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Preliminary Abstract Book

#EBMT26

Preliminary Abstract Book Statement

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Abstracts included in this book are categorized by topics according to their presentation format and session allocation, as indicated by the following codes:

- **OS (number)** – Oral presentations scheduled within the Oral Sessions
- **A (number)** – Poster presentations scheduled for Poster Session A (Monday, 23rd of March)
- **B (number)** – Poster presentations scheduled for Poster Session B (Tuesday, 24th of March)
- **P (number)** – Electronic poster presentations (ePosters), displayed on screens in the designated ePoster area

Abstracts can be searched within the online programme by entering the abstract code or title at the following link: https://ebmt2026.abstractserver.com/programme/#/programme/1/horizontal

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GENERAL TOPICS

Transplant and Cellular Therapies – Basic and Translational

GS2-4

CD19/CD84 IF-BETTER DUAL CAR T CELLS DEMONSTRATE SUPERIOR CONTROL OF CD19-LOW B-ALL THAN SINGLE CART19

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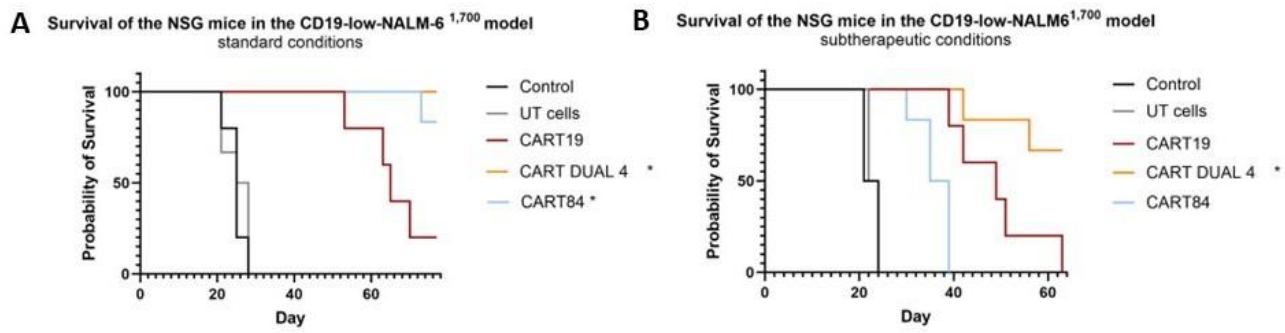
Background: Relapse driven by reduced or absent CD19 expression could limit the long-term efficacy of CD19-directed CAR T-cell therapy in B-ALL, underscoring the need for approaches that maintain function when antigen density falls below the activation threshold.

Methods: To model antigen-low relapse, CD19-low NALM6 variants were generated using CRISPR/Cas9 disruption followed by controlled CD19 re-expression under a truncated promoter. A series of CD19/CD84 dual-targeting CAR T cells were engineered, including an AND-gated construct (DUAL 1m; anti-CD19 scFv–CD3ζ–P2A–anti-CD84 scFv–4-1BB) and IF-BETTER designs, DUAL 4 (anti-CD19 scFv–4-1BB–CD3ζ–P2A–anti-CD84 scFv–4-1BB) and DUAL 5 (anti-CD19 scFv–4-1BB–CD3ζ–P2A–anti-CD84 scFv–CD28). All dual constructs incorporated a mutated CD8α hinge (C164S/C181S) to prevent unintended dimerization. Immune phenotype was characterized through analysis of T-cell subsets and activation/exhaustion markers. CAR T-cell function was evaluated through cytotoxicity and in vitro tumor rechallenge assays, as well as avidity analysis; in vivo efficacy was assessed in two NSG xenografts with WT or CD19-low NALM6 cells. In the CD19-low NALM6 in vivo model, two CAR T-cell doses were evaluated: 5×10^6 and 2×10^6 CAR T cells. Hematologic toxicity was tested by co-culture with $CD34^+$ progenitor cells, and activity was additionally tested on primary B-ALL samples.

Results:



Both IF-BETTER constructs expanded efficiently and preserved a memory-like T-cell distribution comparable to conventional CART19, without premature exhaustion. In cytotoxicity assays, DUAL 4 and DUAL 5 killed $CD19^+$ NALM6-WT, with activation strictly dependent on CD19 engagement despite measurable CD84 expression on target cells, and no cytotoxicity was observed against $CD19^-$ $CD84^+$ MOLM-13 acute myeloid leukemia cells. In long-term in vitro rechallenge assays, IF-BETTER CAR T cells exhibited greater functional persistence, with DUAL 4 maintaining sequential tumor clearance for substantially more rounds than single CART19. In vivo, both DUAL 4 and DUAL 5 achieved tumor control and survival outcomes indistinguishable from single CART19 in the NALM6 WT xenograft.In CD19-low disease models, IF-BETTER DUAL 4 outperformed single CART19. In vitro, DUAL 4 achieved higher cytotoxicity than single CART19. In vivo, DUAL 4 improved tumor control and survival in CD19-low xenografts at both CAR T-cell doses, achieving statistically significant survival benefit in both settings. Importantly, despite CD84 being present on hematopoietic progenitors, DUAL 4 did not eliminate $CD19^-CD34^+$ cells, indicating that CD19 engagement is required for its activation and supporting the safety of this design. Finally, across primary B-ALL samples, IF-BETTER DUAL 4 achieved high cytotoxicity comparable to or exceeding single CART19, supporting its translational relevance.

Conclusions: CD84 emerges as a compelling co-target for CD19-directed CAR T-cell therapy, providing a biologically meaningful co-stimulation without compromising antigen specificity. The IF-BETTER architecture yields dual CD19/CD84 CAR T cells with functional persistence and strict dependence on CD19 for full activation. The DUAL 4 construct matches CART19 performance in CD19-high settings while delivering markedly improved efficacy against CD19-low B-ALL. Overall, these findings support CD19/CD84 IF-BETTER CAR T cells as a promising strategy to prevent or overcome CD19-low relapse in B-ALL.

Disclosure: Nothing to declare

OS03-04

DECITABINE PREVENTS POST-TRANSPLANT RELAPSE IN ACUTE MYELOID LEUKEMIA BY IMMUNOMETABOLIC REPROGRAMMING OF MACROPHAGES VIA THE H3K4ME3–ACOD1–ITACONATE AXIS

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Background: Decitabine (DAC) maintenance therapy has been shown to markedly lower the risk of relapse in acute myeloid leukemia (AML) following hematopoietic stem cell transplantation (HSCT). However, the immunomodulatory mechanisms underlying this benefit remain incompletely defined. This study investigates how DAC reshapes the post-transplant immune microenvironment, identifying the H3K4me3–ACOD1–itaconate axis as a pivotal mediator of macrophage metabolic reprogramming.

Methods:

- Clinical Cohorts: Prospective (n=30) and Retrospective (n=40) analysis of bone marrow samples pre- and post-HSCT (1, 3, 6, 12 months).
- Multi-Omics: RNA-seq, CUT&Tag, ChIP-qPCR, Untargeted Metabolomics, LC-MS/MS, Isotope Tracing.
- Functional Assays: Seahorse XF analysis, Flow Cytometry, In vitro gain/loss-of-function.
- In Vivo: Humanized AML mouse model with bioluminescence imaging.

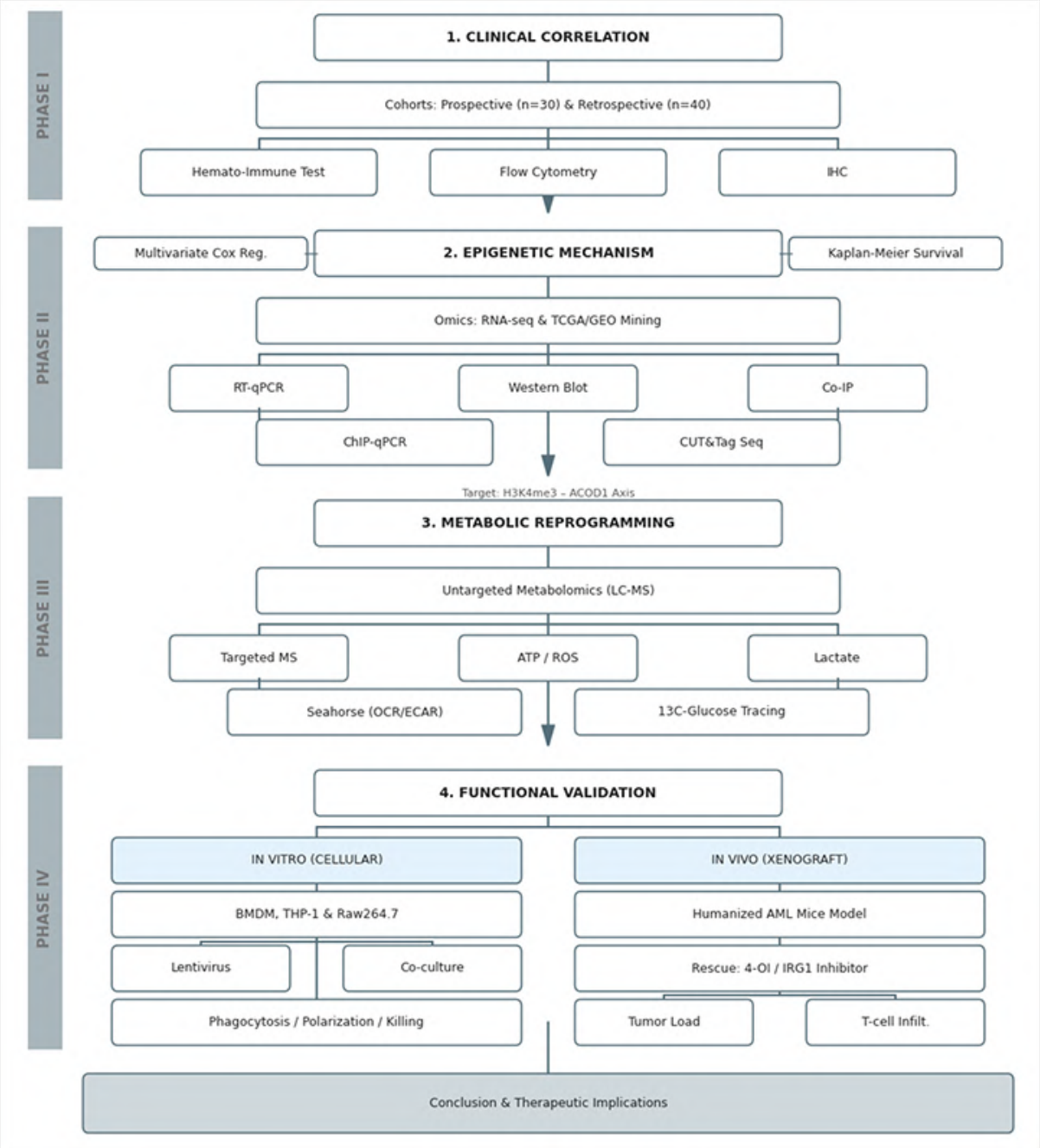

Figure 1 | *Schematic Overview of the Experimental Design. The study is divided into four phases: clinical correlation, epigenetic mechanism, metabolic reprogramming, and functional validation.*

Results: In a prospective cohort (n=30), longitudinal flow cytometric profiling of bone marrow macrophages at pre-transplant and 1, 3, 6, and 12 months post-HSCT revealed

divergent polarization trajectories. Non-relapsed patients maintained elevated CD80 expression throughout follow-up, whereas relapsed cases exhibited progressive accumulation of $CD163^+$ and $CD206^+$ macrophages, with CD206 MFI reaching ~9,000 at 12 months. Kaplan-Meier analysis demonstrated superior median overall survival in patients with M1-predominant profiles (495 vs 385 days, $p<0.05$). Multivariate Cox regression identified M1 polarization as an independent protective factor against relapse (HR 0.42, 95% CI 0.21–0.84).
Retrospective validation (n=40) confirmed significant upregulation of M1 markers (CD80, iNOS) in non-relapsed patients ($p=0.0001$, $p=0.0003$), while CD163 and CD206 were elevated in relapsed cases ($p=0.0193$, $p=0.0075$ for relapse×time interaction). IRG1 showed dynamic regulation with significant time-dependent changes correlating with relapse risk ($p=0.0001$ for interaction term).
Integrated RNA-seq and CUT&Tag analysis revealed decitabine-mediated suppression of ACOD1 transcription via reduced H3K4me3 enrichment at its promoter (fold-change -2.8, $q<0.001$). Untargeted metabolomics and ^{13}C-isotope tracing confirmed decreased itaconate production and restored TCA cycle flux. Seahorse metabolic profiling demonstrated enhanced glycolytic capacity (ECAR/OCR ratio increased 2.1-fold) and M2a-to-M1 repolarization upon ACOD1 silencing.
In a humanized NSG-AML xenograft model, decitabine treatment increased the M1/M2 ratio 3.2-fold by week 6, suppressed bone marrow IRG1 expression (-65%, $p<0.01$), and reduced tumor burden by bioluminescence imaging (mean radiance decreased 78% vs vehicle, $p<0.001$). Pharmacological IRG1 inhibition partially abrogated these effects. Median survival was significantly prolonged in the decitabine arm (58 vs 42 days, log-rank $p=0.012$), with M1 predominance conferring independent survival benefit on multivariate analysis.

Conclusions: Decitabine modulates the H3K4me3–ACOD1–itaconate axis, reprogramming macrophage metabolism and polarization to improve the immune microenvironment and prolong survival after HSCT in AML patients. These findings reveal a novel immunometabolic mechanism and highlight ACOD1 as a promising therapeutic target for post-transplant relapse prevention.

Clinical Trial Registry: 2022-研第 322-01

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OS13-01

REAL-WORLD EVIDENCE FOR THE SAFETY AND EFFICACY OF GLOFITAMAB COMBINED WITH CAR-T THERAPY IN RELAPSED/REFRACTORY B-CELL LYMPHOMA

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Background: Chimeric antigen receptor T-cell (CAR-T) therapy has substantially improved prognosis for patients with relapsed/refractory B-cell non-Hodgkin lymphoma (r/r B-NHL), yet relapse remains a significant challenge. Glofitamab, a CD20/CD3 bispecific antibody, represents a potent strategy to enhance durable responses. This study aimed to investigate the clinical benefit of combining Glofitamab with CAR-T in a multinational real-world setting, and to define the molecular mechanism for sustaining T-cell function and persistence.

Methods: From January 24, 2024, to July 3, 2025, this multicenter retrospective study included 27 r/r B-NHL patients who received single or dual-targeted CAR-T therapy (CD19/CD19-20/CD19-22) coupled with Glofitamab (bridging and/or maintenance), compared to a control cohort of 34 patients treated with CAR-T alone (Table 1). Among the 27 patients, 17 received Glofitamab bridging therapy (median cycles: 3, range: 2-10), and 18 received maintenance therapy (median cycles: 3, range: 1-12). Primary endpoints included ORR, CR rate, PFS, and OS. Mechanistic dissection utilized scRNA-seq on post-CAR-T PBMC from 3 Glofitamab-maintained PR patients versus 3 public controls. In vitro assays quantified T cell cytotoxicity, T effector memory phenotype (Tem), and immunological synapse formation.

Results: As of November 25, 2025, at a median follow-up of 11.97 months (range, 1.6-21.2 months), the Glofitamab combination group demonstrated an ORR of 88.9% and a CR rate of 59.3%, both superior to the control group's ORR of 67.6% and CR rate of 44.1%. The combination group achieved significantly superior PFS and OS (Figure 1); median PFS and OS were not reached in the combination group vs. median PFS 12.19 months in the control group ($p < 0.05$). Univariate Cox regression analysis suggested that Glofitamab bridging and maintenance were protective factors for PFS. Advanced stage (Ann Arbor stage 3-4) was identified as a risk factor for disease PFS. Safety analysis showed no increased risk of high-grade CRS or ICANS in the combination group. Mechanistically, scRNA-seq analysis revealed concurrent upregulation of multiple activation pathways (Cytotoxicity, TCR, NF-kappa B) alongside a critical synchronous activation of the anti-apoptotic pathway. This T-cell viability was strongly correlated with activation of the JAK/STAT signaling pathway. Furthermore, the key JAK/STAT ligand, IL-15, was specifically upregulated in the monocyte and granulocyte

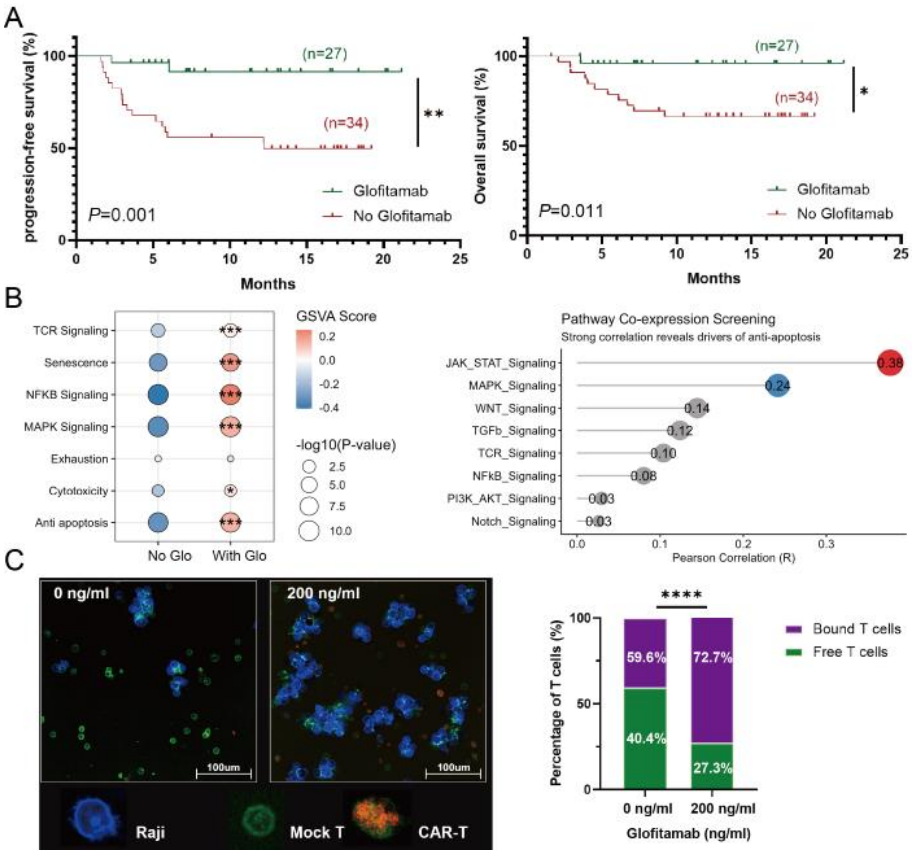
populations. In vitro data validated that Glofitamab significantly enhanced CAR-T cell cytotoxicity and CD107a degranulation, promoted differentiation toward Tem. Confocal microscopy further confirmed Glofitamab role in significantly increased the size of T-cell-tumor cell clusters and the ratio of T-cells engaged in clustering (Figure 1).

Table1. Patients baseline

Patients Characteristics	With Glofitamab (n=27)	No Glofitamab (n=34)	*P* value
Mean age, (range)	54.0 (20.0-75.0)	48.5 (19.0-74.0)	0.346
Gender	11 Female/16 Male	17 Female/17 Male	0.471
Histology lymphoma, n (%)			
DLBCL	24 (88.9%)	25 (73.5%)	0.134
BL	2 (7.4%)	6 (17.6%)	0.239
MCL	0 (0.0%)	2 (5.9%)	0.200
HGBL	0 (0.0%)	1 (2.9%)	0.369
PMBCL	1 (3.7%)	0 (0.0%)	0.258
Elevated LDH, n (%)	18 (66.7%)	13 (38.2%)	**0.027**
Ann Arbor Stage ≥3, n (%)	24 (88.9%)	24 (70.6%)	0.083
IPI, n (%)			
0-2 (low-low intermediate risk)	14 (29.6%)	15 (29.4%)	0.785
3 (high- intermediate risk)	6 (22.2%)	15 (44.1%)	0.074
4-5 (high risk)	7 (25.9%)	4 (11.8%)	0.153
CAR-T combined with ASCT	15 (55.6%)	19 (56.0%)	0.980
CAR T therapy type, n (%)			

CD19	10 (37.0%)	0 (0.0%)	
CD19/20	1 (3.7%)	18 (53.0%)	
CD19/22	16 (59.3%)	16 (47.0%)	

Figure 1. Glofitamab combination therapy achieves superior PFS and OS, correlating with the activation of a T-cell JAK/STAT and enhanced immunological synapse formation in vitro



Conclusions: This real-world study demonstrates that Glofitamab combined with CAR-T therapy achieves superior PFS and OS in r/r B-NHL. Single-cell data reveal that the clinical benefit correlates with a sustained JAK/STAT survival circuit in T cells, specifically driven by IL-15 from monocytes/granulocytes. Supported by functional data showing enhanced T cell cytotoxicity, Tem differentiation, and immunological synapse formation, these findings highlight Glofitamab combination therapy as a key strategy for enhancing long-term T-cell persistence and immune surveillance post-CAR-T therapy.

Clinical Trial Registry: NCT06879262

Disclosure: The authors of this study declare no conflict of interest.

OS13-02

HIGH TUMOR MUTATIONAL BURDEN DEFINES AN IMMUNE-EVASIVE STATE LIMITING CD19 CAR-T EFFICACY IN LARGE B-CELL LYMPHOMA

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Background: High tumor mutational burden (TMB) expands the neoantigen repertoire but may simultaneously impose selective pressure for disruption of antigen presentation and immune signaling pathways. While elevated TMB is a favorable biomarker in immunotherapies dependent on endogenous T-cell recognition, its biologic consequences in CD19-directed CAR-T therapy have not been systematically examined in large B-cell lymphoma (LBCL).

Methods: Tumor genomic profiling was performed using whole-exome sequencing (WES) and/or clinically validated targeted next-generation sequencing to quantify TMB. Associations between TMB and post–CAR-T outcomes were evaluated using competing-risk regression for relapse/progression and multivariable Cox models for progression-free survival (PFS) and overall survival (OS), adjusting for key clinical covariates. Transcriptomic profiling was used to interrogate immune and inflammatory pathway activity. Comparative analyses were conducted in a large front-line LBCL cohort treated with chemoimmunotherapy, with study-level TMB normalization to account for inter-assay variability.

Results: The study included 114 patients with relapsed/refractory LBCL treated with commercial CD19 CAR-T therapy (48% axicabtagene ciloleucel, 17% lisocabtagene maraleucel, 35% tisagenlecleucel), predominantly in the ≥3rd line. Pre-infusion tumor sequencing was available by WES (n=89), targeted sequencing (n=25), or both (n=65). Median WES-derived TMB was 2.82 mutations/Mb (interquartile range [IQR] 1.86–3.98). Higher WES-derived TMB correlated with genomic instability metrics, de novo LBCL histology, and higher baseline metabolic tumor volume (MTV) (all $p<0.01$), but not with cell of origin, double-hit status, TP53 mutation, MYC rearrangement, or age. Higher TMB was independently associated with inferior outcomes following CAR-T therapy. Patients in the highest TMB quartile (>4.0 mut/Mb) experienced increased risk of relapse or progression (subdistribution HR 2.68, $p<0.001$), inferior PFS (HR 2.32, $p<0.01$), and inferior OS (HR 3.04, $p<0.001$) after multivariable adjustment (Fig. 1A, B).

While high-TMB tumors were enriched for increased numbers of clonal neoantigens with strong predicted patient-specific HLA binding, they concurrently exhibited selective loss of HLA genes predicted to present these neoantigens, alongside mutations affecting antigen-processing and presentation machinery (Fig. 1C). Paired transcriptomic profiling (n=40) demonstrated coordinated downregulation of inflammatory and cytotoxic signaling pathways, including TNF–NFκB, IL2–STAT5, and apoptosis (FDR-adjusted p<0.05; Fig. 1D).
Because WES is not routinely available in clinical practice, TMB was also derived from a clinically deployed targeted sequencing assay (MSK-IMPACT). In patients with panel-based sequencing available (n=90), higher targeted TMB reproduced the adverse associations observed with WES-derived TMB, supporting feasibility of clinical implementation .
To compare the effect of TMB across treatment settings, we evaluated its impact in a front-line multi-study cohort of 2,126 LBCL patients treated with chemoimmunotherapy. In contrast to the CAR-T setting, higher TMB demonstrated a reverse association, with improved PFS among patients in the highest scaled-TMB quartile (HR 0.88, p<0.01; Fig. 1E) .

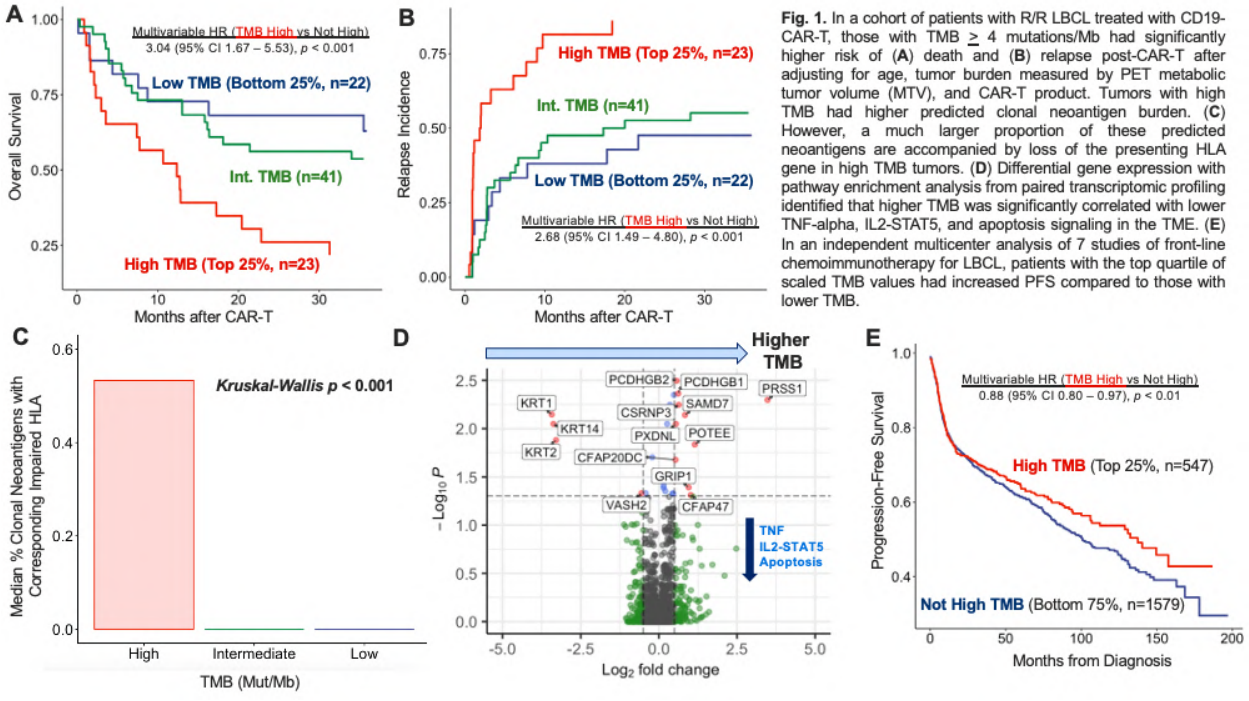

Fig. 1. In a cohort of patients with R/R LBCL treated with CD19-CAR-T, those with TMB ≥ 4 mutations/Mb had significantly higher risk of (**A**) death and (**B**) relapse post-CAR-T after adjusting for age, tumor burden measured by PET metabolic tumor volume (MTV), and CAR-T product. Tumors with high TMB had higher predicted clonal neoantigen burden. (**C**) However, a much larger proportion of these predicted neoantigens are accompanied by loss of the presenting HLA gene in high TMB tumors. (**D**) Differential gene expression with pathway enrichment analysis from paired transcriptomic profiling identified that higher TMB was significantly correlated with lower TNF-alpha, IL2-STAT5, and apoptosis signaling in the TME. (**E**) In an independent multicenter analysis of 7 studies of front-line chemoimmunotherapy for LBCL, patients with the top quartile of scaled TMB values had increased PFS compared to those with lower TMB.

Conclusions: High tumor mutational burden defines an immune-evasive tumor state associated with inferior outcomes after CD19 CAR-T therapy in relapsed/refractory LBCL, characterized by impaired antigen presentation and attenuated immune signaling despite expanded neoantigen repertoires. In contrast, TMB demonstrates a reverse association in front-line chemoimmunotherapy, underscoring its context-dependent impact across immune treatment modalities and supporting its translational utility as a clinically actionable biomarker for CAR-T risk stratification.

Disclosure: Nothing to declare (no conflicts of interest or sources of funding relevant to this abstract).

OS18-04

MYELOID DERIVED SUPPRESSOR CELLS (MDSC) AFFECT IMMEDIATE EFFICACY AND ACUTE TOXICITIES OF ANTI-CD19 CAR-T IN PATIENTS WITH LARGE B-CELL LYMPHOMA

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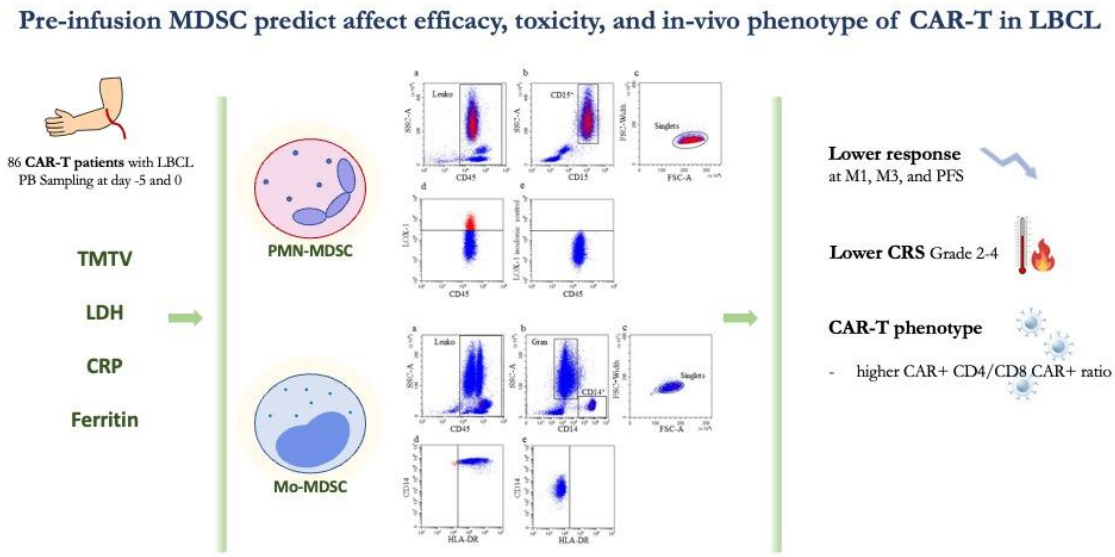
Background: Despite the success of CD19-directed CAR-T-cells in relapsed/refractory (R/R) large B-cell lymphoma (LBCL), a substantial proportion of patients experience treatment failure. **Myeloid-derived suppressor cells** of monocyte (Mo-MDSC) and polymorphonuclear (PMN-MDSC) origin **are key regulators of immune suppression in cancer** and may affect immunotherapy efficacy. Their role in modulating CAR-T-cell efficacy and toxicity is still under investigation. Here, we compared circulating MDSC subsets across CAR-T-cell treated R/R LBCL patients with different outcomes using a common staining panel for the identification of these cells directly in fresh whole blood by multiparameter flow cytometry.

Methods: This prospective observational study included adult patients receiving commercial CAR-T-cell therapy for R/R LBCL. Peripheral blood (PB) was collected before lymphodepletion (LD) and at CAR-T infusion. Mo-MDSC were quantified as $CD45^{+}CD14^{+}HLA\text{-}DR^{neg}$ cells and PMN-MDSC as $CD45^{dim/+}CD15^{+}LOX\text{-}1^{+}$ cells. Data were expressed as cells/μL Additionally, PMN-MDSC maturation status was assessed by differential CD10, CD11b, and CD16 expression. CAR-T-cell expansion was evaluated at days 7, 14, and 30 by $CD3^{+}CAR^{+}$ flow cytometry.
We evaluated the correlation of PMN-MDSC and Mo-MDSC with overall response rate (ORR), progression-free survival (PFS), CAR-T-cell expansion, and toxicities.

Results: Eighty-six patients were included. At 1 and 3 months post-infusion, ORR was 72.9% and 59.1%, respectively. Median PFS was 371 days.
Before LD, immature and mature PMN-**MDSC** significantly **correlated with TMTV and systemic inflammation** (CRP, ferritin and LDH) and Mo-MDSC significantly correlated with CRP. These observations are in line with the complex interrelations between tumor burden and the immune system status.

LD selectively affected PMN-MDSC populations as it decreased immature PMN-MDSC (p<0,01) and increased mature PMN-MDSC although not significantly. There was a trend towards a LD-induced Mo-MDSC decrease.
Despite these changes, immature and mature PMN-MDSC strongly predicted **lack of response at month 1** both when measured before LD (OR 3.76, p<0,001; OR 3.63, p<0.001; respectively) and at CAR-T-cell infusion (OR 1.97, p<0,001; OR 2.34, p<0.001, respectively). Conversely, Mo-MDSC were informative only before LD (OR 6.93, P=0.01). Only immature PMN-MDSC at CAR-T-cell infusion predicted lack of response at month 3 (OR 1.77, p<0.006). The stratification of early response by MDSC was not maintained over time, as neither PMN-MDSC nor Mo-MDSC predicted long-term PFS.
We hypothesized that MDSC had affected CAR-T-cell expansion. Neither PMN-MDSC nor Mo-MDSC associated with quantitative peak (day+7) of CAR-T-cell. However, high mature PMN-MDSC before LD predicted **increased CAR-T CD4/CD8 ratio** (R^2=0.12, p=0.018) in peripheral blood: the concomitance of an unbalanced ratio towards CD4+ associated with a lower response, may enforce the role of CD8+CAR-T-cells in leading the anti-lymphoma effect.



Toxicity was influenced by MDSC. Higher mature PMN-MDSC and Mo-MDSC at CAR-T-cell infusion were associated with a **reduced incidence of grade ≥2 CRS** (OR 0.61, p=0.048 and OR 0.40, p=0.020, respectively) and a lower need for tocilizumab. No association with ICANS was observed.

		CAR+ CD4/CD8 at peak	CRS 2-4	Tocilizumab	Response M1	Response M3	PFS

Baseline (day -5)	**Mature PMN-MDSC**	**Higher**		**Lower**	**Worse**		
	Immature PMN-MDSC			**Lower**	**Worse**		
	Mo-MDSC		**Lower**	**Lower**	**Worse**		
Infusion (day 0)	**Mature PMN-MDSC**		**Lower**	**Lower**	**Worse**	**Worse**	
	Immature PMN-MDSC						
	Mo-MDSC		**Lower**	**Lower**	**Worse**		

Conclusions: Present findings suggest that immune environment influences CAR-T-cell therapy and call for the importance of integrating the MDSC profiling into the clinical management of R/R LBCL. MDSCs might represent a potential therapeutic target in CAR-T-cell bridging or lymphodepleting strategies.

Disclosure: Nothing to declare

A001

PULMONARY AND SYSTEMIC IMMUNE PROFILING REVEALS JAK-STAT SIGNALLING AS A MEDIATOR OF POST-HCT LUNG COMPLICATIONS IN CHILDREN

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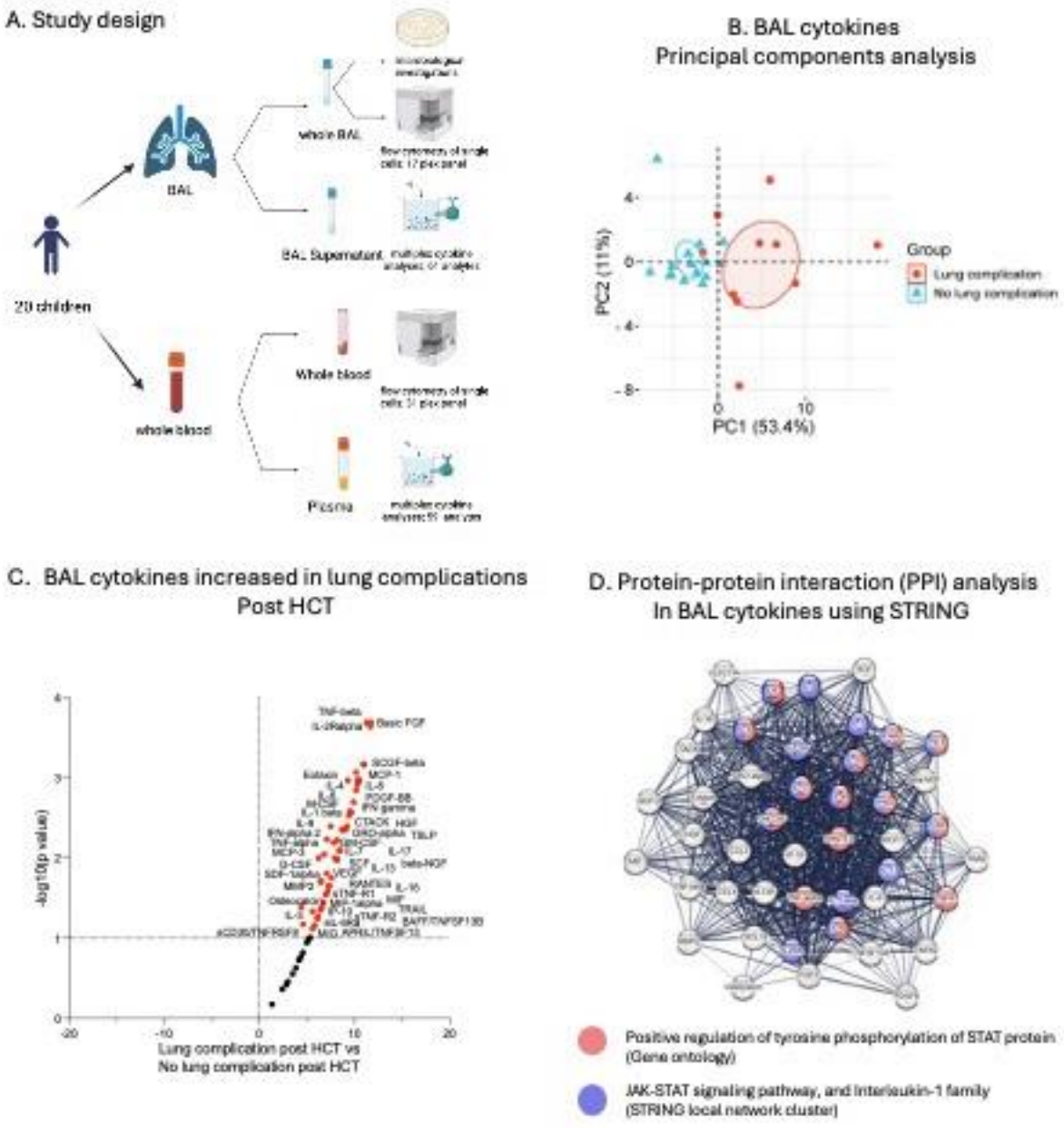
Background: Allogeneic haematopoietic stem cell transplantation is a curative therapy for a range of serious conditions affecting children. Unfortunately, approximately 50% of children undergoing allogeneic HCT develop pulmonary toxicities, which can be life-threatening. There is little known about the biological drivers of these pulmonary diseases and as a result there are few options for risk prediction, early detection and targeted therapies. To further evaluate immune correlates of pulmonary disease pre- and post-HCT, we designed the prospective study 'BREATH', recruiting children undergoing allogenic HCT at a single centre.

Methods: This research aims to identify pathogenic drivers of lung complications and signatures of normal lung immune reconstitution post allogeneic HCT. We aimed to describe, through extensive immunological profiling (utilising flow cytometry and cytokine analyses), patients who maintained 'lung health' as well as those who developed lung disease post-HCT. This prospective longitudinal observational study, 'BREATH', enrolled 20 paediatric patients undergoing HCT at The Royal Children's Hospital in Melbourne and involved the collection of serial paired bronchoalveolar fluid and peripheral blood, combined with detailed clinical data. Patients were eligible to have biospecimen samples collected up to 12 months post the day of stem cell infusion. Patients were only eligible for one biospecimen collection timepoint pre-HCT but eligible for multiple repeated timepoints in the first year post-HCT. Mann-Whitney U tests were used to compare the concentration of analytes (pg./mL) and proportions of cell populations (% of live CD45+ cells) between groups (HCT lung health, HCT lung complication and controls). For lung complication timepoints where paired lung assays were available (n = 8, 6 patients)—that is, cell proportion data obtained by flow cytometry analysis of BAL and soluble analyte data obtained by cytokine profiling of BAL (20 analytes as part of JAK-STAT pathway)—we performed correlation analyses using two-tailed Spearman correlation. For all statistical analyses, a p value < 0.05 was considered significant.

Results: Overall, 40% of children developed a lung complication post-HCT and required a clinically indicated BAL. In total, 49 sample timepoints were collected with a median of 2.6 timepoints per patient (range 1–6). Our primary aim was to identify if children post HCT who developed a lung complication had a unique inflammatory signal compared to children who do not develop lung complications. We found enrichment of the JAK-STAT and IL-1 signalling and profibrotic pathways in both the lung and whole blood, at the time of post-HCT lung complication. Changes in granulocyte and alveolar macrophages populations in BAL were correlated with soluble mediators of the JAK-STAT pathway in these patients with lung disease.



Pulmonary and Systemic Immune Profiling Reveals JAK-STAT Signalling as a Mediator of Post-HCT Lung Complications in Children

Conclusions: This research represents a potential pathogenic pathway for why these patients may develop lung complications as well as a potential therapeutic target (e.g. the JAK-STAT inhibitor ruxolitinib) which requires investigation in larger studies. Improved

understanding of the mechanisms driving this lung disease will enable improved diagnostics and pave the way for the introduction of novel therapeutic approaches.

Clinical Trial Registry: N/A

Disclosure: There are no conflicts of interest to disclose. This research was funded through the following philanthropic organisations; My Room, The Kids Cancer Project & The Bella Tripp Foundation

A002

VERSATILE ALLOGENEIC VIRUS-SPECIFIC CAR-T CELLS FOR HEMATOLOGIC MALIGNANCIES

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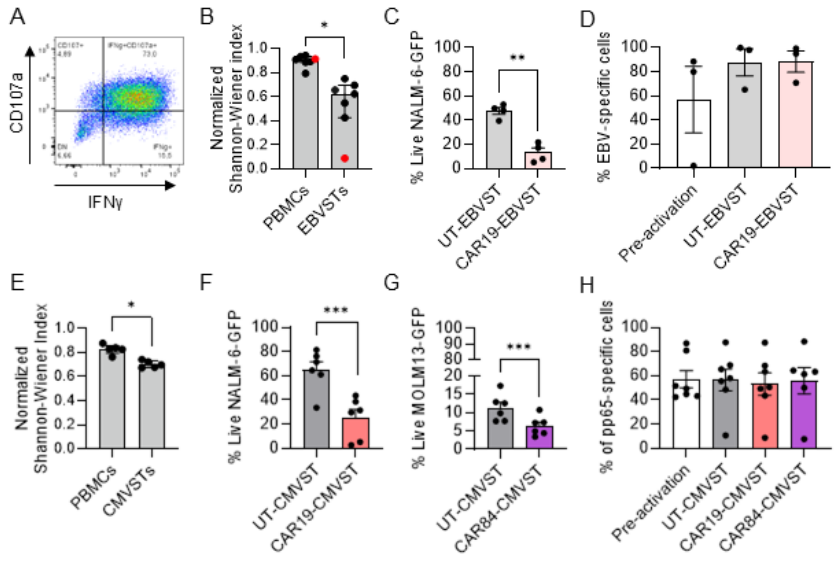
Background: Chimeric antigen receptor (CAR) T-cell therapy has reshaped treatment paradigms for hematologic malignancies, yet truly off-the-shelf products remain hindered by alloreactivity, limited persistence, and the need for gene editing. Virus-specific T cells (VSTs) targeting Epstein–Barr virus (EBV) or cytomegalovirus (CMV) exhibit long-term persistence, viral-restricted TCR repertoires, and a low risk of graft-versus-host disease (GVHD), making them an attractive platform for allogeneic CAR T-cell development. This study evaluates the engineering of EBV- and CMV-reactive T cells with CARs targeting CD19 and CD84 to generate dual-functional products for the treatment of B-cell acute lymphoblastic leukemia (B-ALL) and acute myeloid leukemia (AML).

Methods: VSTs were generated from seropositive donor PBMCs using peptide stimulation followed by cytokine-supported expansion. Phenotype, antiviral functionality, and cytotoxic activity were assessed by flow cytometry, intracellular cytokine staining, and killing assays. TRB CDR3 sequencing was used to characterize repertoire narrowing in VST products. Cryopreserved VSTs were reactivated using anti-CD3/CD28 beads or anti-CD3 antibody prior to lentiviral transduction with second-generation CAR19 or CAR84 vectors. CAR expression, viral responsiveness, and CAR-mediated cytotoxicity were analyzed following expansion. Additional experiments evaluated early lentiviral transduction during antigen-driven stimulation.

Results: EBVSTs and CMVSTs expanded efficiently, maintaining high viability and a consistent predominance of CD3+ T cells throughout expansion. Both EBVSTs and CMVSTs exhibited robust antiviral functionality, characterized by degranulation responses and polyfunctional cytokine secretion upon stimulation with the corresponding viral peptides. TRB CDR3 sequencing revealed marked repertoire focusing relative to unmanipulated PBMCs, with enrichment of clonotypes previously associated with CMV and EBV-epitopes. Functionally, VSTs selectively eliminated autologous or partially HLA-matched allogeneic targets only when pulsed with the appropriate viral peptides, confirming preserved antiviral specificity and absence of detectable alloreactivity.
We next optimized CAR-VST manufacturing from cryopreserved VSTs, mimicking the use of donor-derived VST banks. Anti-CD3/CD28 bead stimulation consistently yielded high CAR19 and CAR84 expression. However, this approach substantially reduced antiviral responsiveness across donors, indicating loss of virus specificity upon strong polyclonal activation. In contrast, anti-CD3 antibody-mediated activation supported efficient CAR transduction while maintaining EBV- or CMV-directed responses. CAR19-EBVST and CAR19-CMVSTs generated under these conditions expressed CAR19, eliminated CD19+ B-ALL targets, and responded to viral peptides. Likewise, CAR84-CMVSTs expressed CAR84, preserved CMV specificity, and displayed cytotoxicity against CD84+ AML cells.



Functional activity, repertoire diversity, and cytotoxicity of EBV- and CMV-specific T cells (VST) before and after CAR transduction. **(A)** Representative dot plots of CD107a and IFN-γ expression in $CD3^+CD8^+$ EBVSTs following overnight stimulation with EBV peptide pools in the presence of monensin and brefeldin. **(B)** TRB CDR3aa diversity (normalized Shannon–Wiener index) in PBMCs and expanded EBVSTs (paired t-test; N=7). **(C)** Cytotoxicity of untransduced (UT) or CAR19-transduced EBVSTs against NALM-6 cells at a 2:1 E:T ratio for 24h (paired t-test vs. UT; N=3–4). **(D)** Frequency of EBV-reactive $CD3^+CD8^+$ T cells ($CD107a^+$, IFN-γ^+, or double-positive) in thawed EBVSTs stimulated as in A before or after expansion with OKT-3 and UT or CAR19-transduced (one-way ANOVA; N=3). **(E)** TRB CDR3aa diversity in PBMCs and expanded CMVSTs (paired t-test; N=5). **(F)** Cytotoxicity of UT or CAR19-CMVSTs against NALM-6 at a 2:1 E:T ratio for 24h (paired t-test vs. UT; N=6). **(G)** Cytotoxicity of UT or CAR84-CMVSTs against MOLM-13 at a 2:1 E:T ratio for 24 h (paired t-test vs. UT; N=6). **(H)** Frequency of virus-reactive $CD3^+CD8^+$ cells in thawed CMVSTs stimulated as in A before or after expansion with OKT-3 and UT, CAR19- or CAR84-transduced (one-way ANOVA; N=7). All data are shown as mean ± S.E.M. *p < 0.05; **p < 0.01; ***p < 0.005.

Finally, lentiviral transduction during the antigen-driven VST expansion phase was evaluated to enable generation of a fully allogeneic CAR-VST product. Early transduction preserved proliferative capacity and leveraged physiological TCR stimulation rather than non-specific activation. Early-transduced CAR19-CMVSTs achieved stable CAR expression, maintained potent cytotoxicity against CD19+ target cells, and retained CMV specificity. Early-transduced CAR84-CMVSTs exhibited a more variable CAR expression, yet maintained cytotoxicity against CD84+ target cells.

Conclusions: VSTs constitute a selective T-cell population with virus-focused repertoires and minimal alloreactivity that can be engineered to express CARs while preserving antiviral function. Anti-CD3 antibody-based activation and early transduction strategies support scalable production of dual-functional CAR-VSTs. This framework advances the development of donor-derived, off-the-shelf CAR T-cell platforms.

Disclosure: Maria Val-Casals: employee of Gyala Therapeutics, S.L
Nela Klein-González: employee of Gyala Therapeutics, S.L
Lorena Pérez-Amill: former employee of Gyala Therapeutics, S.L
Mercedes Armand-Ugón: former employee of Gyala Therapeutics, S.L
Sergio Peña: employee of Gyala Therapeutics, S.L

A003

IMMUNE MODULATION BY CAR-T CELLS: EXTRACELLULAR VESICLES AND SECRETOME AS DRIVERS OF MONOCYTE ACTIVATION

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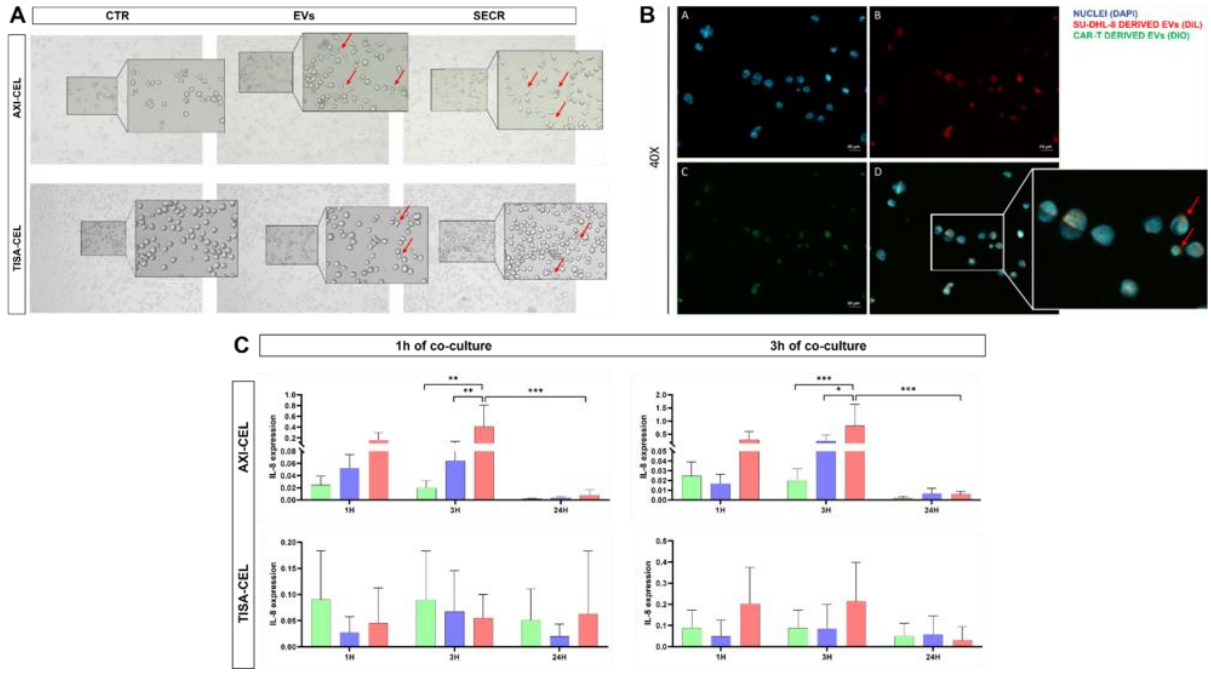
Background: Chimeric Antigen Receptor-T (CAR-T) cell therapy has transformed the treatment of $CD19^+$ B cell malignancies. However, its clinical success is tempered by acute and late toxicities with unclear mechanisms. Increasing evidence points to inflammation and innate immune activation as key drivers, with the monocyte–macrophage compartment playing a central role. Yet CAR-T effects on monocytes remain poorly characterized. We investigated how CAR-T cells interact with monocytes and trigger immune activation.

Methods: CAR-T cells (axicabtagene ciloleucel, axi-cel, and tisagenlecleucel, tisa-cel) were isolated from infusion bag washes of eight Non-Hodgkin Lymphoma patients (with Diffuse Large B-Cell Lymphoma or Follicular Lymphoma) with low-grade CRS and ICANS. To investigate the role of CAR-T-released particles in monocyte activation, cells were co-cultured for 1-3 h with $CD19^+$ SU-DHL-8 lymphoma cells. Extracellular Vesicles (EVs) and the complete secretome (SECR) were collected and used to treat THP-1 monocytes for 1, 3, and 24h. Monocyte-to-macrophage transition was analysed morphologically and molecularly. EV uptake was assessed by fluorescence microscopy, and cytokine expression quantified by digital PCR.

Results: Neither EVs nor SEC significantly affected THP-1 proliferation in either axi-cel or tisa-cel products. When treated for 1-3h with both EVs and SEC, monocytes adopted an irregular shape, with pseudopods formation. This aspect was more evident in cells treated with axi-cel-derived EVs and SEC (Fig.1A) and weren't appreciable after 24h. To assess if these changes were actually related to the monocyte's differentiation, the quantification of *PPM1A* transcript was performed via dPCR. EVs and SEC obtained after 1h of co-culture of

axi-cel products induced *PPM1A* overexpression after 24h of treatment, while EVs and SEC obtained after 3h of co-culture induced the overexpression also after 1-3h post-treatment. Surprisingly, cells treated with tisa-cel-derived EVs and SEC showed an opposite trend, with an increased expression after 1h of treatment with EVs and SEC, not observed after 24h. Collectively, these findings suggest that CAR-T-derived factors promote monocyte differentiation toward a macrophage-like phenotype rather than proliferation. Fluorescence microscopy confirmed EVs uptake by monocytes, indicating their key role in cells activation (Fig.1B). Cytokine analysis revealed significant over-expression of *IL-8*, after 1-3h with axi-cel-derived EVs and SEC, but not after 24h. In tisa-cel context just the treatment with EVs and SEC obtained after 3h of co-culture induce cytokines overexpression after 1-3h, but not after 24h (Fig.1C). *TNF-α*, *ICAM1*, and *IL-1β* transcripts shows the same trend. No effects were observed using EVs or SEC from naive SU-DHL-8.



Conclusions: For the first time, we demonstrate that CAR-T cells release factors capable of inducing monocyte-to-macrophage transition and transient pro-inflammatory activation. These findings highlight a key role for CAR-T-derived EVs and SECR in modulating innate immune responses, with potential implications for clinical outcomes and toxicities in CAR-T-treated patients.

Disclosure: Nothing to declare.

A004

LARGE SCALE MANUFACTURING OF GMP GRADE CORD BLOOD DERIVED MEGAKARYOCYTES FOR CHEMOTHERAPY INDUCED THROMBOCYTOPENIA

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Background: The global shortage of donor platelets underscores the urgent need for reliable and sustainable alternatives. Close to 3 million platelet units are transfused annually in Europe, mostly in patients receiving chemotherapy or bone marrow transplantation. These patients often require multiple transfusions due to the short lifespan of transfused platelets (3–5 days), high consumption rate, and the development of immune refractoriness to platelet transfusions. Currently, platelet supply depends exclusively on adult donor apheresis. This supply is limited by both the short storage lifespan of platelets and reliance on donor availability. We thus developed a large-scale, multi-phase, good manufacturing practice (GMP) compliant method to generate platelets and megakaryocytes (MKs) *ex vivo,* using $CD34^+$ cord blood (CB) cells co-cultured with CB-derived mesenchymal stem cells (MSCs) in bioreactors. Our strategy utilizes the large global cord blood bank inventories as a renewable platelets source.

Methods: CB-derived $CD34^+$ cells were cultured on CB-MSCs monolayers with dynamically titrated cytokines to mimic the bone marrow microenvironment across distinct developmental stages. Supplements included a caspase-3 inhibitor, a histone deacetylase inhibitor, and a ROCK inhibitor to enhance MK viability and platelet production. Cells were expanded and differentiated through sequential co-culture phases: (1) CD34+ cells expansion with GMP media with early differentiation cytokines (TPO, SCF, FLT3L, IL-3, IL-6), (2) expansion of progenitors and differentiation to immature megakaryocytes using MK differentiation media (TPO, SCF, IL-11, IL-6 supplemented with histone deacetylase inhibitor), (3) maturation and large-scale expansion of megakaryocytes in a static bioreactor supplemented with a caspase 3 inhibitor, (4) final maturation of enriched CD61+ cells and platelet production (induced via shear force in a closed, hollow-fiber bioreactor), in the presence of a ROCK inhibitor. On Day 24, cultures were harvested, yielding a combined MK/platelets product.

Results: After 24 days, cultures yielded ~50 × 10^6 pure (>95%), mature MKs and ~0.5 × 10^{10} platelets. The MK were polyploid, and platelet functionality was confirmed by thrombin-induced aggregation, demonstrating robust aggregation *in vitro*. The product was tested for endotoxin, mycoplasma and sterility. Following infusion of the final product (containing 4.2 × 10^6 MKs and 0.15 × 10^8 platelets) into sublethally irradiated thrombocytopenic NSG mice, human $CD41^+$/$CD61^+$ platelets were detected in peripheral circulation within 1 hour. Moreover, platelets produced *in vivo* by the infused MKs, emerged by day 4, reaching their

highest levels by day 11. Notably, human platelets persisted in some mice at day 21, confirming both the rapid and durable thrombopoietic activity of the combined MK/platelet product. The product was well-tolerated with no observed toxicity. Our results highlight the clinical potential of this approach. The novelty of this approach includes the transfusion of a product containing both megakaryocytes and platelets, offering a promising strategy for addressing platelet shortages and improving patient outcomes.

Conclusions: We have developed a scalable platform for clinical use, generating MKs and platelets from CB. The combined infusion of MKs and platelets enables both immediate and sustained platelet reconstitution. Additionally, we have designed a phase I clinical trial to evaluate the safety and efficacy of this approach.

Disclosure: NY Blood Center- consulting, Adaptimmune- Scientific Advisory Board, Navan- Scientific Advisory Board, Celaid Therapeutics- consulting, Zelluna Immunotherapy- Scientific Advisory Board, FibroBiologics- Scientific Advisory Board, Axio- Scientific Advisory Board, Orca Biosystems- Scientific Advisory Board, Takeda- License agreement, Affimed- License agreement, Prana X- License agreement

A005

GENETIC MECHANISMS UNDERLYING CLONAL EVOLUTION DURING RELAPSE FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PHILADELPHIA CHROMOSOME–POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA

Jing Zheng[1,2], *Yanmin Zhao*[1], *Yi Luo*[1], *Jian Yu*[1], *Xiaoyu Lai*[1], *Jinuo Wang*[1], *Yishan Ye*[1], *Lizhen Liu*[1], *Huarui Fu*[1], *Luxin Yang*[1], *Yibo Wu*[1], *Jie Sun*[1], *Weiyan Zheng*[1], *Jingsong He*[1], *Yi Zhao*[1], *Wenjun Wu*[1], *Zhen Cai*[1], *Guoqing Wei*[1], *He Huang*[1], *Jimin Shi*[1]
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Background: (1) Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph^+ALL) is a high-risk subtype due to the BCR::ABL1 fusion gene. While tyrosine kinase inhibitors (TKIs) and allogeneic hematopoietic stem cell transplantation (allo-HSCT) have improved outcomes, relapse after transplantation remains a major issue, driven by genetic clonal evolution. This study aims to uncover the genetic mechanisms behind post-allo-HSCT relapse in Ph^+ALL, identify key driver genes and pathways using a multi-omics approach, and provide a foundation for early detection and prevention of relapse.

Methods: We retrospectively analyzed clinical data and collected bone marrow samples at various stages (diagnosis, post-transplant, and/or relapse) from 112 Ph^+ ALL patients who underwent allo-HSCT, including 44 relapsed and 68 non-relapsed cases. We used integrated cytogenetic and genomic analyses, including G-banding karyotyping and high-throughput sequencing with a 74-gene panel, to study clonal evolution. Bioinformatics tools, such as GO and KEGG pathway analyses, PPI network construction via STRING, core gene identification with Cytoscape, and miRNA–gene and transcription factor–gene network analyses, were

employed to understand clonal evolution patterns. Statistical analyses were conducted using SPSS version 25.0, with significance set at P<0.05.

Results: (1) 1. **Clonal Evolution Dynamics**: After allo-HSCT in Ph⁺ ALL, clonal architecture changed significantly. The relapse group had a higher ABL1 mutation rate than the non-relapse group (31.8% vs. 4.4%, P<0.001), with 93% being the T315I drug-resistance mutation. IKZF1 deletions were common at diagnosis (29.5%) but reduced at relapse (2.3%, P=0.001), indicating clonal replacement. 2. **Cytogenetic Subgroup Evolution**: 2.1. +der(22) Subgroup: JAK2 mutations were more frequent (14.3% vs. 1.2%, P=0.017), suggesting a link between chromosome 22 gain and JAK–STAT pathway activation. 2.2. +8 Subgroup: CDKN2B mutations were more common (16.7% vs. 1.0%, P=0.026), implicating trisomy 8 in cell-cycle control issues. 2.3. −7 Subgroup: Increased mutations in ABL1, CREBBP, and TP53 (P<0.05) suggest that chromosome 7 loss may lead to genome instability and mutational accumulation. 2.4. Complex Karyotype Subgroup: TET2 and JAK2 mutations (P<0.05) are linked to chromosomal instability and epigenetic issues. 3. **Multi-Omics Regulatory Network**: A PPI network identified 14 core genes, including TP53 and ABL1. GO and KEGG analyses showed enrichment in pathways like histone modification and p53 signaling. The T315I mutation alters interactions among ABL1, microRNAs (e.g., hsa-miR-203a-3p), and transcription factors (e.g., CREBBP), leading to abnormal pathway activation. 4. **Clinical Prognostic Associations**: ABL1 mutations are an independent risk factor for relapse post-transplant, with mutation carriers having lower complete remission (57.1% vs. 86.7%, P=0.030) and overall survival rates (26.5% vs. 73.3%, P=0.005). Patients with T315I mutations had significantly shorter survival after relapse than those without (7.6 vs. 29.2 months, P=0.001). A positive measurable residual disease (MRD) status before transplantation predicted the development of ABL1 (P=0.035) and CDKN2B (P=0.021) mutations, suggesting its role in predicting clonal evolution.

Conclusions: (1) This study identifies cytogenetically background-specific clonal evolution in post-transplant Ph⁺ ALL and elucidates ABL1 (especially T315I), TP53, JAK2 and their interaction networks as central drivers. These findings support individualized risk stratification and mutation-guided combination targeted therapy to prevent relapse.

Disclosure: Nothing to declare

A006

GRAFT PLATFORM AND VIRAL REACTIVATION IMPRINT LONG-TERM ALPHABETA AND GAMMADELTA T-CELL CLONAL AND TRANSCRIPTIONAL REMODELING AFTER ALLO-HSCT

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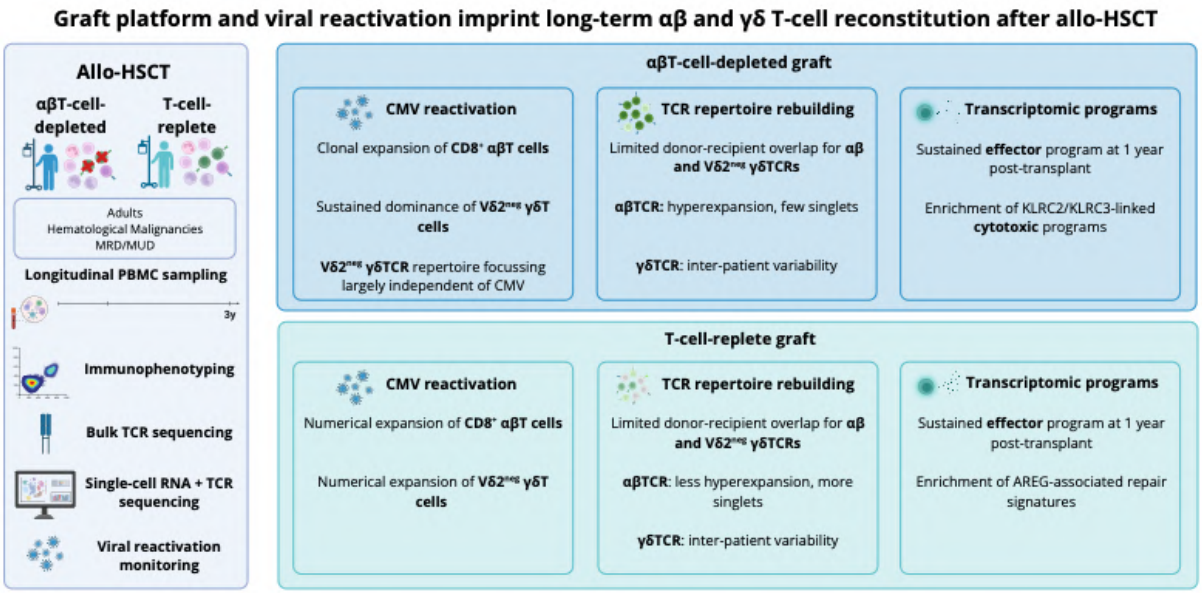
Background: Immune reconstitution after allogeneic hematopoietic stem cell transplantation (allo-HSCT) is shaped by many factors, including graft composition and viral reactivations. However, how graft engineering strategies and CMV/EBV reactivation jointly govern long-term αβ and γδ T cell numerical recovery, clonal architecture, and functional polarization remains poorly understood. We investigated how graft platform (abT-cell-depleted vs T-cell-replete) and CMV/EBV reactivation shape long-term abT cell and gdT cell numerical recovery, clonal architecture, and functional programs.

Methods: We analyzed 213 adult patients, transplanted for hematologic malignancies with matched related or unrelated donors, who received either αβT cell-depleted (n=146) or T-cell-replete (n=67) grafts. Longitudinal immune phenotyping was performed for up to three years and integrated with bulk- and single-cell-T cell receptor (TCR) repertoire and transcriptomic profiling. Clonotypes were defined by CDR3 sequence identity.

Results: CMV-reactivation was associated with pronounced CD8+ abT cell expansion across both platforms. Furthermore, CMV-reactivation was associated with sustained numerical dominance of $Vd2^{neg}$ gdT cells in recipients of ab-T-cell-depleted grafts. In this cohort, $Vd2^{neg}$ gdT cells underwent early polyclonal expansion, followed by repertoire focusing, which was largely independent of CMV reactivation. In contrast, abT cells remained clonally restricted. Reduced early $Vδ2^{pos}$ γδTCR diversity was associated with subsequent EBV reactivation. Single-cell TCR profiling one year post-transplant showed marked hyperexpansion of abTCR clonotypes and a low frequency of TCR singlets in recipients of abT-cell-depleted allo-HSCT. In contrast, gdTCR repertoires showed more inter-patient than inter-platform variability. Limited donor-recipient overlap for abTCRs and $Vd2^{neg}$ gdTCRs indicated that these repertoires are largely newly generated post-transplant.
Transcriptomic analyses demonstrated predominantly effector programmes across T cell subsets one year after allo-HSCT, which were markedly different transcriptomically compared to their donors. Platform-dependent polarization was observed, with enrichment of AREG-associated tissue-repair signatures in T-cell-replete recipients and KLRC2/KLRC3-linked cytotoxic programs in αβT cell-depleted recipients.

Conclusions: Long-term T-cell reconstitution after allo-HSCT is durably imprinted by the graft platform, with viral reactivation amplifying cytotoxic lineages without fully dictating repertoire architecture, and distinct rebuilding rules for αβ and γδ lineages. Defining these platform- and virus-associated trajectories may inform immune monitoring strategies and the rational timing of post-transplant immunomodulatory therapeutic interventions.



Disclosure: **Conflict of Interest:** JK reports on patents dealing with gdTCRs and engineering strategies and received research grants from Novartis and Miltenyi Biotech. MdW reports on grant support from KWF (#13493), Leukemiefonds.nl, Oncode accelerator and I&I Boostgrant and Research support from Miltenyi and Novartis.

A007

ACCELERATING PATIENT CRITICAL TIME METRICS VIA RAPID POINT-OF-CARE MANUFACTURING OF LEUKAPHERESIS-FREE THIRD-GENERATION CD19 CAR-T CELLS

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Background: CAR-T therapy has transformed the treatment of B-cell malignancies. However, the manufacturing of commercially available CAR-Ts requiring leukapheresis and centralized production is time-consuming and costly. The complex supply chain of the commercial products leads to prolongation of critical time metrics ("brain-to-vein" or "vein-to-vein" time) that limits timely patient access to treatment. Here, we aimed to develop and validate a rapid, simplified and GMP-compliant manufacturing platform of third-generation CD19-CAR-Ts from small peripheral blood volumes using G-Rex technology.

Methods: Two manufacturing protocols using a CAR-19 γ-retroviral vector(BCM, Houston) were evaluated: (a)"Expansion-in-G-Rex", involving anti-CD3/CD28 peripheral blood mononuclear cell (PBMCs) activation, transduction in plates on day 2, and transfer to G-Rex-bioreactors for expansion(day 6-9); (b)"Transduction-in-G-Rex", where activated PBMCs were transferred directly to G-Rex (day 2) for transduction and expansion. Three seeding densities (0.25, 0.5, 0.8 $\times 10^6$ cells/cm²) and two viral vector volumes (0.4, 0.75ml/cm²) were tested. Metabolic parameters guided harvest timing. Expansion, phenotype, transduction efficiency, proliferation and cytotoxicity were assessed by FCM, while specificity was evaluated by ELISPOT.

Results: The "Expansion-in-G-Rex" protocol yielded high transduction efficiency (58-81%) and expansion (26-32 fold). However, it required 2-3weeks to complete and involved multiple handlings. To overcome these limitations, we developed the "Transduction-in-G-Rex" protocol, in which both transduction and expansion were performed in G-Rex. The optimal condition (0.25×10^6 cells/cm², 0.4ml/cm² vector) enabled up to 120-fold CAR-T expansion within only 7 days, demonstrating that transduction directly in G-Rex markedly accelerates cell kinetics. GMP validation using PBMCs from one healthy donor and two DLBCL patients confirmed the method's robustness, resulting in 164±53-fold expansion within 8-9 days, producing $1.2\pm0.7\times10^9$ cells with high CAR expression (67±3%), low vector copy number (1.4±0.2), and a polyclonal CD8+/CD4+ composition (48±14%/50±14%, respectively). Phenotypically, CAR-T cells were enriched in naïve (26±7%) and memory subsets (central memory:32±5%, effector memory:33±10%), expressed high activation markers (CD69+:59±14%, CD25+:52±5%), and exhibited a favorable functional profile with increased CD27 and CD62L (68±3%, 58±10%, respectively) and low expression of exhaustion/senescence markers (PD-1^+:11±2%, CTLA-4^+:2.9±0.2%, $CD27^-/CD45RA^+/CD57^+$:6±2%). Functionally, the CAR-T-products showed robust proliferative responses upon CD3 re-stimulation compared to baseline (divided:84% vs 0%, $p<0.0001$; proliferation index:2.9 vs 0, $p=0.0004$) and strong, antigen-specific IFN-γ secretion and cytotoxicity against $CD19^+$ Raji cells compared to untransduced T cells (SFC/25,000 cells:795±51 vs 89±38, p=0,0004; % lysis Raji cells:82±2% vs 31±6%, $p<0.0001$). Activity was specific, as reactivity against $CD19^-$/K562 targets was minimal and comparable to untransduced T-cells (SFC/25,000 cells:38±12 vs 21±16, p=0.0001; %lysis: 43±7% vs 46±2%, p=0.7).

Conclusions: The "Transduction-in-G-Rex" protocol enables rapid, scalable, GMP-compliant and highly efficient CAR-T cell manufacturing from small blood volumes, requiring minimal handling, reduced viral vector input and no leukapheresis, thus addressing major cost and complexity drivers of CAR-T production. Collectively, its robustness, scalability, and ability to generate clinical-scale doses support its suitability for decentralized, point-of-care manufacturing, with the potential to considerably shorten patient time-to-treatment and improve patient access to CAR-T therapy.

Disclosure: Nothing to declare.

A008

OPTIMIZING CONDITIONING REGIMENS FOR HSCT: TMLI AS AN ORGAN-SPARING ALTERNATIVE TO TBI

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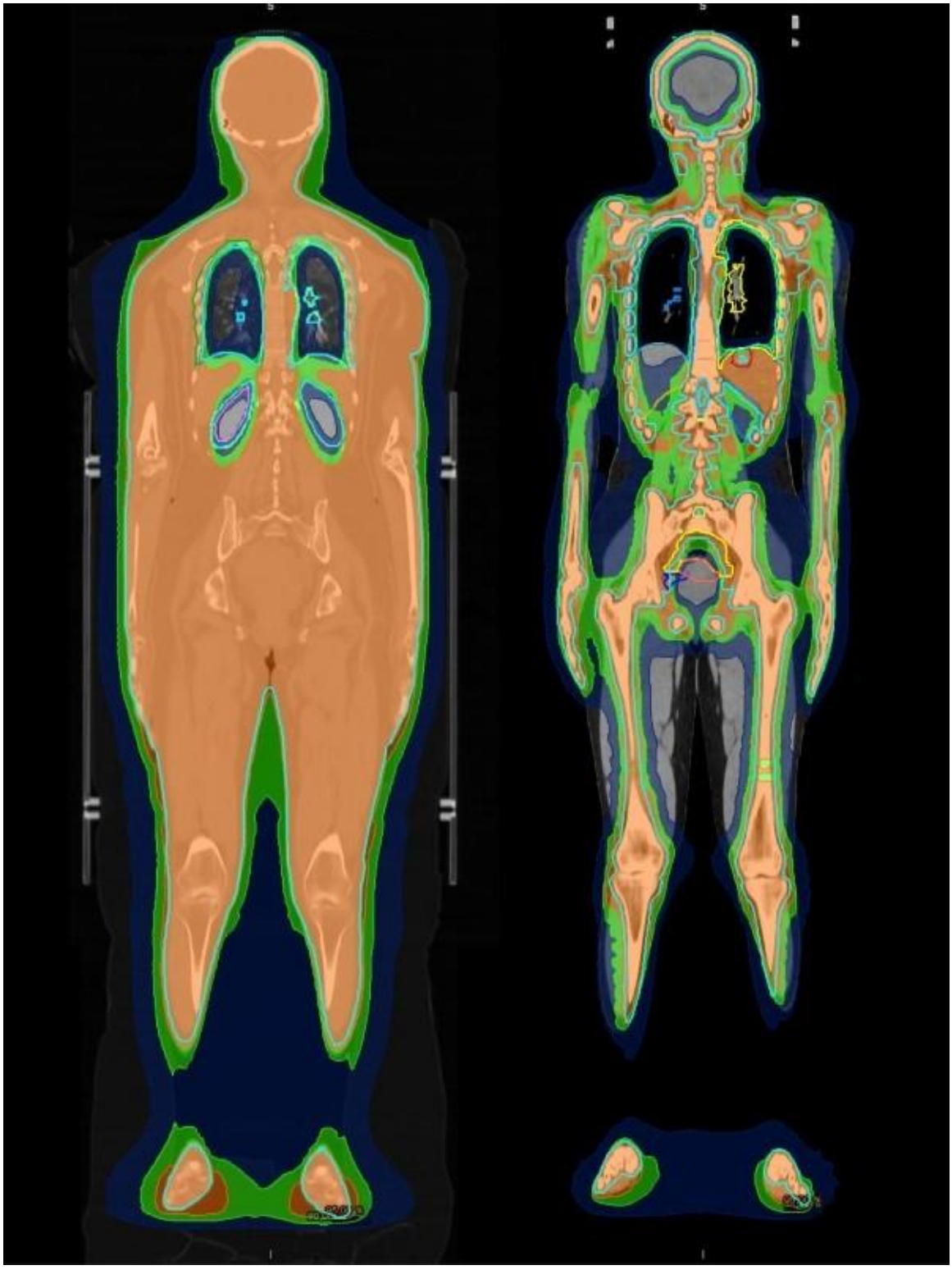
Background: Total Body Irradiation (TBI) remains a cornerstone of myeloablative conditioning for hematopoietic stem cell transplantation (HSCT), enabling immunosuppression, eradication of residual malignancy, and creation of marrow "space." However, its broader use is limited by toxicity, damage to organs at risk (OARs), the risk of secondary malignancies, and reduced suitability for patients with comorbidities. Targeted Total Marrow and Lymphoid Irradiation (TMLI), delivered with the Radixact X9 helical tomotherapy system, offers an organ-sparing alternative by enabling precise high-dose delivery to hematopoietic and lymphoid tissues while minimizing exposure to surrounding organs. Based on a review of the current clinical landscape, we conducted this study to present our center's initial experience. The primary objective was a dosimetric comparison of TMLI and intensity modulated IM-TBI for myeloablative conditioning prior to HSCT, with the specific aim of quantitatively assessing the organ-sparing benefits of TMLI.

Methods: A dosimetric comparison was performed for 65 patients (IM-TBI: n=32; TMLI: n=33) treated between January 2024 and October 2025 using the Radixact X9 system, all planned to a total dose of 12 Gy. Dose-volume histograms (DVHs) for 16 OARs were analyzed, and mean doses and relative differences were calculated.

Results: Planning target volume (PTV) coverage was comparable between techniques (IM-TBI: 96.6% vs TMLI: 95.2%). TMLI resulted in substantial reductions in mean dose to most OARs. The most pronounced reductions (>40%) were observed in gastrointestinal structures: oral cavity (67.2%), stomach (43.9%), and rectum (45.6%). Significant sparing (25–40%) was achieved for the liver (38.2%), heart (37.0%), breasts (36.6%), larynx (36.6%), intestines (35.5%), salivary glands (31.7%), central nervous system structures (brain 26.4%, brainstem 28.9%), and urinary bladder (29.2%). Kidney dose was reduced by 22.1%. Lung doses were comparable between techniques (2.7% reduction). A modest dose increase was observed for the eyes (13.5%) and lenses (4.2%), although absolute lens doses remained within clinically acceptable limits (<3 Gy). Overall, the mean dose to critical structures was reduced by 33.7% with TMLI (6.74 Gy vs 10.17 Gy for IM-TBI).



Conclusions: This analysis confirms the superior organ-sparing capability of TMLI compared with IM-TBI, consistent with international experience. The most clinically relevant dose reductions were observed in OARs highly susceptible to acute and late toxicities (e.g., CNS, gastrointestinal tract, heart, liver), which may translate into improved conditioning safety, reduced long-term complications, and enhanced post-HSCT quality of life. Although TMLI produced a small dose increase to the eyes, the absolute values are unlikely to result in clinically significant ophthalmologic toxicity. Kidney sparing is particularly important given the potential for combined nephrotoxicity with chemotherapy. Overall, TMLI provides a more selective conditioning modality that effectively targets marrow and lymphoid tissues while optimizing protection of vital organs, potentially expanding HSCT eligibility in comorbid patients and enabling safe dose escalation in selected clinical scenarios.

Disclosure: Nothing to declare

A009

SEQUENTIAL MONITORING OF EXTRACELLULAR VESICLES UNCOVERS EARLY ENDOTHELIAL PERTURBATIONS ASSOCIATED WITH ACUTE GVHD

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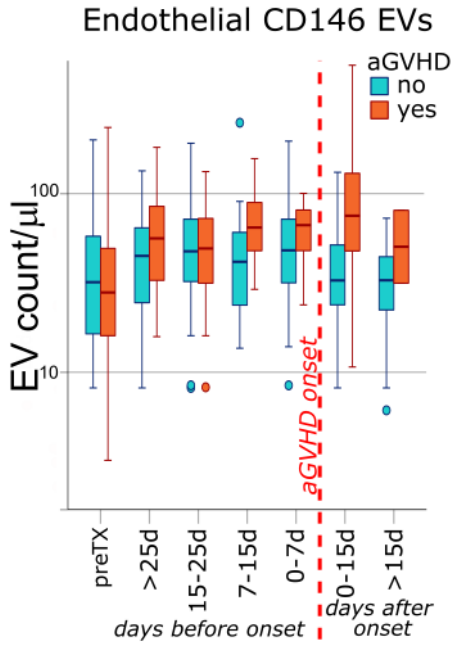
Background: Acute Graft-versus-Host Disease (aGVHD) remains a major complication after allogeneic hematopoietic stem cell transplantation (HSCT), and the absence of reliable early biomarkers continues to hinder timely diagnosis and intervention. We investigated extracellular vesicle (EV) membrane proteins as potential biomarkers and identified a possible association between aGVHD risk and CD146 expression. CD146, a cell adhesion molecule expressed on activated endothelial cells as well as selected lymphocyte subsets and macrophages, may reflect early endothelial dysfunction. This study employed a patented polychromatic flow cytometry (PFC) protocol to characterize post-transplant EV kinetics and determine the cellular origin of $CD146^+$ EVs associated with aGVHD.

Methods: Eighty HSCT recipients were monitored longitudinally; 19 developed aGVHD (grade II: n=10; grade III–IV: n=9). Serial blood samples were obtained from pre-transplant baseline through day +180, with EV profiling performed at 0, 3, 7, 10, 14, 18, 24, 28, 35, 45, 60, 70, 80, and 90 days post-HSCT. A patented BD® PFC assay quantified and phenotyped EV populations using phalloidin-FITC, a lipophilic cationic dye, and markers CD31, CD45, CD41a, and CD146. This multiparametric approach enabled precise enumeration (via BD Trucount Absolute Counting Tubes) of leukocyte-derived (LK), platelet-derived, and endothelial cell–derived (EC) EVs, including activated $CD146^+$ subsets. Associations between EV phenotypes, evaluated as absolute counts and proportional changes from baseline, and subsequent aGVHD were analyzed using logistic regression.

Results: Platelet-derived EVs showed dynamics strongly correlated with platelet count recovery (rho = 0.75; p < 0.001), supporting the biological robustness of the analytical workflow. Total LK EVs and CD146⁺ LK EVs, although elevated relative to healthy donors, did not demonstrate significant temporal changes nor predictive value for aGVHD. In contrast, EC-derived EVs exhibited pronounced early post-transplant kinetics. A distinct rise in EC EVs, particularly the CD146⁺ subpopulation, emerged within the first two weeks after HSCT, consistent with early endothelial activation or injury. Importantly, CD146⁺ EC EV levels were significantly associated with subsequent aGVHD, both as absolute concentrations (Figure1: OR 1.11 p = 0.038) and as proportional increases over time (OR 1.094 p = 0.043). Furthermore, the ratio of CD146⁺ EC EVs to total EC EVs proved highly informative: this ratio increased well before clinical onset of aGVHD, indicating early endothelial stress. Its predictive relevance held for both absolute values (OR 1.248 p = 0.043) and dynamic changes (OR 1.183 p = 0.033). These temporal patterns support a model in which endothelial perturbation precedes the immune dysregulation that culminates in aGVHD, aligning with current mechanistic concepts of transplant-associated vascular injury.



Conclusions: This study demonstrates that endothelial-derived CD146⁺ EVs undergo early post-HSCT alterations reflective of endothelial dysfunction and correlate with later development of aGVHD. CD146⁺ EC EVs represent promising, non-invasive biomarkers capable of identifying high-risk patients before clinical symptoms emerge. A prospective validation study is ongoing, integrating expanded immunophenotyping with the MACSPlex EV platform to establish robust, clinically applicable biomarkers.

Disclosure: Nothing to declare

A010

RESTORATION OF PULMONARY ENDOTHELIAL HEALTH AND OVERALL SURVIVAL *FOLLOWING ALLOGENEIC HSCT THROUGH MINICIRCLE FOXF1 MRNA NANOPARTICLE THERAPY IN JUVENILE MICE*

Clayton Long[1,2], *Ying-Wei Lan*[2], *Jonathan Do*[2], *Hana Roushdy*[2], *Xia Mai*[2], *Roberta Adams*[1,2,3], *Tanya Kalin*[1,2], *Mostafa H. Elberry*[2]
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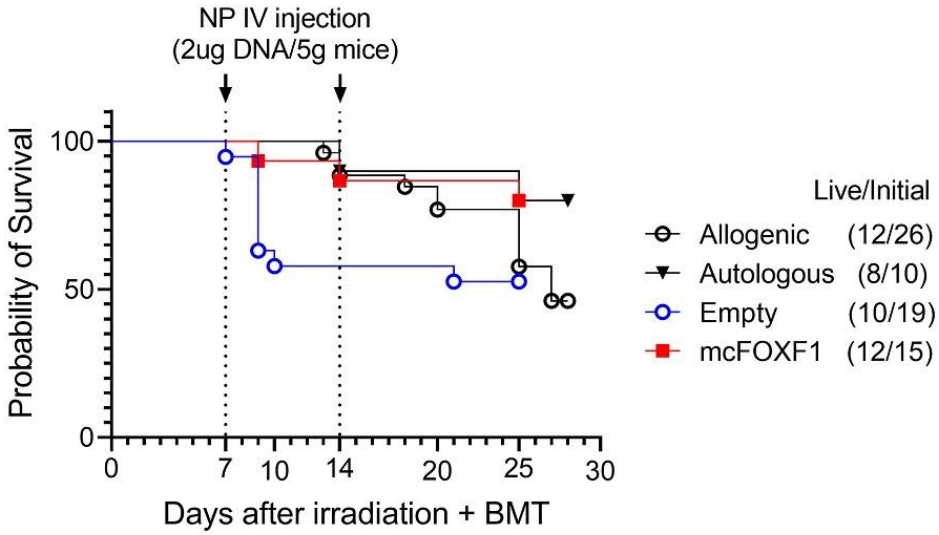
Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative therapy for many malignant and non-malignant pediatric diseases but is frequently complicated by endothelial injury. Pulmonary endothelial cells (ECs) are particularly vulnerable, contributing to severe post-transplant complications such as idiopathic pneumonia syndrome, diffuse alveolar hemorrhage, and pulmonary thrombotic microangiopathy. FOXF1 is a lung-enriched transcription factor essential for pulmonary vascular development, endothelial maintenance, and repair. Congenital FOXF1 loss leads to pulmonary hemorrhage and death in infancy. Acquired FOXF1 downregulation has been linked to acute lung injury and fibrosis. Its role in transplant-associated pulmonary endothelial injury and its therapeutic potential remains incompletely defined. We hypothesized that allogeneic HSCT induces sustained pulmonary EC loss through FOXF1 downregulation and that targeted FOXF1 restoration could rescue endothelial injury and improve survival.

Methods: Juvenile mice (postnatal day 8–10) underwent total body irradiation (13 Gy, split dose) followed by intravenous injection of 3 × 10^6 bone marrow cells. Experimental groups included syngeneic (autologous) HSCT, allogeneic HSCT (BALB/c → C57BL/6), and non-irradiated controls. Pulmonary tissue and blood were collected at days 7, 14, and 28 post-transplant. Pulmonary ECs were quantified by flow cytometry and FOXF1 expression was assessed in sorted ECs by qPCR. To evaluate therapeutic rescue, a subset of allogeneic HSCT mice received intravenous nanoparticle-mediated minicircle FOXF1 (mcFOXF1) mRNA delivery on days 7 and 14 post-transplant. The negative control included allogeneic HSCT mice injected at the same timepoints with empty minicircle (Empty) infusions not containing FOXF1mRNA. Survival, endothelial recovery, FOXF1 expression, and lung histopathology were assessed.

Results:



Allogeneic HSCT resulted in reduced survival and weight loss but full donor engraftment, consistent with systemic graft-versus-host disease. Compared with autologous and control mice, allogeneic HSCT mice demonstrated a marked and persistent reduction in pulmonary ECs at all time points, accompanied by sustained FOXF1 downregulation. In contrast, autologous HSCT mice showed transient FOXF1 suppression and EC loss with pulmonary EC recovery by day 28 and improved survival. Lung tissue from allogenic HSCT mice showed significant inflammation and alveolar destruction compared to autologous HSCT. Therapeutic delivery of mcFOXF1 significantly improved survival in allogeneic HSCT with similar survival curves as autologous models. Given comparable outcomes and shared biological interpretation, Empty and Allogeneic groups were combined into a single control group, increasing statistical power. Compared to the pooled allogenic group, mcFOXF1 nanoparticle treatment significantly reduced mortality (20% vs 51%; RR 0.39, 95% CI 0.14–1.12; $p = 0.04$). Further analysis showed that mcFOXF1 was able to restore the pulmonary EC population in conjunction with increased endogenous FOXF1 expression. Histologic evaluation showed reduced inflammatory lung remodeling with improved alveolar architecture.

Conclusions: Allogeneic HSCT induces sustained pulmonary endothelial loss associated with FOXF1 downregulation in juvenile mice compared to autologous HSCT. Transient restoration of FOXF1 using nanoparticle-delivered mRNA to pulmonary endothelial cells is sufficient to rescue the endothelial population and alveolar integrity with improvement in survival. These findings identify FOXF1 as a central regulator of transplant-associated pulmonary injury and support FOXF1 targeted therapy as a novel, endothelial-specific strategy to mitigate lung complications following HSCT.

Disclosure: There are no conflicts of interest or disclosures to report.

A011

PHARMACOLOGICAL MODULATION OF CAR30 AND CAR19 T CELL STEMNESS AND *EX VIVO* EXPANSION WITH PI3K AND CBP/P300 INHIBITION

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Background: Increasing the proportion of stem memory T-cells (T_{SCM}) in CART infusion products (IP) is associated with improved clinical outcomes. The goal is to analyze the impact of Idelalisib [PI3K inhibitor (PI3Ki), that blocks differentiation] and SGC-CBP30 [inhibitor of CBP/p300 (CBP/p300i), epigenetic expansion promotor] in *ex vivo* CART anti-CD30 (CAR30T) and CART anti-CD19 (CAR19T) cultures.

Methods: T-cells from relapsed and refractory (R/R) Hodgkin Lymphoma (HL) patients were transduced with 4-1BBz-CAR30 and subjected to PI3Ki (0.5μM, 1μM), CBP/p300i (0.5μM, 1μM, 2μM) or a dual-treatment [DT, a combination of PI3Ki (0.5μM) and CBP/p300i (0.5μM)] and untreated (UT) as control. T-cells from R/R B cell non-Hodgkin Lymphoma (BNHL) were transduced with 4-1BBz-CAR19 and PI3Ki (0.5μM), CBP/p300i (0.5μM), DT and UT cultures were performed. CART cultures were performed during 10 days. CART cells composition was determined by flow cytometry. CAR30T cytotoxicity assays were performed against L540 (HL) and CAR19T against Raji (BNHL) at different effector-target ratios.

Results: PI3Ki CAR30T preserved viability and fold-expansion (UT, 15.1±4.4 vs 0.5μM,13.9±4.2; p=0.89) and augmented T_{SCM} proportion (UT vs 0.5μM: $CD4^+$ 4.0%±1.2 vs 14.3%±4.3, p<0.05; $CD8^+$ 9.2%±1.3 vs 30.7%±4.5, p<0.05); however, displayed lower antitumor effect (0.5μM and 1μM vs UT, p<0.05).
CBP30/p300i CAR30T enhanced viability (UT 64.4%±7.0; 0.5μM, 71.7%±6.4 p<0.01; 1μM, 74.3%±6.6, p<0.05) and fold-expansion (UT, 12.7±4.4 vs 0.5μM, 26.3±9.4; p<0.05). CBP/p300i preserved T_{SCM} (UT vs 0.5μM: $CD4^+$ 2.4%±1.1 vs 8.5%±3.9, p=0.072; $CD8^+$ 4.1% ±2.0 vs 14.3% ±6.8, p=0.09) and antitumor efficacy (0.5μM p=0.54; 1μM p=0.30). To enhance expansion and T_{SCM}, DT CAR30T were performed. No differences in fold-expansion was observed in DT (14.0±6.7) compared to PI3Ki (8.7±2.8 p=0.32) or UT (10.8±4.4, p=0.30); CBP/p300i remained higher (22.4±6.9 p<0.05). T_{SCM} in DT ($CD4^+$ 14.7%±3.5; $CD8^+$ 23.7%±4.5) increased similarly to PI3Ki ($CD4^+$ 14.8%±4.6, p=0.94; $CD8^+$ 25.1%±8.6, p=0.71) and exceeded UT ($CD4^+$, 4.2%±1.4, p<0.05; $CD8^+$, 7.2%±2.5, p<0.05) and CBP/p300i ($CD4^+$, 6.8%±2.3, p<0.01; $CD8^+$, 9.9%±4.5, p<0.05). DT cytotoxic capacity was similar to CBP/p300i (p=0.9) and UT (p=0.31), but higher than PI3Ki (p<0.05). CBP/p300i and DT CAR19T enhanced viability at day 6 (UT, 65.7%±3.1 vs CBP/p300i, 75.3%±4.5, p<0.05; UT vs DT 75.4%±4.6, p<0.05), but no PI3Ki (67.4%±4.5 p=0.42). On day 10, only CBP/p300i maintained viability (UT 66.0%±5.2 vs CBP/p300i 58.5%±5.5 p=0.06; UT vs PI3Ki 46.4%±6.9, p<0.05; UT vs DT 47.6%±2.04, p<0.05). CBP/p300i

increased capacity expansion (p<0.01), particularly on day 6 when cell count doubled (UT, $4.1\pm1.9x10^5$ vs CBP/p300i, $8.0\pm1.3x10^5$ p<0.05). CBP/p300i preserved T_{SCM} (UT vs CBP/p300i; $CD4^+$, 6.5%±3.1 vs 7.2%±3.0 p=0.14; $CD8^+$, 5.4%±1.8 vs 6.7%±1.8 p=0.17). Antitumor activity was maintained in CBP/p300i (p=0.15) but decreased in PI3Ki (p<0.01) and DT(p<0.05).

Conclusions: Combination of CBP/p300i and PI3Ki resulted in a CAR30T-IP with increased expansion, T_{SCM} and *in vitro* antitumor effect over single agent use. CBP/p300i resulted in a CAR19T-IP with enhanced expansion without T-cell differentiation maintaining antitumor effect. Targeted pharmacological inhibition may contribute to generate enhanced antitumor efficacy CART products.

Disclosure: Nothing to declare

A012

INFLAMMATORY AND STROMAL ALTERATIONS OF THE HEMATOPOIETIC NICHE ASSOCIATED WITH POST–CAR-T CYTOPENIAS

*Martín Gómez Redondo[1,2], Sandra Muntión Olave[1,2], Silvia Preciado Pérez[1,2], Almudena Navarro Bailón[2,1], **Carmen Santos Marcos**[2,1], Ana África Martín López[2,1], Juan Flores Montero[1,2], Estefanía Pérez López[2,1], Magdalena Sierra Pacho[2,1], Marta Rodríguez González[2,1], Diego Bueno Sacristán[2,1], María Belén Vidriales Vicente[2,1], Miriam López Parra[2,1], Lucía López Corral[2,1], Almudena Cabero Martínez[2,1], Fermín Sánchez-Guijo Martín[2,1]*
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Background: Persistent cytopenias following CAR-T therapy are one of the most clinically relevant toxicities of this treatment. Their pathophysiology is not fully understood, but studies seem to point to a multifactorial origin involving inflammatory damage that affect HSCs and the hematopoietic niche. The aim of this study was to identify the mechanisms of inflammation and hematopoietic dysregulation and the bone marrow microenvironment associated with the development of long-term cytopenias after therapy.

Methods: This single-center study included 35 consecutive Diffuse Large B Cell Lymphoma patients treated with axicabtagene ciloleucel whom peripheral blood and bone marrow (BM) samples were taken prior to lymphodepletion and on day +28 after infusion. Plasma from both compartments was analyzed using Luminex to assess inflammatory and hematopoietic regulatory cytokines. In BM, hematopoietic capacity was evaluated using clonogenic assays (CFU-GM, BFU-E, and CFU-F), and the phenotype of the monocyte/macrophage population was characterized by flow cytometry. In addition, mesenchymal stem cells (MSCs) were isolated and expanded for studies of gene expression, DNA damage, and ROS production. Results were compared between patients with and without grade 2–4 cytopenias at day 100 after CAR-T infusion.

Results: Patients with neutropenia had a baseline inflammatory state prior to treatment, with elevated concentrations of OPN, IL18, and CXCL10 in BM plasma, and dysregulation of

the hematopoietic compartment and niche with lower levels of IL7 and ANG1. At 28 days, they have reduced concentrations of CXCL12. Treatment significantly decreased CFU-GM and BFU-E production in both groups. In BM macrophages, we observed a significant increase in CD64, associated with a proinflammatory phenotype. In MSCs, an increase in phosphorylated ATM was detected after therapy, and elevated ROS production was observed in BM mononuclear cells prior to treatment. Finally, gene expression analysis in MSCs from neutropenic patients showed increased levels of S100A9, along with higher basal expression of PPARG and lower expression of ALPL on day +28, suggesting the presence of a disbalanced pro-inflammatory stroma with an adipogenic differentiation predisposition and reduced osteogenic capacity, and therefore less favorable for hematopoietic recovery.

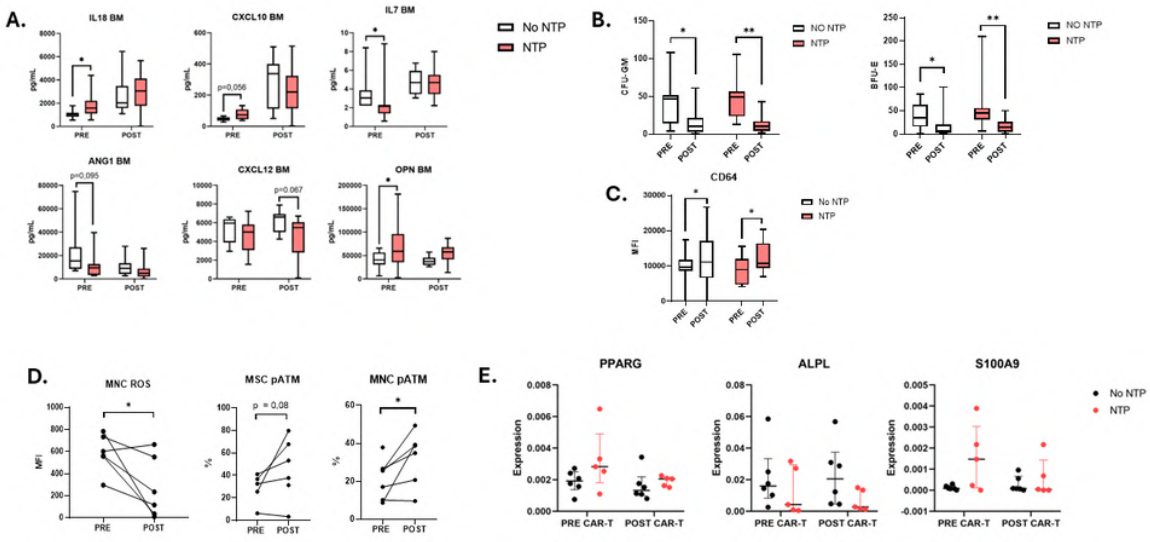

Figure 1. Multiparametric analysis of bone marrow and MSCs in patients treated with CAR-T. A. Quantification of cytokines in bone marrow plasma. B. Hematopoietic clonogenic assays (CFU-GM and BFU-E). C. Phenotyping of bone marrow macrophages by flow cytometry. D. Evaluation of oxidative stress and ATM activation in bone marrow mononuclear cells and MSCs. E. Gene expression of MSCs associated with differentiation and inflammatory response. NTP: grade 2–4 neutropenia; No NTP: absence of neutropenia.

Conclusions: Our findings suggest that post-CAR-T cytopenias develop in a microenvironment that is already altered prior to treatment, characterized by inflammation and niche dysregulation.

Disclosure: Funding: GRS 2182/A/2020, GRS2887/A1/2023 (Gerencia Regional de Salud de Castilla y León) and PI23/01107 (ISCIII, co-funded by the European Union), Red de Terapias Avanzadas (TERAV, RD24/0014/0034) and Centro en Red de Medicina Regenerativa y Terapia Celular de Castilla y León.

Conflict of interest: FSG reports research funding and travel support from Gilead-Kite. ACM reports receiving honoraria for speaking engagements from Gilead-Kite. The remaining authors declare no conflicts of interest.

A013

EVALUATION OF THE STATUS OF THE HEMATOPOIETIC NICHE PRE-LYMPHODEPLETION IN THE DEVELOPMENT OF POST–CAR-T HEMATOTOXICITY

Carmen Santos Marcos[1], *Almudena Navarro Bailón*[1], *Magdalena Sierra Pacho*[1], *Juan Alejandro Flores Montero*[1], *Diego Bueno Sacristán*[1], *Marta Rodríguez González*[1], *Ana África Martín López*[1], *Estefanía Pérez López*[1], *Almudena Cabero Martínez*[1], *Martín Gómez Redondo*[1], *Sandra Muntión Olave*[1], *Silvia Preciado Pérez*[1], *María Belén Vidriales Vicente*[1], *Miriam López Parra*[1], *Lucía López Corral*[1], *Fermín Sánchez-Guijo*[1]
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Background: Post-treatment cytopenias are among the most frequent long-term complications of chimeric antigen receptor T-cell (CAR-T) therapy. Their pathophysiology has not been fully elucidated, with inflammatory response and bone marrow hematopoietic reserve proposed as relevant factors in their development.

Methods: This study aimed to analyze the pre-CAR-T characteristics of the hematopoietic bone marrow (BM) niche, and to evaluate their correlation with the degree of cytopenias during the first 28 days after infusion.
A prospective study was conducted including 17 patients with diffuse large B-cell lymphoma treated consecutively with *axicabtagene ciloleucel* at our institution. Bone marrow aspirates and biopsies were obtained before lymphodepletion and subjected to cytomorphological, histopathological, and flow cytometric analyses to evaluate cellularity, mesenchymal stromal cells (MSC), and hematopoietic precursors. The resulting data were correlated with the presence of persistent cytopenias. Patients were stratified according to the median duration of each cytopenia during the first 28 days post-infusion (4 days for anemia, 9 days for neutropenia and 1 day for thrombocytopenia).

Results: Baseline clinical characteristics and hematological variables are summarized in Table 1. Most patients (82%) presented a low CAR-HEMATOTOX score. Cytokine release syndrome occurred in 94% (predominantly grade 1), and nearly half developed neurotoxicity. Anemia was the most common post-CAR-T cytopenia (94%), followed by thrombocytopenia (88%) and neutropenia (70%). The presence of pre-lymphodepletion anemia and thrombocytopenia was associated with persistent cytopenias during early follow-up ($p = 0.029$ and $p = 0.002$, respectively). Poorer bone marrow cellularity was observed in patients with persistent cytopenias, although the difference was not statistically significant (Figure 1A). Flow cytometry revealed significantly lower CD34+ progenitor counts ($p = 0.04$) in patients with persistent cytopenias (Figure 1B).

Table 1. Descriptive analysis of baseline characteristics and clinical variables (n=17 patients).

Variable	Results n (%)
Gender:	10 (59%) 7 (41%)

• Female • Male	
Age: • Less than or equal to 60 • Greater than 60	13 (76%) 4 (24%)
Medium number of prior lines of therapy	1 (range: 1-5)
Pre-lymphodepletion disease status: • Progression • Partial response • Complete response	9 (53%) 7 (41%) 1 (6%)
CAR-HEMATOTOX Score: • Low (0-1) • High (2 or greater)	14 (82%) 3 (18%)
Cytokine release syndrome (CRS): • Grade 1 • Grade 2 • Early (24h)	12 (75%) 4 (25%) 10 (62%)
Neurotoxicity (ICANS): • Grade 1 • Grade 3	3 (43%) 4 (57%)
Treatment of complications: • Tocilizumab • Dexamethasone • Anakinra • Siltuximab	16 (94%) 14 (88%) 2 (12%) 1 (6%)
Response on day +30: • Complete response • Partial response	13 (76%) 3 (18%) 1 (6%)

• Stable disease	

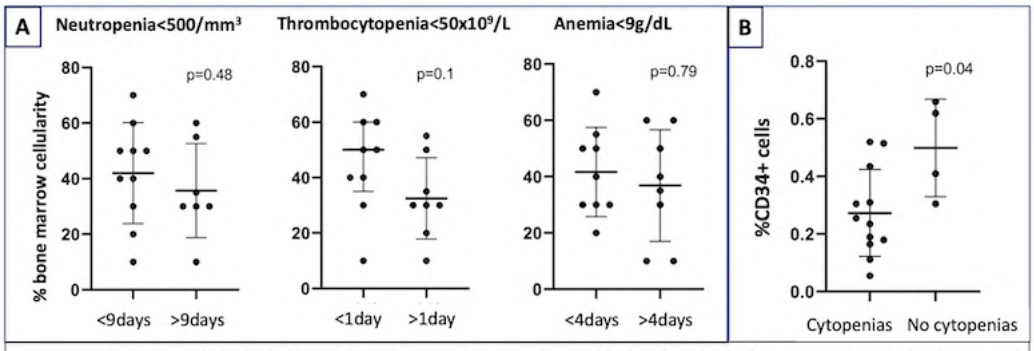

Figure 1. A. Percentage (%) of cellularity in bone marrow biopsies obtained before lymphodepletion according to the duration of cytopenias in the first 28 days after CAR-T infusion. **B.** Percentage (%) of CD34+ cells by flow cytometry in bone marrow pre-lymphodepletion according to the presence or absence of persistent cytopenias in the first 28 days.
Visually assessed by the same pathologist.

Conclusions: A decreased hematopoietic reserve pre-lymphodepletion, with the presence of peripheral blood cytopenias, lower bone marrow cellularity, and a lower number of hematopoietic progenitors, is associated with the development of persistent cytopenias after CAR-T cell therapy during the early follow-up period. The sample size of the study is being expanded and BM samples obtained on day +28 are being evaluated to further investigate the pathophysiology of these cytopenias.

Disclosure:

- F Sánchez-Guijo has received research funding and travel grants from Gilead Kite.
- E Pérez López has received travel grants from Gilead Kite.
- M López Parra declares receiving honoraria from Gilead Kite.

A014

CLINICAL RELEVANCE OF NON-HLA REGIONS DIFFERENCES IN ADDITION TO HLA MOLECULAR MISMATHCES BETWEEN DONOR AND RECIPIENT IN HAPLO-HSCT USING PTCY

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Background: Despite improvements in haploidentical hematopoietic stem cell transplantation (haplo-HSCT) using post-transplant cyclophosphamide (PTCy), outcomes remain suboptimal. Exploring genetic regions beyond HLA may enhance donor selection and transplant success.
The aim of this study was to evaluate the clinical impact of short tandem repeat (STR) disparities between donor and recipient in haplo-HSCT, and their biological relevance alongside HLA molecular mismatches and NK cell alloreactivity.

Methods: This study included 145 patients undergoing related-donor haplo-HSCT. Fifteen STR loci were analyzed using PowerPlex® 16HS (Promega). STR disparity was defined as the presence of an allele in one individual absent in the other, assessed bidirectionally and in GvH/HvG directions. HLA typing was performed via NGS and PCR-SSO, with peptide mismatch load quantified by the PIRCHE algorithm. KIR genotyping and NK alloreactivity were evaluated using missing-ligand and licensing models.

Results: Univariate analysis showed that patients with ≥10 bidirectional STR mismatches had lower relapse rates at 3 years (40% vs. 60%, HR: 0.37). >2 GvH-direction mismatches were associated with improved GRFS (HR: 0.55). Multivariate analysis confirmed ≥10 STR mismatches (HR: 0.29) and low HvG PIRCHE scores (<28) as independent predictors of reduced relapse. High DRI (HR: 2.52) and major ABO incompatibility (HR: 4.88) correlated with worse outcomes. GRFS was improved with >2 GvH STR mismatches and low HvG PIRCHE scores, but worsened with HCT-CI >3 and >2 iKIR mismatches.

Conclusions: STR and KIR mismatches contribute significantly to post-transplant outcomes in haplo-HSCT with PTCy, complementing HLA-based risk stratification. STR disparity may reflect graft-versus-leukemia (GvL) effects, suggesting its utility in donor selection alongside PIRCHE and NK models.

Disclosure: NOTHING TO DECLARE

A015

CD33-CAR INKT CELLS MITIGATE THE IMPACT OF ANTIGENIC HETEROGENEITY IN ACUTE MYELOID LEUKEMIA THROUGH DIRECT CYTOTOXICITY AND ACTIVATION OF CONVENTIONAL T CELLS

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Background: Acute myeloid leukemia (AML) displays extensive inter- and intra-patient antigenic heterogeneity, a major limitation for CAR-based therapies. Cellular platforms capable of coupling potent direct cytotoxicity with the capacity to engage endogenous immune responses may mitigate the impact of antigenic heterogeneity. Invariant natural killer T (iNKT) cells are uniquely suited for allogeneic immunotherapy due to their lack of alloreactivity. Moreover, iNKT cells can promote cross-priming of conventional T cells (PMID: 34376537), offering a strategy to extend tumor control beyond the targeted antigen. To exploit this potential against AML, we generated CD33-directed CAR iNKT cells, we assessed their antitumor activity against CD33-expressing AML cell lines *in vitro* and *in vivo*, we tested their immunomodulatory effects in primary bone marrow samples, and their ability to address antigenic heterogeneity in a mixed tumor *in vitro* system.

Methods: Human iNKT cells were isolated from peripheral blood using the 6B11 monoclonal antibody and magnetic bead enrichment. Purified iNKT cells were activated with anti-CD3 and anti-CD28 antibodies, transduced with a second-generation CD33-CAR containing a CD28 co-stimulatory and a CD3ζ signaling domains, and subsequently restimulated and expanded with α-galactosylceramide (α-GalCer) in the presence of IL-15. Transduction efficacy was assessed by flow cytometry using protein L staining. Cytotoxicity against CD33+ AML cell lines was evaluated in vitro and in vivo in xenograft models. Primary AML bone marrow samples, obtained from AML patients at initial diagnosis, were used to assess blast killing, modulation of HLA class I/II expression on residual blasts, and activation of endogenous T cells after 48 hours of co-culture with CD33-CAR iNKT cells. Antigen heterogeneity was modelled by co-culturing CD33-expressing GFP+ and CD33-knockout (KO) mCherry+ MOLM-14 cells with CD33-CAR iNKT cells alone or in combination with conventional T cells.

Results: CD33-CAR iNKT cells were efficiently generated at high purity and with robust transduction efficacy and expansion across multiple donors. They mediated potent CD33-dependent cytotoxicity against the OCI-AML-3 and the MOLM-14 AML cell lines *in vitro* and significantly extended animal survival *in vivo* in a MOLM-14 xenograft model. In primary AML bone marrow samples, CD33-CAR iNKT cells eliminated primary AML blasts and induced upregulation of HLA class I/II molecules on residual leukemic cells. This was accompanied by activation of endogenous bone-marrow T cells, reflected by increased CD38 and HLA-DR expression, consistent with the previously reported iNKT-mediated immunomodulatory and cross-activating functions. In antigen-heterogeneous co-cultures, CD33-CAR iNKT cells alone selectively eliminated CD33-expressing MOLM-14 cells but did not control CD33-KO cells. However, when both CD33-CAR iNKT cells and conventional T cells were added to the co-culture, we observed a tumor growth inhibition of both CD33-expressing and CD33-KO MOLM-14 cells, resulting in almost 50% reduction in CD33-KO MOLM-14 expansion.

Conclusions: Our findings indicate that CD33-CAR iNKT cells not only exert potent antigen-specific cytotoxicity against AML but can also initiate conventional T cell responses, leading to an antitumor effect that goes beyond the target antigen expressing cells. Altogether, these data support the development of CAR iNKT cells as a robust allogeneic, off-the-shelf immunotherapy for AML.

Clinical Trial Registry: NA

Disclosure: CB: has received research funding from Kite/Gilead, Novartis, BMS/Celgene. YC: has received institutional consulting fees for advisory board from MSD, Novartis, Incyte, BMS, Pfizer, Abbvie, Roche, Jazz, Gilead, Amgen, Astra-Zeneca, Servier, Takeda, Pierre Fabre, Medac; Travel support from MSD, Roche, Novartis, Pfizer, BMS, Gilead, Amgen, Incyte, Abbvie, Janssen, Astra-Zeneca, Jazz, Pierre Fabre, Sanofi all via the institution. CM: Consultancy Astra-Zeneca, Link Cell Thérapies, Ensoma, RedTree Venture Capital, Tune Therapeutics, Nektar, Immatics, GBMNewCo, Grace Science, CARGO therapeutics; Research Funding Tune Therapeutics; Patents & Royalties CARGO therapeutics. RSN: Consultancy Stratus Therapeutics, Restem, Biorasi, Amgen. FS: has received institutional consulting fees from BMS/Celgene, Incyte, Kite/Gilead; speaker fees from Kite/Gilead, Incyte; travel support from Kite/Gilead, Novartis, AstraZeneca, Neovii, Janssen; research funding from Kite/Gilead, Novartis, BMS/Celgene.

A017

HLA–KIR INTERACTIONS AS PREDICTIVE BIOMARKERS OF NK ALLOREACTIVITY IN HAPLOIDENTICAL TRANSPLANTATION WITH PTCY

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Background: Natural killer (NK) cell reconstitution and KIR receptor–mediated alloreactivity after allogeneic hematopoietic stem cell transplantation (HSCT) from an HLA-haploidentical donor (haplo-HSCT) have gained increasing attention due to their potential contribution to the graft-versus-leukemia (GvL) effect. However, the clinical relevance of NK alloreactivity remains controversial, particularly in unmanipulated graft strategies employing post-transplant cyclophosphamide (PTCy), where T-cell depletion is not performed.
This study aimed to evaluate the clinical impact of predicted KIR alloreactivity in haplo-HSCT with PTCy, using graft-versus-host disease and relapse-free survival (GRFS) as a composite endpoint to reflect global transplant success.

Methods: A total of 145 patients with hematological malignancies who underwent haplo-HSCT with PTCy were retrospectively analyzed. HLA typing of recipients was performed by next-generation sequencing (NGS), while donor HLA typing was performed by PCR-SSO whenever haplotype segregation within the family was available. The second-field resolution of the non-shared donor haplotype was inferred using the most frequent allele from the HaploStats database.
Donor–recipient pairs were genotyped for KIR genes using the KIR-SSO assay. NK alloreactivity was assessed according to several predictive interaction models, including the inhibitory KIR mismatch (iKIRmm), missing-ligand, and missing-licensing models. Clinical follow-up extended to 36 months post-transplant.

Results: The most common indications for transplantation were acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), representing 52% of the cohort. Forty-eight patients (33%) had previously undergone HSCT. Reduced-intensity conditioning (RIC) was used in 72% of cases. The hematopoietic cell transplantation–comorbidity index (HCT-CI) was ≥3 in 30% of patients, and the disease risk index (DRI) was high or very high in 17%. Prediction of NK-KIR alloreactivity based on HLA–KIR interaction models revealed that the presence of multiple inhibitory KIR mismatches (iKIRmm) was significantly associated with inferior GRFS. Using the missing-ligand model, patients with multiple iKIR mismatches showed a median GRFS of 5 months compared with 25 months in the overall cohort (HR: 2.46, p = 0.001). A similar association was observed when applying the missing-licensing model (HR: 2.41, p = 0.015).
In multivariate analysis, both the missing-ligand (HR: 2.16, p = 0.008) and missing-licensing (HR: 2.27, p = 0.022) models remained independent predictors of reduced GRFS. Additionally, an HCT-CI ≥3 independently predicted inferior GRFS (HR: 1.79, p = 0.019 and HR: 1.91, p = 0.008, respectively).
These results were exponentially more pronounced in patients who received RIC and whose underlying pathology was myeloid.

Conclusions: Assessment of HLA–KIR interaction models to predict NK-KIR alloreactivity may represent a valuable approach to optimizing donor selection in haploidentical HSCT. Identifying donor–recipient combinations with unfavorable KIR interaction profiles could improve patient stratification and clinical outcomes, contributing to more personalized and immunogenetically informed transplant strategies.

Disclosure: NA

A019

EXTRACELLULAR VESICLES AS NONINVASIVE BIOMARKERS OF IMMUNE AND ENDOTHELIAL ACTIVATION IN CAR T-CELL THERAPY RECIPIENTS

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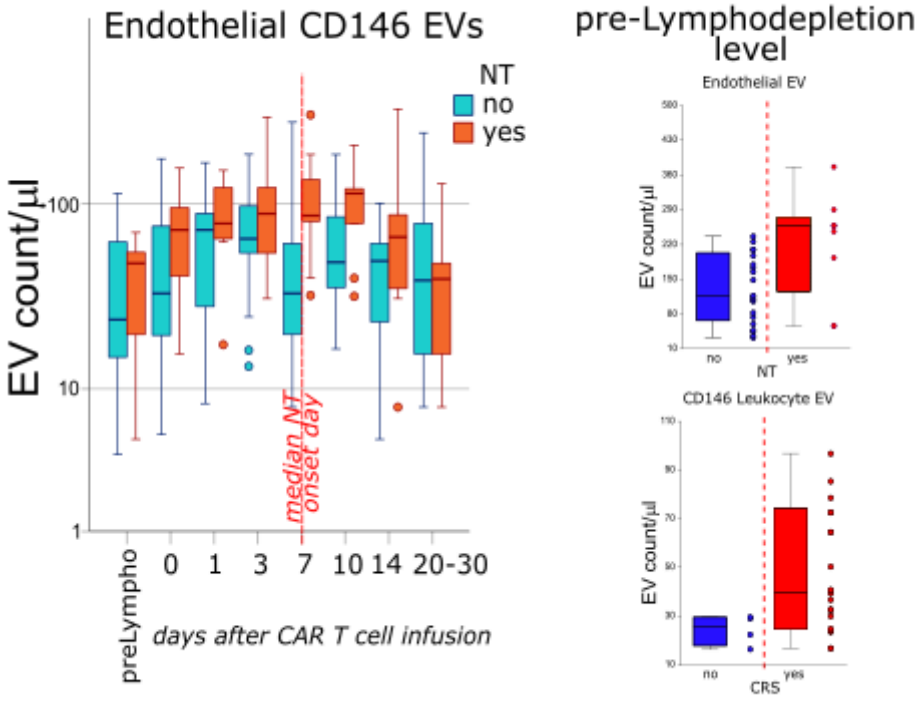
Background: CAR T-cell therapy has transformed the management of hematologic malignancies, yet the development of cytokine release syndrome (CRS), neurotoxicity (NT), and prolonged cytopenias highlights the need for early and reliable biomarkers. Existing predictive tools rely on parameters that typically emerge only after toxicity becomes clinically apparent. Extracellular vesicles (EVs) have shown promise as biomarkers, but their early kinetic behavior remains insufficiently characterized. To address this gap, we employed a patented polychromatic flow cytometry (PFC) assay to evaluate whether specific EV signatures could serve as early indicators of toxicity.

Methods: Thirty patients treated with commercial CAR T-cell products [axicabtagene ciloleucel (n=21), tisagenlecleucel (n=6), or brexucabtagene autoleucel (n=3)] were enrolled. Blood samples were collected pre-lymphodepletion (pre-Lym) and at days 0, 1, 3, 7, 10, 14, and 20-30 post-infusion. Most patients (n=20) had diffuse large B-cell lymphoma; the remaining had follicular lymphoma (n=6), mantle cell lymphoma (n=3), or high-grade B-cell lymphoma (n=1). PFC enabled absolute quantification of EVs derived from leukocytes (LK), endothelial cells (EC), platelets, and activated subsets using phalloidin, LCD, and antibodies targeting CD31, CD45, CD41a, and CD146 in BD Trucount™ tubes (acquired on a BD FACSLyric). Associations between EV kinetics and toxicity were analyzed using Mann-Whitney tests (M-W), logistic regression models (LRM), and receiver operating characteristic (ROC) curve analysis, performed with STATA 15 and SPSS 25.

Results: CRS developed in 26 patients (grades 1–2), and NT occurred in 9. A key finding was the strong association between elevated pre-Lym $CD146^+$ LK EV levels and subsequent CRS onset. Their strong predictive performance (ROC 0.911) suggests these EVs may serve as sensitive pre-infusion biomarkers. Patients who developed prolonged cytopenias (n=11) also exhibited significantly higher baseline levels of total EVs, $CD146^+$ EVs, and LK EVs. Mann-Whitney testing showed that both absolute $CD146^+$ LK EV counts and their proportional increase within total LK EVs were associated with CRS ($p=0.010$ and $p=0.033$, respectively), a trend further supported by LRM (OR 1.104 $p=0.064$). Regarding NT, pre-Lym EC EVs and $CD146^+$ LK EVs were significantly higher in patients who developed NT (M-W $p=0.049$ and $p=0.040$, respectively). Notably, an increase in $CD146^+$ EC EVs preceded NT onset (median day 7), with strong statistical significance (M-W $p=0.003$; LRM OR 1.012 $p=0.044$), highlighting a dynamic endothelial activation process that temporally aligns with emerging

neurological symptoms.



Conclusions: EV profiling identified distinct immunologic and vascular signatures associated with CRS and NT, supporting their utility as real-time indicators of CAR T-mediated inflammation. This prospective analysis demonstrates that CD146⁺ EVs, particularly those derived from LK and EC compartments, are powerful, noninvasive biomarkers capable of anticipating CAR T-related toxicities before clinical onset. Elevated pre-Lym CD146⁺ LK EVs strongly predicted CRS, whereas rising CD146⁺ EC EVs distinguished patients progressing toward NT. These findings underscore the translational potential of PFC-based EV monitoring as a tool for early risk stratification and personalized management in CAR T recipients. Future analyses will expand EV profiling to include immunologic, inflammatory, and endothelial damage markers.

Disclosure: Nothing to declare

A020

SHORT-TERM POST-TRANSPLANT PROTEOMICS REVEAL TEMPORAL AND DISEASE-SPECIFIC TRAJECTORIES IN MYELOID MALIGNANCIES

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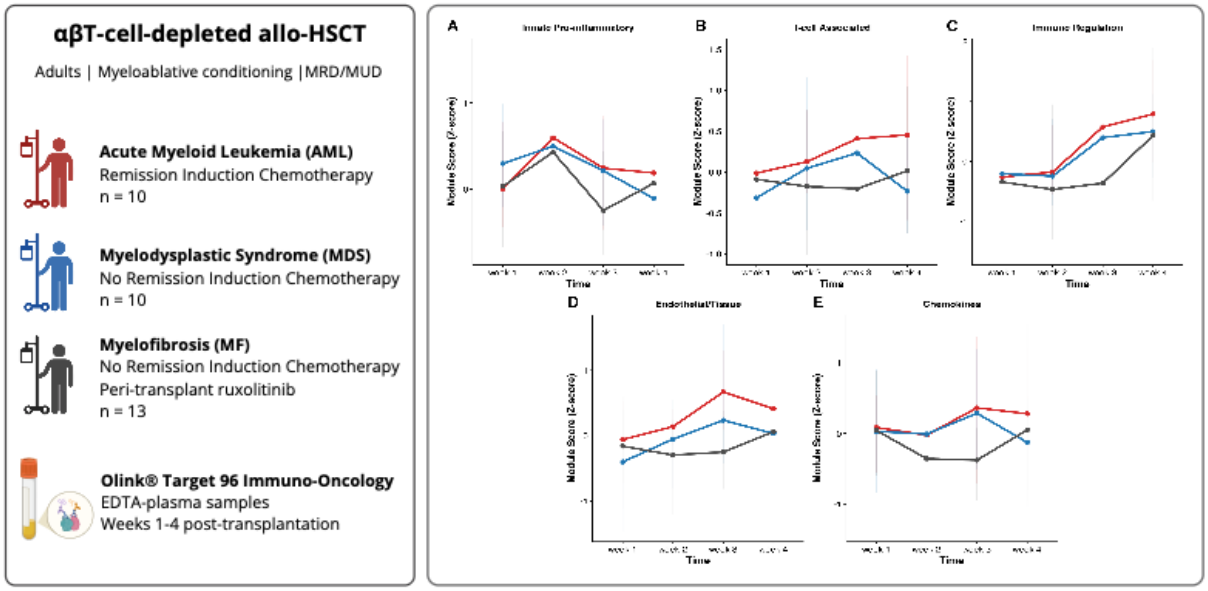
Background: Allogeneic hematopoietic stem cell transplantation is the only curative treatment option for myeloid malignancies. Non-relapse mortality (NRM) remains high in myelodysplastic syndrome (MDS) and myelofibrosis (MF) but is lower in acute myeloid leukemia (AML). Peri-transplant ruxolitinib has been shown to reduce NRM in MF, suggesting that early immune events can be important drivers for later complications. We hypothesize that post-transplant immune dynamics can be initiated already before engraftment and are shaped by disease-specific host conditions. To investigate this, we profiled longitudinal changes in 92 immune-related proteins in patients with AML, MDS, and MF during the first four weeks after allogeneic transplantation.

Methods: We performed a single-center, retrospective analysis, including AML (n =10), MDS (n=10), and MF (n=13) patients who had undergone allogeneic stem cell transplantation. All patients received a myeloablative conditioning regimen and an *ex vivo* αβTCR +/- CD19-depleted allograft. MF patients received 5mg ruxolitinib twice daily from day -5 to day +14. We used the Olink® Target 96 Immuno-Oncology assay to measure 92 immune-related proteins in weekly EDTA-plasma samples (weeks 1-4 post-transplant). Using this method, protein expression was converted into normalized protein expression (NPX) units, expressed on a log2 scale. The data were corrected for batch effects before further analysis. We performed unsupervised analyses to assess global temporal and disease-associated patterns. Subsequently, based on biological function, proteins of interest were grouped into five predefined modules: pro-inflammatory cytokines, T-cell-associated cytokines, immune-regulatory proteins, endothelial/tissue injury-related proteins, and chemokines. For each module, a module score was calculated per sample by aggregating NPX values across proteins within the module (e.g., mean NPX), enabling longitudinal comparison of module trajectories across disease groups.

Results: The time point of sampling explained the largest source of variation in the PCA, suggesting that immune-related protein expression was mostly driven by the time after transplantation. Proteins driving the first principal components included pro-inflammatory cytokines (e.g. IL-6, IL-8), T-cell-associated proteins (e.g. IFN-γ, GZMB, GZMA), immune regulatory proteins (e.g. LAG-3, PD-L1), endothelial-related proteins (e.g. ANGPT1, ANGPT2), and chemokines (e.g. CX3CL1, CCL3). Module scores for these five protein groups highlighted marked time-dependent changes with distinct trajectories per disease group (Figure 1). While cytokine, immune regulation, and chemokine trajectories were similar in AML and MDS during the first three weeks post-transplantation, MDS module scores decreased in week four, diverging from AML. In contrast, module scores for all protein groups were lower in the MF group during weeks two and three but increased after week three.

Short-Term Post-Transplant Proteomics Reveal Temporal and Disease-Specific Trajectories in Myeloid Malignancies



Conclusions: Longitudinal profiling of 92 immune-related proteins indicates that early post-transplant immune dynamics are time-driven but modulated by underlying disease and peri-transplantation interventions. In MF patients treated with peri-transplant ruxolitinib, early module scores were lower but increased after week three, suggesting a transient dampening of the initial immune response. AML and MDS showed similar early trajectories that diverged at later time points. Overall, these results support the use of multiplex protein panels to capture disease-specific immune trajectories, which should be linked to clinical outcomes in future studies.

Disclosure: MdW reports on grant support from KWF (#13493), Leukemiefonds.nl, Oncode accelerator and I&I Boostgrant and Research support from Miltenyi and Novartis. JK reports on patents dealing with gdTCRs and engineering strategies and received research grants from Novartis and Miltenyi Biotech.

A021

IMMUNE PROFILE AND PROTEOME OF PLASMA EXTRACELLULAR VESICLES REVEAL A MYELOID-DRIVEN SIGNATURE ASSOCIATED WITH THE RISK OF RELAPSE AFTER CD19.CAR-T CELL THERAPY

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Background: The therapeutic success obtained with immunotherapies, including chimeric antigen receptor T-cell (CAR-T) therapy, represents the results of many years of research based on the understanding of T-cell biology. However, the complex immunosuppressive tumor microenvironment poses significant challenges to their efficacy. Extracellular vesicles (EVs) have emerged as promising biomarkers in immunotherapy due to their stability in circulation, their ability to reflect the molecular state of their cells of origin, and their suitability for noninvasive liquid biopsy. This strategy aimed to characterize the immune cell subsets, transcriptional and proteomic features associated with clinical response.

Methods: This is a monocenter prospective tissue study conducted on 40 patients receiving AIFA-approved CD19.CAR-T cell products for relapsed/refractory B-cell lymphomas at IRCCS-Azienda Ospedaliero-Universitaria of Bologna. Nineteen patients were in complete response at 1-year after infusion. The others (n=21) had a disease progression during the follow-up. The study was approved by the local Ethical Committee in agreement with the Helsinki Declaration. We used a combining approach integrating multiparametric flow cytometry, single cell-transcriptomic (scRNAseq) analysis and mass spectrometry analysis of EVs. Specifically, we performed:

1. Immune profile on fresh peripheral blood mononuclear cells (PBMCs) before lymphodepletion (PLD) to day+30 after CAR-T cell therapy.
2. scRNAseq on PBMCs at CAR-T cell expansion peak (day+7) and day+90.
3. Proteomic characterization of EVs isolated from plasma by size exclusion chromatography at day+3 after infusion.

Results: Among all cell subsets analyzed, the most striking finding was the abundance of an inflammatory $CD8^+$ T cell subset (defined as $CD45RA^+CD57^+$) and polymorphonuclear (PMN)-MDSC ($CD11b^+CD14^-CD15^+HLA\text{-}DR^{-/low}CD33^+$) at PLD time point in patients who did not respond to treatment compared to those achieving a durable response. Correlation heatmaps revealed a positive association among PMN-MDSC and biochemical parameters. Specifically, PMN-MDSC positively correlated with inflammatory markers including triglycerides, ferritin,

and C-reactive protein. Consistently, the transcriptomic analysis showed an enrichment of myeloid genes attributable to MDSC signature in patients who relapsed immediately or later, in contrast with those who achieved a durable response.
Proteomic analysis of plasma EVs further underscored a clear stratification of the patient cohort according to clinical outcome. Patients achieving a durable response exhibited higher levels of peroxisome proliferation-activated receptor delta (PPARδ), a regulator of myeloid-cell immunosuppressive programs, together with increased expression of the insulin-like growth factors IGF1 and IGF2 and their binding proteins IGFBP3 and IGFBP5, pointing to a role for insulin signaling in mediating clinical benefit. In contrast, non-responders displayed markedly elevated levels of inflammatory markers, including serum amyloid A-4 (SAA4) and Orosomucoid 2 (ORM2).

Conclusions: Our data provides preliminary insights on how the interplay between inflammation, myeloid immunosuppression, and metabolic programs may critically shape clinical outcomes and inform the development of predictive biomarkers and targeted interventions.

Clinical Trial Registry: NCT04892433

Disclosure: PLZ: scientific advisory boards: Secura Bio BIO, Celltrion, Gilead, Janssen-Cilag, BS, Servier, Sandoz, MSD, TG Therap., Takeda, Roche, EUSA Pharma, Kiowa Kirin, Novartis, ADC Therap., Incyte, Beigene; consultancy: EUSA Pharma, MSD, Novartis; speaker's bureau: Celltrion, Gilead, Janssen-Cilag, BMS, Servier, MSD, TG Therap., Takeda, Roche, EUSA Pharma, Kiowa Kirin, Novartis, Incyte, Beigene. FB: scientific advisory boards and speaker fees: NEOVII, NOVARTIS, KITE, GILEAD, PFIZER, CELGENE, MSD. The remaining authors have no conflicts of interest to disclose.
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A023

IMPACT OF CELLULAR COMPOSITION OF LEUKAPHERESIS PRODUCT ON OVERALL NUCLEATED CELL VIABILITY AFTER CRYOPRESERVATION

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Background: According to the recommendations of the European Society for Blood and Marrow Transplantation (EBMT), a key quality parameter of a cryopreserved hematopoietic stem cell (HSC) graft is the overall viability of nucleated cells (NC), which should be ≥70%. However, this integral parameter is comprised of the viability of various cell populations (neutrophils, lymphocytes, monocytes, CD34+ cells), which may have different resistance to cryopreservation.

Methods: We analyzed 75 leukapheresis products. NC viability was assessed by flow cytometry using 7-aminoactinomycin D staining. The cellular composition was determined on a hematology analyzer.

Results: It was established that different cell populations of the leukapheresis product tolerate low-temperature storage differently. Post-thaw viability parameters are presented in Table 1.

Table 1. Viability (%) of cell populations in the leukapheresis product after cryopreservation

Parameter	N	Minimum	Median	Maximum	Mean	Std Dev
NEUTR in product	75	4.00	29.60	72.50	30.74	17.40
MONO in product	75	38.10	88.30	98.30	82.75	15.52
LYMPH in product	75	26.80	86.80	99.00	83.63	13.83
CD34+ in product	75	16.30	90.70	99.50	82.86	19.43

No statistically significant associations were found between the viability of different fractions ($R^2 < 0.34$ for all pairs), indicating independent mechanisms of their cryodamage. A key finding was the direct dependence of the overall NC viability indicator on the initial neutrophil proportion: in containers with NC viability <50%, the initial neutrophil proportion exceeded 60%.

Conclusions:

1. Neutrophils are the population most vulnerable to cryogenic damage in the leukapheresis product; their mean viability does not exceed 31%.
2. The overall NC viability mandated by the EBMT may critically depend on the cellular composition of the graft. A high initial proportion of neutrophils (>60%) may cause the overall viability to fall below the 70% threshold.
3. Thus, assessment of the cellular composition and individual viability of cell populations may provide a more accurate and informative characterization of cryopreserved graft quality compared to using only the integral parameter.

Disclosure: Nothing to declare

A024

THE IMPACT OF INFUSED LYMPHOCYTES SUBSETS ON CLINICAL OUTCOMES IN MUD/HAPLO HCT SETTING WITH CD34+ POSITIVE SELECTION AND COINFUSION OF A CONTROLLED NUMBER OF CD3+

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Background: The most frequent technique used for counterbalance partial incompatible HCT is CD34+ selection, mostly to minimizes GvHD, but his approach could delay immune reconstitution and increase risk of viral and fungal infection. On the other hand, the use of PBSC implies the infusion of a relevant higher number of T cells 5 to 10 times more as compared with Bone Marrow (BM). Since in our centre most part of our patients are primary immunodeficiencies, we applied a procedure to minimize the risk of severe GvHD infusing a controlled number of CD3 positive cells. More recently we have applied this approach also in the haploidentical setting.

Methods: We report on 34 HCT procedures (15 from MUD and 19 Haploidentical donor) in 33 pediatric patients (1 patient received 2 HCT) between 2021 and 2025 in the BMT Unit of the Children's Hospital of Brescia. CD34+ selection has been realized by a Milteny column with an ideal coinfusion of CD3 positive cells of $30x10^6$/Kg. We hypothesized that a different lymphocyte subset distribution in the infused product could have an impact on the incidence of GVHD and analyzed lymphocytes distribution in the infused product in patients who later developed aGVHD grade II-IV (group A) and patient who did not (group B). Mann-Whitney test was used for comparison between groups.

Results: 2-y overall survival was 92.9% for MUD compared with 85.1% for haplo. All HCT engrafted except for 2 cases of primary graft failure (2 patients transplanted for TBD) in the haplo group; these patients were excluded from the analysis on GVHD incidence. 3/15 (20.0%) patients experienced aGVHD grade II-IV in the MUD group in contrast to 5/17 (29.4%) in the haplo group. 1/15 (6.7%) and 2/17 (11.8) developed cGVHD in the MUD and haplo groups, respectively.
The median number of infused CD3+ TCR a/b cells was 27.2*10^6/Kg for the MUD group and 27.5*10^6/Kg for the haplo group. No differences were found in the distribution of lymphocytes subsets in patients who later developed aGVHD grade II-IV. In particular median numbers (*10^6/ Kg R) of infused cells for group A and B were: CD4+ 13.8 vs 17.7 (p 0.34), CD8+ 10.0 VS 9.8 (P 0.30); CD20+ 5.5 vs 6.1 (p 0.72); CD56+CD16+ 1.5 vs 2.1 (p 0.62). No difference was observed in the percentage of CD45RA+ and CD45RO+ (% of infused CD3+) that were 54.3 vs 58.0 and 45.7 vs 42.1 respectively, or in the percentage of γδ T cells (4 vs 2.8).

Conclusions: Our results show that MUD and Haploidentical donor guarantee a similar follow up, with similar control of severity of GvHD, with only few children with limited chronic GvHD. The method allows to graft primary immunodeficiencies patients while limiting the

number of infused CD3+ cells. Moreover, our data, though on a limited number of patients, show that differences in lymphocyte subset distribution on the infused graft do not have an impact on the incidence of GVHD. More extensive analysis are needed to determine the optimal number of CD3+ in different settings of HCT.

Disclosure: Nothing to declare.

A025

RELEVANCE OF HLA-B LEADER DIMORPHISM AND MOLECULAR COMPATIBILITY IN HAPLOIDENTICAL HSCT WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE: EXPERIENCE OF A SPANISH COHORT

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Background: The shortage of fully HLA-matched donors for hematopoietic stem cell transplantation (HSCT) has driven the expansion of alternative donor strategies, notably haploidentical HSCT (haplo-HSCT) using post-transplant cyclophosphamide (PTCy). This approach has significantly improved the feasibility and safety of transplantation by mitigating the detrimental effects of HLA mismatches. However, the immunological criteria for selecting the most suitable donor remain a matter of debate, particularly regarding the contribution of molecular HLA compatibility and the influence of HLA-B leader dimorphism on transplant outcomes.
The present study aimed to evaluate the immunogenic impact of HLA mismatches and the role of HLA-B leader dimorphism in haplo-HSCT with PTCy, focusing on their association with chronic graft-versus-host disease (cGvHD) and graft-versus-host disease–free/relapse-free survival (GRFS).

Methods: A retrospective single-center analysis was conducted on a cohort of 190 patients who underwent haplo-HSCT and their respective donors. High-resolution typing of HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 loci was performed using PCR-SSOP and/or next-generation sequencing (NGS) methodologies. The degree of HLA compatibility was assessed using the Predicted Indirectly Recognizable HLA Epitopes (PIRCHE) algorithm, expressed as the PIRCHE Score (PS). Additionally, HLA-B leader dimorphism and matching were determined through BLEAT and IPD-IMGT/HLA databases.

Results: The median age of the patients was 57 years, with 56% being male. The predominant indications for transplantation were acute myeloid leukemia and myelodysplastic syndromes, accounting for 52% of the cases. The median follow-up period was 36 months.
Receiver Operating Characteristic (ROC) curve analysis demonstrated that patients with a

PIRCHE Score for HLA-B (PS-B) greater than 1 showed a higher incidence of cGvHD (hazard ratio [HR]: 1.81, p = 0.038). A similar trend was observed in cases with HLA-B leader mismatching (HR: 1.69, p = 0.065) and when the TM dimorphism was present in the recipient's HLA-B leader (HR: 2.21, p = 0.021). Both variables remained independent risk factors for cGvHD in multivariate analysis.
Furthermore, patients with a total PIRCHE Score (PS) exceeding 49, as defined by ROC curve cut-off, presented a significantly reduced GRFS (HR: 2.01, p < 0.001). Comparable results were obtained for patients with a hematopoietic cell transplantation-comorbidity index (HCT-CI) ≥ 3 (HR: 1.85, p = 0.004) and for donor–recipient combinations characterized by the HLA-B leader MTM variant (HR: 2.16, p = 0.029). In the multivariate model, both the PIRCHE algorithm–derived score and the HLA-B leader matching status were identified as independent predictors of inferior GRFS.

Conclusions: In conclusion, this study highlights the potential clinical relevance of molecular HLA compatibility parameters in haploidentical HSCT with PTCy. The integration of PIRCHE-based assessments and HLA-B leader dimorphism analysis may enhance donor selection strategies by identifying patients at increased risk of developing cGvHD or experiencing reduced GRFS. These molecular markers could serve as valuable prognostic tools, contributing to more precise immunogenetic matching and improved transplant outcomes in the context of haploidentical transplantation.

Disclosure: NA

A026

GENERATION OF CHIMERIC ANTIGEN RECEPTORS AGAINST MURINE CD123 ALLOWS BIOLOGIC ASSESSMENTS IN IMMUNOLOGICALLY COHERENT IN VIVO SYSTEMS

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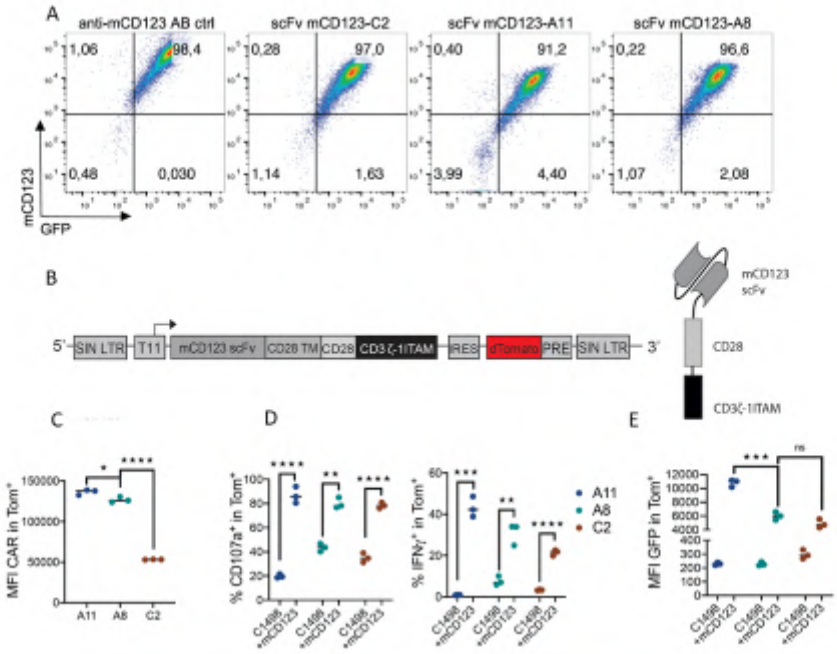
Background: The remarkable early success of CD19-directed CAR T cells in humans reduced the perceived need for detailed mechanistic studies in murine systems. However, emerging limitations now raise critical questions that cannot be adequately addressed in humans or humanized mouse models. To overcome this, we generated CARs targeting murine CD123 (mCD123), an AML-associated antigen, enabling in vivo studies within an immunologically coherent system.

Methods: Antibody selection was performed via phage display. A synthetic murine CD123 peptide, designed from genetic sequence data, was immobilized on high-binding 96-well plates. Additionally, 4 µg of recombinant murine CD123 with a human Fc tag in PBS was

coated onto 96-well plates. Before exposure to the coated wells, HAL9/10 libraries (5×10^{10} phage particles) were preincubated with 4 µg of an unrelated human Fc–tagged protein to deplete Fc-binding phage. The supernatant was then transferred to antigen-coated wells, and bound phage were eluted for subsequent panning rounds. Eluted phage were transferred to 96-deep-well plates for infection, followed by centrifugation and resuspension of the pellets. Three rounds of panning were completed. After the third round, single-clone plates were screened via ELISA. Soluble scFv fragments were produced in 96-well polypropylene MTPs, and supernatants containing monoclonal scFvs were applied to CD123-coated plates. Binding was detected using murine mAb 9E10, which recognizes the C-terminal c-myc tag.

Results: Binders were screened against the murine $CD123^{+}$ myeloid leukemia cell line C1498-mCD123-GFP (Figure 1A). Three candidates—SH1836b-C2, -A11, and -A8—were selected and cloned into a murine second-generation CAR backbone containing a CD28 co-stimulatory domain, a CD3ζ signaling domain, and a single functional ITAM, termed im12328z1 (Figure 1B). CAR expression was regulated by a tetracycline-inducible (Tet-on) T11 promoter and linked to an IRES-driven dTomato (iTom) reporter. Despite sharing an identical backbone, the resulting CARs exhibited distinct functional profiles. im12328z1-A11 showed the highest expression levels (Figure 1C). When stimulated in vitro with mCD123-expressing target cells, im12328z1-A11–transduced murine primary T cells displayed stronger antigen-specific activation compared with SH1836b-C2 and -A8 (Figure 1D). In NFAT reporter cells expressing a GFP-based inducible system, im12328z1-A11 triggered the strongest antigen-dependent response with minimal tonic signaling (Figure 1E). im12328z1-A11 also mediated potent antigen-dependent cytotoxicity against C1498-mCD123 cells in vitro (Figure 2H). In vivo, co-transfer of im12328z1-transduced murine primary T cells rescued syngeneic hematopoietic stem cell recipients from a lethal dose of mCD123-expressing leukemia.

Conclusions: Antigen-display is a powerful approach for generating CARs against non-human antigens with human equivalents, enabling thorough evaluation of their biological properties in vivo. Early identification of limitations or unexpected toxicities in such models may significantly inform and improve the design of future human CAR T-cell trials.



Clinical Trial Registry: Does not apply

Disclosure: Nothing to disclose

A027

THE RATIO THAT MATTERS - HOW CD4:CD8 BALANCE SHAPES CAR T-CELL EFFICACY AND SAFETY

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Background: The growing number of CAR T-cell therapies reported to the EBMT Registry highlights the expanding clinical relevance of this modality. Alongside its therapeutic success, cytokine release syndrome (CRS) remains key treatment-limiting toxicity. Emerging evidence indicates that the CD4:CD8 composition of CAR-T products may influence both therapeutic responses and toxicity profiles. Therefore, we systematically evaluated defined CD4:CD8 CAR-T cell ratios to explore their potential impact on functional behavior and cytokine profiles, as well as the use of new manufacturing technologies that would make such strategy viable in a GMP setting.

Methods: To assess the impact of CD4:CD8 CAR T-cell composition on cytokine secretion, target-cell killing and cytotoxicity profiles, defined CAR T-cell ratios were co-cultured with tumor cell lines. Functional analyses included flow-cytometric characterization of CAR T-cell differentiation, viability and activation profile, as well as multiplex cytokine secretion analyses, and exploratory cytotoxicity in short term cultures. To demonstrate the feasibility in a closed GMP manufacturing workflow, CAR T-cells were generated from PBMCs of healthy donors and subsequently sorted into defined CD4:CD8 ratios using a fully GMP compatible Sony CGX10 Cell Isolation System.

Results: Across CD4:CD8 CAR T-cell ratios ranging from 1:10 to 10:1, no significant differences were observed in CAR T-cell viability or survival after tumor cell contact. In contrast, tumor-cell apoptosis increased in a CD8-dependent manner, with higher proportions of $CD8^+$ CAR T-cells producing correspondingly higher apoptotic indices, and the inverse pattern observed for CD4-enriched ratios. Phenotypic analysis showed that expression of activation (CD25) and exhaustion markers (PD-1, TIM-3, LAG-3) remained comparable across all tested ratios. However, cytokine secretion profiles differed markedly. Increasing the proportion of $CD8^+$ CAR T-cells was associated with elevated secretion of Perforin and Granzyme-B, consistent with FACS data showing enhanced tumor-cell killing in CD8-enriched ratios. Rising proportions of $CD4^+$ CAR T-cells were associated with elevated release of multiple inflammatory cytokines. Finally, clinical scale apheresis products and CAR T-cell products were successfully sorted to defined CD4:CD8 ratios in a closed system utilizing the Sony CGX10, further allowing for the addition of stemness markers in the definition of the sorted cell populations.

Conclusions: Overall, our findings demonstrate that CD4:CD8 CAR T-cell composition is a critical determinant of functional activity and inflammatory potential. CD8-enriched ratios enhanced tumor-cell killing, whereas CD4-enriched ratios markedly amplified cytokine release profiles associated with severe immune toxicities. Although these ratios had minimal impact on CAR T-cell intrinsic phenotype, they shaped effector function and inflammatory output, suggesting that CD4:CD8 composition could serve as a potential parameter to consider when aiming to minimizing CRS-related risks. The Sony CGX10 Cell Isolation System offers a solution that supports translation of this approach while providing fully GMP compliant conditions. Using this setup, additional refinement of CAR T-cell products by definition and isolation of desirable subpopulations (e.g., CAR+, naïve, Tscm, non-exhausted) is feasible and can be explored further at clinical scale.

Disclosure: Tea Gogishvili and Marc-Aurele Brun employees of Sony Biotechnology/Corporation

A028

TRANSFORMING CAR-T ACCESSIBILITY: A PATHWAY TO AFFORDABLE CELL THERAPY FOR B-CELL MALIGNANCIES IN INDIA AND OTHER LMICS

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Background: CAR-T cell therapy has transformed outcomes for relapsed or refractory B-cell malignancies, yet access in low- and middle-income countries (LMICs) remains extremely limited due to high costs, complex manufacturing requirements, and long vein-to-vein timelines. Cartogene Therapeutics aims to address this gap by in-licensing CGT19, a validated CD19 CAR-T construct from Vector BioMed, USA, and establishing a cost-efficient, scalable manufacturing platform in India. CGT19 is a third-generation construct incorporating FMC63 variable regions, CD8 hinge and transmembrane domains, a 4-1BB co-stimulatory domain, and a CD3ζ activation domain, designed to enhance persistence and cytotoxic activity. Preclinical evidence supports its suitability for deployment in resource-constrained regions.

Methods: Vector BioMed conducted in-vitro and in-vivo studies to characterize CGT19. Human T cells were transduced with a lentiviral vector encoding the CGT19 CAR, and assessed for transduction efficiency, vector copy number (VCN), phenotype, and CD19-specific tumor killing. In-vivo antitumor activity was evaluated in CD19-positive xenograft mouse models using serial bioluminescence imaging.
To translate CGT19 into an affordable therapeutic option for India, Cartogene Therapeutics will implement a rapid 7-day manufacturing platform adapted for LMIC settings. T-cell enrichment is performed using a proprietary negative selection method (IsoPure™), followed by Day-0 transduction on the Sepax C-Pro Cell Processing System. Expansion occurs in G-Rex 100M devices to ensure consistent yield with minimal manual handling. Final steps include harvest, wash, formulation, and cryopreservation, with release testing performed for Safety, Purity, Identity, and Potency (SPIP). The process is designed to reduce dependency on complex infrastructure, lower production costs, and support high operational reliability.

Results: In-vitro studies demonstrated high transduction efficiency, generating approximately 70% CAR-expressing T cells with a VCN of ~3. CGT19 exhibited potent CD19-specific cytotoxicity in tumor-killing assays. In xenograft models, CAR-T–treated mice achieved complete tumor clearance, with no detectable bioluminescent signal by Day 55 post-engraftment, confirming strong and durable antitumor activity.
The 7-day manufacturing platform offers major advantages for LMIC application. The substantially shortened production cycle enables a vein-to-vein time up to three-fold faster than many global commercial CAR-T products. Process automation and standardized expansion enhance reproducibility and reduce operator-dependent variability. Importantly, the streamlined workflow enables an estimated throughput of approximately 700 therapies per year, significantly increasing treatment accessibility in India. This high throughput,

combined with a reduced cost base, is expected to support broader patient access while maintaining clinical efficacy comparable to international reference products.

Conclusions: CGT19, supported by strong preclinical activity and a rapid, scalable 7-day manufacturing platform, represents a practical and affordable pathway to expand CAR-T access in India and other LMICs. By integrating a validated CD19 CAR construct with a high-throughput, resource-appropriate production system capable of delivering up to 700 therapies annually, Cartogene Therapeutics aims to reduce the global CAR-T access gap and establish a reproducible model for deploying advanced cell therapies in resource-limited healthcare settings.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

A029

COMPARATIVE IN VITRO EXPANSION OF REGULATORY T CELLS FROM CORD BLOOD AND MOBILIZED PERIPHERAL BLOOD STEM CELLS WITH RAPAMYCIN

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Background: Regulatory T cell (Treg)–based cellular therapies require reliable ex vivo expansion strategies; however, the comparative stability and functional quality of umbilical cord blood–derived (UCB) versus mobilized peripheral blood stem cell–derived Tregs (mPBSC), particularly under rapamycin-based conditions, remain incompletely defined.

Methods: $CD4^+CD25^+$ regulatory T cells were isolated from mobilized peripheral blood stem cells (mPBSC) and umbilical cord blood (CB) units (n=10; 5 mPBSC and 5 CB). Cells were expanded for 14 days with anti-CD3/anti-CD28 stimulation, IL-2 (1000 IU/mL), and with or without rapamycin (100 nM). Expansion rate, purity, viability, and suppressive function were assessed. Phenotypic and stability profiling included CD45RA/RO, FoxP3, CD69, CD27, PD-1, and TIM-3. FOXP3 TSDR methylation was evaluated as a marker of lineage stability. All parameters were compared between sources and culture conditions.

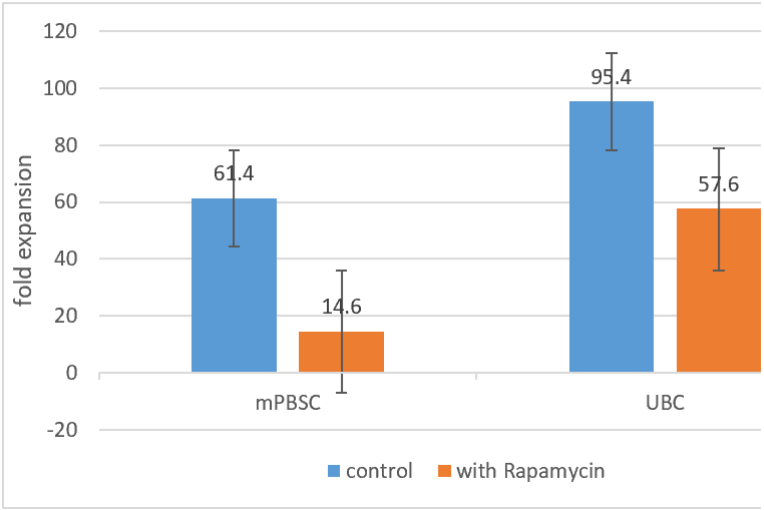
Results: CB-Tregs demonstrated higher post-expansion purity (94.8 ± 0.2% vs. 91.7 ± 0.3%) and significantly greater fold expansion (57.6 ± 19.8-fold vs. 14.6 ± 3.2-fold) compared with mPBSC-Tregs, particularly in the presence of rapamycin (Figure 1). The

characteristics of expanded Tregs derived from umbilical cord blood (CB) and mobilized peripheral blood stem cells (mPBSC) are summarized in Table 1. Cell viability after expansion was comparable between the two sources (98.5 ± 1.0% vs. 98.5 ± 0.6%). Phenotypic analysis showed that CB-Tregs predominantly expressed CD45RA, whereas mPBSC-Tregs exhibited increased CD45RO expression. CD69 expression was lower in CB-Tregs, while CD27 expression was higher compared with mPBSC-Tregs. PD-1 and TIM-3 expression levels were higher in mPBSC-Tregs and reduced in CB-Tregs expanded with rapamycin. Suppression assays demonstrated higher suppressive activity in CB-Tregs compared with mPBSC-Tregs. Analysis of FOXP3 methylation revealed an unmethylated pattern at the analyzed loci in CB-Tregs (n = 5), whereas among mPBSC-derived Treg products, methylation was detected in 2 of 5 samples and was not detected in the remaining 3 samples.

Table 1. Characteristics of Tregs expanded from mPBSC& UCB sources

	MPBSC (MEAN±sd)		UCB (MEAN±sd)	
	control	with Rapa	control	With Rapa
Absolute Treg yields(×103/μl)	6140±4719	1460±320	9540±2037	5760±1980
Fold expansion	61.4±47.1	14.6±3.2	95.4±20.3	57.6±19.8
Purity(%)	88.8±0.5	91.7±0.3	93.7±0.5	94.8±0.2
Viability (%)	98.6 ± 0.5	98.5±1.0	99.2 ± 0.4	98.5±0.6

Figure 1. Fold expansion difference of Treg derived from mPBSC and UBC in the presence and absence of rapamycin



Conclusions: In this study, our findings suggest that CB-Tregs represent a more stable and reliable source for ex vivo expansion, demonstrating superior proliferative capacity, phenotypic preservation, suppressive function, and epigenetic stability compared with mPBSC-Tregs. The reduced stability and function observed in mPBSC-Tregs may be partly influenced by the cytokine-rich inflammatory environment generated during G-CSF mobilization, which can transiently activate peripheral T cells and potentially predispose them to exhaustion or diminished regulatory stability. Together, these observations support the potential superiority of CB-Tregs for future clinical applications, particularly in the prevention of GVHD.

Disclosure: Nothing to declare.

A030

THE INFLUENCE OF LUSPATERCEPT ON BONE MARROW MESENCHYMAL STROMAL CELLS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PATIENTS WITH MYELODYSPLASTIC NEOPLASMS AND ACUTE MYELOID LEUKEMIA

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Background: Myelodysplastic neoplasms (MDS) and acute myeloid leukemia (AML) are the most common indications for allogeneic hematopoietic stem cell transplantation (HSCT) in adult patients. Problems related to poor graft function and rejection are linked to the altered mesenchymal stromal cells (MSCs). Different genes are involved in this process encoding both soluble and cell surface proteins. Secreted factors include key hematopoietic cytokines thrombopoietin (THPO) and stem cell factor (KITLG) along with main stem cell homing chemokine CXCL12. Cell-cell and cell-matrix contacts are highly dependent on adhesion molecules like integrins (ITGB1), cadherins (CDH2), and immunoglobulin superfamily members (VCAM1). The drug luspatercept has demonstrated efficacy for anemia treatment in patients with MDS, affecting also the ability of MSCs to support normal hematopoiesis. It is assumed that these effects could be translated to the post-transplant period.

Methods: The study included 23 patients (11 men and 12 women) with established diagnoses of AML (n=8) and MDS (n=15). The median age was 52 years (19-65). The median time from diagnosis to HSCT was 303 days (73-5342). The median post-HSCT follow-up time was 476 days (79-855). MSCs were isolated from patients' bone marrow at two time points: before HSCT (median 17 days (7-38)) and after HSCT (median 57 days (20-101)). At both time points MSCs were cultured in duplicate: an experimental sample with luspatercept and a control sample without luspatercept. Quantitative PCR was performed to

assess the mRNA expression levels of the genes ITGB1, KITLG, CDH2, VCAM1, THPO, and CXCL12.

Results: When comparing gene expression levels before HSCT, an increase in the expression of ITGB1 ($p<0.02$), KITLG ($p<0.02$), VCAM1 ($p<0.03$), and CXCL12 ($p<0.007$) genes was revealed in the luspatercept group compared to the control. When comparing gene expression levels after HSCT, an increase in the expression of ITGB1 ($p<0.001$), KITLG ($p<0.001$), CDH2 ($p<0.003$), VCAM1 ($p<0.002$), THPO ($p<0.003$), and CXCL12 ($p<0.002$) genes was found in the luspatercept group compared to the control. When comparing control samples from the time points before and after HSCT, the expression level was significantly increased for the ITGB1 ($p<0.002$), KITLG ($p<0.001$), CDH2 ($p<0.02$), and VCAM1 ($p<0.001$) genes post-HSCT compared to pre-HSCT. When comparing samples with luspatercept from the time points before and after HSCT, the expression level was significantly increased for the KITLG gene ($p<0.05$) post-HSCT compared to pre-HSCT. No significant correlation was found between the expression of the studied genes and the time to blood count recovery or the number of transfusions after HSCT. No cases of graft failure were observed, and the incidence of severe poor graft function (the need for red blood cell and/or platelet transfusions after engraftment) was 61% (38-77) at 1 year after HSCT. In univariate proportional hazard model we found no significant association between gene expression levels and overall or progression-free survival.

Conclusions: The obtained in vitro data indicate the ability of luspatercept to enhance the expression of genes responsible for hematopoietic support in bone marrow MSCs of patients with MDS and AML. Further studies are needed to confirm these results and determine the clinical significance of luspatercept use after HSCT.

Disclosure: Authors declare no conflict of interest.
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A032

DEMONSTRATING THE FEASIBILITY OF REFREEZING PREVIOUSLY CRYOPRESERVED BONE MARROW FOLLOWING REPROCESSING

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Background: Cryopreserved cellular therapy products are typically maintained below −140 °C until infusion. However, circumstances may necessitate thawing and refreezing during the product life cycle, including additional testing, removal of cellular debris, adjustment of composition, or further manufacturing steps. The decision to reprocess rather than remanufacture must balance feasibility, cost, source material availability, and potential impact on product quality. Given the widespread perception that repeated freeze–thaw cycles severely reduce cell viability, limited evidence exists to guide the optimization of reprocessing techniques. This study evaluated the feasibility of recovering functional cells from thawed

and re-cryopreserved whole bone marrow (BM) and explored methods to minimize viability loss.

Methods: BM was isolated from vertebral bodies obtained from consented deceased organ donors. White blood cell (WBC) concentration was adjusted to 1.4×10^8 cells/mL. Samples were cryopreserved in 5% dimethyl sulfoxide (DMSO) at 65 mL per 270 mL cryostorage bag, cooled at −1 °C/minute in a −80 °C freezer, and transferred after 12 hours to vapor-phase liquid nitrogen. Thawing was performed using a Barkey Varitherm device, with DMSO dilution achieved using medium containing 2.5% human serum albumin (HSA) and 10 U Benzonase in Plasma-Lyte A. Re-cryopreservation was performed by adding 5% DMSO to the thawing medium, followed by filtration (Fresenius Kabi BM filtration kit), repackaging, passive freezing at −80 °C overnight, and transfer to liquid nitrogen storage.
Cell counts, viability, and colony-forming unit (CFU) assays were obtained before and after reprocessing. Viable $CD34^+$ cell enumeration followed the ISHAGE protocol using a Novocyte flow cytometer (Agilent). A refined thawing method was also tested, in which thawing medium was added gradually (13 mL/min for 5 minutes) to reduce osmotic shock.

Results: Initial evaluation of two cryopreserved BM lots demonstrated that reprocessing did not significantly compromise viability or clonogenicity, provided that the starting $CD34^+$ viability was ≥40% and CFU-GM frequency ≥10 CFU/10^5 WBC. Further testing on BM from three donors confirmed maintenance of functionality. Mean $CD34^+$ viability increased from 87.8 ± 5.6% to 93.2 ± 5.4% ($p = 0.2$), likely reflecting removal of nonviable cells during filtration. CFU frequency declined modestly from 60 ± 29.4 to 51.7 ± 11.8 CFU/10^5 WBC (<30% reduction), indicating preservation of the majority of hematopoietic progenitors. Implementation of the gradual-dilution thawing method further improved post-thaw outcomes. $CD34^+$ viability increased by 6.7 ± 10.1%, and CFU output decreased minimally by 1.1 ± 27.5% ($n = 3$) compared with immediately post-thaw samples, suggesting that HSA, Benzonase, and controlled dilution help mitigate thaw-related stress.

Conclusions: Reprocessing of previously cryopreserved BM is feasible and can be accomplished without substantial loss of cell viability or clonogenic function. Although modest yield reductions were observed, the recovered material retained sufficient functional capacity to justify reprocessing over remanufacture in appropriate cases. This approach offers operational and economic advantages in managing cellular therapy inventories. Ongoing investigations aim to refine thawing and refreezing parameters and to define standardized, validated conditions for safe reprocessing of cryopreserved BM products.

Clinical Trial Registry: NA

Disclosure: Erik Woods- is a paid employee of Ossium Health
Nicholas Weinstein- is a paid employee of Ossium Health
Max Jacobs- is a paid employee of Ossium Health
Sagar Munjal- is a paid employee of Ossium Health
Brian Johnstone is a paid employee of Ossium Health

A033

EXTRACORPOREAL PHOTOPHERESIS FOR DELAYED NEUROTOXICITY SYNDROME AFTER BCMA CAR T-CELL THERAPY

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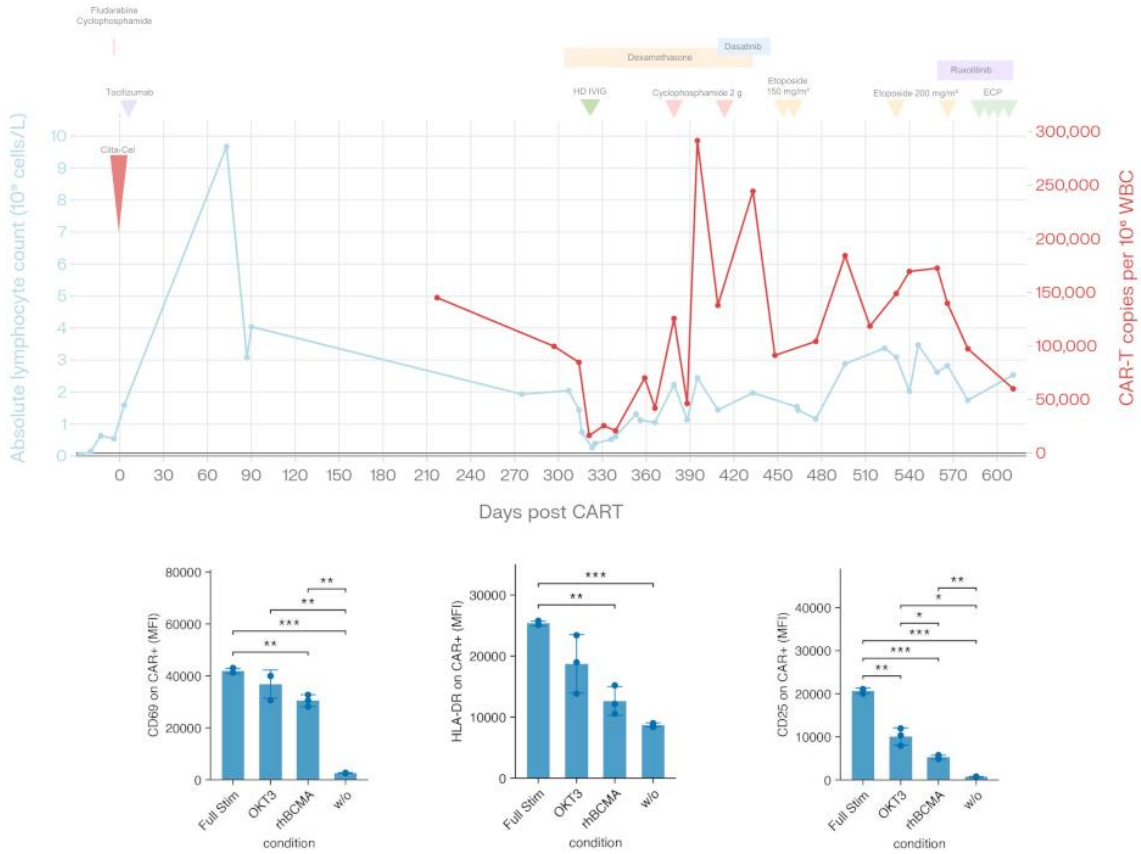
Background: Prolonged hyperexpansion and increased absolute lymphocyte counts after cilta-cel, a BCMA-targeting CAR-T cell (CART) product targeting multiple myeloma (MM) cells, are associated with potentially life-threatening immune-mediated neurotoxicity syndromes including movement and neurocognitive toxicity mimicking parkinsonism. Still, optimal treatment strategies remain undefined. Extracorporeal photopheresis (ECP) is an established treatment modality for graft-versus-host disease, (solid organ) transplant rejection and indolent leukemic T-cell neoplasms but has not been described for the treatment of autologous CART-related diseases.

Methods: We treated a previously neurologically unremarkable 44 yr old male patient with cilta-cel in 4th line for high-risk MM without acute complications despite of CRS °II that was readily controlled with tocilizumab. 3 months after CART infusion he developed an absolute lymphocytosis paralleled by a progressive hypokinetic-dystonic movement disorder with only marginal response to symptomatic pharmacotherapy diagnosed by an expert neurologist. Cranial MRI and CSF sampling with extensive workup showed no signs of infection or malignant disease but mild lymphocytic pleocytosis (12 cells/ul, no qPCR performed). Gradual worsening of neurologic symptoms was accompanied by high CART copy numbers (dPCR) in peripheral blood (pB) which prompted lymphotoxic therapy. However, neither CART hyperexpansion nor the clinical course were durably affected by high-dose steroids, intravenous immunoglobulins, cyclophosphamide, and dasatinib. Repeated therapy with etoposide (150-200 mg/m²) led to a transient decline of CART numbers with consecutive symptomatic improvement but rapid relapse and subsequent refractoriness. Ruxolitinib dosed at up to 20 mg BID did not meaningfully reduce CART copies nor led to relevant symptomatic improvement.
ECP was performed using the Therakos CellEx device according to standard protocols processing 1500 ml of whole blood per session. Methoxysalen (Uvadex) was used as UV radiosensitizer. CART qPCR detecting the lentiviral LTR sequence was multiplexed with RPP30 (housekeeping gene) to normalize cells to 10^6 peripheral blood white blood cells (WBC). qPCR was only available since late 2024. CARTs were detected by fluorochrome-labeled recombinant BCMA in flow cytometry. Short-term CART culture was performed according to published protocols. CARTs were ex vivo stimulated with recombinant BCMA (rhBCMA) or OKT3 as positive control.

Results: Extensive immunophenotyping demonstrated peripheral T-cell lymphocytosis without signs for malignant transformation before initiation of ECP and evidence of activated CART in pB that showed BCMA-specific upregulation of activation markers CD25, CD69 and HLA-DR in vitro, demonstrating inflammatory potential.
Around 20 months after CART infusion, we initiated ECP. Already after 4 sessions the patient

showed an improvement of symptoms and declining CART in pB despite discontinuation of ruxolitinib.
The patient retained complete remission of MM evidenced by ongoing suppression of free light chains and absence of extramedullary disease on PET/CT scan. He continues to receive ECP and extended follow up will be presented at the meeting.
Therapeutic interventions, CART copies and absolute lymphocyte counts and in vitro stimulation assay pre ECP are depicted in Fig. 1.



Conclusions: This preliminary data indicates that ECP might represent a promising therapeutic approach for toxicities related to hyperexpanding CARTs irresponsive to extensive lymphotoxic therapies.

Disclosure: Nothing to declare.

A034

SINGLE-CELL MAPPING PORTRAYS THE LINEAGE SPECTRUM OF EPSTEIN-BARR VIRUS INFECTION AND UNVEILS CLINICAL IMPLICATIONS OF CD70 IN PATIENTS WITH PTLD

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Background: Epstein-Barr virus (EBV)-related post-transplant lymphoproliferative disorder (EBV$^+$ PTLD) is a life-threatening complication that can occur as a result of immunosuppression after hematopoietic stem cell transplantation (HSCT). The remaining unclear pathogenesis and limited treatment options of EBV$^+$ PTLD result in the poor prognosis.

Methods: Bulk and single-cell RNA sequencing (scRNA-seq) were performed on bone marrow and peripheral cells derived from patients with EBV$^+$ PTLD and matched transplant donors. The expression of EBV genes and host genes was analyzed simultaneously by constructing a hybrid reference genome of EBV and human. The quantitative real-time polymerase chain reaction (qRT-PCR) method was employed to verify the differently expressed genes in PTLD.

Results: The bulk transcriptome analysis revealed the expression characteristics of EBV$^+$ PTLD patients, including the over-expressed CD70, uncontrolled proliferation, impaired apoptosis, activated innate immunity and suppressed adaptive immunity, and enhanced T-cell exhaustion. scRNA-seq analysis exhibited a comprehensive cell atlas of EBV$^+$ PTLD, and unveiled the broad EBV infection involving in the full spectrum of the hematopoietic system, even for the hematopoietic stem cells of the patients with PTLD. Further analysis confirmed the latency III/lytic expression program of EBV genes in patients with high infection burden, rather, latent type I/II in patients with low EBV infection. The overwhelming majority of infected B cells were derived from memory B cells, and presented universal and abnormal differentiation patterns, especially for the irregular generation of immunoglobulin antibody isotypes. Moreover, EBV-infected T cells showed significantly inhibited T cell receptors signal, reduced IL2 secretion capacity, and elevated T-cell exhaustion. The re-clustering analysis of B cells, T cells, natural killer cells, and myeloid cells uncovered the heterogeneous cell subpopulations, among which the most highly infected exhausted B cells were likely contributed to treatment evasion. The specifically over-expressed CD70 was recurrently proved by scRNA-seq data and qRT-PCR experiment in EBV$^+$ PTLD patients, illustrating its clinical implications as a biomarker for the diagnosis and immunotherapy in EBV$^+$ PTLD patients.

Conclusions: Collectively, scRNA-seq of EBV$^+$ PTLD provides valuable insights into the lineage distribution and latency programs of EBV infection and offers important candidate solutions for the diagnosis and targeted treatment in the future.

Disclosure: Nothing to declare.

A036

DECIPHERING THE HDAC6-MEDIATED REGULATION OF MLLT3 IN MYELOID PROGENITOR CELL FATE: INSIGHTS INTO STEM CELL DIFFERENTIATION DYNAMICS

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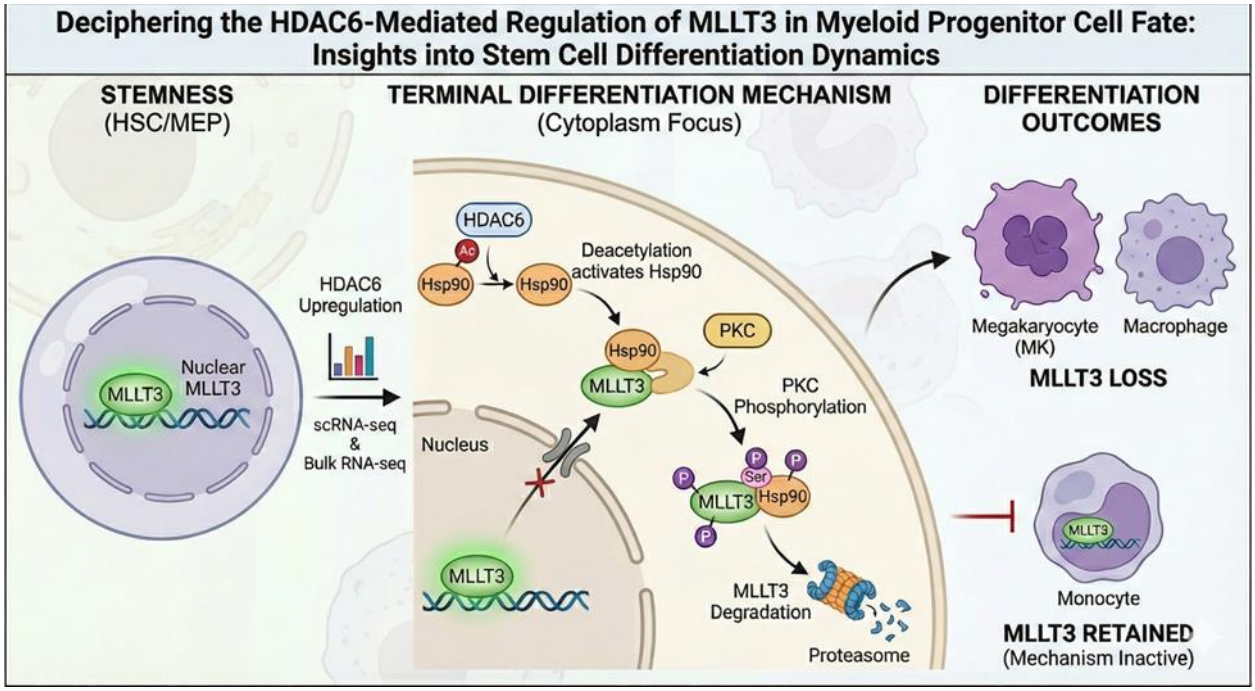
Background: Mixed-lineage leukemia translocated to 3 (MLLT3) is a critical factor in maintaining the stemness of hematopoietic stem cells. While it is established that the loss of MLLT3 in megakaryocyte-erythrocyte progenitor (MEP) cells drives differentiation into megakaryocytes (MKs), the specific regulatory mechanisms that govern MLLT3 during this differentiation process have remained unclear.

Methods: To address this gap, this study utilized single-cell data and bulk RNA sequencing, complemented by FACS, qPCR, and Western blot analyses, to investigate the molecular drivers of terminal differentiation. The research focused on the capacity of histone deacetylase 6 (HDAC6) to modulate MLLT3 levels via Heat Shock Protein 90 (Hsp90) activation during myeloid lineage differentiation into MKs, monocytes, and macrophages.

Results: The study demonstrated that HDAC6 plays a pivotal role by deacetylating and activating Hsp90. This activation enables Hsp90 to retain MLLT3 in the cytoplasm. Subsequently, Protein Kinase C (PKC) phosphorylates MLLT3 at serine residues, leading to the loss of MLLT3. Notably, this specific mechanism was observed during the differentiation of MKs and macrophages but was absent during monocyte differentiation.

Conclusions: Supported by transcriptomic evidence, these findings elucidate the regulatory mechanisms underlying myeloid lineage commitment. By identifying the interplay between HDAC6, Hsp90, and PKC in regulating MLLT3, this study offers valuable insights into stem cell biology and opens new avenues for future therapeutic applications.



Graphical Abstract Legend

Disclosure: Nothing to declare.

P001

PATENTING CORD BLOOD CELLS: AN HISTORICAL PERSPECTIVE

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Background: Haematopoietic stem cell transplantation (HSCT) has undergone rapid and remarkable development over the past 75 years. Since the first cord blood HSCT was performed in 1988 at Saint-Louis Hospital in Paris by a French-American team on a child with Fanconi Anemia, cord blood has been widely used as a source of haematopoietic stem cells for transplant. However, in 1996 the biotechnology company Biocyte Corporation submitted a patent application to the European Patent Office (EPO) for the storage and use of cord blood for allogeneic transplants, gene therapy and clinical and research purposes. Fearing that the patent would increase the cost of transplants worldwide and limit the future use of cord blood, a prompt and strong opposition against the patent application raised from the scientific community, including Eurocord, Netcord, EBMT and the International Society for Cellular Therapy as well as from the wide academic world.

Methods: The president of Eurocord (EG), along with companies such as Thermogenesis and Astra Medica, filled an appeal against Biocyte Corporation with the European Patent Office (EPO) in Munich. The arguments against the patent were as follows : 1) commercial exploitation of parts of the human body ; 2) violation of the principle of free and anonymous donation ; 3) granting of monopolistic power to a single company ; 4) delay to cord blood research resulting from the payment of royalties ; and 5) lack of novelty.

Results: In 1999, the EPO accepted the argument concerning the lack of novelty as grounds for revoking Biocyte Corporation's patent. Previous studies, such as the 1983 study from Koike Kenichi on the viability of haematopoietic stem cells from cord blood and the 1985 Spanish thesis by Juan Besalduch Vidal, had shown that cord blood contains sufficient stem cells for non-HLA-identical transplants so that it can be stored in public cord blood banks and thawed for clinical use.

Conclusions: 1) Thanks to opposition from the scientific Community and work carried out prior to Biocyte Corporation's patent application, transplant centres, cord blood banks, and researchers around the world are not required to pay royalties to a company since unprocessed cord blood cannot be patented, in the same way as bone marrow or peripheral blood stem cells for transplant ; 2) it is a matter of discussion that on a strictly legal level, only the principle of scientific novelty and not an ethical principle, has been recognized as valid for the purposes of recognizing a patent even in the case of use of human biological material for therapeutic purposes. The public donation of stem cells from cord blood, bone marrow and peripheral blood should be supported and warranted worldwide.

Disclosure: Nothing to declare

P002

ALTERED PRE-TRANSPLANT GUT MICROBIOTA PROFILES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: TOWARD MICROBIOTA-INFORMED RISK STRATIFICATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative strategy for hematologic malignancies; however, transplant-related complications remain a significant determinant of outcome. The intestinal microbiota has emerged as an essential regulator of mucosal integrity and immune responses relevant to allo-HSCT. Patients with hematologic malignancies frequently enter transplantation with a markedly altered gut microbiota due to prior chemotherapy, recurrent antibiotic exposure, and disease-related factors, resulting in reduced microbial diversity and shifts in community structure. Such pre-transplant dysbiosis may predispose to adverse post-transplant outcomes,

including infectious complications, graft-versus-host disease (GVHD), and non-relapse mortality.
This study aimed to characterize alterations in gut microbiota composition and alpha diversity in patients before allo-HSCT compared to healthy controls, and to explore the relationship between pre-transplant therapeutic exposures and early post-transplant outcomes.

Methods: This prospective, observational study included adult patients with hematologic malignancies undergoing allo-HSCT at the Fundeni Clinical Institute. Fecal samples were collected from 56 patients before the initiation of conditioning therapy and from 27 healthy donors serving as controls. Microbial DNA was extracted from stool samples, and the V4–V5 hypervariable regions of the bacterial 16S rRNA gene were amplified by polymerase chain reaction (PCR) and sequenced on an Illumina platform. Bioinformatic processing was performed using QIIME 2, including demultiplexing, denoising with DADA2, and generation of amplicon sequence variant (ASV) tables. Wilcoxon rank-sum tests were used to compare alpha diversity between patients and controls. Beta diversity was assessed using Bray–Curtis dissimilarity, and Principal Coordinate Analysis was performed to explore clustering patterns. Baseline microbiota features were analyzed in relation to early post-transplant outcomes, with follow-up extending to day +100.

Results: The cohort comprised 56 adult patients undergoing allo-HSCT, with a median age of 42.4 years (IQR 17.2); 59.6% were male, and acute myeloid leukemia was the most frequent indication for transplantation (56.1%). Most patients had good performance status (ECOG 0–1 in 96.4%) and low-to-intermediate transplant risk (HCT-CI 0–2 in 92.9%). Before allo-HSCT and baseline stool sample collection, patients were heavily pretreated: 71.9% received cytotoxic chemotherapy, 35.1% immunotherapy, 31.6% hypomethylating agents, 19.3% venetoclax, and 12.3% monoclonal antibodies. Additionally, 54.4% were exposed to systemic antibiotics before transplantation, most commonly beta-lactams (35.1%), followed by aminoglycosides and anti-staphylococcal agents (24.6%). At baseline, patients exhibited significantly lower gut microbiota alpha diversity than healthy donors, as assessed by the Shannon index. Beta-diversity analysis demonstrated distinct clustering of patient and control samples on principal coordinate analysis, indicating substantial differences in microbial community structure.

Conclusions: Adult patients undergoing allo-HSCT present with a profoundly altered gut microbiota already before transplantation, likely reflecting extensive prior exposure to chemotherapy and antibiotics. These findings are consistent with previously published data and reinforce existing evidence that reduced baseline gut microbiota diversity may influence early post-transplant outcomes. Together, these observations support the rationale for microbiota-informed risk stratification and interventional strategies in allo-HSCT. Further prospective and longitudinal studies in larger cohorts are warranted better to define the clinical relevance of pre-transplant microbiota alterations.

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Operational and Development of the National Center of Competence in the field of Cancer", contract no. 760009/30.12.2022, code CF 14/16.11.2022.

P003

THE ROLE OF SALVAGE ALLOGENEIC HEMATOPOIETIC STEMM CELL TRANSPLANTATION FOR RELAPSED OR REFRACTORY AML IN NON REMISSION: INSIGHTS FROM REAL-WORLD EXPERIENCE

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Background: Relapsed and refractory (R/R) acute myeloid leukemia (AML) represents a significant therapeutic challenge, with limited treatment options and poor survival outcomes. While salvage allogeneic hematopoietic stem cell transplantation (allo HSCT) remains the only curative strategy with potential efficacy for these patients, its application in patients who fail to achieve complete remission (CR) before transplantation remains controversial due to historically poor survival rates. To date, there is no consensus on how to optimize transplantation strategies for this high-risk cohort, necessitating urgent real-world evidence to guide clinical practice.

Methods: This retrospective study analyzed 120 R/R AML patients who underwent allo-HSCT in non-CR status at Seoul National University Hospital between 2005 and 2024. Overall survival (OS) was estimated using the Kaplan–Meier method, while relapse and non-relapse mortality (NRM) were assessed within a competing-risks framework. Prognostic factors were analyzed using univariate and multivariate Cox regression models.

Results: The median OS was 5.2 months, with a 3-year OS probability of 23%. At three years, the cumulative incidence of relapse was 45.7%, while NRM reached 51.1%. In multivariable analysis, several variables retained independent associations with poorer survival, including age ≥ 50 years (HR 2.90, 95% CI 1.59–5.29; P = 0.001), adverse cytogenetics (HR 2.39, 95% CI 1.46–3.91; P = 0.001), and a bone marrow blast count ≥ 20% at the time of transplantation (HR 1.86, 95% CI 1.15–3.02; P = 0.012). Patients receiving grafts from matched unrelated donors or 1–2 antigen–mismatched unrelated donors experienced higher mortality compared with those transplanted from matched sibling donors. Among post-transplant complications, severe acute graft-versus host disease (GVHD) was associated with markedly inferior survival, whereas chronic GVHD did not significantly affect OS.

Conclusions: Salvage allo-HSCT in non-CR R/R AML shows substantial variability in outcomes, highlighting the importance of careful patient and donor selection, particularly regarding age, cytogenetic risk, disease burden, and donor type. Severe aGVHD was clearly associated with markedly worse survival. These findings highlight the need for individualized donor choice and early control of aGVHD to improve outcomes in this high-risk group.

Disclosure: All authors declare that there are no actual or potential conflicts of interest related to this manuscript.

P004

PERSONALIZED THERAPY GUIDED BY EX VIVO DRUG RESPONSE PROFILING ENABLES ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN RELAPSED/REFRACTORY ACUTE LEUKEMIA WITH IMMATURE PHENOTYPE

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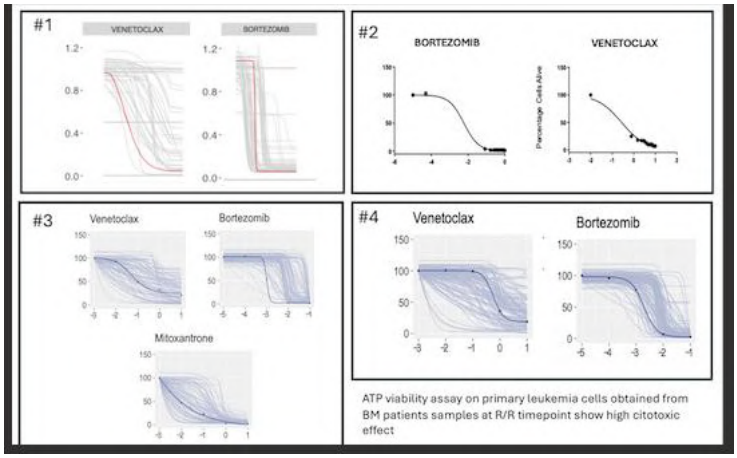
Background: Disease status at the time of allogenic bone marrow transplantation (HSCT) significantly influences the outcome in high risk acute leukemia, with patients achieving complete remission pre HSCT demonstrating superior overall survival and reduced relapse rates compared to those with active disease. However, a substantial proportion of patients with highly refractory or relapsed (R/R) leukemia fail to achieve adequate disease control with conventional therapies, precluding them from proceeding to potentially curative transplantation. Therefore, identifying effective bridging strategies that can successfully reduce disease burden in relapsed/refractory (R/R) patients is crucial to expand transplant eligibility and offer this therapeutic option to a major proportion of patients . In this context an alternative strategy is to develop individualized approaches assessing susceptibility of leukemic cells to specific small molecules by performing ex vivo drug response profiling (DRP). DRP can be performed within an actionable timeframe and could predict in vivo response, leading to a personalized therapy and bridging to transplant.

Methods: We report a case series of 4 patients with R/R AL. Patient characteristics are summarized in Table 1. Treatment regimens were selected based on ex vivo drug sensitivity profiles: three patients received venetoclax plus bortezomib (VEBO), while one patient (pt#3) received VEBO plus mitoxantrone.



At the time of transplantation, two patients (pt#2 and pt#4) had achieved complete remission (CR); notably, one of these patients (pt#2) had previously undergone allogeneic HSCT. The remaining two patients demonstrated significant reduction in disease burden prior to transplantation. All patients received a myeloablative conditioning regimen, two of them Total Body Irradiation based (pt#1 and pt#3). One patient had a matched unrelated donor, three an haploidentical donor. The choice of T depleted o repleted haploidentical transplantation was guided by patient condition, disease status and HCT-CI at time of transplantation.

PT	age	diagnosis	CI-FISH	gene mutations	prior lines of therapy	disease status at DRP	DRP oriented therapy	disease status at HSCT	HSCT
#1	27	near ETP ALL	DDX3X-MLLT10	NOTCH1, JAK3, NRAS, SUZ12, PHF6, MED12	HyperCVAD, LAL0904	refractory	VEN800-Bortezomib	PR	MAC-MUD
#2	36	AUL	PICALM-MLLT10	FLT3 ITD	HyperCVAD,FLAI, HSCT (sibling)	relapse	VEN800-Bortezomib	CR	MAC-Haplo PTCy
#3	59	T-ALL (cortical) + ETP	trisomy 21, TRADrearrangement	/	LAL1913 (4 cycles)	relapse	VEN400-Bortezomib-Mitoxantrone	PR	MAC-Haplo abTCD

#4	37	near ETP ALL	PICALM-MLLT10, MECOM, monosomy7, ETV6-CDKN1B del, TRAD-NKX2	NOTCH1, RUNX1, SUX12, WT1, PTPN11	LAL1913 (9 cycles+maintenance)	relapse	VEN800-Bortezomib	CR	MAC-Haplo PTCy

Results: All four patients proceeded to allogeneic HSCT following two cycles of DRP-guided therapy. Patient #1 experienced fatal veno-occlusive disease (VOD) during the engraftment period of his second allogenic transplantation. Patient #2 maintained Complete response (CR) for 12 months post-transplant. Patient #3 experienced disease relapse at 6 months post-HSCT. Patient #4 remains in ongoing CR at 3 years post-transplantation.

Conclusions: Although limited to a small patient cohort, ex vivo drug screening platform successfully guided therapeutic option in R/R AL patients, with very high risk phenotype enabling successful bridging to allogeneic transplantation significantly reducing disease burden.

Disclosure: Nothing to declare.

P005

RETHINKING CONTAMINATION CONTROLS IN CHIMERISM TESTING: THE CASE AGAINST NTCS

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Background: Modern next-generation sequencing (NGS)-based molecular assays offer a rich array of metrics and informatics tools to monitor assay performance. These advancements challenge the necessity of traditional quality control concept such as no-template controls (NTCs) and their application. In our laboratory's validation and clinical use of the CareDx AlloSeq HCT assay for chimerism monitoring, we evaluated the effectiveness of replacing NTCs with single-genome controls and contrived samples.
NTCs are conventionally used to detect contamination. However, in the context of chimerism testing, they frequently fail to generate sufficient read depth due to the absence of input material. This failure renders them uninformative, as any contamination present is unlikely to reach the detection threshold. A failed NTC result does not confirm assay integrity; it simply provides no usable data. In contrast, single-genome controls and sensitivity mixtures offer robust, interpretable metrics that can actively monitor assay performance and detect contamination.

Methods: We conducted twelve validation runs, nearly 200 clinical runs, and four additional study runs using single-genome controls and contrived mixtures. These included samples intentionally contaminated with bleach (a commonly used surface disinfectant and

decontaminant, but also a powerful PCR inhibitor) and unanticipated contributors. In each case, we recorded contributor proportions, software-detected genotype errors, and key assay metrics such as cluster density and read depth.

Results: Initial assessments revealed that including an NTC reduced read depth by approximately 30% across all batched samples compared to runs using single-genome contamination controls, probably due to the massice creation of non-specific products of amplification). Because the AlloSeq HCT software relies on defined donor and recipient genotypes, the detection of unexpected alleles serves as a reliable indicator of contamination. To test this, we spiked wipe samples from bleach-dampened and DNA-contaminated surfaces into single-genome controls. These samples either flagged errors for unanticipated genotypes or showed degraded performance, validating the sensitivity of this approach.

Conclusions: Over hundreds of runs, our contrived sensitivity controls have consistently enabled robust performance monitoring. The informatics systems in place are sufficiently sensitive to detect contamination and deviations in assay setup, eliminating the need for legacy NTCs and potentially redundant wipe tests. These findings support a streamlined, data-driven approach to quality control in chimerism testing, improving both assay reliability and operational efficiency.

Disclosure: Thierry Viard and Narin Tangprasertchai are CareDx employees and Stock holders.

P006

TRACKING BACK INNOVATION IN DIFFERENT CLASSES OF NEWLY-DEVELOPED MEDICINAL PRODUCTS THROUGH THE LINKAGE BETWEEN NOBEL AND GALIEN PRIZES SUPPORTS A SPECIFIC STATUS FOR ADVANCED THERAPIES

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Background: Advanced therapies – Advanced Therapy Medicinal Products or ATMPs as per EC Regulation 1394/2007 – are different in many aspects from other classes of medicinal products, whether chemically synthesized or manufactured through a biological process. By adopting a 'lex specialis' for ATMPs, the European Union has acknowledged the specificity of ATMPs, especially on the basis of the innovative dimension of their manufacturing process and of their interest for public health and economics. However, one can wonder about the origin and recognition of their innovativeness while innovation is a notion contingent to its context of use and ATMPs are facing several commercialization failures, although denoting that innovation does not always equal adoption..

Methods: In this study, we attempted to grade the levels of innovation that characterize different categories of medicinal products that were brought to the market over the last four decades.
As a proxy to the flow from "discovery" to "innovation", we have listed Nobel prizes in Physiology or Medicine or Nobel prizes in Biochemistry from 1920 on one hand, and Galien prizes awarded to innovations based on biological elements (biomedical innovations) on the other hand, and searched for links between the two categories of awards.
We subset the biomedical innovations that were most frequently awarded a Galien prize into three groups: "products of recombinant DNA technology", "products of antibody engineering" and "advanced therapies" (ATMPs).

Results: First, our study highlights that one Nobel prize can lead to several biomedical innovations.
Second, it is quite remarkable that the vast majority of Galien prizes has been awarded to biological medicinal products (biologicals).
Third, the links between Nobel prizes and Galien prizes are not homogenous among the three groups targeted in our analysis, showing difference in the recognition of innovation.
From 1999 onwards, "Products of antibody engineering" have received many Galien prizes – many of them in recent years - stemming from a quite low number of Nobel prizes. It continues to produce significant impacts in several medical fields.
"Products of recombinant DNA technology" have also received an important although smaller number of Galien Prizes; overall, these were awarded in an earlier period starting in 1987.
In 2017, a Gallien prize was awarded for the first time to an ATMP. In total, ATMPs have been awarded a smaller number of Galien prizes. However, their design and development can be tracked back to a higher number of Nobel prizes in physiology or chemistry, some of them that were awarded recently.

Conclusions: Our analysis suggests that the rapid incorporation of a combination of breakthrough technologies based on several scientific discoveries recognized by Nobel prizes is key to their development and manufacturing, supporting their recognition and regulation as a distinct class of therapeutics.

Clinical Trial Registry: N.A.

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P007

HARVESTING CD3 POSITIVE LYMPHOCYTES IN PEDIATRIC PATIENTS FOR CAR-T CELL MANUFACTURING

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Background: CD3+ are the targets for Leukapheresis in patients undergoing CAR-T cell therapy. We here report our inhouse experience to harvest T-cells form pediatric and adolescent patients with the AMICUS™ device.

Methods: We reviewed retrospectively the patients charts for the patients data and apheresis settings and results of the products harvested. All products were manufactured by Novartis Company (Kymriah™). Every patients and/or their relatives give written informed consent for the harvesting procedure, the treatment with CAR-T cells and the use of the data setting. We calculated the collection efficiency (CE) for Lymphocytes , Granulocytes, Monocytes, Erythrocytes and Thrombocytes taken blood smear immediately before and after the procedure. Products were than cryopreserved and shipped to Novartis facilities for CAR-T cell manufactoring. The specification form the manufacturer for the T-cell yield was 1 10^{09} cells in the product. (SD 1500 l

Results: From July 2016 to June 2025 we performed 23 procedures in 23 patients (14 male 9 female; median age 11.6y min 1.2 - max 19.4y; median bw 35 kg, min 10 - max 87 kg) with B-cell leukemias (n=22), Burkitt-Lymphoma (n=1). The setting of the AMICUS device in median 6 cycles with 1250 ml cycle volume, ACD-A ratio 1:12, MNC setpoint 0.6, RBC setpoint 6.8, MNC setpoint 1.5 - 2.3, PPP flush 10 ml. Due to the CD3+ cell count we managed the whole blood to be processed. In median 8737 ml (SD 1500 ml) whole blood were processed, corresponding to 240 ml (SD 25 ml) whole blood /kg bw, with a median CD3+ cell count before the procedure of 1250 cell/µl (SD 350cells/µl). For the CD3+ cells we calculated a CE of 55.3%, total Lymphocytes 55,2%, Monocytes 41.3%, Granulocytes 3.5%, Thrombocytes 19.4%, MNC 53.2%. In all patients we had a sufficient yield of more than 1x10^{09} CD3+ cells in the product, with one exeption. In one case it was 0.92x10^{09}. No side effects were noted in the patients during or after the procedure. Venous acces was central venous access only (n=11) and peripheral access only (n=4) or a combination of PVC and CVC. The content of Erythrocytes in the product is in median 8.5% (3.7 - 15%). With this preliminary data we now calculate the minimum whole blood to be processed by the formular: (1000.000.000 CD3+ cells/CD3+ cell count/ml)* (CE(=0.5)) = whole blood to processed.
One product could not be manufactured due to HCV positivity in the IDM at harvest, 2 products has not fullfilled the quality criteria after manufacturing.

Conclusions: We conclude, that Lymphcyte apheresis performed with the AMICUS device is feasable and results in good standard products for manufacturing CAR-T cells.

Disclosure: No conflict of interest.

Transplant and Cellular Therapies - Clinical

GS2-5

DURABLE CLINICAL BENEFITS WITH EXAGAMGLOGENE AUTOTEMCEL FOR GREATER THAN 6 YEARS OF FOLLOW-UP IN TRANSFUSION-DEPENDENT THALASSEMIA AND SICKLE CELL DISEASE WITH RECURRENT VASO-OCCLUSIVE CRISES

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Background: Exagamglogene autotemcel (exa-cel) is a one-time, *ex vivo* CRISPR/Cas9 gene-edited, autologous cell therapy approved for patients ≥12 years (y) old with transfusion-dependent β-thalassemia (TDT) or sickle cell disease (SCD) with recurrent vaso-occlusive crises (VOCs). We report long-term efficacy and safety from the phase 3 CLIMB THAL-111, CLIMB SCD-121, and CLIMB-131 trials.

Methods: CLIMB-111 (TDT) and CLIMB-121 (SCD) are 2-year, phase 3 studies of exa-cel in participants aged 12-35y. Participants then enroll in CLIMB-131 for up to 13 y follow-up. The CLIMB-111 primary endpoint is transfusion independence: proportion of participants maintaining a weighted average hemoglobin ≥9 g/dL without RBC transfusion for ≥12 consecutive months (TI12). The CLIMB-121 primary endpoint is the proportion of participants free of severe VOCs for ≥12 consecutive months (VF12); the key secondary endpoint is the proportion of participants free from inpatient hospitalization for severe VOCs for ≥12 consecutive months (HF12). As an ad hoc analysis, the overall survival (OS) rate (proportion who survived death from any cause) and event-free survival (EFS) rate as typically defined for allogeneic bone marrow transplant (proportion who survived death from any cause, graft-versus-host-disease [GVHD], or graft failure, whichever occurred earliest) were evaluated. Data are from July 20, 2025; final CLIMB-121 results are presented.

Results: In CLIMB-111, 56 participants (mean age: 21.2y) received exa-cel; median follow-up was 49.6 (19.4,78.6) months. All participants were evaluable for TI12; 98.2% (55/56) achieved TI12 in CLIMB-111/CLIMB-131. After exa-cel, all participants engrafted neutrophils and platelets at a median of 29 (12,56) days and 43.5 (20,200) days, respectively. As of July 2025, 69.6% (39/56) of CLIMB-111/CLIMB-131 participants had discontinued iron removal therapy (IRT) for ≥6 months with levels of serum ferritin, liver iron content, and T2* cardiac iron content generally stable with no increase over time post-IRT discontinuation.
In CLIMB-121, 46 participants (mean age: 21.4y) received exa-cel; median follow-up was 44.7 (8.9,73.7) months. Of 45 participants evaluable for VF12/HF12, 100% (45/45) achieved VF12 and HF12 in CLIMB-121/CLIMB-131. After exa-cel, all participants engrafted neutrophils and platelets at a median of 27 (15,40) and 34.5 (23,126) days, respectively. In SCD participants, clinically meaningful improvements in hemolysis markers (lactate dehydrogenase, haptoglobin, reticulocyte count, indirect bilirubin) were observed compared to baseline and were maintained over time.
In TDT and SCD, durable increases in total and fetal hemoglobin were observed. Allelic editing was stable over time in both bone marrow and peripheral blood. OS and EFS rates at 2 years were the same: 100% for TDT and 97.8% for SCD (1 death due to COVID-19, previously reported; individual was not immunized against SARS-CoV-2). There were no events of GVHD or graft failure in any participant.
Exa-cel safety profile was consistent with myeloablative conditioning and autologous transplant in both TDT and SCD. There were no malignancies through follow-up in CLIMB-131.

Conclusions: Exa-cel demonstrated durable clinical benefits for >6 years of follow-up in TDT and SCD participants. The safety profile was consistent with busulfan myeloablative conditioning and autologous transplant; there were no malignancies. These data continue to support exa-cel as a one-time functional cure for TDT and SCD.

Clinical Trial Registry: NCT03745287, NCT03655678, NCT04208529

Disclosure: Franco Locatelli: advisory board for Amgen, Neovii, Novartis, Sanofi, Vertex Pharmaceuticals Incorporated; speaker's bureau for Amgen, Bluebird Bio, Gilead, Jazz Pharmaceuticals, Medac, Miltenyi, Neovii, Novartis, SOBI
Haydar Frangoul: received consulting fees from Vertex, Editas Medicine, BioLineRx and Rocket Pharma; honoraria from Jazz Pharmaceuticals; advisory fees from Rocket

Pharmaceuticals; served in a leadership or fiduciary position for Vertex
Akshay Sharma, Selim Corbacioglu, Mattia Algeri: advisory board member for Vertex
Roland Meisel: received consulting fees from Vertex
Josu de la Fuente: advisory board member for Vertex, Sanofi, MAAT Pharma, Sangamo; received honoraria from Vertex
Markus Mapara: received consulting fees from Bluebird Bio, CRISPR Therapeutics, Incyte Corporation, Ossium Health; advisory board member for Bluebird Bio, CRISPR Therapeutics, Incyte Corporation.
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Ben Carpenter: advisory board member for Vertex; received honoraria from Bluebird Bio
Janet Kwiatkowski: received consulting fees from Forma Therapeutics, Vertex, Agios, BioMarin, Chiesi, Bristol Myers Squibb, Bluebird Bio, Editas Medicine, CRISPR/Vertex, Imara, Silence Therapeutics, Novo-Nordisk; received research funding from Forma Therapeutics, Agios, Bluebird Bio, Pfizer, CRISPR/Vertex, Imara, Apopharma
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Kevin Boerner, Tina Liu, Sakellarios Zairis, William Hobbs are employees of Vertex Pharmaceuticals Incorporated and may hold Vertex stock/stock options.
Stephan Grupp: received consultancy fees from Novartis, Jazz, Adaptimmune, Vertex, Allogene, Cabaletta; honoraria from Novartis; research funding from Novartis, Kite, Servier, Jazz, Cellectis, Vertex; advisory board member for Allogene.

GS2-6

NON-RELAPSE MORTALITY FOLLOWING CAR-T CELL THERAPY: A STUDY BY THE EBMT TRANSPLANT COMPLICATIONS WORKING PARTY

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Background: Non-relapse mortality (NRM) is a significant concern following CAR T-cell infusion, with a recent meta-analysis identifying NRM of 5-10% following CAR T-cell infusion for haematological malignancies (1). However, this study comprised pooled data from a mixture of clinical trials and real-world data reports, with varying reporting criteria and limited long-term follow-up (1). Therefore, disease- and product-specific estimates of NRM in large real-world cohorts remain needed.
This retrospective EBMT registry study evaluated the risk of NRM for different disease indications and CAR-T products and identified the leading causes of NRM.

Methods: We identified and included adult patients ≥18 years of age at the time of first CAR-T infusion, who received a licensed CAR-T product between 2019 and 2023 for a haematological malignancy.

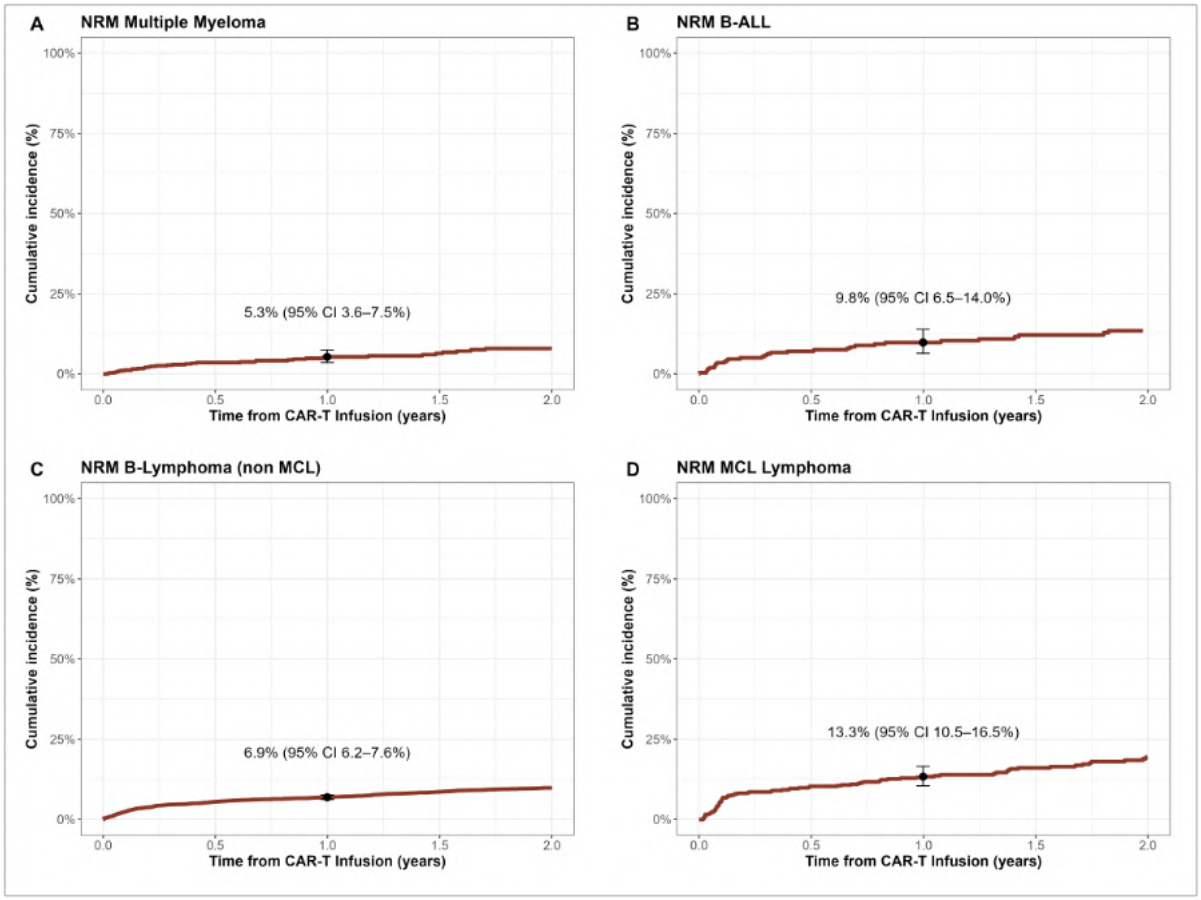
Results: 6928 patients were included, of whom 258 received CAR T-cell therapy for B-acute lymphoblastic leukaemia (B-ALL), 514 for mantle cell lymphoma (MCL), 5573 for B-cell lymphoma (BCL), and 583 for multiple myeloma (MM). There were 2,887 deaths, and the leading cause was disease progression/relapse (80.4%).
Table 1 summarizes NRM by disease indication and CAR-T product, and Figure 1 depicts the cumulative incidence of NRM by disease. The highest NRM at 1-year post-infusion was observed in MCL patients treated with brexu-cel (13.3%), followed by B-ALL patients treated with brexu-cel (11.4%). The lowest NRM at 1 year was seen in BCL patients treated with liso-cel (3.99%).

Table 1: Non-relapse mortality by disease indication and CAR T product

Diagnosis and CAR T product	NRM at 6 months (% (95% CI))	NRM at 1 year (% (95% CI))	NRM at 2 years (% (95% CI))

B-ALL Tisa-cel	6.90% (3.64%, 11.6%)	9.00% (5.14%, 14.2%)	10.9% (6.42%, 16.6%)
B-ALL Brexu-cel	7.45% (3.26%, 14.0%)	11.4% (5.74%, 19.1%)	19.0% (10.6%, 29.3%)
BCL Liso-cel	3.99% (1.29%, 9.19%)	3.99% (1.29%, 9.19%)	6.07% (2.05%, 13.3%)
BCL Tisa-cel	5.24% (4.23%, 6.39%)	6.31% (5.19%, 7.58%)	9.42% (7.93%, 11.1%)
BCL Axi-cel	5.68% (4.97%, 6.46%)	7.26% (6.44%, 8.14%)	10.1% (9.09%, 11.3%)
MCL Brexu-cel	10.3% (7.83%, 13.1%)	13.3% (10.5%, 16.5%)	19.4% (15.6%, 23.7%)
MM Ide-cel	3.24% (1.90%, 5.16%)	4.59% (2.89%, 6.87%)	Not Applicable (Insufficient FU)
MM Cilta-cel	4.85% (1.78%, 10.3%)	8.75% (4.01%, 15.8%)	Not Applicable (Insufficient FU)

In multivariable analysis, the risk of NRM was increased in B-ALL patients with ECOG ≥1 (HR 3.47, p=0.03), and in MM patients with active disease at lymphodepletion (HR [CR/PR vs. active disease] 0.42, p=0.05). Among BCL patients, higher NRM was associated with older age at CAR-T infusion (HR 1.16, p<0.001), male sex (HR 1.34, p=0.003), ECOG ≥1 (HR 2.00, p<0.001), and disease status (HR [PR vs. active disease] 0.75, p=0.01). The leading cause of NRM was infection (n=191, 35.4% of NRM), cell therapy-related causes (n=177, 32.8% of NRM), and secondary malignancies (n=51, 9.5% of NRM).



Conclusions: This study highlights the significant NRM associated with CAR T-cell therapy and differences across diseases and therapeutic products. Infections were the leading cause of NRM, underscoring the need for improved, product-specific strategies for infection prevention, surveillance, and management to further enhance CAR-T outcomes.

References: 1. Cordas Dos Santos DM, Tix T, Shouval R, Gafter-Gvili A, Alberge JB, Cliff ERS, et al. A systematic review and meta-analysis of nonrelapse mortality after CAR T cell therapy. Nat Med. 2024;30(9):2667-78.

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LWP1-2

COMPARATIVE EFFICACY OF AXICABTAGENE CILOLEUCEL AND LISOCABTAGENE MARALEUCEL IN SECOND LINE TREATMENT OF RELAPSED/REFRACTORY LARGE B-CELL LYMPHOMA – AN EBMT ANALYSIS

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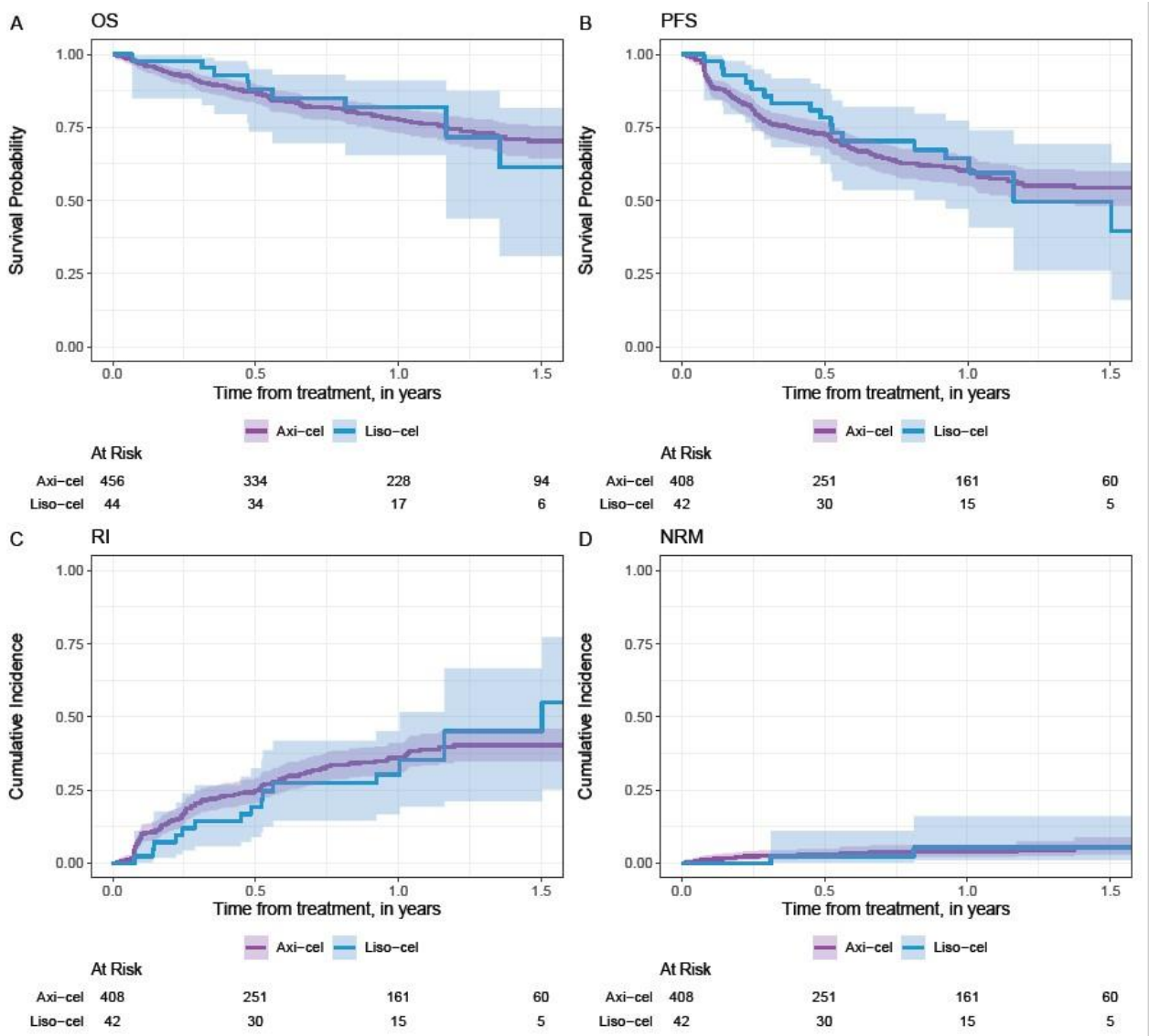
Background: Both axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel (liso-cel) are approved for second line treatment of relapsed/refratory (r/r) large b-cell lymphoma (LBCL). Differences in the design of the pivotal trials complicate direct comparisons of their efficacy. In the ≥3rd-line setting, real-world analyses have significantly influenced the use of the approved CAR T-cell products. This EBMT analysis evaluates potential differences in efficacy between axi-cel and liso-cel in the second-line treatment of r/r LBCL.

Methods: Patients with LBCL registered in the EBMT registry from 01/2022 until 12/2024 receiving either axi- or liso-cel in second line were included. Kaplan-Meyer estimates were used to calculate overall (OS) and progression-free survival (PFS) from the day of CAR T-cell infusion, cumulative incidences were applied for relapse incidence (RI) and non-relapse mortality (NRM). To mitigate selection bias, propensity score matching (PSM) was employed, including the following variables: treatment year, disease status at CAR T-cell infusion, HCT-CI, time between diagnosis and infusion and lymphodepleting regimen.

Results: Of 515 included patients, 44 were treated with liso-cel and 471 received axi-cel. Median age of the whole cohort was 63 years (range 54 - 70) and the majority of patients were male (64%). At cell therapy, 91% of patients had an ECOG performance status of 0-1, 77% presented with Ann Arbor stage III-IV and 41% had elevated LDH. The majority of patients had refractory disease at the time of CAR T-cell infusion (58%). The two cohorts differed significantly only in the frequency of extranodal involvement (39% in the axi-cel group vs 21% for liso-cel patients, p = 0.048) and the year of CAR T-cell infusion (76% of axi-cel infusions in 2022 and 2023 vs 45.5% of liso-cel infusions in this period). With a

median follow-up of 1.1 years, OS at 1 year for all patients was 77.9% (95% CI 73.6-81.6), 77.5% (95% CI 73-81.4) for axi-cel patients and 81.9% (95% CI 65.5-91) for liso-cel patients. PFS at 1 year was 60.7% (95% CI 55.6-65.3) for the entire cohort and 60.3% (95% CI 55-65.2) for patients who received axi-cel vs 64.4% (95% CI 47.2-77.3) for patients treated with liso-cel. The relapse incidence was 35.9% (95% CI 30.9-41) 1 year after axi-cel infusion and 30.3% (95% CI 16.6-45.1) after liso-cel treatment. One-year NRM was 3.7% (95% CI 2.1-6) and 5.3% (95% CI 0.9-16) for axi-cel and liso-cel, respectively. Propensity score matching confirmed similar results for both productsfor OS, PFS, RI and NRM.

Conclusions: In this real-world analysis, patients with r/r LBCL receiving axi-cel or liso-cel infusion in the second line setting achieved excellent 1-year survival outcomes, consistent with pivotal trial data. Both products demonstrated similar results in terms of OS, PFS and RI. NRM is notably low for both axi- and liso-cel, highlighting that both products are not only highly efficacious but also safe. Treatment selection can therefore be tailored to individual patient characteristics, such as comorbidities and other clinical factors. Ongoing data collection on toxicity profiles, including the incidence of ICANS and CRS, will further inform treatment decisions.



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Gabriel Brisou reports honoraria from Incyte, Kite Gilead, BMS, Novartis, Abbvie and Roche, worked as consultant for Incyte, Kite Gilead, BMS, Novartis, Miltenyi Biomedicine, Abbvie and Roche and received travel support from Incyte, Kite Gilead, BMS, and Novartis.
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OS02-01

DISEASE STATUS AT LYMPHODEPLETION RATHER THAN BRIDGING MODALITY PREDICTS OUTCOMES FOLLOWING CD19-DIRECTED CAR T-CELL THERAPY IN LARGE B-CELL LYMPHOMA

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Background: CD19-directed CAR T-cell therapy (CART) induces durable remissions in a subset of patients with relapsed/refractory large B-cell lymphoma (R/R LBCL). Bridging therapy (BT) between leukapheresis and lymphodepletion is used in many patients, but the optimal modality and its impact on outcomes remain uncertain. Here, we evaluated the impact of BT modality and disease status at lymphodepletion on the outcomes following CART in a large international cohort.

Methods: We analyzed 1,134 adults with R/R LBCL treated with commercial CD19-directed CART cells (axicabtagene ciloleucel or tisagenlecleucel) at 38 EBMT centers (2018–2023). BT was defined as any anti-lymphoma treatment between leukapheresis and lymphodepletion and was categorized into Pola-BR, low-dose regimens, classical salvage chemo-immunotherapy, or radiotherapy (RT). Outcomes were analyzed using Kaplan-Meier plots and multivariable Cox models adjusted for clinical covariates and CART product, with changes in disease status from apheresis to lymphodepletion classified as improved, stable, or worse.

Results: Of 1,134 patients, 900 pts (79%) received BT and 234 (21%) proceeded to CART without BT. BT usage marked a higher-risk population at lymphodepletion, with significantly increased LDH levels (49.3% vs 39.1%), bulky disease (17.0% vs 6.8%), and ECOG ≥2 (16.9% vs 7.9%). With a median follow-up of 36.2 vs 35.1 months, the 3-year PFS was 34.3% vs 44.7% and the OS 44.4% vs 57.4% in the BT versus No-BT groups, respectively. In multivariable models adjusting for age, sex, transformed histology, prior auto-HCT, number of prior treatment lines, disease status at apheresis, LDH at lymphodepletion, ECOG at CART, and CART product, absence of BT remained associated with more favorable outcomes (OS HR 0.63, 95%CI 0.49–0.82; PFS HR 0.69, 95%CI 0.55–0.87), mostly caused by lower RI in these patients. Overall, 25.6% of patients improved their disease status between apheresis and lymphodepletion (28.2% in BT vs. 9.9% in No-BT, $p<0.001$). Patients with improvement of the disease status had a 3-year OS of 63.2% vs 41.8% (stable) and 39.8% (worsened; $p<0.0001$) and a 3-year PFS of 48.6% vs 32.1% and 34.2%, respectively ($p<0.0001$). This was particularly pronounced among BT recipients, with 3-year PFS rates of 47.5%, 28.9%, and 27.7% for improved, stable, and worsened disease status, respectively. BT modality influenced conversion rates and rates of progression (highest/lowest with Pola-BR and RT), but in multivariable analyses using the same covariates, no BT modality was associated with OS, PFS, RI, or NRM. Toxicity profiles, including CRS, ICANS, were comparable between BT and No-BT cohorts.

Conclusions: In this large registry cohort, BT was used in 79% of patients intended for CART and identified patients with a higher risk of failure following CART. BT exposure was associated with inferior survival even after adjustment for baseline disease and patient characteristics, and no individual BT modality conferred a clear survival advantage. Improvement in disease status before lymphodepletion was a significant determinant of outcome. These data support the use of BT when necessary, aiming to improve the disease status at lymphodepletion. Our data underscore the need for prospective studies to refine BT strategies that safely achieve disease control without compromising CART efficacy.

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OS02-02

THREE-YEAR EFFICACY AND LONGITUDINAL SAFETY OF LISOCABTAGENE MARALEUCEL (LISO-CEL) IN PATIENTS WITH THIRD-LINE OR LATER (3L+) FOLLICULAR LYMPHOMA (FL) FROM TRANSCEND FL

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Background: In the primary analysis of TRANSCEND FL (NCT04245839), an open-label, pivotal study, liso-cel showed high response rates and favorable safety in patients with R/R FL. Here, we report 3-year follow-up results in patients with 3L+ FL, including efficacy, safety, and longitudinal safety analyses for key AEs.

Methods: Patients were eligible if they had R/R FL after ≥ 2 prior lines of combination systemic therapy, including an anti-CD20 antibody and an alkylator. Patients received liso-cel after lymphodepleting chemotherapy (LDC). Bridging therapy was allowed with reconfirmation of PET-positive disease before LDC. The primary endpoint was ORR per independent review committee by PET/CT using Lugano 2014 criteria. Secondary endpoints included CR rate, duration of response, PFS, OS, and safety. Additional post hoc analyses included time to next treatment and efficacy by progression of disease ≤ 24 months from

first-line chemoimmunotherapy (POD24) status (yes vs no) and by prior bendamustine exposure before leukapheresis (yes vs no). Incidences of infections, second primary malignancies (SPM), hypogammaglobulinemia, and grade ≥ 3 cytopenia (overall and by lineage) were assessed over time from Day 0–15, Day 16–30, at 3-month intervals until Month 12, at 6-month intervals until Month 36, and from Month 37 until end of study.

Results: At data cutoff (03/31/2025), 107 patients with 3L+ FL received liso-cel and were evaluable for safety; 103 were efficacy evaluable. Median (range) age was 62 years (23–80); 95 (89%) had Ann Arbor stage III/IV disease; and 61 (57%) were high risk per Follicular Lymphoma International Prognostic Index. Fifty-nine patients (55%) had POD24, 69 (64%) were double refractory to anti-CD20 antibody and an alkylator, and 65 (61%) had prior bendamustine exposure.
Median (range) on-study follow-up was 41.5 months (0.3–54.0). Response rates were high overall and regardless of POD24 status or prior bendamustine exposure (**Table 1**). Treatment-emergent (TE) AE rates were consistent with the primary and 2-year follow-up analyses. Grade 3 cytokine release syndrome was reported in 1% (no grade 4/5), grade 3 neurological events in 2% (no grade 4/5). SPMs were reported in 11 patients (10%; 4 additional patients since the 2-year follow-up analysis; no secondary T-cell malignancies). Grade ≥ 3 infections were reported in 13 (12%) patients, including 7 (7%) in the TE period (≤ 90 d after infusion) and 8 (7%) in the post-TE period (3 more patients since the 2-year analysis). AE incidences over time are shown in **Table 2.**

Conclusions: In patients with 3L+ FL, a single infusion of liso-cel demonstrated remarkable efficacy, with durable responses and high 3-year survival rates, regardless of POD24 status or prior bendamustine exposure. No new safety signals were identified. Grade ≥ 3 neutropenia and hypogammaglobulinemia decreased over time and severe infections remained low, further underscoring the favorable long-term safety profile of liso-cel in patients with 3L+ FL.

Table 1. Efficacy outcomes

	3L+ FL (n = 103)	**POD24 (n = 57)**	**Non-POD24 (n = 46)**	**Prior bendamustine exposure (n = 61)**	**No prior bendamustine exposure (n = 42)**
ORR (95% CI)	97.1 (91.7–99.4)	96.5 (87.9–99.6)	97.8 (88.5–99.9)	96.7 (88.7–99.6)	97.6 (87.4–99.9)
CR rate (95% CI)	94.2 (87.8–97.8)	94.7 (85.4–98.9)	93.5 (82.1–98.6)	93.4 (84.1–98.7)	95.2 (83.8–99.4)
36-month DOR rate, % (95% CI)	70.0 (59.7–78.2)	60.4 (45.8–72.3)	81.6 (66.4–90.4)	70.4 (56.7–80.5)	69.3 (52.1–81.4)

36-month PFS rate, % (95% CI)	67.9 (57.6–76.2)	58.0 (43.4–70.0)	79.9 (64.8–89.0)	68.0 (54.5–78.3)	67.5 (50.3–79.9)
36-month OS rate, % (95% CI)	86.2 (77.8–91.6)	82.2 (69.5–90.0)	91.1 (78.1–96.6)	81.4 (68.9–89.3)	92.9 (79.5–97.6)
Free of next treatment at 36-month rate, % (95% CI)	75.3 (65.7–82.6)	67.7 (53.7–78.3)	84.6 (70.4–92.4)	73.1 (59.8–82.6)	78.5 (62.7–88.2)

3L+, third line or later; DOR, duration of response; POD24, progression of disease ≤ 24 months from first-line chemoimmunotherapy.

Table 2 . Summary of selected AEs over time (liso-cel–treated set)[a]

	Day 0–15	Day 16–30	Month 2–3	Month 4–6	Month 7–9	Month 10–12	Month 13–18	Month 19–24	Month 25–30	Month 31–36	Month 37–EOS
Grade ≥ 3 neutropenia, n (%)	85 (79)	26 (25)	26 (25)	12 (14)	6 (7)	9 (12)	7 (10)	5 (6)	4 (10)	3 (7.5)	4 (7)
Grade ≥ 3 anemia, n (%)	18 (17)	8 (8)	5 (5)	0	0	0	0	0	1 (2)	1 (3)	1 (2)
Grade ≥ 3 thrombocytopenia,' n (%)	20 (19)	19 (18)	14 (14)	5 (6)	5 (6)	0	2 (3)	1 (1)	2 5)	1 (3)	2 (4)
Hypogammaglobulinemia, n (%)	52 (65)	62 (62)	60 (61)	47 (61)	45 (56)	40 (57)	45 (62)	41 (53)	20 (53)	16 (42)	26 (48)
Any-grade infection, n (%)	10 (9)	5 (5)	13 (12)	5 (5)	3 (3)	3 (3)	4 (4)	4 (4)	6 (7)	5 (6)	2 (2)
Grade ≥ 3 infections, n (%)	2 (2)	3 (3)	4 (4)	1 (1)	2 (2)	1 (1)	1 (1)	1 (1)	3 (3)	3 (4)	1 (1)

[a]Proportions for grade ≥ 3 cytopenias and hypogammaglobulinemia were calculated using the denominator as the number of patients with a laboratory parameter assessment in each time period. From M25—M36, > 50% of patients on study had missing values for laboratory parameters. Proportions for infections were calculated using the number of patients on study in each time period: D0—D15, n = 107; D16—D30, n = 106; M2—M3, n = 106; M4—M6, n = 105; M7—M9, n = 100; M10—M12, n = 97; M13—M18, n = 97; M19—M24, n = 94; M25—M30, n = 90; M31—M36, n = 85; M37—EOS, n = 81.
Monthly ranges start on the first day of the first month and end on the last day of the last month. Each patient is counted once in each time period but is counted again if having an event in another time period. Results are consistent when patients who started subsequent antilymphoma therapy were excluded at the initiation of subsequent therapy.
D, Day; EOS, end of study; liso-cel, lisocabtagene maraleucel; M, Month.

Clinical Trial Registry: NCT04245839

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OS02-03

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION COMBINED WITH CAR-T CELL THERAPY SIGNIFICANTLY IMPROVES PROGRESSION-FREE SURVIVAL IN RELAPSED REFRACTORY CENTRAL NERVOUS SYSTEM LYMPHOMA

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Background: Relapsed or refractory Central nervous system lymphoma(R/R CNSL) is challenging to manage clinically. CAR-T therapy has demonstrated efficacy in relapsed and refractory large B-cell lymphoma, with some studies indicating a favourable response rate for R/R CNSL. Nevertheless, disease-free survival and long-term outcomes are suboptimal.Our study aims to explore the efficacy of CAR-T and the factors affecting its long-term survival in R/R CNSL. Additionally, we analysed the safety and effectiveness of ASCT combined with CAR-T therapy.

Methods: This single-centre retrospective study included 153 patients with relapsed/refractory CNS lymphoma (R/R CNSL) treated with CAR-T therapy at Beijing GoBroad Hospital from September 2019 to September 2025. Overall, 51% were male, and the median age was 56 years (range, 19–79). PCNSL accounted for 53% of cases (81/153)

and SCNSL for 47% (72/153), The common histology in SCNSL was DLBCL(n=55), followed by HGBL(n=5), PMBL(n=3) and others.
A total of 83 patients had received ≥3 prior treatment lines. IELSG (PCNSL) or IPI (SCNSL) scoring identified 27% as low-risk, 59% intermediate-risk, and 14% high-risk. Most patients were refractory to HD-MTX (85%), and 58% had received MTX within 6 months before CAR-T. BTKi resistance was present in 64%, and 18% had failed prior ASCT.
Parenchymal involvement occurred in 74%, cerebrospinal fluid in 8%, and both in 18%.
Patients received a median of 2 cycles (0–5) of bridging therapy, achieving a 71% objective response rate (CR 84; PR 24). Based on bridging response, patients were classified into Bridging-Effective (CR/PR) and Bridging-Ineffective (SD/PD) groups. In the BE group, 49%(53/108) underwent ASCT combined with CAR-T therapy.

Table 1:Baseline of different treatment in the effective group after bridging therapy

Variable	CAR-T(N=55)	ASCT+CAR-T(N=53)	p-value
Age(>60)	27/55(49.1%)	6/53(11.3%)	0.736
Sex(male)	26/55(47.3%)	26/53(49.1%)	0.278
Risk category -Low risk -Intermediate risk -High risk	14/55(25.5) 34/55(61.8%) 7/55(12.7%)	21/53(39.6%) 28/53(52.8%) 4/53(7.5%)	0.118
ECOG ≥2	20/55(37.7%)	21/53(39.6%)	**0.0001**
Histology -PCNSL -SCNSL	20/55(36.4%) 35/55(63.6%)	23/53(43.4%) 30/53(56.6%)	**0.005**
TP53 mutation	6/55(10.9%)	8/53(15.1%)	0.272
Previous HD-MTX resistance	48/55(87.3%)	51/53(96.2%)	**0.001**
Previous BTK inhibitor resistance	35/55(63.6%)	35/53(66.0%)	0.761
Previous auto-HCT	14/55(25.5%)	9/53(17.0%)	0.067
Previous regimen lines≥3	28/55(50.9%)	31/53(58.5%)	0.833

Results: The 3-month ORR was 79% (121/153), and CRR is 69% (106/153). Incidences of any-grade CRS and ICANS were 69% (105/153) and 14% (21/153), with severe (≥3) CRS and ICANS at 6% (6/105) and 24 % (5/21), respectively. BE group exhibited significantly higher 3-month ORR (91% vs. 56%) and CRR (87% vs. 33%) compared to BI group. Median follow-up time was 26months. Median Progression-Free Survival (PFS) for BE group was 49 months, significantly longer than BI group's 6 months (P<0.0001).
Median Overall Survival (OS) was not reached for BE group, while it was 13 months for BI group (P<0.0001).1-year OS rates were 93% vs. 57% (P<0.01), and 1-year PFS rates were 75% vs. 27% (P<0.01) for BE and BI groups, respectively.
2-year OS rates were 78.5%vs. 29% (P<0.01), and 1-year PFS rates were 67% vs. 14% (P<0.01) for BE and BI groups, respectively.
Among the 108 BE group patients, Median PFS in ASCT combined with CAR-T cohort was significantly prolonged (57.11 vs. 27.35 months, p=0.001). Median OS was not reached in both cohort（p=0.053). No statistical difference was observed in CRS and ICANS between the two cohorts.

Conclusions: Effective bridging therapy can significantly improve the efficacy of CART in the treatment of R/R CNSL. After bridging therapy is effective, the treatment model of ASCT combined with CAR-T can significantly improve Progression-free survival.

Disclosure: Nothing to declare.

OS02-05

IMPACT OF PRIOR B-CELL-DIRECTED IMMUNOTHERAPY ON THE OUTCOME OF CD19 CAR T-CELL THERAPY IN AGGRESSIVE B-CELL LYMPHOMA

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Background: B-cell-directed immunotherapies (BCDI), such as CD19 chimeric antigen receptor T-cell therapy (CAR-T), antibody-drug conjugates including polatuzumab vedotin (pola), and bispecific antibodies (BSA) have revolutionized the treatment of large B-cell lymphoma (LBCL). The optimal sequencing of BCDI and CAR-T remains unclear, while prolonged B-cell depletion may contribute to CAR-T-associated non-relapse mortality (NRM). In a collaborative analysis by the EBMT and the GoCART coalition, we evaluated the impact of prior BCDI exposure on outcomes after CD19 CAR-T in a large retrospective cohort.

Methods: We analyzed 1128 adult patients with LBCL who underwent CD19 CAR-T between 2018 and July 2023 at 38 European centers reported to the EBMT registry. BCDI exposure (excluding rituximab) prior to CAR-T, including bridging therapy, was categorized as BSA, pola-based regimens, and other BCDI, including obinutuzumab, brentuximab vedotin, and loncastixumab tesirine.

Results: Among 1,128 patients, 376 (33.2%) received BCDI other than rituximab before CAR-T (BCDI group) and 752 (66.7%) did not (non-BCDI group). Within the BCDI group, 189 (50.3%) received BCDI as bridging only and 187 (49.7%) prior to apheresis (median of 3 lines including BCDI). BCDI-exposed patients more often had ≥3 prior treatment lines (54.8% vs. 43.0%, p<0.001), more frequent axicabtagene ciloleucel usage (63.8% vs. 56.0%, p=0.012), and higher complete/partial remission (CR/PR) rates at lymphodepletion (40.2% vs. 29.1%, p<0.001).
Three-year overall survival (OS) was numerically inferior with prior BCDI (41.3% vs. 49.7%, p=0.07), without differences in progression-free survival (PFS) (35.0% vs. 37.2%), relapse incidence (52.0% vs. 51.5%), or NRM (13.0% vs. 11.3%). Post–CAR-T CR rates (51.8% vs. 54.8%) and overall response rate (73.8% vs. 73.1%) were not statistically different, as were cytokine release syndrome (83.9% vs. 84.8%), Immune Effector Cell-Associated Neurotoxicity Syndrome (31.3% vs. 32.9%), and 2-year grade III/IV infections (22.2% vs. 21.8%). In multivariable analysis, prior BCDI showed a borderline association with inferior OS (HR 1.21, 95% CI 1.00–1.47, p=0.06).
Within BCDI-exposed patients, BCDI type was associated with different 2.5-year OS (BSA 48.0%, pola-based (often including bendamustine) 39.8%, other BCDI 59.9%; p=0.03). After matching patients, OS was lower with pola than with BSA (HR 1.84 [0.95–3.57], p=0.07), and favored other BCDI over pola (HR 0.61, p=0.11), with a trend toward improved PFS (HR 0.63, p=0.09). Analysis of BCDI administration timing is under way but shows different univariable 3-year OS by BCDI exposure relative to apheresis (post-apheresis only 47.1%, pre-apheresis only 41.2%, both pre- and post-apheresis 22.6%).

Conclusions: Our data suggest that prior BCDI exposure may be associated with inferior OS after CAR-T without affecting NRM, with this effect potentially confined to patients receiving BCDI before apheresis. Matched analyses indicated a signal toward inferior OS with pola-based regimens; however, these findings are hypothesis-generating and limited by residual confounding (e.g. bendamustine use with pola), retrospective design, and small subgroup sizes.

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OS03-08

DO 2 YEAR PATIENT OUTCOMES DIFFER BY DONOR TYPE USING CONTEMPORARY GRAFT VS HOST DISEASE PROPHYLAXIS POST-TRANSPLANT? A CIBMTR RETROSPECTIVE ANALYSIS

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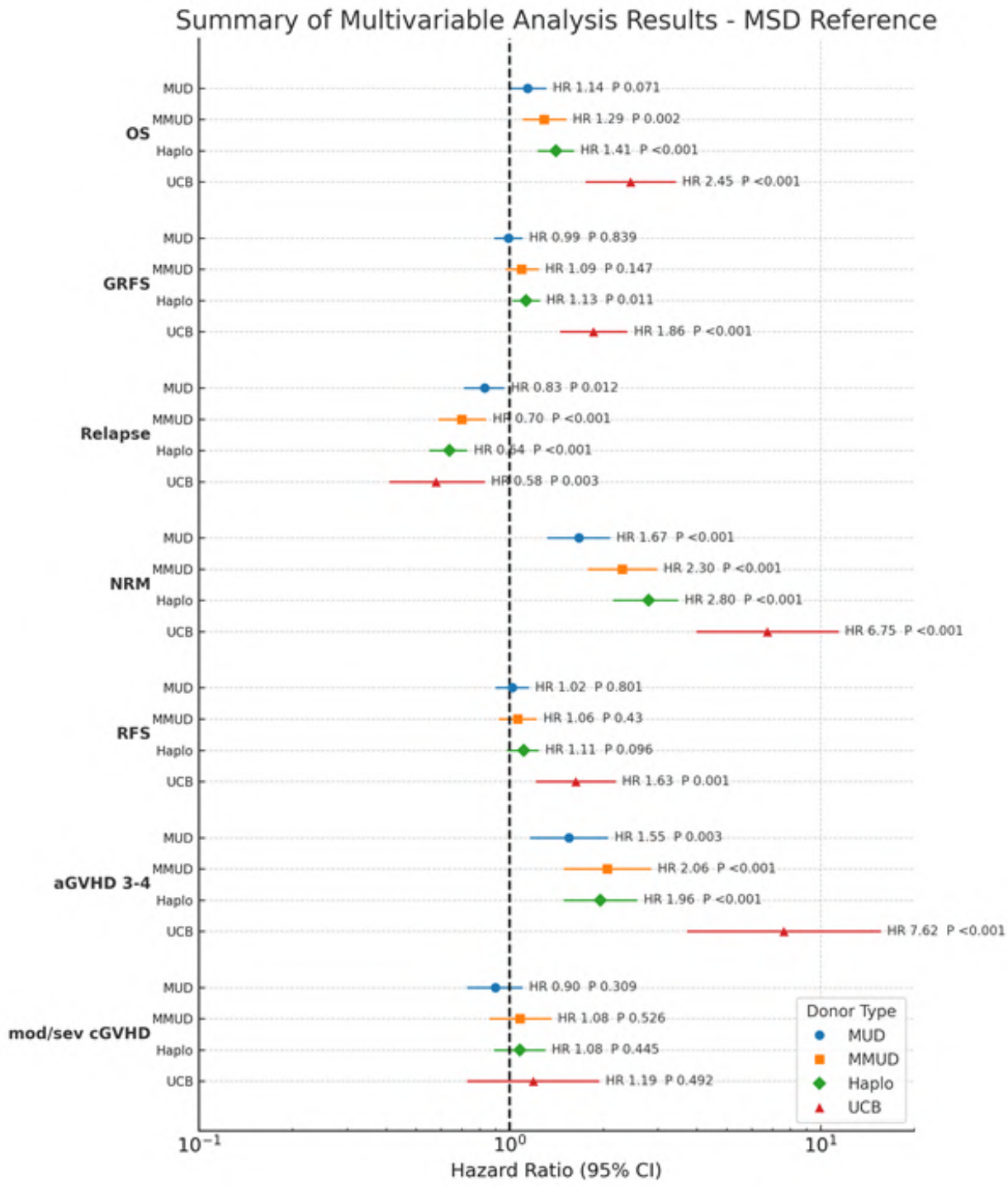
Background: Post-transplant cyclophosphamide (PTCy) based graft vs host disease (GvHD) prophylaxis expands access to allogeneic hematopoietic cell transplantation (HCT) through the safe and effective use of mismatched related (haplo) and unrelated donors (MMUD). A previous analysis from our group evaluating HCTs from 2017-2022 demonstrated that outcome disparities persist at 1-year post-HCT between matched (sibling/related [MSD] and unrelated [MUD]) donors compared to mismatched sources, but such differences have diminished in magnitude using contemporary GVHD prophylaxis. We sought to expand the population (adding cases from 2023) and evaluate longer term outcomes to determine if differences persist beyond one year of follow-up.

Methods: We conducted a retrospective registry analysis of all contemporary donor types using the Center for International Blood and Marrow Transplant Research (CIBMTR) database. The primary objective was to compare overall and GVHD-free, relapse-free survival (GRFS) at 2 years post HCT among donor types. Secondary objectives were to compare cumulative incidence of relapse, disease-free survival (DFS), non-relapse mortality (NRM), acute GVHD (aGVHD) grades 2-4 and 3-4 and moderate/severe chronic GVHD (cGVHD). The cohort included adult patients (≥18 years old) with acute leukemia (ALL and AML) or myelodysplastic syndrome (MDS) transplanted in the U.S. from 2017-2023. Donor types included MSD, 8/8 HLA MUD, 7/8 HLA MMUD, haplo and umbilical cord blood (UCB). All patients received PTCy without ATG with the exception of UCB recipients who received CNI-based GVHD prophylaxis without ATG as standard of care per current American Society for Transplantation and Cellular Therapy (ASTCT) guidelines.

Results: The study cohort included 13,336 patients from 166 centers. The distribution by donor type and disease were as follows: MSD=1263, MUD=4117, MMUD=1426, Haplo=5811, UCB=719 and ALL=2551, AML=7305, MDS=3480, respectively. Median donor age in years differed by type and was older for related donor sources: MSD=53, MUD=27, MMUD=28 and haplo=35. Peripheral blood allografts were used in 89% of MSD/MUD/MMUD/haplo HCT. 40% received myeloablative conditioning with >50% in both the MSD and UCB groups. Median survival time was 23.2 months (interquartile range 11.0-39.7 months) and analysis limited to 24 months. In multivariable analyses (Figure), OS was highest in MSD and MUD and lowest in UCB. Compared to MSD (reference), GRFS was worse in haplo and UCB and did not differ with MUD or MMUD. Relapse was lower in MUD, MMUD, haplo and UCB compared to MSD, but offset by higher NRM. aGVHD 3-4 risk was higher in MUD, MMUD, haplo and UCB, but cGVHD risk did not differ among groups.



Conclusions: In this extended follow-up analysis of recipients of alloHCT in the contemporary PTCy era, outcomes still vary by donor type at two years post-HCT. MSD and

MUD result in similar OS and GRFS. MMUD and haplo compare favorably. Conventional UCB had worse outcomes overall. Results suggest donor selection strategies should favor MSD and MUD, if available, followed by MMUD and haplo over UCB.

Disclosure: Mahasweta Gooptu - Advisory Board Member: Syndax, Incyte
Bronwen E. Shaw - Consulting: Orcabio
All other authors have nothing to declare.

OS07-01

NOVEL COMPOSITE END-POINTS TOXICITY/PROGRESSION-FREE SURVIVAL (TFPFS) AND TOXICITY-FREE COMPLETE REMISSION (TFCR) AFTER CART19 CELL THERAPY FOR LARGE B CELL LYMPHOMA (LBCL): CELL THERAPY CONSORTIUM ANALYSIS

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Background:

The success of any CAR-T product is typically assessed by disease response and rates of immune complications; both vary significantly among CART19 products for patients with LBCL. We explored the utility of integrated efficacy/toxicity composite end-points to yield insights into net clinical benefit.

Methods: To evaluate the combined contribution of efficacy and toxicity in first 100 days post CAR19-T, we defined a novel composite end-point: toxicity-progression free survival at day 100 (tPFS100). Events included relapse/progression, death and grade ≥3 cytokine release syndrome (CRS) or grade ≥3 immune effector-associated encephalopathy (ICANS). In addition, at day 100, each patient was assigned to one of 3 groups: non CR group, toxicity-free complete response at day 100 (tfCR100) and CR group with grade ≥3 CRS or ICANS toxicity (CRwt).

Results:

We included 627 consecutive CAR19-T cell recipients with LBCL reported to Cell Therapy Consortium (CTC) between 2017-2023; median age was 64 yrs (18-86), 12% had ECOG≥2 and 57% had refractory disease. Most common product infused was axi-cel (53%) followed by tisa-cel (33%) and liso-cel (13%).

At day 100 post CAR19-T, composite tPFS100 in entire cohort was 61% (95% CI: 57-65%). Product specific tPFS100 was highest for liso-cel 70% (95%CI 62-80%) compared to 53% (47-60%) for tisa-cel and 46% (95%CI 41-51%) for axi-cel. In MVA, high LDH (2.40; 95%CI 1.87-3.09; p=0.01) and advanced stage III-IV (HR 1.38; 1-1.9; p=0.04) were risk factors for inferior tfPFS100. Liso-cel/age >65 yrs and tisa-cell/age >65yrs were protective (HR 0.21 and HR 0.7).
We determined that 242 pts (49%) achieved tfCR100, 66 patients (10%) experienced CRwt and 320 (51%) did not achieve CR by day 100.
The tfCR100 rates were similar by age and differed significantly by CAR-T product: 32.9 % (Axi-cel), 37.2% (Tisa-cel) and 65.1% (Liso-cel; p<0.01). Factors favorably associated with tfCR included normal LDH and ECOG £1. After CART19 therapy, tfCR group had lower rates of neutropenia <500, thrombocytopenia, infection rates, peak CRP and ferritin, ICU utilization and shorter length of hospital stay compared to CRwt patients.
At a median follow-up of 22.4 months (range 21-80.7), adjusted 2-year OS among tfCR100 group was 86% (95% 80-91) compared to 63% (49-75%) for the CRwt group (p=0.01). Among patients without CR100, 31% (25-36%; p<0.01) survived to 2 years post CAR19-T. Notably, non-relapse mortality was significantly lower in the tfCR100 group (5%; 95% CI: 2–9%) compared to CRwt (26%; 95% CI: 14–38%; p < 0.01). The 2-year cumulative incidence of relapse did not differ significantly between two CR groups (26%; vs. 21%; p = 0.44). As a result, tfCR100 group yield significantly better PFS (72%; 95%CI(64-79%) compared to CRwt group (54; 95% CI 43-64%; p<0.01).

Conclusions:

Our data demonstrate that about half of CAR19-T recipients experience CR without advanced CRS or ICANS; thus, products differ significantly in early endpoint tfPFS100 with observed superiority of liso-cel. The emergence of these novel tools that may be valuable in benchmarking cell therapies, health economic modeling, and guiding future strategies to optimize safety and efficacy of CAR-T therapy.

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OS07-02

FRAILTY ASSESSMENT AND THEIR PROGNOSTIC SIGNIFICANCE IN CAR T-CELL THERAPY. RESULTS FROM A PROSPECTIVE AND LONGITUDINAL SINGLE-CENTER STUDY

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Background: Frailty syndrome in patients with hematological malignancies has been increasingly associated with inferior outcomes. Based on this evidence, our institution launched a prospective, longitudinal, observational study in April 2023 to evaluate frailty in all candidates for CAR T-cell therapy and to assess its impact on clinical outcomes. This analysis summarizes the results obtained during this investigation.

Methods: All patients with lymphoproliferative disorders (LPD) or acute lymphoblastic leukemia (ALL) eligible for commercial (axicabtagene autoleucel) or academic (ARI0001) CD19 CAR T-cell therapy were prospectively included after providing informed consent. Frailty was assessed using the HCT Frailty Scale (Salas et al., 2023) at first consultation (prior to leukapheresis) and before lymphodepletion for CAR T-cell infusion. Quality of life (QoL) was evaluated using the EQ-5D-3L questionnaire before lymphodepletion. All assessments were integrated into clinical practice and conducted by nursing staff, requiring a median of 10–15 minutes per patient, and no additional resources. The study had no funding, and no interventions were implemented based on frailty status during the study period.

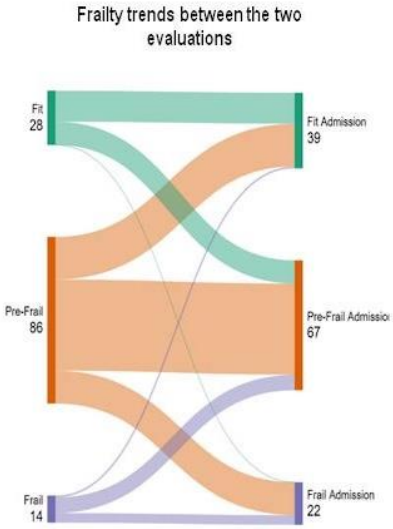
Results: A total of 132 consecutive patients were included, 44 (33%) with ALL and 88 (67%) with LPD. At first consultation, 28 (21%) patients were classified as fit, 86 (65%) as pre-frail, and 18 (13%) as frail. Frail patients were older than fit and pre-frail patients (median age 62 vs. 52 and 55 years; p=0.015) and more frequently female (44.4% vs. 10.7% and 38.3%; p=0.015) (Table 1).
Before lymphodepletion, frailty distribution changed significantly, confirming its dynamic nature: 39 (29.5%) patients were fit, 67 (50.9%) pre-frail, and 26 (19.7%) frail (Figure 1). Frail patients remained older, more frequently female (61.5% vs. 25.6% and 26.9%; p=0.003), and more often had ECOG ≥1 (49.9% vs. 13.9% and 22.2%; p=0.042). No differences were observed regarding baseline diagnosis, disease status, bridging therapy, or CAR T-cell product (Table 1).
Outcome analyses were performed according to frailty status before lymphodepletion (Table 1). Rates of cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome (ICANS) were similar across groups. However, proportions of ICU admission were higher in frail patients (26.4%) than in fit (15.2%) and pre-frail (13.4%) patients (P=0.163). QoL was significantly worse in frail patients across all EQ-5D domains (mobility, self-care, usual activities, pain/discomfort, and anxiety (all p<0.05). With a median follow-up of 251

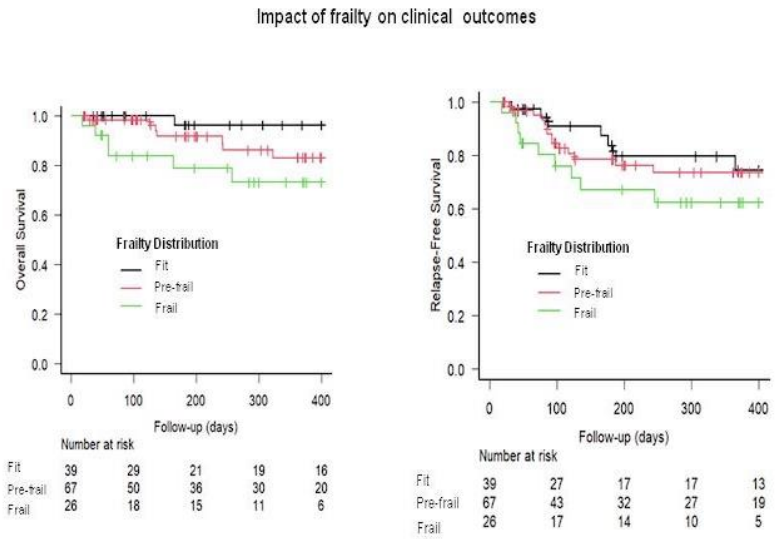
days, frailty was associated with inferior overall survival (OS): 1-year OS rates were 96.3% in fit, 83.2% in pre-frail, and 73.3% in frail patients (p=0.044) (Figure 1). Relapse rates were similar across groups (30.8% vs. 15.4% and 22.4%, p=0.338). The main cause of death was relapse, while non-relapse mortality occurred in 1 of 39 fit patients and 1 of 26 frail patients.

Table 1. Main Results According to Fit, Pre-Frail and Frail States

Information at First Consultation	**All N=132**	**Fit N=28 (21.2)**	**Pre-Frail N=86 (65.2)**	**Frail N=18 (13.6)**	**P value**
Age (range)	55 (47-76)	52 (29-74)	55 (18-76)	62 (38-75)	0.015
Sex					
Male	88 (66.7)	25 (89.3)	53 (61.6)	10 (55.5)	0.015
Female	44 (33.3)	3 (10.7)	33 (38.3)	8 (44.4)	
Baseline Diagnosis					
Acute lymphoblastic leukemia	44 (33.3)	10 (35.7)	29 (33.7)	8 (44.4)	0.755
Lymphoproliferative disorder	88 (66.7)	18 (64.2)	60 (69.7)	10 (55.5)	
Type of CAR-T					
AXI-CEL	54 (40.9)	11 (39.2)	36 (41.8)	7 (38.8)	0.955
ARI0001	78 (59.1)	17 (60.7)	50 (58.1)	11 (61.1)	
Information at CAR T-cell Admission	**All N=132**	**Fit N=39 (29.5)**	**Pre-Frail N=67 (50.9)**	**Frail N=26 (19.7)**	**P value**
Age (range)	55 (47-76)	52 (31-76)	55 (26-76)	61 (18-74)	0.032
Sex					
Male	88 (66.7)	29 (74.3)	49 (73.1)	10 (38.5)	0.003
Female	44 (33.3)	10 (25.6)	18 (26.9)	16 (61.5)	
Baseline Diagnosis					
Acute lymphoblastic leukemia	44 (33.3)	14 (35.9)	22 (32.8)	8 (30.7)	0.884
Lymphoproliferative disorder	88 (66.7)	25 (64.1)	45 (67.1)	18 (69.2)	
Bridge Therapy					
Yes	131 (99.2)	39 (100)	66 (98.5)	26 (100)	0.926
ECOG					
0	90 (75.0)	31 (86.1)	48 (77.4)	11 (50.1)	0.042
1	25 (20.8)	4 (11.1)	12 (19.4)	9 (40.9)	
2	5 (4.1)	1 (2.8)	2 (3.2)	2 (9.0)	
Missing Data	12 (9)	3 (7.6)	5 (7.4)	4 (15.3)	

Disease Status Remission MRD POS Partial Response Progression / Refractory Disease	 13 (9.8) 11 (8.3) 107 (81)	 2 (5.1) 4 (10.2) 33 (84.6)	 9 (13.4) 7 (10.4) 50 (74.6)	 2 (7.6) 0 24 (92)	0.252
Type of CAR-T AXICEL ARI0001	 54 (40.9) 78 (59.1)	 15 (38.5) 24 (61.5)	 26 (38.8) 41 (61.2)	 13 (50.0) 13 (50.0)	0.575
CRS Any grade Grade 2-5	 85 (64.4) 20 (15.2)	 21 (53.8) 6 (15.4)	 45 (67.2) 9 (13.4)	 19 (73.1) 5 (19.2)	 0.226 0.708
ICANS Any grade Grade 2-5	 33 (25.0) 19 (14.3)	 10 (25.6) 7 (17.9)	 15 (22.3) 8 (11.9)	 8 (30.8) 4 (15.3)	 0.7 0.714
ICU Admission	20 (15.2)	4 (10.3)	9 (13.4)	7 (26.9)	0.163
Disease Relapse (Yes)	29 (22.0)	6 (15.4)	15 (22.4)	8 (30.8)	0.338
Death **NRM**	14 (10.6) 3 (2.3)	1 (2.6) 1 (2.6)	7 (10.4) 0	6 (23.1) 2 (7.7)	0.031





Conclusions: Frailty was prevalent and dynamic among CAR T-cell candidates. Frailty was associated with poorer QoL and inferior survival. These findings suggest that routine frailty assessment and consideration of interventions to address frailty prior to CAR T-cell therapy may be beneficial in this group of patients.

Disclosure: Authors have no conflicts of interest.

OS07-03

THE INFLAMIX SCORE PREDICTS VERY SEVERE CRS AND ICU ADMISSION, AS WELL AS PROGNOSIS, IN PATIENTS WITH LBCL TREATED WITH CAR-T THERAPY

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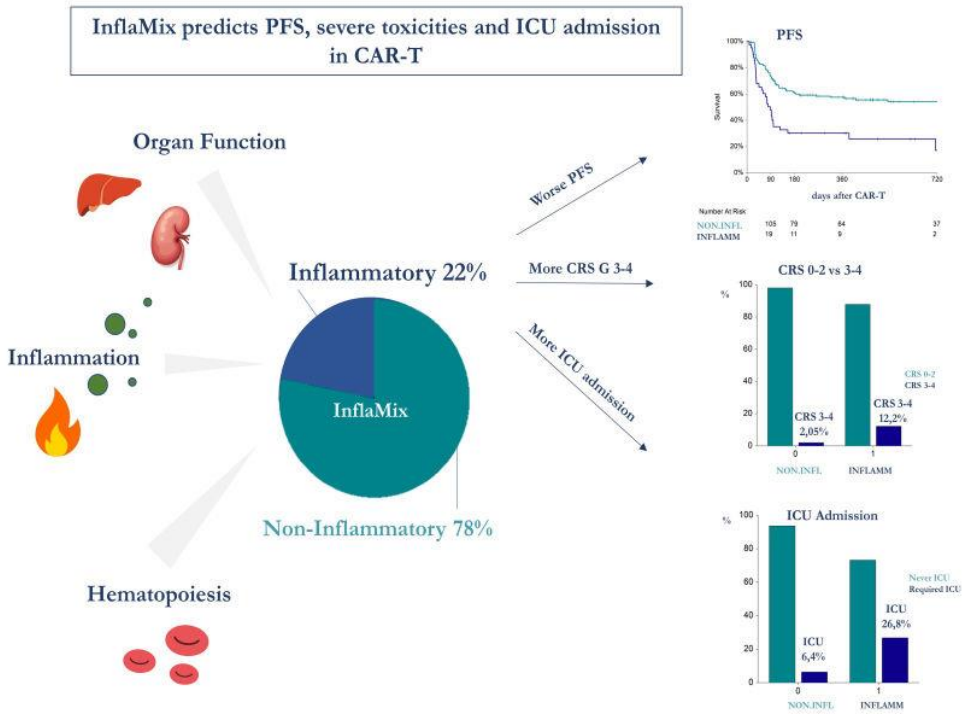
Background: InflaMix is a multiparametric inflammation-based score developed to characterize pre-infusion inflammatory profiles and organ function in candidates for CAR-T therapy. InflaMix can be calculated online from at least two of the following values (hemoglobin, albumin, LDH, CRP, ALP, AST, cytokines (IL-6, IL-10, TNFα), ferritin, D-dimer, WBCs and platelets) and dichotomize patients in Inflammatory and Non-Inflammatory. Early studies suggested a role in predicting toxicity and clinical outcomes. Despite significant advances in CAR-T cell therapy for relapsed/refractory large B-cell lymphoma (R/R LBCL), early prediction of severe inflammatory toxicities and poor outcomes remains challenging. We report a real-world validation of InflaMix in relapsed/refractory large B-cell lymphoma (LBCL), with some insight on prediction of severe toxicities and Intensive Care (ICU) admission, useful for empowering resources allocation strategies.

Methods: A total of 188 LBCL patients infused with commercial anti-CD19 CAR-T cells in two hub centers were retrospectively evaluated and categorized as Non-Inflammatory (n=147, 78%) or Inflammatory (n=41, 22%) according to the InflaMix obtained ≤48 hours before infusion. Clinical endpoints included CRS/ICANS severity, use of tocilizumab and corticosteroids, ICU admission, early infections (day 0–30), cytopenias (early/late ICAHT), progression-free survival (PFS), and competing-risk cumulative incidence of relapse and non-relapse mortality (NRM).

Results: InflaMix confirmed a strong prognostic relevance: inflammatory patients had inferior PFS compared to the non-inflammatory group, with 1-year PFS of 30% vs 57% (HR 2.38; 95% CI 1.54–3.67; p<0.001). Competing-risk analysis showed higher relapse incidence in the inflammatory group (Gray's p=0.004), while NRM stood around 7.5% at 1 year and did not differ significantly (Gray's p=0.722).
Inflammatory patients showed a significantly higher incidence of grade 3–4 CRS (12.2% vs 2.05%, OR 3.13; 95% CI 1.70–5.76, p<0.001,) and an increased risk of ICU admission (26.8% vs 6.4%, OR 2.95, 95% CI 1.77–4.92; p<0.001). In contrast, the association with grade ≥2 ICANS did not reach statistical significance (OR 1.51, CI 0.78-2.89; p=0.215).



No significant correlations were found with the use of tocilizumab (OR 1.55, CI 0.76-3.12; p=0.223), the use of corticosteroids (OR 1.33, CI 0.77-2.27; p=0.299), early infections (OR 1.55, CI 0.86-2.78; p=0.141), or cytopenias (early/late ICAHT) (OR 0.92 CI 0.51-166, p=0.803; OR 0.59 CI 0.15-2.2, p=0.432, respectively).

Conclusions: These results confirm InflaMix as a powerful baseline prognostic tool capable of predicting high-grade CRS (which require vasopressors and/or high flow respiratory support), the need for ICU-level care and inferior PFS. By capturing multidimensional aspects of systemic inflammation and organ function at pre-infusion, InflaMix provides clinically meaningful risk stratification relevant for patient counseling, toxicity mitigation strategies, and optimization of critical-care resource allocation in high-volume CAR-T programs.

Disclosure: Nothing to disclose.

OS07-04

A BASELINE INFLAMMATORY SIGNATURE IDENTIFIES IMPAIRED CD8⁺ T-CELL RECONSTITUTION AND RELAPSE RISK AFTER ALLOHCT IN AML, INDEPENDENT OF TP53 MUTATION AND MRD

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Background:

Maladaptive inflammation confers adverse risk to T cell immunotherapies including immune checkpoint inhibition and CAR-T. However, its effects on hematopoietic cell transplant (HCT) allograft function and efficacy are unknown. *InflaMix*, a point of care tool developed using an unsupervised computational approach in CAR-T cohorts (Raj, *Nat Med* 2025), provides a pragmatic method to quantify deleterious inflammatory states. We hypothesized that *InflaMix* classification before allogeneic HCT (alloHCT) identifies AML patients at risk of treatment failure independent of other high-risk factors such as *TP53* mutation.

Methods: We conducted a single center observational analysis of adults undergoing first standard of care alloHCT for AML between 2014–2024 (n=421). *InflaMix* was derived from laboratory and cytokine variables obtained within 14 days pre-alloHCT (including IL-6, IL-10, TNF, albumin, LDH, hemoglobin, AST, alkaline phosphatase, and CRP). Patients were then classified in inflammatory vs non-inflammatory clusters. Primary endpoints were overall survival (OS), cumulative incidence of measurable residual disease (MRD) relapse assessed by multiparameter flow cytometry (MFC), and non-relapse mortality (NRM). Multivariable Cox models and Fine-Gray models were adjusted for age, conditioning intensity, HLA match, GVHD prophylaxis, *TP53* status, cord blood use, and baseline MRD. *TP53* status was defined by either *TP53* mutation of copy number loss noted by next generation sequencing or 17p chromosomal loss by cytogenetics. Secondary endpoints included graft-versus-host disease-free, relapse-free survival (GRFS) and immune reconstitution.

Results: *InflaMix* classified 43 patients (10.2%) as inflammatory and 378 (89.8%) as non-inflammatory (Table 1). In our multivariable analysis, inflammatory status was independently associated with inferior overall survival (HR 1.59, 95% CI 1.01–2.52, p=0.047). In a competing risks analysis, inflammatory status was associated with a higher cumulative incidence of MRD-defined relapse (sHR 1.59, 95% CI 1.03–2.45, p=0.037) and a trend toward increased non-relapse mortality that did not reach statistical significance (sHR 1.86, 95% CI 0.97–3.56, p=0.060) (Fig. 1A-C). Longitudinal immune profiling demonstrated persistently impaired CD8⁺ T-cell reconstitution following alloHCT among inflammatory patients compared with non-inflammatory patients (Fig. 1D). Consistent with these findings,

inflammatory status was associated with inferior graft-versus-host disease-free, relapse-free survival (HR 1.47, 95% CI 1.04–2.09, p=0.030).

Characteristic	Non-inflammatory n = 378[1]	Inflammatory n = 43[1]
Age	63 (52, 69)	63 (57, 68)
Sex		
F	172 (46%)	22 (51%)
M	206 (54%)	21 (49%)
Conditioning Intensity		
Ablative	155 (41%)	16 (37%)
Reduced intensity	210 (56%)	25 (58%)
Non-ablative	13 (3%)	2 (5%)
HLA match		
Haploidentical	31 (8%)	4 (10%)
Matched	262 (69%)	26 (60%)
Mismatched	85 (23%)	13 (30%)
Graft Source		
Bone Marrow	32 (9%)	8 (19%)
Cord Blood	28 (7%)	5 (11%)
Peripheral Blood Stem Cells	318 (84%)	30 (70%)
Donor Type		
Related	104 (28%)	9 (21%)
Unrelated	274 (72%)	34 (79%)
GVHD prophylaxis		
PTCy-based	112 (30%)	9 (21%)
Non-PTCy-based	225 (59%)	33 (77%)
Ex vivo T cell depletion	41 (11%)	1 (2%)
TP53 mutation status		
TP53^{mut}	44 (12%)	14 (33%)
TP53^{wt}	334 (88%)	29 (67%)
Acute GVHD		
Yes	228 (65%)	29 (69%)
No	125 (35%)	13 (31%)
Unknown	25	1

[1] median (q1, q3); n (%)

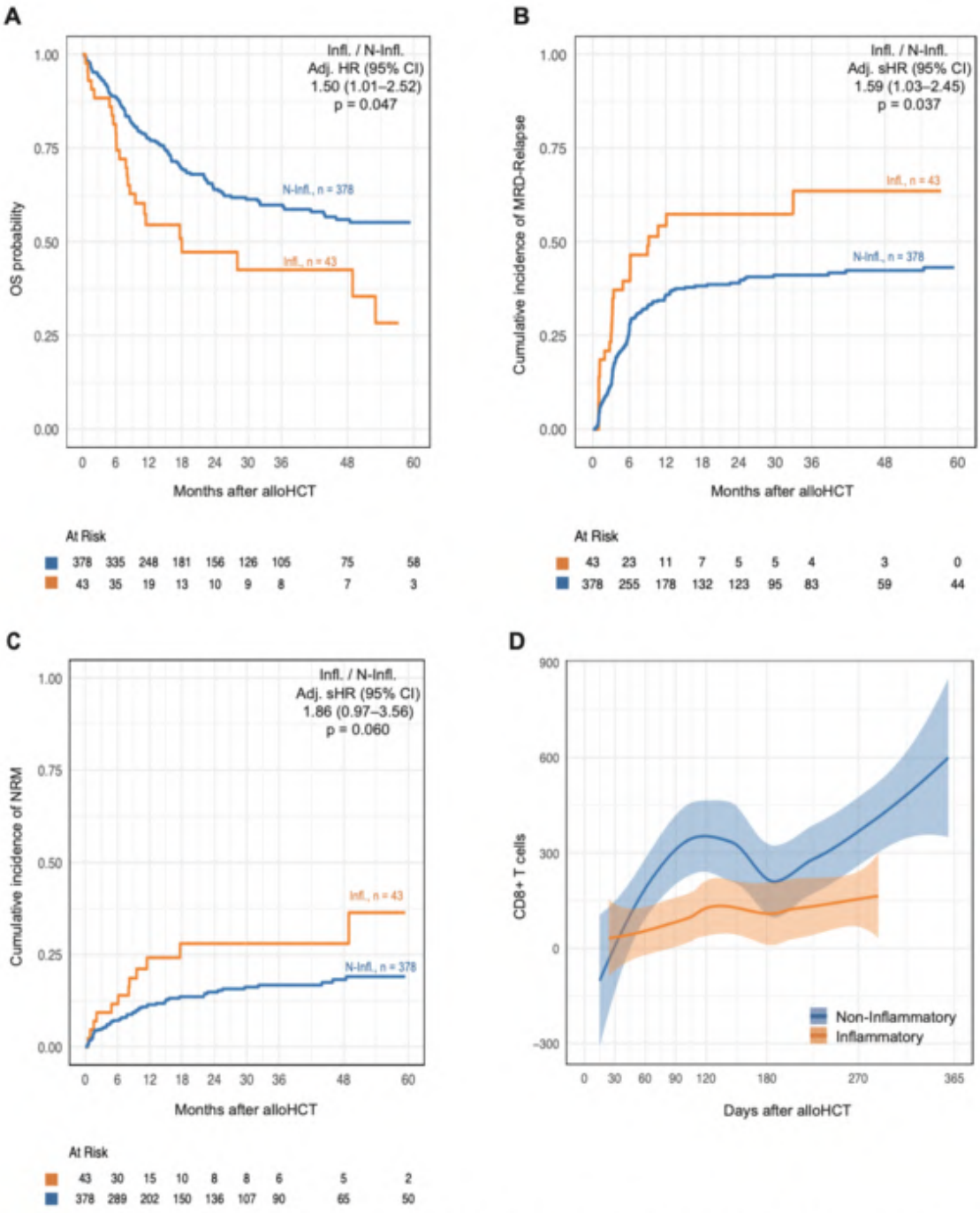

Figure 1 | Pre-transplant inflammatory status is associated with overall survival, relapse risk, non-relapse mortality, and immune reconstitution following alloHCT in AML. (A) Kaplan–Meier estimates of overall survival (OS) stratified by inflammatory (Infl.) versus non-inflammatory (N-Infl.) status following allogeneic hematopoietic cell transplantation (alloHCT). **(B)** Cumulative incidence of MRD-defined relapse and **(C)** cumulative incidence of non-relapse mortality (NRM), accounting for competing risks and stratified by inflammatory status. **(D)** Smoothed trajectories of CD8+ T-cell reconstitution over time following alloHCT, stratified by inflammatory status. Hazard ratios (HRs) for OS and subdistribution hazard ratios (sHRs) for competing-risks endpoints were estimated using multivariable Cox and Fine–Gray models, respectively.

Conclusions: A pre-alloHCT inflammatory state captured by *InflaMix* confers prognostic value over *TP53* mutation status and pre-transplant MRD, independently identifying adults with AML at increased risk of post-transplant relapse and mortality. Notably, inflammatory clustering correlated with impaired post-transplant $CD8^+$ T-cell reconstitution, potentially explaining the heightened risk of relapse and non-relapse mortality. These findings suggest that systemic inflammation prior to transplant may link relapse biology and post-transplant immune dysfunction, identifying a high-risk population that may benefit from inflammation-informed risk stratification and targeted interventions.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

OS07-05

CARE-BMT RISK SCORE: CARDIOVASCULAR RISK STRATIFICATION IN 104 CONSECUTIVE PATIENTS UNDERGOING ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Cardiovascular complications remain a major cause of morbidity and mortality after allogenic stem cell transplantation (allo-HCT). Identifying high-risk patients during pre-transplant assessment is essential, especially in the context of PTCy-based GvHD prophylaxis, which carries potential cardiotoxicity. The recent American Heart Association (AHA) scientific statement recommends the use of CARE-BMT Risk Score to improve cardiovascular risk stratification and to guide management in transplant candidates. We aimed to evaluate the predictive performance of the CARE-BMT Risk Score in a cohort of patients undergoing allo-HCT with PTCy and to describe the main characteristics of early and late cardiovascular events (CE).

Methods: We retrospectively analyzed all consecutive adult patients who underwent allo-HCT with PTCy as GvHD prophylaxis at our center between April 2023 and September 2024. Patients were stratified into CARE-BMT risk categories according to AHA recommendations. CE were evaluated at day +100 and 1-year post-transplant. CE included cardiovascular death, non-fatal myocardial infarction, stroke, new-onset heart failure, new atrial fibrillation/flutter and sustained ventricular tachycardia. Pre-transplant cardiologic evaluation included baseline pro-BNP and T-troponin, measured before conditioning.

Results: Patients and transplant characteristics are reported in Table 1. A total of 104 patients were included, with a median age of 54 years (range 19-74). According to the CARE-BMT Risk Score, 53 patients (51%) were classified as high-risk and 51 (49%) as intermediate-risk. PTCy was administered at 50 mg/kg in 94 patients, while 10 (2 intermediate- and 8 high-risk) received a reduced dose of 40 mg/kg according to institutional policy.
Overall, 8 patients (7.7%) experienced CE after HCT, all among the high-risk group. Within the first 100 days after allo-HCT, CE included 1 stroke and 5 arrhythmias (4 atrial fibrillation and 1 atrial flutter). At 1-year, 1 cardiovascular death and 1 paroxysmal supraventricular tachycardia were observed. 15.1% of high-risk patients and 0% of intermediate-risk experienced a CE (p<0.01).
Baseline elevation of both pro-BNP and T-troponin was detected in 17 patients, 15 of whom belonged to the high-risk category. High-risk patients with baseline elevation of both pro-BNP and T-troponin showed a higher incidence of CE (33.3% *vs* 7.9%, p=0.03).

Table 1. Patient and allo-HCT characteristics

Characteristics of patients	Overall population, n	%
Age		
<50 y	31	30
50-54 y	12	11
55-64 y	34	33
≥ 65 y	27	26
Disease		
Acute myeloid leukemia	50	48
Acute lymphoblastic leukemia	12	11
Chronic lymphocytic leukemia	3	3
Myelodysplasia and Myeloproliferative neoplasms	29	28
Lymphoma and Myeloma	9	9
Non-malignant disease	1	1
Disease status at transplant		
Complete/partial remission	70	67
Active disease	34	33
Donor type		
Matched-related donor (MRD)	12	12
Matched-unrelated donor (MUD)	72	69
Mismatched-related donor (MMRD)	20	19
Cardiovascular history		

Arrhythmias	4	4
Cerebrovascular event	2	2
Dyslipidemia/diabetes	13	12
Heart failure	3	3
Hypertension	22	21
Peripheral arterial disease	2	2
Acute coronary syndrome	6	6
CARE-BMT risk score		
High (≥5)	53	51
5 point	28	
6 point	14	
7 point	9	
8 point	2	
Intermediate (2-4)	51	49
2 point	14	
3 point	13	
4 point	24	
Low (≤2)	0	

Conclusions: The CARE-BMT Risk Score confirmed its ability to identify patients at increased cardiovascular risk after allo-HCT in our single center experience. Moreover, baseline pro-BNP and T-troponin further improved our ability to stratify these high-risk patients, suggesting that combined biomarker assessment may provide additional predictive value beyond the CARE-BMT Risk Score. Additional studies are warranted to optimize cardiovascular risk prediction, guide individualized transplant strategies (including PTCy dose modulation), and assess long-term outcomes.

Disclosure: Nothing to declare.

OS08-04

CD19 CHIMERIC ANTIGEN RECEPTOR T CELLS GENERATED USING A PIGGYBAC TRANSPOSON VECTOR FOR ACUTE LYMPHOBLASTIC LEUKEMIA: A PHASE I STUDY

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Background: CD19-directed chimeric antigen receptor T cell (CD19 CAR-T cell) therapy achieves high remission rates in patients with relapsed or refractory B-cell hematologic malignancies. However, its widespread implementation is hampered by the substantial manufacturing costs associated with viral vector-based production. To overcome this issue, we developed a clinically effective, cost-efficient CAR-T platform by generating CAR-T cells

using a nonviral piggyBac transposon gene-transfer system and initiated a Phase I clinical trial to evaluate toxicity, the maximum tolerated dose, and clinical efficacy. Here, we report the trial findings.

Methods: CD19 CAR-T cells were generated using a CD19 CAR-expressing transposon vector together with a piggyBac transposase expression vector. The Phase I trial employed a modified 3+3 dose-escalation design, enrolling pediatric and adult patients with relapsed or refractory B-precursor acute lymphoblastic leukemia. Patients in Cohort 1 (age: 16–60 years) and 2 (age: 1–15 years) received 1×10^5 CAR-T cells/kg, while patients in Cohorts 3 and 4 (age: 1–60 years) received 3×10^5 CAR-T cells/kg and 1×10^6 CAR-T cells/kg, respectively. All patients underwent lymphodepletion (fludarabine [25 mg/m²/day] and cyclophosphamide [250 mg/m²/day] for 3 consecutive days), followed by a single infusion of the CAR-T cell product. Safety, cytokine release syndrome (CRS), neurotoxicity, expansion kinetics, early antileukemic responses, and long-term outcomes were systematically assessed.

Results: As of December 2025, a total of 12 patients (n = 3 in each cohort) had received the CAR-T cell infusion. Flow cytometry analysis confirmed CAR-T cell expansion, with detectable circulating CAR-T cells in all patients. Generally, peak expansion occurred approximately 7–10 days after infusion, demonstrating expansion kinetics comparable to those reported for conventional viral vector-derived CAR-T products, with no evidence of delayed or impaired proliferation associated with our nonviral piggyBac platform. No dose-limiting toxicities (DLTs; defined as [1] Grade ≥4 nonhematologic toxicities, [2] Grade ≥4 CRS, [3] Grade 4 graft-versus-host disease, or [4] Grade 3 nonhematologic toxicities or Grade 3 CRS that failed to improve to Grade 2 within 4 weeks of infusion) were observed. CRS occurred in six patients (Grade 3, n = 1; Grade 1–2, n = 5). At 28 days after infusion, four patients achieved complete remission, seven achieved complete remission with incomplete hematologic recovery, and one showed no response. The median follow-up was 33 months (range, 3–70), with a 2-year disease-free survival (DFS) of 73.3% (n = 12), including three documented relapses. Among the nine patients who had isolated extramedullary relapse at enrollment, the 2-year DFS was 75.0%.

Conclusions: In this first-in-human trial, piggyBac transposon-engineered CD19 CAR-T therapy demonstrated an excellent safety profile, with no DLTs or severe adverse events. The therapy achieved high remission rates and durable disease control, even in individuals with isolated extramedullary relapse. Collectively, these findings support the safety, biological robustness, and long-term efficacy of this nonviral CAR-T platform, highlighting its potential as a scalable, low-cost alternative suitable for broader clinical implementation.

Clinical Trial Registry: jRCTa040190099

Disclosure: Yoshiyuki Takahashi has IP licensing agreements with Japan Tissue Engineering Co. Ltd (J-TEC) and receives research funding from J-TEC.
Nobuhiro Nishio has IP licensing agreements with Japan Tissue Engineering Co. Ltd (J-TEC).
All other authors declare no conflicts of interest.

OS08-05

CD7-TARGETED CHIMERIC ANTIGEN RECEPTOR (CAR)-T CELL THERAPY SHOWS GOOD EFFICACY AND SAFETY IN REFRACTORY/RELAPSED MIXED PHENOTYPE ACUTE LEUKEMIA (MPAL)

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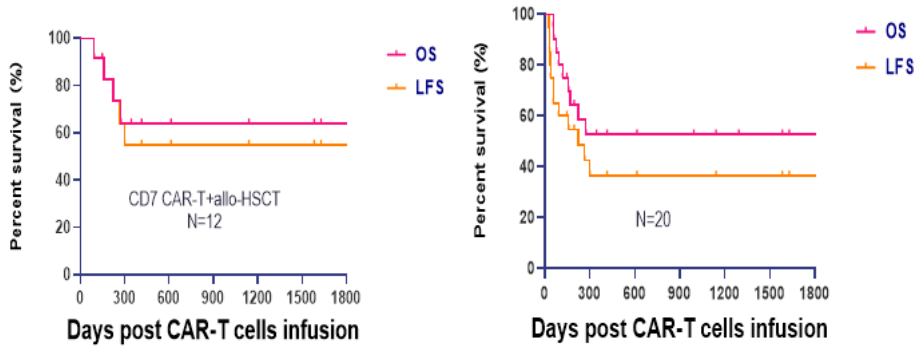
Background: Mixed-phenotype acute leukemia (MPAL) is a rare and aggressive malignancy. Patients with relapsed or refractory (r/r) disease have limited therapeutic options. Here, we report the safety and efficacy of CD7CAR-T for r/r CD7-positive MPAL from our phase I clinical trial (https://clinicaltrials.gov NCT04938115).

Methods: Peripheral blood (PB) mononuclear cells were collected from 19 patients and 1 from prior transplant donor. A novel approach was used to generate "naturally selected" CD7 CAR (NS7CAR) T cells that overcome CD7-directed fratricide without gene editing. NS7CAR is a second-generation murine-based CAR containing 4-1BB and CD3ζ co-stimulatory domains. Before CAR-T cell infusion, patients received bridging chemotherapy to control rapid disease progression, followed by a lymphodepleting regimen of fludarabine (30 mg/m^2/d) and cyclophosphamide (300 mg/m^2/d) for three days (day -5 to day -3). The median production time for NS7CAR-T was 14 days.

Results: Twenty patients with CD7-positive expression ≥ 80% MAPL were enrolled and received NS7CAR-T therapy. The median age was 26.5(8-58) years. At enrollment, the median bone marrow (BM) blasts by flow cytometry (FCM) were 12.0% (0.08-74.4%), and 8 patients had extramedullary disease (EMD). Six patients were relapsed from prior allogeneic hematopoietic stem cell transplantation (allo-HSCT). All patients received a single NS7CAR-T infusion, 5 with a low d
ose (1-5 × 10^5/kg) and 15 with a medium dose (1.0 × 10^6/kg). The median transduction efficiency was 96.6% (32.0-99.1%).
About 1-month post-infusion, in BM, 18/20 (90%) patients achieved minimal residual disease (MRD)-negative complete remission (CR). Among the 8 patients with EMD, the overall response rate was 6/8 (75%), including 5 CR and 1 partial response, and 2 showed no response. Overall, 15/20 patients achieved CR both in BM and EMD.
With a median follow-up of 248 days (range: 55–1810), the 3-year overall survival (OS) and leukemia-free survival (LFS) for the entire cohort were 52.6% and 36.4%. Within 3 months after CAR-T, 12 patients in CR underwent consolidative allo-HSCT (including 3 second transplants), resulting in a 3-year OS and LFS of 64.2% and 55%, respectively. For the remaining 3 CR patients, 1 remained leukemia-free till 194 days, and 2 died.



Among the other 7 patients less than CR, 3 died from disease progression, and 4 received salvage transplantation, of whom 2 died.
Following NS7CAR-T infusion, most patients developed mild cytokine release syndrome (CRS) (95% ≤ grade II), and only 1 experienced grade III CRS. None had neurotoxicity. Two of the 6 patients with prior transplant history developed GVHD (1 grade I, 1 grade IV).
The median peak proportion of circulating CD7 CAR-T cells in PB by FCM was 82.5% (25.8–96.5%), occurring on day 14 (7–25). By qPCR, the median peak CAR-T copy number was 3.64 × 10^5 copies/μg DNA (0.28–15.7 × 10^5), observed on day 19 (10–29).

Conclusions: This study demonstrates that NS7CAR-T cells are a promising therapeutic option for CD7-positive MPAL, including patients who relapsed after transplantation. Consolidative allo-HSCT further improves survival outcomes. Further studies with longer follow-up and larger cohorts are warranted to confirm the long-term efficacy and durability of NS7CAR-T therapy in MPAL.

Clinical Trial Registry: NCT04938115, https://clinicaltrials.gov

Disclosure: All the listed authors have no conflict of interest to declare.

OS08-06

LONG-TERM OUTCOMES OF SEQUENTIAL CD7 CAR-T THERAPY AND SECOND ALLOGENEIC TRANSPLANTATION FOR T-ALL/LBL RELAPSED AFTER A PRIOR ALLO-TRANSPLANT

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Background: Relapsed T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) after allogeneic hematopoietic stem cell transplantation (allo-HSCT) has a poor prognosis with limited therapeutic options. While CD7-targeted chimeric antigen receptor (CAR) T-cell therapy can induce remission, the long-term outcomes remain suboptimal. The role of a

consolidative second allo-HSCT following CAR-T-induced remission is not well defined. The purpose of this study is to evaluate the long-term efficacy and safety of a second allo-HSCT performed following CD7 CAR-T therapy for T-ALL/LBL patients who relapsed after a prior transplant.

Methods: This study included 18 patients (16 T-ALL, 2 T-LBL) who, after post-first-transplant relapse, achieved bone marrow minimal residual disease (MRD)-negative complete remission (CR) with CD7 CAR-T therapy and proceeded to a second allo-HSCT at our centers between January 2021 and January 2021. Outcomes including survival, relapse, and transplant-related complications were analyzed. Follow-up was until September 30, 2025, with a median post-second-transplant follow-up of 510 days (range: 32-1352).

Results: Their first allo-HSCT was performed using matched sibling (n=4), haploidentical (n=13), or unrelated (n=1) donors. Following the first transplant, 16 patients experienced morphological relapse and 2 patients had MRD-positive. Extramedullary disease was present in 12 patients at the time of relapse. Prior to the second transplant, CD7 CAR-T cells were administered, derived from the original transplant donor in 5 patients and from the recipient in 13 patients.
The median age at second HSCT was 29.7 years (range: 13.8-55.4). Prior to second HSCT, all 18 patients (100%) achieved MRD-negative CR in bone marrow. Of 12 patients with extramedullary disease, 11 (91.7%) achieved CR and 1 achieved partial remission (PR) after CD7 CAR-T. All patients received a transplant from a different donor at the time of the second HSCT. Donors for the second transplant were haploidentical (n=15) or matched unrelated (n=3). Conditioning regimens were TBI-based (n=10), busulfan/ melphalan -based (n=8). The estimated 3-year overall survival (OS) and leukemia-free survival (LFS) after the second transplant were 46.4% (95% CI: 21.9-71.0%) and 44.4% (95% CI: 21.5-67.4%), respectively. The 3-year cumulative incidence of relapse (CIR) and non-relapse mortality (NRM) were 16.7% (95% CI: 5.9-46.8%) and 48.0% (95% CI: 28.8-80.2%), respectively. The day-100 cumulative incidences of grade II-IV and grade III-IV acute graft-versus-host disease (aGVHD) were 66.7% (95% CI: 48.1-92.4%) and 44.4% (95% CI: 26.5-74.5%), respectively. The 1-year cumulative incidence of chronic GVHD (cGVHD) and moderate-severe cGVHD was 34.7% (95% CI: 18.1-66.5%) and 11.1% (95% CI: 3.0-41.0%), respectively. The day-100 cumulative incidences of CMV and EBV viremia were 66.7% (95% CI: 48.1-92.4%) and 22.2% (95% CI: 9.4-52.7%), respectively.
Nine patients died after the second transplant: 3 from infection, 2 from GVHD, 1 from TA-TMA, 1 from relapse, 1 from kidney failure, and 1 from intracranial hemorrhage.

Characteristics	Patients(n=18)
ETP-ALL/LBL	
Yes	4(22.2%)
No	18(77.8%)
Relapse/MRD involvements site when CD7-CAR-T therapy enrollment; n (%)	

BM MRD positive only	2(11.1%)
BM morphological relapse alone	4(22.2%)
BM+EMD relapse	11(61.1%)
EMD relapse alone	1(5.6%)
Lines of treatment prior to NS7CAR-T after relapse following the first allo-HSCT; median (range)	2(1-4)
Number of chemotherapy cycles prior to NS7CAR-T after relapse following the first allo-HSCT; median (range)	2(0-7)
BM blasts before CAR-T enrollment by FCM; median (range)	5.4%(0-91.0%)
BM blasts before CAR-T infusion by FCM; median(range)	0.8%(0-94.5%)
Dose of CD7-CAR-T cells; n (%)	
5×10^5/kg	6(33.3%)
1×10^6/kg	12(66.7%)
Transfection rate of CAR; median (range)	96.4%(59.4%-99.1%)

Conclusions: For T-ALL/LBL patients relapsing after a first allo-HSCT, CD7 CAR-T therapy can effectively induce remission, making a consolidative second allo-HSCT feasible. This sequential approach offers a potential curative strategy for this high-risk population. However, significant transplant-related mortality, primarily from infections and GVHD, remains a major challenge. Further investigation with larger cohorts and longer follow-up is warranted to optimize this treatment strategy.

Disclosure: Nothing to declare.

OS08-08

FIRST-IN-HUMAN TRIAL OF IL15-ACTIVATED CIK CELL THERAPY POST-HCT: DURABLE REMISSION AND SEROTHERAPY-ASSOCIATED IMMUNE RECONSTITUTION IN HIGH-RISK HEMATOLOGIC MALIGNANCIES

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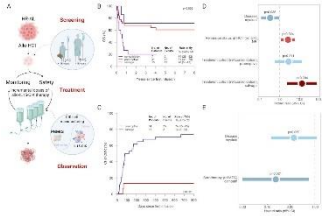
Background: Early relapse after allogeneic hematopoietic stem cell transplantation (HCT) remains a major cause of treatment failure and poor survival, particularly in pediatric patients and individuals with substantial treatment-related toxicity, for whom effective salvage options are often unavailable or unapproved. This clinical gap underscores the need for preventive, well-tolerated, and broadly accessible post-HCT immunotherapies. We conducted a first-in-human, disease-burden–guided study to evaluate the feasibility, safety, and efficacy of donor-derived IL-15–activated cytokine-induced killer cells (IL15-CIK), which combine T-cell and natural killer cell properties, for post-HCT disease control.

Methods: Combined outcomes from a prospective, multicenter phase I/II trial (EudraCT 2013-005446-11) and a parallel pilot study are reported, comprising 56 cases with high-risk leukemia treated with IL15-CIK monotherapy for relapse prevention or relapse management following HLA-matched or HLA-mismatched transplantation (n=28 each). According to disease status at first infusion, cases were stratified into consolidation (n=7; complete molecular remission [CMR]), preemptive (n=34; complete remission [CR] with impending relapse and <5% bone marrow blasts), or salvage cohorts (n=15; overt relapse with ≥5% bone marrow blasts). In total, 169 IL15-CIK infusions were administered without lymphodepletion or graft-versus-host disease (GvHD) prophylaxis, either as single infusions (29%) or within predefined dose-escalation regimens (71%).

Results: Centralized, on-demand IL15-CIK manufacturing and shipment to five centers in Germany proved feasible and scalable, with treatment being well tolerated. Therapy-related adverse events and GvHD were infrequent, predominantly mild, and clinically manageable. Acute GvHD grades 1–2 and grade 3 occurred in 27% and 4% of patients, respectively, with no extensive chronic GvHD or treatment-related mortality observed. Beyond early responses at day 100, the cumulative incidence of CMR at day 700 reached 74% in the preemptive cohort compared with 13% in the salvage cohort, highlighting the advantage of early, preventive intervention. After a median follow-up of 7.3 years (range, 6.8–8.7), 5-year overall survival (OS) was 71% in the consolidation cohort, 61% in the preemptive cohort, and 20% in the salvage cohort. Five-year progression-free survival was 50% overall and reached 69% in pediatric acute myeloid leukemia, a population with substantial unmet clinical need. To inform future risk-adapted strategies, predictors of outcome were analyzed. In multivariable analysis, myeloid malignancy (vs lymphoblastic) was independently associated with superior OS (p=0.036), whereas high leukemic burden at first IL15-CIK infusion (≥5% bone marrow blasts; p=0.004) and refractory disease at HCT (p=0.024) were associated with inferior OS. Prior serotherapy emerged as the only factor significantly associated with cumulative incidence of relapse (p=0.021), with lower relapse rates observed after Campath compared with ATG.

Conclusions: Donor-derived IL15-CIK monotherapy is feasible, safe, and confers durable relapse-preventive activity after allogeneic HCT. Treatment efficacy is primarily determined by disease burden at the time of intervention, while prior serotherapy emerges as a key modulator of post-HCT relapse risk. Beyond the IL15-CIK platform, these findings have broader implications for post-transplant immunotherapy and support IL15-CIK as a viable alternative to donor lymphocyte infusion.



Clinical Trial Registry: EudraCT 2013-005446-11

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All other authors declare no conflicts of interest.

OS12-02

COST-EFFECTIVENESS OF ORCA-T VS ALLO-HCT WITH CONVENTIONAL GVHD PROPHYLAXIS FOR THE TREATMENT OF ADVANCED HEMATOLOGIC MALIGNANCIES IN THE UNITED STATES

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) is a potentially curative therapy for patients with hematologic malignancies, but its success is limited by GVHD, which is associated with substantial morbidity, mortality, and economic burden. Orca-T, an investigational, high-precision cell therapy, demonstrated improvement in survival free

of moderate-to-severe chronic GVHD compared to conventional allo-HCT with tacrolimus/methotrexate (TAC/MTX) in the pivotal Phase 3 Precision- T trial. Given the rising costs of GVHD therapies and the long-term care burden, assessing the economic value of Orca-T is essential. To assess the cost effectiveness of Orca-T compared to conventional allo-HCT with TAC/MTX GVHD prophylaxis from a US health system perspective.

Methods: A three-state partitioned survival model (relapse-free, relapsed, and dead) with monthly cycles and a lifetime horizon was developed. The intervention arm included Orca-T with single-agent tacrolimus, while the comparator arm included conventional allo-HCT with TAC/MTX GVHD prophylaxis. Overall survival and relapse-free survival data from the Phase 3 Precision-T study were incorporated using a cure-mixture modeling approach to estimate long-term survival and relapse status for patients. Costs included conditioning regimens, index procedure length of stay, Orca-T acquisition, donor procurement (conventional allo-HCT with TAC/MTX only), acute GVHD (aGVHD) and chronic GVHD (cGVHD) management, infection management, and terminal care. Model outcomes included life-years, quality-adjusted life-years (QALYs), and direct healthcare costs. Both costs and outcomes were discounted at 3% annually.

Results: Orca-T was associated with lower lifetime costs of $1,412,864 compared to $2,253,413 for conventional allo-HCT with TAC/MTX with a lifetime cost savings of $840,548 per patient. The costs associated with Orca-T acquisition were offset by savings from aGVHD, infection, and cGVHD management costs. The cGVHD management costs were $797,650 for Orca-T compared to $2,068,847 for conventional allo-HCT with TAC/MTX. Orca-T was also associated with 15.80 QALYs compared to 11.45 QALYs with conventional allo-HCT with TAC/MTX over a patient's lifetime. Given the combination of cost savings and QALY gains, Orca-T is dominant over conventional allo-HCT with TAC/MTX.

Conclusions: Over a patient's lifetime, the model demonstrated that Orca-T can reduce the overall economic burden compared to conventional allo-HCT with TAC/MTX, with the majority of cost savings driven by reductions in aGVHD, infection, and cGVHD management costs. Given the considerable clinical and economic impact of these complications, Orca-T represents a high value therapeutic option for adults with advanced hematologic malignancies, offering both superior clinical outcomes and economic benefits.

Clinical Trial Registry: NCT05316701 https://clinicaltrials.gov/study/NCT05316701

Disclosure: Rawan Faramand reports Sanofi consultancy and support from Orca Bio for travel for the ASCO 2024 annual meeting. Anna Pavlova reports being an employee and equity holder at Orca Bio. James Scott McClellan reports being an employee, officer, and equity holder at Orca Bio. Matia Saeedian has nothing to declare. Miguel-Angel Perales reports equity ownership in Orca Bio. Andrea Blank reports being an employee and equity holder at Orca Bio. Rocio Manghani reports being employed by Orca Bio. Shivani Yadav has nothing to declare.

OS13-03

HOSPITAL EXEMPTION FOR HEIDAGENLECLEUCEL (HEIDI-CEL), A THIRD GENERATION CD19.CAR T CELL PRODUCT IN GERMANY

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Background: Chimeric antigen receptor (CAR)-transduced T cells have become an important instrument in the armamentarium of the hematologist for the treatment of CD19+ disease in patients. Hitherto, no commerical CAR-T-cell product has been approved on the market for patients with chronic lymphatic leukemia (CLL). In a lengthy and cumbersome process, we established in-house manufacturing of CD19.CAR-T-cell products for CLL patients in accordance with Good Manufacturing Practice (GMP). Here, we describe the entire way from an investigator-initiated trial (IIT) up to the achievement of a hospital exemption which enables us to open new medical and financial strategies in current clinical practice in Germany.

Methods: In our investigator-initiated trial (IIT) HD-CAR-1 trial (NCT03676504 (clinicaltrials.gov); EudraCT-No. 2016-004808-60), 43 patients with CD19+ leukemias and non-Hodgkin's lymphoma consented treatment by our in house-product heidagenlecleucel (Heidi-cel). Subsequently, the patients underwent leukapheresis. In our GMP core facility, we manufactured 3rd generation Heidi-cel, i.e. (CD28/4-1BB) CAR-T-cells. Patients obtained the CAR-T-cells after standard conditioning with fludarabine and cyclophosphamide, and were followed-up clinically.
To obtain a hospital exemption, we submitted non-clinical and clinical data, quality data, a risk mitigation plan (RMP), a pharmacovigilance surveillance master file (PSMF) as well as a product information (PI) to the federal regulatory authority Paul-Ehrlich-Institut (PEI).

Results: For all patients undergoing leukapheresis, a CAR-T-cell product was successfully manufactured. Nine heavily pretreated patients with refractory or relapsed CLL obtained CD19.CAR-T cells at escalated dose levels up to 200 × 10^6 CAR-T-cells/m^2. In-house CD19.CAR-T-cell manufacturing was successful for all patients. Not even a single case of neurotoxicity (ICANS) was observed. One case of grade 3 cytokine release syndrome was reported. By day 90, six patients (67%) achieved a CR, five of these (83%) with undetectable MRD. With a median follow-up of 27 months, 2-year PFS and OS were 30% and 69%, respectively.
Based on these encouraging results, we started a harsh and meticulous review process with our regulators at the PEI. After 2.5 years of a responsorial submission process, we eventually obtained a hospital exemption for r/r CLL patients from the PEI.

Conclusions: This is a report on the definitively first time in Germany, that the PEI issued a hospital exemption for an ATMP, i.e. for our in-house manufactured CAR T cell product, designated heidagenlecleucel (Heidi-cel). This is remarkable for various reasons: simplification of logistics, increased flexibility, development and clinical testing of own approaches, achievement of autarky by strengthening of know-how in vector design and

production of genetically modified cells and thus cost reduction in the German healthcare system.

Clinical Trial Registry: HD-CAR-1 trial (NCT03676504 (clinicaltrials.gov); EudraCT-No. 2016-004808-60)

Disclosure: The authors have nothing to declare with respect to this work. This academic trial has been funded by the NCT Heidelberg and the University Hospital Heidelberg (UKHD).

OS13-05

COMPARATIVE OUTCOMES OF LISOCABTAGENE MARALEUCEL (LISO-CEL) VERSUS AN EXTERNAL CONTROL ARM (ECA) IN PATIENTS WITH THIRD-LINE OR LATER (3L+) RELAPSED/REFRACTORY (R/R) MANTLE CELL LYMPHOMA (MCL)

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Background: In the MCL cohort of TRANSCEND NHL 001 (NCT02631044), the CD19-directed CAR T cell product liso-cel demonstrated high CR rate and deep, durable responses in heavily pretreated patients with 3L+ R/R MCL (Wang M, et al. *J Clin Oncol* 2024). This study compared efficacy outcomes observed with liso-cel in the MCL cohort with standard-of-care (SOC) treatments used in routine clinical practice.

Methods: An ECA cohort was developed using real-world data from the United States (Flatiron Health database; data cutoff: 02/28/2024) and clinical/hospital sites in 4 European countries (France, Germany, Spain, and United Kingdom; data cutoff: 06/30/2024), applying key eligibility criteria from the MCL cohort of TRANSCEND NHL 001. Propensity score methodologies balanced the ECA to the TRANSCEND NHL 001 MCL cohort by prespecified baseline characteristics and prognostic factors (age, refractory to last therapy, ECOG score, MCL morphology, number of prior therapies, prior ASCT, refractory to Bruton tyrosine kinase inhibitor [BTKi] therapy, and simplified mantle cell lymphoma International Prognostic Index score). Balancing was performed using trimmed, stabilized inverse probability of treatment weighting (IPTW).
The primary analysis utilized the liso-cel–treated efficacy analysis cohort (LTEAC [n=75]; patients with PET-positive disease who failed ≥2 prior lines of systemic therapy, including a BTKi, alkylating agent, and rituximab [or other CD20-targeted agent] and received liso-cel at a target dose of 100×10^6 CAR^+ T cells). Sensitivity analyses included: the liso-cel efficacy

analysis cohort (LEAC [n=81]; the LTEAC plus 6 patients who received liso-cel at a target dose of 50×10^6 CAR^+ T cells) and the leukapheresed cohort (LKC [n=104]; all eligible patients who underwent leukapheresis).
The primary endpoint was ORR. Secondary endpoints included CR rate, PFS, time to next treatment (TTNT), OS, and duration of response (DOR). Response data were by investigator assessment. Generalized linear models estimated relative risk for ORR and CR rate, and Cox proportional hazards models estimated HR for PFS, TTNT, OS, and DOR.

Results: A total of 457 patients (Europe, n=197; United States, n=260) were included in the ECA. SOC regimens used in the 3L+ R/R MCL setting included chemoimmunotherapy (22.1%), covalent BTKi (19.7%), lenalidomide-based regimens (17.7%), bortezomib-based regimens (10.9%), CD19 CAR T cell therapy (brexucabtagene autoleucel; 10.1%), venetoclax-based regimens (6.3%), noncovalent BTKi (4.2%), chemotherapy (3.9%), and HSCT (2.6%).
After IPTW adjustment, liso-cel treatment was associated with statistically significant improved outcomes versus SOC for the primary (ORR) and secondary endpoints (CR rate, PFS, and OS; **Table**). Notably, patients who received liso-cel achieved an ORR approximately twice as high (79.6%) and a CR rate nearly 3 times greater (64.5%) than those treated with SOC (39.4% and 21.6%, respectively). Liso-cel reduced the risk of progression or death by 35.0% and the risk of death by 40.0%. TTNT and DOR also numerically favored liso-cel. Sensitivity analyses were consistent with the primary analysis.

Conclusions: Liso-cel demonstrated significantly better efficacy than SOC therapies, establishing its role as an important new treatment for patients with 3L+ R/R MCL who have received a minimum of 2 prior lines of systemic therapy, including treatment with a BTKi.

Table. Comparison of efficacy endpoints adjusted for trimmed, stabilized IPTW between the LTEAC, LEAC, LKC, and ECA cohort

	LTEAC (n=75) vs ECA cohort (n=457)	**LEAC (n=81) vs ECA cohort (n=457)**	**LKC (n=104) vs ECA cohort (n=457)**
ORR	***RR, 2.0 (1.7–2.5)***	***RR, 2.0 (1.7–2.5)***	***RR, 1.7 (1.4–2.2)***
CR rate	***RR, 3.0 (2.3–4.0)***	***RR, 3.1 (2.3–4.1)***	***RR, 2.7 (2.0–3.6)***
PFS	***HR, 0.65 (0.44–0.97)***	***HR, 0.63 (0.43–0.93)***	***HR, 0.57 (0.39–0.84)***
OS	***HR, 0.60 (0.39–0.93)***	***HR, 0.58 (0.38–0.88)***	***HR, 0.59 (0.39–0.88)***
TTNT	HR, 0.71 (0.46–1.10)	HR, 0.68 (0.45–1.05)	***HR, 0.64 (0.43–0.96)***

Table. Comparison of efficacy endpoints adjusted for trimmed, stabilized IPTW between the LTEAC, LEAC, LKC, and ECA cohort

DOR[a]	HR, 0.92 (0.57–1.47)	HR, 0.88 (0.55–1.43)	–

Results are RR or HR (95% CI). RR >1 or HR <1 indicate favorable results for liso-cel versus SOC treatments. Statistically significant results are bolded and *italicized*.
[a]DOR was calculated among responders (n=64 [85.3%] in the LTEAC, n=67 [82.7%] in the LEAC, and n=180 [39.4%] in the ECA cohort). DOR was not prespecified to be analyzed in the sensitivity analysis between leukapheresed cohort and ECA cohort.
LTEAC (n=75): included patients with MCL who had PET-positive disease at the time of liso-cel administration or after bridging therapy had failed ≥2 prior lines of systemic therapy, including an alkylating agent, a BTKi, and rituximab (or other CD20-targeted agent) and were treated at a target dose of 100×10^6 CAR^+ T cells (DL2) with conforming product. LTEAC is the PAS in the TRANSCEND NHL 001 MCL cohort.
LEAC (n=81): included patients with MCL who had PET-positive disease at baseline or after bridging therapy and had failed ≥2 prior lines of systemic therapy, including an alkylating agent, a BTKi, and rituximab (or other CD20-targeted agent) and were treated at DL2 and DL1 (a target dose of 50×10^6 CAR^+ T cells) with conforming product.
LKC (n=104): included all patients with MCL who met all inclusion/exclusion criteria, underwent leukapheresis, and had disease that failed ≥2 prior lines of systemic therapy, including an alkylating agent, a BTKi, and rituximab (or other CD20-targeted agent).
DL, dose level; PAS, primary analysis set; RR, relative risk.

Clinical Trial Registry: NCT02631044

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Thymofox; patents, royalties, other intellectual property rights with Juno Therapeutics (institution); research funding from Seres Therapeutics; and stocks in Seres Therapeutics.

OS13-06

OUTPATIENT USE OF LISOCABTAGENE MARALEUCEL (LISO-CEL) IN PATIENTS WITH RELAPSED OR REFRACTORY (R/R) LARGE B-CELL LYMPHOMA (LBCL): REAL-WORLD DATA FROM THE CIBMTR REGISTRY

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Background: Liso-cel is an autologous, CD19-directed CAR T cell product with consistent efficacy across B-cell malignancies, including R/R LBCL. Its well-established safety profile has made outpatient delivery commonplace. Here, we describe real-world outcomes for patients with R/R LBCL who received liso-cel as standard of care (SOC) therapy in the inpatient or outpatient setting.

Methods: This observational study included patients in the United States with R/R LBCL who received commercial liso-cel as second-line or later treatment in the inpatient or outpatient setting between 02/2021 and 02/2025 and had ≥ 1 postinfusion assessment reported in the Center for International Blood & Marrow Transplant Research (CIBMTR). Outcomes included rates of AEs of special interest, nonrelapse mortality (NRM), postinfusion hospitalizations in the outpatient group, ORR, CR rate, duration of response (DOR), PFS, and OS. Results are reported descriptively.

Results: Of 1116 eligible patients, 34% (n=375) were intended for outpatient treatment, as reported to the CIBMTR, including 82 of 195 (42%) patients who received liso-cel as second-line treatment. Among patients treated in the inpatient versus outpatient setting, respectively, median (range) age was 71.5 years (21.5–91.2) and 69.8 years (25.0–86.1), most patients were male (59% and 61%), 16% and 12% had high-grade B-cell lymphoma,

26% and 26% had ≥ 2 extranodal involvement sites, and 5% and 4% had secondary CNS involvement, while 48% versus 37% had elevated LDH before infusion, and 10% versus 3% had ECOG PS ≥ 2; ≥ 1 comorbidities were reported for 72% and 65% (including cardiac, 36% and 32%; pulmonary, 30% and 26%; active infections requiring ongoing treatment, 6% and 3%) of patients in the inpatient and outpatient groups, respectively. Median (range) number of prior lines of therapy was 3 (1–13) and 3 (1–16) in the inpatient and outpatient groups, and 65% and 62% received bridging therapy, respectively. Median (95% CI) follow-up was 12.7 months (12.5–13) and 12.6 months (12.4–12.8) in the inpatient and outpatient groups, respectively.
Overall incidences of cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) events were similar between groups; most CRS and ICANS events were low grade (**Table 1**). Incidences of other AEs of special interest were also similar. Among outpatients, 46% were not hospitalized after infusion; of those hospitalized, median (IQR) time to hospitalization was 5 days (3–8) and duration of stay was 5 days (3–9).
Response rates were high in both the inpatient (ORR, 80%; CR rate, 70%) and outpatient settings (ORR, 83%; CR rate, 74%), with consistent 12-month DOR (59% and 63%), PFS (49% and 56%), and OS (65% and 74%) rates, respectively (**Table 2**).

Conclusions: These results continue to demonstrate that one-time treatment with liso-cel results in deep, clinically meaningful efficacy in the SOC setting across a broad population of patients with R/R LBCL. Despite the few differences in baseline characteristics, outcomes were consistent across inpatient and outpatient care settings. The well-established safety profile of liso-cel is conducive to outpatient treatment, allowing ~50% of patients to remain out of the hospital after infusion.

Table 1. Safety outcomes in inpatient versus outpatient settings

	Inpatient (n = 741)	**Outpatient (n = 375)**
CRS, % Any grade Grade 2 Grade ≥ 3	 52 15 3	 49 11 2
ICANS, % Any grade Grade 2 Grade ≥ 3	 28 5 10	 22 4 8
Grade 4 thrombocytopenia and/or neutropenia at 30 days after infusion, %	12	14

Table 1. Safety outcomes in inpatient versus outpatient settings

Clinically significant infections any time after infusion, %	48	42
Deaths, % PD	37 25	30 21
12-month NRM, % (95% CI)	7.1 (5.2–9.4)	4.1 (2.2–6.8)

CRS, cytokine response syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; liso-cel, lisocabtagene maraleucel; NRM, nonrelapse mortality; PD, progressive disease.

Table 2. Effectiveness outcomes in inpatient versus outpatient settings

	Inpatient (n = 741)	Outpatient (n = 375)
ORR, % (95% CI)	80 (77–83)	83 (79–87)
CR rate, % (95% CI)	70 (66–73)	74 (69–79)
DOR		
Median (95% CI), months	NR (NR–NR)	NR (NR–NR)
12-month rate, % (95% CI)	59 (54–63)	63 (56–69)
PFS		
Median (95% CI), months	11.8 (8.8–NR)	NR (NR–NR)
12-month rate, % (95% CI)	49 (45–53)	56 (50–61)
OS		
Median (95% CI), months	NR (NR–NR)	NR (NR–NR)
12-month rate, % (95% CI)	65 (61–68)	74 (68–78)

DOR, duration of response; NR, not reached.

Clinical Trial Registry: Not applicable.

Disclosure: **MB:** research funding, consulting, honoraria, and/or stockholding in Ahura Biopharma, AstraZeneca/Gracell, Bristol Myers Squibb, Gilead/Kite, Janssen, Novartis, Sanofi; **KP:** research funding, consulting, and/or honorarium from AbbVie, Adaptive Biotechnologies, Adicet Bio, ADC Therapeutics, Arcus Biosciences, Arvinas, AstraZeneca, AvenCell Therapeutics, BeiGene, BeOne Medicines, Bristol Myers Squibb, Caribou Biosciences, Century Therapeutics, CRISPR Therapeutics, Fate Therapeutics, Genentech/Roche, Kite, Indapta Therapeutics, Janssen, Lilly, Loxo Oncology, Lyell Immunopharma, MEI Pharma, Merck, Nurix Therapeutics, Pfizer, Pharmacyclics, Sana Biotechnology, Sanofi, Xencor; **ML:** consulting and/or honoraria from AbbVie, Acrotech

Biopharma, ADC Therapeutics, AstraZeneca, Bristol Myers Squibb, Fate Therapeutics, Genentech, Incyte Corporation, Ipsen, Janssen, Kite, Lyell Immunopharma, Loxo Oncology, Pfizer, Recordati, Regeneron, Veeva, viTToria Biotherapeutics; **KS:** honoraria from Bristol Myers Squibb, Curio Science, Kite, Targeted Oncology; **UR:** consulting, advisory board, and/or speaker's bureau for Bristol Myers Squibb, Janssen, Ossium Health; **YL:** research funding and/or consulting from Adicet Bio, Bristol Myers Squibb, Caribou Biosciences, Chimeric Therapeutics, Fosun Kite, Gilead/Kite, Genentech, Janssen, Legend Biotech, Nektar Therapeutics, NexImmune, Pfizer, Regeneron, Sanofi, Tessera Therapeutics, Vineti; **SI:** Consulting for AbbVie, ADC Therapeutics, Argenx, Acrotech Biopharma; **JLC:** research funding and/or consulting from AbbVie, ADC Therapeutics, Genentech/Roche, Genmab, Kite, Lilly, Merck, Novartis, Regeneron; **SA:** research funding and/or consultancy from ADC Therapeutics, Bristol Myers Squibb, Caribou Biosciences, Genmab, Gilead/Kite, Janssen, Nektar Therapeutics; **II**: consulting from Bristol Myers Squibb, Celgene; **MF:** research funding, consulting, patents/royalites from inpatients related to chimeric antigen receptors and T cell manufacturing, and/or stock holding from Bristol Myers Squibb/Juno Therapeutics, CytoAgents, Gilead Sciences, ImmunoFree, Novartis, Sobi; **DB, DR:** employment and stock from Bristol Myers Squibb; **MCP:** research funding, consulting, and/or honoraria from Amgen, Bristol Myers Squibb, Celgene, Gilead/Kite, Janssen, Medigene, Novartis, Pfizer; **BDH:** research funding, consultancy, and/or honoraria from AbbVie, ADC Therapeutics, Astellas Pharma, Bristol Myers Squibb, Caribou Biosciences, Genentech, Genmab, In8Bio, Johnson & Johnson, Kite, Novartis, Poseida Therapeutics, Regeneron.

OS13-07

QUANTIFYING DAY-TO-DAY RISK OF CYTOKINE RELEASE SYNDROME (CRS) AND NEUROLOGICAL EVENTS (NE) AFTER LISOCABTAGENE MARALEUCEL (LISO-CEL) INFUSION: POOLED ANALYSIS FROM 7 CLINICAL TRIALS

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Background: CRS and NEs are adverse events associated with CAR T cell therapy. Regulatory authorities such as the FDA and EMA recently reduced the time patients are

required to remain close to the healthcare facility after infusion from 4 to 2 weeks. Here, we quantify the probability of new onset CRS or NEs at specific time points after liso-cel infusion.

Methods: Time to first onset of CRS or NE data were pooled for liso-cel–treated patients from clinical trials in second-line (2L) or third-line or later (3L+) large B-cell lymphoma (LBCL; TRANSCEND NHL 001, TRANSCEND WORLD, PLATFORM, OUTREACH, TRANSFORM, PILOT) and 2L or later (2L+) FL (TRANSCEND FL). We estimated, for Days 1–30 after infusion (Day 1=infusion day), the probability of future CRS/NE onset at each landmark as the proportion of patients under observation with onset on that day or later, divided by those still at risk (alive and in study), regardless of prior onset.
Additional analyses estimated the future risk of CRS/NEs within the same time period (Days 1–30 after infusion) based on prior occurrence of CRS/NEs and the probability of CRS/NEs within the first 15 days after infusion (the close monitoring period) in patients without prior CRS/NEs. All analyses are descriptive; no formal hypothesis testing was performed.

Results: Of 691 patients who received liso-cel across 7 clinical trials, 51% (n=355) did not experience CRS/NEs. For patients with any-grade CRS/NEs (n=336; grade ≥3 at first onset, n=12), 96% occurred on or before Day 15 after infusion; median time to onset of CRS and NEs was 5 and 8 days, respectively, and median time to resolution was 4 and 7 days. The risk of future any-grade CRS/NEs decreased steadily over time to 1% on Day 30 (**Table**, **Figure**), and the risk of experiencing a maximum grade ≥3 CRS/NE remained low throughout the 30-day period (≤8%).
Patients without prior CRS/NEs had numerically lower risks of experiencing any-grade CRS/NEs within 30 days after infusion compared with patients who previously experienced CRS/NEs (Day 15, 4% vs 7%, respectively; **Table**). The overall risk of grade ≥3 CRS/NEs was ≤8% and ≤13%, respectively, for patients without versus with prior CRS/NEs, and decreased to ≤1% by Day 15 regardless of prior CRS/NE status.
From Day 1, risk of any-grade or maximum grade ≥3 CRS/NEs within 15 days of infusion for patients without prior CRS/NEs decreased over time (**Table**). On Day 7, the probability of future grade ≥3 CRS/NEs was 3%, suggesting patients without prior CRS/NEs may be candidates for early discharge before Day 15, contingent on institutional protocols and risk tolerance.

Conclusions: Data from liso-cel clinical trials in patients with 2L/3L+ LBCL and 2L+ FL indicate that 96% of CRS/NEs occurred within 15 days after infusion and were predominantly low grade. The risk of future CRS/NEs decreased progressively over time, with an estimated 4% risk at Day 15 in patients without prior events. These findings provide quantitative residual risk estimates that may help physicians decide when to discharge patients after liso-cel infusion, particularly from inpatient settings.

Table. Risk of future CRS or NEs

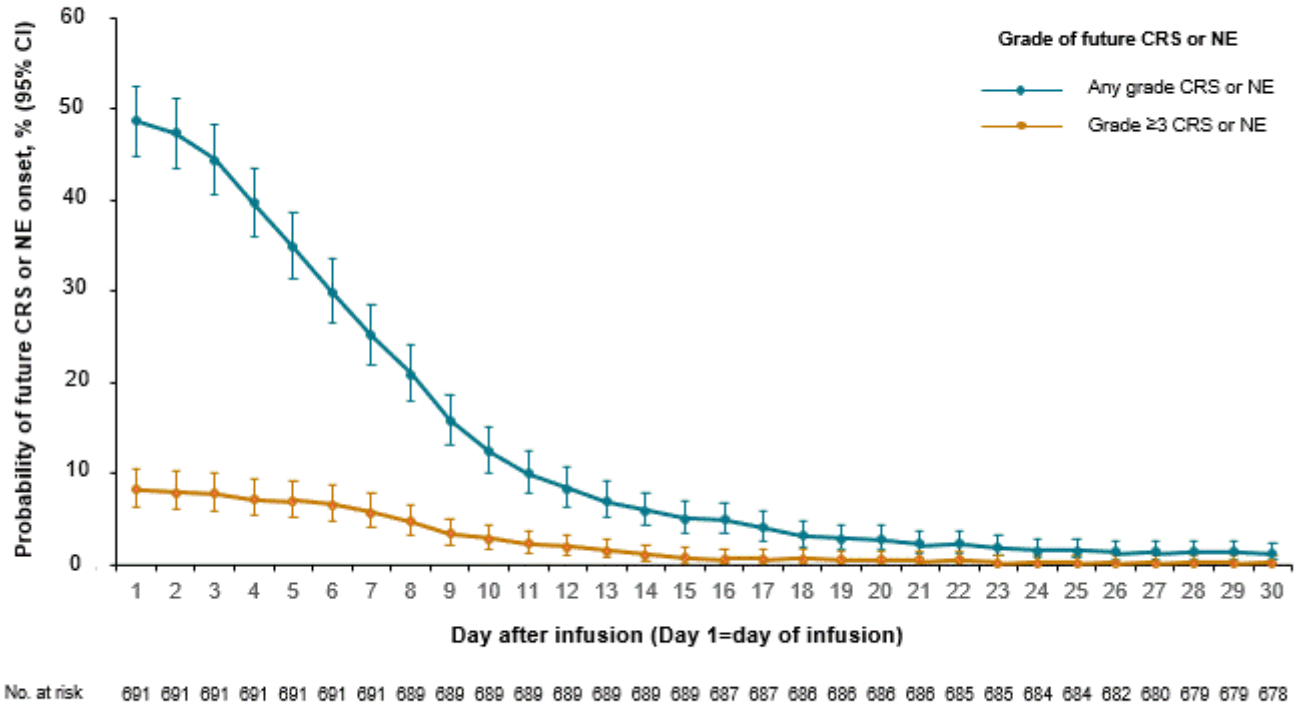
	Overall cumulative risk	**No prior CRS and/or NE**	**Prior CRS and/or NE**	**15-day analysis No prior CRS and/or NE**

Table. Risk of future CRS or NEs

	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3	Any grade	Grade ≥3
On Day 1, % (95% CI)	49 (45–52)	8 (6–11)	49 (45–52)	8 (6–11)	NA	NA	47 (43–50)	8 (6–10)
On Day 5, % (95% CI)	35 (31–39)	7 (5–9)	34 (30–39)	6 (4–8)	37 (29–45)	13 (8–19)	32 (28–36)	5 (3–7)
On Day 7, % (95% CI)	25 (22–29)	6 (4–8)	23 (19–27)	4 (2–6)	30 (24–36)	10 (6–14)	20 (16–24)	3 (2–5)
On Day 10, % (95% CI)	12 (10–15)	3 (2–4)	10 (7–14)	2 (1–4)	16 (12–20)	4 (2–7)	7 (4–10)	2 (1–3)
On Day 15, % (95% CI)	5 (4–7)	1 (0.3–2)	4 (2–6)	1 (0.1–2)	7 (4–10)	1 (0.3–3)	0 (0–1)	0 (0–1)
On Day 30, % (95% CI)	1 (1–3)	0.3 (0–1)	1 (0.5–3)	1 (0.1–2)	1 (0.3–3)	0 (0–1)	NA	NA

NA, not assessed.

Figure. Risk of future CRS or NEs over 30 days



Clinical Trial Registry: NCT02631044; NCT03484702; NCT03310619; NCT03744676; NCT03575351; NCT03483103; NCT04245839

Disclosure: **VO-M:** consultancy and/or advisory role for Bristol Myers Squibb and Pfizer; **PBa:** advisory board and consultancy from Amgen, AstraZeneca, Autolus, Celgene, a Bristol-Myers Squibb Company, Gilead/Kite, Incyte Corporation, Novartis, Pfizer, and Pierre Fabre; **RL:** honoraria, advisory boards, consultancy, and/or travel support from Bristol Myers Squibb, Kite, Roche, and Takeda; **PM:** nothing to disclose; **KA:** travel support from Bristol Myers Squibb, Gilead, and Novartis; **PBo:** consultancy, research funding, and/or honoraria from AbbVie, Amgen, BeiGene, Bristol Myers Squibb, Celgene, a Bristol-Myers Squibb Company, Gilead, Incyte Corporation, Miltenyi Biotec, MSD, Novartis, Roche, and Takeda Oncology; **PC:** advisory board and/or honoraria from AbbVie, ADC Therapeutics, Amgen, BeiGene, Celgene, a Bristol-Myers Squibb Company, Daiichi Sankyo, Gilead/Kite, GlaxoSmithKline, Incyte Corporation, Janssen, KyowaKirin, Nerviano Medical Science, Novartis, Roche, Sanofi and Takeda; **MN:** Consultancy and/or honoraria from Bristol Myers Squibb and Gilead; **DB:** current employment and stock holder in Bristol Myers Squibb; **SB:** current employment and stockholder in Bristol Myers Squibb; and **PJM:** current employment

and stockholder in Bristol Myers Squibb; **FM:** Consultancy and/or honoraria from AbbVie, AstraZeneca, Bristol Myers Squibb, Gilead/Kite, Janssen, Miltenyi Biotec, Roche, and Takeda.

OS14-01

ORCA-T DEMONSTRATES FAVORABLE QUALITY OF LIFE AND HEALTHCARE RESOURCE USE COMPARED TO STANDARD ALLOHSCT PLUS TAC/MTX FOR GVHD PREVENTION IN RANDOMIZED PHASE3 CLINICAL TRIAL (PRECISION-T)

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Background: Conventional allogeneic hematopoietic stem cell transplantation (alloHSCT) is associated with increased toxicity and infections due to multiagent immunosuppression. Orca-T, a high-precision engineered allogeneic T cell immunotherapy utilizing single-agent GVHD prophylaxis, demonstrated superior survival free of chronic GVHD (HR = 0.26; p < 0.00001), significantly lower moderate to severe chronic GVHD (12.6% vs 44.0%; p < 0.001), and fewer serious infections and deaths at 1 year versus alloHSCT in a phase 3 trial. This study compares health-related quality of life (HRQoL) and hospitalization patterns between arms.

Methods: Adults aged 18–65 undergoing myeloablative alloHSCT for acute leukemia in remission or high-risk MDS (≤10% BM blasts) with matched related or unrelated donors were randomized 1:1 to Orca-T + tacrolimus or unmanipulated PBSC + Tac/MTX. Exploratory outcomes included HRQoL and hospitalization. HRQoL was measured using the FACT-BMT instrument (0–164 scale; higher scores indicate better HRQoL) at baseline and predefined intervals. A repeated measures model assessed change over time. Duration of initial hospitalization, rehospitalization rates, total hospitalized days, and rehospitalization-free survival were compared between arms.

Results: Safety analyses included 88 Orca-T and 94 Tac/MTX patients, with grade 3–4 acute GVHD rates of 5.7% vs 9.6% and moderate–severe chronic GVHD of 12.5% vs 34.0%. Survey completion was >85% at baseline and ~66% at 1 year. FACT-BMT scores were consistently higher for Orca-T, with smaller declines at day 14 (−7.74 vs −13.69) and recovery above baseline by day 100 (1.34 vs −3.12), sustained through day 365. Subscale scores exceeded baseline earlier and were ≥2-fold higher by day 365. Median hospitalization was 24.5 vs 24.0 days; rehospitalizations 27.3% vs 45.7%; total hospitalized days 30.6 vs 40.8; ICU admissions 1 vs 4. Rehospitalization-free survival at 18 months was 66.4% (95% CI 54.0–76.2) vs 33.8% (95% CI 18.5–49.9) (p = 0.0096; HR 0.53 [0.32–0.86]).

Conclusions: Orca-T recipients experienced higher HRQoL, faster recovery, fewer ICU stays, lower rehospitalization rates, and improved rehospitalization-free survival compared to Tac/MTX, suggesting improved early post-transplant recovery and reduced GVHD symptom burden.

Clinical Trial Registry: NCT04013685 https://clinicaltrials.gov/study/NCT04013685

Disclosure: Arpita Gandhi, MD reports consulting fees from CareDx, educational events for MJH Sciences – speakers bureaus and OncLive – panel, consulting for Orca Bio, and travel funds for EBMT 2025 oral presentation. Anna Purdum reports being an employee for Orca Bio. Anna Pavlova, MD, PhD reports being an employee and equity holder for Orca Bio. Ai Li, PhD reports being an employee for Orca Bio. James Scott McClellan, MD, PhD reports being an employee, officer, and equity holder for Orca Bio. Bronwen Shaw has nothing to declare. Rachel Cusatis has nothing to declare.

OS14-02

CLINICAL OUTCOMES IN ORCA-T AND REGISTRY-BASED POST-TRANSPLANT CYCLOPHOSPHAMIDE PATIENTS: AN OBSERVATIONAL COMPARISON

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Background: Orca-T is an investigational precision cell therapy for allogeneic treatment of hematological disorders. In a Phase 1b clinical trial (NCT04013685) with patients having acute leukemias or MDS, Orca-T exhibited an excellent safety profile and low rates of severe Graft-versus-Host Disease (GVHD). In a Phase 3 randomized trial (NCT05316701), in comparison to calcineurin inhibitor/methotrexate prophylaxis, Orca-T met the primary endpoint of improving moderate-to-severe chronic GVHD-free survival (cGFS). Here we retrospectively compared the clinical outcomes of Orca-T patients to those receiving post-transplant cyclophosphamide (PTCy) for GVHD prophylaxis.

Methods: The Orca-T patients in this study (n=164) included all participants in the Ph3 trial who received Orca-T (n=88), as well as participants in the ph1b trial who met the Ph3 eligibility criteria (n=76). The PTCy patients (n=380) included those in the CIBMTR registry who received PTCy + tacrolimus ± mmf and had pre-transplant demographic and clinical profiles that were similar to the Orca-T patients. Additional inclusion criteria were ages 18-65, intermediate- to high-risk AML or ALL in CR or MDS, rmyeloablative conditioning, and an 8/8 HLA-matched donor. The endpoints compared were overall survival (OS), relapse-free survival (RFS), cGFS, and the cumulative incidences of non-relapse mortality (NRM), relapse, gr. 3-4 acute GVHD, and moderate-severe chronic GVHD. Competing risks were death for the cumulative incidences of relapse and GVHD, and relapse for NRM. Time-to-event outcomes were analyzed from the transplantation date until the first event or date of last contact. Standard survival and competing risk methods were used; $p<.05$ defined significance.

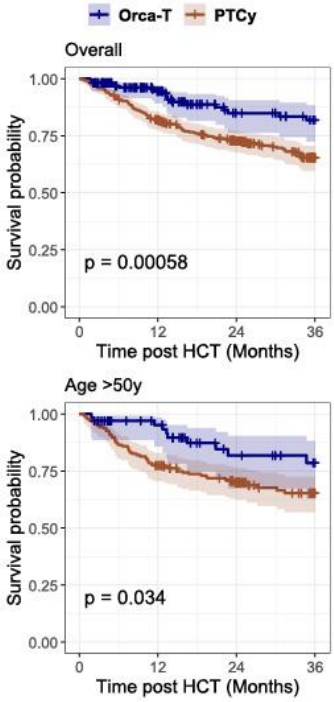
Results: Orca-T patients, in comparison to the PTCy patients, exhibited increased OS ($p<.001$), increased RFS ($p=.045$), and decreased NRM ($p=.033$) (Table 1 and Fig. 1). GRFS, relapse, and aGVHD grades 3-4 estimates did not significantly differ between the treatment groups. The 1-year cumulative incidence of moderate-severe cGVHD was lower in the PTCy group, but the cGFS rates were not significantly different.
The increased OS effect of Orca-T was consistently observed in subgroups of patients (e.g., age, HCT-CI, DRI, disease type) that can be associated with disparate clinical outcomes. Noteworthy was the increased OS ($p=.034$) and decreased NRM ($p=.048$) in patients >50 years of age.

Table 1. Clinical Outcomes.

	Orca-T	PTCy	P-value[2]
Overall Estimates (N)	164	380	
Overall survival			**<.001**
1-year	94% (89-97%) [1]	82% (78-86%)	
2-year	85% (76-90%)	73% (68-77%)	
3-year	82% (72-88%)	65% (60-70%)	
RFS			**0.045**
1-year	78% (70-84%)	70% (65-74%)	
NRM			**0.033**
1-year	2.7% (0.87-6.4%)	7.7% (5.3-11%)	
Age group >50y (N)	67	177	
Overall survival			**0.034**
1-year	95% (86-98%)	77% (71-83%)	
2-year	82% (67- 90%)	70% (62-76%)	
3-year	79% (63- 88%)	65% (57-72%)	
RFS			0.2
1-year	76% (63-85%)	68% (60-74%)	
NRM			**0.048**
1-year	3.0% (0.56-9.4%)	12% (7.7-17%)	

[1] Point estimate (95% CI)
[2] Log-rank test (survival) or Gray's test (cumulative incidence)

Figure 1. Overall Survival.



Conclusions: In conclusion, Orca-T patients, in comparison to PTCy patients in the CIBMTR registry, exhibited increased OS, increased RFS, and decreased NRM. These observations were consistently observed in stratified analyses, with further separation in clinical effect between Orca-T and PTCy in patients >50 years of age.

Clinical Trial Registry: NCT04013685 https://clinicaltrials.gov/study/NCT04013685
NCT05316701 https://clinicaltrials.gov/study/NCT05316701

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Behring, PeerView; advisory Sanofi, Maat Pharma; DSMB participation. Antonio Jimenez Jimenez, MD – honorarium AML lecture; research funding AbbVie. Satyajit Kosuri, MD – consulting Incyte, Sanofi; honoraria Sanofi, AbbVie; advisory roles/travel support. Yi-Bin Chen, MD – consulting Incyte, CSL Behring, MaaT, Ironwood, LifeMine, ProTGen, Generation Bio; trial committees Novo Nordisk, Editas, Alexion, Daiichi; stock ImmunoFree, Phesi. John Magenau, MD; Alireza Eghtedar, MD; Joseph P. McGuirk, DO – nothing to declare. Samer A. Srour, MB ChB, MS – ASH 2025 presentation Orca Bio. Anna Pavlova, MD, PhD; Nathaniel Fernhoff, PhD; James Scott McClellan, MD, PhD; Scott Killian, MPH, PhD – employment and equity Orca Bio. Robert Negrin, MD – consulting Amgen, Strada, Biorasi, Apia Bio, Cellenko, ReStem; patents licensed Orca Bio; advisory Kura Oncology, University of Pennsylvania; ASH leadership; stock Strada. Everett Meyer, MD, PhD – Orca Biosystems trial funding.

OS14-03

POST-TRANSPLANT CYCLOPHOSPHAMIDE-BASED GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS AFTER MISMATCHED UNRELATED DONOR PERIPHERAL BLOOD STEM CELL TRANSPLANTATION – 2-YEAR OUTCOMES FROM THE NMDP-SPONSORED ACCESS TRIAL

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Background: ACCESS is a CIBMTR run phase II, non-randomized, multicenter trial that assessed peripheral blood graft (PBSC) use in the setting of a GVHD prophylaxis regimen of cyclophosphamide, tacrolimus, and mycophenolate mofetil (PTCy) in two adult strata: myeloablative conditioning (MAC) and reduced-intensity or nonmyeloablative (RIC) conditioning before HCT from a ≤35 year old MMUD (4-7/8 match at HLA-A, B, C and -DRB1). The primary outcome was overall survival (OS) at 1-year post-HCT and was 83.8% and 78.6% in MAC and RIC, respectively (Al Malki et al. JCO 2025). Here we present longer term outcomes and compared to two similar trials also using PTCy GVHD prophylaxis.

Methods: In the current analysis using long term outcome data reported as standard to the CIBMTR registry, we evaluated 2-year outcomes for the patients enrolled on and reported in the primary ACCESS results publication along with comparative cohorts from the 15-MMUD

phase II trial (15-MMUD) (Shaw et al. JCO 2021), bone marrow in MMUD MAC and RIC, and the Blood and Marrow Transplant Clinical Trials Network 1703 randomized phase III trial (1703) (Bolanos-Meade et al. NEJM 2023), PBSC using PTCy in matched related and unrelated RIC.

Results: A total of 145 patients on ACCESS (n=75 MAC, n=70 RIC) were included, 80 on 15-MMUD (n=40 MAC, n=40 RIC) and 208 on 1703 (all RIC) with 59%, 48% and 13% self-identifying within an underrepresented group, respectively. Median follow-up on ACCESS was 24.2 months (range: 0.4-40.3 months). Primary disease was predominately acute leukemia in all cohorts. HLA matching varied by cohort: ACCESS – 7/8=68%, <7/8=32%; 15-MMUD – 7/8=61%, <7/8=39%; and 1703 – 7/8=3%, <7/8=0%.
In the MAC groups, the 2-year OS was 72.5% (95% Confidence Interval, 60.7-81.3%) and 62.4% (45.6-75.4%) (Figure) and GVHD-free, relapse-free survival (GRFS) was 32.7% (22.2-43.5%) and 28.0% (15.0-42.5%) for ACCESS and 15-MMUD, respectively. Relapse at 2 years was 31.4% (21.1-42.2%) on ACCESS and 27.6% (14.7-42.1%) on 15-MMUD. Chronic GVHD requiring immunosuppression (cGVHD IST) at 2 years was 26.5% (16.8-37.1%) and 25.6% (13.1-40.2%) on ACCESS and 15-MMUD, respectively.
In the RIC groups, the 2-year OS was 72.8% (60.7-81.7%), 74.8% (58.2-85.6%) and 67.2% (60.3-73.1%) (Figure) and GRFS was 41.5% (29.8-52.8%), 38.0% (23.0-52.9%) and 36.5% (29.8-43.3%) for ACCESS ,15-MMUD and 1703, respectively. Relapse at 2-years was 26.5% (16.6-37.4%) on ACCESS, 32.8% (18.7-47.6%) on 15-MMUD and 33.2% (26.7-39.8%) on 1703. cGVHD IST at 2 years was 17.1% (9.4-26.9%), 17.5% (7.6-30.8%) and 18.9% (13.8-24.6%) on ACCESS, 15-MMUD and 1703, respectively. Additional outcomes at 2 years and acute GVHD at 6 months are shown in the table.

Figure: Overall Survival following HCT for MAC (A) and RIC (B) cohorts from ACCESS, 15-MMUD and BMT CTN 1703

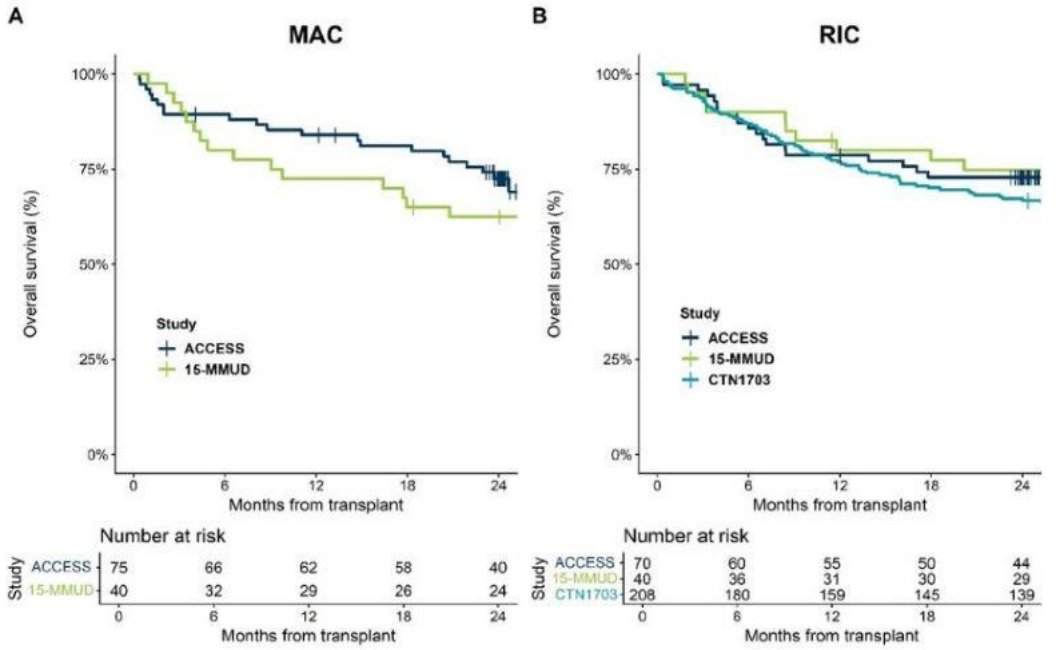

Table: Estimates for OS, GRFS, cGVHD, cGVHD requiring IST, relapse/progression, and relapse/progression-free survival at 2 years post-transplant – MAC cohorts from ACCESS and 15-MMUD and RIC cohorts from ACCESS, 15-MMUD and BMT CTN 1703

	Myeloablative Conditioning (MAC)		Reduced Intensity Conditioning (RIC)		
	ACCESS MAC PBSC (N = 75)	**15-MMUD MAC BM (N=40)**	**ACCESS RIC PBSC (N = 70)**	**15-MMUD RIC BM (N=40)**	**BMT CTN 1703 RIC PBSC (N=208)**
Outcomes	**Prob (95% CI)**	**Prob (95% CI)**	**Prob (95% CI)**	**Prob (95% CI)**	**Prob (95% CI)**
Overall Survival	72.5 (60.7-81.3)%	62.4 (45.6-75.4)%	72.8 (60.7-81.7)%	74.8 (58.2-85.6)%	67.2 (60.3-73.1)%

Table: Estimates for OS, GRFS, cGVHD, cGVHD requiring IST, relapse/progression, and relapse/progression-free survival at 2 years post-transplant – MAC cohorts from ACCESS and 15-MMUD and RIC cohorts from ACCESS, 15-MMUD and BMT CTN 1703

Chronic GVHD	44.6 (31.3-56.9)%	46.8 (29-62.9)%		28.7 (17.3-41.2)%	21.5 (9.3-37.1)%	33.5 (26-41.1)%
cGVHD requiring IST	26.5 (16.8-37.1)%	25.6 (13.1-40.2)%		17.1 (9.4-26.9)%	17.5 (7.6-30.8)%	18.9 (13.8-24.6)%
Relapse	31.4 (21.1-42.2)%	27.6 (14.7-42.1)%		26.5 (16.6-37.4)%	32.8 (18.7-47.6)%	33.2 (26.7-39.8)%
Relapse-free survival	55.1 (43-65.6)%	54.9 (38.3-68.7)%		57.5 (44.9-68.2)%	59.7 (42.9-73.1)%	53.8 (46.6-60.4)%
GRFS	32.7 (22.2-43.5)%	28.0 (15.0-42.5)%		41.5 (29.8-52.8)%	38.0 (23.0-52.9)%	36.5 (29.8-43.3)%
Non-relapse mortality	13.5 (6.9-22.4%)	17.5 (7.6-30.8)%		16.0 (8.5-25.7)%	7.5 (1.9-18.4)%	13.0 (8.8-18.1)%
6mo Grade 2-4 aGVHD	30.7 (20.6-41.3)%	47.5 (34.5-60.7)%		44.3 (32.4-55.5)%	35 (23.1-48)%	54.8 (47.7-61.3)%
6mo Grade 3-4 aGVHD	8.0 (3.2-15.6)%	20 (10.6-31.5)%		10.0 (4.4-18.4)%	2.5 (0.1-8.2)%	6.8 (3.9-10.8)%

Conclusions: PTCy-based GVHD prophylaxis after MMUD HSCT with PBSC grafts results in favorable 2-year OS, GRFS and other outcomes. The results on ACCESS are comparable to those observed on the 1703 trial utilizing matched related and unrelated donors and 15-MMUD using MMUD with bone marrow grafts. Using MMUDs at all match levels expands donor availability to all patients regardless of ancestry and should be considered as a viable alternative when fully matched related or unrelated donors are unavailable.

Clinical Trial Registry: ACCESS - NCT04904588, https://www.clinicaltrials.gov/study/NCT04904588

15-MMUD - NCT02793544, https://www.clinicaltrials.gov/study/NCT02793544
BMT CTN 1703 - NCT03959241, https://www.clinicaltrials.gov/study/NCT03959241

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Mahasweta Gooptu - Advisory Board Member: Syndax, Incyte
Brian C. Shaffer - Consulting: Gamida Cell; Research Support: Incyte, Genetech
Bronwen E. Shaw - Consulting: Orcabio

All other authors have nothing to declare.

OS14-05

BETTER OUTCOMES WITH HAPLOIDENTICAL THAN MATCHED SIBLING DONORS FOR AML PATIENTS TRANSPLANTED IN MRD+ CR: A STUDY FROM GLOBAL COMMITTEE AND ALWP OF THE EBMT

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Background: Disease relapse is a major challenge for acute myeloid leukemia patients after allogeneic hematopoietic cell transplantation (allo-HCT). The risk of post-transplant relapse significantly increases in patients who are transplanted in complete remission with detectable measurable disease (MRD positive) as opposed to MRD negative. Haploidentical donor (HAPLO) grafts may exert a higher graft-versus-leukemia effect than human leukocyte antigen (HLA)-matched donors. In a European Society for Blood and Marrow Transplantation (EBMT) global multi-center, registry-based analysis, we compared the outcomes following allo-HCT from either a HAPLO, matched sibling donor (MSD), or a 10/10 HLA-matched unrelated donor (MUD).

Methods: Data from 3385 adult AML patients receiving a first allo-HCT in first or second complete remission (CR1/CR2) from 269 EBMT centers between 2015 and 2022 were analyzed. 2765 patients were transplanted in CR1 and 620 in CR2. All had detectable measurable residual disease by molecular biology (MRD positive). Transplants from HLA-mismatched UD (<10/10), umbilical cord blood, or grafts with *ex*-vivo manipulation were excluded. HAPLOs were restricted to recipients with post-transplant cyclophosphamide (PTCy) as graft-versus-host disease (GVHD) prophylaxis. Multivariable Cox regression models were used to evaluate the impact of donor types on outcomes.

Results: Results from 3385 HCTs were analyzed comprising 609 (18%) HAPLO, 1057 (31%) MSD and 1719 (51%) MUD. For the entire study population, the median age was 55 years (range: 18-83). In the HAPLO group, the proportion of patients transplanted in CR2 was higher (22%) than in the MSD (15%) or MUD (18%) groups (p< 0.001). Peripheral blood was the major graft source (91%) and reduced-intensity conditioning (RIC) was usedfor approximately half (49%) of the study population. Primary disease relapse was the major cause of death in each of the three cohorts.
On multivariable analysis, compared with HAPLO HCT (as reference group), MSD HCT (hazard ratio [HR]=1.55, 95% CI 1.26-1.91; p<0.001) was associated with a significantly higher risk of disease relapse (HR=1.55, 95% CI 1.26-1.91; p<0.001)and lower non-relapse mortality (NRM) (HR=0.63, 95% CI 0.46-0.86; p=0.004) leading to an inferior LFS (HR=1.19, 95% CI 1.01-1.41; p=0.048) and a lower GVHD/relapse free survival (GRFS) (HR=1.22, 95% CI 1.05-1.41; p=0.01). Interestingly, in reference to HAPLO, although MUD HCT was associated with a higher incidence of disease relapse (HR=1.26, 95% CI 1.03-1.54; p=0.03), there was no significant differences concerning LFS, GRFS and OS.
We also found, as expected, that HCT at CR2 was associated with a significantly higher incidence of relapse (HR=1.5, 95% CI 1.27-1.78; p<0.001) compared with at CR1 and therefore significantly poorer survival outcomes (OS, LFS and GRFS). Myeloablative conditioning regimen was associated with a significantly lower relapse incidence (HR=0.75, 95% CI 0.64-0.87; p<0.001) and significantly superior survival outcomes (OS, LFS and GRFS) compared with reduced intensity conditioning. Finally, older patient age (by 10-year intervals) was associated with higher NRM (HR=1.23, 95% CI 1.12-1.36; p<0.001) and poorer OS (HR=1.10, 95% CI 1.04-1.17; p<0.001).

Conclusions: For AML patients transplanted in MRD positive complete remission, HAPLO HCTs were associated with better LFS and GRFS than MSD HCTs, primarily due to better relapse prevention.

Disclosure: Nothing to declare.

OS14-06

IMPACT OF ABO COMPATIBILITY ON OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC ALL: RESULTS FROM FORUM

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Background: ABO incompatibility occurs in approximately 40% of all allogeneic hematopoietic stem cell transplants (allo-HSCT) in Caucasian populations. Inferior outcomes after ABO major-incompatible transplantation have been reported, although findings across studies are inconsistent. Suggested adverse effects include delayed engraftment, increased graft rejection, higher incidence or severity of graft-versus-host disease (GvHD), and increased transplant-related mortality (TRM). The clinical significance of ABO incompatibility in pediatric populations remains insufficiently defined due to limited data. The FORUM trial offers a unique opportunity to evaluate this question in a large, prospectively conducted and well-controlled pediatric cohort. We therefore assessed the impact of ABO incompatibility on transplantation outcomes in children with acute lymphoblastic leukemia (ALL) enrolled in the international FORUM trial.

Methods: The FORUM (For Omitting Radiation Under Majority Age) trial is a prospective, global, multicenter, open-label phase III study (EudraCT 2012-003032-22; ClinicalTrials.gov: NCT01949129). We retrospectively analyzed 1,564 pediatric patients who received allo-HSCT from matched sibling or matched unrelated donors to determine the influence of ABO incompatibility on safety, efficacy, and survival outcomes. The data cut-off was November 2025. Patients were stratified into two cohorts based on age: (1) ≥4 years with matched sibling or matched donors (MSD/MD; n=1,328) and (2) <4 years with MSD/MD donors (n=236). Transplants were further hierarchically categorized as ABO-compatible, ABO major-incompatible, or ABO minor-incompatible. In Cohort 1, 650, 376, and 302 patients were included in each respective group; in Cohort 2, 105, 78, and 53 patients were included. Stem

cell sources included bone marrow, peripheral blood stem cells, and cord blood. Three-year overall survival (OS) and event-free survival (EFS) were assessed.

Results: The median follow-up was 3 years.
In Cohort 1 (≥4 years, MSD/MD), ABO incompatibility was not significantly associated with survival. OS and EFS were similar across ABO groups (OS: 0.77 for ABO-compatible, 0.80 for major-incompatible, 0.79 for minor-incompatible; p=0.722; EFS: 0.70, 0.68, 0.69; p=0.850).
In Cohort 2 (<4 years, MSD/MD), major ABO incompatibility showed a non-significant trend toward lower survival, while minor-incompatible transplants showed outcomes comparable to ABO-compatible transplants (OS: 0.74, 0.67, 0.79; p=0.246; EFS: 0.58, 0.50, 0.59; p=0.222).
Across both cohorts, ABO incompatibility had no impact on rates of acute GvHD or engraftment.

Conclusions: Our large study showed no impact of ABO incompatibility on outcomes in children ≥4 years undergoing allo-HSCT. In children <4 years, major ABO incompatibility was associated with a slight, non-significant reduction in OS and EFS, while outcomes after minor-incompatible transplantation were comparable to ABO-compatible procedures. Overall, major ABO mismatches should not limit donor selection in pediatric allo-HSCT.

Clinical Trial Registry: The FORUM (For Omitting Radiation Under Majority Age) trial is a prospective, global, multicenter, open-label phase III study (EudraCT 2012-003032-22; ClinicalTrials.gov: NCT01949129).

Disclosure: Herbert Pichler reports travel grants from Jazz Pharmaceuticals and Sanofi and speakers bureau fees from Vertex and Novartis.
Andrea Jarisch declares speaker fees from Novartis, Medac, Vertex, Merck and advisory board participation with Vertex and Novartis.
Peter Bader reports travel grants from Medac, Novartis, Vertex; and speakers bureau fees from Medac, Novartis, Amgen.
The remaining authors declare no competing financial interests.

OS14-08

ALLOGENEIC STEM CELLS TRANSPLANTATION IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS PREVIOUSLY TREATED BY TISAGENLECLEUCEL FOR B-CELL PRECURSOR ACUTE LYMPHOBLASTIC LEUKEMIA: A FRENCH RETROSPECTIVE SFGM-TC STUDY

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Emilie Dourthe[1]
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Background: Anti-CD19 CAR T-cells have transformed the prognosis of relapsed/refractory (R/R) B-cell acute lymphoblastic leukemia (B-ALL) in children, adolescents and young adults (AYA). Despite initial response rates exceeding 90%, durability of remission remains uncertain and more than 50% of patients relapse. These results required to optimize the post CAR T-cells management strategies and specifically asking the role of a consolidation treatment with allogeneic hematopoietic stem cell transplantation (allo-HSCT). Efficacy and toxicity of this procedure after CAR T-cells remain underreported. Here, we present the French experience of pediatric and AYA patients undergoing allo-HSCT after CAR T-cells for R/R B-ALL.

Methods: This national SFGM-TC retrospective study included children and AYA who received allo-HSCT after tisagenlecleucel for R/R B-ALL in SFCE or AYA centers (2016–2023). Data were collected from the PROMISE registry and patient records.

Results: Forty patients underwent allo-HSCT after a median of 6.3 months (range: 2–28.5) post CAR T-cells for early failure/relapse (n=23), early B-cell recovery (BCR) (n=13) and pre-planned consolidation or persistent cytopenia (n=4).Twenty-nine patients received treatment between CAR T-cells therapy and allo-HSCT (immunotherapy: n=19, chemotherapy: n=10).
At 2 year, EFS was 46% (95% CI: 32–66%), OS 57% (95% CI: 43–76%), CIR 31% (95% CI: 16–47%), and NRM 23% (95% CI: 11–37%).
Allogeneic HSCT toxicity was not different according to indication, with a rate of aGVHD of 43% (grade 3+: 13%), SOS of 33% (grade 3+: 13%) and cGVHD of 17%. In the whole cohort, the 2y GRFS was 36% (95%CI: 23%-56%).
Among the 18 deceased patients (45%), 10 died in complete remission from allo-HSCT complications, after a median time of 1.4 months (range: 0–25.4 months).
In multivariate analysis, early BCR was associated with better OS (77%, 95% CI: 57–100%; HR = 0.17; p = 0.027) and lower CIR (16%, 95% CI: 2–42%).
Twelve patients had previously undergone a 1st allo-HSCT (median interval between transplants: 29 months, range: 12–100). Prior allo-HSCT did not significantly impact survival (2-y OS: 58% for 1st allo HSCT vs 55% for 2nd allo HSCT) or toxicity profile after allo-HSCT (2-y NRM: 25% for 1st allo HSCT vs 18% for 2nd allo HSCT).
Among the 11 patients who relapsed after allo-HSCT the 2-year OS was 24% (95%CI: 9-74%). Two patients were successfully re-treated with subsequent CD19-directed CAR T cells therapy.

Conclusions: In this real-world analysis, allo-HSCT after CAR T-cells is associated with high NRM even after 1st allo-HSCT comparing to historically results for patients receiving allo-HSCT without previous CAR T-cells. This result is similar with a single center retrospective analysis where pre-transplant CAR T-cell therapy was associated with inferior survival and increased NRM compared to patients receiving only allo-HSCT (Chok et al, ASH 2025).

Importantly, indications of allo-HSCT lead the prognosis of patients in terms of survival offering a curative perspective for patients with early BCR precising the favorable results of allo-HSCT after CAR T-cells published by the CHOP (Myers et al., Haematologica, 2025).

Disclosure: Nothing to declare.

OS17-05

BEYOND PROGNOSTIC RISK: TIME-DEPENDENT INTERACTION ANALYSIS IDENTIFIES ASXL1, RUNX1, AND A MUTATED ASXL1/RUNX1/BCOR/BCORL1 CLUSTER AS PREDICTORS OF TRANSPLANT BENEFIT IN AML IN FIRST REMISSION

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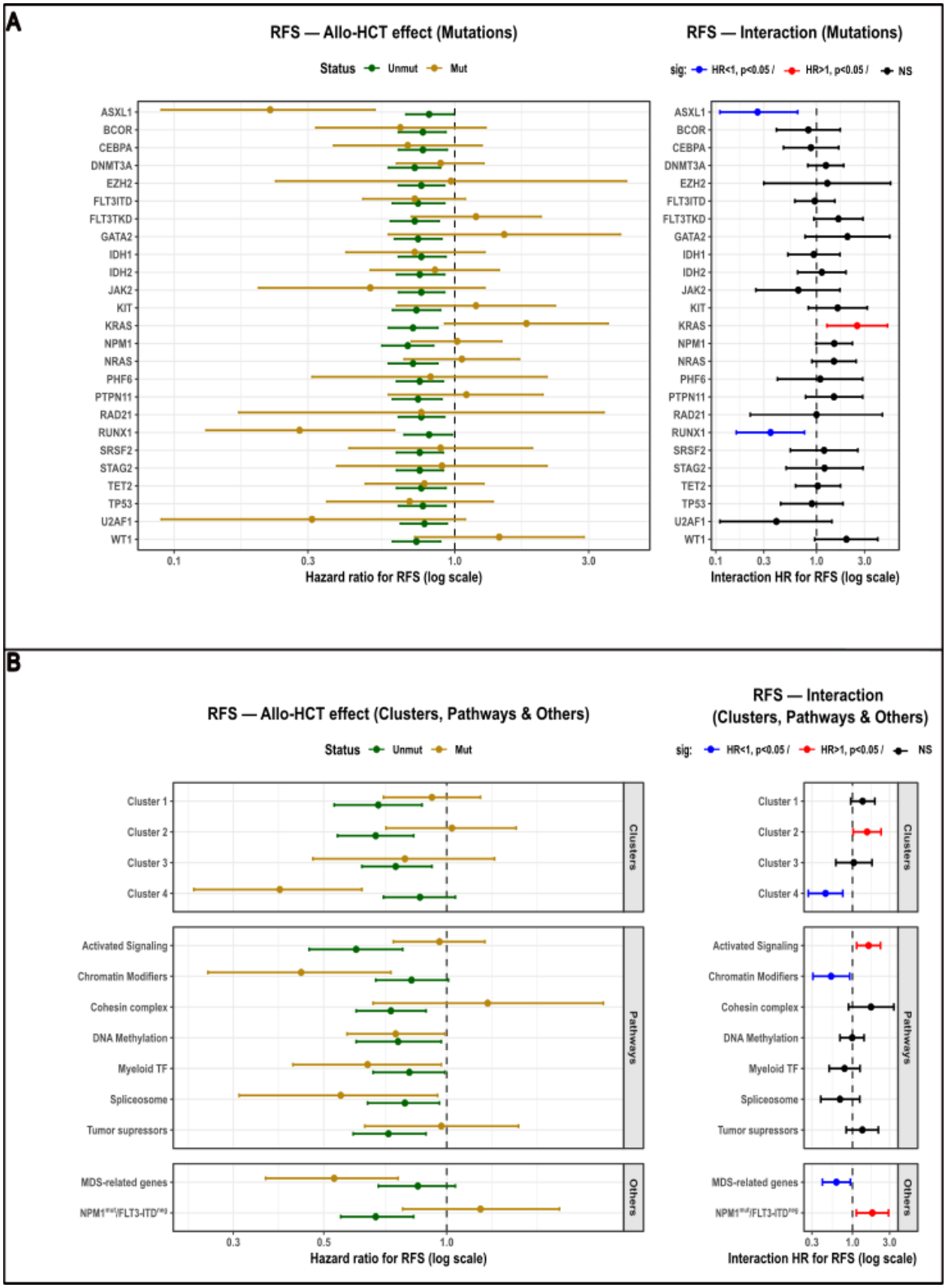
Background: Allogeneic hematopoietic stem cell transplantation (allo-HCT) is a key consolidation strategy for intermediate- and high-risk acute myeloid leukemia (AML) in first complete remission (CR1). However, whether specific genomic subgroups derive true therapeutic benefit from allo-HCT—rather than simply reflecting adverse prognosis—remains unclear. Most prior studies rely on static survival comparisons, which are susceptible to immortal-time bias, and do not formally test whether transplant benefit differs by mutational status. We applied a time-dependent interaction framework to identify molecular predictors of relapse-free survival (RFS) and overall survival (OS) benefit from allo-HCT.

Methods: We conducted a multicenter, retrospective study of 1,228 adult AML patients who achieved CR1, with next-generation sequencing data at diagnosis across five academic centers. Allo-HCT was modelled as a time-dependent covariate to minimize immortal time bias. Multivariable Cox regression models adjusted for age, white blood cell count, and cytogenetic risk. Somatic mutations were grouped into molecular clusters using pairwise Fisher's exact tests with false discovery rate correction, defining a co-mutated cluster 4 (ASXL1, RUNX1, BCOR, BCORL1). Interaction terms between mutation status and the time-dependent transplant variable were used to test whether transplant benefit differed by genomic subgroup formally.

Results: Among 1,228 patients, 593 (48.3%) underwent allo-HCT at a median of 107 days post-CR1. In time-dependent models, allo-HCT conferred marked RFS benefit in ASXL1-mutated patients (hazard ratio [HR] 0.22) with significant interaction (interaction HR 0.26,

p=0.004), indicating substantially greater benefit versus ASXL1-unmutated patients (HR 0.82). Similarly, RUNX1-mutated AML showed significant RFS improvement with allo-HCT (HR 0.29; interaction HR 0.35, p=0.01) versus RUNX1-unmutated disease (HR 0.81). At the pathway level, chromatin modifier mutations (interaction HR 0.53, p=0.02) and MDS-related gene mutations (interaction HR 0.62, p=0.03) predicted significant RFS benefit. Cluster 4 analysis showed pronounced RFS benefit from allo-HCT (interaction HR 0.45, p<0.01), Figure 1.For OS, significant interactions were observed in ASXL1-mutated (interaction HR 0.28, p=0.01) and RUNX1-mutated patients (interaction HR 0.37, p=0.0), with neutral transplant effects in unmutated groups. Cluster 4 demonstrated a significant OS benefit (interaction HR 0.50, p=0.01). Improvements were primarily driven by reduced relapse incidence.

Conclusions:


A
RFS — Allo-HCT effect (Mutations)
Status Unmut Mut
RFS — Interaction (Mutations)
sig: HR<1, p<0.05 / HR>1, p<0.05 / NS
ASXL1
BCOR
CEBPA
DNMT3A
EZH2
FLT3ITD
FLT3TKD
GATA2
IDH1
IDH2
JAK2
KIT
KRAS
NPM1
NRAS
PHF6
PTPN11
RAD21
RUNX1
SRSF2
STAG2
TET2
TP53
U2AF1
WT1
0.1
0.3
1.0
3.0
Hazard ratio for RFS (log scale)
Interaction HR for RFS (log scale)
B
RFS — Allo-HCT effect (Clusters, Pathways & Others)
RFS — Interaction
(Clusters, Pathways & Others)
Status Unmut Mut
sig: HR<1, p<0.05 / HR>1, p<0.05 / NS
Cluster 1
Cluster 2
Cluster 3
Cluster 4
Clusters
Activated Signaling
Chromatin Modifiers
Cohesin complex
DNA Methylation
Myeloid TF
Spliceosome
Tumor supressors
Pathways
MDS-related genes
NPM1mut/FLT3-ITDpos
Others
0.3
0.5
1.0
3.0
Hazard ratio for RFS (log scale)
Interaction HR for RFS (log scale)

Using time-dependent interaction analysis, we demonstrate that ASXL1, RUNX1, chromatin modifiers, and MDS-related mutations—and a mutated ASXL1/RUNX1/BCOR/BCORL1 cluster—identify AML patients deriving substantial survival benefit from allo-HCT in CR1. These mutations function as predictive biomarkers of transplant response, not merely adverse prognostic markers, supporting genomically guided transplant decision-making in AML.

Disclosure: No conflict of interest.

OS18-01

ULTRA-LOW-DOSE IL-10-EXPRESSING CAR-T CELLS ACHIEVE ROBUST COMPLETE REMISSION IN R/R DLBCL: RESULTS UPDATE OF A PHASE I TRIAL

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Background: Chimeric antigen receptor (CAR)-T cell therapy has transformed the management of relapsed/refractory (R/R) diffuse large B-cell lymphoma (DLBCL), yet suboptimal complete remission (CR) rates and limited T-cell persistence remain major challenges. IL-10 engineering enhances CAR-T cell function in solid tumor models, but its clinical relevance in lymphoma remains unknown. To address this, we conducted an open-label, single-arm, investigator-initiated phase I trial (NCT06120166) evaluating the IL-10-expressing CD19 CAR-T product, META 10-19, in patients with R/R DLBCL.
The primary objective was to assess the safety and tolerability of META 10-19. Secondary

objectives included the characterization of pharmacokinetics, *in vivo* expansion, cytokine profiles and preliminary antitumor efficacy.

Methods: Between December 2023 and April 2025, 13 patients with R/R DLBCL were enrolled and received a single infusion of META 10-19 across three dose levels (DLs): DL1 (2.0×10^4 cells/kg; n=3), DL2 (2.0×10^3 cells/kg; n=7, including 4 in dose expansion), and DL3 (5.0×10^3 cells/kg; n=3). All patients received standard fludarabine/ cyclophosphamide lymphodepletion. Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were graded using Lee 2014 and ASTCT 2019 criteria. Adverse events were assessed through CTCAE 5.0. Pharmacokinetics and immune correlates were evaluated through flow cytometry, serum cytokine analyses, and single-cell RNA sequencing (scRNA-Seq).

Results: As of November 15th, 2025, the objective response rate was 100%, comprising 11 patients achieving CR (91.7%) and 1 achieving partial remission (PR, 8.3%). CRS occurred in 12 patients (Grade 1: 8; Grade 2: 3; Grade 3: 1), while ICANS in 2 patients (Grade 1: 1; Grade 2: 1). All patients exhibited robust *in vivo* expansion of META 10-19 (median peak: 660.7 cells/μL), accompanied by marked increases in serum IL-10 levels (median peak: 1,221.59 pg/mL). scRNA-Seq showed that IL-10^+ $CD8^+$ CAR-T cells displayed transcriptional programs with heightened proliferation, activation, type 2 immune response, and IL-10 signaling, compared to IL-10^- $CD8^+$ CAR-T cells.

Conclusions: Ultra-low-dose of META 10-19 demonstrated potent antitumor activity, manageable safety, and exceptional proliferative capacity in R/R DLBCL. The doses used (2×10^3 - 2×10^4 CAR-T cells/kg) are the lowest reported in clinical CAR-T therapy to date, defining a new benchmark for potency and clinical scalability. As one of the first cytokine-engineered CAR-T products evaluated in R/R DLBCL patients, META 10-19 introduces a novel therapeutic paradigm for aggressive B-cell malignancies. Larger studies with extended follow-up are warranted to validate long-term durability and broader applications across hematologic and solid tumors.

Clinical Trial Registry: NCT06120166
https://clinicaltrials.gov/study/NCT06120166

Disclosure: Y.G. and L.T. are inventors of these patents relevant to the findings, co-founders, shareholders and advisors for Leman Biotech. The interests of L.T. were reviewed and managed by École Polytechnique Fédérale de Lausanne. The interests of Y.G. were reviewed and managed by Zhejiang University. D.B., B.C., Y.C., J.R., C.L., Y.L. and Q.C. are employees of Leman Biotech. The remaining authors declare no competing interests.

OS18-02

A GLOBAL PHASE 1B STUDY OF PRIZLO-CEL, A DUAL TARGETING CD20/CD19 CHIMERIC ANTIGEN RECEPTOR (CAR)-T CELL THERAPY, FOR PATIENTS WITH RELAPSED/REFRACTORY LARGE B CELL LYMPHOMA

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Background: CAR-T cell therapies have transformed the treatment landscape of relapsed/refractory (R/R) large B cell lymphoma (LBCL). However, >50% of patients relapse, in part due to CD19 tumor antigen escape. Dual targeting of two validated B-cell antigens, CD20 and CD19, may prevent relapses associated with CD19 antigen loss.
Prizlo-cel is an investigational dual targeting CD20/CD19 CAR-T cell therapy with an optimized CAR design and a differentiated CD20 binder. We report preliminary efficacy, safety, and biomarker analyses from the first global phase 1b (NCT05421663) study of prizlo-cel in CAR-T naive patients with R/R LBCL.

Methods: Prizlo-cel dose levels tested were 2.0 million (M) CAR-T cells/kg (n=18), 150M (n=8) and 75M (n=25) CAR-T cells. Primary objectives include safety and recommended phase 2 dose. Secondary objectives include preliminary efficacy and pharmacokinetics. Biomarker analyses include peripheral blood T cell expansion and B-cell depletion, tumor-

based CD20 and CD19 target expression and gene expression-based tumor microenvironment (TME; LymphoMAP) analysis.

Results: As of April 2025, 51 patients with R/R LBCL were infused; 39% had ≥2 prior lines of therapy; 67% had bridging therapy. Median follow-up was 8mo.
Across all doses, Grade 3 ICANS were reported in 4 (8%) of patients. Grade 3 CRS events were observed in 2 (4%) patients. All events were in the absence of prophylactic steroids.
Across all doses in 44 evaluable patients, ORR was 91% and CR rate was 75%. High response rates were achieved irrespective of number of prior lines of therapy.
Cellular kinetics showed comparable CAR-T cellular expansion, including CD4+ and CD8+ CAR-T cells at peak expansion, and comparable B-cell depletion across doses. Moreover, few Grade 3 ICANS and CRS events were observed with comparable CAR-T expansion across doses.
High response rates were observed across varying levels of CD20 or CD19 expression. In 31 patients with CD20 and CD19 high/medium (H-score >100), ORR and CR rates were 100% and 90%, respectively. In 11 patients with low expression of one or both antigens (CD20 or CD19 H-score <100), ORR and CR rates were 82% and 73%, respectively. Initial findings from 30 patients with available gene expression data showed 100% ORR across all LymphoMAP archetypes, with high CR rates across lymph node (94%), fibroblast/macrophage (83%), and T exhausted (80%) TME archetypes.

Conclusions: Initial findings from this global phase 1b study showed that prizlo-cel has a favorable safety profile, with low and manageable rates of Grade 3 CRS and ICANS, and high CR rates in CAR-T–naïve patients with R/R LBCL. High response rates were observed across a range of CD20 and CD19 expression levels and immunosuppressive TME archetypes. Taken together, these data suggest that dual antigen targeting of CD20 and CD19 with prizlo-cel via an optimized CAR-T construct may overcome the limitations of single-antigen CAR-T cell therapies, with the potential of improving clinical outcomes.

Clinical Trial Registry: NCT05421663

Disclosure: Margot Jak, Luke Mountjoy, Jacob Haaber Christensen, Yasmina Serroukh, and Laura Magnano have nothing to disclose
Krish Patel is a consultant/advisory board member for AstraZeneca, ADC Therapeutics, Abbvie, BeiGene, BMS, Caribou, Century Therapeutics, Fate Therapeutics, Genentech/Roche, Janssen, Kite, Lilly/Loxo, Merck, Nurix Therapeutics, Pfizer and received research funding (institution): Accutar, Arvinas, AstraZeneca, Abbvie, Bristol Myers Squibb, Caribou, CRISPR therapeutics, Century Therapeutics, Fate Therapeutics, Genentech/Roche, Janssen, Kite, Lilly/Loxo, Merck, Nurix Therapeutics, Pfizer, and Xencor
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OS18-03

PHASE I/IIA MULTICENTER TRIAL OF NON-VIRAL SLEEPING BEAUTY TRANSPOSON-ENGINEERED CD19 CAR-T CELLS (TRANSPOCART19) IN RELAPSED/REFRACTORY B-CELL LYMPHOMAS: RESULTS FROM DOSE LEVELS 1 AND 2

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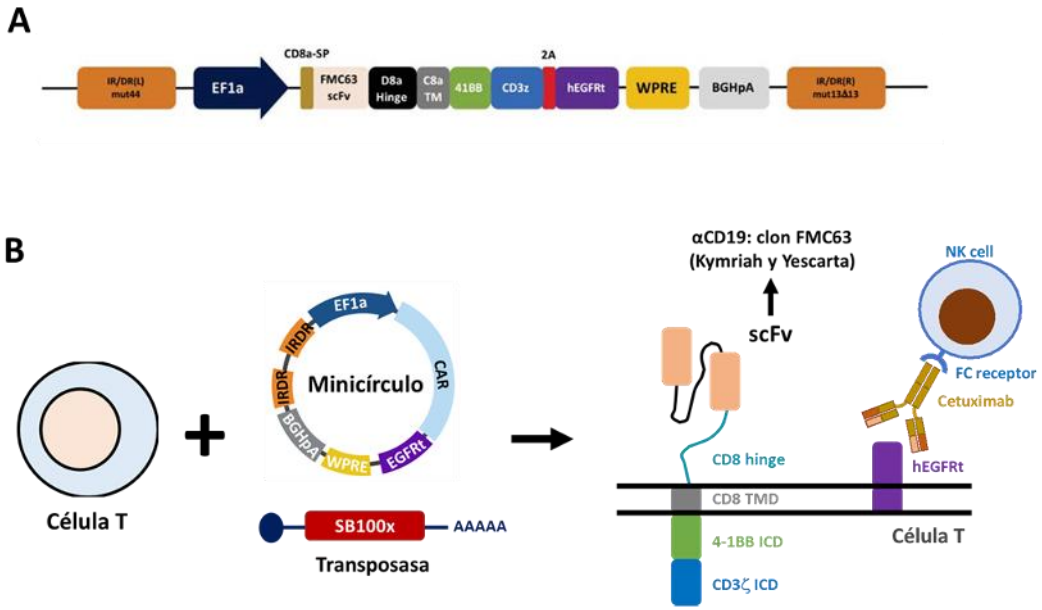
Background:



TranspoCART19 is an academic project designed to develop an innovative, virus-free CAR-T cell therapy for adults with relapsed/refractory (R/R) B-cell lymphomas. Using the *Sleeping Beauty* transposon system, the TranspoCART19 product encodes a 4-1BB-costimulated anti-CD19 CAR together with a truncated EGFR safety switch. Following successful preclinical development and regulatory approval, a multicenter phase I/IIa clinical trial (NCT06378190) was initiated in May 2023.

Methods: This is an open-label, multicenter, non-randomized phase I/IIa trial evaluating safety, feasibility, and preliminary efficacy. Dose escalation follows a 3+3 design with three dose levels (1, 3, and 5 $\times 10^6$ CAR-T/kg), followed by an expansion cohort at the recommended phase II dose. The CAR-T product is infused fractionally (10%, 30%, 60% on days 0, +1, +4). This abstract summarizes safety and preliminary efficacy findings from patients treated in the first two dose levels of the ongoing dose-escalation phase.

Results: As of November 2025, 10 patients were enrolled and seven received TranspoCART19 (four at 1×10^6/kg; three at 3×10^6/kg), while three additional patients have completed apheresis and manufacturing and are pending infusion (Dose Level 3). Manufacturing was successful for all apheresed patients, with no manufacturing failures or out-of-specification products. Patient-level characteristics and outcomes are summarized in the Table.
Safety: No DLTs were reported. Across all infused patients, CRS occurred in 3/7 cases, all grade 1 and self-limited except for one requiring a single dose of tocilizumab. The only patient who developed ICANS was the one with rapidly progressive primary CNS lymphoma, who progressed early and was withdrawn on day +20, subsequently dying from progressive disease on day +31 (he was replaced per DSMB rules to complete dose level 1). He had a possible grade 3 ICANS, although grading was unreliable due to markedly abnormal neurological status at baseline (ICE 5–8). No other patient developed ICANS or any neurological adverse events. There were no cases of IEC-HS. Cytopenias were transient or intermittent, responsive to supportive care, and no patient developed an aplastic phenotype. After a median follow-up of 199 days (range, 62–519), four SAEs have been reported: two febrile neutropenia, one abdominal sepsis, and one papillary thyroid carcinoma in a patient with a pre-CAR-T benign thyroid lesion. No treatment-related deaths occurred.
Efficacy: With the exception of the patient with rapidly progressive primary CNS lymphoma who experienced early disease progression, all six remaining patients achieved complete metabolic response at first assessment (day +28), which has been maintained in subsequent evaluations. In-vivo expansion of TranspoCART19 was detected in all patients, with CAR-T peaks at day +14 and detectable persistence up to day +56 in three out of four patients with available data.

Baseline Characteristics and Outcomes of TranspoCART19-Treated Patients (n = 7)

Variable	Patient 002-1	Patient 001-1	Patient 001-2	Patient 001-3	Patient 001-4	Patient 004-1	Patient 004-2
Dose level	1×10^6/kg	1×10^6/kg	1×10^6/kg	1×10^6/kg	3×10^6/kg	3×10^6/kg	3×10^6/kg

Variable	Patient 002-1	Patient 001-1	Patient 001-2	Patient 001-3	Patient 001-4	Patient 004-1	Patient 004-2
Age (years)	53	53	67	73	74	68	68
Sex	F	M	F	M	F	M	M
ECOG	0	2	1	1	1	0	0
Diagnosis	Marginal zone lymphoma	Primary CNS lymphoma	Difuse large B-cell lymphoma	Follicular lymphoma	Follicular lymphoma	Follicular lymphoma	Follicular lymphoma
Lines of prior therapy	8	3	2	2	4	3	2
Bridging therapy	R-GemOx	Dex + ibrutinib; R-IE; Dex maintenance	Pola-GemOx	None	None	None	R-CVP
Disease preLD	PR	PD	PD	PD	PD	PD	PR
Hematotox score	2	2	0	1	1	NA	NA
CRS (grade)	0	1 (toci x 1)	0	0	1	0	1
ICANS (grade)	0	3 (grading was not reliable)	0	0	0	0	0
Infections (grade ≥3)	Febrile neutropenia	None	Abdominal sepsis and papillary thyroid carcinoma	None	None	None	None

Variable	Patient 002-1	Patient 001-1	Patient 001-2	Patient 001-3	Patient 001-4	Patient 004-1	Patient 004-2
Day +28 response	CR	PD	CR	CR	CR	CR	CR
Day +100 response	CR	NA	CR	CR	CR	Not due yet	Not due yet
Day +180 response	CR	NA	CR	CR	Not due yet		
Day +365 response	CR	NA	CR	Not due yet			
Status at last follow-up	Ongoing CR	Dead due PD	Ongoing CR	Ongoing CR	Ongoing CR	Ongoing CR	Ongoing CR

Conclusions: Manufacturing feasibility was confirmed, with all apheresed patients producing a product that met release criteria. TranspoCART19 also demonstrated a highly favorable safety profile across two dose levels and promising early efficacy, with sustained metabolic complete responses in all evaluable patients. These results support continuation of dose escalation and subsequent expansion.

Clinical Trial Registry: NCT06378190

Disclosure: Nothing to declare.

OS18-07

EXTENDED CLINICAL AND GENOMIC EVALUATION OF CTX130, A CD70-DIRECTED ALLOGENEIC CAR T THERAPY, IN ADULT T-CELL LEUKEMIA/LYMPHOMA: RESULTS FROM THE FIRST-IN-HUMAN COBALT-LYM PHASE I TRIAL

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Background: Adult T-cell leukemia/lymphoma (ATLL) is a rare, aggressive $CD4^+$ T-cell malignancy driven by HTLV-I infection and associated with poor outcomes, particularly in the relapsed/refractory setting where effective therapies are lacking. CD70 is aberrantly expressed in ATLL and contributes to immune escape through CD27-mediated signaling, making it a compelling immunotherapeutic target. CTX130 is an allogeneic CRISPR-Cas9–

engineered CAR T-cell product directed against CD70. We report clinical outcomes and genomic correlates from six patients with relapsed/refractory ATLL treated with CTX130 in the Phase I COBALT-LYM trial, including next-generation sequencing (NGS) findings from four patients.

Methods: This single-arm, open-label Phase I study evaluated CTX130 in patients with relapsed or refractory T-cell malignancies at sites in the USA, Australia, and Canada. We describe the experience from our center's ATLL cohort. Patients were required to have received ≥1 prior systemic therapy and have ECOG 0–1. All underwent lymphodepletion with fludarabine and cyclophosphamide before CTX130 infusion; repeat dosing was allowed per protocol. The primary endpoint was safety. Secondary endpoints included overall response rate (ORR), progression-free survival (PFS), and overall survival (OS). NGS was performed (NeoGenomics) on peripheral blood samples from four patients to characterize mutational profiles and assess clonal dynamics pre- and post-treatment.

Results: Six patients with previously treated ATLL received CTX130 between August 28, 2020, and May 30, 2023, with follow-up through July 2025. Median age was 54 years (range 33–72), with a median of one prior therapy (range 1–5). Two patients (29%) had acute/leukemic ATLL and four (71%) had lymphomatous disease. CTX130 dose levels ranged from 3×10^7 to 9×10^8 CAR T cells; three patients received a second infusion. No cytokine release syndrome (CRS) or ICANS was observed. Grade ≥3 adverse events consisted primarily of infections and neutropenia.
The ORR was 50% (three of six patients), including two complete responses (CRs) and one partial response (PR). Median PFS was 2.5 months, and median OS was 7.8 months. Two patients remained alive as of July 2025, with one achieving prolonged survival of 37.5 months. NGS demonstrated dynamic genomic changes in two patients with paired samples, including shifts in variant allele frequencies and acquisition of new mutations. A STAT3 mutation emerged post-therapy in one long-term responder, consistent with reports associating STAT3 alterations with more indolent ATLL biology. These findings suggest that CAR T-cell–mediated immune pressure may drive clonal remodeling and, in select patients, contribute to more favorable disease trajectories.

Conclusions: CTX130 showed encouraging activity and manageable toxicity in relapsed/refractory ATLL, producing a 50% ORR in a population with historically limited treatment options. The presence of two long-term survivors represents the first documented durable remissions from our center's ATLL CAR T program. Genomic analyses indicate that ATLL can undergo clonal adaptation under CAR T-cell pressure, warranting deeper investigation into predictors of response. These results support ongoing development of CD70-targeted therapies, including next-generation CTX131, and highlight the need for larger studies to refine patient selection and integrate molecular biomarkers into therapeutic decision-making.

Clinical Trial Registry: NCT04502446
https://clinicaltrials.gov/study/NCT04502446

Disclosure: No conflicts of interest to report.

OS18-08

ADOPTIVE TRANSFER OF MULTIVIRUS-SPECIFIC T CELLS AGAINST REFRACTORY CMV, ADV AND EBV INFECTIONS AFTER STEM CELL TRANSPLANTATION – INTERIM RESULTS FROM THE "TRACE" PHASE-III TRIAL

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Background: Patients with chemo-refractory CMV, EBV, or AdV infections following allogeneic stem cell transplantation (SCT) are exposed to a high morbidity and mortality, with limited approved treatment options. Adoptive transfer of multivirus-specific T cells has shown promising results in early studies. TRACE was the first placebo-controlled phase-III trial evaluating the efficacy and safety of multivirus-specific T-cell infusion in this patient population. The primary endpoints are viral clearance (two consecutive negative PCRs) and progression rates between Day 7 and Week 8 after investigational medical product (IMP) infusion. Incidence and severity of graft-versus-host disease (GvHD) as well as the frequency of *in vivo* expanded virus-specific T-cells are amongst the secondary endpoints.

Methods: TRACE is a prospective, multicentre, double-blind, placebo-controlled randomized phase-III trial conducted across 33 European centres. The IMP is produced in 7 decentralized academic GMP units. Patients can be included, if viremia is resistant to at least two weeks of antiviral first-line therapy. Only IMPs produced using cells from the original SCT donor are accepted. The IMP consists of donor-derived CD4+ and CD8+ T lymphocytes enriched for CMV, EBV, and AdV specificity using the CliniMACS IFNy-Capture System after exposure to overlapping peptide mix. Patients are randomized 2:1 (verum:placebo). The pre-planned interim analysis was performed after 39 evaluable patients (57% of the aimed total). Significance levels were adjusted for multiple testing.

Results: Harmonization of academic GMP production across all participating countries (Italy, Germany, the Netherlands, Belgium, France and Spain) was successful, including diagnostic methods and reproducible quality control, to allow inter-center-comparability. In the interim analysis, 2 primary efficacy endpoints were assessed in 39 evaluable patients across the 2 treatment groups (placebo or verum) in a blinded manner. First, viral clearance showed a remarkable clearance rate of 56% in group A compared to only 36% in group B. Second, 76% of patients did not progress in group A compared to 57% in group B. Neither test was statistically significant, therefore the clinical trial continues with both treatment arms. Of the

39 evaluable patients, 26% were enrolled due to AdV, 51% due to CMV and 3% due to EBV infection, and 20% presented with multiple viral infections. Induction of a virus-specific T cell response *in vivo* could be successfully detected. Safety analysis was performed, with GvHD as AE of special interest and no safety concerns have been raised. In light of this last evidence, the independent advisory board ("Scientific Ethics Advisory and Data Safety Monitoring Board") recommended the study to continue.

Conclusions: Set-up and conduct of a phase-III IIT aimed at restoring pathogen-specific immunity is feasible. TRACE is designed to provide evidence for the efficacy and safety of multivirus-specific T-cell infusion in patients with chemo-refractory viral infections post-SCT. Given the high need to generate efficacy data, this approach may represent a novel therapeutic option for this vulnerable patient population.

Clinical Trial Registry: ClinicalTrials.gov ID: NCT04832607
EUCT: 2024-512321-84-00
DRKS: DRKS00018985
https://www.uniklinik-freiburg.de/trace-study.html

Disclosure: LH is an employee of Miltenyi Biomedicine. Miltenyi Biotec B.V. & Co. KG supports IMP manufacturing for the clinical trial.

Paed3-04

SEROTHERAPY IN CORD BLOOD HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH MALIGNANCIES: RESULTS OF A RETROSPECTIVE MULTICENTER STUDY BY AIEOP (ASSOCIAZIONE ITALIANA ONCOEMATOLOGIA PEDIATRICA)

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Background: The role of T-cell depletion/modulation by serotherapy in cord blood hematopoietic stem cell transplantation (CB-HSCT) has not been fully elucidated, and recent studies suggest that CB-HSCT without serotherapy may be the optimal option in high-risk

and relapsed/refractory pediatric myeloid malignancies, because of an acceptable non-relapse mortality (NRM) combined to a strong graft-versus-leukemia effect.

Methods: In this multicenter study, we retrospectively analyzed the outcome of a cohort of pediatric patients (n=289) with malignant diseases undergoing unrelated CB-HSCT from 01/01/2000 to 31/12/2022 who did (ATG; n=252) or did not receive (no-ATG; n=37) serotherapy as part of their GvHD prophylaxis. Overall, 88 patients (30%) underwent transplant in advanced disease phase defined as either after the failure of a previous transplant or without heamatological remission at the time conditioning was initiated.

Results: The study involved 21 centers. The median duration of the follow-up of the entire study population was of 9 years (IQR 5,3-12,6) with no differences in the two subgroups. Median time to neutrophil engraftment was 24 days (range 12-76) in ATG group and 28 days (range 10-47) in no-ATG group (p=0.44). At day + 45 the cumulative incidence of graft failure was 2,4% (95%CI 1,1-5,3) in ATG group and 5,5% (95%CI 1,4-21,3) in no-ATG group (p=0,28).
In univariable analysis, the composite endpoint of 5-year chronic GvHD-free, relapse-free survival (cGRFS) was 47,2% (95% CI: 39–55%) and 60% (95% CI:38 –81%) in ATG and no-ATG group, respectively (p = 0.39). In multivariable analysis, only disease phase showed a statistically significant correlation with cGRFS [early disease phase RR 0,67 (95%CI 0,52-0,88) p=0.004]The cumulative incidence of NRM was 30% (95%CI 24-36) in ATG patients and 36% (95%CI 22-57) in no-ATG patients (p=0.6), while the cumulative incidence of relapse (CIR) was 19% (95%CI 14-25) and 25% (95%CI 14-45) in ATG patients and non-ATG patients, respectively (p= 0.34). In patients with advanced disease phase, a CIR of 29% (95% CI: 21–40) was observed. In multivariable analysis, disease phase and year of HSCT were related to NRM (early disease phase RR 0.34 95%CI 0.16-0.71 p= 0.004, transplant year before 2010 RR 0.38 95%CI 0.19-0.75 p= 0.005); disease phase correlated with relapse (early disease phase RR 0.52 95%CI 0.32-0.85 p= 0.001).
Cumulative incidence of grade II-IV aGvHD was 32% (95%CI 26-38) and 26% (95%CI 15-48) in ATG and no ATG subgroups (p=0.63), respectively. Cumulative incidence of cGVHD was 16% (95%CI 11-23) in ATG patients and 8% (95%CI 1-50) in no-ATG patients (p=0.43).

Conclusions: In conclusion our study suggests that the use of ATG for GvHD prophylaxis in CB-HSCT from unrelated donors, differently from transplantation using bone marrow or peripheral blood as stem cell source, does not correlate with a better outcome, and confirms a strong graft-versus-leukemia effects of this stem cell source, as previously demonstrated by other studies.

Disclosure: Nothing to declare.

Paed4-07

TREOSULFAN-BASED REDUCED-TOXICITY CONDITIONING IN CHILDREN WITH INBORN ERRORS OF IMMUNITY: REPORT OF RETROSPECTIVE STUDY FROM A SINGLE CENTER IN CANADA

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Background: Children with inborn errors of immunity (IEI) display diverse symptoms. Allogeneic hematopoeitic stem cell transplant (HSCT) is the main cure, with traditional myeloablative conditioning (busulfan and cyclophosphamide) providing good engraftment but high toxicity (veno-oclussive disease) and long-term risks. Since 2016, the Hospital for Sick Children in Toronto has used Treosulfan-based conditioning for IEI patients. We performed a retrospective review to assess outcomes and survival with this regimen.

Methods: We retrospectively reviewed charts of IEI patients under 18 years who received allogeneic HSCT with Treosulfan-based reduced-toxicity conditioning at Sick Children's Hospital from July 2016 to June 2025, following REB approval. Outcomes were compared to published North American Busulfan-based cohorts. We evaluated overall survival, transplant-related mortality, acute and chronic complications, chimerism, immune reconstitution, IVIG independence, and vaccine response.

Results: Between July 2016 and June 2025, ninety-four children diagnosed with inborn errors of immunity (IEI) underwent allogeneic hematopoietic stem cell transplantation (HSCT) at The Hospital for Sick Children. The median follow-up period was 36 months, ranging from 3 months to 8 years. The median age at transplant was 2 years (range: 2 months to 17 years), with males comprising 62% of the cohort.
The IEI diagnoses included haemophagocytic lymphohistiocytosis (HLH; n=20), severe combined immunodeficiency (SCID; n=18), chronic granulomatous disease (CGD; n=12), combined immunodeficiency (CID; n=5), and other IEI disorders (n=39). All patients received a Treosulfan-based conditioning regimen, predominantly Treosulfan/Fludarabine/Cyclophosphamide (n=79), Treosulfan/Fludarabine (n=14), or Treosulfan/Fludarabine/Thiotepa (n=1). Serotherapy with antithymocyte globulin (ATG) was administered to all individuals.
Donor types included cord unrelated donors (CURD; n=38), matched unrelated donors (MUD; n=21), matched sibling donors (MSD; n=19), mismatched unrelated donors (MMUD; n=9), and haploidentical donors (n=7). Sources of stem cells were peripheral blood (n=37), bone marrow grafts (n=19), and cord blood (n=38).
The overall survival rate was 91%, similar to the historical PIDTC range (67%-95%). There were eight deaths: survival rates were 83% in SCID, 85% in HLH, and 91% in CGD groups. Acute GVHD occurred in 51% of patients (44/86), with grade III-IV seen in 6.8% (6/86). Chronic GVHD was reported in 41% (36/86), but severe cases comprised only 4%. VOD developed in 3.6% (3/86). Chimerism analysis showed full donor chimerism in 51% (44/86) and mixed in 48% (42/86). Most patients (94%) were off IVIG at analysis.

Conclusions: This is the first North American study of IEI children receiving Treosulfan-based conditioning, demonstrating excellent results with reduced transplant mortality, lower VOD rates, acceptable GVHD rates, and IVIG independence.

Clinical Trial Registry: NA

Disclosure: Nothing to disclose

A037

EMAPALUMAB INDUCES RAPID, DURABLE RESPONSES AND RELIABLE BRIDGING TO CURATIVE HSCT IN PATIENTS WITH PRIMARY HLH: POOLED ANALYSIS OF PROSPECTIVE TRIALS NI-0501-04, NI-0501-05 AND NI-0501-09

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Background: Emapalumab, a fully human anti-interferon-γ (IFNγ) monoclonal antibody, is FDA-approved for adult/paediatric patients with pHLH with refractory, recurrent or progressive disease or intolerance to conventional HLH therapy. Primary hemophagocytic lymphohistiocytosis (pHLH) is a life-threatening, genetically driven, IFNγ–mediated hyperinflammatory disorder. Allogeneic hematopoietic stem-cell transplantation (HSCT) still remains the only potentially curative therapy, but optimal conditioning and transplant success depend on achieving adequate disease control beforehand. The pivotal NI-0501-04 study first showed, and the NI-0501-09 study later confirmed, that emapalumab rapidly controls hyperinflammation and enables successful HSCT in patients with pHLH (Locatelli et al., 2020, 2025).

Methods: We conducted a pooled analysis of 3 prospective studies (NI-0501-04 [2013 to 2019; n=45], NI-0501-05 [2021; n=37 of 45 in NI-0501-04], NI-0501-09 [2019 to 2022; n=35] for a total of 80 emapalumab-treated patients. Clinical responses were based on an investigator's global assessment, classified as complete response [CR] (complete response or non-active disease), partial response [PR] (partial response or HLH improvement) or no response [NR] (progressive disease, reactivation, worsening or death). Investigator-assessed OR was defined as achieving either CR or PR. Patients who received ≥3 emapalumab doses with investigator assessments made up the response-evaluable set at week 8 or EOT (n=62) and the best-response set (n=71); those with ≥3-month follow-up formed the bridging-success survival set (n=73). Safety was not evaluated in this pooled analysis. Analyses were descriptive.

Results: At baseline, the median age was 0.8 years (range 0.01–16.67); 54% (43/80) were males; 31% (25/80) had central nervous system involvement and 66% (53/80) had received prior HLH therapy. At Week 8/EOT, 55/62 evaluable patients achieved OR (89%), including CR in 14/62 (23%). Considering best response up to Week 8/EOT, 67/71 patients responded (94%) and 23/71 attained CR (32%). Median time to first OR was 16 days.
Bridging-success survival was achieved by 57/73 patients (78%): 51 proceeded to HSCT and 6, without HSCT, were alive ≥3 months after EOT (median 358 days; [95% CI 109-380]). An assessment of CR or PR by Week 8 conferred a greater probability of bridging success than NR (93% and 90%, respectively vs 43%).
GC tapering by at least 25% and 50% from baseline occurred within 14 days for 29/73 patients (40%) and 19/73 patients (26%), respectively. By EOT, 35/73 (48%) and 26/73 (36%) achieved those same reductions.

Conclusions: In pHLH, emapalumab rapidly achieves clinically meaningful and durable disease control, enables GC reduction, and successfully bridges to HSCT or ≥3 months survival without HSCT in 78% of patients. These findings reinforce emapalumab's role as an effective IFNγ neutralizing bridge to curative HSCT in a high-risk pediatric population.

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Clinical Trial Registry: NI-0501-04 (NCT01818492): A Phase 2/3, Open-label, Single Arm, Multicentre Study to Assess Safety, Tolerability, Pharmacokinetics and Efficacy of Intravenous Multiple Administrations of NI-0501, an Anti-interferon Gamma (Anti-IFNγ) Monoclonal Antibody, in Paediatric Patients with Primary Haemophagocytic Lymphohistiocytosis (HLH)
NI-0501-05 (NCT02069899): A Study for Long-term Follow-up of Hemophagocytic Lymphohistiocytosis (HLH) Participants Who Received Treatment With Emapalumab (NI-0501), an Anti-interferon Gamma Monoclonal Antibody
NI-0501-09 (NCT03312751): Study to Assess the Efficacy and Safety of Emapalumab in Primary Haemophagocytic Lymphohistiocytosis

Disclosure: Franco Locatelli: Speaker`s Bureau: Miltenyi, Amgen, Novartis, BMS, Gilead, Sobi; Advisory Board: Amgen, Novartis, Sanofi, Vertex;
Michael B. Jordan: Honoraria: Sobi; Research Funding: Sobi; Didier Halimi: Consultancy: Sobi;
Elena Burillo: employee: Sobi; Divested equity in a private or publicly-traded company in the past 24 months: Sobi; Current equity holder in publicly-traded company: Sobi;
Brian D. Jamieson: Employee: Sobi, Inc.; Emmanuel Monnet: Patents: MerckSerono, Novimmune, Sobi; Divested equity in a private or publicly-traded company in the past 24 months: Sobi; Current equity holder in publicly-traded company: Sobi, Sanofi; Employee: Sobi;
Andrew Danquah: Employee: Sobi.

A038

INTERIM CLINICAL OUTCOMES IN ORCA-T WITH REDUCED INTENSITY CONDITIONING: AN OBSERVATIONAL COMPARISON TO REGISTRY-BASED POST-TRANSPLANT CYCLOPHOSPHAMIDE PATIENTS

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Background: Orca-T is an investigational precision cell therapy that has been evaluated in the context of myeloablative conditioning for allogeneic treatment of hematological disorders. In a ph1b clinical trial (NCT04013685) in patients with acute leukemias and MDS, Orca-T exhibited an excellent safety profile and low rates of serious graft-versus-host disease (GVHD). In a ph3 randomized trial (NCT05316701), in comparison to calcineurin inhibitor/methotrexate prophylaxis, Orca-T met the primary endpoint of improving moderate-to-severe chronic GVHD-free survival. Studies of Orca-T combined with reduced intensity conditioning (RIC) are ongoing. Here we report interim clinical outcomes in Orca-T patients who received RIC in comparison to a registry cohort who received RIC plus post-transplant cyclophosphamide (PTCy).

Methods: Patients on a single-center ph1 study (NCT05088356) of Orca T in RIC who were diagnosed with ALL, AML, or MDS (n=46) were included in this evaluation. The other patients with myelofibrosis or a haploidentical donor were excluded (n=7). Contemporaneous patient level data were obtained from CIBMTR-NMDP. The comparator group included adults in the CIBMTR registry treated with RIC + PTCy + tacrolimus ± mycophenolate (n=587). The pre-transplant demographic and clinical characteristics were similar between cohorts. The included participants were adults ages 60-75, had intermediate- to high-risk AML, ALL or MDS, received RIC, and had a 7/8 or 8/8 HLA-matched donor. We studied the following endpoints: overall survival (OS), relapse-free survival (RFS), GVHD and relapse-free survival (GRFS), moderate-severe chronic GVHD-free survival (cGFS), and the cumulative incidences of non-relapse mortality (NRM), relapse, grades 3-4 acute GVHD and moderate-severe chronic GVHD. Standard survival and competing risk methods were used; $p<.05$ defined significance.

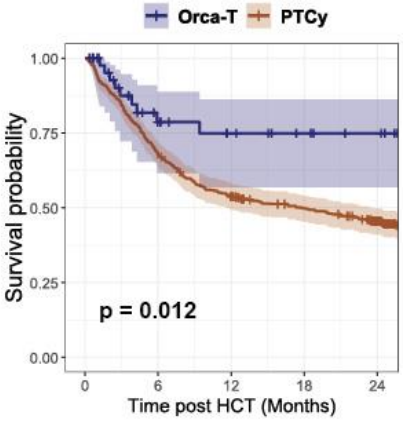
Results: Although this is a retrospective analysis, each of the clinical outcome estimates strongly favored Orca-T, with RFS (p=.034), GRFS (p=.012), and cGFS (p=.034) (Table 1). Notably, the 1-year GRFS estimate for Orca-T of 75% (95% CI = 57-86%) was remarkably high (Figure 1). While the cumulative incidence estimates of serious GVHD were low in both groups, none of the Orca-T patients experienced gr. 3-4 aGVHD.

Table 1. Clinical Outcomes.

Outcome[1]	Orca-T (N=46)	PTCy (N=587)	P-value[2]
Overall survival	86% (70-94%)	72% (68-75%)	0.066
RFS	81% (65-91%)	61% (57-65%)	**0.034**
GRFS	75% (57-86%)	54% (49-58%)	**0.012**
cGFS	79% (61-90%)	64% (60-67%)	**0.034**
NRM	8.1% (2.0-20%)	16% (13-19%)	0.4
Relapse	10% (3.2-23%)	23% (20-27%)	0.067
aGVHD gr.3-4	0.00% (—%)	5.8% (4.1-7.9%)	0.12
cGVHD mod-sev	6.9% (1.1-20%)	10% (7.9-13%)	0.4

[1] 1-year estimate (95% CI)
[2] Log-rank test (survival) or Gray's test (cumulative incidence)

Figure 1. GRFS.



Conclusions: Interim analyses of RIC + Orca-T patients revealed low GVHD, relapse, and NRM rates. Comparison to RIC + PTCy patients in the CIBMTR registry suggested a clinical benefit of RIC + Orca-T. These findings provide insight for improving clinical outcomes in older patients and high comorbidity patients unable to receive myeloablative conditioning regimens.

Clinical Trial Registry: NCT04013685 https://clinicaltrials.gov/study/NCT04013685 NCT05316701 https://clinicaltrials.gov/study/NCT05316701

Disclosure: Alejandro Villar-Prados: presentation for Tandem 2026 for Orca Bio; Anna Pavlova, MD, PhD: employee and equity holder at Orca Bio; Nathaniel B. Fernhoff, PhD: employee, officer, and equity holder at Orca Bio; James Scott McClellan, MD, PhD: employee, officer, and equity holder at Orca Bio; Scott Killian, MPH, PhD: employed by Orca Bio; Robert S. Negrin, MD: consulting fees from Amgen, Garuda (now Strada Therapeutics), Biorasi, Apia Bio, Cellenko, and ReStem; Patents planned, issued, or pending for methods for allogeneic transplantation licensed to Orca Bio; participation on data safety monitoring boards or advisory boards for Kura Oncology and University of Pennsylvania; leadership roles as Vice President and President Elect of the American Society of Hematology; stock or stock options in Garuda Therapeutics (now Strada Therapeutics); Everett H. Meyer, MD, PhD: Orca Biosystems clinical trial funding.

A039

CONTEMPORARY CAUSES OF ACUTE TRANSPLANT-RELATED MORTALITY (TRM) AFTER ALLOGRAFT IN A COHORT OF 2312 PAEDIATRIC PATIENTS: A REPORT FROM THE BSBMTCT, PAEDIATRIC GROUP

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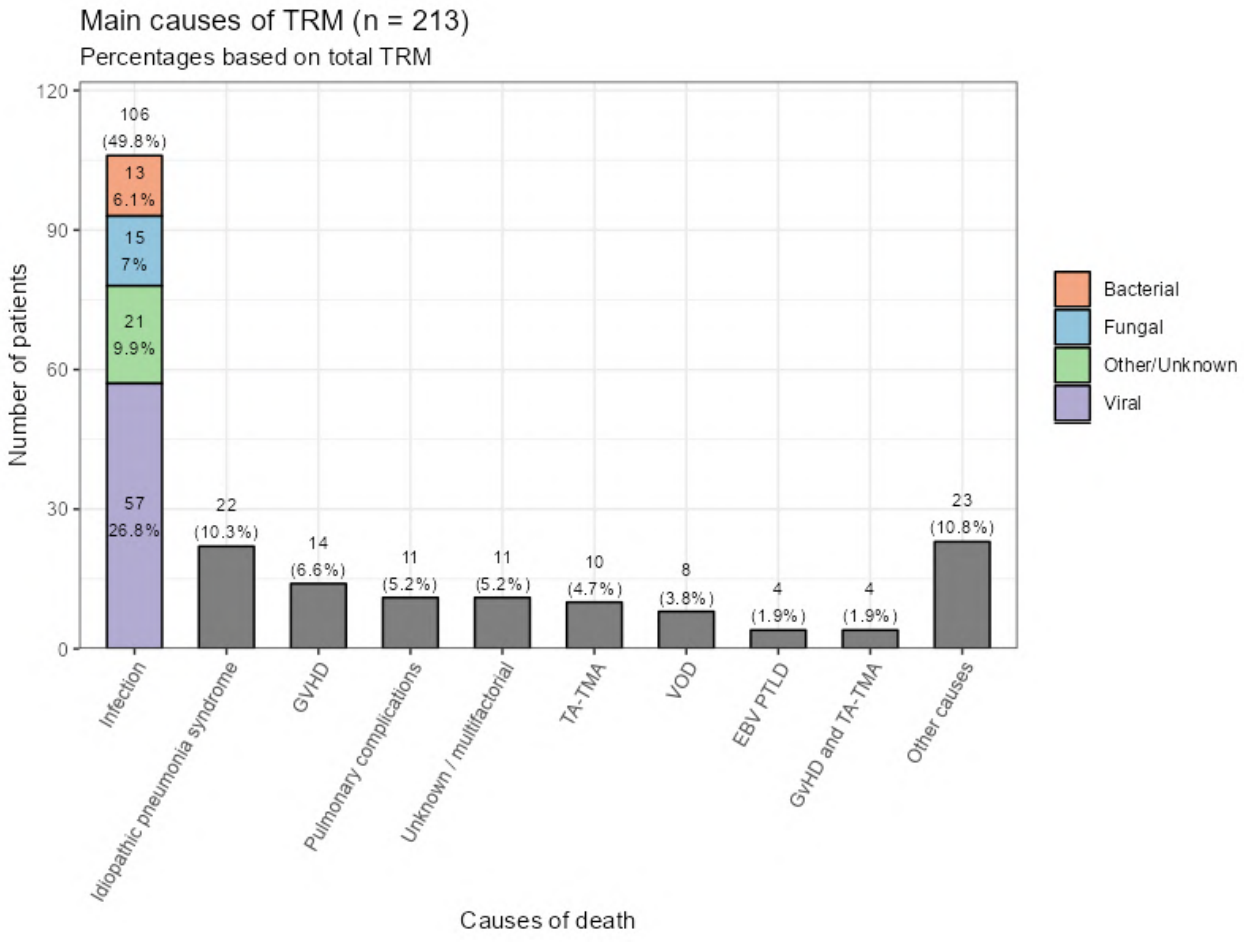
Background: A retrospective analysis of all paediatric patients undergoing allogeneic hematopoietic stem cell transplant (HSCT) in all 13 British Society of Bone Marrow Transplant and Cellular Therapies (BSBMTCT) centres from 2017 to 2023 was performed to determine the contemporary rate and causes of TRM.

Methods: Data from annual national audit meetings were reviewed for cause of death, which was then classified as relapse or TRM. The proportion of TRM was compared across groups.

Results: A total of 2312 patients (0 – 19 years, median = 7y) received allogeneic HSCT during the study period. Follow-up time varied from 10 months to 21 months depending on date of transplant and the annual data collection cut-off.
Overall mortality was 14% (334/2312 patients). Relapse rate was 5% at time of analysis although this is likely to increase with longer follow-up. The overall TRM was 9% (213/2312 patients). Over time, this fell from 12.5% in 2017 to 6.9% in 2023 (p = 0.44). Patients with TRM died at a median of 80 (+/-54) days after transplant.
The main causes of TRM are shown in Figure 1. Infection accounted for almost half of TRM. Viral infections predominated (27% of TRM), particularly adenovirus [29 patients (14%

overall TRM), cytomegalovirus [15 (7%)], and parainfluenza [11 (5%)]. Graft-versus-host disease (GVHD) by itself or in combination with other diagnoses was the cause of TRM in 33 patients (14.3 %). The "other causes" category (11%) mostly included cases of directed organ or systemic drug toxicity.
When analysing the difference in TRM proportion across groups (table 1) we observed a higher TRM in patients with a diagnosis of inborn errors of metabolism (15.4%) and inborn errors of immunity (IEI) (11.3%), whereas TRM in patients with haemoglobinopathies (4.2%) and bone marrow failure (3.7%) was very low. In patients with leukaemia, TRM was lower in those transplanted in CR1 than with advanced disease (p< 0.01). In terms of donor type, MSD had the lowest TRM (5.7%), and haploidentical transplants the highest (16.4%) (p <0.01). Difference between MSD (5.7%) and MUD (9.3%) was borderline significant (p = 0.05). Use of bone marrow as graft source was associated with a significantly lower TRM (7%) compared to PBSC (11.9%) and umbilical cord (11.7%) (p = <0.01). TRM was comparable in recipients of myeloablative (10.7%) and reduced intensity conditioning (11%), but significantly lower in those who received non-myeloablative conditioning (4.1%) (p<0.05). TRM was significantly higher in second transplants (p<0.01).



	Number of patients in each subgroup (%)	Number of deaths due to TRM	Statistical comparison
Diagnoses: • Leukaemia • Inborn errors of Immunity • Bone marrow failure • Non-malignant haematological conditions (SCD, thalassaemia) • Inborn errors of metabolism • Myelodysplasia • Lymphoma • Graft failure • Autoimmune diseases • Other conditions • No diagnosis documented	867 (37%) 478 (21%) 349 (15%) 238 (10%) 149 (6%) 123 (5%) 57 (3%) 29 (1%) 11 (0.5%) 6 (0.3%) 5 (0.2%)	84 (9.7%) " 54 (11.3%) # 13 (3.7%) " # > 10 (4.2%)* } 23 (15.4%)* > } 11 (8.9%) 2 (3.5%) 10 (34.5%) " # } 4 (36.4%) 2 (33.3%) -	" # > * } p < 0.05
Malignant vs non-malignant (n = 2307) • Malignant • Non-malignant	926 (40%) 1381 (60%)	87 (9.3%) 126 (9.1%)	p = 0.87
Disease status in patients with leukaemia (n = 850) • CR1	445 (52%) 303 (36%) 32 (4%)	25 (5.6%)* 43 (14.2%)* 4	* p < 0.01

• CR2 • >CR2 • Refractory • Secondary	58 (7%) 11 (1%)	(12.5%) 8 (13.8%) 2 (18.2%)	
Donor type (n = 2309) • MSD (+MFD) • MUD • Mismatch donor (MMUD, MMFD, includes 9/10) • Haploidentical	598 (26%) 1000 (43%) 479 (21%) 232 (10%)	34 (5.7%) * 93 (9.3%) " 46 (9.6%) 38 (16.4%) * "	* " p < 0.05
Source (n = 2290) • Bone Marrow • PBSC • Cord	1221 (53%) 700 (30%) 369 (16%)	85 (7%) * " 83 (11.9%) * 43 (11.7%) "	* " p < 0.05
Conditioning (n = 2312)[+] • MA (TBI-based, Bu-based) • RTC (FluTreoThiotepa) • RIC (TreoFlu) • Non-MA (FluCy) • No conditioning	1044 (45%) 727 (31%) 271 (12%) 246 (11%) 24 (1%)	112 (10.7%) * 55 (7.6%) 30 (11.1%) " 10 (4.1%) * " 6 (25%)	* " p<0.05
Serotherapy (n = 2312) • Alemtuzumab • ATG • No serotherapy	952 (41%) 743 (32%) 616 (27%)	86 (9%) 74 (9.9%) 53 (8.6%)	p = 0.7

HSCT number • First transplant • Second transplant	2246 (97%) 66 (3%)	196 (8.7 %) * 17 (25.8%) *	* p < 0.05
For statistical comparison, Chi-square test or Fisher's exact test (if <5 events in any outcome) were applied using RStudio software. Matching symbols indicate subgroups with statistical significance within a group. +For conditioning regimens, the most prevalent drug combinations are shown in parenthesis. *Bu: Busulfan; CR: complete remission; Cy: cyclophosphamide; Flu: fludarabine; HSCT: hematopoietic stem cell transplant; MA: myeloablative; MFD: matched family donor; MSD: matched sibling donor; NMA: non-myeloablative; PBSC: peripheral blood stem cells; RIC: reduced intensity conditioning; RTC: reduced toxicity conditioning; SCD: sickle-cell disease; TBI: total body irradiation; Treo: treosulfan; TRM: transplant-related mortality*			

Conclusions: TRM in children undergoing HSCT has reduced over time but remains significant. Overall TRM in our cohort is comparable to published series but shows a higher proportion of infectious deaths. Our data identify key areas to focus resources on to improve outcomes. Infections, particularly viral infections are currently the leading cause of TRM,

highlighting the need for novel anti-virals and strategies to enhance immune reconstitution. Further work is needed to understand the pathogenesis of IPS and TA-TMA enabling prevention of these complications.

Disclosure: Oana Mirci-Danicar declares consultancy work for Alexion.
Rest of authors have nothing to declare.

A040

CLINICAL BENEFITS OF RUXOLITINIB IN MODERATE-TO-SEVERE CRS: REDUCED SEVERE ICANS AND STEROID USE WITH PRESERVED SURVIVAL AFTER PEDIATRIC CAR-T THERAPY

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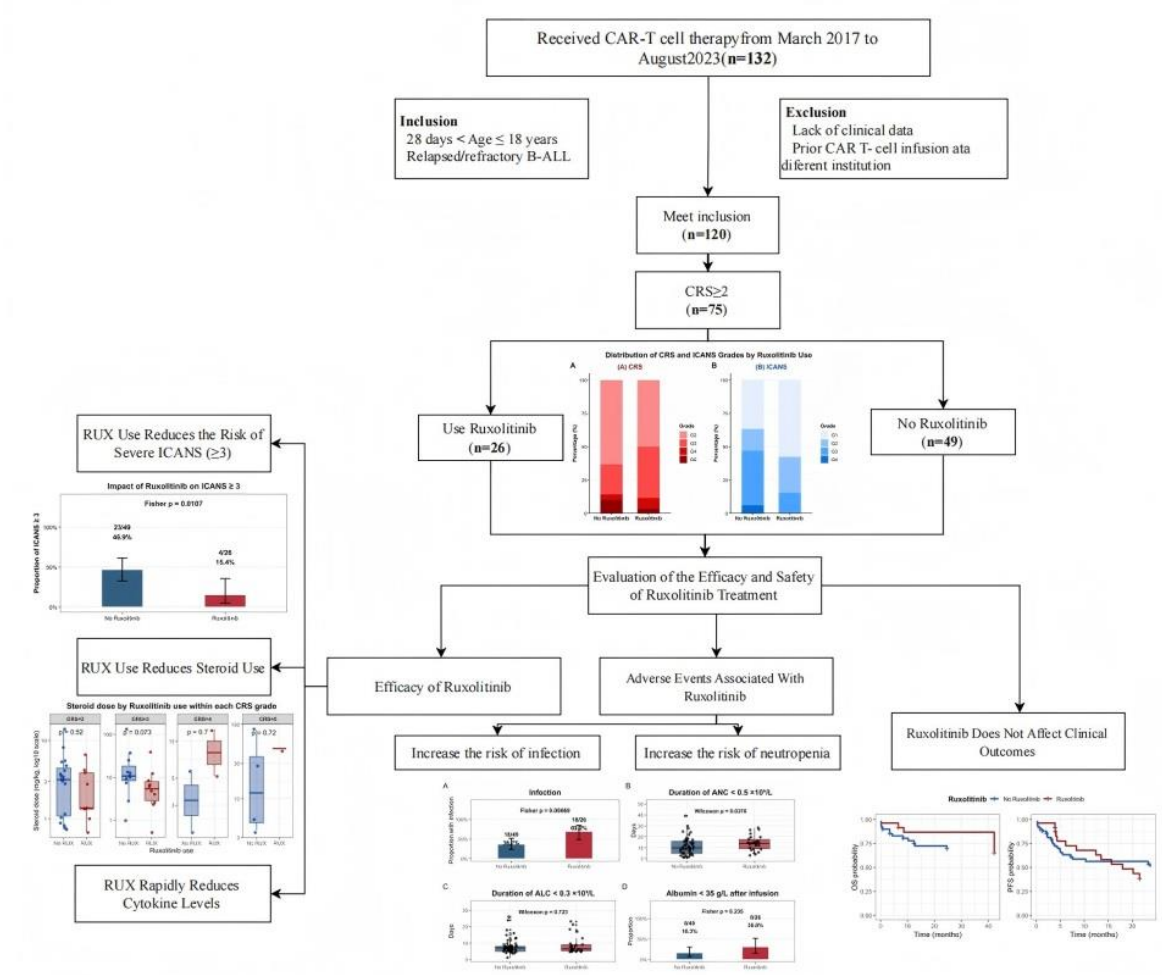
Background: Cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) remain major complications in children with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL) undergoing CAR-T-cell therapy. Ruxolitinib (RUX), a JAK1/2 inhibitor, has recently been incorporated into CRS management protocols, yet its impact on neurotoxicity, steroid exposure, and clinical outcomes has not been clearly defined. This study evaluated the efficacy and safety of RUX in patients who developed CRS of grade 2 or higher following CAR-T infusion.

Methods: From a cohort of 132 pediatric CAR-T recipients, 75 patients who experienced CRS ≥ grade 2 were included. Clinical characteristics, ICANS grade, cumulative steroid exposure, neutropenia duration, infection, and long-term survival were compared between patients who received RUX and those who did not. Steroid dose was further analyzed within individual CRS severity strata to assess potential differences in RUX responsiveness.

Results: Ruxolitinib use was associated with a marked reduction in severe neurotoxicity. The incidence of ICANS ≥ grade 3 was 15.4% in the RUX group compared with 46.9% in the non-RUX group (Fisher p = 0.0107), demonstrating a significant protective effect. In analyses stratified by CRS grade, patients with CRS = 2 showed lower steroid doses in the RUX group, although the difference was not statistically significant (median 1.37 vs 3.18 mg/kg, p = 0.52). Patients with CRS = 3 exhibited a more pronounced reduction, with RUX users receiving substantially lower steroid amounts compared with controls (median 4.44 vs 10.66 mg/kg), and the difference approached statistical significance (p = 0.073). Steroid comparisons within CRS grades 4 and 5 were limited by very small sample sizes, permitting descriptive reporting only. Ruxolitinib use was associated with prolonged myelosuppression, with a significantly longer duration of neutropenia (median 14 vs 10 days, p = 0.0188) and a numerically increased infection rate. Importantly, RUX did not negatively impact long-term efficacy. One-, two-, and three-year overall survival rates were 86.5%, 86.5%, and 86.5% in the RUX group, compared with 77.7%, 72.3%, and 69.3% among non-RUX patients. Progression-free survival was likewise comparable between groups at all time points,

indicating no detrimental survival effect.



Conclusions: Among pediatric B-ALL patients who developed CRS ≥ grade 2 after CAR-T therapy, ruxolitinib significantly reduced the risk of severe ICANS and demonstrated a consistent steroid-sparing trend, particularly in CRS = 3 patients. Although RUX increased the duration of neutropenia and infection risk, these effects did not compromise overall or progression-free survival. These findings support ruxolitinib as a promising adjunctive strategy for CRS management with meaningful neuroprotective benefits and acceptable safety in the context of CAR-T–related toxicity.

Clinical Trial Registry: None

Disclosure: No conflict of interest

A041

RELAPSED OR REFRACTORY POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS: REAL-LIFE MULTICENTER ITALIAN EXPERIENCE WITH TABELECLEUCEL

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Background: Epstein Barr virus associated post-transplant lymphoproliferative disease (EBV+PTLD) is a rare complication occurring after either stem cell (HSCT) or solid organ transplantation (SOT), with a very poor outcome if first line therapy fails, ranging from 1-4 months. Tabelecleucel is an allogeneic EBV-specific T-cell immunotherapy that targets EBV-positive cells selectively based on human leukocyte antigen (HLA) restriction. The phase 3 ALLELE study demonstrated an overall response rate (ORR) of 51%, with a complete remission (CR) rate of 28% and an overall survival (OS) of 84% at 12 months for responding patients, without significant toxicities. In Italy Tabelecleucel became available as monotherapy in adult and pediatric patients with R/R EBV-related PTLD, who have received at least one prior therapy, from February 2023 as compassionate use and from March 2025 as commercial use.

Methods: This retrospective observational analysis describes the preliminary Italian real-life experience with use of tabelecleucel. Adult patients diagnosed with R/R PTLD candidated and referred to treatment with tebelecleucel used both compassionately and commercially were included.

Results: From January 2024 to September 2025, 19 patients were enrolled across 8 Italian centers. The median age at the time of immunotherapy was 49 years (range 29–76), with a predominance of male patients (63.2%) and good performance status. Seven patients (36.8%) received prior HSCT and 12 (63.2%) received SOT: 6 heart, 2 lung, 2 kidney, 1 combined, and 1 liver transplant. Sixteen patients (84.2%) had monomorphic PTLD (mostly DLBCL). PTLD-adapted prognostic index was high in 10 patients (52.6%), 16 cases (84.2%)

had an extranodal localization, 2 (10.5%) with central nervous system involvement, 13 (68.4%) with IV stage disease. In 17 out of 19 cases the origin of the PTLD was documented (10 from patient, 7 from the donor). In 8 cases this attribution was made on the basis of high-resolution HLA typing. The median time from transplant to PTLD onset was 21 months (range 1-227) and 11 cases (58.0%) had early-onset. The median time from PTLD diagnosis to tabelecleucel treatment was 3 months (range 0.9–131). Sixteen patients (84.2%) received rituximab monotherapy as first line treatment. The median number of tabelecleucel cycles was 2 (range 0–6): 3 patients did not receive tabelecleucel (1 death, 2 unavailability of tabelecleucel lots). Two lot switchs were required. No significant toxicity was reported. The ORR was 37.5%, with 5 of 16 treated cases (31.3%) achieving CR. In the subcohort of SOT recipients, ORR was 60%, with 5 of 10 patients (50%) achieving CR; while, among HSCT recipients ORR was 0%. After a median follow-up of 11 months, 11 of 19 patients were alive.

Conclusions: The preliminary Italian experience supports the efficacy and safety of tabelecleucel, consistent with the results of the ALLELE trial in SOT. In our cohort no response to tabelecleucel was observed in PTLD after HSCT, remarkably 3 of these patients did not meet ALLELE inclusion criteria. It is essential to identify early potential candidates for this promising new therapy, which is now readily accessible in our country.

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Chiara Consoli: nothing to declare
Monica Rondi: nothing to declare
Chiara Nozzoli: nothing to declare
Ilaria Cutini: nothing to declare
Fabrizio Vianello: nothing to declare
Daniele Avenoso: nothing to declare
Cristina Tecchio: nothing to declare
Giorgia Battipaglia: Speaker Pierre Fabre
Cinzia Pellegrini: nothing to declare
Enrico Maffini: nothing to declare
Patrizia Chiusolo: nothing to declare
Luisa Giaccone: nothing to declare
Silvia Giorgi: nothing to declare
Michele Clerico: nothing to declare
Benedetto Bruno: Consultancy Pierre Fabre
Federica Cavallo: Consultancy Kyte, Bristol Myers Squibb, Roche, Astrazeneca, Sobi, Gentili, Incyte, Pierre Fabre, Speaker Lilly, Novartis, Honoraria: BeOne.

A042

LISOCABTAGENE MARALEUCEL VERSUS AXICABTAGENE CILOLEUCEL IN R/R LARGE B-CELL LYMPHOMA: A META-ANALYSIS OF REAL-WORLD COMPARATIVE STUDIES

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Seiwald[1], Ana Fonseca[1], Mariana Serpa[1], Erick Xavier[1], Luciana Tucunduva[1], Yana Novis[1], Michael Scordo[5], Xavier Deschênes-Simard[6]
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Background: Axicabtagene ciloleucel (axi-cel) and lisocabtagene maraleucel (liso-cel) are standard-of-care CAR T-cell therapies for R/R LBCL. In the absence of head-to-head randomized controlled trials (RCTs), real-world evidence (RWE) studies have emerged.

Methods: We conducted a systematic review and meta-analysis to synthesize the available RWE (both fully published studies and recently presented abstracts) comparing the efficacy and safety of liso-cel versus axi-cel in patients with R/R LBCL.Following a pre-registered protocol (PROSPERO CRD420251218794), we searched PubMed, Embase, Cochrane, and major conference abstracts for comparative studies of liso-cel vs. axi-cel in R/R LBCL. Dichotomous safety and efficacy outcomes were pooled via random-effects meta-analysis. Time-to-event outcomes were extracted or calculated from reconstructed individual patient data (IPD) from published Kaplan-Meier curves.

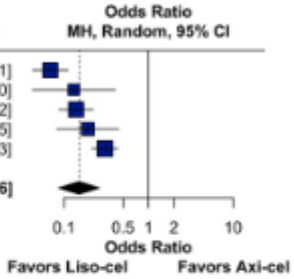
Results: Five studies were included, totaling 2,205 patients. When comparing liso-cel to axi-cel,the meta-analysis of efficacy demonstrated no statistical difference in overall response rate (ORR) (OR 1.34, 95% CI: 0.63–2.83) or complete response rate (CRR) (OR 1.18, 95% CI: 0.96–1.45). Liso-cel was associated with lower odds of any-grade cytokine release syndrome (CRS) (OR 0.15, 95% CI: 0.09–0.26) and lower grade ≥3 CRS (OR 0.24, 95% CI: 0.08–0.69). Liso-cel was also associated with lower odds of any-grade immune effector cell-associated neurotoxicity syndrome (ICANS) (OR 0.30, 95% CI: 0.23–0.39) and, notably, significantly lower odds of grade ≥3 ICANS (OR 0.42, 95% CI: 0.19–0.93). Survival analyses, restricted to the 729 patients with extractable IPD from fully published studies, showed comparable outcomes: progression-free survival (PFS) (HR 1.07, 95% CI: 0.86-1.33), overall survival (OS) (HR 1.02, 95% CI: 0.78-1.33), and duration of response (DOR) (HR 1.03, 95% CI: 0.79-1.35).

CRS (Any Grade)

A

Study	Liso-cel Events	Liso-cel Total	Axi-cel Events	Axi-cel Total	Weight	Odds Ratio	95% CI
Brisou 2025	65	127	563	600	22.7%	0.07	[0.04; 0.11]
Looka 2025	20	37	45	50	12.9%	0.13	[0.04; 0.40]
Deschenes-Simard 2025	70	138	303	344	22.9%	0.14	[0.09; 0.22]
Portuguese 2025	37	58	92	102	16.8%	0.19	[0.08; 0.45]
Melody 2025	96	185	440	564	24.7%	0.30	[0.21; 0.43]
Total (95% CI)	**288**	**545**	**1443**	**1660**	**100.0%**	**0.15**	**[0.09; 0.26]**

Heterogeneity: $Tau^2 = 0.2955$; $Chi^2 = 25.08$, df = 4 ($P < 0.0001$); $I^2 = 84.0\%$

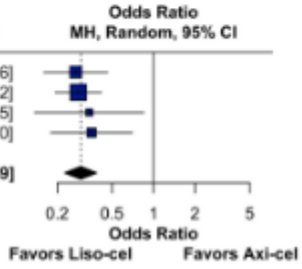


ICANS (Any Grade)

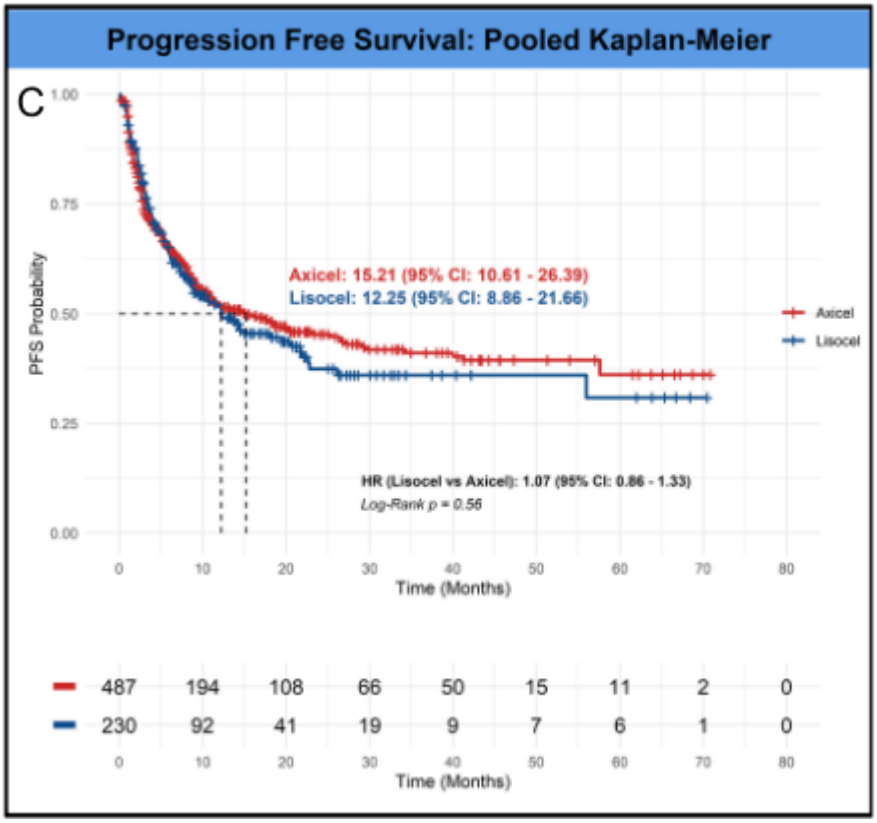
B

Study	Liso-cel Events	Liso-cel Total	Axi-cel Events	Axi-cel Total	Weight	Odds Ratio	95% CI
Deschenes-Simard 2025	19	138	127	344	25.9%	0.27	[0.16; 0.46]
Melody 2025	41	185	282	564	49.5%	0.28	[0.19; 0.42]
Looka 2025	10	37	26	50	8.8%	0.34	[0.14; 0.85]
Portuguese 2025	18	58	57	102	15.8%	0.36	[0.18; 0.70]
Total (95% CI)	**88**	**418**	**492**	**1060**	**100.0%**	**0.30**	**[0.23; 0.39]**

Heterogeneity: $Tau^2 = 0$; $Chi^2 = 0.50$, df = 3 ($P = 0.9184$); $I^2 = 0.0\%$



Progression Free Survival: Pooled Kaplan-Meier



Conclusions: This meta-analysis of RWE suggests that liso-cel and axi-cel offer comparable efficacy and survival outcomes in the treatment of R/R LBCL. Liso-cel was, however, associated with a substantially better toxicity profile, including significantly lower rates of CRS and ICANS.

Disclosure: *Michael Scordo* served as a paid consultant for McKinsey & Company, Angiocrine Bioscience, Inc., and Omeros Corporation; received research funding from Angiocrine Bioscience, Inc., Omeros Corporation, Amgen Inc., Bristol Myers Squibb, and Sanofi; served on ad hoc advisory boards for Kite – A Gilead Company, Bristol Myers Squibb, and Miltenyi Biotec; and received honoraria from i3Health, Medscape, CancerNetwork, Intellisphere LLC, Curio Science LLC, and IDEOlogy.
Xavier Deschênes-Simard has served on ad hoc advisory boards for Gilead–Kite Pharma and Bristol Myers Squibb; has received honoraria from Bristol Myers Squibb, Hoffmann-La Roche, and Eli Lilly; and serves as an investigator for Allogene, AbbVie, Hoffmann-La Roche, BeiGene, Epizyme, Iovance, Immatics, and AstraZeneca.

A043

PRELIMINARY SAFETY AND EFFICACY OF MYELOABLATIVE ORCA-Q IN PATIENTS WITH HAPLOIDENTICAL DONORS

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is an option for patients without matched donors. Despite advances, outcomes remain limited by immunological barriers, leading to higher risks of graft-versus-host disease (GVHD), delayed immune recovery, and variable relapse rates. Orca-Q is a precision-engineered, immune cell therapy designed to facilitate immune recovery and maintain GVL while reducing GVHD. with less immunosuppression. This study reports interim results from an ongoing study (NCT03802695).

Methods: Adult patients with high-risk hematologic malignancies who were eligible for myeloablative conditioning (MAC) alloHSCT with a haploidentical donor were enrolled in a dose expansion study using single agent tacrolimus for GVHD prevention. Inclusion criteria were broad, 44 patients in total were treated, and here, we report data for 39 patients age

<65 with AML, ALL, or MDS. Orca-Q was centrally manufactured at an Orca Bio GMP facility (Sacramento, CA) from GCSF-mobilized peripheral blood apheresis products. Patients were followed for GVHD and relapse for one year and for overall survival (OS) thereafter. GVHD-free, relapse-free survival (GRFS) was defined as the time from transplant to the first occurrence of grade 3-4 acute GVHD (aGVHD), moderate to severe chronic GVHD (cGVHD), relapse or death.

Results: Orca-Q was successfully manufactured and administered with a vein-to-vein time of less than 72 hours. 39 patients were treated, baseline characteristics were as follows: Median age 44 years (range 21-64), 77% male; median follow-up was 937 days (range 19-1825). All patients received MAC with one of the following regimens: Bu/Flu/Thio-based, TBI/Flu/Thio, TBI/Flu. Patients who received TBI/Flu/Thio were also analyzed separately. Orca-Q was well-tolerated and all patients engrafted neutrophils by day +19 (median 11 days). Two patients with busulfan-based conditioning experienced secondary graft failure. Clinical outcomes were as follows:

	All patients	Patients with TFT regimen
n=	39	14
Median f/u, days	937	1244
OS at 1, 2, 3 years	80%, 77%, 77%	85%, 85%, 85%
RFS at 1 year	77%	85%
GRFS at 1 year	72%	85%
NRM at 1 year	5.8%	7.7%
Relapse incidence at 1 year	18.2%	8.4%
aGHVD gr3-4 at D+180	8.1%	0%
Mod-to-severe cGVHD at 1 year	0%	0%
BMT CTN Grade 3+ infections at 1-year	5.3%	7.1%

Mean cumulative number of serious adverse events (SAEs) at 1 year was 0.43 for patients with TFT regimen compared to 1.08 for patients with other regimens.

Conclusions: The study demonstrated high engraftment rates, encouraging OS and RFS, and low incidences of severe aGVHD and cGVHD. Notably, outcomes appeared favorable in the TFT subgroup, with improved survival, GRFS, and lower relapse incidence compared to other regimens. These findings support the safety and efficacy of Orca-Q in reducing GVHD

and achieving durable remissions. The Phase 1 study continues to enroll patients to confirm these results.

Clinical Trial Registry: NCT03802695 https://clinicaltrials.gov/study/NCT03802695

Disclosure: Amandeep Salhotra, MD – grants or contracts for research funding – Bristol Myers Squibb, Rigel, Orca Bio; consulting fees – Sanofi; honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events – Sanofi, Incyte. Samer A. Srour, MB ChB, MS – presentation at ASH 2025 for Orca Bio. Mehrdad Abedi, MD – nothing to declare. Edmund K. Waller, MD, PhD – nothing to declare. Hannah Choe, MD – nothing to declare. Anna Pavlova, MD, PhD – employee and equity holder – Orca Bio. Tamara Zharkevich, MD, PhD – employee – Orca Bio. Scott Killian, PhD – employee – Orca Bio. James Scott McClellan, MD, PhD – employee, officer, and equity holder – Orca Bio. Nathaniel B. Fernhoff, PhD – employee, officer, and equity holder – Orca Bio. Robert Lowsky, MD – nothing to declare.

A045

CAR-T-CELL–INDUCED PSEUDOPROGRESSION (CARTIPP): AN EBMT TCWP STUDY

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Background: With expanding use of CAR-T-cell therapy, clinicians report adverse events beyond classical toxicities. Pseudoprogression, a phenomenon known from immune checkpoint inhibition, may occur rapidly with CAR-T-cell therapy. Further to mimicking early malignant progression, it can induce inflammatory swelling that may cause complications depending on the anatomical site. This entity—termed CAR-T-cell-therapy–induced pseudoprogression (CARTiPP)—has been described in small single-center reports and remains insufficiently understood. Characterizing its frequency, clinical presentation and prognostic significance is crucial to guide management. We collected multicentric EBMT data to define clinical features, diagnostic patterns, management strategies and outcomes of CARTiPP across European centers.

Methods: All adult patients (≥18 years) receiving first CAR-T-cell therapy reported to EBMT until June 2024 were eligible if they developed CARTiPP, defined as a transient increase in volume of malignant manifestations within 30 days of infusion followed by regression. Complicated CARTiPP (cCARTiPP) was defined by organ dysfunction, tissue damage or the need for any new therapeutic intervention initiated due to CARTiPP. Data was collected from 2024 until 2025 through two EBMT forms: An initial case-identification form, sent out to 221 EBMT centres and a second, detailed form capturing clinical characteristics, diagnostics, treatments, and outcomes.

Results: 41 patients with CARTiPP from 16 European centres were included. Median age was 57.4 years (53.7% male, 48.8% ECOG 1). Most underlying diseases were diffuse large B-cell lymphoma (DLBCL, 53.7%), mantle cell lymphoma (MCL, 9.8%), and primary mediastinal large B-cell lymphoma (PMBCL, 9.8%). Before lymphodepletion, most patients had relapse or progression, including primary refractory disease (58.5%). Median CARTiPP occurrence was five days (Q1–Q3, 4–7) after infusion. CARTiPP was detected by clinical observation (36.6%), imaging (34.1%), or both (29.3%). 56.1% developed cCARTiPP. In 81.1%, CARTiPP resembled prior disease presentations. Before CARTiPP, 82.9% received anti-inflammatory treatment for CAR-T toxicities, mainly tocilizumab alone (53.7%) or in combination (24.4%). CRS occurred in 37 (90.2%) cases, mostly (89.7%, n=35) before CARTiPP onset. Fifteen patients (36.6%) developed ICANS, mostly (n=11, 73.3%) after CARTiPP onset. CARTiPP-triggered interventions occurred in 34.1% of patients, mainly glucocorticoids (57.1%), suggesting some episodes resolved without escalation. The median follow-up of patients alive was 21.6 months (95% CI, 12–33.6). Relapse incidence at one year after CAR-T infusion was 36.3% (95% CI, 21.2–51.5). One-year overall survival (OS) was 68.6% (95% CI, 51.0–81.0) two-year OS 57.5% (95% CI, 38.9–72.4) (Figure 1). One-year progression-free survival (PFS) was 57.3% (95% CI, 40.5–71.1). One-year non-relapse mortality (NRM) was 7.3% (95% CI, 1.9–18.0).

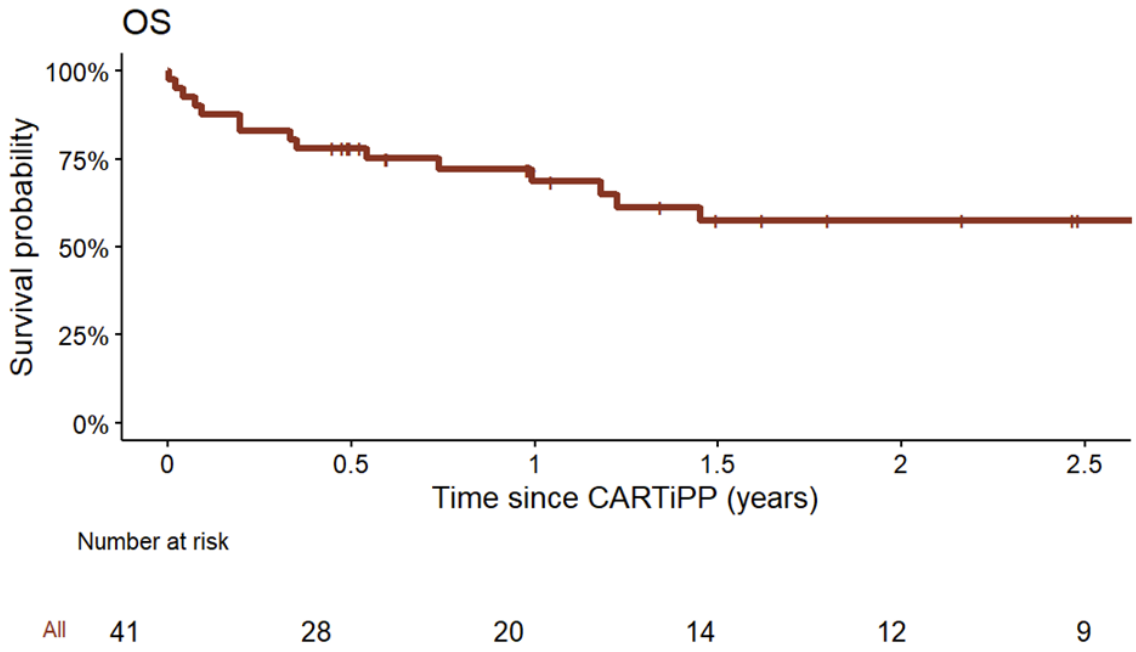

Figure 1: OS after CARTiPP.

Conclusions: This is to our knowledge the first multicenter report of CARTiPP as an early inflammatory flare occurring within days after infusion mimicking disease progression. CARTiPP-patients showed PFS, OS and NRM comparable to published real-world CAR-T cohorts, suggesting CARTiPP may not impact prognosis. Some cases resolved spontaneously, although complicated presentations required timely intervention. CARTiPP may be an often self-limiting phenomenon, needing more standardized diagnostic criteria, imaging confirmation whenever feasible, and structured management recommendations across centres. For lesions near critical anatomical structures, mindful anticipation of transient inflammatory enlargement may help mitigate risks.

Disclosure: Nothing to declare.

A046

CLINICAL BIOMARKERS FOR EARLY RECOGNITION OF SUBOPTIMAL ECULIZUMAB RESPONSE IN TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY

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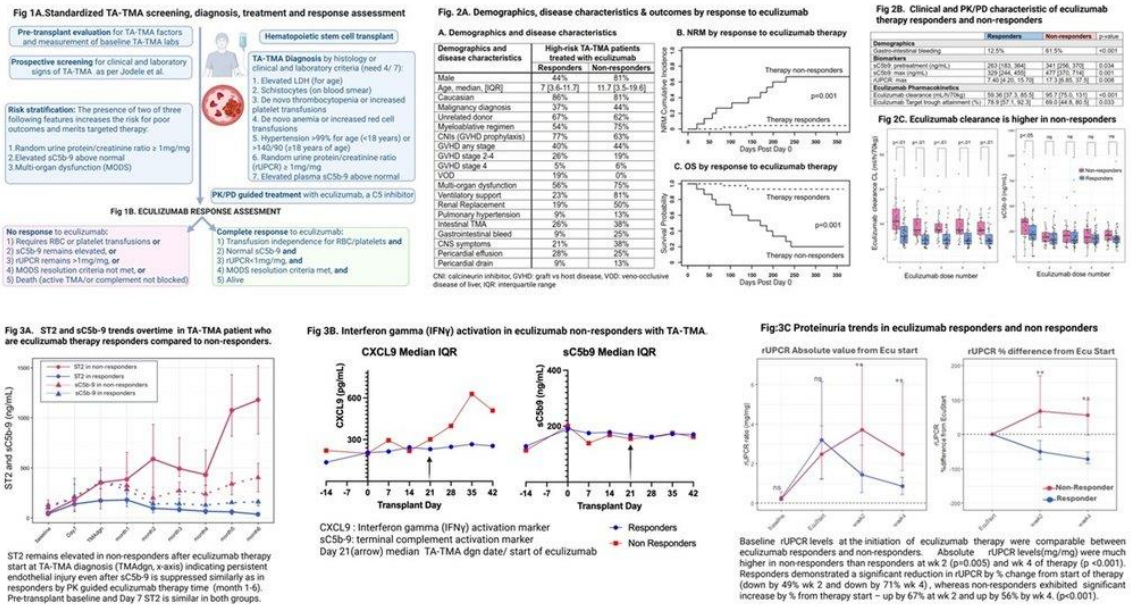
Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is a life-threatening complication of hematopoietic stem cell transplantation (HSCT), driven by endothelial injury and complement activation. Eculizumab, a terminal complement C5 inhibitor, improves survival in high-risk TA-TMA, yet one-third of patients fail to respond. Our study objective was to determine mechanisms of eculizumab non-response and early predictors of outcome in TA-TMA that are critical for improving therapy.

Methods: We prospectively studied 90 children and young adults with high-risk TA-TMA, comparing eculizumab responders (n=60) and non-responders (n=30). All HSCT recipients were prospectively screened for TA-TMA. TA-TMA risk group and response to eculizumab was determined based on published criteria (Fig1). All patients with high-risk TA-TMA received PK/PD-guided eculizumab dosing. We performed novel PK/PD modeling to determine complete complement blockade ("equilibrium"). Complement blockade, PK/PD dynamics, biomarker trajectories for sC5b-9, CXCL9, ST2, proteinuria by random urine protein/creatine ratio (rUPCR), and outcomes were compared in responders and non-responders.

Results: Non-responders displayed greater systemic organ injury and worse survival despite optimized eculizumab dosing and PK/PD monitoring (Fig 2A). PK/PD modeling confirmed that complement blockade can be achieved with intensified dosing, but steady blockade state (equilibrium) requires approximately six weeks of therapy, underscoring that short-term biomarker normalization is not sufficient to declare response (Fig 2B). Importantly, non-responders exhibited persistently elevated rUPCR and rising ST2 despite suppression of sC5b-9, indicating ongoing complement-independent endothelial injury. Longitudinal biomarker profiling showed that non-responders had progressive CXCL9 elevation despite sC5b-9 control, and that adding IFNγ blockade with emapalumab improved eculizumab PK/PD, accelerated complement suppression, and enhanced survival, underscoring the pathogenic role of the complement-interferon loop (Fig3). We showed that elevated sC5b-9 is associated with TA-TMA risk, higher therapy needs and poor outcomes, whereas comprehensive profiling of other complement components did not differentiate responders, and normal C3/C4 values did not exclude TA-TMA highlighting the need for functional biomarkers.

Figures: Determinants of Eculizumab Response in High-Risk Transplant-Associated Thrombotic Microangiopathy



Conclusions: These findings reveal that eculizumab non-response reflects complement independent persistent endothelial injury. Early monitoring of ST2, CXCL9, rUPCR, may identify patients at risk for suboptimal eculizumab response and guide precision therapies that can be integrated with complement blockade. Such strategies will be essential to improve survival and prevent irreversible vascular injury in high-risk TA-TMA.

Clinical Trial Registry: Not applicable.

Disclosure: Consultancy honoraria for Novartis, Omeros, SOBI, Alexion. US patents.

A047

B CELL APLASIA POST CD28 AND 41BB CONTAINING CD19 TARGETING CAR-T CELL THERAPY – SINGLE CENTRE RETROSPECTIVE EXPERIENCE

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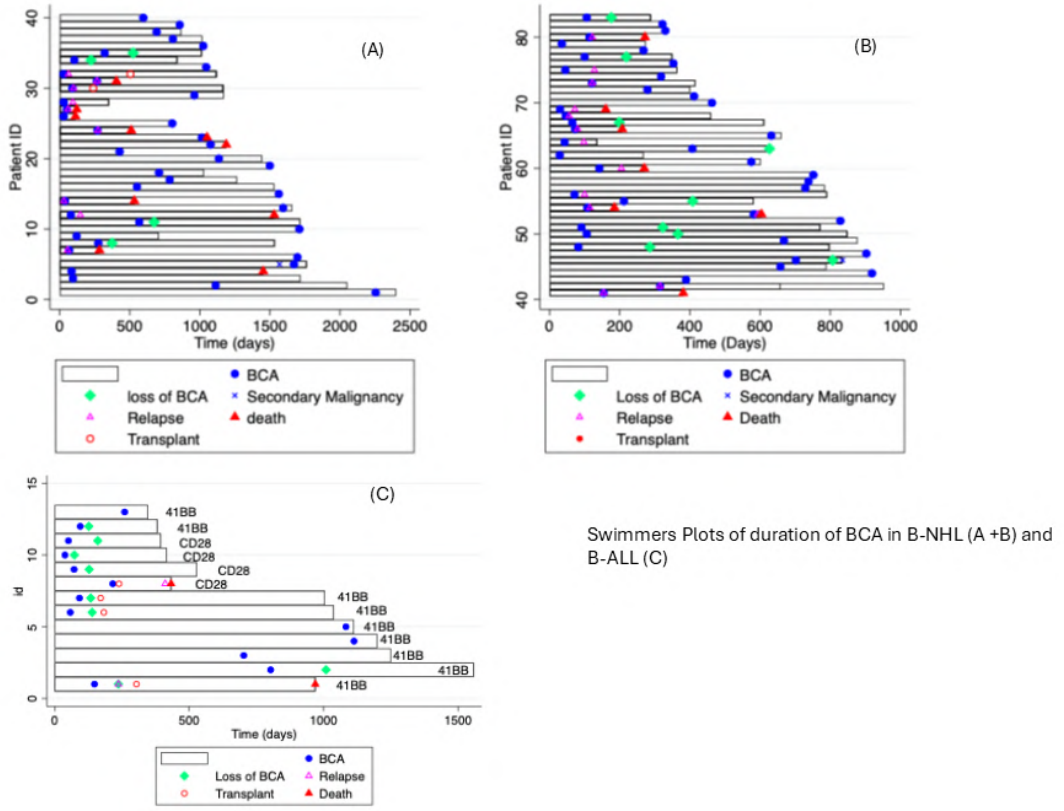
Background: B cell aplasia(BCA) is often used as a surrogate marker for CAR-T persistence. BCA in the setting of CD28 containing CAR-T cell and it's impact on remission duration is less well defined than 41BB.

Methods: This retrospective study analysed outcomes of 115 consecutive CAR-T patients. Probability of Overall Survival(OS), Progression Free Survival(PFS) were calculated by Kaplan Meier. Cumulative Incidence(CI) of relapse risk, non relapse mortality (NRM) and B cell recovery was calculated using competing risk analysis.

Results:



Swimmers Plots of duration of BCA in B-NHL (A +B) and B-ALL (C)

102 patients with B-Non-Hodgkins Lymphoma(B-NHL) and 13 patients with B-Acute Lymphoblastic Leukaemia(B-ALL) were reviewed. Patient characteristics are in Table 1. BCA was assessed at regular time points pre and post CAR-T infusion. Patients who had no immunophenotyping performed or progressed/died before day 100 were not included in BCA and CD4 analysis. BCA was not assessed beyond time of relapse. For B-NHL, 54/83(65%) had BCA pre infusion. All patients were in BCA at least once post CAR-T up until a median of 1.59 years(IQR 0.27-2.11). Of these, 81/83(96%) had received CD28 containing CAR-T cell therapy. 13/83(15.7%) subsequently had loss of BCA at a median of 1 year post infusion(IQR 0.61-1.44). 42/83(50.6%) patients remained in CR with ongoing BCA at time of analysis with a median duration of BCA of 2.21 years(IQR 1.2-2.76). Median OS was 2.12 years (range 0.31-6.68) with estimated 2 year OS and PFS of 79% (95% CI 67-87) and 69%

(57-77). 2 year CI of relapse was 27%(18-37) in those in ongoing BCA vs 0% for those with loss of BCA, p=0.09). 2 year NRM was low in this cohort (ongoing BCA 2% (1-10) vs Loss of BCA 0%.)In the B-ALL cohort where 9/13(69%), 6/13(46.1%) had pre-existing BCA pre infusion. 13/13(100%) had detectable BCA post CAR-T up until a median of 0.41 years(IQR 0.2-0.96) post infusion. 8/13(61.5%) subsequently lost BCA at a median of 0.37 years post CAR-T(IQR 0.35-0.49). 4/13(30.8%) patients were in remission and in ongoing BCA at time of last follow up. Median OS was 2.65 years(range 0.95-4.27) with estimated 2 year OS and PFS of 89% (43-98) and 81% (41-95).
CI of B cell recovery at 6 months was 3%(1-10) for B-NHL patients versus 46%(19-69) for B-ALL patients(p=0.003). CI of CD4 recovery at 1 year was 43%(30-54) in B-NHL compared to 64%(37-87) in B-ALL(p=0.22).

Patient Characteristics Table 1:

Characteristics	NHL, N (%)	ALL, N (%)
Sex		
Male	62(60.8)	5(38.5)
Female	40(39.2)	8(61.5)
Age		
Median	64	22
IQR	54-71	20-35
Range	22-82	18-70
Diagnosis		
ALL		
DLBCL		
FL	69(67.6)	13(100)
tFL	1(1)	
PMBCL	21 (20.6)	
SLL with Richter's	3(2.9)	
transformation	1(1)	
T cell/histiocytic rich large B	1(1)	
cell lymphoma	6 (5.9)	
MCL		
Status Pre CAR-T		
CR	34(33.3)	10(76.9)
PR	45(44.2)	0(0)
SD/PD	23(22.5)	3(23.1)
CAR-T Product		
Kymriah	3(2.9)	9(69.2)
Yescarta	93(91.2)	0(0)
Tecartus	6(5.9)	4(30.8)

Characteristics	NHL, N (%)	ALL, N (%)
CAR Domain		
CD28	99(97.1)	4(30.8)
41BB	3(2.9)	9(69.2)
CAR Haematotox Score		
≥2	36(35.3)	5(38.5)
0-1	66(64.7)	8(61.5)
Prior lines of treatment		
Median	2	2
Minimum	1	1
Maximum	9	3
IQR	1	1
CRS		
Any Grade	98(96.1)	11(84.61)
G≥3	8(7.9)	1(7.69)
ICANS		
Any Grade	50(49.0)	
G≥3	21(21.0)	3(23.1)
		2(15.4)
Toxicity Treatment Steroids		
Yes	64(62.7)	8(61.5)
No	38(37.3)	5(38.5)
Toxicity Treatment Anakinra		
Yes	47(46.1)	6(46.2)
No	55 (53.9)	7(53.8)
Toxicity Treatment Tocilizumab		
Yes	77(75.5)	8(61.5)
No	25(24.5)	5(38.5)
Day 28 response		
CR	62(60.8)	13(100), All MRD negative.
PR	26(25.5)	
PD/relapse	10(9.8)	
SD	2(2)	
Not available	2(2)	

Characteristics	NHL, N (%)	ALL, N (%)
Day 100 response		
CR	69(67.6)	3 (100%), All MRD negative.
PR	5(4.9)	
PD/relapse	17(16.7)	
SD	0(0)	
Not available	11(10.8)	

Conclusions: Prolonged BCA was demonstrated in B-NHL patients in long term remission treated with CD28 containing CAR-T and no excess risk of relapse was seen in those who lost BCA. B cell recovery was seen more frequently in B-ALL patients and this happened at earlier time points. Despite early B cell recovery, durable remissions were seen in the B-ALL cohort. The finding of faster B cell recovery in B-ALL may reflect younger age, higher proportion of prior Allo-SCT and fewer lines of therapy pre CAR-T. A high proportion of patients have BCA pre CAR-T and this calls into question it's utility as a marker for CAR-T persistence in isolation and should be used with immunophenotype-based and ddPCR CAR-T persistence assays.

Clinical Trial Registry: None.

Disclosure: (Francesca Sillito)Honoraria Kite Gilead, Honoraria BMS, International sponsorship MEDAC/Miltenyi Biotec.

A048

LONG-TERM CLINICAL OUTCOMES IN PATIENTS WITH RELAPSED OR REFRACTORY B-CELL NON-HODGKIN LYMPHOMA TREATED WITH PRIZLONCABTAGENE AUTOLEUCEL

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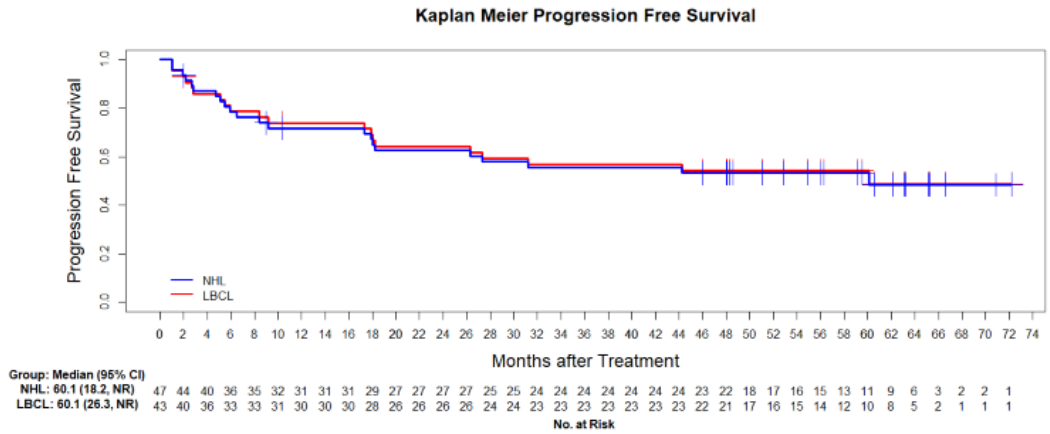
Background: Recent studies have highlighted the curative potential of chimeric antigen receptor T-cell (CAR-T) therapy for large B-cell lymphoma (LBCL). Prizloncabtagene autoleucel, previously known as C-CAR039, is an autologous anti-CD20/CD19 dual-antigen targeting CAR-T therapy for the treatment of patients with relapsed or refractory (r/r) B-cell non-Hodgkin lymphoma (B-NHL). We previously reported the outcomes of 48 patients with r/r B-NHL treated with C-CAR039 at the 2025 EHA Congress (Yu et al. Abstract PS2159). At a median follow-up (mFU) of 45.5 months, the overall response rate (ORR) was 91.5%, with a

complete response (CR) rate of 85.1%. Median progression-free survival (PFS) and overall survival (OS) were not reached, and the estimated 4-year PFS and OS rates were 52.5% and 65.4%, respectively. Here, we report the long-term results with a mFU of 53.9 months.

Methods: Eligible patients had r/r diffuse large B-cell lymphoma (DLBCL), primary mediastinal large B-cell lymphoma (PMBCL), follicular lymphoma (FL), and mantle cell lymphoma (MCL) after ≥2 lines of therapy including an anti-CD20 monoclonal antibody plus an alkylating agent. Patients underwent leukapheresis, followed by lymphodepletion chemotherapy and infusion of C-CAR039 (1.0-5.0×10^6 CAR-T cells/kg). Primary endpoints include safety and tolerability. Secondary endpoints include efficacy and pharmacokinetics.

Results: As of Nov 26, 2025, mFU was 53.9 months (range: 3.1-72.2). Of the 48 infused patients, 44 were LBCL (DLBCL, n = 37; transformed FL, n = 4; PMBCL, n = 3), 3 were FL, and 1 was MCL. One DLBCL patient who had no measurable disease at baseline was excluded from the efficacy analysis. 45 out of 48 (93.8%) patients experienced cytokine release syndrome, with only one being grade 3. Three patients experienced immune effector cell-associated neurotoxicity syndrome, with two cases of grade 1 and one case of grade 2, all at the dose of 5.0×10^6 CAR-T cells/kg.
The clinical response for all patients was matured and consistent with the last report, with 91.5% ORR (95% CI, 79.6-97.6) and 85.1% CR (95% CI, 71.7-93.8). Median PFS was 60.1 months (95% CI, 18.2-NR), median OS was not reached. The estimated 4-year PFS and OS rates were 53.3% (95%CI, 40.4-70.2) and 65.9% (95%CI, 53.6-81.0), respectively.
Among 43 efficacy-evaluable LBCL patients, the ORR was 90.7%, with 86.0% CR. Median PFS was 60.1 months (95% CI, 26.3-NR), median OS was not reached. The estimated 4-year PFS and OS rates were 54.2% (95%CI, 41.0-71.8) and 67.4% (95%CI, 54.7-83.0), respectively. 20/43 (46.5%) remained CR and 28 patients (65.1%) remained alive at this data cutoff date. Notably, no disease progression occurred in any patients beyond 3 years.



Conclusions: With more than 4 years of follow-up, median PFS reached 60.1 months and median OS was not reached. Among LBCL patients, 20 patients (46.5%) maintained response without treatment and 28 patients (65.1%) remained alive. Together, these data

demonstrated excellent durable efficacy and manageable safety profiles. Pivotal studies are ongoing in the US and China, respectively.

Clinical Trial Registry: Number:NCT04317885, #NCT04655677, #NCT04696432, and #NCT04693676
website:clinicaltrials.gov

Disclosure: Aibin Liang, Wenjuan Yu, Ping Li, Lili Zhou, Min Yang, Shiguang Ye, Yan Zhang, Lanfang Li, Jing Zhao, Kevin Zhu, Huilai Zhang, Daobin Zhou, Jie Jin: Nothing to declare
Judy Zhu, Jing Li, Chengxiao Zheng, Liping Lan: Employees of Shanghai AbelZeta Ltd.
Jiaqi Huang, Xin Yao, Yihong Yao: Employees of AbelZeta Inc.

A049

OUTCOME OF AGGRESSIVE B-CELL LYMPHOMA ADMINISTERED WITH CAR T-CELL ALONE OR IN COMBINATION WITH ASCT: A PROPENSITY SCORE MATCHING COHORT STUDY

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Background: Anti-CD19 chimeric antigen receptor T-cell therapy approved for relapsed or refractory large B-cell lymphoma (RR-LBCL) after at least two treatment lines.Autologous hematopoietic stem cell transplantation (ASCT) combined with CAR-T cell therapy is effective against multiple subtypes of RR-LBCL.

Methods: This single-center, propensity score matching (PSM) cohort study analyzed 64 R/R NHL patients. 32 patients received ASCT combined with CAR-T cell therapy, matched 1:1 with 32 patients receiving CAR-T alone based on 10 baseline characteristics (Table 1). The two groups were well balanced across all baseline characteristics after PSM, and were appropriate for further comparative analysis of outcomes.Patients who had previously received CAR-T therapy or ASCT were excluded.The conditioning regimen for the ASCT+CAR-T group was standard BEAM (bis-carmustine, etoposide, cytarabine, and melphalan) , while CAR-T cells were transfused within two days after transfusion of CD34+ HSCs in ASCT+CAR-T.

Results: The dose of CD34+ hematopoietic stem cells (HSCs) ranged from 2.4 to $9.5*10^6$/kg in ASCT+CAR-T group .The median numbers of CAR-T cell reinfusions were 2.2×10^6/kg (range: 0.3-4.5) and 2.8×10^6/kg (range: 0.4-3.5) in the CAR-T group and ASCT+CAR-T group, respectively.
Stem cell engraftment in the ASCT+CAR-T group was unaffected.CAR T-cell expansion did not appear to differ in terms of therapeutic efficacy.
In the ASCT+CAR-T and the CART group, the incidences of grade ≥3 CRS was 12% vs. 6.8%, respectively, while the incidences of grade ≥3 ICANS was 0 vs. 1.4%, respectively.
A response at 3 month occurred in 68.8% of the patients in the ASCT+CAR-T group and in

55.2% of those in the CAR-T group(P=0.302) (with a complete response in 62.5% and 41.4%, respectively)(P=0.127).
The median follow-up period was 38.4 months (95% CI: 0.36,71.67).The 3-year PFS and OS rates for the overall population were 51.58%(95% CI: 37.74,63.77) and 63.73%(95% CI: 49.53,74.91)respectively. Patients who received ASCT+CAR-T had an improving trend in PFS [3-year PFS 60.66%(95% CI: 40.87,75.64) vs. 44.20%(95% CI: 26.11,60.87); P=0.082] ,and OS [3-year OS 74.22%(95% CI: 54.82,86.25) vs. 52.22%(95% CI: 31.23,69.58); P=0.082] compared to patients in the CAR-T group. (Fig.1A,B).
The 3-year incidence of relapse/progression for ASCT+CAR-T was 32.17%(95% CI: 16.45,49.03) compared to 43.15%(95% CI: 24.75,60.30)in the CAR-T group (P=0.316)).
The non-relapse mortality (NRM) rate was 7.17% (95% CI: 1.16,21.07) with ASCT+CAR-T compared to 12.65% (95% CI: 3.87,26.85) in the CAR-T group (P=0.250).(Fig.1C,D)

Table 1 Baseline characteristics-PSM

Variable	CAR-T (N=32)	ASCT+CAR-T (N=32)	Overall (N=64)	P value
Sex				
Male	18(56.3)	17(53.1)	35(54.7)	1.0000
Age (years)				
≤60	27(84.4)	27(84.4)	54(84.4)	1.0000
Histologic subtype				
DLBCL	27(84.4)	23(71.9)	50(78.1)	0.1966
HGBL	4(12.5)	3(9.4)	7(10.9)	
PMBL	1(3.1)	6(18.8)	7(10.9)	
IPI				1.0000
≥3	9(28.1)	9(28.1)	18(28.1)	
ECOG				1.0000
≥2	8(25.0)	8(25.0)	16(25.0)	
Disease stage				1.0000

Table 1 Baseline characteristics-PSM

III or IV	28(87.5)	28(87.5)	56(87.5)	
Cycles of therapy>3	6(18.8)	6(18.8)	12(18.8)	1.0000
Disease status prior to CAR-T therapy				
CR/PR	23(71.9)	23(71.9)	46(71.9)	1.0000
SD/PD	9(28.1)	9(28.1)	18(28.1)	

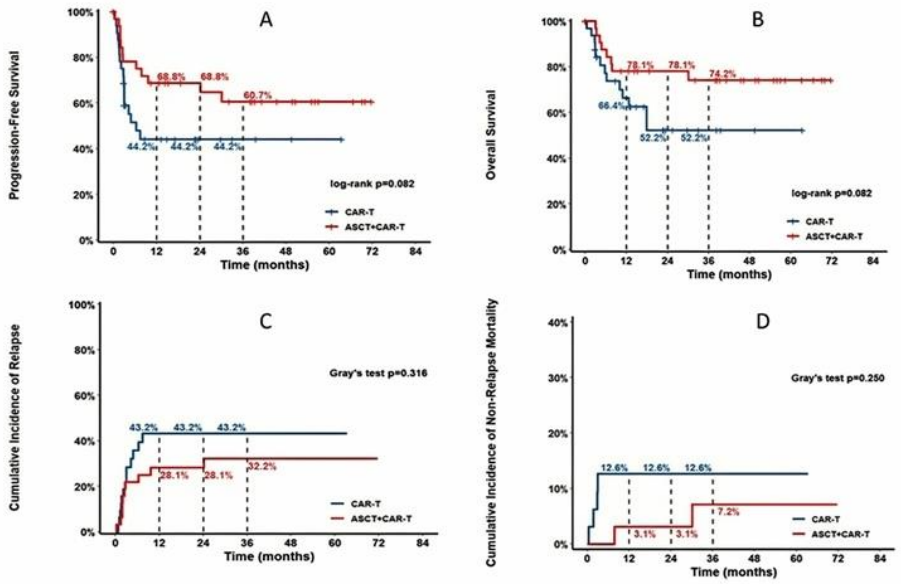

Figure 1 Kaplan–Meier curves comparing progression-free survival (A), overall survival (B), cumulative incidence of relapse (C), and non-relapse mortality (D) between patients with relapsed/refractory large B-cell lymphoma (RR-LBCL) treated with CD19 CAR-T therapy versus ASCT combined with CAR-T (ASCT+CAR-T).

Conclusions: Compared to CAR-T therapy alone, the combination of ASCT and CAR-T therapy showed a trend of improved survival outcomes in patients with relapsed/refractory (R/R) B-cell lymphoma. However, a larger study is required to confirm these findings.

Clinical Trial Registry: ChiCTR2100055062

Disclosure: Nothing to declare

A050

INFLUENCE OF THE HLA MISMATCHED LOCUS ON OUTCOMES IN MISMATCHED UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION USING POST-TRANSPLANT CYCLOPHOSPHAMIDE GVHD PROPHYLAXIS: A CIBMTR RETROSPECTIVE ANALYSIS

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Background: The adoption of post-transplant cyclophosphamide (PTCy) has expanded the use of mismatched unrelated donors (MMUD) in allogeneic HCT. A prior CIBMTR study noted equivalent outcomes between 8/8 matched unrelated donors (MUD) and 7/8 MMUD when PTCy is used. Class I and II MMUD recipients had similar outcomes, whereas a report from the EBMT (Arrieta-Bolaños et al., JCO 2024) reported worse outcomes with class I mismatched donors are associated with an increased risk of mortality even in the PTCy setting. We therefore examined whether the mismatched HLA locus affects outcomes after 7/8 MMUD HCT with PTCy in a large, contemporary U.S. cohort.

Methods: We conducted a retrospective CIBMTR registry analysis of adults (≥18 years) undergoing first allogeneic HCT in the US from 2017-2023 using a 7/8 MMUD and PTCy-based GVHD prophylaxis. The primary objective was to compare overall and GVHD-free, relapse-free survival (GRFS) at 2 years post HCT between MMUD based mismatched HLA locus. Secondary objectives included evaluating relapse, disease-free survival (DFS), non-relapse mortality (NRM), acute GVHD (aGVHD) grades 2-4 and 3-4, moderate/severe chronic GVHD (cGVHD) and primary graft failure (PGF) by mismatched locus. Eligible diagnoses included acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) and myelodysplastic syndromes (MDS).

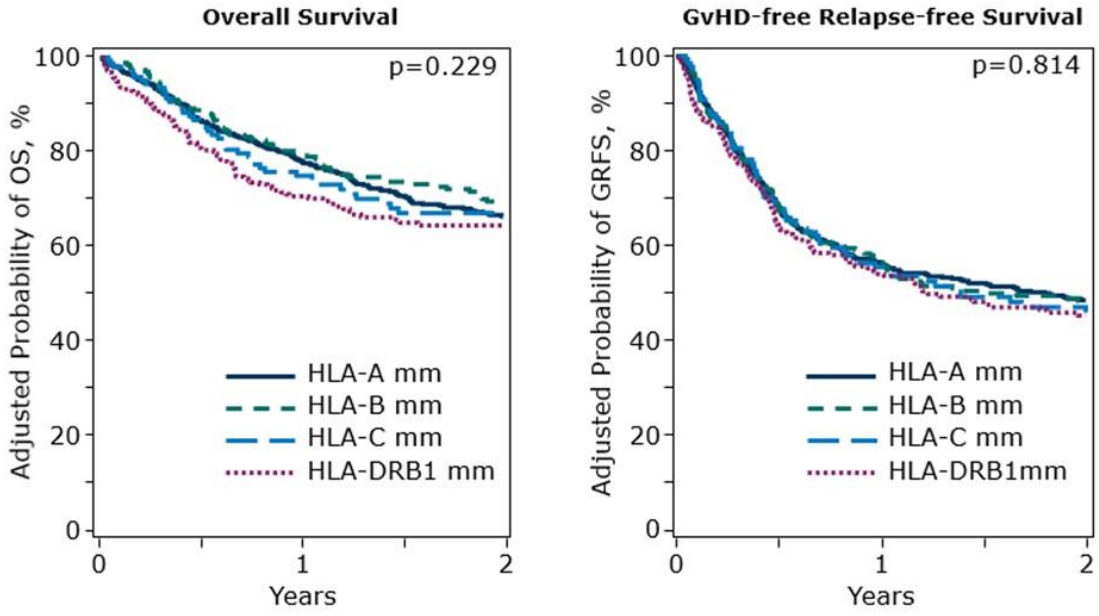
Results: Included were 1,255 patients from 114 centers with AML (n=692), ALL (n=235) and MDS (n=328). Median (range) recipient and donor age was 59.4 (18.7-78.4) and 27.7 years (18.4-61.2), respectively. Fifty two percent of recipients were female, 32% were ethnically diverse and most received peripheral blood grafts (93.2%). The distribution of single-locus mismatches was HLA-A (n=591), HLA-B (n=279), HLA-C (n=128) and HLA-DRB1(n=257). HLA-DQB1 and -DPB1 T cell epitope (TCE) data were available for 99.2% and 96.8% of recipients, respectively. DQB1 mismatches were more common among DRB1 mismatched pairs (49%) versus HLA-A (6%), -B (8%) and -C (7%) MMUD. HLA-DPB1 TCE

matching was similar across groups (20-27% non-permissive). Neither DQB1 mismatching nor DPB1 TCE status was associated with any clinical outcomes in multivariable models. Using the largest group (HLA-A) as the reference mismatched locus, no significant differences were observed in OS, GRFS, relapse, DFS, NRM, aGVHD 2-4 or 3-4 and moderate-severe cGVHD across mismatched loci (table and figure). Primary graft failure (PGF) was higher among DRB1 mismatched pairs (HR 1.94, 95% CI 1.10-3.40, p=0.0211). Whether donor specific antibodies (DSA) were present is not available, limiting interpretation of PGF findings.

Table: Multivariable analysis results

	HLA-A mm n=591 (ref)		**HLA-B mm n=279**		**HLA-C mm n=128**		**HLA-DRB1 mm n**
Outcome*	**HR**	**Overall p-value**	**HR (95% CI)**	**p-value**	**HR (95% CI)**	**p-value**	**HR (95% CI)**
OS	1	0.229	0.9 (0.69, 1.18)	0.440	1.05 (0.75, 1.48)	0.759	1.23 (0.95, 1.6)
GRFS	1	0.814	1.01 (0.82, 1.24)	0.925	1.04 (0.79, 1.36)	0.787	1.11 (0.9, 1.36)
RFS	1	0.453	0.92 (0.72, 1.17)	0.501	1.1 (0.81, 1.49)	0.533	1.14 (0.9, 1.45)
Relapse	1	0.937	1.04 (0.77, 1.4)	0.813	0.89 (0.57, 1.37)	0.596	1.00 (0.72, 1.39)
NRM	1	0.194	0.83 (0.55, 1.24)	0.361	1.32 (0.88, 1.98)	0.182	1.22 (0.84, 1.77)
aGVHD 2-4	1	0.187	1.33 (1.03, 1.73)	0.030	1.16 (0.83, 1.62)	0.373	1.24 (0.91, 1.71)
aGVHD 3-4	1	0.842	1.12 (0.69, 1.82)	0.642	0.98 (0.52, 1.85)	0.956	0.84 (0.49, 1.46)
mod/sev cGVHD	1	0.914	1.02 (0.71, 1.46)	0.933	0.92 (0.56, 1.51)	0.741	0.88 (0.59, 1.31)
Primary Graft Failure	1	0.014	0.56(0.25-1.23)	0.148	1.33(0.61-2.90)	0.468	1.94(1.10-3.40)

Figure: 2-year Probability of overall survival and GVHD-free, relapse-free survival by HLA-mismatched locus in 7/8 MMUD HCT using PTCy-based GVHD prophylaxis



Conclusions: In this large contemporary cohort of 7/8 MMUD HCT with PTCy, we did not observe significant differences in OS, GRFS, relapse, DFS, NRM, aGVHD and cGVHD according to the mismatched HLA locus. PGF risk was higher with HLA-DRB1 mismatched pairs, although this finding is difficult to interpret in the absence of DSA data and should be considered exploratory. DSA to class II molecules have been historically associated with less effective desensitization than DSA to class I. These results support MMUD donor selection strategies that prioritize non-HLA donor characteristics, such as younger donor age rather than the specific HLA mismatched locus. Studies in larger cohorts will be required to confirm these results.

Disclosure: Shannon McCurdy - Advisory Board: Geron. Brian Shaffer - Consulting: Gamida Cell; Research Support: Incyte, Genentech. Bronwen Shaw - Consulting: OrcaBio.

A051

DONOR SELECTION AND CLINICAL OUTCOMES OF ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN ADULTS OLDER THAN 50 YEARS - A SINGLE CENTRE RETROSPECTIVE REVIEW

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Background: Optimal donor selection for older patients undergoing allogeneic haematopoietic stem cell transplantation (allo-HSCT) remains controversial. While matched sibling donors (MSD) have traditionally been considered standard, the benefits of younger alternative donors and the impact of post-transplantation cyclophosphamide (PTCy) prophylaxis remain unclear in this population. To address these issues, we compared the clinical outcomes of four donor types in allo-HSCT patients >50 years old.

Methods: We conducted a retrospective analysis of 493 consecutive patients >50 years old with malignant haematological diseases undergoing MSD, matched unrelated donor (MUD), mismatched unrelated donor (MMUD), or haploidentical allo-HSCT between January 2014 and December 2023. Patients received either PTCy-based (40mg/kg/day on days +3 to +4 with cyclosporine A and mycophenolate mofetil) or conventional calcineurin inhibitor-based graft-*versus*-host-disease (GVHD) prophylaxis. Outcomes analyzed included engraftment, GVHD, non-relapse mortality (NRM), relapse-free survival (RFS), overall survival (OS), and GVHD-free, relapse-free survival (GRFS). Univariate and multivariate analyses with Cox proportional hazards regression and Fine-Gray models were used to identify significant prognostic factors.

Results: Four hundred and ninety-three patients (median age: 57 years; male: 51%) undergoing allo-HSCT (MSD, N=198; MUD, N=101; MMUD, N=58; haploidentical, N=136) were analyzed (Table 1). Haploidentical recipients and MSD donors were significantly older, whereas MMUD and haploidentical recipients had higher disease risk indices. All haploidentical recipients received PTCy prophylaxis and 99% received peripheral blood HSC grafts. Engraftment rates were comparable (94–99% at day 28). The 180-day incidence of grade II-IV acute GVHD was significantly higher in MMUD (42%) compared with MSD (22%), MUD (31%), and haploidentical (16%) groups (P<0.001) (Figure 1A). In multivariate analysis, MMUD and non-PTCy prophylaxis were associated with increased risk of acute GVHD. At 2 years, the incidence of moderate to severe chronic GVHD was highest in MUD (49%) and MSD (43%) *versus* MMUD (25%) and haploidentical (17%) allo-HSCT (P<0.001) (Figure 1B). Risk factors for chronic GVHD included donor age >50 years, female-to-male donation, peripheral blood HSC grafts, and conventional GVHD prophylaxis. NRM was comparable (9–13% at 2 years). Importantly, haploidentical showed superior RFS (72% at 2 years; hazard ratio: 0.62; P=0.016) compared with MSD allo-HSCT. Haploidentical also demonstrated significantly superior GRFS (58% at 2 years) compared with other allo-HSCT (23–30%) (P<0.001) (Figure 1C). However, this advantage was primarily attributable to PTCy prophylaxis in multivariate analysis. OS was similar (62–74% at 2 years). In the high disease risk subgroup, haploidentical showed improved RFS compared with MSD allo-HSCT (62% *versus* 36%; P=0.051) (Figure 1D). Male sex and high disease risk index

independently predicted worse survival outcomes.

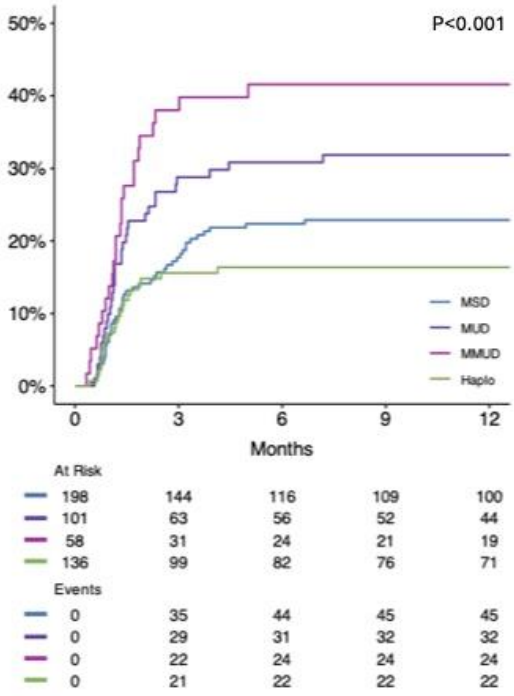
Table 1. Demographic and Clinical Characteristic at Baseline.

Characteristic	MSD (N=198)	MUD (N=101)	MMUD (N=58)	Haplo (N=136)
Recipient age – mean ± SD, yr	57 ± 4	57 ± 4	57 ± 4	59 ± 5
Donor age – mean ± SD, yr	55 ± 6	32 ± 7	36 ± 8	34 ± 11
Median follow-up – mo (95% CI)	61 (57-71)	66 (59-82)	65 (42-99)	25 (22-31)
Male sex – no. (%)	101 (51)	49 (49)	29 (50)	73 (54)
Disease – no. (%)				
AML	89 (45)	45 (45)	31 (53)	68 (50)
ALL	31 (16)	15 (15)	13 (22)	18 (13)
MDS	25 (13)	15 (15)	4 (7)	18 (13)
MPN	14 (7)	6 (6)	3 (5)	7 (5)
NHL	16 (8)	9 (9)	6 (10)	14 (10)
Others*	23 (12)	11 (11)	1 (2)	11 (8)
AML – no. (%)				
Favorable	16 (18)	8 (18)	7 (23)	5 (7)
Intermediate	56 (63)	26 (58)	10 (32)	34 (50)
Adverse	17 (19)	11 (24)	14 (45)	29 (43)
ALL – no. (%)				
Ph +ve	9 (29)	7 (47)	5 (39)	10 (56)
Ph -ve	16 (52)	7 (47)	6 (46)	4 (22)
T-ALL	6 (19)	1 (7)	2 (15)	4 (22)
Disease risk index				
Low	32 (16)	15 (15)	9 (16)	12 (9)
Intermediate	138 (70)	65 (64)	29 (50)	89 (65)
High	27 (14)	21 (21)	19 (33)	35 (26)
Very high	1 (1)	0	1 (2)	0
HCT-CI				
≥1 – no. (%)	43 (22)	33 (33)	10 (17)	31 (23)
≥2 – no. (%)	16 (8)	13 (13)	5 (9)	10 (7)
Gender match (donor / recipient) – no. (%)				
Female / Female	46 (23)	25 (25)	12 (21)	24 (18)
Female / Male	46 (23)	11 (11)	8 (14)	27 (20)
Male / Male	55 (28)	38 (38)	21 (36)	46 (34)
Male / Female	51 (26)	27 (27)	17 (29)	39 (29)

CMV status (donor / recipient) – no. (%)				
Pos / Pos	173 (87)	58 (58)	37 (64)	81 (60)
Neg / Pos	11 (6)	39 (39)	14 (24)	49 (36)
Pos / Neg	11 (6)	2 (2)	3 (5)	2 (2)
Neg / Neg	3 (2)	2 (2)	4 (7)	4 (3)
Blood group match – no. (%)				
Bidirectional	16 (8)	17 (17)	10 (17)	7 (5)
Major mismatch	34 (17)	23 (23)	18 (31)	25 (18)
Minor mismatch	31 (16)	30 (30)	17 (29)	22 (16)
No mismatch	117 (59)	31 (31)	13 (22)	82 (60)
Stem cell source – no (%)				
Peripheral blood (PB)	154 (78)	69 (68)	41 (71)	135 (99%)
Bone marrow (BM)	42 (21)	32 (32)	17 (29)	1 (1)
BM + PB	2 (1)	0	0	0
Conditioning intensity – no. (%)				
MAC	100 (51)	39 (39)	25 (43)	27 (20)
RIC	98 (50)	62 (61)	33 (57)	109 (80)
Prior transplantation – no. (%)				
Autologous	3 (2)	4 (4)	0	2 (2)
Allogeneic	1 (1)	4 (4)	2 (3)	6 (4)
GVHD prophylaxis – no. (%)				
PTCy + CsA + MMF	0	0	23 (40)	136 (100)
ShMTX + CsA	198 (100)	0	0	0
ShMTX + CsA + MMF	0	101 (100)	35 (60)	0

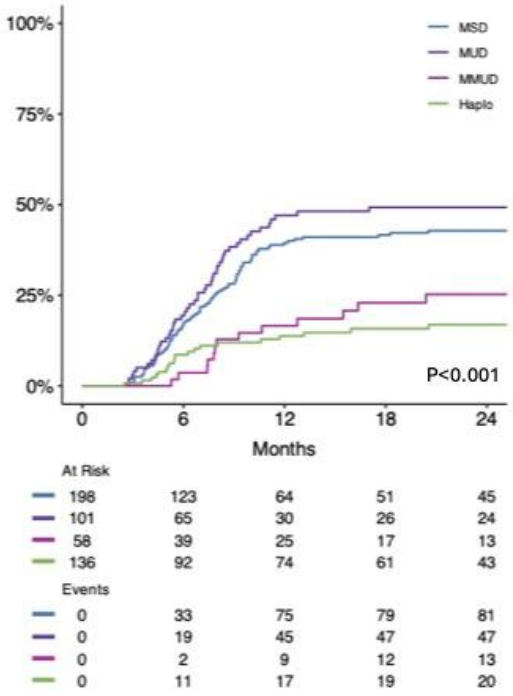
Figure 1.

A



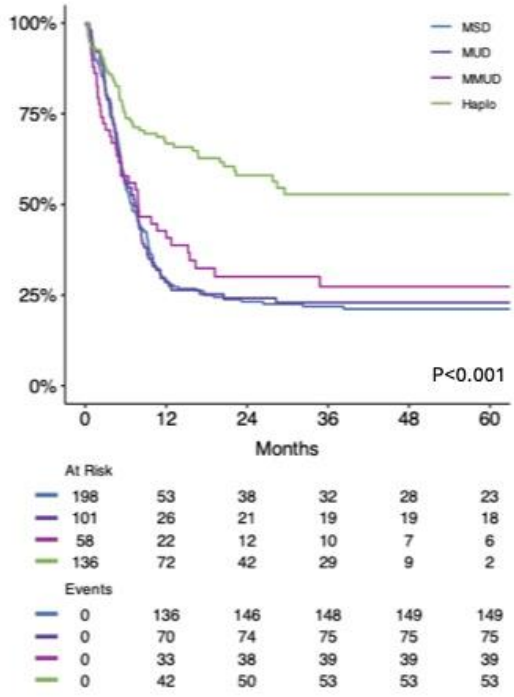
At Risk					
MSD	198	144	116	109	100
MUD	101	63	56	52	44
MMUD	58	31	24	21	19
Haplo	136	99	82	76	71
Events					
MSD	0	35	44	45	45
MUD	0	29	31	32	32
MMUD	0	22	24	24	24
Haplo	0	21	22	22	22

B



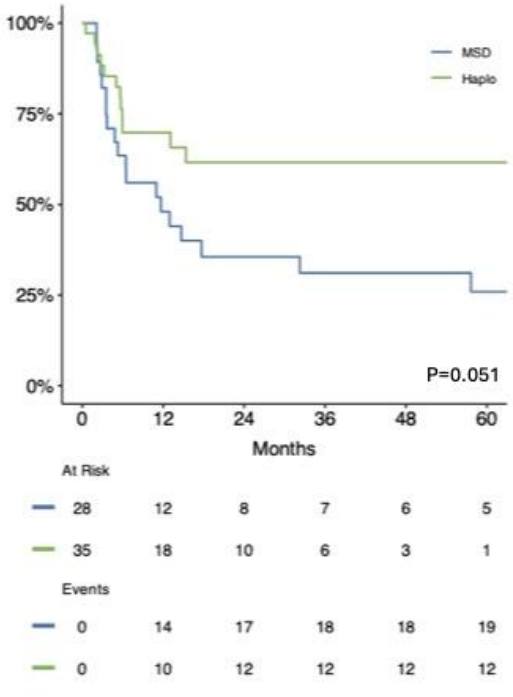
At Risk					
MSD	198	123	64	51	45
MUD	101	65	30	26	24
MMUD	58	39	25	17	13
Haplo	136	92	74	61	43
Events					
MSD	0	33	75	79	81
MUD	0	19	45	47	47
MMUD	0	2	9	12	13
Haplo	0	11	17	19	20

C



At Risk					
MSD	198	53	38	32	28	23
MUD	101	26	21	19	19	18
MMUD	58	22	12	10	7	6
Haplo	136	72	42	29	9	2
Events						
MSD	0	136	146	148	149	149
MUD	0	70	74	75	75	75
MMUD	0	33	38	39	39	39
Haplo	0	42	50	53	53	53

D



At Risk						
MSD	28	12	8	7	6	5
Haplo	35	18	10	6	3	1
Events						
MSD	0	14	17	18	18	19
Haplo	0	10	12	12	12	12

Conclusions: In patients > 50 years old, MUD allo-HSCT with younger donors and conventional GVHD prophylaxis achieved outcomes comparable with those of older MSD allo-HSCT. Notably, haploidentical allo-HSCT with PTCy demonstrated superior RFS and GRFS compared with MSD allo-HSCT with conventional GVHD prophylaxis, suggesting that alternative donor approaches with optimized GVHD prophylaxis might be advantageous in this older population. Disease risk index remained an important independent predictor of outcomes in all donor types.

Disclosure: Nothing to declare

A052

BCMA CAR T-CELL THERAPY DEMONSTRATES EARLY SAFETY AND EFFICACY SIGNALS IN REFRACTORY SYSTEMIC SCLEROSIS AND ANTIPHOSPHOLIPID SYNDROME: PHASE I RESULTS IN AUTOIMMUNE DISEASES

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Background: Chimeric antigen receptor (CAR) T-cell therapy offers a targeted strategy to eliminate autoreactive B cells in severe autoimmune diseases. B-cell maturation antigen (BCMA), expressed on plasmablasts and plasma cells, represents a promising therapeutic target. We report updated safety and preliminary efficacy data from an ongoing Phase 1 trial of BCMA-directed CAR T cells (HBI0101) in patients with refractory autoimmune rheumatic diseases (ARDs) (NCT07085676).

Methods: HBI0101 is an autologous BCMA-targeted CAR T-cell product generated by retroviral transduction of patient-derived T cells. The construct, developed at Hadassah Medical Center, has previously been administered to 145 patients with relapsed/refractory multiple myeloma and 20 patients with amyloidosis. In the initial safety phase (October 2024–November 2025), eight patients with refractory systemic lupus erythematosus (SLE), systemic sclerosis (SSc), idiopathic inflammatory myopathy (IIM), and antiphospholipid syndrome (APS) coexisting with SLE received lymphodepleting chemotherapy followed by infusion of 450×10^6 CAR-positive (CAR^+) T cells (n=6) or 800×10^6 CAR^+ T cells (n=2). Adverse events (AEs) and clinical responses were prospectively monitored.

Results:

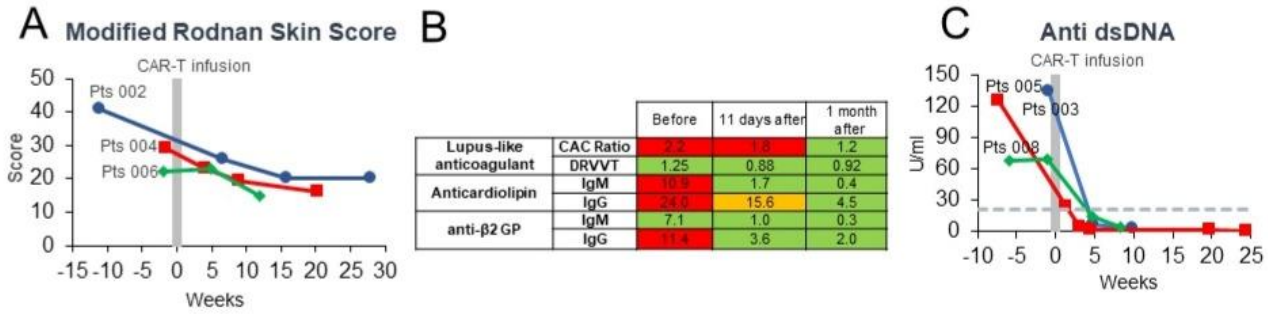

Figure 1. Representative laboratory and clinical responses following BCMA-directed CAR T-cell therapy. (A) Changes in Modified Rodnan Skin Score (mRSS) in three patients with systemic sclerosis. (B) Longitudinal changes in lupus anticoagulant assays in a patient with antiphospholipid syndrome who received CAR-T BCMA (red = above reference range; orange = above reference range with improvement; green = within normal range). (C) Longitudinal changes in anti–double-stranded DNA (anti-dsDNA) antibody levels in patients with systemic lupus erythematosus.

Clinical responses were observed across multiple autoimmune phenotypes, with a maximum follow-up of 12 months (mean: 169 days). Three patients with SSc showed rapid reductions in skin fibrosis, with Modified Rodnan Skin Score improving from 41 and 34 to 20, and from 27 to 15 within 2 months (Figure 1A); skin biopsy in one patient demonstrated early histological resolution of fibrosis. A patient with severe APS and diffuse alveolar hemorrhage showed cessation of pulmonary bleeding, improved oxygen dependence, and gradual corticosteroid tapering; antiphospholipid antibodies normalized (Figure 1B). SLE patients showed marked clinical improvement, including normalization of anti–double-stranded DNA antibodies (Figure 1C). One patient with severe SLE and lupus nephritis experienced resolution of edema and systemic symptoms, normalization of complement, serum albumin, hemoglobin, and anti-dsDNA titers, along with progressive improvement in proteinuria and serum creatinine, permitting corticosteroid and antihypertensive tapering. A patient with IIM showed improved muscle strength (iliopsoas manual muscle testing from 2/2+ to 5−/4+) and sustained decline in serum creatine phosphokinase; however, disease relapse occurred at 9 months.BCMA-directed CAR T-cell therapy was generally well tolerated. Lymphopenia from chemotherapy occurred in all patients. Grade 3–4 neutropenia occurred in 2 patients and was managed supportively. Cytokine release syndrome (CRS) was limited to Grade 1–2 events (Grade 2 in 4 patients; Grade 1 in 2 patients); two patients experienced no CRS. Tocilizumab was administered to 6 patients (median dose 1.5, range 1–3), and high-dose corticosteroids were required in one patient. No immune effector cell–associated neurotoxicity syndrome (ICANS) was observed.

Conclusions: BCMA-targeted CAR T-cell therapy demonstrated a favorable safety profile with no dose-limiting toxicities or unexpected adverse events. All treated patients showed clinical or biological responses lasting up to 9 months. Notably, we report the first clinical responses to BCMA-directed CAR T-cell therapy in SSc and APS. These interim data support the safety, feasibility, and therapeutic potential of BCMA-targeted CAR T cells as a novel, antigen-specific treatment strategy for refractory autoimmune diseases.

Clinical Trial Registry: NCT07085676

Disclosure: Nothing to declare

A054

FLUDARABINE EXPOSURE IMPACTS BCMA-DIRECTED CAR-T THERAPY EFFICACY IN RELAPSED OR REFRACTORY MULTIPLE MYELOMA

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Background: Fludarabine (Flu) dosing is based on the body surface area. Adjustments for patients with reduced creatinine clearance (CrCl) are based on the package insert and are not tailored to CAR-T. While Flu exposure (area under the curve, AUC) has been linked with CAR-T outcomes in large B-cell lymphoma (Scordo, 2023) and B-cell acute lymphoblastic leukemia (Dekker, 2022), its significance in relapsed/refractory multiple myeloma (RRMM) remains to be fully established.

Methods: This retrospective study included patients with RRMM treated with CAR-T directed at the B-cell maturation antigen (BCMA). To estimate the Flu AUC using clinically available parameters, a validated pharmacokinetic model was used (Langenhorst, 2019). Absolute lymphocyte count (ALC; days 0-30) was used as a surrogate for CAR-T expansion (Saldarriaga, 2024). Overall response was defined as a partial response or better based on the International Myeloma Working Group response criteria. Cox proportional hazard models were used to estimate the association between Flu AUC and progression-free survival (PFS) and overall survival (OS). The relationship between Flu AUC and overall response rate (ORR), cytokine release syndrome (CRS), and immune effector cell-associated neurotoxicity syndrome (ICANS) was examined using logistic regression. Associations with blood counts were estimated using linear regression. Multivariable analyses (MVA) included age, sex, CAR-T product, cytogenetics and extra-medullary disease.

Results: We included 161 patients: 119 (74%) were treated with cilta-cel and 42 (26%) with ide-cel (Table 1). Flu AUC ranged from 11.2 to 22.25 mg*h/L (Figure 1A). Patients with a CrCl <80mL/min had higher Flu AUC than those with a CrCl≥80mL/min (17.37 vs 15.48mg*h/L, p<0.001; Figure 1B). On univariable analysis (UVA), higher Flu AUC was associated with more day 0-30 thrombocytopenia (p=0.019) and higher day 0-30 peak ALC (p=0.033). There was no association on UVA with ICANS, CRS, day 30-90 thrombocytopenia or day 0-90 neutropenia. On MVA, higher Flu AUC was associated with increased ORR (OR 1.37, 95%CI 1.03-1.89, p=0.038), MRD negativity (OR 0.65, 95%CI 0.49-0.85, p=0.003) and PFS (HR 0.78, 95%CI 0.68-0.91, p<0.001), but not OS (p=0.39). Analyzing each cell product individually, the impact of Flu AUC on PFS was observed in cilta-cel (HR 0.72, 95% CI 0.56-0.91, p=0.007) but was not statistically significant in ide-cel (HR 0.83, 95% CI 0.68-

1.02, p=0.077). Optimal Flu AUC to minimize relapse risk in cilta-cel was > 16.1 mg*h/L (Figure 1C).

Table 1: Baseline characteristics, stratified by creatinine clearance

Characteristics	CrCl<80mL/min (N=63)	CrCl≥80mL/min (N=98)	P-value
Age, mean [min, max]	70 [46, 86]	61 [42, 80]	<0.001
Female sex	27 (43%)	44 (45%)	0.9
High-risk cytogenetics	31 (49%)	49 (50%)	>0.9
Extra-medullary disease	10 (16%)	30 (31%)	0.04
Bone marrow plasma cell >50%	5 (8.1%)	16 (16%)	0.2
Cilta-cel	45 (71%)	74 (76%)	0.6
Ide-cel	18 (29%)	24 (24%)	0.6
Fludarabine exposure (mg*h/L), mean [min, max]	17.4 [12.3, 22.5]	15.48 [11.2, 20.2]	<0.001

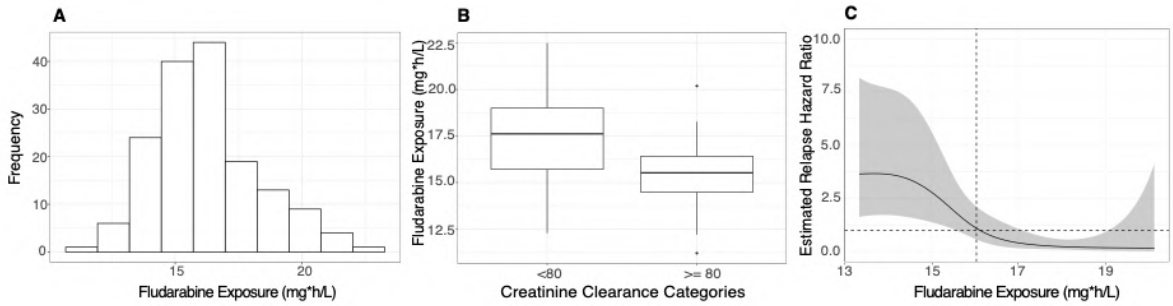

Figure 1: Fludarabine exposure prior to BCMA-directed CAR-T (A) Estimated fludarabine distribution; (B) Estimated fludarabine exposure is higher in the group with CrCl<80mL/min than CrCl≥80mL/min (C) Increased fludarabine exposure reduces risk of relapse in cilta-cel.

Conclusions: Flu AUC varies across CrCl despite standard dose adjustments. Higher Flu AUC is associated with improved CAR-T efficacy, which was particularly notable in cilta-cel, potentially suggesting product-specific differences between BCMA-directed CAR-T therapies.

However, limited ide-cel sample size may have reduced the power to detect an effect. The correlation between higher Flu AUC and ALC suggests a potential effect on CAR-T expansion. Personalized Flu dosing may represent a simple intervention to improve outcomes in RRMM.

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A055

OUTCOME OF CAR-T CELL THERAPY IN OLDER PATIENTS. A STUDY FROM THE EBMT TRANSPLANT COMPLICATIONS WORKING PARTY

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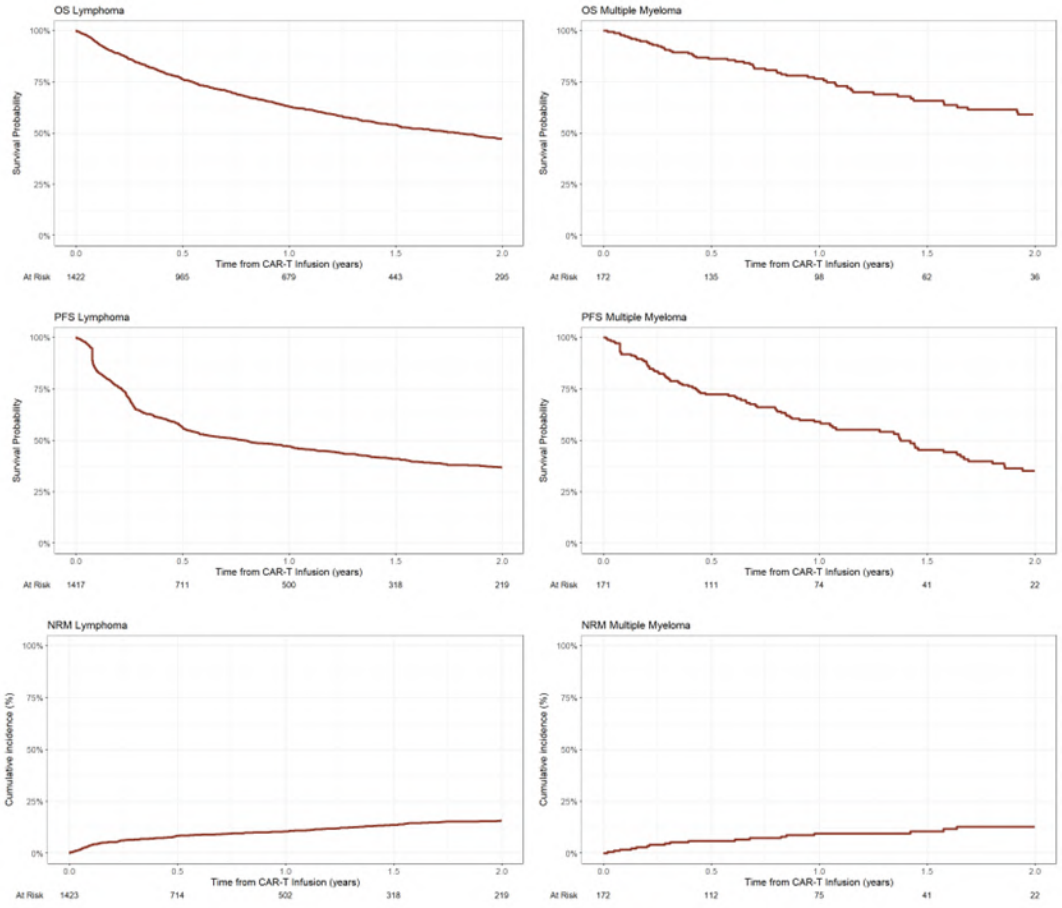
Background: CAR T-cell therapy has transformed the management of B-cell malignancies. Early clinical trial eligibility criteria and toxicity profiles suggested that advanced age might limit access. Although later studies confirmed feasibility, real-world data in patients ≥70 years remain limited. We evaluated outcomes and safety of CAR T-cell therapy in this population using the EBMT registry.

Methods: We included all patients aged ≥70 years at infusion who received a licensed CAR-T cell product between 2019 and 2023. Univariable analyses used Kaplan–Meier and cumulative incidence (CI) functions; multivariable analyses used Cox cause-specific models.

Results: We included 1,595 patients, of whom 1,423 had non-Hodgkin lymphoma (NHL, including mantle-cell lymphoma, n=197) and 172 had multiple myeloma (MM). Median age at infusion was 73.7 years (range 70.0–91.3). Most patients had an ECOG of 0–1 (91.5%). Prior autologous HCT was more frequent in MM (73
.2%) than in NHL (14.8%). At infusion, 35.1% of NHL patients and 38.3% of MM patients were in complete or partial remission.In univariable analyses, NHL patients showed an OS of 63.0% (95% CI: 60.4–65.7%) and PFS was 47.1% (95% CI: 44.3–49.7%) at 1 year. For MM, OS was 76.5% (95% CI: 70.0–83.5%) and PFS was 59.0% (95% CI: 50.8–66.3%) at 1 year. The CI of relapse at 1 year was 42.4% (95% CI: 39.8–45.1%) for NHL and 31.3% (95% CI: 24.2–38.6%) for MM. NRM at 1 year was similar, reaching 10.6% (95% CI: 9.0–12.3%) in NHL, and 9.5% (95% CI: 5.5–14.7%) in MM. Disease progression accounted for 75.6% and 71.4% of deaths in NHL and MM.
Multivariable analyses showed that treatment with axi-cel was associated with superior OS (HR 1.28, 95% CI:1.07–1.53; p=0.006), PFS (HR 1.41, 95% CI: 1.20–1.64; p<0.001), and lower relapse incidence (RI) compared with axi-cel. Male sex was associated with shorter OS (HR 1.21, 95% CI: 1.01–1.45; p=0.04) and higher NRM. ECOG ≥1 was similarly linked to poorer OS (HR 1.52, 95% CI: 1.27–1.81; p<0.001), PFS (HR: 1.34, 95% CI: 1.15–1.56; p<0.001), NRM and RI. Compared to patients in active disease, achieving a PR or a CR at infusion was associated with improved OS, (HR: 0.66, 95% CI: 0.54–0.82; p<0.001) and (HR: 0.52, 95% CI: 0.37–0.73; p<0.001) respectively, as were PFS and RI. Finally, a longer interval between initial diagnosis and CAR T-cell infusion is associated with better OS (HR [1-year]: 0.96, 95% CI:0.94–0.98; p<0.001), PFS (HR: 0.96, 95% CI: 0.95–0.98; p<0.001). In the MM subgroup, the use of ide-cel was associated with worse PFS (HR: 2.52, 95% CI: 1.19–5.30; p=0.02) and RI, while an ECOG≥1 was associated with shorter OS (HR: 2.80, 95% CI: 1.35–5.79; p=0.006), PFS (HR: 2.54, 95% CI: 1.49–4.33; p<0.001) and higher RI.



Conclusions: In this large real-world cohort of patients aged ≥70 years, CAR T-cell therapy showed marginally higher NRM and lower RI compared with younger populations in other studies. This suggests efficacity and safety of CAR-T in older populations.

Clinical Trial Registry: N/A

Disclosure: No COI directly linked to this work.

A056

HAPLOIDENTICAL DONOR-DERIVED CAR-T CELLS CO-INFUSED WITH THE ALLOGENIC GRAFT ON THE PLATFORM OF T CELL DEPLETION OR POST-TRANSPLANT CYCLOPHOSPHAMIDE IN CHILDREN WITH ADVANCED B-CELL NEOPLASMS

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Background: Autologous CAR T cells induce high rate of deep remissions among children with rR/R B-ALL. In a significant proportion of cases cure is achieved only with HSCT as post-CAR-T consolidation. Seeking to combine the cytoreductive and curative power of HSCT with the antigen-specific activity of CAR-T we devised an approach with simultaneous infusion of hematopoietic stem cell graft and CAR-T cells, derived from the same donor. Two GVHD prevention platforms were used: ex-vivo T cell depletion and PtCy. We report here pooled analysis of prospective trial patients and compassionate use program.

Methods: A total of 38 pts with R/R BCP-ALL and B-NHL/leukemia were enrolled. The main characteristics of the group are presented in Table 1.

Table1 Clinical Characteristics of Patients

38 patients	
median age	9,6 y
Sex Male female	 23 15
Diagnosis BCP-ALL B-NHL/leukemia	 34 4
Remission status **AD** BM >5% BM>5%+ExD ExD **MRD positive** **CR (MRD negative)**	 **24** 10 7 7 **11** **3**
Previous therapy HSCT	 13

blinatumomab inotuzumab blinatumomab+inotuzumab CAR-T cell infusion	23 1 5 11
Conditioning regimen TBI Treosulfan	 19 19
ex-vivo T cell depletion	27
post-transplant cyclophosphamide	11
Donor type Haploidentical	 38

27 patients received T-cell depleted graft, GVHD prophylaxis included abatacept. In this subgroup CAR-T products included CD19 CAR- T (n=5), CD1922 tandem CAR-T (n=19), and cocktail CD19 and CD22 CAR-T (n=3). Eleven pts were transplanted with PtCy-based GVHD prophylaxis, in this subgroup CAR-T cells were infused on day +5 after HSCT and were represented by either by CD19-22 tandem CAR- T (n=1), CD19 CAR- T(n=1) or by CD19 and CD22 cocktail product (n=9). In the PtCy group GVHD prophylaxis included abatacept, vedolizumab and CsA or baricitinib.

Results: There was no suspected conflict between the graft and CAR-T cells. Primary engraftment was observed in 36 of 38 pts (one pt died before engraftment and one relapsed early), all engrafted patients achieved MRD-negative CR at day +28 after HSCT. The median time to CAR-T cell peak expansion was 14 days regardless of depletion platform.
CRS occurred in 21 (55%) patients and only two pts had grade 3 CRS. Also 21 patients had neurologic events (ICANS grade 1, n=13, grade 2, n=6 and grade 3, n=2). Twelve patients had aGvHD, grade 2 (n=10), grade 3(n=1) and grade 4 (n=1), 5 patients had mild chronic GvHD. There were no significant differences in CAR-T toxicity between depletion and PtCy groups.
Six patients died in CR and one before engraftment due to infection and VOD.
Leukemia relapse was observed in nine children (8 from HD burden and one from MRD group) at a median time of 174 days after allograft, 3 pts had CD 19 negative relapse.
23 (58%) patients are alive (22 in CR, 1 with disease progression) with a median follow-up of 2,9 years (0,33-5,8). EFS and OS in patients with high disease burden was 45% and 41%, in MRD group 82% and 81%. EFS and OS at 2,6 years in whole group are 59% and 57%, respectively, without differences between T-cell depletion and ptCy groups.

Conclusions: Our early experience suggests that allogenic CAR-T cells can be safely infused simultaneously with the HSC graft both on the platform of T cell depletion and PtCy-based GVHD prophylaxis. The infusions did not compromise engraftment and GvHD control, while specific CAR-T toxicity was mild and manageable. We have documented CAR-T expansion and persistence. Prospective testing of the approach is warranted.

Disclosure: Nothing to declare.

A059

COMPARATIVE VALIDATION OF NEUTROPHIL-BASED MODELS (CAR-HEMATOTOX, ALL-HEMATOTOX, AND E-IPM) FOR PREDICTING EARLY T-ICAHT–DEFINED PLATELET RECOVERY AFTER CAR-T THERAPY

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Background: Immune effector cell–associated hematotoxicity (ICAHT) is a common complication after CAR-T therapy. A thrombocytopenia-focused ICAHT grading system (T-ICAHT) has recently been developed to standardize the assessment of platelet recovery (Kai Rejeski, et al. Blood 2025). Whether established neutrophil-centered models—CAR-HEMATOTOX (CAR-HT), ALL-HEMATOTOX (ALL-HT), and the early Inflammatory Prognostic Model (eIPM) for N-ICAHT—can be repurposed to effectively predict T-ICAHT across different hematologic malignancies treated with CAR-T remains unknown.

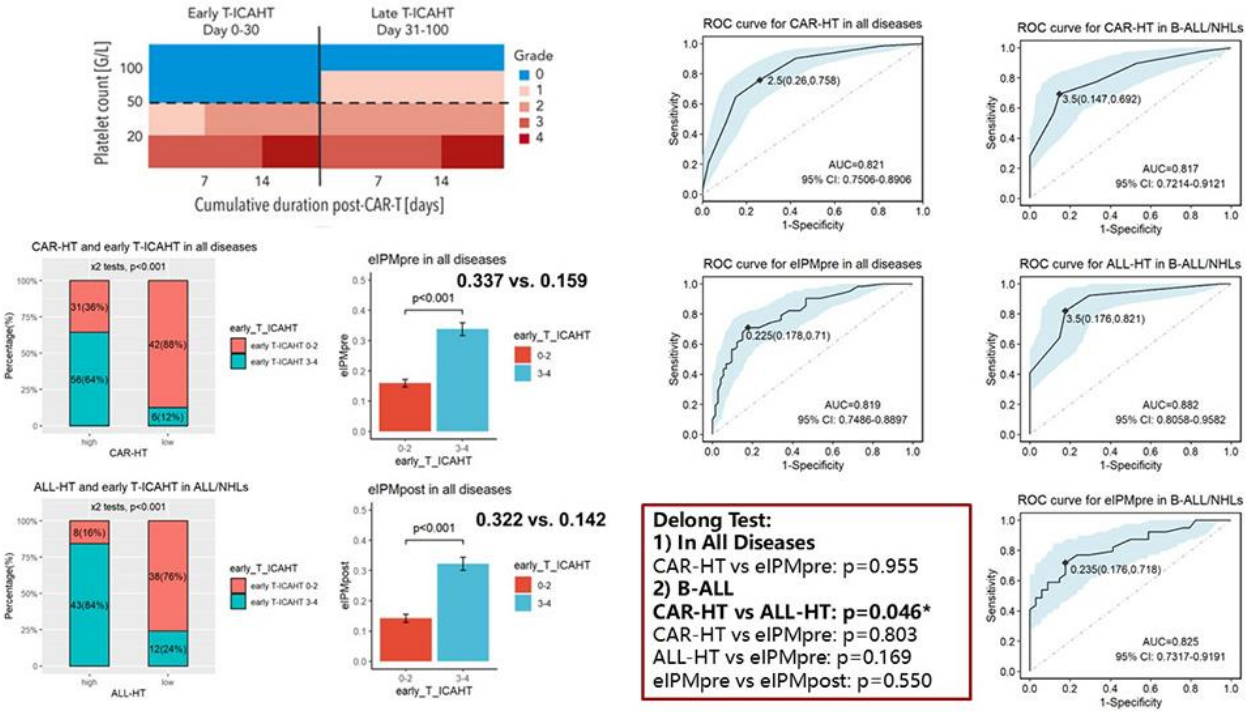
Methods: In this prospective cohort, 135 patients received CAR-T therapy between 2022 and 2025, including autologous CD19 CAR-T (brexucabtagene autoleucel or academic 4-1BB–based CAR-T) for B-ALL/B-cell non-Hodgkin lymphoma (n=73), CD7 CAR-T for T-ALL/T-cell NHL (n=28), and BCMA CAR-T for multiple myeloma (n=34). Early T-ICAHT was graded on a four-grade scale according to the cumulative depth and duration of thrombocytopenia within 30 days after infusion, and late T-ICAHT was defined by thrombocytopenia severity between days 31 and 100. Patients were censored at the time of subsequent allo-HSCT. The predictive performance of CAR-HT, ALL-HT, and eIPM for early T-ICAHT was compared, with ROC curves evaluated using DeLong's test.

Results: Grade 3–4 early T-ICAHT occurred in 39/73 (53.4%) of B-ALL/NHL, 16/28 (57.1%) of T-ALL/NHL, and 7/34 (20.6%) of MM patients. In the overall cohort, grade 3–4 early T-ICAHT was associated with significantly inferior outcomes, including inferior 1-year OS (63% vs. 97%, $P<0.001$) and DFS (43% vs. 80%, $P<0.001$) compared with grade 0–2. The prognostic impact on OS was disease-specific: grade 3–4 early T-ICAHT predicted inferior 1-year OS in T-ALL/NHL (0% vs. 100%, $P=0.004$) but not in B-ALL/NHL (94% vs. 92%, $P=0.50$). In contrast, early T-ICAHT was consistently associated with inferior DFS in both B-ALL/NHL (45% vs. 72%, $P=0.039$) and T-ALL/NHL (0% vs. 73%, $P=0.053$).
CAR-HT classified 64.4% of patients as high risk, and ALL-HT identified 50.5% of ALL/NHL patients as high risk. CAR-HT effectively discriminated patients at high risk for grade 3–4 early T-ICAHT (high risk: grade 3–4, 64% vs. grade 0–2, 36%; low risk: grade 3–4, 12% vs. grade 0–2, 88%; $P<0.001$), with consistent performance in B-ALL/NHL ($P<0.001$) and T-ALL/NHL ($P=0.031$). ALL-HT similarly distinguished high- and low-risk early T-ICAHT in ALL/NHL (high risk: grade 3–4, 84% vs. grade 0–2, 16%; low risk: grade 3–4, 24% vs. grade 0–2, 76%; $P<0.001$), with consistent performance in B-ALL/NHL ($P<0.001$) and T-

ALL/NHL (*P*=0.019). Both eIPM_pre and eIPM_post were strongly associated with grade 3–4 early T-ICAHT in the overall cohort (*P*<0.001), in B-ALL/NHL (*P*<0.001), and in MM (eIPM_pre, *P*=0.010; eIPM_post, *P*=0.006), but showed reduced discriminatory ability in T-ALL/NHL (eIPM_pre, *P*=0.029; eIPM_post, *P*=0.057).
ROC analysis for grade 3-4 early T-ICAHT demonstrated comparable predictive performance of CAR-HT, eIPM_pre, and eIPM_post in MM and T-ALL/NHL. In B-ALL/NHL, ALL-HT showed higher discrimination than CAR-HT (AUC 0.882 vs. 0.817), with a significant difference by DeLong's test (P=0.046).

Characteristics		Characteristics		ICAHT	B-ALL/NHL (N=73)	T-ALL/NHL (N=28)	MM (N=34)	Avg. PLT Infusion Units
Age, Median (Range)	41 (6-83)	Prior allo-HSCT, yes, n(%)	49 (36.3%)	N-ICAHT 1, n (%)	15(20.6%)	7 (25.0%)	19 (55.9%)	0.2
Sex, Male, n(%)	80 (59.3%)	Prior allo-HSCT, no, n(%)	86 (63.7%)	N-ICAHT 2, n(%)	12 (16.4%)	5 (17.9%)	5 (14.7%)	0.7
Sex, Female, n(%)	55 (40.7%)	Median BM blasts Before FC	Median (Interquartile range)	N-ICAHT 3, n (%)	26 (35.6%)	11 (39.2%)	10 (29.4%)	3.9
Disease and Target, n(%)		B-ALL/NHL	25.0%(6.0%-65.0%)	N-ICAHT 4, n (%)	20 (27.4%)	5 (17.9%)	0 (0.0%)	13.4
B-ALL/NHL, CD19 or CD19-22	73(54.1%)	T-ALL/NHL	7.0% (0%-55.5%)	T-ICAHT 0, n(%)	20 (27.4%)	5 (17.9%)	17 (50.0%)	0
T-ALL/NHL, CD7	28 (20.7%)	CRS 0-1, n(%)	81（60.0%)	T-ICAHT 1,	5 (6.9%)	2 (7.1%)	6 (17.6%)	0.1

				n (%)				
MM, BCMA	34 (25.2%)	CRS 2+, n(%)	54（40.0%)	T-ICAHT 2, n (%)	9 (12.3%)	5 (17.9 %)	4 (11.8 %)	0.1
Co-stimulatory CD28, n(%)	13 (9.6%)	ICANS 0-1, n(%)	128 (94.8%)	T-ICAHT 3, n (%)	17 (23.3%)	10 (35.7 %)	4 (11.8 %)	2.7
Co-stimulatory 4-1BB, n(%)	122 (90.4%)	ICANS 2+, n(%)	7 (5.2%)	T-ICAHT 4, n (%)	22 (30.1%)	6 (21.4 %)	3 (8.8%)	13.4



Conclusions: CAR-HT, ALL-HT, and eIPM effectively identify patients at higher risk of post-infusion thrombocytopenia within 30 days after CAR-T therapy. In ALL with predominant bone marrow blast involvement, ALL-HT may provide superior predictive performance.

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A060

IMPACT OF THIOTEPA-BUSULFAN CONDITIONING ON CMML TRANSPLANT SCORE PERFORMANCE

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Background: Allogeneic stem cell transplantation (allo-SCT) remains the only curative therapy for patients with CMML. Given the high transplant-related mortality and morbidity (Kröger et al., 2002), risk scores are essential to identify patients who most likely benefit. The CMML transplant score, developed by Gagelmann et al., incorporates ASXL1/NRAS mutations, bone marrow blasts >2%, and comorbidity index.
While predictive of overall survival (OS) and non-relapse mortality (NRM), the effect of conditioning regimen on score performance remains unknown. Recently, thiotepa–busulfan (TB) conditioning has been associated with markedly reduced relapse rates and improved Survival in CMML, (Massoud et al., 2024), raising the question whether intensified disease control may alter the prognostic relevance of established transplant risk scores.

Methods: A retrospective cohort analysis was performed including 54 consecutive patients who underwent allo-SCT for CMML between 2019 and October 2025 at the University Medical Center Hamburg-Eppendorf. The CMML transplant score was applied to all patients.
Primary analysis evaluated score discrimination in the entire cohort. Secondary analysis focused on the TB conditioning subgroup (n=30) to assess whether this conditioning modifies score prognostic value. The CMML transplant score was calculated according to Gagelmann et al. For analysis, we dichotomized at ≥5 points, representing the most relevant prognostic inflection in the original model (transition from scores 0–4 to 5–7). Patients were classified as lower-risk (0–4) or higher-risk (≥5).

Results: In the overall cohort (median age 66 years, 74% male), the CMML transplant score retained prognostic discrimination for OS (p=0.02) and PFS (p=0.04). In the TB conditioning subgroup (n=30, 58% of total cohort) no patient relapsed regardless of risk score However, OS varied by score group: at 1 year 100% for lower-risk (n=9) and 51% for higher-risk n=21) patients, p = 0.11. Though not reaching statistical significance, probably due to

sample size, the numerical differences indicate the CMML transplant score may retain its prognostic performance in CMML patients conditioned using TB. Survival differences were driven entirely by NRM rather than disease progression.
The most frequent main cause of death of TB patients was septic shock (7), followed by unknown (2), cardiac arrest (1), respiratory (1) and multiorgan failure (1). Comorbidity burden may contribute substantially, as 83% of deceased patients (10 of 12) had impaired lung function pre-transplant (DLCO < 65%), compared with 50% in the overall TB group and 48% in the full cohort.

Table Patients donor and transplant Characteristics

Variable	Overall cohort (N = 54)	TB subgroup (N = 30)
CPSS-Mol risk group Low	0 (0%)	0 (0%)
CPSS-Mol risk group Intermediate-1	10 (19%)	6 (20%)
CPSS-Mol risk group Intermediate-2	24 (44%)	13 (43%)
CPSS-Mol risk group High	18 (33%)	10 (33%)
CPSS-Mol risk group Very high	2 (4%)	1 (3%)
Transplant year, median (range)	2022 (2019-2025)	2024 (2019-2025)
MRD	7 (13%)	4 (13%)
Haplo	8 (15%)	0 (0%)
MUD	35 (65%)	24 (80%)
MMUD	4 (7%)	2 (7%)
Conditioning Thiotepa-busulfan (TB)	30 (56%)	30 (100%)
Conditioning Fludarabine-busulfan (FB)	7 (13%)	0 (0%)
Conditioning Treosulfan-fludarabine	12 (22%)	0 (0%)
Other	5 (9%)	0 (0%)
Male	40 (74%)	23 (77%)
Female	14 (26%)	7 (23%)

Patient age, years, median (range)	66 (41-80)	64 (42-76)
CMV Negative	20 (37%)	15 (50%)
CMV Positive	34 (63%)	15 (50%)

Conclusions: TB conditioning eliminates relapse risk across all risk groups of the CMML transplant score, validating our previous comparative study findings. While this intensive approach achieves superior disease control, the risk-benefit equation shifts from disease progression to treatment-related toxicity. The CMML Transplant score however appears to retain its prognostic performance.

Disclosure: Nothing to declare.

A061

TRUNCATING GENE ALTERATIONS AND PROMOTER HYPERMETHYLATION DRIVE CD7⁻ RELAPSE AFTER CD7 CAR-T THERAPY: A PATIENT-INFORMED MECHANISM STUDY

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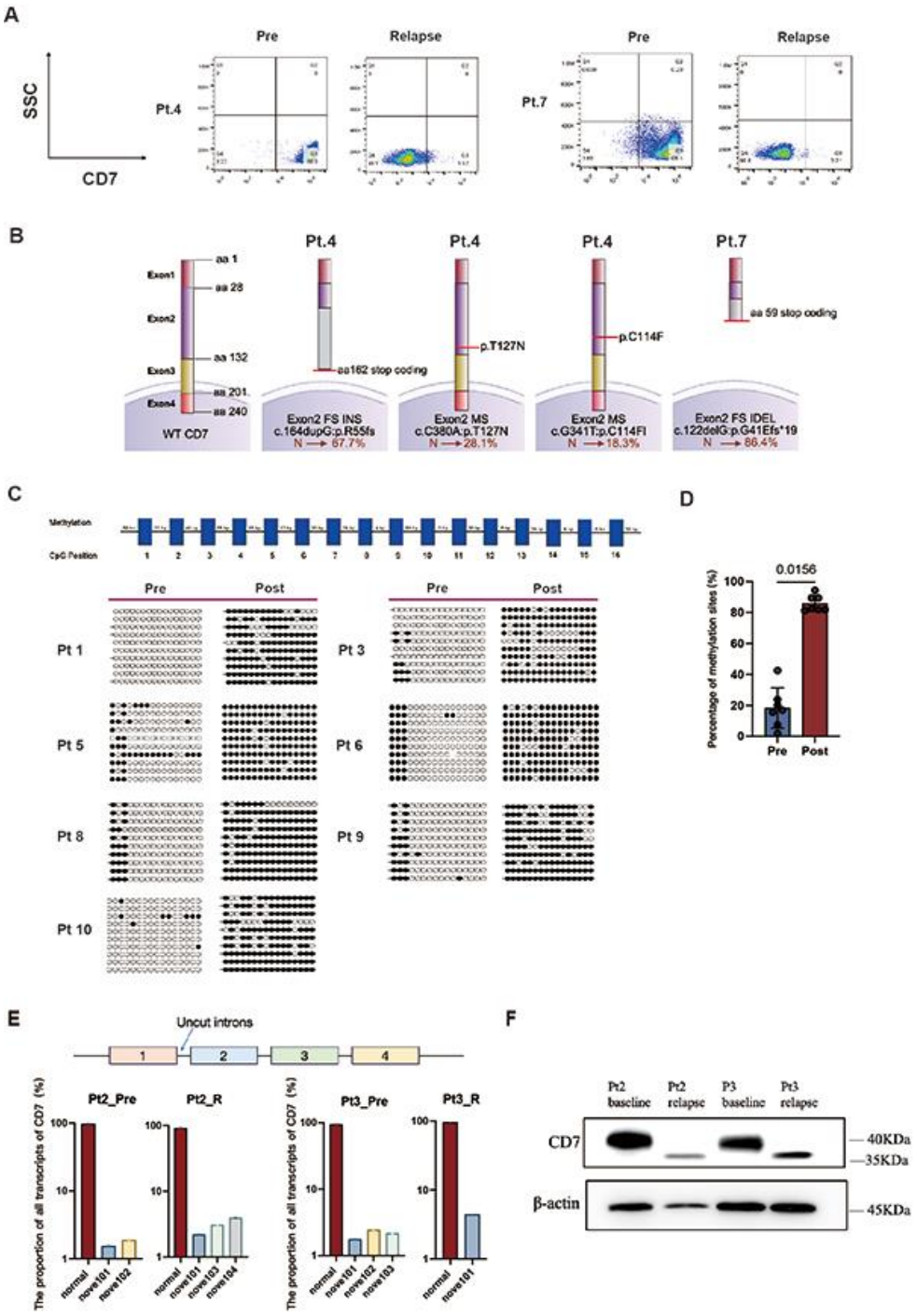
Background: The CD7 antigen, emerging as a novel target for chimeric antigen receptor (CAR) T-cell therapy, particularly as a novel strategy to bridge to allogeneic hematopoietic stem-cell transplantation (HSCT). However, antigen loss-mediated relapse remains a major challenge. Recent clinical data indicate that 30%-51.7% of relapses result from CD7 protein loss [Tan Y et al., J Hematol Oncol. 2023] [Pan J et al., J Hematol Oncol 2021]. The mechanisms underlying the antigen loss remain to be further explored.

Methods: Herein, we analyzed paired specimens collected at screening (pre-treatment) and clinical relapse from 10 patients with T-cell hematologic malignancies (5 T-ALL, 3 T-LBL, 2 HSTL) who experienced CD7-negative relapse ($CD7^-$/relapse). $CD7^+$ tumor cells (pre-treatment) and $CD7^-$ tumor cells (relapse) were prospectively isolated by flow cytometry sorting. Whole-exome sequencing (WES) was conducted to identify acquired somatic mutations, while bisulfite sequencing PCR (BSP) was used to evaluate the methylation status of the *CD7* promoter region spanning from −300 to +200 bp. (ClinicalTrials.gov identifiers: NCT04599556, NCT04538599, and NCT05716113).In addition, we focused on two patients with sufficient samples to further explore alternatively spliced CD7 transcripts and protein sequencing analysis.

Results: In two patients (Pt4 and Pt7), acquired truncating mutations in *CD7* exon 2 were identified as the dominant resistance mechanism. These mutations (frameshift insertion exon2:c.164dupG:p.R55fs in Pt4 and deletion exon2:c.122delG:p.G41Efs*19 in Pt7) were predicted to yield nonfunctional, truncated CD7 proteins lacking the transmembrane domain,

considering either biallelic mutations or upregulation of the mutation copy. Additionally, Pt4 harbored subclonal missense single nucleotide variants (exon2:c.C380A:p.T127N, 28.1%; exon2:c.G341T:p.C114F, 18.3%), indicating clonal heterogeneity.
Notably, non-truncating mutations and mild CD7 (-300 to +200 bp) methylation were concurrently observed in Pt2. A missense mutation (exon2:c.G124C:p.A42P [24.2% VAF]) and an in-frame deletion (c.271_273del:p.91_91del [26.7% VAF]) within the extracellular domain were detected, potentially impairing epitope recognition. These findings suggest a combination of deleterious mutations and ensuing epigenetic silencing.
No genetic alterations were detected in the remaining seven patients. However, analysis of these relapsed samples revealed hypermethylation within a moderate CpG island located in the *CD7* promoter region (-300 to +200 bp). In vitro, azacitidine treatment restored *CD7* mRNA and intracellular protein expression in hypermethylated CD7-negative T-ALL cell lines (Hut78 and H9), supporting methylation-driven transcriptional silencing as a resistance mechanism. Western blot analysis of $CD7^{-}$ tumor cells from Pt3 and Pt4 revealed the presence of low-molecular-weight CD7 isoforms, which were confirmed by protein sequencing to identify N-terminally truncated CD7. Additionally, there has been no discovery of alternative splicing that forms a dominant advantage.



(A) Flow cytometric analysis of CD7 surface expression at pretreatment and relapse in Pt4 and Pt7.
(B) Acquired mutations in CD7 were detected in relapsed samples from Pt4 and Pt7.
These mutations are predicted to result in a truncated protein lacking the transmembrane domain.
(C) Methylation status of the CD7 promoter region. Filled circles represent methylated CpG sites.
(D) Methylation levels were significantly elevated in relapsed samples (10 clones) compared to pretreatment samples (10 clones).(E) Proportion of different splice variants of CD7 transcripts
(F) Western blot analysis reveals a lower molecular weight band in the relapsed sample from Pt2 and Pt3.

Conclusions: Our study elucidates that the dominant mechanism underlying $CD7^-$ relapse is methylation-driven epigenetic silencing under immune pressure. Some patients may develop truncating mutations and rapidly gain clonal advantage and progress.

Clinical Trial Registry: ClinicalTrials.gov identifiers: NCT04599556, NCT04538599, and NCT05716113.

Disclosure: The authors have no conflicts of interest to disclose.

A062

BU/CY/FLU-ATG VERSUS BU/CY-ATG CONDITIONING REGIMEN IN HAPLOIDENTICAL CELL TRANSPLANTATION FOR SEVERE ACQUIRED APLASTIC ANEMIA

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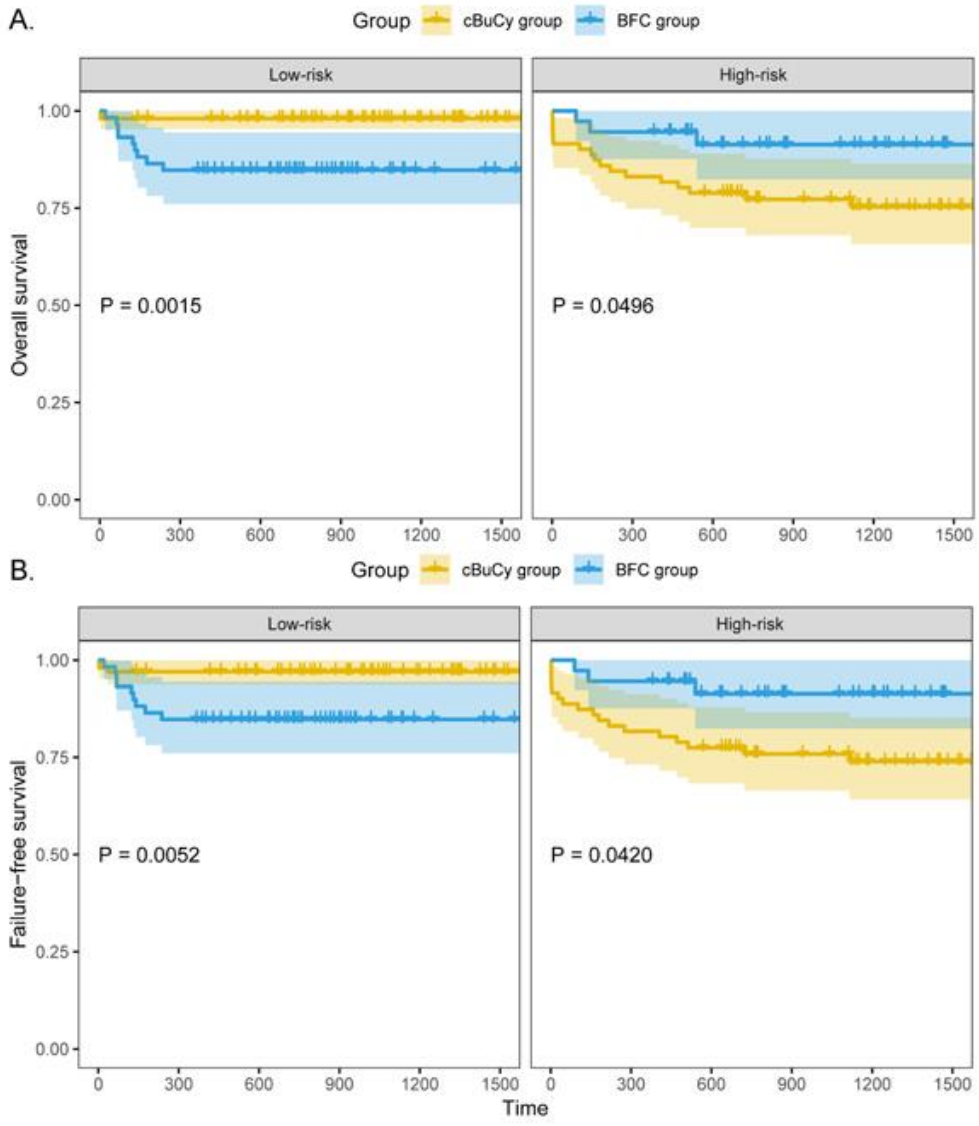
Background: The optimal conditioning regimen for haploidentical hematopoietic cell transplantation (haplo-HCT) in patients with severe acquired aplastic anemia (SAA) remains undefined. In G-CSF/ATG-based haplo-HCT, the conventional busulfan 6.4 mg/kg and cyclophosphamide 200 mg/kg (cBuCy) conditioning regimen and fludarabine (Flu)-based regimens are widely adopted. Scattered reports have showed promising outcomes using the two regimens. However, comparisons between cBuCy and Flu-based conditioning regimens are limited.

Methods: In this study, we tried to comprehensively compare transplant outcomes following haplo-HCT with cBuCy regimen and a Flu-based regimen, comprising busulfan 6.4 mg/kg, Flu 150 mg/m^2, and cyclophosphamide 100 mg/kg (BFC regimen). Patients undergoing haplo-HCT with the cBuCy regimen and the reduced-toxicity BFC regimen between 2012 and 2021 at PKUPH were reviewed. To minimize the impact of selection bias and confounding factors, we performed a propensity score matching (PSM) analysis. Patient age, sex, the interval between SAA diagnosis and HCT, and donor-recipient ABO matching group were included in the propensity score model. Finally, this study retrospectively compared two conditioning regimens (cBuCy cohort, n = 172; and BFC cohort, n = 96] in SAA patients who underwent haplo-HCT for SAA.

Results: The BFC and cBuCy regimens achieved comparable 4-year overall survival (OS; 87.3% vs. 88.5%, P = 0.634) and failure-free survival (FFS; 87.3% vs. 87.4%, P = 0.834). However, BFC regimen led to increased Epstein-Barr virus reactivation (P < 0.001) and post-transplant severe pneumonia (P = 0.004 at 1 year). Multivariable analysis identified poorer performance status and a higher Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) as adverse factors for survival following haplo-HCT. Compared to those without any risk factor, patients with 1 factor (P = 0.016 for OS, and 0.014 for FFS) or 2 factors (P < 0.001 for OS and FFS) had increased risk of worse survival. Patients were then divided into

low-risk (no risk factor) and high-risk (1-2 factors) groups. Compared to cBuCy regimen, BFC regimen achieved better OS (P = 0.0496) and FFS (P = 0.042) in high-risk patients, while survival rates in the low-risk subgroup were relatively lower (P = 0.0015 for OS and 0.0052 for FFS).



Conclusions: Conclusively, we found both the BFC and cBuCy regimens were feasible for conditioning SAA patients undergoing haplo-HCT. Patients with poorer performance status and higher HCT-CI may benefit from the Flu-based conditioning, while cBuCy conditioning regimen can result in favorable outcomes in low-risk patients.

Disclosure: Nothing to declare.

A063

THE CAST STRATEGY (CAR-T/ASCT/SEQUENTIAL CAR-T) WITH LOW-DOSE FRACTIONATED RT BRIDGING IN HEAVILY PRE-TREATED R/R CNSL ：A PROOF-OF-CONCEPT STUDY

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Background: The prognosis for patients with ultra-refractory Central Nervous System Lymphoma (CNSL), particularly those with high-risk features like TP53 mutations, is dismal. These patients exhibit profound resistance to multiple lines of therapy, including BTK inhibitors, presenting a critical unmet medical need. We hypothesized that a multi-modal, synergistic platform was required to overcome this therapeutic resistance. We therefore designed and evaluated a novel protocol: CAR-T, Autologous Stem Cell Transplant, and Sequential CAR-T (CAST), bridged by low-dose radiotherapy.

Methods: Between March 2024 and June 2025, five heavily pretreated adults (median age 46; median 4 prior lines) with rapidly progressive, chemorefractory R/R CNSL (4 PCNSL, 1 SCNSL; 3/5 TP53-mutated) were enrolled. The CAST protocol comprised four distinct phases: 1) Low-dose radiotherapy bridge (7.5-10.5 Gy WBRT/CSI) for cytoreduction and to potentially enhance CAR-T trafficking. 2) A first infusion of CD19 CAR-T cells (2×10^6/kg). 3) 1-3 months later, high-dose chemotherapy (BEAM or TBC) followed by autologous stem cell transplant (ASCT; median 2.8×10^6 CD34+/kg). 4) A second, non-overlapping CAR-T infusion (CD22 or CD20; 2×10^6/kg) administered at day +3 to +5 post-ASCT to target potential antigen escape. Primary endpoints included overall response (PET/MRI), minimal residual disease in CSF (MRD, by flow cytometry), safety (CRS/ICANS), and survival.

Figure 1. Schematic of the CAST "Sandwich" Strategy (CAR-T/ASCT/Sequential CAR–T) with Low–Dose WBRT/CSI Bridging for Ultra-Refractory R/R CNSL

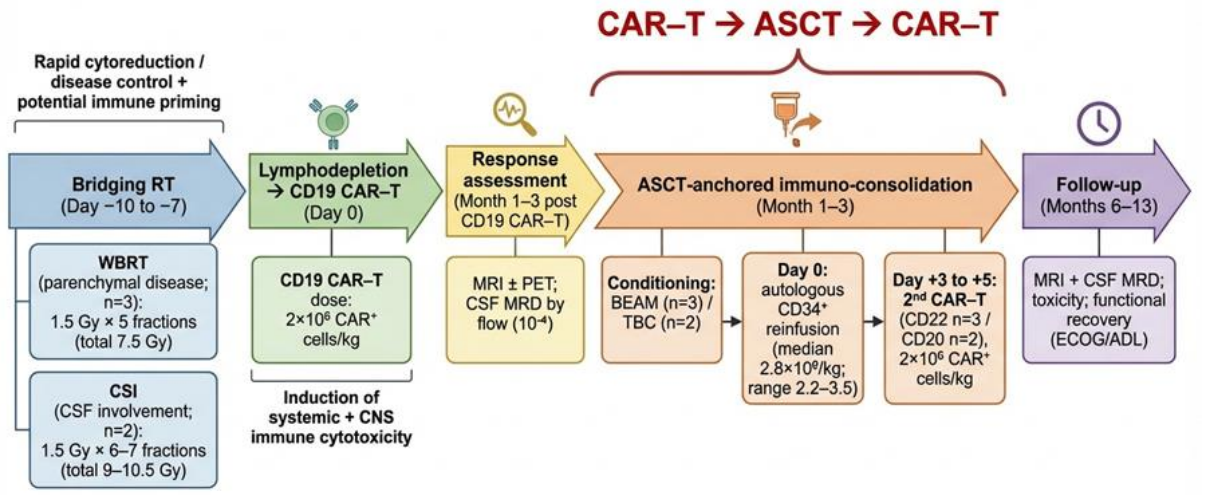

Figure 1. Schematic of the CAST "Sandwich" Strategy (CAR-T/ASCT/Sequential CAR-T) with Low-Dose WBRT/CSI Bridging for Ultra-Refractory R/R CNSL

Results: All five patients successfully completed the entire CAST protocol. Following the initial CD19 CAR-T, 3 patients achieved CR and 2 achieved PR. Significantly, after completion of the full protocol, all 5 patients (100%) converted to and maintained a deep complete remission, confirmed by both imaging and sustained CSF MRD negativity. With a median follow-up of 8 months (range 6-13), all patients remain in continuous remission with no disease progression or deaths observed. The intensive regimen was notably well-tolerated. All cytokine release syndrome (CRS) events were Grade 1-2; no Grade ≥3 CRS or ICANS occurred, and there was no treatment-related mortality. Delayed thrombocytopenia, observed in 3 patients, was effectively managed without clinical sequelae. At last follow-up, all patients maintained an excellent performance status (ECOG 0-1).

Conclusions: This initial study demonstrates that the "CAST" strategy is a feasible, safe, and highly effective approach, inducing 100% deep and durable molecular remissions in an ultra-high-risk CNSL population with no other viable options. By integrating radiation biology, transplant medicine, and dual-target cellular immunotherapy into a unified, mechanistically rational platform, this strategy offers a potential curative pathway for these patients. These promising results provide a strong rationale for an expanded, multicenter Phase II trial to validate these findings.

Clinical Trial Registry: ChiCTR1900025419(https://www.chictr.org.cn)

Disclosure: Nothing to declare

A064

L-IPM: A NOVEL SCORE SYSTEM FOR PREDICTING LATE IMMUNE EFFECTOR CELL-ASSOCIATED HEMATOTOXICITY (ICAHT) AFTER CAR-T THERAPY AND COMPARISON WITH CAR-HEMATOTOX, ALL-HEMATOTOX, AND E-IPM

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Background: Immune effector cell–associated hematotoxicity (ICAHT) profoundly affects long-term outcomes after CAR-T therapy. According to the EHA/EBMT consensus (Blood, 2023), ICAHT is classified as early (day 0–30) or late (≥day 30) neutropenia-associated ICAHT (N-ICAHT). Although CAR-HEMATOTOX, ALL-HEMATOTOX, and eIPM were developed primarily to predict early ICAHT, predictive tools for late N-ICAHT remain limited. This study aimed to develop an effective model to predict late N-ICAHT using routinely available variables.

Methods: A consecutive cohort of 135 patients with hematologic malignancies who received either commercial CAR-T products, including Brexu-cel or investigational CD19, BCMA or CD7 targeted CAR-T between 2022 and 2025 was enrolled. Multivariable logistic regression was used to develop a point-based risk score (Late Inflammatory Prognostic Model Score, L-IPM_{score}), and LASSO regression was applied for machine learning–based model construction (L-IPM_{index}) to predict late N-ICAHT. Model discrimination was assessed using ROC and the DeLong test.
Candidate variables included age, sex, diagnosis, prior HSCT, CRS grade, ICANS grade, IEC-HS, early N-ICAHT grade, and log-transformed peak ferritin, IL-6, and D-dimer levels within 0–30 days. Grade 3–4 late N-ICAHT was used as the dependent variable. Univariate logistic regression was performed, and variables with $p<0.10$ were entered into LASSO regression. The optimal lambda was selected at $\lambda=0.033$ by cross-validation.

Results: The **L-IPM_{score}** was based on four variables assessed within day 0–30 after CAR-T infusion—peak D-dimer, IL-6, ferritin, and early N-ICAHT grade. One point was assigned for each variable exceeding the cutoff (D-dimer ≥5,000 ng/mL, IL-6 ≥168 pg/mL, ferritin ≥2,000 ng/mL, or early N-ICAHT grade 3–4), yielding a total score of 0–4. Patients were categorized as low risk (0–1) or high risk (≥2) for late N-ICAHT by **L-IPM_{score}**. The fitted LASSO model was defined as: 0.427 × (early N-ICAHT Grade) + 0.155 × ln(peak IL-6) + 0.001 × ln(peak ferritin) − 2.330, and was designated as the **L-IPM_{index}**.
Low **L-IPM_{score}** patients (0–1, n=58) were predominantly grade 0–2 late N-ICAHT(91.5%) with only 8.5% grade 3-4 events, whereas high **L-IPM_{score}** patients (≥2, n=77) were enriched for severe toxicity, with grade 3–4 late N-ICAHT in 64.9%. Using the median **L-IPM_{index}** of 0.4185 as the cut-off, low-risk patients (n=67) were predominantly distributed in lower toxicity grades, with 77.7% experiencing grade 0–2 late N-ICAHT. In contrast, high **L-IPM_{index}** patients (n=68) showed a clear shift toward severe toxicity, with 58.8% developing

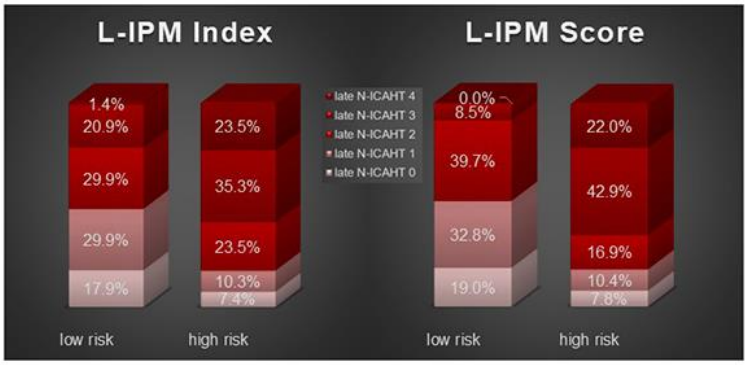
grade 3–4 late N-ICAHT.
ROC analyses for grade 3–4 late N-ICAHT demonstrated incremental improvement in predictive performance across models. CAR-HEMATOTOX showed modest discrimination (AUC = 0.673, 95% CI 0.583–0.764), comparable to eIPMpre (AUC = 0.689, 95% CI 0.597–0.781). The **L-IPM$_{index}$** exhibited improved accuracy (AUC = 0.728, 95% CI 0.643–0.814). Notably, the **L-IPM$_{score}$** achieved the highest discriminatory ability (AUC = 0.887, 95% CI 0.835–0.938); DeLong's test confirmed significant differences between the **L-IPM$_{score}$** and all other scoring systems (all $p < 0.001$), indicating superior performance in identifying late N-ICAHT.

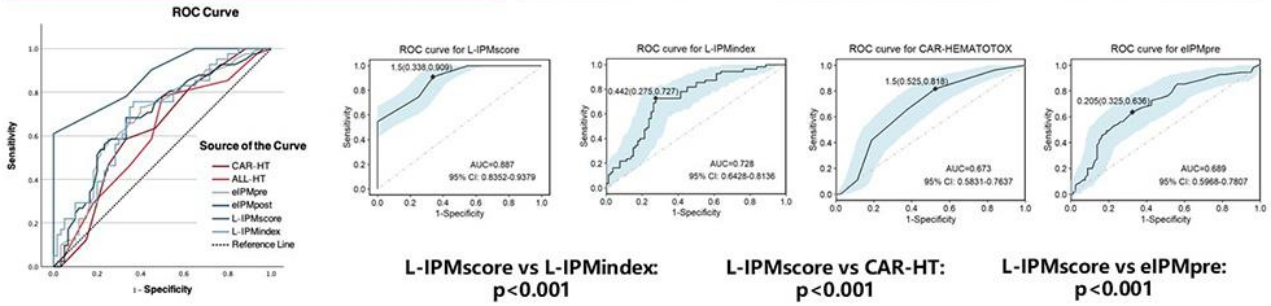
Characteristics	**Whole Cohort (n=135)**	**Late N-ICAHT 0-2(n=80)**	**Late N-ICAHT 3-4(n=55)**	***P value***	**Characteristics**	**Whole Cohort (n=135)**	**Late N-ICAHT 0-2(n=80)**	**Late N-ICAHT 3-4(n=55)**	***P value***
Age, median (IQR)	41(24.5-55.0)	41.5(24.0-59.0)	41(25.5-52.5)	0.507	**Early N-ICAHT, n(%)**				
B-ALL/NHL, n(%)	73	48	25	0.111	1	41(30.4%)	34(42.5%)	7 (12.7%)	**<0.001**
T-ALL/NHL, n(%)	28	12	16		2	22(16.3%)	14 (17.5%)	8 (14.5%)	
MM,n(%)	34	20	14		3	47(34.8%)	23 (28.8%)	24 (43.6%)	
Co-stimulatory n(CD28/4-1BB)	13/122	8/72	5/50	0.860	4	25(18.5%)	9(11.3%)	16 (29.1%)	
Prior HSCT, Yes n(%)	49	28	21	0.706	**CRS 0-1,n(%)**	81(60.0%)	50 (62.5%)	31 (56.4%)	0.475
Median BM blasts%					CRS 2+,n(%)	54(40.0%)	30 (37.5%)	24 (43.6%)	

Before FC m(IQR)									
B-ALL/NHL	25.00 (6.0-65.0)	21.00 (6.0-64.0)	50.0 (6.0-74.5)	0.317	ICANS 0-1, n(%)	128(94.8%)	77(96.3%)	51(92.7%)	0.609
T-ALL/NHL	7.00 (0.0-55.5)	6.00 (0.0-26.3)	10.5 (0.0-60.8)	0.450	ICANS 2+, n(%)	7(5.2%)	3(3.8%)	4 (7.3%)	

Features 0-30 days	0 point	1 point
D-dimer peak	<5000ng/mL	≥5000ng/mL
IL-6 peak	<168pg/mL	≥168pg/mL
Ferritin peak	<2000ng/mL	≥2000ng/mL
Early N-ICAHT	1-2	3-4
L-IPM Score	Low Risk	High Risk
Total Points	0-1	≥2

L-IPM Index= 0.427×(early N-ICAHT)+0.155×ln(peak IL-6)+0.001×ln(peak Ferritin)-2.330; 0.4185 as cutoff





Conclusions: The L-IPM system may serve as a practical and user-friendly tool for predicting late N-ICAHT in CAR-T recipients.

Disclosure: ML has received honoraria for lectures from Novartis, BeOne, Takeda, and Fosun Kite

A065

IMPACT OF TREATMENT SEQUENCE OF GLOFITAMAB AND CAR-T THERAPY ON EFFICACY, SURVIVAL, AND TARGET ANTIGEN EXPRESSION IN RELAPSED/REFRACTORY B-NHL

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Background: Both CAR-T cell therapy and CD20×CD3 bispecific antibodies (bsAbs) have demonstrated efficacy in relapsed/refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL). As these immunotherapies are increasingly used in parallel, some patients with suboptimal response or relapse after one therapy may still benefit from the alternative modality. This study investigates how the sequence of CAR-T and bsAb administration influences treatment response, survival, and antigen expression in R/R B-NHL.

Methods: We retrospectively analyzed R/R B-NHL patients treated at Beijing Gaobo Hospital from October 2023 to October 2025. Patients who received bsAb either before CAR-T as bridging/first-line therapy or after CAR-T progression were included. According to treatment sequence, patients were divided into two groups: **Group A (n=19)** received CAR-T first, then bsAb; **Group B (n=11)** received bsAb first, then CAR-T. Outcomes analyzed included objective response rate (ORR), complete response rate (CRR), progression-free survival (PFS), overall survival (OS), and target antigen expression post-treatment.

Results: Among 30 patients, 86.6% were male; median age was 44 years (range 24–75), and 93.3% were stage III–IV. Histologies included DLBCL (n=21), Burkitt lymphoma (n=5), CNSL (n=2), and others (n=2).
Group A (CAR-T → bsAb) had a median follow-up of 18.1 months, with ORR 68.4% (13/19), CRR 42.1% (8/19), median PFS 19.4 months, and median OS 32.8 months.
Group B (bsAb → CAR-T) had a median follow-up of 4.1 months, with ORR 54.5% (6/11), CRR 27.3% (3/11), median PFS 4.4 months, and median OS 8.5 months.
Among patients with paired biopsies, CD19 loss after CAR-T occurred in 20% (2/10), while CD20 loss after bsAb occurred in 100% (5/5).
Prior response to the first immunotherapy significantly affected ORR ($p<0.05$). Patients who responded to the initial therapy achieved an ORR of 86.7% (13/15) after sequential treatment, compared with 40.0% (6/15) in non-responders. Similarly, prior responders showed longer PFS and OS (median PFS 31.1 vs 5.4 months, $p=0.029$; median OS 32.9 vs 7.4 months, $p=0.027$).

Description of CD19/CD20 (immunohistochemistry) status in the two patient sets according to the timing of the biopsy

Characteristic	Group A (CAR-T → bsAb)		Group B (bsAb → CAR-T)	
CD19 status before CAR T-cell Negative Positive	0 17 0 2	0.0% 89.5% 0.0% 10.5%	0 6 5 0	0.0% 54.5% 45.5% 0.0%

Description of CD19/CD20 (immunohistochemistry) status in the two patient sets according to the timing of the biopsy

Not tested Missing				
CD19 status after CAR T-cell Negative Positive Not tested Missing	 1 8 8 2	 5.3% 42.1% 42.1% 10.5%	 1 0 10 0	 9.1% 0.0% 90.9% 0.0%
CD20 status before CD3/CD20 BsAb Negative Positive Not tested Missing	 1 15 1 2	 5.3% 78.9% 5.3% 10.5%	 1 10 0 0	 9.1% 90.9% 0.0% 0.0%
CD20 status after CD3/CD20 BsAb Negative Positive Not tested Missing	 3 0 14 2	 15.8% 0.0% 73.7% 10.5%	 2 0 9 0	 18.2% 0.0% 81.8% 0.0%

Conclusions: The sequence of immunotherapy may influence survival, with CAR-T followed by bsAb potentially providing longer PFS. Bispecific antibody therapy is associated with higher rates of CD20 antigen loss compared to CAR-T–induced CD19 loss, which may contribute to resistance. Patients who initially respond to one immunotherapy may still benefit from the alternative modality upon relapse, supporting sequential treatment strategies in R/R B-NHL.

Disclosure: Nothing Disclosure

A066

CD19 CAR-T THERAPY IN TRANSFORMED FOLLICULAR LYMPHOMA: A REAL-WORLD COHORT OF 43 PATIENTS

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Background: Transformed follicular lymphoma (tFL) carries a poor prognosis, particularly after multiple lines of therapy. Although CD19-directed CAR-T therapy has improved outcomes in relapsed/refractory (r/r) large B-cell lymphoma, real-world evidence in tFL—especially data incorporating detailed molecular features—remains limited.

Methods: We retrospectively analyzed 43 pathologically confirmed tFL patients treated with CD19 CAR-T therapy at our center between 2019 and 2025. Baseline characteristics, prior therapies, bridging regimens, safety, treatment response, and molecular findings (IHC/FISH/NGS) were collected. Overall survival (OS) and progression-free survival (PFS) were estimated using the Kaplan–Meier method.

Results: **Baseline characteristics:** The median age was 50 years (range, 26–68), and 53% (23/43) were male. ECOG ≥2 was observed in 30% (13/43). Fourteen patients (33%) were primary refractory, and the median number of prior therapy lines was 3 (range, 2–7).
Bridging therapy: Forty-one patients (41/43) required bridging treatment prior to infusion, with a median of 1 cycle (range, 1–4). Venetoclax-based multidrug regimens were commonly applied; 30/43 received BCL-2 inhibitors and 18/43 received BTK inhibitors.
Molecular features: After transformation, 12/43 showed double-expressor phenotype by IHC. Among 26 patients with FISH testing, 3 had double/triple-hit abnormalities; excluding these, BCL2 rearrangements were present in 8/23. NGS was available for 36/43 patients, with TP53 mutations detected in 19/36.
Median time from FL diagnosis to histologic transformation was 1.83 years (range, 0–13.58). Median MYC expression after transformation was 30% (range, negative–80%), and median Ki-67 was 70% (10%–90%).
Safety: Incidence of CRS of any grade and ≥grade 3 was 34/43 and 5/43, respectively. ICANS occurred in 5/43 patients, with grade ≥3 in 4/43.
Efficacy: At 3 months, ORR and CRR were 56% (24/43) and 47% (20/43), respectively. With a median follow-up of 37.87 months (95% CI, −16.37 to 59.37), 1-year PFS and OS were 45.4% and 66.9%, and 3-year PFS and OS were 41.7% and 63.2%.
Subgroup analyses: When survival was calculated from the date of histologic transformation, 3-year and 5-year OS rates were both 64.7%.
One-year OS for patients with versus without TP53 mutations was 56.4% vs. 76.5% (p=0.433).
One-year OS for patients with versus without BCL2 rearrangement was 45.5% vs. 73.3% (p=0.235).

Conclusions: Despite modest early ORR/CRR, CD19 CAR-T therapy yielded durable long-term survival in this real-world tFL cohort, with a 3-year OS of 63.2%, comparable to—if not exceeding—large international datasets such as CIBMTR. CD19 CAR-T remains an important therapeutic option for heavily pretreated tFL.

Disclosure: Nothing to disclosure

A067

ANTIBIOTIC TIMING AND IMPACT ON SURVIVAL OUTCOMES IN ANTI-CD19 AND ANTI-BCMA CAR-T CELL THERAPY

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Background: Patients undergoing chimeric antigen receptor T-cell (CAR-T) therapy are often treated with antibiotics in the post CAR-T period due to fevers in the setting of cytokine release syndrome. Prior work has suggested that broad spectrum antibiotics in post- and pre-CAR-T period may be deleterious to efficacy and overall survival (OS) in patients with B-cell malignancies. Particularly, PIM (piperacillin-tazobactam, imipenem, meropenem) are implicated with poor outcomes. This relates to dysregulation of gut microbiome and possible hematopoietic impairment. We aimed to investigate the effect of pre- and post-CAR-T antibiotics in patients receiving anti-CD19 and anti-BCMA CAR-T therapy.

Methods: This is a single-center retrospective study of adults with multiple myeloma, B-cell lymphoma, and acute lymphoblastic leukemia treated with CD19 and BCMA targeting CAR-T therapy at our center between April 2017 and August 2024. CD19 products included lisocabtagene maraleucel, tisagenlecleucel, brexucabtagene autoleucel, and axicabtagene ciloleucel. BCMA products included idecabtagene vicleucel and ciltacabtagene autoleucel. Recipients of experimental CAR-T products included as "other". We collected data on pre-CAR-T therapy antibiotic exposure (defined as antibiotics received 30 days pre-CAR-T infusion), post-CAR-T therapy exposure (antibiotics received on day of infusion up to 30 days after). Primary outcomes were progression free survival (PFS) and OS. Secondary outcome was progression at first PET-CT scan. We constructed Cox regression models to model survival outcomes adjusted for age, prior lines of therapy, and infection rate.

Results: Of 329 patients, 96 received anti-CD19 CAR-T, 198 received anti-BCMA CAR-T and 35 were enrolled in trials for experimental products. The median age was 61 with 60% male. Patients receiving anti-CD19 CAR-T were more likely to receive pre-CAR-T antibiotics than patients receiving anti-BCMA CAR-T (17.7% vs. 7.5%, p-value 0.016). Median duration of pre-CAR-T antibiotic was 7 days for CD19 and 8 days for BCMA CAR-T. Majority of patients

received antibiotics post-CAR-T, 83% CD19 patients, 57% BCMA patients, and 66% other products. Patients receiving CD19 were on longer duration of post-CAR-T antibiotics (defined as >5 days versus ≤5 days) than BCMA patients (62.5% vs 42.4%, p-value 0.0026). Median duration of post-CAR-T antibiotics was 7 days for CD19 and 6 days for BCMA. Post CAR-T antibiotics were largely fourth generation cephalosporins such as cefepime, with vancomycin. Few patients received PIM. Median OS with no pre-CAR-T antibiotics was 559 days [IQR 212,973], and 216 days [IQR 91,727] with pre-CAR-T antibiotics. After multivariable adjustment, pre-CAR-T antibiotic exposure was still associated with worse OS (HR 2.52 [1.03,6.16]). Also true for subset analyses: BCMA patients with pre-CAR-T antibiotics had worse OS (HR 2.6 [1.1, 6.3]) as did CD19 (HR 2.45 [1.01,5.9]) than without pre-CAR-T antibiotics. Post-CAR-T antibiotics had no effect on OS. Neither pre nor post-CAR-T antibiotics had statistically significant effect on PFS nor progression at first PET-CT scan.

Conclusions: Exposure to antibiotics in 30 days pre-CAR-T is associated with worse OS, even when adjusted for age, prior lines of therapy, and infection rate. Post-CAR-T antibiotics did not have an effect on PFS, OS or progression at first PET-CT scan. Clinicians should be judicious with antibiotic exposure in the 30 days prior to CAR-T therapy.

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A068

IMMUNOGENETIC AND CLINICAL DETERMINANTS OF CYTOKINE RELEASE SYNDROME AFTER HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH POSTRANSPLANTATION CYCLOPHOSPHAMIDE

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Background: Cytokine release syndrome (CRS) is recognized as an early inflammatory complication after haploidentical hematopoietic stem cell transplantation (haplo-HSCT). However, the determinants of CRS, its severity patterns, and the potential contribution of immunogenetic factors remain incompletely defined.
The aim was to evaluate the incidence and risk factors for CRS after haplo-HSCT, focusing on CRS occurrence and its severity. We explored the potential role of PIRCHE score in the graft-versus-host (GvH) and host-versus-graft (HvG) directions and HLA-B leader peptide mismatches, in the development of CRS. We also assessed the impact of CRS on post-transplant outcomes.

Methods: We conducted a retrospective single-center study including 198 consecutive patients undergoing haplo-HSCT. CRS was graded according to ASTCT criteria. Immunogenetic evaluation included calculation of PIRCHE scores in GvH and HvG directions and classification of donor–recipient HLA-B leader peptide genotype and match/mismatch. Logistic regression analyses were performed to identify factors associated with CRS occurrence, grade ≥2 CRS, and early (within 24 hours) grade ≥2 CRS. Post-transplant outcomes were analyzed using competing-risks methodology (Fine–Gray models), with relapse or death treated as competing events. Multivariable models included clinically relevant variables and factors with $p<0.10$ in univariate analyses.

Results: CRS occurred in 76.4% of patients; grade ≥2 CRS and early grade ≥2 CRS were observed in 14.9% and 12.6% of cases, respectively.
In multivariable analysis, reduced-intensity conditioning (RIC) was independently associated with CRS occurrence (OR 3.15, 95% CI 1.46–6.77; p=0.003), whereas recipient CMV seropositivity showed a protective trend.
Grade ≥2 CRS was also independently associated with RIC transplantation (OR 3.51, 95% CI 1.01–12.26; p=0.049), while a TMM donor–recipient HLA-B leader genotype showed a trend toward increased risk (OR 3.84, 95% CI 0.83–17.76; p=0.085).
In the analysis of early grade ≥2 CRS, increasing donor age was independently associated with higher risk (OR 1.04 per year, 95% CI 1.003–1.071; p=0.030), together with specific donor–recipient HLA-B leader mismatches (TMM or MTM pairs; OR 4.49, 95% CI 1.33–15.24; p=0.016). Total PIRCHE score in the GvH (OR 1.01, 95% CI 1.00–1.03; p=0.048) and HvG (OR 1.01, 95% CI 0.99–1.03; p=0.064) directions showed associations in univariate analysis but did not retain statistical significance after multivariable adjustment.
CRS occurrence or severity was not associated with NRM, chronic GVHD, relapse, GRFS, or OS; however, CRS (any grade) was associated with severe acute GVHD (grade 3–4). In a multivariable competing-risks analysis focused on grade 3–4 aGVHD, transplantation from a

sibling donor (vs parent or offspring) independently increased the risk (HR 3.90, 95% CI 1.86–8.18; p=0.0003), whereas CRS occurrence was associated with a significantly reduced risk of severe aGVHD (sHR 0.32, 95% CI 0.16–0.63; p=0.001), and higher PIRCHE-B GvH scores showed a consistent trend toward a lower incidence of severe aGVHD (HR 0.85, 95% CI 0.71–1.00; p=0.051).

Conclusions: CRS is a frequent early complication after haplo-HSCT and is influenced by conditioning intensity, donor age, and immunogenetic factors. The incorporation of PIRCHE scores and HLA-B leader matching suggests that CRS may reflect donor–recipient immunogenicity.

Disclosure: No

A070

SALVAGE STRATEGIES AND OUTCOMES AFTER EARLY-LINE CD19 CAR T-CELL THERAPY FAILURE IN LARGE B-CELL LYMPHOMA

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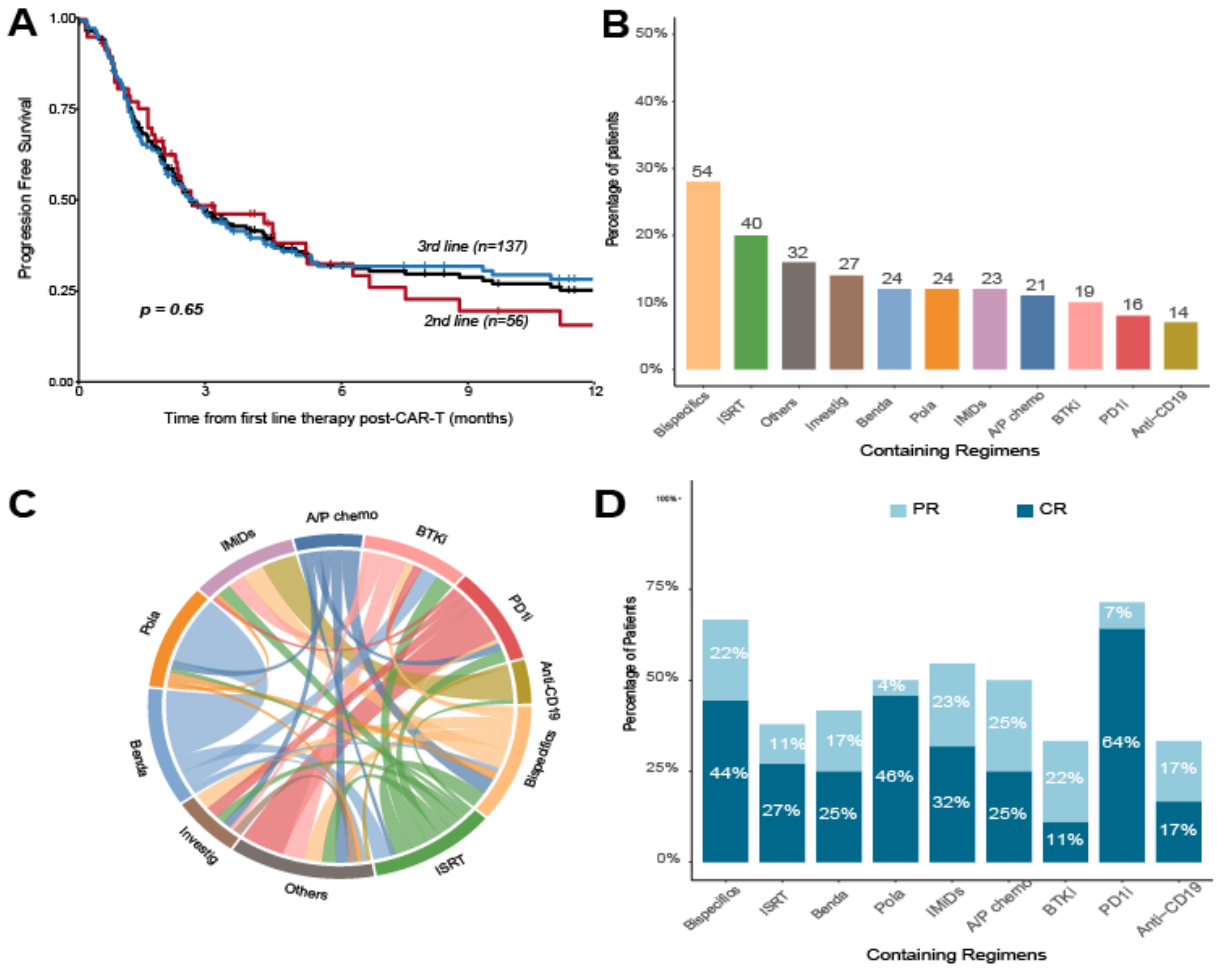
Background: The approval of CD19 chimeric antigen receptor (CAR) T-cell therapy in the second-line setting for large B-cell lymphoma (LBCL) has altered treatment sequencing and

expanded the population at risk for post–CAR-T relapse. However, evidence guiding management after CAR-T failure is largely derived from later-line cohorts. We therefore evaluated outcomes and first salvage strategies in a large international cohort of patients relapsing after early-line CD19 CAR-T therapy.

Methods: We conducted an international, retrospective, multicenter cohort study across five institutions, including adults with LBCL treated with commercial or point-of-care CD19 CAR-T therapy in the second or third-line. Outcomes were assessed from initiation of first salvage therapy. Progression-free survival (PFS) and overall survival (OS) were estimated using Kaplan–Meier methods. Associations between clinical variables and outcomes were evaluated using univariable and multivariable Cox proportional hazards models.

Results: Among 562 LBCL patients treated with CD19 CAR-T therapy, the cumulative incidence of relapse or progression was 41% (95% CI, 37–45). Of the 243 patients who relapsed or progressed, 198 (81%) received salvage therapy. In the salvage-treated cohort, median age was 65 years (IQR, 54–73). Prior CAR-T exposure included axicabtagene ciloleucel (51%), isoantigenic maraleucel (24%), tisagenlecleucel (22%), and point-of-care products (4%); 70% had received CAR-T therapy in the third-line setting.
The overall response rate (ORR) to first salvage therapy was 50%, including 34% complete and 16% partial responses. With a median follow-up of 25 months (IQR, 10–43), 1-year OS and PFS after salvage were similar between patients who received CAR-T therapy in the second versus third-line (OS, 42% vs 44%, p=0.93; PFS, 18% vs 28%, p=0.80; **Fig. 1A**). In multivariable analyses adjusting for age, CAR-T product, time from CAR-T to relapse or progression, and pre-salvage LDH, CAR-T treatment line was not associated with OS, PFS, or response. In contrast, relapse or progression within 3 months of CAR-T therapy was strongly associated with inferior PFS (HR, 3.03; 95% CI, 1.7–5.2).
Post–CAR-T salvage strategies were heterogeneous (**Fig. 1B–C**), most commonly including bispecific antibodies (n=54), involved-site radiotherapy (n=40), bendamustine-based therapy (n=24), and polatuzumab-containing therapy (n=24); treatment categories were not mutually exclusive. Response rates varied by treatment component, with the highest ORR observed among patients receiving checkpoint inhibitor–based therapy (71%) and bispecific antibody–containing therapy (66%) (**Fig. 1D**). One-year OS, analyzed by treatment component exposure, was highest in patients treated with checkpoint inhibitors (67%), followed by bispecific antibodies (57%), and lowest among those receiving anthracycline- or platinum-based therapy (21%). Despite these differences, EFS remained modest across approaches, ranging from 42% with bispecific antibody–containing therapy to 5% with bendamustine- or anthracycline/platinum-based therapy.



Conclusions: In this large multicenter cohort of LBCL patients relapsing after early-line CD19 CAR-T therapy, salvage treatment achieved clinically meaningful responses regardless of prior CAR-T treatment line. Early post–CAR-T relapse identified a high-risk subgroup with poor outcomes. Immunotherapy-based salvage strategies showed the most favorable activity, supporting their preferential consideration and underscoring the need for prospective studies to optimize post–CAR-T treatment sequencing.

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A071

INCIDENCE OF SINUSOIDAL OBSTRUCTION SYNDROME (VOD/SOS) DIAGNOSED BY DOPPLER ULTRASOUND/LIVER ELASTOGRAPHY IN PATIENTS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Sinusoidal Obstruction Syndrome (SOS) is a rare but potentially life-threatening complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). While ultrasound and liver elastography contribute to the early diagnosis of SOS, their predictive value in the pre-transplant setting remains unclear.

Methods: We conducted a real-world, single-center study between January 2017 and December 2024 in patients undergoing allo-HSCT at the University Hospital of Nancy. The primary objective was to assess the association of pre-transplant ultrasound and color Doppler (US-Doppler) according to Lassau criteria, as well as Liver Stiffness Measurement (LSM), with the subsequent development of SOS. Secondary objectives included evaluating the incidence and severity of SOS and its impact on patient outcomes.

Results: A total of 431 patients were included, and pre-transplant US-Doppler with LSM was performed in 347. The cumulative incidence of SOS at day 120 was 8.35% (n = 36; 95% CI, 5.74–10.97), with a median time to onset of 12 days (range, 1–119). According to the 2023 European Society for Blood and Marrow Transplantation (EBMT) diagnostic criteria, 21 patients developed severe SOS and 7 developed very severe SOS. Twenty-nine patients received defibrotide, with a median treatment duration of 21 days (range, 3–60). The median duration of intensive care unit stay among patients with very severe SOS was 13 days (range, 3–34). In univariate analysis, beyond the classical clinical parameters associated to a higher risk of SOS, pre-transplant US-Doppler and LSM were also associated with an increased risk of SOS. In multivariate analysis, the main pre-transplant risk factors significantly associated with SOS were the presence of ≥3 US-Doppler criteria (HR, 4.06; 95% CI,1.14–14.48; p = 0.031) and mean pre-transplant liver stiffness ≥7.5 kPa (HR, 2.74; 95% CI, 1.20–5.92; p = 0.012). SOS incidence was 8.81 fold increased in patients with both LSM≥ 7.5 kPa and ≥3 US-doppler SOS criteria at baseline (n=8) compared to patients with LSM <7.5 kPa and less than 3 US-doppler criteria.

Conclusions: Pre-transplant liver assessment using US-Doppler and LSM is significantly associated with subsequent SOS development, suggesting that these non-invasive approaches may serve as valuable predictive biomarkers. Prospective validation in larger multicenter studies is warranted.

Clinical Trial Registry: NCT04141735

Disclosure: Nothing to declare

A072

PERI-TRANSPLANT PALLIATIVE CARE AND/OR COMORBIDITY MANAGEMENT FOR OLDER, MEDICALLY INFIRM, AND/OR FRAIL RECIPIENTS OF ALLOGENEIC TRANSPLANTS – PHASE II AND INTERIM PHASE III TRIAL ANALYSES

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Background: Patients (pts) with hematopoietic cell transplantation comorbidity index (HCT-CI) scores of ≥3), older age (≥65 years), and/or who are frail per gait speed (<0.8 meters/second) have increased morbidity and mortality after allo-HCT compared to younger and healthier counterparts. We report results of a seamless phase II/III prospective, randomized clinical trial conducted at 11 transplant centers to test new approaches to improve quality of life (QOL) in this pt population.

Methods: Phase II compared peri-transplant specialist-administered supportive and palliative care (SPC), peri-transplant patient-administered management of comorbidities (MC, e.g. physical exercise, stress reduction, education, and as needed cardio-pulmonary rehabilitation as needed), both (SPC+MC), and usual care (UC) for change in Functional Assessment of Cancer Therapy – Bone Marrow Transplantation (FACT-BMT) scores from baseline to day 90 (D90). Pts deceased prior to D90 were assigned FACT-BMT score=0. The winning phase II arm (the experimental arm with the best change in FACT-BMT from baseline to day 90) moved forward versus UC in phase III. Interventions started within 2 weeks before day 0 and continued for a total of 10 weeks each. Patients received weekly reminders for the MC arm. We calculated FACT-BMT Trial Outcome Index (TOI) for all patients and total scores for a subset of patients with available data for all 5 subscales. Clinicaltrials.gov #: NCT03870750

Results: Phase-II was completed after enrolling 35 pts to each of the 4 study arms. Calculating the difference between FACT-BMT scores on D90 minus baseline, excluding missing data, indicated that SPC resulted in a small improvement in QOL compared to either MC or SPC+MC (Table 1); hence SPC was deemed the winning phase II arm and moved forward to Phase III.
Phase-III planned interim analysis was conducted after enrolling 158 SPC pts and 153 UC pts. The SPC and UC arms were well balanced with median age (both 68 years), HCT-CI ≥3 (49% vs 55%), frailty per gait speed (13% vs 12%), female sex (41% vs 34%), non-white race (9.5% vs 11.5%), and Hispanic or unreported ethnicity (7.7% vs 5.7%), respectively. After median follow-up of 362 days, 45 pts had died in each arm.
The mean QOL difference between baseline and D90 FACT-BMT TOI scores was 2.83 for SPC and 4.27 for UC (difference of differences, -1.44, 95% CI of difference, -5.03 to 2.14, p=0.43). Similar findings (p=0.92) were seen when using total scores in a subset (n=204) of pts. Fitting a generalized linear model that included baseline, D30, and D90 values, without assigning a value of 0 to those who died before D90, and testing the null hypothesis that the slope of scores differed between SPC and UC resulted in p=0.85 for TOI scores and p=0.98 for total scores. Comparison of mortality yielded a hazard ratio of 1.13 [0.75-1.73] for SPC vs. UC (Figure).

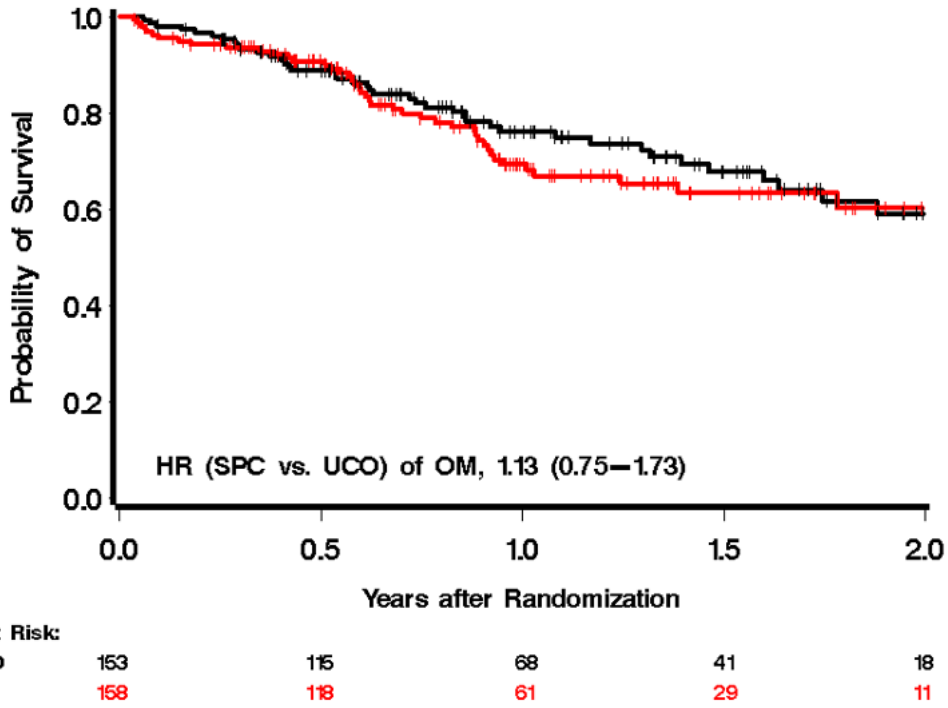
Table 1: Change in FACT-BMT (baseline value minus D90 value) comparing the 4 arms of phase II.

Group	Mean difference (SD)	Median difference (range)
SPC (n=28)	2.93 (28.52)	-0.25 (-38.22 to 100)

CM (n=18)	18.37 (33.80)	9.50 (-11 to 98.33)
SPC+CM (n=27)	15.76 (32.69)	7.67 (-32 to 90)

SPC – Supportive and Palliative Care
CM – Comorbidity management
SD – standard deviation

Figure. Kaplan Meier survival curve comparing Supportive and Palliative Care (SPC) and Usual Care Outcome (UCO).



Conclusions: Specialist-administered SPC showed no meaningful improvement in D90 QOL, nor a survival advantage, compared to UC in older, comorbid, and/or frail allo-HCT recipients, resulting in the cessation of this Phase II/III trial. Different approaches to use SPC for patient support during allo-HCT are needed.

Clinical Trial Registry: Clinicaltrials.gov #: NCT03870750

Study Details | NCT03870750 | Identifying Best Approach in Improving Quality of Life and Survival After a Donor Stem Cell Transplant in Older, Medically Infirm, or Frail Patients With Blood Diseases | ClinicalTrials.gov

Disclosure: Ronald Sobecks is on an advisory board for Care Dx, Inc.
Remaining authors have nothing to declare.

A073

POST-TRANSPLANT CYCLOPHOSPHAMIDE DOSE REDUCTION ENABLES FASTER GRANULOCYTE ENGRAFTMENT WHILE MAINTAINING EFFICACY IN PREVENTING GVHD

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Background: Post-transplant cyclophosphamide (PTCy) is an established strategy for the prophylaxis of graft-versus-host disease (GVHD) following allogeneic hematopoietic stem cell transplantation (allo-HSCT). While the standard high-dose regimen (100mg/kg) is widely used, non-negligible toxicity prompts evaluation of reduced-dose regimens.

Methods: We retrospectively analysed data from 367 consecutive adult recipients of first allo-HSCT at the Institute of Hematology and Blood Transfusion in Prague between 1/2018 and 6/2025, who received post-transplant cyclophosphamide (together with cyclosporin and mycophenolate-mofetil) as GVHD prophylaxis. Based on previous reports and preliminary data, we have reduced PTCy dose in all patients undergoing HSCT from 2x50mg/kg to 2x35mg/kg since 6/2024 with the aim of decreasing toxicity while maintaining efficacy. Endpoints included cumulative incidence of neutrophil and platelet engraftment, acute and chronic GVHD, relapse, non-relapse mortality (NRM), overall (OS) and disease-free survival (DFS). Comparisons used appropriate statistical tests, including competing-risk methods for cumulative incidence (CI) analyses; survival was evaluated by the Kaplan-Meier method. Multivariate analysis was performed to adjust for baseline differences.

Results: Baseline characteristics differed between the 70 mg/kg group (n = 60) and the 100mg/kg group (n = 307)—the 70mg/kg group was older (mean age 53 vs 48 years, p = 0.005), had a higher comorbidity burden (HCT-CI > 2 in 38% vs 24%, p= 0.04), and a different donor composition (more matched related donors—12% vs 0.3%, fewer haploidentical donors—18% vs 32%; p < 0.001). The 70 mg/kg cohort achieved a significantly shorter time to neutrophil engraftment (median 18.5 vs 21 days), confirmed with competing-risk cumulative incidence analysis (p < 0.001). Median time to platelet engraftment was also shorter in the 70mg/kg cohort (18 vs 20 days), however, competing risks analysis did not show significant difference (60-day CI of 95% vs 93.2%; p = 0.128). We did not find any significant differences between the 70mg/kg and 100mg/kg cohorts in cumulative incidence of acute GVHD (120-day CI of 48,3% vs 44,6%; p = 0.426) or chronic GVHD (1-year CI of 34,5% vs 28%; p = 0.61). Cumulative incidence of relapse was numerically lower with PTCy 70mg/kg but did not reach statistical significance (1-year CI of 11% vs 22%; p = 0.071). NRM was similar between groups (p = 0.802). OS and DFS curves were comparable between both groups (1-year OS of 87% vs 80%; p = 0.2; 1-year DFS of

78% vs 69%; p = 0.16). In multivariate analysis, no variable—including age, HCT-CI, or donor type—was significantly associated with an increased risk of death.

Conclusions: In this retrospective analysis, reduced-dose PTCy (70mg/kg) for GVHD prophylaxis demonstrated comparable efficacy to standard-dose PTCy (100mg/kg) in terms of GVHD prevention, relapse incidence, NRM, and survival outcomes, despite being administered to an older and higher-risk patient population. Reduced-dose PTCy (70mg/kg) was associated with faster neutrophil engraftment. These findings support the feasibility of PTCy dose reduction to 70mg/kg without compromising key clinical outcomes and suggest potential benefits for early hematologic recovery. Prospective studies are warranted to validate these results and to clarify the optimal PTCy dosing.

Disclosure: Nothing to declare.

A075

OUTCOME OF PATIENTS TREATED FOR T-ALL WITH HSCT IN THE FORUM-1 STUDY

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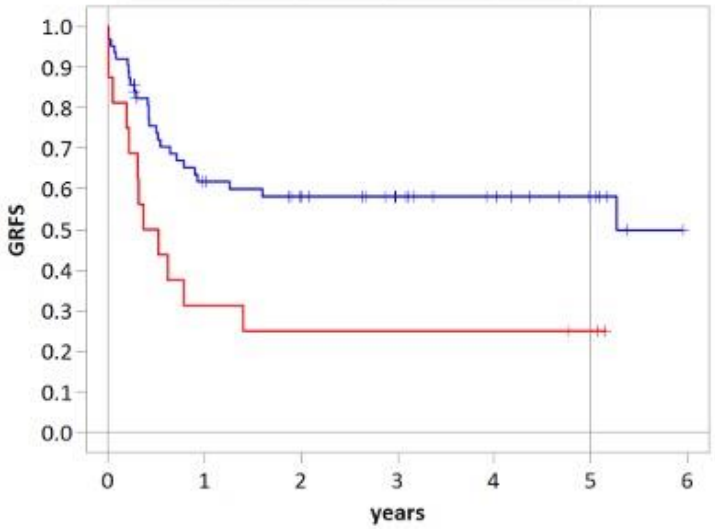
Background: The prognosis of relapsed T-acute lymphoblastic leukemia (T-ALL) remains poor. Few innovative targeted therapies or immunotherapies are available in this setting in contrast to B-ALL. The indication for allogeneic hematopoietic stem cell transplantation (HSCT) is broader in T-ALL : high-risk patients in first complete remission (CR) and almost all patients in CR2. Evaluating the toxicity and efficacy of this procedure is crucial for defining the best standard of care for these patients.

Methods: We report results of the prospective international FORUM-1 study (NCT01949129) of T-ALL patients treated with TBI-etoposide or myeloablative Busulfan or Treosulfan based

regimens according to age (≤ or > 4 years) or remission status before HSCT (CR1 or CR2 or later).

Results:

conditioning	Patients	3-yrs EFS	3-yrs GRFS	3-yrs OS
TBI	63	0.67±0.06	0.58±0.06	0.72±0.06
CHEMO	16	0.31±0.12	0.25±0.11	0.38±0.12
p-value		0.010	0.014	0.005



Between 2013 and October 2025, 392 T-ALL patients received HSCT from an HLA-identical sibling donor (MSD) or 9-10/10 HLA-compatible matched unrelated donor (MD).
Among 38 patients ≤4 years old, 5 (13%) received TBI-etoposide (all >2 years old) and 87% were in CR1. At 3 years, the EFS and OS were 66% and 73% respectively with a CI-NRM of 5% and a CIR of 29%.
Among the 231 patients > 4 years old in CR1, at a median age of 10.2 years (4.1-18.6), 157 (68%) received TBI-etoposide. At 3 years, the EFS and OS were 76% and 78% respectively with a CI NRM of 7% and CIR of 16%. There was no difference in EFS, OS, GRFS, CI-NRM or CIR according to type of donor nor conditioning (3y EFS 76% vs 74% and OS 77% vs 77% respectively in TBI-etoposide vs chemo-conditioning group).
Among the 84 patients > 4 years old in CR2 or later, at a median age of 10.3 years (4-19.5), 67 (80%) received TBI-etoposide. The timing of relapse was distributed as follows: very early 38%, early 27%, late 30%. At 3 years, the EFS and OS were 60% and 65% respectively with a GRFS of 52%, a CI-NRM of 13% and CIR of 26%. There was no significant difference in EFS, OS, GRFS, CI NRM or CIR according to donor type or site or timing of the previous relapse. In contrast, there was a significant superiority of TBI-etoposide over chemo-conditioning for 3 year-EFS (67% vs 31%, p-value=0.01), OS (72% vs 38%, p-value=0.005), GRFS (58% vs 25%, p-value=0.014) and CIR (19% vs 56%, p-value=0.002) but no difference in CI NRM (14% vs 13%).
Of note, no significant difference in the number of patients with viral infection, SOS incidence or acute GvHD was identified between patients receiving HSCT in CR1 or CR2.

Conclusions: Allo HSCT allows cure of many patients with T-ALL, especially when transplanted in CR1. Use of TBI in combination with etoposide must be preferred in patients with ≥CR2. In patients transplanted in CR1, chemo-based conditioning achieved similar survival outcome as TBI-etoposide.

Clinical Trial Registry: NCT01949129

Disclosure: HP reports travel grants from Jazz Pharmaceuticals and Sanofi and speakers bureau fees from Vertex and Novartis.

A076

AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION (AUTOHCT) FOR PLASMABLASTIC LYMPHOMA (PBL): AN EBMT LYMPHOMA WORKING PARTY STUDY

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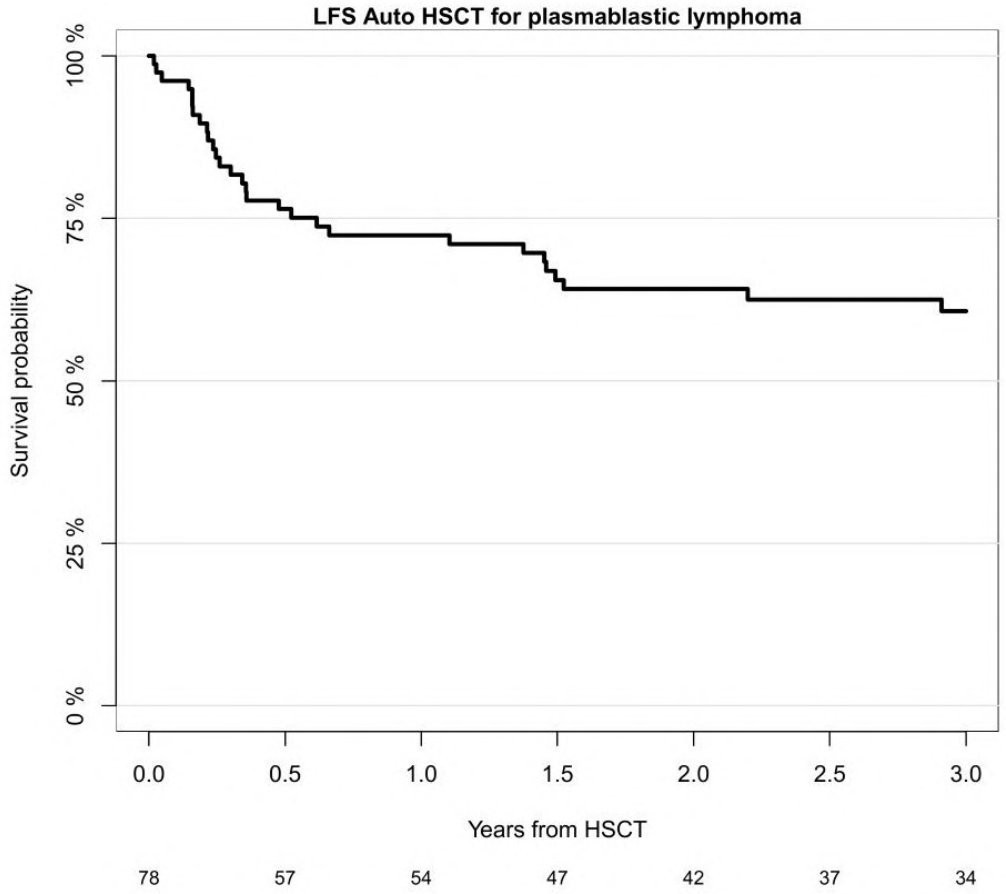
Background: PBL is a rare form of aggressive B-cell lymphoma. PBL lacks classic B-cell markers but expresses plasmacytic markers. It is commonly associated with HIV infection. The first-line therapy most commonly consists of CHOP chemotherapy, although long-term remission can only be achieved in a minority of patients. Due to its aggressive clinical course, autoHCT is often performed as consolidation therapy after first-line or salvage therapy. However, this practice is currently supported only by small retrospective analyses which, however, show encouraging outcomes. We therefore aimed to study the outcome of PBL after autoHCT for the first time on a reasonable sample size.

Methods: This EBMT registry analysis included adult patients who underwent a first autoHCT for PBL between 2016 and 2022. Diagnostic reports were collected for all patients and were grouped by an expert pathologist according to diagnostic certainty: high, moderate or low. Criteria for high certainty were (1) PBL diagnosis explicitly indicated in the report, (2) site of biopsy compatible with PBL, and (3) absence of CD20 and/or the presence of EBV. Statistical analysis was descriptive, employing univariate and multivariate comparisons to assess the impact of baseline characteristics on survival endpoints.

Results: A total of 78 patients with diagnostic reports meeting high/moderate/low certainty were included. Eighty-three per cent were male, and 32% were HIV-positive. Median age was 51 years (range 23 - 74). AutoHCT was performed after first-line therapy in 56% of patients and after second-line therapy in 32% of patients. The majority of patients were in partial (40%) or complete (55%) remission prior to autoHCT. Conditioning was performed according to BEAM or similar protocols in 73% of the patients. Diagnostic certainty was high in 45% and moderate in 23% of patients. After a median follow-up of 4.5 years, 2-year rates of OS, lymphoma-free survival (LFS), relapse incidence (RI), and non-relapse mortality (NRM) were 79%, 64%, 31%, and 5%, respectively (Figure 1).



Notably, on multivariate analysis, relapse incidence tended to be lower in HIV-positive patients (hazard ratio (HR) 0.35; 95% CI 0.1–1.25). Age, sex, and lines of treatment did not correlate with disease-related outcomes. Neither baseline characteristic correlated with NRM. 2-year LFS and RI in patients with high, moderate, and low diagnostic certainty were 68%, 55%, and 42% (p=0.151); and 20%,34%, and 50% (p=0.105), respectively.

Conclusions: This first large analysis on autologous transplantation in patients with PBL suggests markedly favorable disease control of consolidative autoHCT, contrasting the often limited potential of standard lymphoma-type induction in this entity. This notion is supported by the observation that autoHCT efficacy seems to correlate with diagnostic certainty. In line with previous very preliminary reports, our analysis supports the use of autoHCT in eligible patients with PBL.

Disclosure: The authors declare no competing financial interests.

A077

EXCELLENT OUTCOME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PEDIATRIC AND ADULT NUP98-REARRANGED ACUTE MYELOID LEUKEMIA: A SINGLE-CENTER REAL-WORLD STUDY

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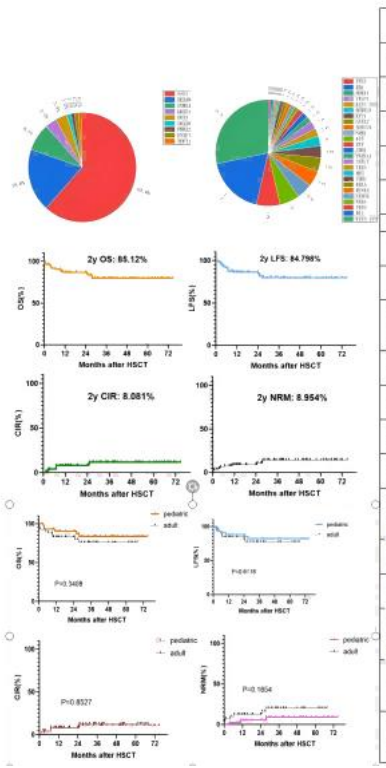
Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective and curative treatment for NUP98-rearranged acute myeloid leukemia (NUP98-r AML). However, prognostic factors following allo-HSCT remain poorly defined.

Methods: We retrospectively analyzed pediatric and adult patients with NUP98-r AML confirmed by RT-PCR who underwent allo-HSCT between January 2021 and December 2024. Minimal residual disease (MRD) was monitored pre- and post-HSCT using multiparameter flow cytometry (MFC) and RT-PCR.

Results: Among 86 included patients (4.61% of all AML transplants during the period), 44 (51.16%) were pediatric. Median age was 15 years (range 0.83–59). At diagnosis, 23 patients (26.74%) had white blood cell counts ≥100×10⁹/L. Nine fusion partners were identified, most commonly NSD1 (61.63%), followed by HOXA9 (18.60%), with HOXA9 more frequent in adults than children (28.5% vs. 9.0%, P=0.005). Co-mutations included FLT3-ITD (56.98%) and WT1 (52.33%). According to cytogenetic risk stratification, 70.93% were high-risk. Pre-HSCT, 67.44% were in complete remission (CR); among these, 75.86% were MRD-positive by both MFC and NUP98-r. HCT-CI score was ≥1 in 54.65%. Donors were haploidentical donor in 83.72%. BU-based Myeloablative conditioning (MAC) was used in 88.37% the remaining was TBI-based MAC. Post-transplant NUP98-r positivity rates were 40.70%, 9.30%, and 3.49% at 1, 2, and 3 months, respectively. After a median follow-up of 29.2 months, 2-year overall survival (OS), leukemia-free survival (LFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM) were 85.12%, 84.80%, 8.08%, and 8.95%, respectively, with no significant differences between adults and children. Multivariate analysis identified non-remission (NR) pre-HSCT as an independent predictor of inferior OS (HR 3.31, P=0.023) and LFS (HR 2.73, P=0.031). NUP98-r positivity at 1 month post-HSCT was associated with worse OS (HR 5.54, P=0.03) and LFS (HR 4.82, P=0.017); positivity at 2 months with inferior LFS (HR 3.91, P=0.039); and positivity at 3 months with poorer LFS (HR 7.59, P=0.009) and higher CIR (HR 19.45, P<0.001). In the CR subgroup, dual-positive MRD (MFC and NUP98-r) pre-HSCT predicted worse OS (HR 6.11, P=0.037), LFS (HR 10.10, P=0.005), and CIR (HR 13.02, P=0.016). Among pediatric patients, NR pre-HSCT correlated with inferior OS (HR 5.62, P=0.047). In adults, TBI-based versus BU-based MAC was associated with poorer OS (HR 17.05, P<0.001), LFS (HR 9.21, P=0.002), and higher NRM (HR 30.62, P<0.001).



	Total(n=86)	Pediatric(n=44)	Adult(n=42)	P v
Gender/male	46 (53.49)	25 (56.82)	21 (50.00)	0.562
WBC≥100 at diagnosis, n (%)	23 (26.74)	10 (22.73)	13 (30.95)	0.389
NUP98 type, n(%)				0.005
NSD1	53 (61.63)	29 (65.91)	24 (57.14)	
HOXA9	16 (18.60)	4 (9.09)	12 (28.57)	
KDM5A	7 (8.14)	7 (15.91)	0 (0.00)	
FLT3_ITD, n (%)	49 (56.98)	26 (59.09)	23 (54.76)	0.685
WT1, n (%)	45 (52.33)	22 (50.00)	23 (54.76)	0.659
Cytogenetic risk stratification(adverse), n (%)	61 (70.93)	34 (77.27)	27 (64.29)	0.185
HCT_CI(socre ≥1), n (%)	47 (54.65)	22 (50.00)	25 (59.52)	0.375
CR status pre-HSCT(NR), n (%)	58 (67.44)	32 (72.73)	26 (61.90)	0.284
MFC-MRD pos pre-HSCT, n (%)	45 (52.33)	20 (45.45)	25 (59.52)	0.192
NUP98-r pos pre-HSCT, n (%)	64 (74.42)	29 (65.91)	35 (83.33)	0.162
Myeloablative conditioning(BUsed)	76 (88.37)	38 (86.36)	38 (90.48)	0.796
Intensitified MAC	40 (46.51)	15 (34.09)	25 (59.52)	0.018
Donor type(HID), n (%)	72 (83.72)	39 (88.64)	33 (78.57)	0.206
NUP98-r pos post-HSCT at 1 m, n (%)	35 (40.70)	6 (13.64)	29 (69.05)	0.001
NUP98-r pos post-HSCT at 2 m, n (%)	8 (9.30)	5 (11.36)	3 (7.14)	0.827
NUP98-r pos post-HSCT at 13m, n (%)	3 (3.49)	2 (4.55)	1 (2.38)	0.356

Univariable Analysis of Transplant Outcomes of all Patients

	OS		LFS		CIR		NRM	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Sex, female vs male	1.45 (0.53-4.00)	0.472	1.60 (0.63-4.05)	0.324	1.19 (0.30-4.67)	0.81	1.87 (0.55-6.41)	0.32
Age, adult vs child	1.64 (0.58-4.61)	0.348	1.76 (0.68-4.54)	0.244	1.01 (0.26-3.93)	0.98	2.56 (0.67-9.74)	0.17
WBC, ≥100 vs < 100, ×10^9/L	1.32 (0.45-3.88)	0.608	1.01 (0.36-2.84)	0.963	0.37 (0.05-2.94)	0.35	1.82 (0.53-6.21)	0.34
NUP98-NSD, Yes vs No	0.50 (0.18-1.38)	0.182	0.44 (0.17-1.12)	0.085	0.19 (0.04-0.93)	**0.041**	0.92 (0.26-3.24)	0.89
FLT3 ITD, Yes vs No	0.63 (0.23-1.75)	0.377	0.57 (0.22-1.44)	0.235	0.76 (0.19-2.99)	0.69	0.49 (0.14-1.68)	0.25
WT1, Yes vs No	0.83 (0.30-2.30)	0.726	0.94 (0.37-2.37)	0.895	0.92 (0.24-3.52)	0.9	0.94 (0.28-3.15)	0.93
ELN2022, Adverse vs Intermediat	1.15 (0.37-3.61)	0.811	1.51 (0.50-4.58)	0.470	0.69 (0.17-2.81)	0.6	3.73 (0.47-29.76)	0.21
HCT CI, ≥1 vs <1	2.38 (0.76-7.49)	0.138	1.40 (0.54-3.60)	0.492	0.26 (0.05-1.32)	0.11	7.82 (1.03-59.41)	**0.047**
Disease status at HSCT, NR vs CR	3.31 (1.18-9.32)	**0.023**	2.78 (1.10-7.05)	**0.031**	1.20 (0.28-5.23)	0.8	4.86 (1.27-18.59)	**0.021**
CR subgroup, MFC-MRD Pos NUP98 Pos vs others	6.11 (1.11-33.48)	0.037	10.10 (2.02-50.39)	0.005	13.02 (1.62-104.54)	0.016	5.33 (0.50-57.34)	0.17
Intensed, Yes vs No	0.80 (0.28-2.25)	0.671	0.95 (0.37-2.40)	0.912	1.19 (0.30-4.69)	0.8	0.78 (0.22-2.73)	0.7
Regemen, TBI vs BU	5.16 (1.62-16.44)	**0.005**	3.59 (1.17-11.03)	**0.025**	0.00 (0.00-0.00)	<0.001	9.63 (2.79-33.20)	**<0.001**
doner type, HID vs others	1.13 (0.26-5.03)	0.868	1.47 (0.34-6.42)	0.607	1.25 (0.16-9.53)	0.83	1.56 (0.21-11.78)	0.67
Pre-NUP98r, Pos vs Neg	5.06 (0.66-38.49)	0.117	6.45 (0.86-48.51)	0.070	2.42 (0.32-18.49)	0.39	NE	NE
NUP98r at 1m, Pos versus Neg	5.84 (1.18-26.11)	0.03	4.82 (1.32-17.52)	0.017	3.29 (0.66-16.29)	0.15	4.04 (0.44-36.72)	0.22
NUP98r at 2m, Pos versus Neg	3.21 (0.68-15.20)	0.141	3.91 (1.07-14.26)	0.039	5.32 (0.92-30.67)	0.061	4.45 (0.46-42.77)	0.2
NUP98r at 3m, Pos versus Neg	NE	NE	7.59 (1.65-34.92)	0.009	19.45 (3.14-120.37)	0.001	NE	NE

Multivariable analysis of Transplant Outcomes of all Patients

	OS		LFS		CIR		NRM	
	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P	HR (95%CI)	P
Disease status at HSCT, NR vs CR	3.31 (1.18-9.32)	0.023	2.73 (1.10-7.05)	0.031	NE	NE	6.50 (1.29-32.72)	0.023
HCT CI, ≥1 vs <1	NE	NE	NE	NE	NE	NE	14.01 (2.50-78.53)	0.003
Regemen, TBI vs BU	NE	NE	NE	NE	NE	NE	18.60 (4.72-73.31)	<0.001

Conclusions: Allo-HSCT yields encouraging outcomes in NUP98-r AML, with no survival difference between pediatric and adult patients. Pre-HSCT NR status and early post-HSCT detection of NUP98-r are strongly associated with poorer prognosis. Among CR patients, dual MRD positivity before transplant further identifies a high-risk subgroup. In adults, TBI-based MAC may confer inferior survival outcomes compared to BU-based regimens.

Clinical Trial Registry: NO

Disclosure: Nothing to declare.

A078

OUTCOMES OF ALLO-HCT IN AML PATIENTS HARBORING NUP98 REARRANGEMENTS: A STUDY OF THE EBMT GLOBAL COMMITTEE, ACUTE LEUKEMIA WORKING PARTY, AND PEDIATRIC DISEASES WORKING PARTY

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Background: Acute myeloid leukemia (AML) featuring NUP98 gene fusions resulting from chromosomal rearrangements at 11p15 is recognized as a high-risk subtype. Given the low incidence of these genetic abnormalities in AML, the therapeutic value of allogeneic hematopoietic cell transplantation (allo-HCT) in this population has not been clearly established.

Methods:

We retrospectively analyzed 147 AML patients with NUP98 fusions or 11p15 rearrangements undergoing first allo-HCT. Data were contributed by 87 EBMT-affiliated centers between 2010 and 2022.

Results:

The cohort included 109 adult patients (median age at transplantation: 46.3 years, range 18.1–73.5) and 38 pediatric patients (median age: 9.4 years, range 0.4–18). In adults, the most common fusions were NUP98-NSD1 (24.8%) and NUP98-HOXA9 (19.3%); in children, NUP98-NSD1 predominated (68.4%), followed by NUP98-KDM5A (13.2%). At transplantation, 112 patients were in CR1, 14 in ≥CR2, and 21 had active disease. CR1 rates were 72.5% in adults vs. 86.8% in children (P=0.04), with active leukemia in 18.3% of adults vs. 2.6% of children. Myeloablative conditioning was used in 67.1% overall, more frequently in children (89.5%) than adults (59.3%; P<0.001).

Donors comprised haploidentical relatives (n=30), HLA-matched siblings (n=34), unrelated donors (n=68; 44 fully matched 10/10, 15 mismatched 9/10, 1 mismatched 8/10, 8 incomplete typing), cord blood (n=12), other matched relatives (n=2), and one-locus mismatched relatives (n=1). Peripheral blood stem cells were the primary source in adults (n=88), whereas bone marrow predominated in children (n=22), followed by peripheral blood (n=8) and cord blood (n=8).

Median follow-up was 2.9 years (95% CI, 2–3.5). Day-30 neutrophil engraftment rate was 93.0% (95% CI, 87.2–96.2; 95.2% adults, 86.5% children). Two-year overall survival (OS) was 69.9% (95% CI, 60.3–77.6), leukemia-free survival (LFS) 52.0% (95% CI, 42.6–60.7), and GVHD-free/relapse-free survival (GRFS) 40.6% (95% CI, 31.4–49.6). Two-year relapse incidence (RI) was 39.1% (95% CI, 30.1–48.0) and non-relapse mortality (NRM) 8.9% (95% CI, 4.8–14.4). Day-100 cumulative incidence of grade II–IV acute GVHD was 22.6% (95% CI, 16.1–29.7; grade III–IV, 9.9% [95% CI, 5.7–15.5]). Two-year chronic GVHD incidence was 23.2% (95% CI, 16.0–31.3), including extensive disease in 8.2% (95% CI, 3.9–14.3).

Univariate analysis revealed trends favoring pediatric patients: 2-year OS 78.7% (95% CI, 60.2–89.3) versus 66.4% (95% CI, 54.5–75.8) in adults (P=0.16); LFS 55.8% versus 50.6% (P=0.65); RI 41.6% versus 38.2% (P=0.58); NRM 2.6% versus 11.1% (P=0.10). Grade II–IV acute GVHD occurred in 13.2% of children versus 26.0% of adults (P=0.11; grade III–IV, 7.9% vs. 10.6%; P=0.63). Chronic GVHD was significantly lower in children (9.6% vs. 28.3%; P=0.045), with no extensive cases versus 11.3% in adults (P=0.14). GRFS was 52.1% in children versus 36.1% in adults (P=0.28). Transplantation with active disease was associated with inferior LFS, higher RI, and worse GRFS, whereas myeloablative conditioning correlated with superior 2-year OS.

Conclusions: This represents the most extensive series to date examining allo-HCT outcomes in NUP98-rearranged AML, encompassing both adult and pediatric cases from this uncommon subgroup. Allo-HCT appears to offer a valuable curative approach for individuals with NUP98-rearranged AML.

Disclosure: Nothing to declare.

A079

IMPORTANCE OF GRAFT COMPOSITION ON EBV REACTIVATION RISK FOLLOWING MODERN GVHD PROPHYLAXIS

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Background: Epstein-Barr virus (EBV) reactivation is a frequent complication after allogeneic (allo) hematopoietic cell transplantation (HCT) and can lead to post-transplant lymphoproliferative disorder (PTLD). While anti-thymocyte globulin (ATG) and post-transplant cyclophosphamide (PTCy) are well-established prophylactic strategies to prevent graft-versus-host disease (GVHD), their comparative impact on EBV reactivation remains insufficiently characterized.

Methods: We conducted a retrospective single-center study in consecutive recipients of allo HCT from a matched related/unrelated, mismatched unrelated or haploidentical donor between January 1, 2019, and December 31, 2024. Patients received either rabbit ATG or

post-transplant cyclophosphamide for GVHD prophylaxis. Primary endpoints were cumulative incidences of positive EBV DNAemia and high level EBV DNAemia (≥ 10^4 copies/mL) by month +6, measured using a whole blood quantitative PCR weekly from D+14 to D+100 then every 2 weeks. Secondary endpoints were incidence of probable/proven PTLD at 2 years, acute GVHD at 6 months, chronic GVHD and non-relapse mortality, as well as overall (OS), and progression-free survival (PFS). We also assessed risk factors for EBV DNAemia. Data on graft cellular content, engraftment, immune reconstitution, CMV reactivation and humoral response to post-transplant hepatitis B revaccination were also analysed.

Results: A total of 286 adults patients were included (Table 1). Of these, 215 patients received ATG and 71 PTCy. High-level EBV DNAemia occurred more frequently in the ATG group (74.9% vs. 49.3%, $p < 0.0001$), particularly at higher doses (4.5 vs. 2.5 mg/kg). In ATG recipients, high CD19+ B-cell doses (≥ 3.88 x 10^7/kg) and an elevated CD19+/CD8+ ratio (≥ 0.84) in grafts were independently associated with the cumulative incidence of high EBV DNAemia, a relationship not observed with PTCy (Figure 1). We observed no PTLD in the PTCy group while, 5 cases occurred in ATG recipients, 4 of whom had received a graft with a high CD19+/CD8+ ratio. In multivariable analysis, use of ATG (HR 3.0; 95%CI 1.6-5.7; p = 0.00084) and an elevated CD19+/CD8+ ratio in the graft (HR = 2.08; 95%CI: 1.4-3.1; p = 0.00025) emerged as the strongest independent predictors of high EBV DNAemia. ATG-treated patients exhibited delayed $CD4^+$ T-cell reconstitution and prolonged $CD4^+/CD8^+$ ratio inversion. Rituximab (RTX) had no impact on OS or PFS but was associated with sustained B-cell depletion, hypogammaglobulinemia, impaired hepatitis B immunity after vaccination with less patients achieving protective anti-HBsAg antibody levels (≥ 10 IU/mL) (p = 0.0176) and reduced anti-HBsAg antibody titers (p = 0.0064).

Table 1. Epstein-Barr virus related outcomes

		ATG N=215 (%)	PTCy N=71 (%)	p-v
EBV DNAemia at +6 months (copies/mL)	Any	161 (74.9)	35 (49.3)	0.00
	< 10 000	86 (40.0)	16 (22.5)	
	10 000 - 50 000	57 (35.4)	12 (16.9)	
	50 001 - 100 000	11 (6.8)	2 (2.8)	
	> 100 000	18 (11.2)	2 (2.8)	
Onset of EBV ≥10^4 copies/mL	Median time, days post HCT (range)	36 (17-165)	86 (39-109)	<0.00
EBV treatment	None	83 (38.6)	18 (51.4)	0
	RTX 1-4 doses	78 (36.4)	17 (48.6)	
	Median time of RTX in months (range)	1.7 (1.1-5.9)	3.6 (1.6-5.3)	<0.00

EBV outcome (among those with EBV reactivation)	Spontaneous resolution	82 (50.9)	15 (42.9)	
	Resolved following RTX[1]	76 (47.2)	16 (45.7)	0.00
	Stable[2]	0	4 (11.4)	
	Progression or death prior evaluation	3 (1.8)	0	
PTLD	Any (polymorphic/monomorphic)	5 (2.2)	0	0
	Median time of response, days (range)	40 (27-55)	NA	N
6 years survival post RTX	OS with RTX (95%CI)	64.2 (43.7-78.9)	80.7 (51.1-93.4)	0
	OS with no RTX (95%CI)	73.9 (63.4-81.9)	69.0 (48.5-82.7)	0
	PFS with RTX (95%CI)	58.3 (41.2-71.9)	63.9 (53.9-72.3)	0
	PFS with no RTX (95%CI)	75.6 (47.3-90.1)	66.6 (47.9-79.9)	0

p-values calculated using Fisher's exact test (categorical variables) and the Mann–Whitney U test (continuous variables).

[1] # of viral copies = 0 is considered as resolved.[2] # of viral copies remained the same ±

15%.

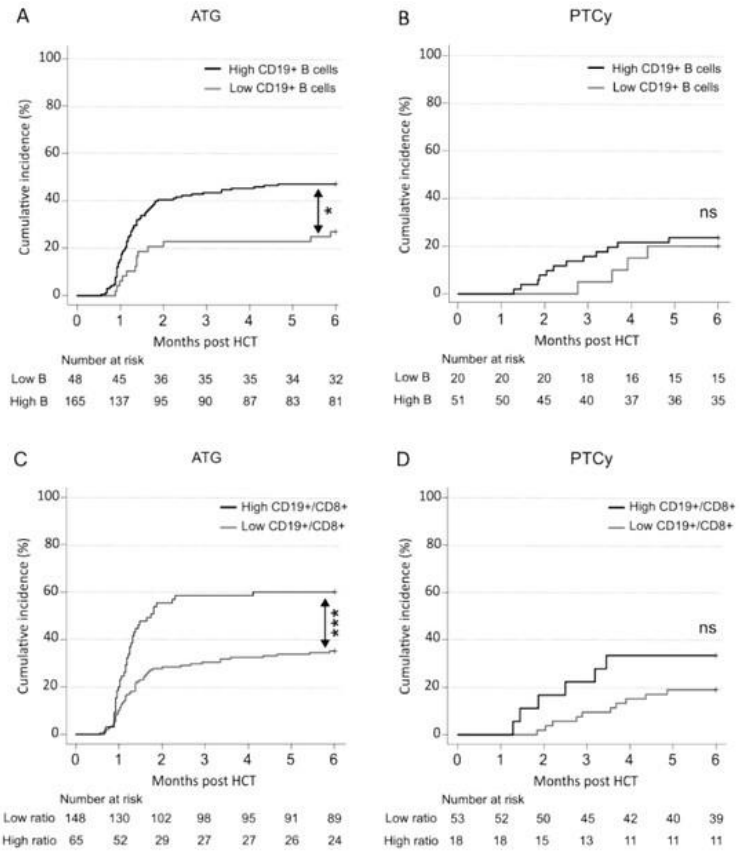

Figure 1. Association between graft B-cell content and cumulative incidence of EBV DNAemia ≥ 10^4 copies/mL post allogeneic transplant. (A) Cumulative incidence of high EBV DNAemia according to a threshold of 3.88 x 10^7 CD19+/kg in the ATG group. (B) Same analysis in the PTCy group (threshold: 4.78 x 10^7 CD19+ cells/kg). Cumulative incidence of high EBV DNAemia based on the CD19+/CD8+ ratio (threshold: 0.84) in the ATG group (C) and in the PTCy group (D). *$p < 0.05$; ***$p < 0.001$.

Conclusions: A high CD19+/CD8+ ratio in infused grafts was associated with a higher risk of high-level EBV reactivation in ATG-based GVHD prophylaxis but not after PTCy, highlighting distinct immune regulation and depletion patterns, as well as divergent early T-cell reconstitution dynamics. This new predictive factor may help identify patients who might

benefit from more aggressive management such as increased monitoring frequency, lower treatment threshold, or even primary prophylaxis.

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A080

PATIENTS WITH RELAPSED/REFRACTORY SYSTEMIC LIGHT CHAIN AMYLOIDOSIS ACHIEVE DEEP HEMATOLOGIC AND ORGAN RESPONSES WITH THE NOVEL MDC-CAR-BCMA001

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Background: B-cell maturation antigen (BCMA) has emerged as an attractive immunotherapeutic target in plasma cell disorders, however no commercial BCMA-directed chimeric antigen receptor (CAR) T-cell therapy is available for systemic light chain (AL) amyloidosis. We pursued compassionate use of the in-house manufactured 2nd-generation BCMA-directed MDC-CAR-BCMA001 in patients with relapsed/refractory AL amyloidosis and report on our updated findings in this challenging patient group.

Methods: Seven patients were treated with a fixed dose of 800 x 10^6 BCMA-directed CAR T-cells after lymphodepleting chemotherapy with fludarabine/cyclophosphamide (4/7) or bendamustine (3/7 – in cases of neuropathy or severe nephropathy). Leukapheresis, manufacturing and administration of CAR T-cells were performed in-house.

Results: Median age of the patients was 62 years (range: 57-70 years); underlying plasma cell disorder was monoclonal gammopathy in one case, smoldering myeloma in four and concurrent symptomatic multiple myeloma in the two remaining cases. Six out of seven patients had at least triple-class refractory disease and were not in remission prior to CAR T-cell infusion remission (4/7 progressive disease). Overall response was observed in 6/7 patients (86%, 3 complete remissions and 3 very good partial remissions) with a median time to best response of only 13 days. All evaluable patients (3/3) achieved measurable residual disease negativity. In responders, near-total suppression of amyloidogenic serum free light chain levels was achieved. Organ responses including near-complete cardiac and near-complete renal responses as well as improvements in neuropathy and myopathy were

observed in 4/7 patients at a median of 140 days. Six out of seven patients are alive and 3/6 responders are in sustained remission after a median follow-up of 327 days (including deep remissions over two years with long-lasting CAR T-cell persistence). All patients experienced manageable cytokine release syndrome (max. grade 3), rapidly resolving after tocilizumab and/or dexamethasone. Reversible deterioration of amyloid-involved organ function was observed in one patient. Neither immune effector cell-associated neurotoxicity nor higher-grade late hematotoxicity were observed.

Conclusions: MDC-CAR-BCMA001 shows a manageable toxicity profile with high efficacy even in heavily pretreated patients, making it a suitable construct for treating the vulnerable cohort of AL amyloidosis patients. Long-lasting, deep hematologic responses translate into excellent organ responses even in patients with advanced organ disease. These findings warrant further prospective evaluation, as planned in the phase I *CLEAR AL* trial (EU CT No. 2025-520790-39-00).

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A082

ARE TRANSPLANT-DERIVED COMORBIDITY INDICES FIT FOR CAR-T THERAPY? A MULTICENTER COMPARATIVE ANALYSIS

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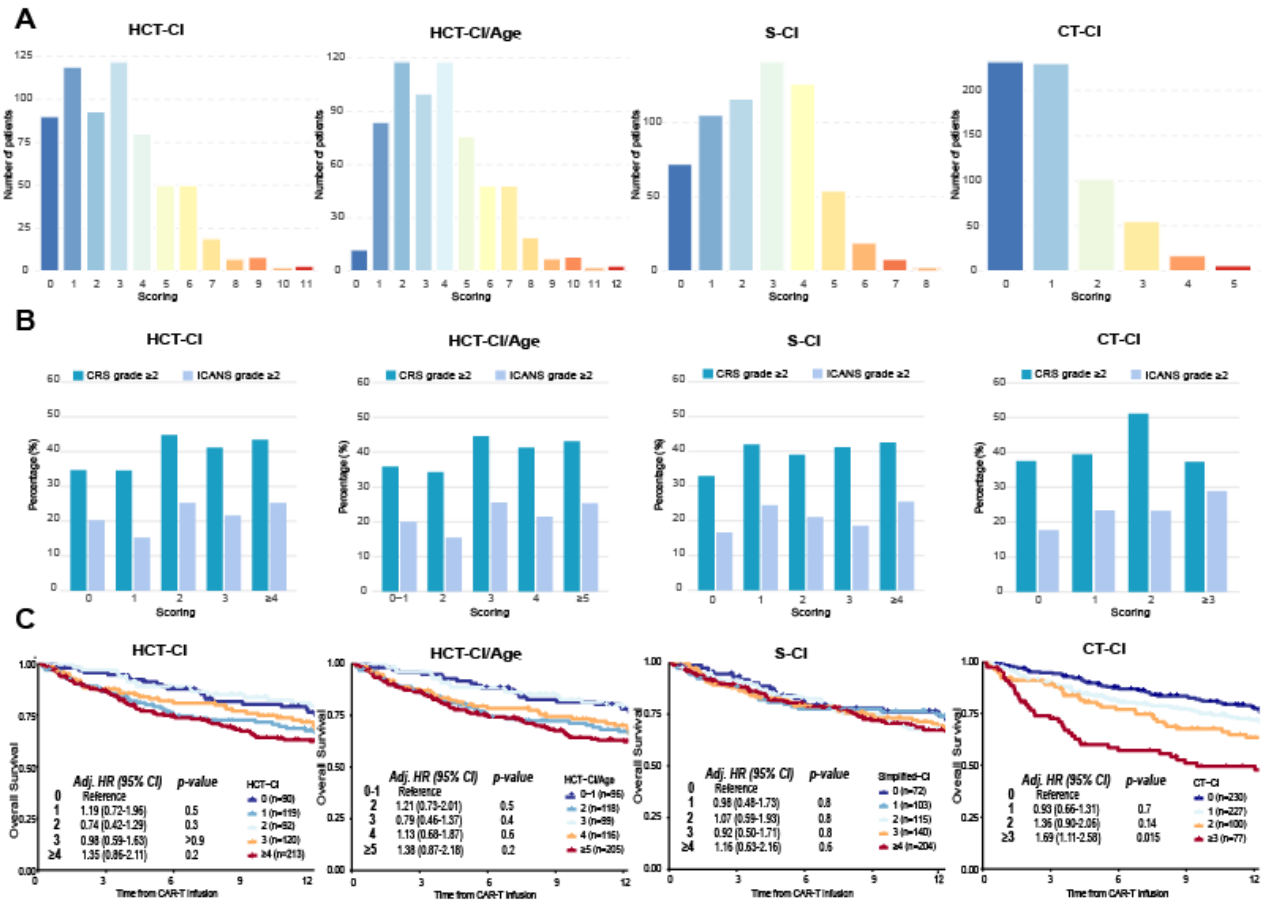
Background: Comorbidity indices are central to fitness assessment and risk stratification before hematopoietic cell transplantation, yet their utility in the CAR-T setting remains uncertain. Given the distinct clinical profile and toxicity spectrum of CAR-T recipients, it is unclear whether transplant-derived tools meaningfully inform outcomes. We therefore evaluated the clinical utility of four comorbidity indices in large B-cell lymphoma (LBCL) patients treated with commercial CAR-T across multiple centers.

Methods: We conducted an international, multi-center retrospective study across five centers, including adults with LBCL treated with commercial CAR-T products between 2016-2025. Comorbidities were assessed using: the Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), the Comorbidity-Age Index (HCT-CI/Age), the Simplified-Comorbidity Index (S-CI), and the Cellular Therapy-Comorbidity Index (CT-CI). Primary endpoints were 1-year overall survival (OS) and progression-free survival (PFS); non-relapse mortality (NRM) was evaluated as a secondary endpoint. Correlations between indices were quantified using Spearman's rank coefficient. Discriminative ability for OS/PFS was evaluated with Harrell's C-index. Cox models for OS/PFS and Fine–Gray competing risk regression for NRM. Multivariable models included clinically relevant covariates and were stratified by center.

Results: Among 642 patients (median age 65 years; IQR 56–72), 57% received axi-cel, 19% liso-cel, and 23% tisa-cel; 79% received bridging therapy, and 68% received ≤2 lines of pre-apheresis treatments. Grade ≥2 CRS and grade ≥2 ICANS occurred in 40% and 22% of patients, respectively. With a median follow-up of 26.1 months (IQR 12.3–43.2), 1-year OS was 70% (95% CI 66–74) and 1-year PFS was 49% (95% CI 45–53), while 1-year NRM was 4.4% (95% CI 2.9–6.2).Overall, patients receiving CAR-T were highly comorbid (Fig.1A). Correlation between indices varied substantially, with the strongest correlation observed between HCT-CI and HCT-CI/Age (ρ=0.99) and the weakest between CT-CI and S-CI (ρ=0.18). Rates of grade ≥2 ICANS increased with higher comorbidity burden, ranging from

17-20% in the lowest category to 25-29% in the highest categories (Fig.1B). Similar pattern was observed for grade ≥2 CRS, which were as high as 43% in the highest categories (Fig.1B).
Higher comorbidity scores were associated with shorter OS for all indices except the S-CI (Fig.1C). In multivariable analysis adjusting for age, performance status, LDH pre-lymphodepletion, CAR-T product, and bridging therapy, only CT-CI≥3 remained significantly associated with inferior OS (Adj.HR 1.69, 95% CI 1.11–2.58; p=0.015). Two-year OS estimates were 32% for CT-CI≥3 versus 67% for CT-CI=0. A high CT-CI was also the only index associated with inferior PFS (Adj.HR 1.48, 95% CI 1.02–2.16; p=0.038). None of the indices discriminated NRM risk.
Discrimination across indices was limited: C-indices for OS ranged from 0.53 with S-CI to 0.60 with CT-CI, and for PFS from 0.52-0.58. Calibration was similarly poor across all models.



Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI; Sorror, *Blood* 2025); Comorbidity-Age Index (HCT-CIAge; Sorror, *JCO* 2014); Simplified-Comorbidity Index (S-CI; Shouval, *Blood Adv* 2022); Cellular Therapy-Comorbidity Index (CT-CI; Greenbaum, *Blood Adv* 2025)

Conclusions: In this large international study established comorbidity indices showed limited prognostic value in LBCL patients undergoing CAR-T therapy. Among all indices evaluated, only the CT-CI meaningfully stratified OS and PFS, and none predicted NRM.

These findings suggest that transplant-derived comorbidity tools may not adequately capture risk in CAR-T recipients, highlighting the need for CAR-T–specific fitness assessments.

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A083

INCIDENCE AND RISK FACTORS OF PRIMARY GRAFT FAILURE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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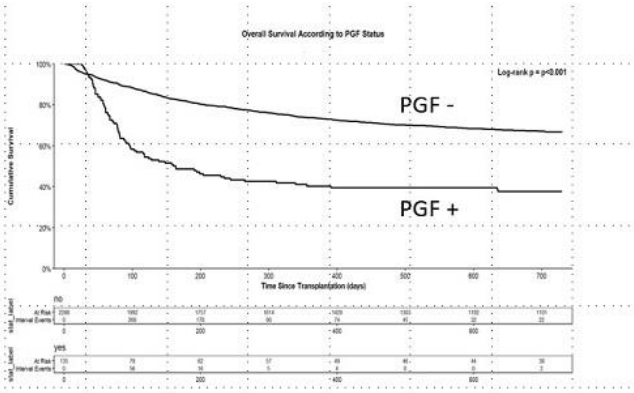
Background: Primary graft failure (PGF) remains a severe, life-threatening complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) with limited data on the incidence and predictors in heterogeneous cohorts.

Methods: We conducted a retrospective analysis of 2423 consecutive adult (n= 1621) and pediatric (n=802) patients who underwent allo-HSCT between 2002 and 2023 with a median follow-up of 629 days (range: 1 day-21ye⁹ars). PGF was defined as failure to achieve neutrophil engraftment (ANC >0.5×10⁹/L) by day +28 post-HSCT without relapse of underlying malignant disease. Secondary graft failure (sGF) was defined as loss of donor hematopoiesis of underlying malignant disease. Gray's method was used to estimate cumulative incidence (CI) of PGF and sGF with competing risks (relapse, death without PGF). Risk factors for PGF were analyzed using Cox regression.

Results:

Characteristics of the cohort	N=2423
Period	
2002_2012	191 (7.88%)
2013_2023	2232 (92.1%)
Age	
median (range)	26 (range:0.00-76.0)
<18	802 (33%)
>18	1621 (67%)
Diagnosis	
Aplastic anemia	130 (5.4%)
Inborn_or_nonmalignant	115 (4.8%)
Leukemia	1608 (66.4%)
Lymphoprilifetative diseases and multiple myeloma	198 (8.2%)
Myelodysplastic syndrom	114 (4.7%)
Myeloprolyferative diseases	226 (9.33%)
Solid tumors	32 (1.32%)
State of malignant disease	
Active_disease	625 (29%)
Other	1554 (71.1%)
Donor type	
Haploidentical	736 (30.4%)
MMUD	347 (14.3%)
MRD	478 (19.7%)
MUD	862 (35.6%)
Source of the graft	
BM	1151 (47.4%)
PBSC	1257 (52%)
Other	15 (0,6%)
Patients' sex	
Female	1048 (43%)
Male	1375 (57%)
Donors' sex	
Female	911 (38%)
Male	1506 (62%)
Female_to_female	424 (17.5%)
Female_to_male	487 (20.2%)
Male_to_female	622 (25.7%)
Male_to_male	883 (36.5%)
ABO compartability	
Bidirectional	213 (8.97%)
Major	521 (21.9%)
Matched	1077 (45.4%)
Minor	563 (23.7%)
Engraftment	
Death before day +28	88 (4%)
Relapse/progression before day +28	26 (1%)
No engraftment	153 (6%)
Engraftment	2156 (89%)
Time of engraftment	
median (range)	20.0 (6 -51)



Multivariable analysis of PGF risk factors

Variable		N	Hazard ratio	p
Adult		2401	1.30 (0.84, 2.02)	0.230
HSCT_type	haplo	732	Reference	
	MMUD	345	0.45 (0.25, 0.81)	0.008
	MRD	467	0.06 (0.03, 0.14)	<0.001
	MUD	857	0.24 (0.14, 0.39)	<0.001
Diagnosis_group	AA	128	Reference	
	Inborn_or_nonmalignant	114	0.67 (0.28, 1.60)	0.369
	Leukemia	1592	0.37 (0.19, 0.70)	0.002
	Lymphomas&MM	197	0.27 (0.09, 0.77)	0.015
	MDS	112	1.10 (0.46, 2.68)	0.825
	Myeloprolyferative	226	0.76 (0.36, 1.63)	0.480
	Solid	32	0.17 (0.04, 0.80)	0.025
Source1	BM	1146	Reference	
	PBSC	1255	0.35 (0.22, 0.57)	<0.001
Female_to_male	Female_to_female	421	Reference	
	Female_to_male	482	1.44 (0.83, 2.48)	0.194
	Male_to_female	617	0.92 (0.52, 1.63)	0.778
	Male_to_male	881	0.88 (0.52, 1.50)	0.648

The overall incidence of PGF was 5.6% (n=135) and the 2 year CI of sGF was 2.2%. In multivariate analysis, independent factors significantly associated with a reduced risk of PGF were: diagnosis of leukemia (HR=0.37, 95%CI 0.19-0.70, p=0.002), lymphoprolipherative diseases/multiple myeloma (HR=0.27, CI 0.09-0.77, p=0.015), and solid tumor (HR=0.17, CI 0.04-0.80, p=0.025) compared to aplastic anemia (AA); use of matched related donor (MRD, HR=0.06, CI 0.03-0.14, p<0.001), matched unrelated (MUD, HR=0.24, CI 0.14-0.39, p<0.001), or mismatched unrelated (MMUD, HR=0.45, CI 0.25-0.81, p=0.008) donor compared to haploidentical donor; and peripheral blood stem cells (PBSC) vs. bone marrow (BM) (HR=0.35, CI 0.22-0.57, p<0.001). PGF patients were younger (median 17 vs. 26 years, p<0.001). Two year OS was 37% in PGF patients vs. 78% in patients with engraftment.

Conclusions: PGF is a rare but devastating complication of allo-HSCT. The highest risk is associated with haploidentical transplantation and use of bone marrow as a source. These

findings underscore the critical need for developing preventive strategies for high-risk patients and an aggressive salvage approach once PGF occurs.

Disclosure: Nothing ot disclose.

A085

CLINICAL OUTCOMES IN MYELODYSPLASTIC SYNDROME PATIENTS TREATED WITH ORCA-T OR POST-TRANSPLANT CYCLOPHOSPHAMIDE PATIENTS: A REGISTRY-BASED COMPARISON

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Background: Allogeneic hematopoietic stem cell transplantation (alloHSCT) is the only potentially curative intervention for myelodysplastic syndrome (MDS), but novel strategies are needed to reduce relapse and improve survival. Orca-T is an investigational precision cell therapy for treatment of hematological malignancies. In a Phase 1b clinical trial (NCT04013685), Orca-T exhibited an excellent safety profile and low rates of severe Graft-versus-Host disease (GVHD). In a Phase 3 prospectively randomized trial (NCT05316701), Orca-T met the primary endpoint of improving moderate-to-severe chronic GVHD-free survival in comparison to calcineurin inhibitor/methotrexate prophylaxis. The goal of the present study was to compare the clinical outcomes of myelodysplastic syndrome (MDS) patients who received either Orca-T or post-transplant cyclophosphamide (PTCy) for the control of GVHD.

Methods: The Orca-T patients in this study included all MDS patients in the Ph3 trial who received Orca-T and all MDS patients in the Ph1b trial who met the Ph3 eligibility criteria. For comparison to PTCy patients, a dataset was acquired from CIBMTR-NMDP. The PTCy patients in this study included those in the CIBMTR registry who had a diagnosis of MDS, received PTCy + tacrolimus ± mycophenolate, and had pre-transplant demographic and clinical profiles that were similar to the Orca-T patients. Additional inclusion criteria were ages 18-65, myeloablative conditioning regimen, and an 8/8 HLA-matched donor. We studied the following endpoints: overall survival (OS), relapse-free survival (RFS), GVHD and relapse-free survival (GRFS), moderate-severe chronic GVHD-free survival (cGFS), and the cumulative incidences of non-relapse mortality (NRM), relapse, grades 3-4 acute GVHD and moderate-severe chronic GVHD. Standard survival and competing risk methods were used; $p<.05$ defined significance.

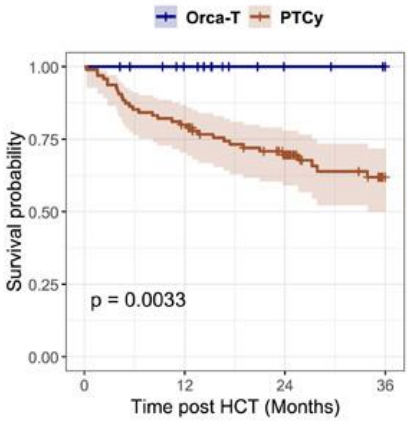
Results: Orca-T MDS patients (n=25), in comparison to PTCy MDS patients (n=95), exhibited increased OS (p=.003), increased RFS (p=.005), and decreased relapse (p=.026) (Table 1 and Fig. 1). The 1-year estimates for NRM, GRFS and gr. 3-4 aGVHD favored Orca-T, but did not reach statistical significance. The cumulative incidence of moderate-to-severe cGVHD was lower in the PTCy group, but cGFS was similar. The analysis consistently showed lower overall survival estimates for PTCy patients across various subgroups, defined by recipient age, sex, HCT-CI, KPS, and donor type. Thus, differences in demographic and clinical characteristics between the treatment groups are unlikely to explain the overall observed difference in OS.

Table 1. Clinical Outcomes.

Outcome[1]	Orca-T (N=25)	PTCy (N=95)	P-value[2]
Overall survival			**0.003**
1-year	100% (—%)	80% (70-87%)	
2-year	100% (—%)	70% (59-78%)	
3-year	100% (—%)	62% (50-72%)	
RFS	95% (69-99%)	64% (53-73%)	**0.005**
GRFS	67% (43-83%)	51% (40-61%)	0.11
NRM	0% (—%)	9.9% (4.8-17%)	0.11
Relapse	5.0% (0.31-21%)	26% (18-36%)	**0.026**

[1] 1-year estimate (95% CI)
[2] Log-rank test (survival) or Gray's test (cumulative incidence)

Figure 1. Overall Survival.



Conclusions: In conclusion, MDS patients treated with Orca-T, in comparison to PTCy, exhibited increased OS, increased RFS, decreased relapse, and decreased NRM. These observations provide evidence supporting the use of Orca-T for improved clinical outcomes.

Clinical Trial Registry: NCT05316701 https://clinicaltrials.gov/study/NCT05316701

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A086

MACROPHAGE ACTIVATION BEFORE LYMPHODEPLETION CAN PREDICT CRS, ICANS, AND LATE CYTOPENIA AFTER CD19 CAR-T CELL THERAPY FOR HEMATOLOGICAL CANCER

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Background: CAR-T cell therapy is challenged by immune-related toxicities, including cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity (ICANS), and late cytopenia. Growing evidence suggests that macrophage activation plays a key role in the pathophysiology of these toxicities. We investigated whether circulating markers of macrophage activation (soluble mannose receptor, sMR and sCD163) could predict the severity of CRS, ICANS, and late cytopenia after CD19 CAR-T therapy.

Methods: We included 35 patients treated with CD19 CAR-T therapy for B-ALL (*n*=14) or B-NHL (*n*=21) at Rigshospitalet in Denmark from 2019-2025 (Table). Patients received tisagenlecleucel (*n*=13), axicabtagene ciloleucel (*n*=10), or an academic CAR-T product (DK-CLIC-1901, *n*=12). sMR and sCD163 levels were measured using in-house ELISA assays in plasma collected before lymphodepleting chemotherapy (pre-LD), on day of CAR-T infusion, daily from day +1 to +8, and on days +10, +12, +14, and +90 post-infusion. 156 healthy controls with a median age of 27 years (range: 7.7-69) were included for comparison.

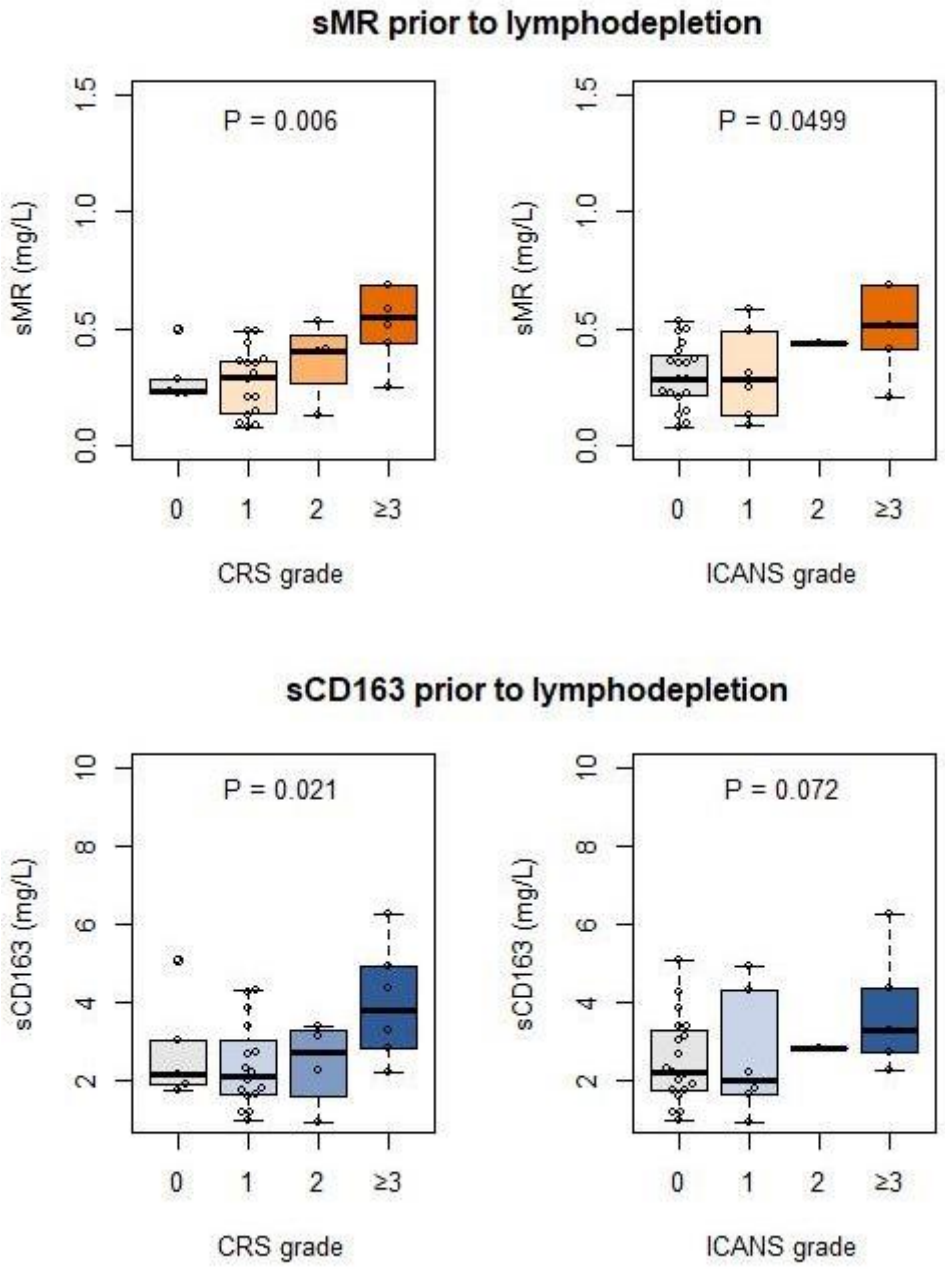
Patient and treatment characteristics	**N=35**
Age at infusion (years), median (range)	40 (1.7-71.8)
Male sex, n (%)	29 (82.9%)
Diagnosis, n (%) B-ALL B-NHL	14 (40.0%) 21 (60.0%)

No. of prior lines of therapy, median (range)	2 (1-5)
Prior HSCT, n (%) Allogeneic HSCT Autologous HSCT	7 (20.0%) 2 (5.7%)
Refractory to previous treatment line, n (%)	20 (57.1%)
Pre-LD LDH (U/L), median (range)	228 (142-2230)
Elevated pre-LD LDH, n (%)	19 (54.3%)
Bridging therapy, n (%) Chemotherapy-based regimens IT therapy only Radiotherapy ± steroids Targeted therapy Steroids only None	9 (25.7%) 5 (14.3%) 3 (8.6%) 4 (11.4%) 5 (14.3%) 9 (25.7%)
CAR-T product, n (%) Tisa-cel (Kymriah®) Axi-cel (Yescarta®) DK-CLIC-1901	13 (37.1%) 10 (28.6%) 12 (34.3%)
CAR-T dose (cells × 10^6/kg), median (range)	2.0 (0.23-4.8)

Days from leukapheresis to infusion, median (range)	33 (13-58)

Results: Pre-LD levels of sMR and sCD163 were significantly elevated in patients compared with healthy controls (median 0.35 vs. 0.18 mg/L, P<0.0001, and 2.32 vs. 1.45 mg/L, P<0.0001, respectively). After CAR-T infusion, both markers rose and peaked at day +6 for sMR (0.50 mg/L) and day +12 for sCD163 (4.1 mg/L). Pre-LD levels of sMR and sCD163 were not associated with diagnosis, prior lines of therapy, bridging therapy, or same-day CRP, IL-6 or LDH levels (all P≥0.05).
Grade ≥3 CRS and ICANS occurred in 17% and 14% of patients. sMR and sCD163 levels were significantly higher pre-LD in patients developing grade ≥3 CRS compared with grade 0-2 and tended to be higher in patients with grade ≥3 ICANS (Figure). In Cox regression analyses, the pre-LD levels of both markers were associated with increased risk of severe CRS (sMR: HR=2.7 per doubling, P=0.008; sCD163: HR=4.5 per doubling, P=0.034). Similarly, pre-LD sMR levels were associated with a higher risk of severe ICANS (HR=2.7 per doubling, P=0.027). Furthermore, high pre-LD LDH levels were associated with increased risk of severe CRS (HR=2.09 per doubling, P=0.011), while age, diagnosis, CAR-T product, and CAR-T cell dose were not associated with CRS or ICANS in our cohort.
Patients with grade ≥3 neutropenia (52% by ICAHT), thrombocytopenia (38%), and anemia (21%) between day +30 and +90 had higher pre-LD sMR levels compared with grade 0-2 (P=0.0008, P=0.002, and P=0.02, respectively), and higher pre-LD sCD163 levels were observed in patients with late grade ≥3 thrombocytopenia (P=0.04). In a logistic regression, higher sMR levels pre-LD were associated with increased risk of late grade ≥3 ICAHT (OR=7.2 per doubling, P=0.012) and prolonged grade ≥3 thrombocytopenia (OR=13.6 per

doubling, P=0.016).



Conclusions: Elevated levels of sMR and sCD163 before the start of lymphodepletion were associated with the development of severe CRS, ICANS, and late cytopenia in patients treated with CD19 CAR-T therapy, indicating a potential role as risk biomarkers. Our findings further support the emerging evidence of a role of activated macrophages in the

pathogenesis of CAR-T-related toxicities and point to macrophage-targeted interventions as a possible therapeutic strategy.

Disclosure: Nothing to declare.

A087

CAR-T BRIDGING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH REFRACTORY/RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Acute lymphoblastic leukemia (ALL) is the most common malignant tumor in children, accounting for 75%-80% of pediatric acute leukemia. Among these, 15%-20% of patients experience refractory or relapsed disease, resulting in extremely poor long-term prognosis. In recent years, the clinical application of CAR-T has improved prognosis for children with refractory or relapsed ALL. Furthermore,bridging hematopoietic stem cell transplantation (HSCT) following combination chemotherapy or CAR-T has significantly enhanced the long-term survival rates for these patients.Herein,we investigate the efficacy and safety of sequential allogeneic hematopoietic stem cell transplantation for pediatric patients with refractory/relapsed acute lymphoblastic leukemia (R/R ALL) who achieved CAR-T cell therapy.

Methods: A retrospective study was conducted on 40 pediatric R/R ALL patients who accepted allogeneic hematopoietic stem cell transplantation following CAR-T between January 2017 and October 2025 In West China Second University of Sichuan University.

Results: A total of 40 patients were enrolled, comprising 19 males and 21 females, with 38 cases of B-cell ALL and 2 cases of T-cell ALL.The median age of the enrolled patients was 4.5 (0.5-14.0) years.Among 40 patients,fifteen patients(38%) received CD7,CD19 or CD22 mono-target CAR-T, fourteen patients(35%) received CD19/CD22 dual-target CAR-T, and twelve patients(27%) received multi-target CAR-T, such as CD19/CD22/CD72 or CD19/CD22/CD133. Patient and transplant characteristics are shown in Table 1. All the patients received MRD remission after CAR-T therapy by flow cytometry except 3 patients still had positive fusion genes. In the transplantation group, donors included Haploidentical (n=25), Cord Blood (n=7), Matched Unrelated Donor (n=4), Matched Sibling Donor (n=3), and Mismatched Unrelated Donor (n=1). All patients achieved hematopoietic reconstitution. Neutrophil engraftment (defined as ANC≥0.5 *10^9/L for three consecutive days) was achieved at a median of 12(10-34) days post-transplant.The median time to platelet engraftment (defined as PLT≥20*10^9/L for 7 consecutive days without transfusion support) was 18(7-43)days.With a median follow-up of 20(1-92) months, the Overall Survival(OS) was 67%,and the Leukemia-Free Survival(LFS) rate was 61%.The OS was 49% for mono-target CAR-T group, 78% for dual-target CAR-T group, and 100% for multi-target CAR-T

group respectively. The OS was 68% for patients with negative fusion genes prior to transplantation, compared to 33% for those with positive fusion genes (p=0.04).The incidence of grade II-IV acute GVHD was 15%, and the incidence of chronic GVHD was 40%. Engraftment syndrome was observed in 27 patients.Ten patients experienced relapse, resulting in a cumulative incidence of relapse (CIR) of 33%. Among these, Two patients received donor-derived CAR-T therapy upon relapse and achieved remission again, with sustained monitoring showing negative MRD,while eight died after relapse. Among the eight deceased cases, six were from the mono-target CAR-T group and two from the dual-target CAR-T group.

Conclusions: CAR-T Bridging allo-HSCT can improve long-term survival in pediatric patients with R/R ALL. Among them, children who received dual-target or multi-target CAR-T therapy prior to transplantation appeared to have better outcomes than those who received mono-target CAR-T.Furthermore,whether the fusion gene is negative before transplantation is a key factor affecting the prognosis of pediatric patients.

Disclosure: Nothing to declare from all authors in relation to this study.

A088

OUTCOMES OF DONOR LYMPHOCYTE INFUSION FOR MEASURABLE RESIDUAL DISEASE AND RELAPSE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A SINGLE-CENTRE RETROSPECTIVE ANALYSIS

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Background: Donor lymphocyte infusion (DLI) is a key intervention for relapse after allogeneic stem cell transplantation (alloSCT). Identifying predictors of response and optimal timing remains critical to improving outcomes.

Methods:

We analysed 43 consecutive patients who received donor lymphocyte infusions (DLI) following allogeneic stem cell transplantation (alloSCT) for haematological malignancies between 2015 and 2025. Indications for DLI were categorised as frank relapse (n=30), measurable residual disease (MRD) relapse or persistence (n=7), or mixed chimerism (n=6). MRD relapse was defined by molecular disease detection in the absence of morphological relapse. Frank relapse was defined by ≥5% bone marrow blasts and/or the presence of extramedullary disease. Complete response (CR) was defined as morphological remission with <5% bone marrow blasts; CR with incomplete count recovery (CRi) and morphologic leukaemia-free state (MLFS) were included as CR. For MRD-directed DLI, response was defined as molecular MRD clearance, for mixed chimerism, response was defined as reversion to full donor chimerism. Survival analyses were landmarked from the date of first DLI . Primary endpoints were CR, overall survival (OS), and progression-free survival (PFS). Multivariable Cox regression was used to identify independent predictors of outcome.

Results: Baseline patient, disease, and transplant characteristics are summarised in Table 1. Median time from alloSCT to first DLI was 14.5 months(range 1.2–41.3), and median time from relapse to DLI was 1.6 months(range 0.2–16.9). The CR rate was 51.2%, significantly higher in MRD compared with frank-relapse indications (85.7% vs. 40.0%; p=0.042). Acute and chronic GVHD post-DLI occurred more frequently in responders (31.8% vs. 4.8%, p=0.046; 54.5% vs. 23.8%, p=0.062). Adjunct therapies were administered to 28 patients (65%), with a median of one agent (range 1–3); complete response rates were similar between adjunct-therapy and DLI-only groups (46.4% vs. 60.0%; p=0.53).

With a median follow-up of 25.0 months, median OS for the cohort was 10.4 months, with a 1-year OS of 43.2%. Patients receiving DLI pre-emptively for MRD relapse showed superior 1-year OS compared with frank relapse (85.7% vs. 33.5%; p=0.033). Median OS was 8 months in the frank-relapse group and was not reached in the MRD-relapse group (HR 0.14; 95% CI 0.02–1.04; p=0.05).

Patients receiving pre-emptive DLI for MRD relapse also demonstrated numerically superior disease control (median PFS 25 vs 8 months; 1-year PFS 62.5% vs. 31.6%; p=0.01).

In multivariable analysis, the development of chronic GVHD post-DLI independently predicted improved OS (HR 0.27; 95% CI 0.09–0.80; p=0.018) and PFS (HR 0.33; 95% CI 0.14–0.81; p=0.015). Age, number of DLI cycles, cumulative CD3+ dose, adjunct therapy, and acute GVHD did not independently impact survival.

Characteristic	N	Percentage
Total Patients (N)	43	100%
Median Age at Transplant	55 years (range 16–67)	-
Male : Female Ratio	1.26 : 1	-
Indications for AlloSCT		
AML	33	76.7%
B-ALL	3	7.0%
MDS/MPN	6	14.0%
CML	1	2.3%
European LeukemiaNet 2022 (AML)		
Adverse	14	42.4%
Intermediate	9	27.3%
Favorable	10	30.3%
Trackable MRD Marker (Y=1/N=0)		
Present	16	37.2%
Absent	26	60.5%
Disease Status at Transplant		
CR1	24	55.8%
≥CR2	9	20.9%
PR	2	4.7%
MLFS	1	2.3%
Active Disease	6	14.0%
Conditioning Regimen		
Myeloablative (MAC)	23	53.5%
Reduced Intensity (RIC)	20	46.5%
Donor Type		
Matched Related Donor (MRD)	20	46.5%
Matched Unrelated Donor (MUD)	18	41.9%
Mismatched Unrelated Donor (MMUD)	2	4.7%
Haploidentical Donor	3	7.0%

Conclusions: In our experience, DLI was associated with clinically significant response both when given alone or in combination with chemotherapy. Efficacy appears enhanced when administered preemptively for MRD relapse compared with frank relapse. The development of chronic GVHD post-DLI is a strong independent prognostic factor, highlighting a potent graft-versus-leukemia effect. These findings support the continued use of DLI for disease relapse after transplantation, as well as further investigation of the use of DLI to MRD relapse.

Disclosure: None to disclose.

A089

SECONDARY MALIGNANCY RISK AFTER ALLOGENEIC HSCT WITH PTCY OR ATG PROPHYLAXIS: A RETROSPECTIVE STUDY

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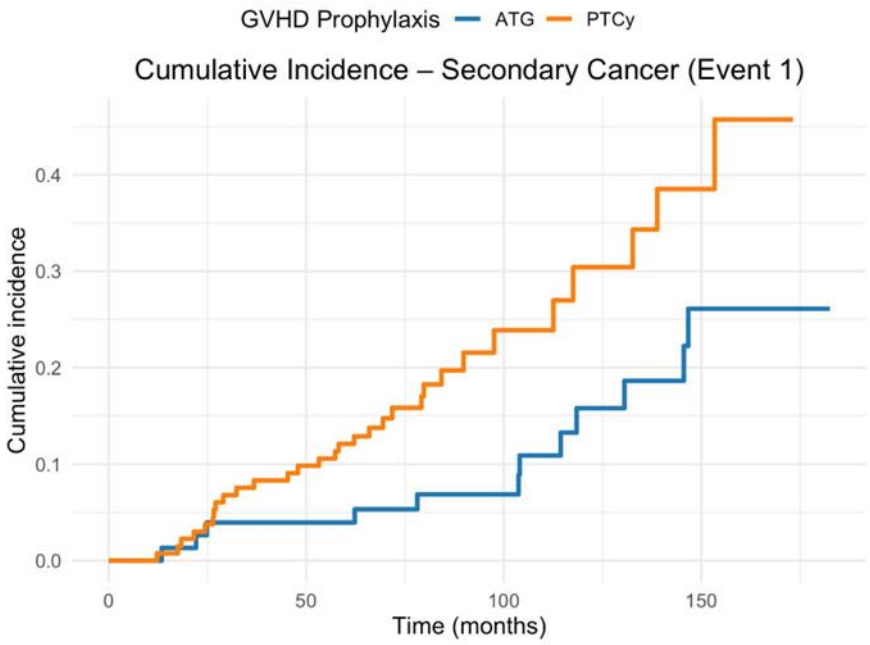
Background: Long-term survival after allogeneic stem cell transplantation has improved, but secondary malignancies have emerged as a major cause of late non-relapse mortality, underscoring the need for tailored lifelong surveillance.

Methods: We retrospectively analyzed 223 adults who underwent allo-HSCT between 2009 and 2019 and received either PTCy- or ATG-based GvHD prophylaxis. Only long-term survivors, defined as patients alive ≥2 years post-transplant, were included. The cumulative incidence of secondary malignancies, excluding basal cell carcinomas, was estimated using competing-risk methods (CIF), with death as the competing event. Group comparisons used Gray's test, and risk factors were evaluated through Fine–Gray subdistribution hazard models, with covariates reported with 95% confidence intervals.

Results: GvHD prophylaxis consisted of PTCy-based regimens in 144 patients (65%) or ATG-based in 79 patients (35%). Median age at transplant was 47 (31–72), and 59% of patients were male. Underlying diagnoses included acute myeloid leukemia (18%), acute lymphoblastic leukemia (8%), myelodysplastic syndromes (10%), non-Hodgkin lymphoma (31%), Hodgkin lymphoma (29%), aplastic anemia (1%), and myeloproliferative neoplasms (3%). At the time of allo-HSCT, 72% of patients were in complete remission, 14% were in partial response and 14% had stable or progressive disease. Conditioning included myeloablative (19%), non-myeloablative (27%), and reduced-intensity regimens (54%). Peripheral blood stem cells were used in 69% and bone marrow in 31%, with matched related (26%), matched unrelated (16%), and haploidentical donors (58%).
In total, 42 out of 223 patients (18,8%) developed a secondary cancer, 30 out of 144 (20,8%) in the PTCy group and 12 out of 79 (15,2%) in the ATG group. [Tab1]
With a median follow-up of 101 months, The 5-year cumulative incidence of secondary malignancies was significantly higher in the PTCy cohort than in the ATG group (9.8% vs 3.9%, respectively; p = 0.022) [Fig.1]. In multivariable Fine–Gray analysis, PTCy remained independently associated with increased risk (HR 2.16), while other clinical and transplant-related variables did not emerge as significant predictors. No predominant tumor subtype emerged.
The divergence in cumulative incidence curves became more pronounced after 50 months from transplant, and by 150 months the estimated cumulative risk reached 38.5% in the PTCy group versus 26.1% in the ATG cohort. Importantly, no significant differences were observed in the incidence of solid tumors of viral etiology between the two groups, suggesting that the excess risk is not driven by infection-related cancers.
Despite the higher incidence, survival outcomes were comparable: 5-year OS was 91% with PTCy versus 95% with ATG, and 5-year PFS was 86% and 89%, respectively. Subgroup

analyses showed no significant OS differences across disease status, donor type, stem cell source, or conditioning intensity. Age at transplant was not associated with secondary malignancy risk.



	PTCy	ATG
Patients in cohort, n	144	79
Secondary malignancies included in main analysis, n (%)	30 (20.8%)	12 (15.2%)
5-year cumulative incidence of secondary malignancies	9.8%	3.9%
p value	*	0.022
Estimated cumulative incidence at 150 months	38.5%	26.1%
Tumor subtype, n		
Melanoma	9	0
Squamous cell carcinoma (all sites)	9	5
Other solid tumors†	8	5
Hematologic malignancies‡	4	2
† *Other solid tumors* include: colon adenocarcinoma, breast carcinoma, prostate carcinoma, endometrial carcinoma, lung cancer (including adenocarcinoma), pancreatic cancer, GIST, malignant peripheral nerve sheath tumor, carcinoma of unknown primary		

‡ *Hematologic malignancies* include: myelodysplastic syndrome, acute myeloid leukemia, primary myelofibrosis, Hodgkin lymphoma, Burkitt lymphoma, marginal zone lymphoma

Conclusions: In this cohort of long-term allo-HSCT survivors, PTCy-based GvHD prophylaxis was associated with a significantly higher cumulative incidence of secondary malignancies compared with ATG. Furthermore, these findings underscore the need for enhanced, long-term cancer surveillance strategies, especially in patients receiving PTCy. This surveillance strategy as well as adherence to screening programs should be stressed also beyond the fifth post-transplant year.

Disclosure: No disclosure to declare.

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NOVEL PRECISION ALEMTUZUMAB DOSING RESULTS IN BETTER DAY 0 TARGET RANGE ACHIEVEMENT AND IMPROVED HSCT OUTCOMES IN IEI PATIENTS

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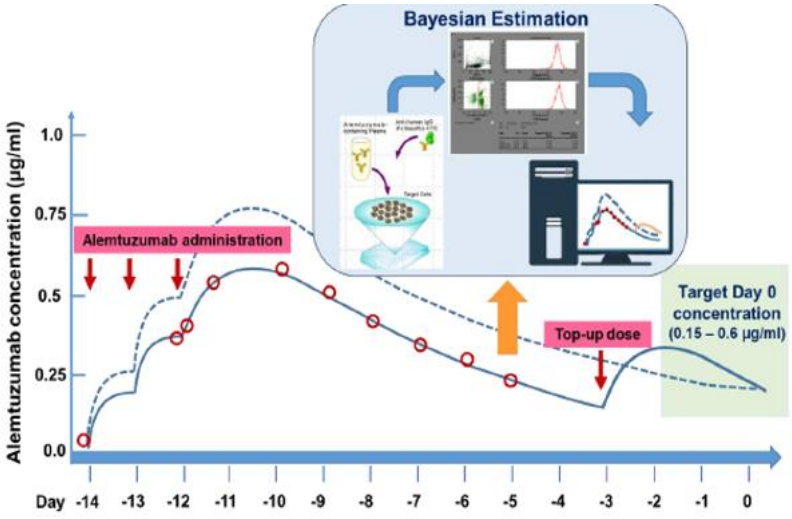
Background: Reduced intensity and reduced toxicity conditioning regimens offer low rates of toxicities and superior survival for patients with inborn errors of immunity undergoing allogeneic hematopoietic stem cell transplant (HCST). However, these approaches can be associated with increased rates of mixed chimerism and secondary graft loss. Peri-transplant alemtuzumab levels impact HCST outcomes; with low levels increasing the risk of acute graft versus host disease (GVHD) and high levels delaying immune reconstitution and increasing the risk of clinically significant mixed chimerism and secondary graft failure. We hypothesized that model-informed precision dosing of alemtuzumab with therapeutic concentration intervention (Precision Alemtuzumab Dosing) could achieve target Day 0 alemtuzumab levels of 0.15-0.9ug/mL in most patients, and minimize the risks of acute GVHD, clinically significant mixed chimerism, and secondary graft failure.

Methods: Prospectively enrolled patients were given model-informed initial alemtuzumab dosing of 10 mg/m2 divided over days -14 to -12. Alemtuzumab levels were measured through Day -5 or -4. Individual PK profiles were estimated using MW\Pharm software (version 2.4) based on our previously reported population PK model. Patients who were projected to clear alemtuzumab by Day 0 to <0.15ug/mL were given additional model-informed individualized "top-up" alemtuzumab dosing on Day -3 or -2 (Figure 1). Mixed chimerism was defined as a whole blood chimerism < 95% on two consecutive measurements within a 2-week period. Clinically significant mixed chimerism was defined as whole blood myeloid chimerism <50%. Secondary interventions evaluated included a CD34+ stem cell boost or a second transplant.

Results: Thirty-three patients of median age 3y2m years (range 3 months-32 years 9m) were treated. The underlying diagnoses and demographic information are presented in Table 1. Sixteen patients (49%) needed a top up dose, and twenty-four patients (73%) achieved Day 0 alemtuzumab levels within the optimal therapeutic range of 0.15-0.9ug/mL. Twenty-nine (88%) were evaluable for Day +100 outcomes. Two patients (7%) developed acute grade I GVHD. Ten patients (35%) experienced mixed chimerism and only one patient who had reactivated HLH during conditioning experienced clinically significant mixed chimerism in all lineages and subsequent secondary graft failure. Thirteen patients (40%) were evaluable for 1-year outcomes. Two patients (15%) had chronic limited skin GVHD. Six patients (46%) had mixed chimerism and only one (8%) had clinically significant mixed chimerism at one year. Five out of thirty-three patients (15%) received a CD34+ selected boost at a median of 6.5 months post-transplant at the discretion of the treating physician. The median myeloid chimerism was 47.8% (range 33%-78%) at the time of the boost.

Median age at transplant (range)	3y2m (43m-32y9m)
Gender Male Female	 16 (48%) 17 (52%)
Diagnosis HLH sJIA CGD WAS SAA XMEN SCID HyperIgE	 12 (36%) 10 (30%) 3 (9%) 3 (9%) 2 (6%) 1 (3%) 1 (3%) 1 (3%)
Preparative Regimen Alemtuzumab/Fludarabine/Melphalan/Thiotepa Alemtuzumab/Busulfan/Fludarabine	 27 (82%) 6 (18%)



Conclusions: Our novel precision alemtuzumab dosing is feasible and results in target range achievement in >70% of patients (compared to historic experience of approximately 25% of patients treated with standard-of-care alemtuzumab dosing regimens). It appears to result in low rates of acute GVHD, clinically significant mixed chimerism, and secondary graft failure at day +100.

Clinical Trial Registry: ClinicalTrials.gov ID NCT03302754.

Disclosure: This study is funded by the NIH - NIH 5R01HD107690-02
Pending patent applications related to precision alemtuzumab dosing for allogeneic HCT: US20230165958A1, EP4142755A1
Michael B. Jordan is a consultant and advisory board member for Novimmune, Sobi.
Ashish Kumar is a consultant for SOBI, Springworks therapeutics and OPNA
Blachy Davila Saldana served on the DSMB for Orchard Therapeutics; and is an ad hoc consultant for Sobi
Parinda Mehta is a board member at Orthogon Therapeutics
Rebecca Marsh is part time employed by Pharming Healthcare - not related to this study

A091

PRELIMINARY BASIS FOR A PREDICTIVE ALGORITHM OF REHABILITATION REQUIREMENTS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is among the most effective strategies for treating hematologic malignancies, and although the benefits of physical activity and rehabilitation are acknowledged across transplant phases, comprehensive and individualized rehabilitative care is still lacking.

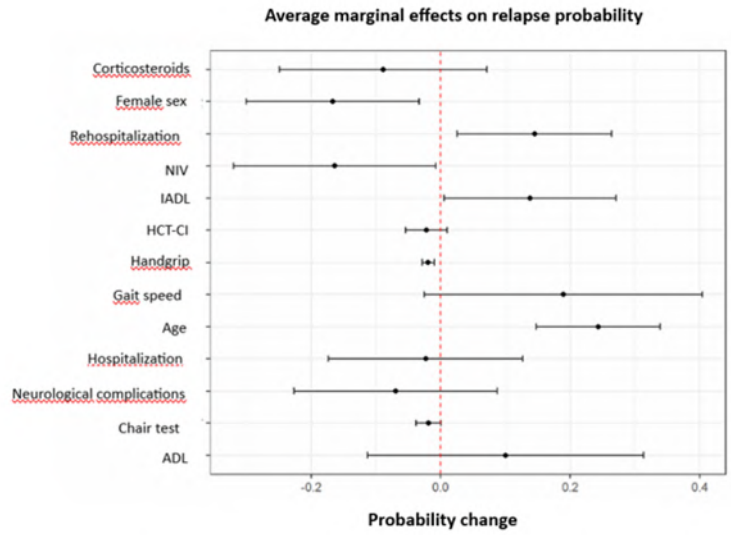
Methods: We therefore aimed to determine whether significant correlations exist among currently available clinical variables to identify the most informative predictors of rehabilitative needs in HSCT patients, with the long-term goal of using such predictors to develop an algorithm capable of early detecting rehabilitation requirements.
Clinical data from the hospitalization period of all patients undergoing allo-HSCT for any diagnosis at the ASST Spedali Civili di Brescia between November 2018 and February 2025 were retrospectively collected. The potential predictors analyzed included sex, age, Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), Patient-Generated Subjective Global Assessment (PG-SGA), 4-Meter Gait Speed, 30-Second Chair Stand Test, Handgrip strength, Activities of Daily Living (ADL), Instrumental Activities of Daily Living (IADL), need for non-invasive ventilation (NIV), onset of neurological complications, use of high-dose steroid therapy, length of hospital stay, and ICU admission. Surrogate endpoints considered indicative of rehabilitative need were relapse occurrence and post-transplant hospital readmission.

Results: Of the 190 patients evaluated, 181 were included in analyses for relapse and 141 for rehospitalization. In relapse comparison tests, relapsed patients showed higher median age (68.4 vs 65.5 years; p=0.032), greater proportion of individuals >60 years (92.1% vs 69.9%; p=0.005), and lower mean handgrip strength (27.9 vs 34.1 kg; p=0.005). In multivariate logistic regression with average marginal effects (AME), age >60 years emerged as the strongest predictor of relapse risk (OR: 17.76; CI: 2.83–362.30; p=0.011; AME: +0.243; p<0.001). Conversely, handgrip strength (OR: 0.86; CI: 0.78–0.93; p<0.001; AME: –0.019 per kg; p<0.001), female sex (OR: 0.23; CI: 0.05–0.90; p=0.042; AME: –0.166; p=0.015), and NIV use (AME: –0.164; p=0.040) were significantly associated with reduced relapse probability (Table and Image 1). Regarding readmission, prolonged hospitalization was the strongest predictor of increased risk (OR: 3.43; CI: 1.30–9.83; p=0.016; AME: +0.251; p=0.010), whereas NIV use (OR: 0.15; CI: 0.03–0.61; p=0.013; AME: –0.323; p=0.001) and gait speed (OR: 0.11; CI: 0.01–1.04; p=0.063; AME: –0.431; p=0.050) were associated with lower rehospitalization likelihood (Table and Image 1)**.**

Predictors	**Relapse**				**Rehospitalization**		
	OR	**95% CI**	**p-value**		**OR**	**95% CI**	**p-value**
Sex (female vs male)	0.23	0.05-0.90	0.042		0.38	0.08-1.75	0.219

Age	17.76	2.83-362.3	0.5		1.16	0.39-3.62	0.787
HCT-CI	0.84	0.64-1.08	0.189		0.83	0.64-1.07	0.163
PGS-GA day 1	-	-	-		1.58	0.58-4.45	0.376
PGS-GA day 28	-	-	-		2.27	0.67-8.55	0.202
Gait speed	4.48	0.91-37.94	0.095		0.11	0.01-1.43	0.105
Chair stand test	0.86	0.73-1.01	0.073		0.98	0.85-1.13	0.771
Handgrip	0.86	0.78-0.93	<0.001		1.03	0.97-1.10	0.350
ADL	2.48	0.29-35.22	0.440		0.55	0.04-7.27	0.641
IADL	3.77	0.81-23.39	0.116		0.38	0.07-2.07	0.263
NIV	0.20	0.01-1.29	0.152		0.14	0.02-0.68	0.022
Neurological complications	0.56	0.12-2.2	0.424		3.83	0.95-17.77	0.068
Days of hospitalization	-	-	-		3.81	1.12-14.86	0.039
High dose corticosteroids	0.47	0.09-1.94	0.325		0.47	0.09-1.94	0.325

Table 1



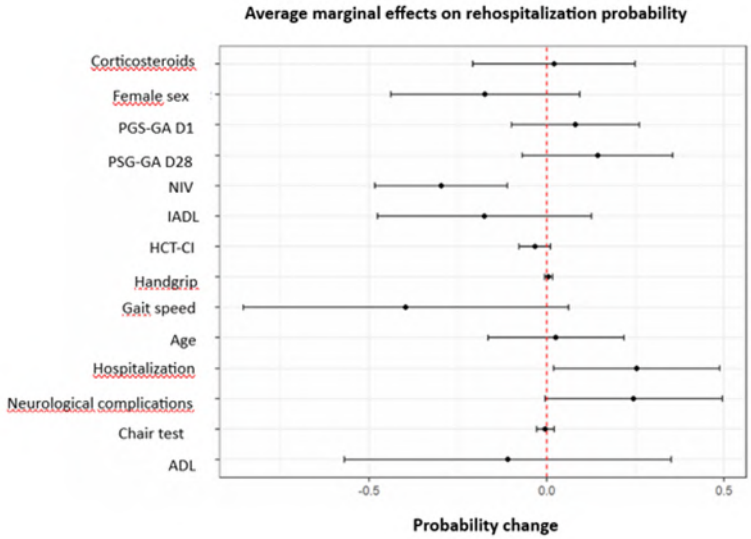


Image 1

Conclusions: Age, sex, handgrip strength, gait speed, NIV use, and hospital-stay duration emerge as significant predictors of rehabilitative needs in HSCT patients. Future prospective studies, focusing on longitudinal assessment of post-transplant evolution are required to

refine predictor selection based on current findings and literature evidence, validate the clinical and rehabilitative impact of identified predictors, and develop a predictive algorithm suitable for practical clinical implementation.

Disclosure: Nothing to declare.

A092

EMAPALUMAB IS ASSOCIATED WITH RAPID AND SUSTAINED BENEFITS IN PHLH SUBGROUPS, INCLUDING CNS INVOLVEMENT AND PREVIOUSLY UNTREATED PATIENTS: ANALYSIS OF TRIALS NI-0501-04, NI-0501-05 AND NI-0501-09

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Background: Emapalumab, a fully human anti-interferon-γ (IFNγ) monoclonal antibody, is FDA-approved for adult and children with primary hemaphagocitic lymphohistiocytosis (pHLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy. We present an expanded analysis of emapalumab treatment in pHLH, focusing on responses in previously untreated patients and in those with central nervous system (CNS) involvement.

Methods: We conducted a pooled analysis of 3 prospective studies (NI-0501-04 [2013 to 2019; n=45], NI-0501-05 [2021; n=37 of 45 in NI-0501-04], NI-0501-09 [2019 to 2022; n=35] for a total of 80 emapalumab-treated patients. Patients who received ≥3 emapalumab doses and had a recorded investigator assessment comprised the response-evaluable set at week 8/EOT (n=68) and the best response-evaluable set (n=74); those with ≥3-month follow-up formed the bridging-success survival set (n=70). Responses were based on treating investigator global assessments, classified as CR (complete response or non-active disease), PR (partial response or HLH improvement) or no response (NR; progressive disease, reactivation, worsening or death). Absolute risk differences (RD) were reported with 95% confidence intervals (CI) calculated with the Exact method and Fisher exact p values (α=0.05). Safety was not evaluated in this pooled analysis. Analyses were descriptive.

Results: Median patient age was 0.8 years (0.01–16.67); 54% were male. CNS involvement was present in 25/77 patients (32%); 27/80 (34%) were previously untreated.
CNS subgroup: At Week 8/EOT, 16/19 evaluable CNS-positive patients (84%) achieved OR (CR 16%, PR 68%), whereas 39/43 evaluable CNS-negative patients (91%) achieved OR (CR 26%, PR 65%). Best OR up to Week 8/EOT were 91% (CNS+) and 96% (CNS-). Median time

to first OR was 16 days in both groups. Bridging-success survival occurred in 15/23 CNS+ patients (65%) and 42/50 CNS- patients (84%), RD −18.8% (95% CI −42.5% to 2.7%; Fisher exact *p*=0.125).
Prior-treatment subgroup: Previously untreated patients (PUP) had an OR of 19/22 (86%) at Week 8/EOT (CR 23%, PR 64%) and 96% best OR up to Week 8/EOT (CR 29%, PR 67%); previously treated patients (PTP) had an OR of 36/40 (90%) at week 8/EOT(CR 22%, PR 68%) and 94% best OR (CR 34%, PR 60%). Median time to first OR was similar across both cohorts (15 days [PUP] and 16 days [PTP], respectively). Bridging-success survival for both cohorts was comparable (76% [PUP] vs 79% [PTP], RD −3.2% (95% CI −26% to 16.4%; Fisher exact *p*=0.772).

Conclusions: Emapalumab shows strong efficacy across pHLH subgroups. OR kinetics were similar across both CNS+ and CNS-, with many CNS+ patients responding and bridging to HSCT or sustaining control. Similar outcomes were observed between both PUP and PTP cohorts with pHLH.
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Clinical Trial Registry: NI-0501-04 (NCT01818492): A Phase 2/3, Open-label, Single Arm, Multicentre Study to Assess Safety, Tolerability, Pharmacokinetics and Efficacy of Intravenous Multiple Administrations of NI-0501, an Anti-interferon Gamma (Anti-IFNγ) Monoclonal Antibody, in Paediatric Patients with Primary Haemophagocytic Lymphohistiocytosis (HLH)
NI-0501-05 (NCT02069899): A Study for Long-term Follow-up of Hemophagocytic Lymphohistiocytosis (HLH) Participants Who Received Treatment With Emapalumab (NI-0501), an Anti-interferon Gamma Monoclonal Antibody
NI-0501-09 (NCT03312751): Study to Assess the Efficacy and Safety of Emapalumab in Primary Haemophagocytic Lymphohistiocytosis

Disclosure: Franco Locatelli: Speaker`s Bureau: Miltenyi, Amgen, Novartis, BMS, Gilead, Sobi; Advisory Board: Amgen, Novartis, Sanofi, Vertex; Michael B. Jordan: Honoraria: Sobi; Research Funding: Sobi; Didier Halimi: Consultancy: Sobi; Elena Burillo: employee: Sobi; Divested equity in a private or publicly-traded company in the past 24 months: Sobi; Current equity holder in publicly-traded company: Sobi; Brian D. Jamieson: Employee: Sobi, Inc.; Emmanuel Monnet: Patents: MerckSerono, Novimmune, Sobi; Divested equity in a private or publicly-traded company in the past 24 months: Sobi; Current equity holder in publicly-traded company: Sobi, Sanofi; Employee: Sobi; Andrew Danquah: Employee: Sobi.

A093

MAAT033 FOR GUT MICROBIOTA OPTIMIZATION TO IMPROVE SURVIVAL AFTER ALLOGENEIC HCT: THE PHOEBUS TRIAL

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Background: Allogeneic hematopoietic transplantation (alloHCT) is a well-established therapy for high-risk hematologic malignancies, with nearly 20,000 procedures reported annually to the European Society for Blood and Marrow Transplantation. Despite its effectiveness, outcomes are often limited by relapse, infections, graft-*versus*-host disease (GvHD) and conditioning-related toxicity. Emerging evidence suggests that gut microbiota diversity plays a critical role in reducing these complications and may even lower relapse risk. Fecal microbiota transplantation offers a promising strategy to restore microbial balance and improve clinical outcomes after alloHCT.

Methods: The PHOEBUS trial is a multi-center randomized, double blinded phase IIb trial evaluating the efficacy of MaaT033 in improving survival of adult alloHCT subjects (Clinicaltrials.gov identifier: NCT05762211).
MaaT033 is a freeze-dried, full-ecosystem, high-richness and diversity, fecal microbiota medicinal product, formulated as delayed-release capsules and derived from healthy pooled allogeneic human fecal material.
388 subjects aged ≥ 50 years with hematologic malignancies for which an alloHCT is indicated will be randomized 1:1 to receive either MaaT033 or placebo, before initiation of the conditioning regimen and after hematopoietic recovery following alloHCT. Stratification is based on the Disease Risk Index and donor-host compatibility.
Inclusion criteria comprise age ≥ 50 years, reduced-toxicity or intensity conditioning regimen, neutrophils >0.5 G/L, and administration of broad-spectrum antibiotics within the last 90 days prior to inclusion. Exclusion criteria comprise non-myeloablative and conventional myeloablative conditioning regimen, *in vitro* T-cell depletion, alloHCT with cord blood cells, use of alemtuzumab, vedolizumab or abatacept for GvHD prophylaxis, and history of chronic digestive disease.
Study recruitment is ongoing in France, Germany, Spain, Belgium, The Netherlands and the UK.

Results: The primary endpoint is evaluation of overall survival at 12 months after alloHCT. Key secondary endpoints include evaluation of GvHD-free survival, and GvHD-free/relapse-free survival at 12 months after alloHCT. Additional endpoints are assessment of the safety of MaaT033, cumulative incidence of acute and chronic GvHD, non-relapse mortality, incidence of severe infections, and quality of life. Exploratory endpoints are the evaluation of the effects of MaaT033 on immune recovery, nutritional status, and healthcare resource utilization.
Subjects receive MaaT033 or placebo (3 capsules/day) for 1 week before the start of the conditioning regimen. Experimental treatment is resumed at neutrophil recovery and pursued for up to 90 days after alloHCT. Subjects are followed for study assessments up to 12 months post-alloHCT, and thereafter every 6 months to monitor survival, relapse, and chronic GvHD. The study will conclude once all participants have at least 24 months of follow-up, unless death or early termination occurs.
Two interim safety analyses, conducted after the first 60 and 120 randomized subjects, were favorable, with no safety signals or excess 90-day post-alloHCT mortality attributable to MaaT033. Additionally, during its third meeting (July 2025), the Data and Safety Monitoring

Board, which meets every 6 months, reviewed the safety data and confirmed that MaaT033 has an acceptable safety profile, recommending that the trial continue as planned.

Conclusions: The PHOEBUS trial explores for the first time the potential of a full microbiota ecosystem therapy to enhance survival in alloHCT recipients. Recruitment is ongoing and preliminary safety assessments are favorable.

Clinical Trial Registry: EU-CT 2022-501831-18-00
https://clinicaltrials.gov/study/NCT05762211

Disclosure: Natalia Gemperle Ortiz and Emilie Plantamura: Employees of MaaT Pharma and holders of stock options in the company.
Joël Doré: Consultant for MaaT Pharma and holder of stock options in the company.

A094

DYNAMIC MONITORING OF THE PROGNOSTIC NUTRITIONAL INDEX (PNI) IN CAR-T THERAPY FOR RELAPSED/REFRACTORY LYMPHOMA: A RETROSPECTIVE STUDY

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Background: The prognostic nutritional index (PNI) is a well-established marker that reflects both nutritional status and systemic inflammation, and serves as a powerful predictor of survival and treatment response across various malignancies. However, evidence regarding the relationship between dynamic PNI changes and clinical outcomes in chimeric antigen receptor T-cell (CAR-T) therapy remains limited. This study investigated temporal changes in PNI during CAR-T treatment and evaluated its association with treatment-related toxicities and survival outcomes in patients with relapsed/refractory (R/R) lymphoma.

Methods: We retrospectively analyzed 372 patients who received CAR-T therapy in our department between December 2018 and January 2024. PNI was calculated using:
PNI = Serum albumin (g/L) + 5 × Lymphocyte count ($\times 10^9$/L).
PNI was measured at four time points: baseline before infusion (D0), and days 7, 14, and 21 after CAR-T infusion. Spearman correlations and logistic regression analyses were performed to assess associations between PNI, cytokine levels, and toxicities. Cox regression models were applied to evaluate the relationship between PNI and survival outcomes.

Results: A total of 372 patients were included (53.0% male; median age 51). Subtypes included DLBCL (n=223), FL (33), PCNSL (23), HGBL (24), PMBL (17), BL (14), and others (51). Median BMI was 22.6 kg/m². ECOG ≥2, IPI ≥3, and stage III–IV were observed in 32.3%, 38.7%, and 91.1% of patients.

After CAR-T infusion, CRS occurred in 76.9% (grade ≥3: 7.0%), and ICANS in 3.0% (grade ≥3: 1.3%). Grade ≥3 cytopenias included neutropenia (43.3%), anemia (33.1%), and thrombocytopenia (11.6%).

PNI dynamics

PNI was stable at baseline, declined sharply to nadir by day 7, and partially recovered by day 21.

PNI and CRS

Lower PNI correlated with more severe CRS, with day-7 PNI showing the strongest association ($P<0.0001$). Baseline, day-14, and day-21 PNI were also significant.

PNI and cytopenias

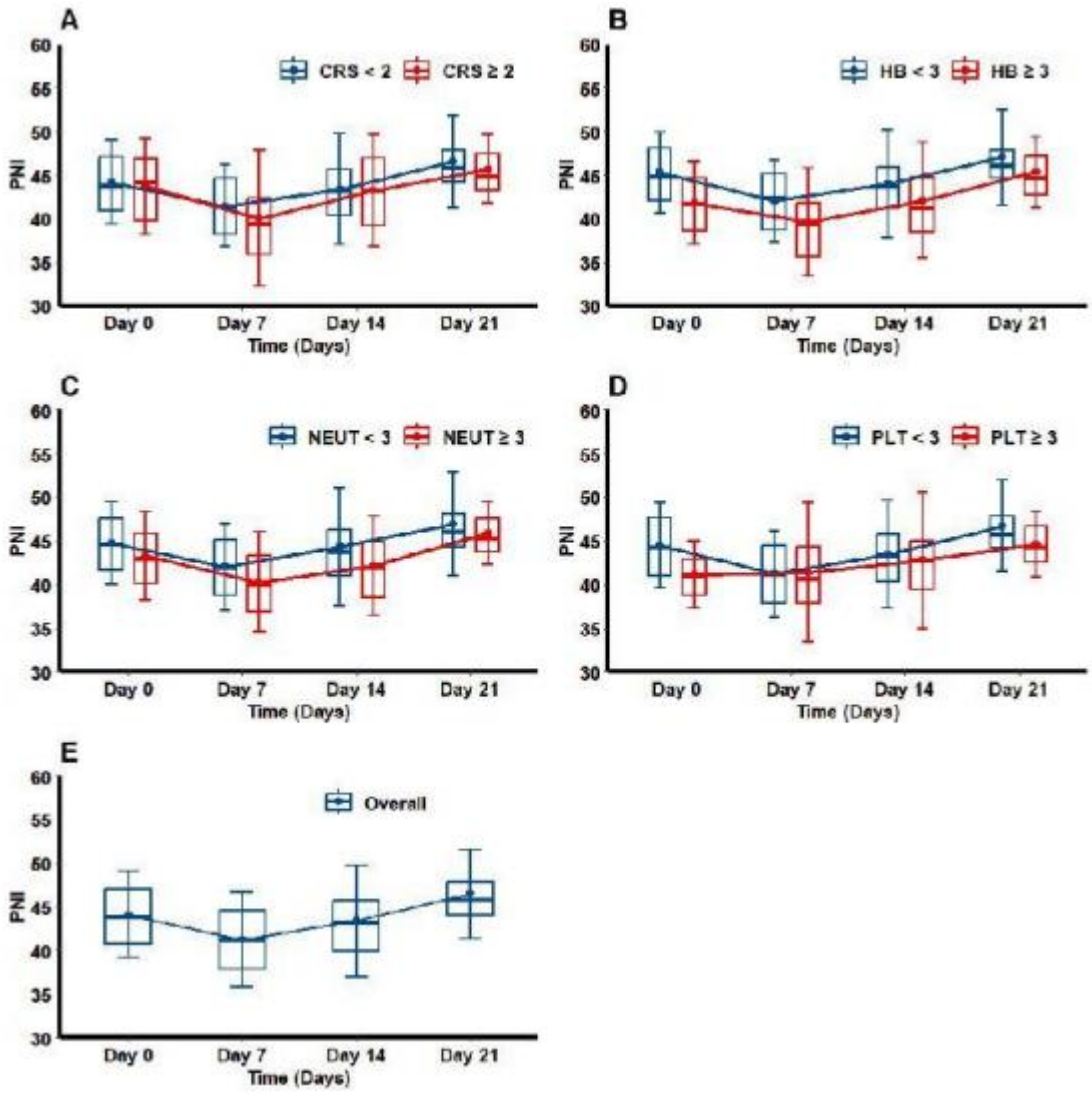
Patients with grade ≥3 neutropenia, anemia, or thrombocytopenia had consistently lower PNI at all timepoints (all $P<0.01$). Baseline PNI independently predicted hematologic toxicity:

- Anemia: OR=0.871, $P<0.001$
- Neutropenia: OR=0.955, $P=0.048$
- Thrombocytopenia: OR=0.867, $P<0.001$

Survival outcomes

At 30.84 months of follow-up, median PFS was 11.11 months; median OS was not reached. Five-year PFS and OS were 40.87% and 53.25%.

PNI at D0, D7, and D14 significantly predicted PFS and OS in univariate analyses. In multivariate models, PNI at D0, D7, and D14 independently predicted OS, while only baseline PNI predicted PFS.



Conclusions: This study demonstrates that PNI undergoes distinct dynamic changes during CAR-T therapy in patients with R/R lymphoma. Lower PNI levels—both at baseline and during treatment—are strongly associated with more severe CRS, higher rates of hematologic toxicities, and poorer long-term survival. A rapid decline in PNI during the early treatment period may serve as an early warning indicator for high-risk patients. Integrating PNI into routine monitoring may improve risk stratification and support individualized clinical management during CAR-T therapy.

Disclosure: Nothing Disclosure

A095

CIRCULATING TUMOR DNA (CTDNA) AND IL-10 OR IL-10/IL-6 RATIO DYNAMIC MONITORING FOR PREDICTING RELAPSE IN RELAPSED/REFRACTORY CNS LYMPHOMA: A RETROSPECTIVE COHORT STUDY

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Background: Central nervous system lymphoma (CNSL) carries a high risk of relapse in the relapsed/refractory setting. Early identification of impending relapse may offer a crucial window for timely clinical intervention. This study evaluated the predictive value of serial cerebrospinal fluid (CSF) circulating tumor DNA (ctDNA), interleukin-10 (IL-10), and the IL-10/IL-6 ratio for relapse in patients with CNSL undergoing CAR-T cell therapy or other treatment modalities.

Methods: We retrospectively analyzed 46 patients with CNSL (primary CNS lymphoma [PCNSL], n = 33; secondary CNS lymphoma [SCNSL], n = 13) treated at Beijing GoBroad Hospital between August 1, 2023, and August 1, 2025. CSF samples were collected at baseline and at multiple time points for ctDNA assessment, flow cytometry, and cytokine profiling. Tumor-specific immunoglobulin gene rearrangements were used to track ctDNA and were compared with imaging and clinical relapse. The median age was 56 years (range, 35–75), and 50% were male. Treatments included autologous stem-cell transplantation (ASCT; n = 13), CAR-T therapy (n = 16), ASCT combined with CAR-T therapy (n = 14), and chemotherapy (n = 3). The median number of ctDNA tests per patient was 1.5 (range, 1–9), and cytokine tests 1 (range, 0–9).

Results: Among the 46 patients, 12 (26.1%) experienced relapse, with 11 detected radiographically and 1 detected by flow cytometry. Of the 12 relapsed patients, 5 (42%) were ctDNA-positive, including 2 patients in whom ctDNA positivity preceded radiographic relapse by an average of 109 days (91–127 days). Seven relapsed patients were ctDNA-negative, and two patients had ctDNA positivity without subsequent relapse.
The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy of ctDNA for relapse prediction were 41.7% (5/12), 94.1% (32/34), 71.4% (5/7), 82.1% (32/39), and 80.4% (37/46), respectively. Fisher's exact test showed a highly significant association between ctDNA status and relapse ($P = 0.009$).ROC curve analysis demonstrated predictive value for CSF IL-10 and IL-10/IL-6 ratio, with AUCs of 0.850 and 0.791, respectively (both $P < 0.05$). The optimal cutoffs for relapse prediction were 1.765 pg/mL for IL-10 and 0.275 for the IL-10/IL-6 ratio. Among the 43 patients with cytokine measurements, the sensitivity, specificity, PPV, NPV, and accuracy for IL-10 and IL-10/IL-6 ratio were 70.0% (7/10), 69.7% (23/33), 41.2% (7/17), 88.5% (23/26), and 69.8% (30/43), respectively. Elevated IL-10 or IL-10/IL-6 ratio was significantly associated with relapse ($P = 0.034$).

Conclusions: CSF ctDNA, IL-10, and the IL-10/IL-6 ratio are significant biomarkers for predicting relapse in CNSL. ctDNA demonstrated the highest specificity and PPV, and ctDNA positivity—particularly when preceding radiographic progression—may serve as an early warning indicator of relapse. In contrast, IL-10 and the IL-10/IL-6 ratio exhibited higher sensitivity and complement the predictive limitations of ctDNA. Both biomarkers showed strong NPVs, underscoring their utility in identifying patients at low risk of relapse. While ctDNA displayed superior overall performance, integrating both ctDNA and cytokine-based markers may enhance relapse prediction in clinical practice for CNSL patients.

Disclosure: Nothing to disclosure

A096

A FIRST-IN-HUMAN STUDY OF HLA-PARTIALLY TO FULLY MATCHED ALLOGENEIC CRYOPRESERVED DECEASED DONOR BONE MARROW TRANSPLANTATION FOR PATIENTS WITH HEMATOLOGIC MALIGNANCIES

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Background: Cryopreserved bone marrow hematopoietic progenitor cells (HPCs) can serve as valuable option to address unmet needs in allogeneic hematopoietic cell transplants (HCT). PRESERVEI (NCT05589896) evaluates cryopreserved, minimally manipulated allogeneic HPCs from deceased donor vertebral body bone marrow (BM) across 4/8–8/8 HLA-matched grafts. These cells are processed using minimal manipulation. This report provides prespecified interim data for Cohort 1 (n=4).

Methods: Four hematologic malignancy patients received donor HPC, marrow. Transplants were performed using 4/8 HLA-matched grafts for patient 1, 3 & 4, and 5/8 HLA-matched for patient 2. CD34+ cell doses were 5.72, 6.11, 5.22, and 7.53 X 10^6 cells/kg, respectively. Graft-versus-host disease (GVHD) prophylaxis included tacrolimus, mycophenolate mofetil (MMF), and post-transplant cyclophosphamide (50 mg/kg on Days +3 and +4). Neutrophil and platelet engraftment times were recorded; safety and GVHD were monitored; relapse and death were tracked.

Results: Patient 1 (age 52, T cell ALL) and patient 2 (age 62, AML) received myeloablative conditioning (MAC) while patient 3 (age 47, HTLV- ATLL) received reduced-intensity conditioning (RIC). Patient 4 (age 58, MDS) received RIC regimen.
Neutrophil engraftment was observed on Days +15, +17, +17 and +17; platelet engraftment observed on Days +18, +28, +20, and +27, respectively for the four patients. No clinically

significant local toxicity reported on day of infusion Grade 1 skin acute GVHD manageable with steroids was reported for patient 4 on day 49 and resolved on day 52. No grade III-IV acute GVHD, or severe chronic GVHD relapse, or death have been reported at the time of initial analysis. Mild chronic GVHD reported in patient 2 manifested by thrombocytopenia, peripheral edema and dysphagia, the patient was managed by methyl prednisone with resolution of symptoms. Secondary graft failure was reported for patient 3 after viral reactivation which was considered not related to the HPC marrow graft. No patient in cohort 1 met prespecified stopping rules.

Table 1: Patient demographics and characteristics for Cohort 1 patients

Patient	Age (years)	Gender (M/F)	Race	Disease	Conditioning Regimen (MAC vs. RIC)	CD34+ Dose (x10^6/kg)
Patient 1	52	Male	Asian	T-cell ALL (CR1)	MAC	5.72
Patient 2	62	Female	White	AML (CR1)	MAC	6.11
Patient 3	47	Female	White	HTLV-ATLL (CR1)	RIC	5.22
Patient 4	58	Male	African American	AML (CR1)	RIC	7.53

CR: Complete Remission, **RIC:** Reduced-Intensity Conditioning), **MAC:** Myeloblative Conditioning

Fig 1: PRESERVE I Cohort 1 patient journey
* Bone Marrow Chimerism

Conclusions: These preliminary encouraging data from cohort 1 demonstrate that transplantation of the cryopreserved off the shelf HPC, marrow cells from deceased donors is feasible and safe for infusion. The interim cohort 1 data highlights the potential of this novel graft source for patients with unmet medical needs. Cohort 2 will proceed per the protocol to further evaluate safety and early efficacy.

Clinical Trial Registry: NCT05589896

Disclosure:

1. Sagar Munjal is an employee of Ossium Health
2. Sagar Patel – Nothing to declare
3. Shahbaz Malik – Nothing to declare
4. Uttam Rao – Nothing to declare
5. Taiga Nishihori – Nothing to declare
6. Preethi Prasad is an employee of Ossium Health
7. Vicki L. Graves is an employee of Ossium Health
8. W. Scott Goebel is a consultant to Ossium Health
9. Erik J. Woods is an employee of Ossium Health

A097

UPFRONT TRANSPLANTATION VS. INTENSIVE REMISSION INDUCTION IN MDS/AML, MDS-EB AND OLIGOBLASTIC AML - LIMITED PREDICTIVE VALUE OF BLAST COUNT AT DIAGNOSIS

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Background: Patients with myelodysplastic neoplasms/acute myeloid leukemia (MDS/AML, ICC2022), MDS with Excess Blasts (MDS-EB) and oligoblastic AML with myelodysplasia-related changes (AML-MR, ICC2022) respond poorly to induction chemotherapy. Furthermore, complications of induction chemotherapy may cause early mortality or morbidity with only 50-60% of patients reaching potentially curative allogeneic hematopoietic stem cell transplantation (alloHSCT). Recent prospective evidence from the ETAL3-ASAP trial supports upfront alloHSCT in relapsed or refractory AML, but there is a lack of evidence to guide this decision at first diagnosis.

Methods: We retrospectively analyzed 232 patients with MDS/AML, MDS-EB and AML-MR with diagnostic bone marrow (BM) blast counts >5% who underwent alloHSCT at our center between 2007 and 2023. Cox regression models were fitted for overall survival (OS), and propensity score matching was used to further adjust for differences in baseline characteristics.

Results: 176 of 232 (75.9%) patients received intensive induction (induction group), while 56 of 232 (24.3 %) underwent upfront alloHSCT (upfront group). There were no differences between groups in age at alloHSCT, sex, HCT-CI score, conditioning intensity and donor matching. Patients in the upfront vs. the induction group more often had favorable ELN risk (18.9% vs. 8.1%, p = 0.058), BM blast counts <20% at diagnosis (81.8% vs. 7.5%, p<0.001), and more frequently showed a Karnofsky performance index (KPI) of 100% (31.5% vs. 17.3%, p = 0.042).Five-year OS was comparable in the upfront group vs. the induction group (57.2% vs. 45.7%, p=0.1). While blast counts at initial diagnosis were not associated with OS (HR 1.39 [0.66-2.94], p=0.389), there was a significant association of blast counts >5% at alloHSCT with inferior OS (HR 1.68, [1.14-2.46], p = 0.008).Interestingly, within the upfront group 5y-OS was not associated with blast counts at alloHSCT <5% vs. 5-9% vs. 10-20% vs. >20% (58.2% vs. 53.5% vs. 50% vs. 68.2%, p =

0.6). Multivariate analysis confirmed ELN risk as a good predictor of OS (HR 2.23 [1.02-5.23], p = 0.045), while application of induction therapy was not associated to outcome (HR 1.12, [0.69-1.81], p=0.637). Furthermore, there was no difference in 5-year OS between patients in remission after induction and patients in the upfront group (59.6% vs 57.2%, p =0.95).

To adjust for potential selection bias in the upfront group, we matched 21 patients in the upfront group to 131 patients in the induction group based on ELN risk, diagnostic BM blast count, and KPI. There were no significant differences between matched patients from the upfront vs. induction group in 5-year OS (38.1% vs. 47.2%, p = 0.98), RFS (47.1% vs. 48.2%, p = 0.89), relapse incidence (32.9% vs 23.4%, p = 0.5), and NRM (32.3% vs 34.3%, p = 0.58), respectively.

Table 1	Variable	Category	n	Overall	Induction	Upfront	p value
Patient characteristics	Age at alloHSCT, years	Mean (SD)	232	56.5 (12.1)	56.3 (12.5)	57.1 (10.6)	0.679
	Sex	Male	232	130 (56.0%)	99 (56.2%)	31 (55.4%)	1.000
		Female		102 (44.0%)	77 (43.8%)	25 (44.6%)	
	Karnofsky performance status	100	216	45 (20.8%)	28 (17.3%)	17 (31.5%)	0.042
		<100		171 (79.2%)	134 (82.7%)	37 (68.5%)	
	HCT-CI	0	226	130 (57.5%)	98 (57.0%)	32 (59.3%)	0.890
		>0		96 (42.5%)	74 (43.0%)	22 (40.7%)	
Disease characteristics	Blasts at diagnosis	5–9% MDS-EB	214	21 (9.8%)	5 (3.1%)	16 (29.1%)	<0.001
		10–19% MDS/AML		36 (16.8%)	7 (4.4%)	29 (52.7%)	
		20–29% AML		26 (12.1%)	22 (13.8%)	4 (7.3%)	
		30–49% AML		35 (16.4%)	34 (21.4%)	1 (1.8%)	

Table 1	Variable	Category	n	Overall	Induction	Upfront	p value
		≥50% AML		96 (44.9%)	91 (57.2%)	5 (9.1%)	
	Cytogenetics	Normal	226	68 (30.1%)	41 (24.1%)	27 (48.2%)	0.001
		Abnormal		158 (69.9%)	129 (75.9%)	29 (51.8%)	
	ELN risk	Favorable	225	24 (10.7%)	14 (8.1%)	10 (18.9%)	0.058
		Intermediate		63 (28.0%)	52 (30.2%)	11 (20.8%)	
		Adverse		138 (61.3%)	106 (61.6%)	32 (60.4%)	
Treatment characteristics	Conditioning intensity	RIC	230	202 (87.8%)	153 (87.4%)	49 (89.1%)	0.926
		MAC		28 (12.2%)	22 (12.6%)	6 (10.9%)	

Table 1. Baseline patient, disease, and treatment characteristics of the cohort

Conclusions: Our results further question the use of diagnostic blast counts as a suitable criterion to allocate patients with MDS/AML and oligoblastic AML-MRC to intensive remission induction prior to alloHSCT.

Disclosure: Nothing to declare.

A098

IMPACT OF POST-TRANSPLANT INTRATHECAL THERAPY ON CENTRAL NERVOUS SYSTEM RELAPSE IN ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: It is well established that central nervous system (CNS) relapse after allogeneic hematopoietic stem cell transplantation (HSCT) carries a very poor prognosis in adults with acute lymphoblastic leukemia (ALL), but isolated CNS relapses remain uncommon. There is no clear consensus regarding the benefit of administering post-transplant IT prophylaxis.

Methods: Multicenter retrospective study that reviewed across 5 Spanish centers, 126 patients aged ≥18 years with ALL who underwent allogeneic HSCT from 2014 to 2025. All patients had received pre-HSCT IT therapy as part of standard treatment protocols and part of the cohort routinely received post-transplant CNS prophylaxis.
The objective was to evaluate the association between post-HSCT IT prophylaxis and CNS relapse, and to identify additional associated factors.

Results: Baseline characteristics are described in Table 1. Seventy-eight patients were male (38%). The median age at diagnosis was 40 years (IQR, 26–51).
The most frequent ALL subtype was Ph-negative, followed by Ph-positive ALL and T-ALL (62 (49.2%), 33 (26.2%), and 23 (18.3%) patients respectively).
Thirty patients (23%) received immunotherapy prior to transplantation.
The median number of pre-HSCT treatment lines was 1 (1–2), and most patients were treated according to PETHEMA protocols.
The median time from diagnosis to transplant was 6 months (IQR 5–11).
At transplant, 75% of patients were in first complete remission, achieving MRD negativity 70%.
Most patients received myeloablative conditioning (103 (82%)), predominantly TBI-based (63%). The median number of pre-HSCT IT was 4 (3–7), and 59 (47%) of the patients received >4 doses.
Seventeen patients (13.5%) received peri-transplant IT during conditioning, and 35 (28%) received post-HSCT prophylactic IT with a median of 4 doses (2–5).
With a median follow-up of 56 months (21–81), OS was 50%. Thirty-four patients (27%) relapsed (30 medullary relapses, and 4 combined relapses) with a median time to combined relapse of 7.5 months (4–13.25). No patient presented with isolated CNS relapse.
Among the 4 patients who experienced combined relapse, two had T-ALL, one Ph-negative ALL with a KMT2Ar, and one MPAL. None had CNS involvement at initial diagnosis.
Two patients underwent HSCT in first complete remission, and three were MRD-negative at transplant.
Overall survival, relapse-free survival, and non-relapse mortality at 2 years were 68% (95% CI, 58–75), 69% (59–77) and 21% (14–29) respectively, Figure 1. The cumulative incidence of relapse at 2 years was 31% (23–41), and the incidence of combined relapse 4% (2–11).
Post-HSCT IT prophylaxis was not associated with a reduced risk of CNS relapse (CI of CNS relapse at 2 years 0% vs 6% (95% CI, 2–16, p=0.20) and no isolated CNS relapses were observed in either group.
Regarding toxicity related to IT, one patient experienced cognitive impairment, other developed a cerebrospinal fluid fistula, and a third patient developed subcortical leukoencephalopathy in the context of TBI and IT.

Variables	**N=126**

Male sex, n (%)	78 (61.9%)
Age at ALL diagnosis, median (IQR), years	40 (26–51)
ALL subtype, n (%) Ph− B-ALL Ph+ B-ALL T-ALL Other / MPAL	 62 (49.2%) 33 (26.2%) 23 (18.3%) 8 (6.3%)
CNS disease at diagnosis, n (%)	18 (14.3%)
WBC at diagnosis, median (IQR), $\times 10^9$/L	13.6 (4.2–87.1)
Cytogenetics, n (%) Diploid Low hypodiploidy / near-haploidy Complex (≥5 abnormalities) Unknown / not available	 11 (8.7%) 6 (4.8%) 7 (5.6%) 65 (51.6%)
TP53 mutation/deletion, n (%)	4 (3.2%)
First-line protocol, n (%) PETHEMA 2003 / 2008 / 2011 / 2019 / 2022 Hyper-CVAD / FLAG-IDA / clinical trial / others	 3 (2.4) / 15 (12) / 31 (24.6) / 41 (32.5) / 7 (5.6) 5 (4) / 6 (4.8) / 17 (13.4) / 1 (0.8)
TKI, n (%) Imatinib Dasatinib Ponatinib	 30 (83%) 2 (6%) 4 (11%)
Blinatumomab/Inotuzumab before HSCT, n (%)	19 (15%) / 11 (8,7%)
Disease status at HSCT, n (%) CR1 CR2 >CR2 / Refractory MRD-negative pre-HSCT, n (%) MMR (for Ph+ or *Ph-like*), n (%)	 95 (75%) 28 (22%) 1 (0.8%) / 3 (2.4%) 103 (82%) 35/36 (97%)
Transplant characteristics	
Conditioning regimen Myeloablative n (%) / TBI-based	103 (82%) / 80 (63%)
Stem cell source, n (%) Peripheral blood / Bone marrow	 97 (77%) / 29 (23%)

Donor type, n (%)	
Matched 10/10	79 (63%)
Mismatched	20 (16%)
Haploidentical	27 (21%)
GVHD prophylaxis, n (%)	
ATLG	56 (44%)
Post-transplant cyclophosphamide	29 (23%)
CNI + MTX	64 (51%)
CNI + MMF	29 (23%)
Other	4 (3%)
IT administered pre-HSCT, median doses (range)	4 (3–7)
>4 ITs	59 (47%)
≤4 ITs	67 (53%)

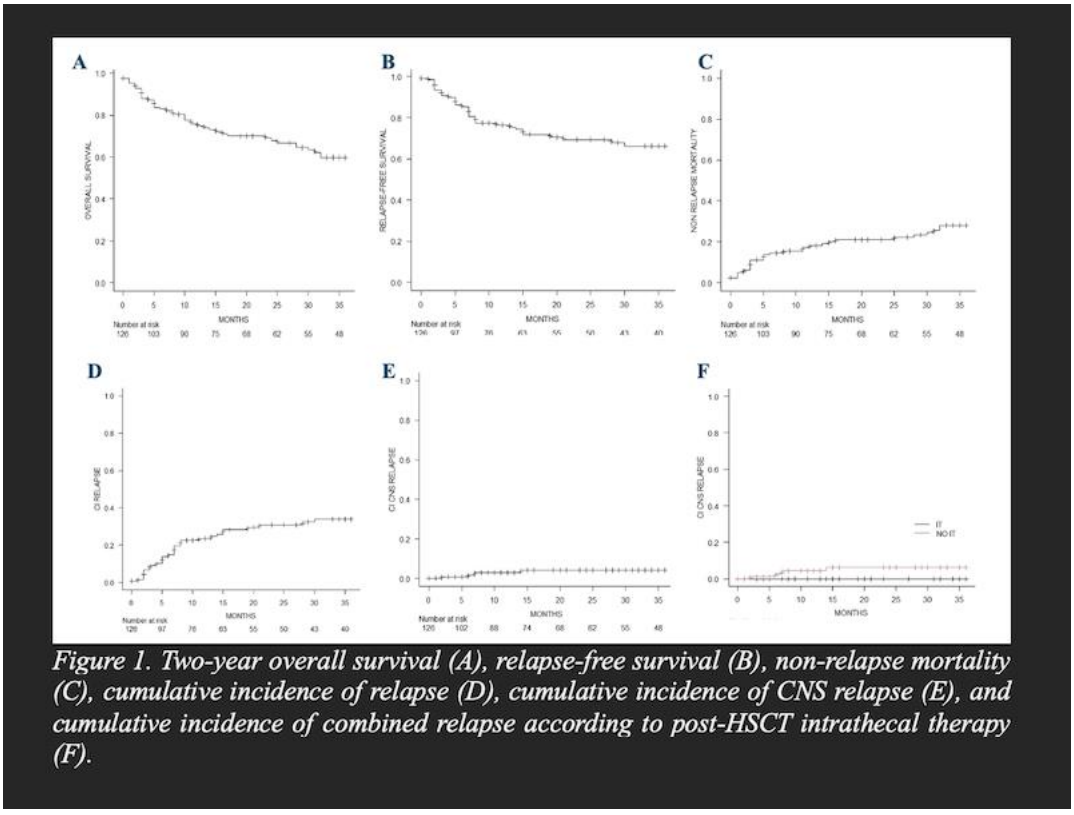

Figure 1. Two-year overall survival (A), relapse-free survival (B), non-relapse mortality (C), cumulative incidence of relapse (D), cumulative incidence of CNS relapse (E), and cumulative incidence of combined relapse according to post-HSCT intrathecal therapy (F).

Conclusions: Peri- or post-HSCT prophylactic IT therapy was not associated with a reduced risk of isolated CNS relapse in this predominantly TBI-based myeloablative transplant cohort; therefore, given its potential morbidity, its use should be individualized.

Disclosure: Nothing to declare.

A099

TIMING OF CALCINEURIN INHIBITOR–MMF AFTER HAPLOIDENTICAL TRANSPLANTATION WITH PTCY: RESULTS OF A PHASE II RANDOMIZED STUDY

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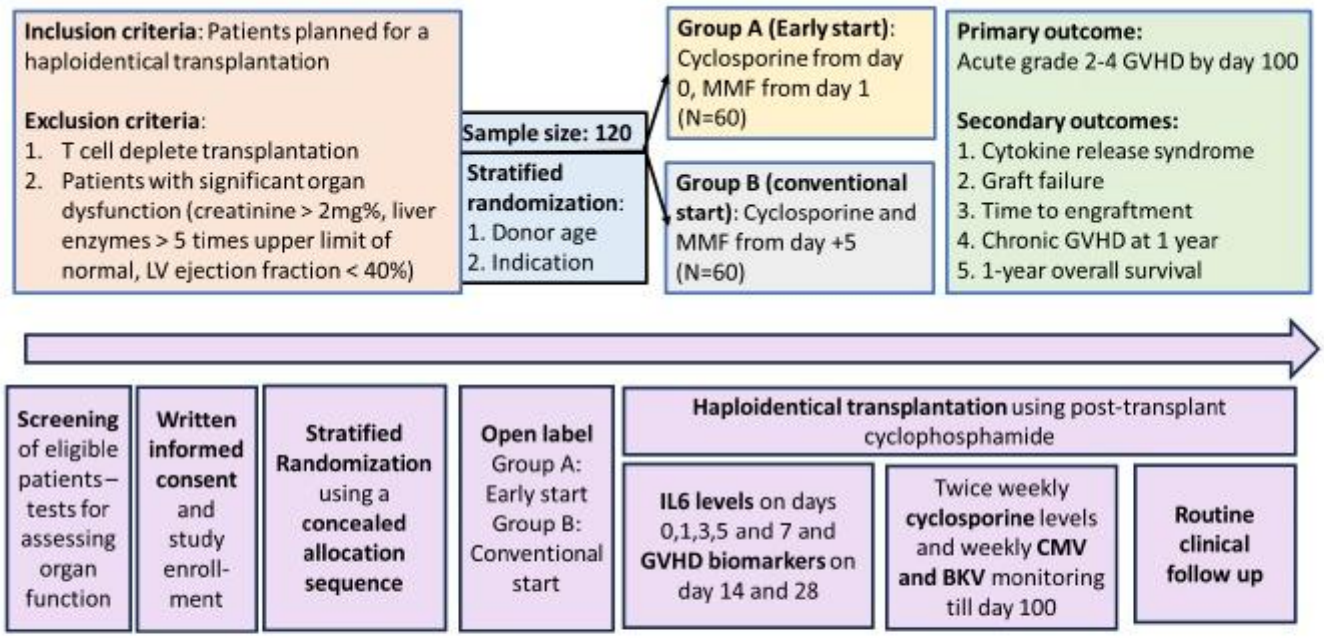
Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) using post-transplant cyclophosphamide (PTCy) has broken immunological barriers and expanded access to transplantation but remains associated with a high incidence of cytokine release syndrome (CRS) and acute graft-versus-host disease (aGVHD). Conventionally, calcineurin inhibitors (CNI) and mycophenolate mofetil (MMF) are initiated on day +5. However, emerging retrospective data suggest that earlier initiation of immunosuppression may reduce CRS without increasing graft failure or GVHD. Prospective randomized data addressing this question are limited. We report a pre-planned interim analysis of an ongoing randomized phase II trial evaluating early versus conventional initiation of CNI/MMF following T-cell replete haplo-HSCT.

Methods: This is an open-label, randomized phase II study (IRB Min No. 16035 dated 24.01.2024) with a planned total sample size of 120 patients undergoing T-cell replete haplo-HSCT for malignant and non-malignant hematologic disorders. Patients were randomized to receive either early immunosuppression (cyclosporine from day 0 and MMF from day 1; intervention arm) or conventional immunosuppression (cyclosporine and MMF from day +5; comparator arm). Randomization was stratified by donor age. Conditioning regimens included myeloablative (MAC), reduced-intensity (RIC), and non-myeloablative (NMA) approaches. Outcomes assessed included CRS, acute GVHD, graft failure, CMV reactivation, relapse, treatment-related mortality (TRM), and overall survival (OS). Categorical variables were compared using chi-square or Fisher's exact tests. The study has been funded by Indian Council of Medical Research (ICMR) Small Extramural Grants – 2024.



MMF = mycophenolate mofetil; GVHD = graft versus host disease; IL6 = interleukin-6; CMV =cytomegalovirus; BKV = Human p

Twice a week monitoring of cyclosporine levels and weekly monitoring for CMV and BK virus constitute the current standard-
management for patients undergoing haploidentical transplantation. There are no additional study-related visits.

Figure: Study schema and study-related procedures

Results: At interim analysis, 64 patients had completed at least 100 days of follow-up (comparator n=34; intervention n=30). Median follow-up was 195 days (range 3–492). Baseline characteristics, including age, disease type, HCT-CI score, conditioning intensity and $CD34^+$ cell dose, were well balanced between arms.
CRS occurred less frequently in the intervention arm compared with the comparator arm (63.3% vs 82.4%, p=0.059). However there was no decrease in the incidence of grade ≥2 CRS between the two arms. Rates of engraftment were comparable, with graft failure observed in one patient in the comparator arm and none in the intervention arm. Median time to platelet recovery was similar between groups, while neutrophil recovery occurred earlier in the intervention arm (15 [13–25] vs 17 [12–35] days, one-sided p=0.026).
The incidence of aGVHD among engrafted patients did not differ significantly (38.2% vs 30%, p=0.80). CMV reactivation was numerically higher in the intervention arm, but not statistically significant (46.7% vs 23.5%, p=0.067). Day-100 NRM (20.0% vs 20.6%) and

overall survival at last follow-up (73.3% vs 79.4%, p=0.768) were similar between both groups.

Transplant characteristics and outcomes	**Comparator (n=34) Median (Range) or N (%)**	**Intervention (n=30) Median (Range) or N (%)**	**p value**
Median age	18(1-50)	23(1-54)	0.850
Male sex	26 (76.5%)	18 (60.0%)	0.185
Pediatric	14 (41.2%)	11 (36.7%)	0.800
Patient CMV IgG Positive	34 (100%)	26 (86.7%)	0.043
Disease type Malignant Non-malignant	 26 (76.5%) 8 (23.5%)	 21 (70.0%) 9 (30.0%)	0.584
Donor sex (Male)	19 (55.9%)	18 (60.0%)	0.803
Donor Age	31 (2-55)	29 (5–53)	0.622
HCT-CI score 0 1 ≥2	 26 (76.5%) 5 (14.7%) 3 (8.8%)	 23 (76.7%) 4 (13.3%) 3 (10.0%)	0.978
Conditioning MAC RIC NMA	 20 (58.8%) 13 (38.2%) 1 (2.9%)	 19 (63.3%) 11 (36.7%) 0 (0%)	0.623
CD34 dose infused (x 10^6/kg)	8.49 (6.24–12.0)	8.8 (6.2–14.3)	0.331
Cytokine release syndrome Grade 1 Grade 2	28 (82.4%) 24 4	19 (63.3%) 18 1	 0.059 0.36
Day of Neutrophil Engraftment	17 (12–35)	15 (13–25)	0.026
Day of platelet engraftment	26 (17–48)	20 (15–39)	0.531
CMV reactivation	8 (23.5%)	14 (46.7%)	0.067

Graft failure	1 (2.9%)	0 (0%)	1.000
Acute GVHD Grade II- IV	13 (38.2%)	10 (30%)	0.802
Overall survival	27 (79.4%)	22 (73.3%)	0.768
TRM Day 30	4 (11.8%)	5 (16.7%)	0.723
TRM Day 100	7 (20.6%)	6 (20.0%)	1.000

Conclusions: In this interim analysis of a randomized phase II trial, early initiation of CNI and MMF following T-cell replete haplo-HSCT with PTCy was associated with a trend towards reduction in CRS and earlier neutrophil recovery, without an increase in aGVHD, graft failure or early mortality. These findings support the safety of early immunosuppression and suggest a potential strategy to mitigate CRS in haploidentical transplantation.

Disclosure: Nothing to declare.

A101

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACQUIRED APLASTIC ANEMIA IN 2024: A CROSS-SECTIONAL STUDY FROM THE CHINESE BLOOD AND MARROW TRANSPLANTATION REGISTRY GROUP (CBMTRG)

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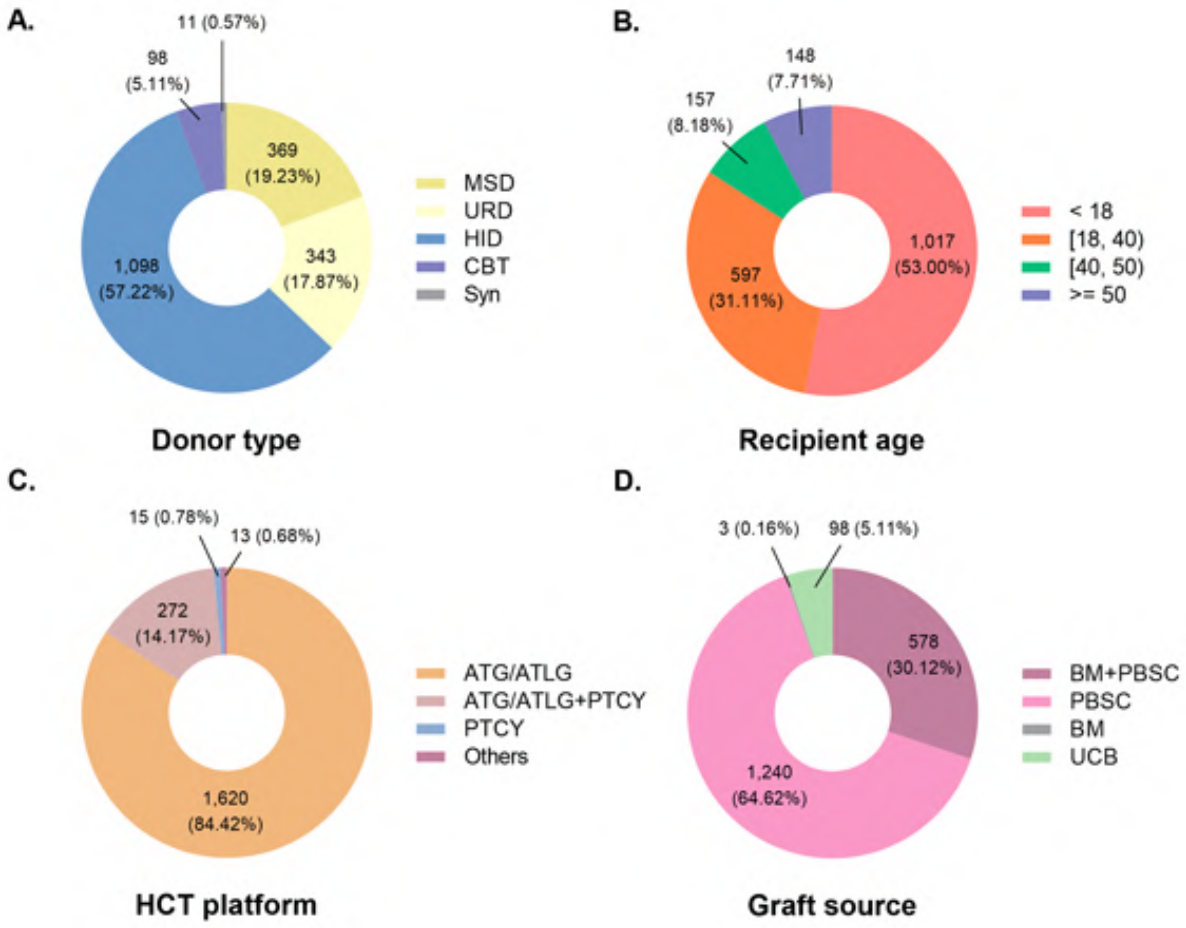
Background: Allogeneic hematopoietic stem cell transplantation (HCT) is well established as curative treatment for aplastic anemia (AA). China holds the largest number of allogeneic HCT cases worldwide, reaching 14,947 cases in 2023. Over the past decades, there have been continuous efforts to augment transplant protocols by improving conditioning regimens, graft-versus-host disease (GVHD) prophylaxis, and donor selection. Hence, HCT has been increasingly considered in individuals with AA in China. And the upper limit of age for HCT among AA recipients has continuously been broken. More than 1,000 cases of transplants for AA have been conducted annually in China since 2018. Compared to Europe and the US, HCT for AA in China can feature distinct characteristics, which stem from the practical experience of transplant centers, donor availability, drug accessibility, etc..

Methods: A nationwide registration of HCT has been organized by the Stem Cell Application Section of the Hematology Branch of the Chinese Medical Association since 2008. Every 6 months, data including transplant numbers, patient gender and age, disease, donor type, stem cell source, conditioning regimen, and GVHD prophylaxis was reported to the CMBTRG via Excel form. This cross-sectional study focused on transplant activity data for AA in China in 2024.

Results: In 2024, 1,919 transplants were reported in 1,893 patients (53.00% pediatrics, 31.11% young adults aged < 40 years, and 15.89% older adults) with AA by 158 actively transplanting centers in China. Haploidentical donor (HID) was the leading donor source of HCT (n = 1,098, 57.22%) for AA in China, which was observed across all age groups. Matched sibling donor (MSD, n = 369) and unrelated donor (URD, n = 343) were used in 19.23% and 17.87% of transplants, respectively. Flu+Cy (35.23%) was the most commonly used regimen for MSD HCT. In the haploidentical and unrelated setting, Bu+Flu+Cy (36.07% and 39.94%, respectively) and Bu+Cy (23.32% and 31.78%, respectively) were the two leading conditioning regimens. The anti-thymocyte globulin/anti-T-lymphocyte globulin (ATG/ATLG)-based platform (n = 1,620, 84.42%) was the predominant transplant modality in China, followed by the ATG/ATLG plus PTCY platform (n = 272, 14.17%). PBSC (n =1,240, 64.62%) and BM plus PBSC (n = 578, 30.12%) were the two leading graft sources. Apart from its use in all URD transplants, PBSC also accounted for 71.54% of MSD (71.54%) and HID (57.01%) transplants. Co-infusions have been employed in 26.35% (n = 506) of transplants to prevent GVHD, which were more likely to be used in pediatrics, PBSC transplants, and alternative HCT with HID and URD. The three-dugs regimen comprising calcineurin inhibitors (CNI), mycophenolate mofetil (MMF), and methotrexate (MTX) was the most commonly used GVHD prophylaxis in the ATG/ATLG-based setting (1258/1620, 77.65%). In the ATG/ATLG+PTCY-based setting, the regimen utilizing CNI±MMF/MTX ranked first (162/272, 59.56%). The prevalence of CNI+MMF+MTX regimen was also observed across MSD (57.45%), URD (70.85%), and HID (78.32%) transplants. Novel GVHD prophylaxis regimens have incorporated aniti-CD25 monoclonal antibody and ruxolitinib.



Conclusions: This survey offers a comprehensive overview of the current HCT landscape in China and serves as a valuable resource for clinical practice.

Disclosure: Nothing to declare.

A103

IRON OVERLOAD (IO) IS ASSOCIATED WITH AN INCREASED RISK OF INFECTIOUS COMPLICATIONS AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT) WITH POST TRANSPLANT CYCLOPHOSPHAMIDE (PTCY) BASED PROPHYLAXIS

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Background: The adverse effect of iron overload (IO) on outcomes of allogeneic hematopoietic cell transplantation (HCT) has been previously described as delayed engraftment and increased non-relapsed mortality (Al Malki et al. BBMT 2020). Additionally, iron is a nutrient for microorganisms and high pre-HCT serum ferritin (SF) levels have been previously associated with an increased risk of invasive fungal infections after HCT (Dadwal et al. BBMT 2011). However, its impact on patients receiving post-transplant cyclophosphamide (PTCy) as GvHD prophylaxis is unknown.

Methods: In this study, we included patients who underwent HCT and received PTCy at the City of Hope National Medical Center between June 2013 and December 2023 for a hematologic disease. We retrospectively analyzed infectious (documented viral, fungal, and bacterial infections) outcomes up to D+100 and stratified patients by pre-HCT SF level of 2000 ng/mL. The study was approved by the institutional review board at City of Hope.

Results: There were 584 consecutive patients who met criteria for analysis and were included in our study. There were 142 and 442 patients who had SF >2000 and $\leq$ 2000 ng/mL, respectively. The median age was similar between the cohorts (52 vs 52.5, p=0.82). The median SF value was 3107 versus 763.6 ng/mL between cohorts, respectively. Iron stain (IS) was done in 194 patients with available pre HCT bone marrow samples with median ISS (IS score) of 3 (range; 0-4). Fifty-nine patients had ISS of 0-2, and 135 patients with ISS of 3-4, with patients in the higher ISS (3-4) group having a higher baseline median SF (1118.2 vs 202.6 ng/mL, p<0.001). The total incidence of any infection up to D+100 post HCT between SF>2000 and $\leq$2000 ng/mL was 77.5% and 64.3% (p=0.003) respectively. There was a higher incidence of fungal (18.3% vs 8.8%, p=0.001) and viral (55.6% vs 43.7%, p=0.01) infections in the SF > 2000 cohort, however bacterial infections were not significantly different (36.5% vs 29.4%, p=0.11).

Conclusions: In conclusion, IO defined by SF of 2000 ng/mL correlated with higher ISS in pre-HCT bone marrow. IO was a strong adverse prognostic factor for infections post-HCT. Better viral and fungal prophylaxis and pre-emptive therapies approach might be necessary for patients with IO undergoing HCT with PTCy-based GvHD prophylaxis platform.

Disclosure: Nothing to declare.

A106

OPTIMIZING ALTERNATIVE DONOR SELECTION IN ALLOGENEIC HSCT: DISEASE- AND CONDITIONING-SPECIFIC ADVANTAGES OF UMBILICAL CORD BLOOD TRANSPLANTS

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) offers curative potential for various hematologic malignancies; however, many patients lack suitable HLA-matched donors. Advances in HLA typing and T-cell depletion have enabled the use of alternative graft sources, but the optimal donor choice in specific clinical settings remains uncertain.

Methods: We retrospectively analyzed 223 consecutive patients who underwent first allogeneic HSCT between January 2015 and December 2023 at Seoul National University Hospital. After excluding recipients of HLA-identical sibling or fully matched unrelated transplants, the final cohort included 146 haploidentical, 39 mismatched unrelated donor (MMUD), and 38 umbilical cord blood (UCB) transplants. Overall survival (OS) and relapse-free survival (RFS) were estimated using the Kaplan–Meier method, and prognostic factors were evaluated using Cox proportional hazards regression.

Results: The 5-year OS rates were 41.9% (95% CI, 34.4–51.0%) for haploidentical, 52.8% (95% CI, 39.0–71.5%) for MMUD, and 59.4% (95% CI, 45.4–77.9%) for UCB transplants ($p = 0.067$). The corresponding RFS rates were 36.8% (95% CI, 29.5–45.8%), 40.7% (95% CI, 27.8–59.6%), and 59.4% (95% CI, 45.4–77.9%), showing significantly inferior outcomes for haploidentical transplants ($p = 0.034$). Conditioning intensity influenced survival differently by donor type. Among UCB recipients, MAC resulted in significantly superior 5-year OS and RFS compared with RIC (OS: 66.5% vs. 28.6%, $p = 0.012$; RFS: 66.5% vs. 28.6%, $p = 0.0085$), whereas no significant difference was observed in haploidentical or MMUD transplants. In lymphoid malignancies, UCB transplantation achieved markedly higher survival compared with other donor sources, with a 5-year OS of 77.8% (95% CI, 60.8–99.6%; $p = 0.028$) and a 5-year RFS of 77.8% (95% CI, 60.8–99.6%; $p = 0.0061$). Among patients in complete remission (CR) at transplantation, UCB again demonstrated superior outcomes, with a 5-year OS of 77.8% compared with 48.5% for haploidentical and 57.2% for MMUD transplants ($p = 0.034$), and a 5-year RFS of 77.8% compared with 40.7% and 37.5%, respectively ($p = 0.0095$). In multivariate analysis, CR at day 100 post-transplantation was the strongest independent predictor of OS (HR = 11.19, $p < 0.001$) and RFS (HR = 12.16, $p < 0.001$), while UCB transplantation was independently associated with improved RFS (HR = 0.22, $p = 0.017$). Acute and chronic graft-versus-host disease incidences were comparable among groups.

Conclusions: UCB transplantation provided favorable long-term outcomes, particularly in lymphoid malignancies when myeloablative conditioning was feasible and disease remission was achieved early. Conditioning intensity and post-transplant remission status were key determinants of long-term survival. These findings support a risk-adapted donor selection strategy incorporating disease type, conditioning intensity, and early remission status to optimize outcomes in alternative donor HSCT.

Disclosure: The authors declare no conflicts of interest. This study was supported by the Seoul National University Hospital (grant number 0320220060).

A107

INFLUENCE OF TIME-OF-DAY OF GRAFT INFUSION ON ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION OUTCOMES: A VALIDATION COHORT STUDY

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a curative therapy for hematologic diseases but remains limited by graft-versus-host disease (GvHD) and non-relapse mortality (NRM). Emerging evidence suggests circadian rhythms influence immune function and transplant outcomes. Hou et al. reported that afternoon PBSC infusions were associated with higher acute GvHD and worse survival, highlighting a potential role for graft timing.

Methods: We retrospectively analyzed 368 adult patients undergoing first allo-HSCT with PBSC at Geneva University Hospitals between 2015 and 2024. Bone marrow and ex vivo manipulated grafts were excluded. Patients were stratified into early versus late infusion groups based on the results of a receiver operating characteristic (ROC) analysis. Clinical and graft characteristics, and outcomes including OS, progression-free survival (PFS), cumulative incidence of relapse, NRM, and acute GvHD were analyzed. Multivariable regression, accounting for covariates significantly different among the two groups, was performed.

Results: The ROC analysis for overall survival (OS), identified 11:17 a.m. as the optimal cutoff for infusion timing in our cohort (AUC = 0.53; sensitivity = 0.90; specificity = 0.23). Early infusion (<11 a.m.) was associated with improved 2-year OS (83% vs 65%, p=0.0078)

and reduced NRM (3.2% vs 13%, p=0.02) compared to late infusion. No differences were observed in relapse rates, PFS, or time to neutrophil engraftment. Acute GvHD incidence showed a non-significant trend towards reduction in the early group. To note, a higher proportion of patients in the early infusion groups received frozen grafts (n=42, 67%) compared to patients in the late infusion group (n=95, 31%; p<0.001). Multivariable analysis including the graft congelation status as covariate confirmed that later infusion remained independently associated with poorer OS (HR 2.29; p=0.015).

Conclusions: Timing of PBSC infusion appears to influence allo-HSCT outcomes, with early morning graft administration improving OS and reducing NRM. Two currently phase 3 randomised clinical trials are ongoing comparing patients undergoing transplantation between 11:30 a.m. and 12:30 p.m. or between 5:30 p.m. and 6:30 p.m. in the context of allo-HSCT for malignant (NCT06294678) or non-malignant (NCT06294691) haematological diseases. Our data support the potential of circadian-informed transplant strategies and underscore the need for prospective trials to validate timing as a simple, low-cost intervention to optimize allo-HSCT outcomes across centers.

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CS: speaker fees from AbbVie; research funding from Bayer
SML: Travel support from Noevii, BeiGene, Gilead, Jazz, Sanofi all via the institution.
SM: GILEAD: travel and accommodation expenses

A108

CLINICAL CHARACTERISTICS, PROGNOSTIC FACTORS, AND TRANSPLANT OUTCOMES IN HEMATOLOGICAL MALIGNANCIES WITH BEHÇET'S DISEASE: A RETROSPECTIVE STUDY OF 114 PATIENTS

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Background: Approximately 10–20% of patients with hematological malignancies (HMs), particularly myelodysplastic syndromes (MDS) and acute leukemia (AL), are reported to have coexisting autoimmune diseases, among which systemic vasculitis represents a common

manifestation. Behçet's disease (BD), a distinct form of systemic vasculitis characterized by pan-vasculitis and recurrent mucocutaneous and systemic inflammatory lesions, has been increasingly recognized in association with HMs. Notably, trisomy 8 (+8), one of the most frequent cytogenetic abnormalities in MDS and AL, has been implicated in the pathogenesis of BD or BD-like syndromes in this context, with a reported prevalence exceeding 70% in MDS patients exhibiting BD-like features.This study aimed to analyze the clinical features, long-term outcomes, and prognostic factors in patients with HMs coexisting with BD, focusing on the efficacy of hematopoietic stem cell transplantation (HSCT).

Methods: We conducted a retrospective analysis, including 29 patients with HMs and BD from the First Affiliated Hospital, Zhejiang University School of Medicine between Jan 2016 and Dec 2024, and 85 cases with complete data identified through a systematic literature review up to May 2025. Statistical analyses, performed using SPSS software, encompassed descriptive statistics, survival analysis (Kaplan-Meier method, log-rank test), and multivariate Cox proportional hazards regression to identify prognostic factors.

Results: The cohort comprised 114 patients (50 male, 64 female) with a median age of 49 years (range: 7-81). Primary HM diagnoses were BD-MDS (n=88, 77.2%), BD-AML (n=24, 21.1%), and BD-ALL (n=2, 1.8%). BD onset preceded HM diagnosis in 57 patients (50.0%). Trisomy 8 (+8) was present in 80 patients (70.2%), and 33 patients (28.9%) underwent allogeneic HSCT (allo-HSCT). Multivariate Cox analysis identified male sex (HR=1.82, 95% CI 1.01-3.29, P=0.048), age ≥60 years (HR=3.15, 95% CI 1.83-5.42, P<0.001), and BD onset preceding HM (HR=2.12, 95% CI 1.19-3.78, P=0.011) as independent adverse prognostic factors for overall survival (OS). Patients with BD-MDS had significantly superior OS compared to those with BD-AL (P<0.001). Allo-HSCT significantly improved OS in the overall cohort (P=0.013). Among all patients, trisomy 8 had no significant impact on OS (P=0.831). However, allo-HSCT recipients with +8 had significantly better OS than non-transplanted +8 patients (P=0.029). Moreover, all 6 surviving patients who underwent HSCT at our center maintained sustained remission of both hematologic malignancies and Behçet's disease through serial follow-up evaluations.

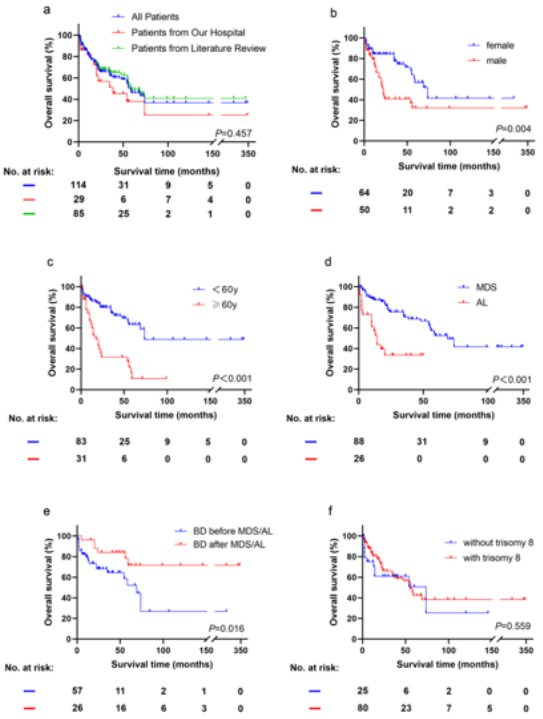

Figure 1. Survival of patients with MDS/AL-BD: (a) Overall survival of patients with MDS/AL-BD. (b) Overall survival of male and female patients. (c) Overall survival of elderly patients(≥ 60y) and young patients(＜60y). (d) Overall survival of MDS and AL patients.(e) Overall survival of patients with BD onset before MDS/AL and patients with MDS/AL onset before BD. (f) Overall survival of patients with and without trisomy 8. The survival time was defined as the period from diagnosis with MDS/AL to death.

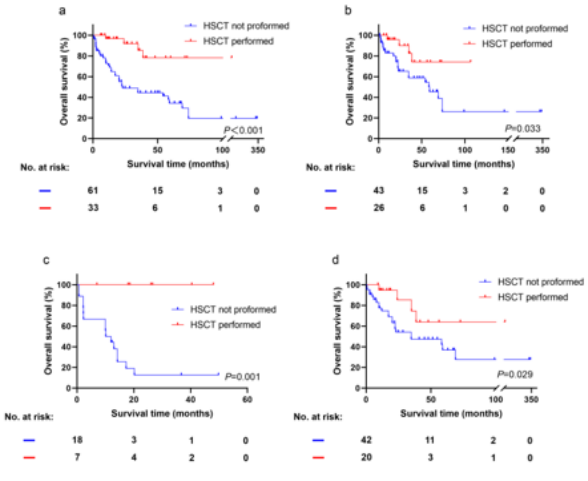

Figure 2. Patients treated with HSCT have better prognosis. (a) Overall survival of patients who received HSCT and those who did not. (b) Overall survival of patients with MDS who received HSCT and those who did not. (c) Overall survival of patients with AL who received HSCT and those who did not. (d) Overall survival of patients with trisomy 8 who received HSCT and those who did not.

Conclusions: BD–HM, particularly with trisomy 8, represents a distinct clinical and biological entity characterized by prominent GI involvement, systemic inflammation, and unique therapeutic challenges. In patients with HMs and BD, male sex, advanced age (≥60 years), and BD onset prior to HM diagnosis are independent adverse prognostic factors. Patients with BD-MDS exhibit significantly better survival than those with BD-AL. These data support early recognition and aggressive management of BD and HM overlap syndrome, with allo-HSCT as

the cornerstone for fit patients, and highlight the potential of targeted immunomodulation as an adjunct or alternative in the future.

Disclosure: Nothing to declare

A109

CUMULATIVE CYCLOSPORINE A EXPOSURE AND LONG-TERM OUTCOMES IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKAEMIA

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Background: Early Cyclosporine A (CsA) exposure influences both graft-versus-host disease (GvHD) control and antileukemic immunity after allogeneic stem cell transplantation (alloHCT). Prior studies relying on median CsA trough concentrations report inconsistent associations with relapse and survival. This may partially be due to the fact that median trough levels incompletely reflect cumulative immunosuppressive burden. We addressed this methodological limitation by reconstructing continuous daily concentration curves to quantify cumulative exposure in a homogeneous cohort of patients suffering from acute myeloid leukaemia (AML).

Methods: All adults receiving first alloHCT with a CsA/ATLG-based GvHD prophylaxis regimen for AML between 2009-2025 at the University Medical Centre Freiburg were included (N=320, Table 1). Daily CsA concentration curves were reconstructed using a unified LOWESS-based smoothing framework. After outlier filtering, LOWESS-smoothing was applied to individual patient measurements and interpolated onto a one-day grid. Daily and cumulative AUC values were derived via trapezoidal integration. Patient-level cumulative exposures for days 0-20 and 0-100 were normalised to a pooled reference curve and dichotomised at the median. To avoid reverse causality, exposure measurement was truncated before day 100 in the event of death, relapse, or the start of systemic immunosuppression for GvHD. Survival outcomes were analysed using Kaplan-Meier, Cox regression, and Fine-Gray competing risk models, adjusted for established clinical covariates including donor type, conditioning intensity, GvHD prophylaxis and risk-adapted dosing by disease risk index (DRI).

Results: High cumulative CsA exposure during days 0-100 was associated with markedly improved overall survival (OS) (Figure 1) and relapse-free survival (RFS). Five-year OS was 66.1% in the high-exposure group versus 43.4% in the low-exposure group (log-rank $p<0.001$), and this advantage remained highly significant in the adjusted Cox model (HR 0.55; 95% CI 0.38-0.79; $p=0.001$). Relapse-free survival similarly favoured high exposure

(HR 0.66; 95% CI 0.47-0.92; p=0.015). Despite numerical differences at five years in non-relapse mortality and relapse, the adjusted Fine–Gray model provided no evidence of a difference (NRM: SHR 0.68, 95% CI 0.41–1.15, p=0.16; relapse: SHR 0.70, 95% CI 0.46–1.12, p=0.11). High early (day 0-20) exposure was additionally associated with a significantly lower risk of chronic GvHD in a landmark analysis (SHR 0.54; 95% CI 0.33-0.90; p=0.015).

		low CsA exposure (N=160)	**high CsA exposure (N=160)**	**Total (N=320)**	**p-value**
Mean CsA level day 0–100 (ng/ml)		199 (185-212)	238 (226-255)	223 (199-242)	<0.001
Patient age at transplantation		62 (51-68)	60(50-69)	62(51-69)	0.91
Donor age at apheresis		29 (23-37)	30 (23-38)	29 (23-37)	0.98
Donor and recipient gender match or mismatch	Match	81 (50.6%)	84 (52.5%)	165 (51.6%)	0.77
	Male donor to female recipient	31 (19.4%)	26 (16.2%)	57 (17.8%)	
	Female donor to male recipient	48 (30.0%)	50 (31.2%)	98 (30.6%)	
Active disease	remission	73 (45.6%)	87 (54.4%)	160 (50.0%)	0.12
	active	87 (54.4%)	73 (45.6%)	160 (50.0%)	
TCI score		2.50 (2.50-3.50)	2.50 (2.50-3.50)	2.50 (2.50-3.50)	0.70
HCT-CI score		3.00 (1.00-4.00)	2.00 (1.00-4.00)	3.00 (1.00-4.00)	0.20
CMV risk	Low	63 (39.4%)	51 (31.9%)	114 (35.6%)	0.033
	Intermediate	7 (4.4%)	19 (11.9%)	26 (8.1%)	
	High	90 (56.2%)	90 (56.2%)	180 (56.2%)	

		low CsA exposure (N=160)	high CsA exposure (N=160)	Total (N=320)	p-value
Donor category	Matched sibling donor	13 (8.1%)	15 (9.4%)	28 (8.8%)	0.093
	Matched unrelated donor	120 (75.0%)	131 (81.9%)	251 (78.4%)	
	Mismatched donor	27 (16.9%)	14 (8.8%)	41 (12.8%)	
GvHD prophylaxis	CyA plus MMF or Myfortic	134 (83.8%)	132 (82.5%)	266 (83.1%)	0.96
	CyA plus MTX	25 (15.6%)	27 (16.9%)	52 (16.2%)	
	Other	1 (0.6%)	1 (0.6%)	2 (0.6%)	

Table 1. Baseline characteristics by Cyclosporine A exposure group. Patients were dichotomised into low and high exposure groups based on the median cumulative CsA exposure index for days 0–100. Continuous variables are reported as median (interquartile range) and were compared using the Wilcoxon rank-sum test. Categorical variables are shown as number and were compared using χ^2 tests or Fisher's exact test.

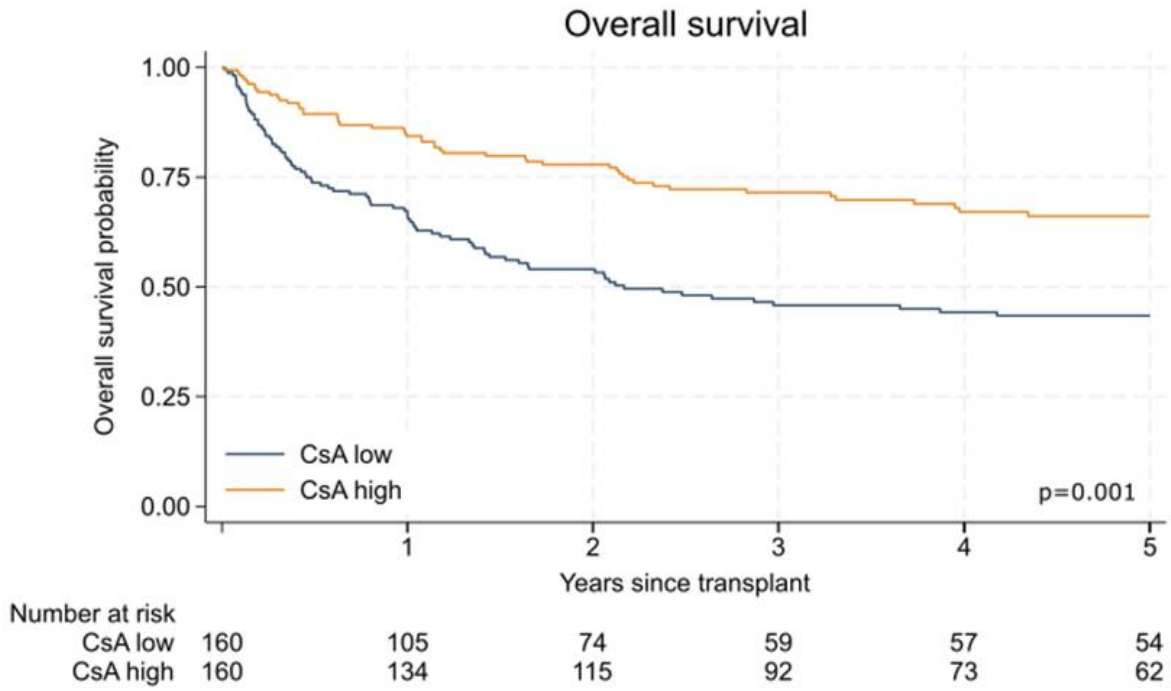

Figure 1. Kaplan–Meier overall survival by CsA exposure (day 0–100). Patients in the high-exposure group showed significantly improved survival over 5 years compared with those in the low-exposure group (log-rank p=0.001).

Conclusions: Higher cumulative CsA exposure in the first 100 days after alloHCT, was associated with markedly improved OS and RFS and less cGvHD, independent of disease risk. These findings suggest that, in contrast to concerns derived from solely trough-based monitoring, greater cumulative exposure within standard therapeutic ranges was not associated with less GvL activity.

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A110

ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH ACUTE LEUKEMIA: LESSONS TO LEARN FROM MULTIMODAL CLUSTERING

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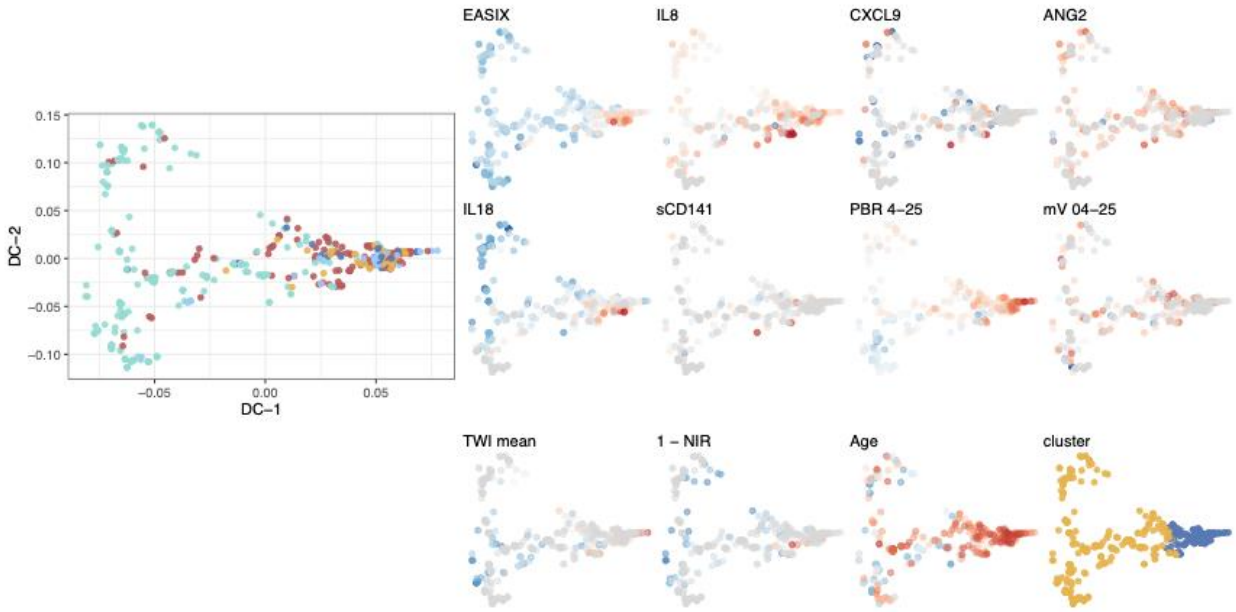
Background: Early mortality after allogeneic hematopoietic stem cell transplantation (alloHSCT) is associated with endothelial cell dysfunction that can be demonstrated already before conditioning therapy. We set out to study whether the reported pre-transplant endothelial alterations may be triggered by cytotoxic therapy and/or neutropenia-associated infections during induction therapy for acute leukemia.

Methods: In the context of a prospective observational study (NCT05502887) we included 152 patients before alloHSCT as well as 102 healthy individuals (controls). We performed longitudinal, comprehensive endothelial assessments on a subset of them diagnosed with acute leukemia, before first induction chemotherapy (n= 30), on day 7-9 after first induction therapy (peripheral blast clearance) (n= 31), directly before second induction chemotherapy (n= 18), and before alloHSCT (n=22).
Sublingual microscopy (Glycocheck®), digital hyperspectral imaging (Tivita®), and serum endothelial markers (endothelial activation and stress index (EASIX), Angiopoietin (ANG)2, CXCL8, CXCL9, interleukin (IL)-18, and soluble thrombomodulin) were measured before alloHSCT and at each time point for the longitudinal sub-cohort. To integrate these diverse measurements into a single interpretable pattern, we used a multimodal clustering approach: the data from all tests were first simplified using UMAP, a dimensionality-reduction method that groups related measurements closer together, and then patients were assigned to clusters using k-medoids, a robust clustering algorithm that identifies representative profiles. This approach allowed us to classify patients into clinically meaningful groups based on shared endothelial characteristics.

Results: The clustering and dimensionality reduction showed a clear difference between patients and controls. Most of the patients were in a single cluster that had significantly elevated endothelial distress markers and was associated with adverse transplantation outcomes, particularly non-relapse mortality. In the longitudinal acute leukemia subcohort, we found a remarkable stability of altered endothelial measures (IL18, Glycocheck®, Tivita®), in patients irrespective of age, from initial diagnosis until the pre-conditioning landmark, whereas EASIX at initial diagnosis reflected tumor load. In contrast, markers of acute endothelial distress (ANG2, CXCL8, sCD141) increased during induction chemotherapy and normalized until transplantation. This could also be seen in the UMAP coordinates and diffusion maps where most of these patients differed from controls for all time points.
The diffusion map analysis clearly separated the two clusters and showed regions of high EASIX, IL18, reduced glycocalyx thickness and low digital perfusion that were highly spatially correlated with the endothelial risk cluster. Most of the acute leukemia patients with high values of endothelial dysfunction markers at initial diagnosis clustered in this region, and their diffusion map positions remained relatively unchanged across time.



Conclusions: In patients with acute leukemia undergoing alloHSCT, multimodal clustering show unique pretransplant patterns driven by endothelial dysfunction-associated markers. Altered sublingual and digital endothelial and perfusion markers together with increased IL18 were present already at initial diagnosis and remained stable during the pretransplant course. Collectively, these results suggest that pre-transplant endothelial integrity alterations in patients with AML are caused by disease related factors rather than by treatment toxicity.

Clinical Trial Registry: NCT05502887

Disclosure: None

A111

TRANSPLANT OUTCOMES WITH SPANISH CORD BLOOD UNITS: SIGNIFICANT IMPROVEMENT OVER TIME

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Background: During the past decades, Spanish cord blood (CB) banks have delivered a large number of cord blood units (CBU) used by EBMT centres. This study addressed whether outcomes of cord blood transplantations (CBTs) using Spanish CBUs have improved over time.

Methods: We retrospectively analysed 1629 CBTs, performed between 2005 and 2023 in 200 EBMT centres, reported to Eurocord registry, which used at least one CBU coming from any of the 7 public Spanish CB banks linked to REDMO (located in Barcelona, n=966; Malaga, n=462; Madrid, n=140; Valencia, n=93; Santiago de Compostela, n=57; Pais Vasco n=28; Tenerife, n=4). Using an intention-to-treat approach (no censoring if a subsequent transplant is performed), the primary endpoint was 5-year overall survival (OS) from the day of CBT. Based on the analysis of continuous risk of death after transplantation, 3 time periods were considered: 2005-2010 (P1, n= 558), 2011-2013 (P2, n= 480) and 2014-2023 (P3, n= 591).

Results: Comparing P3 with P1 period, we observed: (1) lower percentage of patients with acute leukaemia in advanced stage at CBT; (2) more AMLs than ALLs; (3) lower percentage of patients transplanted for lymphoid diseases (lymphomas, myelomas, other chronic lymphoproliferative disorders); (4) higher nucleated and $CD34^+$ cell doses infused; (5) increased use of busulfan for myeloablative conditioning regimens (MACs); (6) less ATG use. Overall, the 5-year OS significantly improved with time, whether considering all, single or double CBTs (**Figure**). The most striking improvements reflected by a statistically significant 5-year OS increase $\geq$ 20%, were observed (1) in males; (2) when recipient age at CBT was $\geq$ 10 and < 40 years; (3) if a MAC including either TBI or a 2-drug busulfan-based TBI-free regimen was used; (4) for single CBTs, when there was a donor/recipient HLA incompatibility restricted to HLA-A and/or HLA-B loci (low-resolution typing for HLA-A and -B, high-resolution for HLA-DRB1) (**Table**). We did not observe any significant improvement over time with RIC. Disease-specific analyses showed a statistically significant 5-year OS improvement $\geq$ 20% in patients with: (1) acute myeloid leukaemias who received either a double CBT after a MAC or a single CBTs after a 2-drug busulfan-based TBI-free MAC (**Table**); (2) acute lymphoblastic leukaemias who received a single CBT with no more than 2 donor/recipient HLA mismatches or with HLA mismatch(es) restricted to the HLA-A locus; (3) myelodysplastic syndromes (Table). No such improvement was observed for non-malignant diseases (**Table**). Notably, all results described above remained significant when adjusted on total nucleated or $CD34^+$ cell dose infused or on recipient age at CBT.

Figure: 5-year overall survival according 3 times periods: P1 (2005-2010), P2 (2011-2013) and P3 (2014-2023)

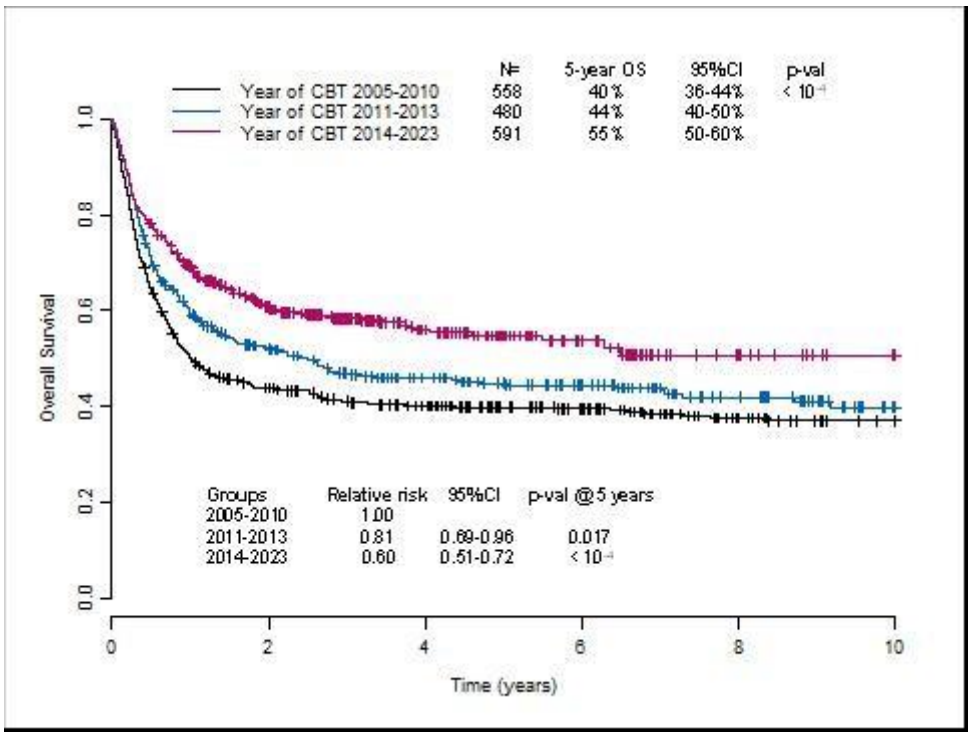

Table: Covariates improving over time

Table	Type of CBT	N=	Kaplan-Meier Estimates			Log-Rank test	Maximum difference
Covariates			P1	P2	P3	p-values	between P1, P2 & P3
All CBTs	single + double CBTs	1629	40%	45%	55%	< 10^{-4}	15%
Single CBTs	single CBTs	1041	44%	47%	58%	< 10^{-4}	14%
Double CBTs	double CBTs	588	33%	42%	49%	0.0016	16%
Overall analyses							

Recipient age at CBT > 10 to < 40 years	single + double CBTs	522	36%	47%	57%	0.0001	21%
Male recipients	single + double CBTs	921	36%	44%	56%	$< 10^{-4}$	20%
TBI-based MACs	single + double CBTs	285	39%	56%	61%	0.0004	22%
Two-drug busulfan-based TBI-free MACs	single + double CBTs	205	49%	53%	72%	0.028	23%
Donor/recipient HLA mismatch restricted to HLA-A and/or -B loci	single CBTs	464	46%	41%	61%	0.0004	20%
Disease-specific analyses							
AMLs with MACs	double CBTs	92	22%	32%	64%	0.0022	42%
AMLs with 2-drug busulfan-based TBI-free MACs	single CBTs	51	36%	43%	81%	0.027	45%
ALLs with 0 to 2 donor/recipient HLA mismatches	single CBTs	249	43%	46%	66%	0.0071	23%
ALLs donor/recipient mismatch restricted to the HLA-A locus	single CBTs	44	29%	58%	71%	0.046	42%

Myelodysplastic syndromes	single + double CBTs	95	20%	52%	55%	0.01	35%
Non-malignant diseases	single + double CBTs	246	59%	68%	73%	0.13	14%

Conclusions: Survival after CBTs using Spanish CBUs has significantly improved during the past decades, especially since 2014. The striking outcome improvements likely resulted from the experience gained through long-term use of classic MAC regimen, such as the busulfan/cyclophosphamide combination, and from a better selection of the CBUs, aiming for higher cell doses and improved donor/recipient HLA matching.

Disclosure: Nothing to declare. No external funding was required.

A112

EFFICACY OF THE TRIPLET THERAPY WITH VENETOCLAX, AZACITIDINE AND GILTERITINIB FOR THE TREATMENT OF FLT3-ITD MUTATED R/R AML PATIENTS BRIDGING TO ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Patients with relapsed or refractory (R/R) acute myeloid leukemia (AML) with FLT3-Internal Tandem Duplication (ITD) mutation have a poor prognosis and high risk of relapse.Triplet therapy with venetoclax[VEN], azacitidine[AZA] and gilteritinib is effective and significantly improves response rates and survival outcomes in this high-risk patient population.

Methods: We analyzed 48 FLT3-ITD mutated AML patients in a retrospective cohort study. Patients with R/R disease or persistent MRD received triplet therapy (VEN, AZA and gilteritinib) and bridged to allo-HSCT between August 2021 and June 2024. Bone marrow aspirates were obtained, cytogenetic and molecular characteristics were collected at the time of diagnosis. HLA-haploidentical donor transplants were performed if no HLA matched sibling or unrelated donor was available. Patients received myeloablative conditioning regimens followed by post-transplant gilteritinib maintenance therapy. The therapeutic process and clinical outcomes were retrospectively analyzed.

Results: 48 adult patients were enrolled in this study, 27 (56.2%) were female and 21 (43.8%) were male. The median age was 41 (range 15-61). Based on prognostic stratification defined by the 2022 European LeukemiaNet (ELN) guidelines, 38 (79.2%) patients were categorized in the Intermediate-risk group and 10 (20.8%) were categorized in the adverse-risk group at diagnosis. At the time of enrollment, 38 (79.2%) patients had R/R disease, of whom 36 cases failed to achieve remission with prior chemotherapy and two cases attained complete remission with MRD positivity. The remaining 10 patients (20.8%) were in CR1 but were detected with persistent positive MRD during chemotherapy.
After one cycle of triplet therapy (VEN, AZA and gilteritinib), 39 (81.3%) patients reached CR/CRi (16 were MRD negative and 23 were MRD positive). The remaining 9 (18.7%) patients showed no treatment response and proceeded to transplantation with active disease. No treatment-related mortality (TRM) was observed. Patients received myeloablative conditioning with a modified Bu/Cy/Cla/Ara-c (busulfan/cyclophosphamide/cladribine/cytarabine) or MCBC (melphalan/cladribine/busulfan/cyclophosphamide) preparative regimen. All patients engrafted successfully, with hematopoietic recovery within 60 days of transplantation. Gilteritinib maintenance therapy started between day +30 to latest day +90 after allo-HSCT. At the time of this analysis, 40 (83.3%) patients remained alive, while disease relapse had occurred in 9 patients (18.8%). The median follow-up of alive patients was 16.6 months (11-43.2). The 1-year overall survival (OS) and relapse-free survival (RFS) were 83.3% (95% CI 72.7-93.9%) and 75.0% (95% CI 62.7-87.3%), respectively. The leading causes of death were leukemia relapse (n=4), followed by grade IV aGVHD (n=3) and severe infection (n=1). The 1-year incidences of relapse and non-relapse mortality (NRM) were 14.6% (95% CI 6.3-26.1%) and 10.4% (95% CI 3.8-21.0%) , respectively. 19 (39.6%) patients experienced aGVHD and 15 (31.3%) experienced cGVHD.

Conclusions: The triplet therapy of VEN, AZA and gilteritinib resulted in high rates of CR/CRi and enhanced the feasibility of HSCT in FLT3-ITD mutated AML patients with R/R disease or persistent MRD. Sequential allo-HSCT followed by gilteritinib maintenance therapy may significantly improve the long-term prognosis in this high-risk group of patients.

Disclosure: None

A113

THE EFFICACY OF MEMORY T CELL DONOR LYMPHOCYTE INFUSION IN AUGMENTING IMMUNE FUNCTION FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Prolonged immune reconstitution associated with allogeneic hematopoietic cell transplantation (allo-HCT) increases the risk of severe infection, a significant cause of mortality in these patients. Despite the improvements in the use of prophylactic strategies and the establishment of first-line treatment, there remains a necessity to formulate a novel therapy for these patients. Memory T cells, defined by expression of CD45RO and absence of CD45RA isoform, has been reported as an effective method to rapidly recover T cell immunity post allo-HCT, which contributed to the enhanced capacity for anti-infection. In this study, we analyzed the efficacy and safety of CD45RA-depleted memory T-cell infusion in treating refractory or persistent viral or fungal infection following allo-HCT.

Methods: In this retrospective study, we screened those allo-HCT receipts who received at least once CD45RA-depleted memory T-cell adoptive cell therapy (ACT) and obtained the required information by using institutional electronic medical records. Between March 2024 and November 2025, 20 adult patients were enrolled.

Results: Baseline characteristics and transplant procedure are described in Table 1. The pathogens treated include viruses (90%), including epstein-barr virus (EBV, 35.0%), Cytomegalovirus (CMV, 10.0%), human parvovirus B19 (10.0%), adenovirus (ADV, 10.0%), herpes simplex virus-1 (HSV1, 15.0%), herpes simplex virus-2 (HSV2, 5.0%), BK virus (BKV, 10.0%), john cunningham virus (5.0%), human herpesvirus 6B (HHV6B, 5.0%), human parainfluenza viruses (HPIVs, 5.0%), and fungi (15.0%), including fusarium (10.0%) and aspergillus (5.0%). 48 infusions of CD45RA-depleted memory T-cell ACT were administrated to the 20 patients with a cumulative dose of 23.2 (range: 4.3–47.7) $\times 10^6$ cells/kg across a median of two cycles (range: 1–4). Memory T cells were obtained from original transplant donor (n=15, 75.0%) and third-party donor (n=5, 25.0%). The first ACT infusion was administered at a median of 98 days (range: 23-774) after allo-HCT, with half of patients (n=10) receiving ACT within 100 days. During the treatment period, 14 (70.0%) patients continued concomitant use of immunosuppressants. After a median follow-up of 52 (range: 16-636) days, 18 patients (90.0%) are alive at time of analysis (December 2025), and 12 patients (60.0%) attained complete remission from the infection. In three patients with fungi infection (including fusarium and aspergillus), a marked improvement in clinical symptoms was observed in these patients. Of 18 patients with viruses infection, the cumulative incidence of negative viral polymerase chain reaction after first ACT was 72.2% (13/18 patients). The median duration to achieve negative test for each virus are 15 days (EBV, one patient continues to test positive), 5 days (CMV), 38 days (B19), 10 days (ADV, one patient continues to test positive), 35 days (HSV1, one patient continues to test positive), 9 days (HSV2), 36 days (BKV, one patient continues to test positive), 33 days (HHV6B) and 36 days (HPIVs). Treatment was well tolerated; adverse events included acute graft versus host disease (GvHD) in 1 patient (5.0%), chronic GvHD in 3 (15.0%) and primary disease relapse in 1 (5.0%).

Characteristics	All
Age at allo-HCT (years), median (range)	46 (25-66)
Sex, *n* (%)	

Male	14 (70.0%)
Female	6 (30.0%)
Conditioning intensity, *n* (%)	
MAC	13 (65.0%)
RIC	7 (35.0%)
Donor type, *n* (%)	
HID	18 (90.0%)
MUD/MMUD	1 (5.0%)
MSD	1 (5.0%)
T-cell depleted, *n* (%)	
Ex vivo	1 (5.0%)
In vivo	
rATG-based	16 (80.0%)
PTCY-based	3 (15.0%)

Tabel 1. Patients'characteristics. Abbreviation: allo-HCT, allogeneic hematopoietic cell transplantation; HID, haploidentical donor; MUD/MMUD, matched/mismatched unrelated donor; MSD, matched sibling donor; MAC, myeloablative conditioning; PTCy, post-transplant cyclophosphamide; rATG, rabbit anti-thymocyte globulin; RIC, reduced-intensity conditioning.

Conclusions: CD45RA-depleted donor memory T cell infusion provides clinical benefit in allo-HCT receipt with refractory and persistent infection, without evidence of the safety concerns reported.

Disclosure: Nothing to declare.

A114

LONG-TERM SURVIVAL AND HIGH-RISK DETERMINANTS FOLLOWING AUTOLOGOUS STEM CELL TRANSPLANT IN MANTLE CELL LYMPHOMA

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Background: High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has been a cornerstone of treatment for mantle cell lymphoma (MCL). However, the therapeutic landscape has shifted away from ASCT in favor of Bruton tyrosine kinase inhibitor (BTKi) containing regimens. Despite this shift, patients with high-risk morphologic features and TP53 aberrations continue to experience inferior outcomes with BTKi-based approaches. In this context, the role of ASCT remains uncertain. The goal of this study was to evaluate outcomes in MCL following ASCT in the setting of these adverse prognostic features.

Methods: We conducted a single center retrospective study of all patients with MCL who underwent ASCT between August 1996 and January 2021 at Mayo Clinic, Rochester, MN. Categorical variables were compared using the Chi-square test and/or Fisher's exact test. Overall survival (OS) and progression free survival (PFS) were evaluated using the Kaplan–Meier method with group comparisons by log-rank test. Patients were stratified by high-risk features including blastoid or pleomorphic morphology, a proliferation index (Ki67) ≥ 30%, TP53 mutations and high mantle cell lymphoma international prognostic index (MIPI) scores.

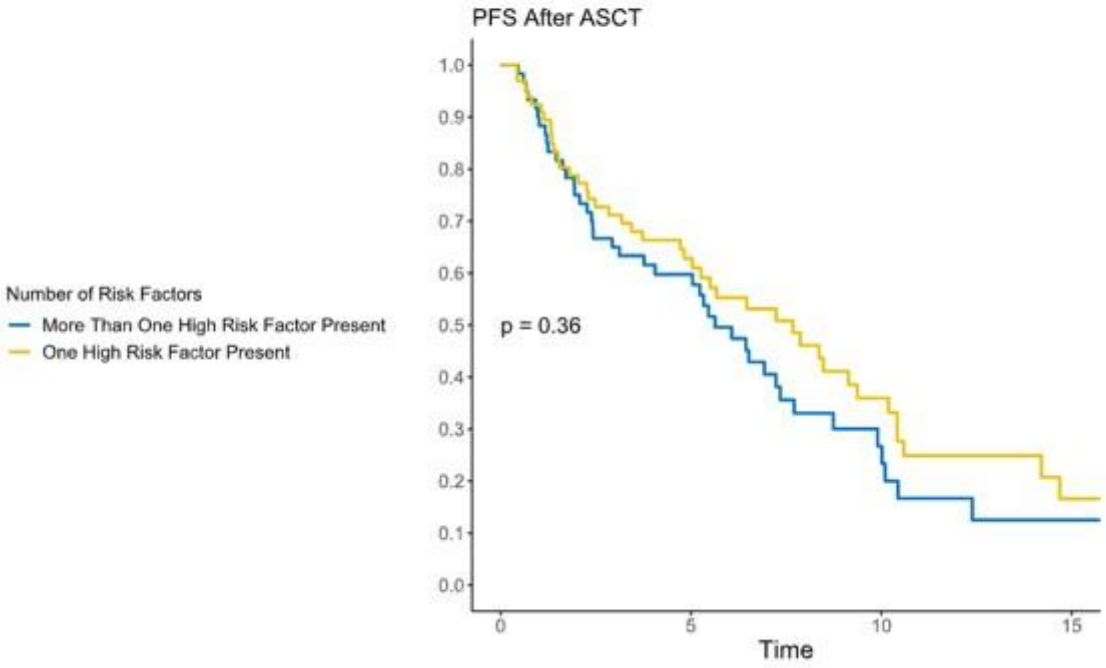
Results: A total of 303 patients were included in the study. The median age at the time of ASCT was 59.9 years and the cohort was predominantly male (78.5%), Caucasian (91.4%) and diagnosed with advanced-stage disease (95%). The median follow-up after ASCT was 11.2 years. The median PFS for the entire cohort was 8.4 years (95% CI, 7.3-10.2) and the median OS was 10.9 years (95% CI 9.5-15.4 years).
Blastoid or pleomorphic morphology, a high proliferation index, and elevated MIPI scores were each significantly associated with shorter PFS and OS, as shown in Table 1. Patients with a single high-risk feature had a trend toward longer PFS compared with those harboring multiple high-risk factors (7.7 vs 5.6 years), although this difference was not statistically significant (p = 0.36), as demonstrated in Figure 1.
The entire cohort was further stratified by PFS (< 5 vs ≥ 5 years) and OS (< 5 vs ≥ 5 years and (< 10 vs ≥ 10 years). Patients with PFS < 5 years were more likely to have aggressive morphology (p=0.007) and high MIPI scores (p=0.05) than those with PFS > 5 years. Conversely, patients with OS ≥ 10 years were less likely to have aggressive morphology (p=0.07) or high risk MIPI scores (p=0.001).
Ninety-two of 303 patients received rituximab maintenance after ASCT, and 149 of 303 ultimately relapsed. Post-ASCT therapies included BTKi in 59 of 303 patients and CAR-T in 11 individuals.

Table1:

		PFS (y)	p-value	OS (y)	p-value
All patients (n=303)		8.4		10.9	
Morphology (n=303)	Aggressive (n=65)	5.3	**< 0.001**	7.6	**0.004**
	Not-aggressive (n=238)	9.9		12. 5	
Proliferation index (n=161)	Ki-67 ≥ 30 % (n=88)	7.7	**0.006**	10.6	**0.004**
	Ki-67 < 30 % (n=73)	10.9		NR	
TP-53 status (n=39)	Mutated (n=12)	5	0.27	NR	0.21
	Wild type (n=27)	6.5		NR	
MIPI (n=164)	High risk (n=52)	5.6	**< 0.001**	7.7	**< 0.001**
	Not high risk (n=112)	10.3		15.8	

Abbreviations: y=years, n=number, NR=not reached.

Figure1:



Conclusions: Our study demonstrates that ASCT can provide durable benefit in MCL, with median PFS exceeding five years across all high-risk categories. These findings support a continued role for ASCT in the management of MCL, including high-risk patients who experience inferior outcomes with BTKi based therapy and in those who are unable to tolerate or have contraindications to BTKi.

Disclosure: "Nothing to declare"

A115

LINK BETWEEN NON DONOR-SPECIFIC ANTI-HLA ANTIBODIES AND INFERIOR KEY OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION -THE "LAIKA" STUDY-

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Background: The role of non-donor-specific anti-HLA antibodies in allogeneic HSCT remains unclear, despite the well-recognized adverse impact of donor-specific antibodies on post-transplant outcomes.

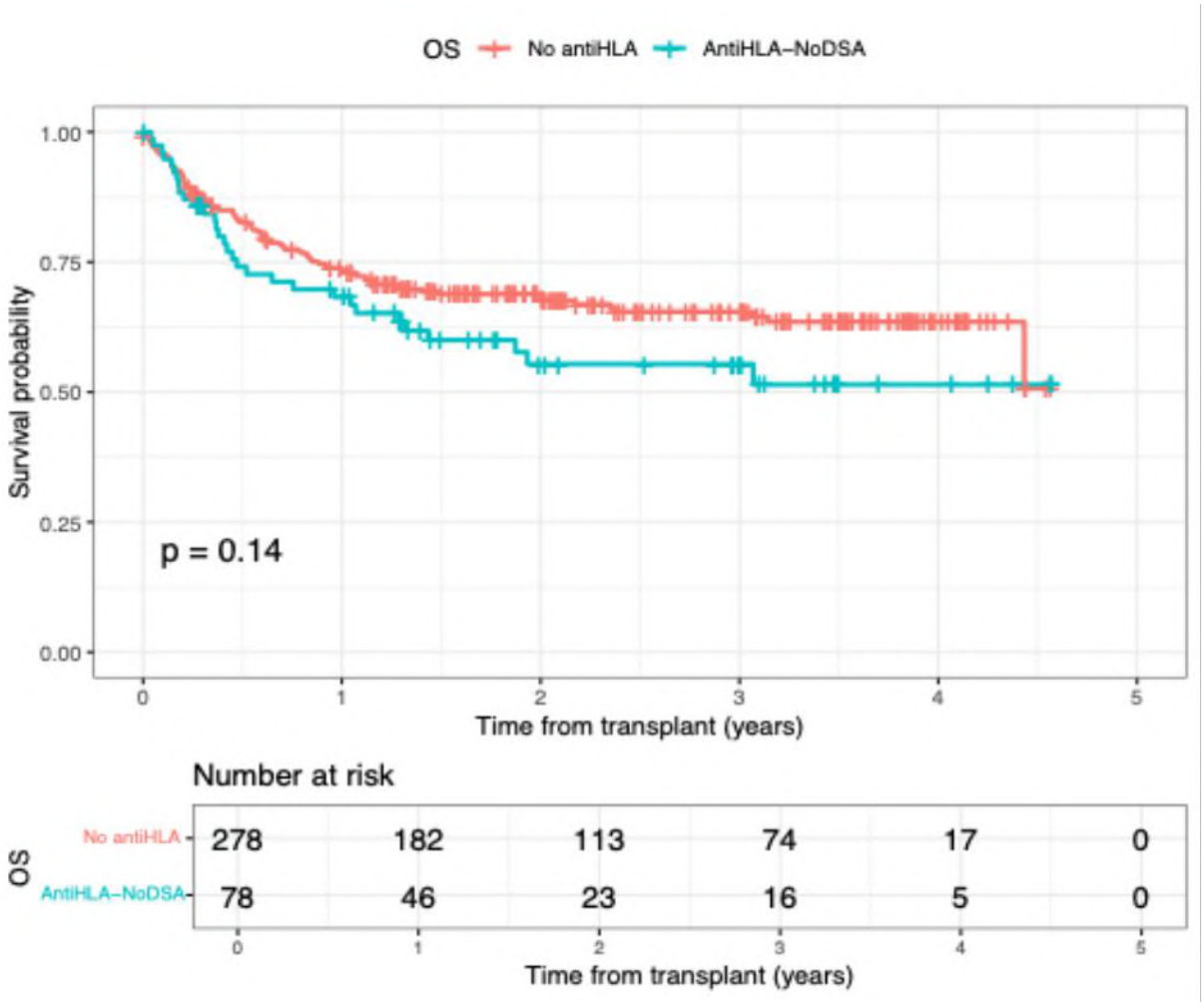
Methods: We conducted a retrospective multicenter study including 401 allogeneic HSCT patients from five Italian transplant centers. Patients were categorized into three groups based on pre-transplant anti-HLA antibody status: no detectable antibodies (No Anti-HLA), non–donor-specific antibodies (AntiHLA-NoDSA), and donor-specific antibodies (DSA). Descriptive statistics were generated for the overall cohort and stratified by antibody group. The association between antibody status and overall survival was evaluated using Kaplan–Meier estimates and Cox proportional hazard models, performed first in univariate analyses and subsequently adjusted for clinically relevant covariates in multivariate models.

Results: Among 401 allogeneic HSCT recipients, No Anti-HLA, AntiHLA-NoDSA and DSA patients were 278 (69%), 78 (19%) and 45 (11%), respectively. The cohort had a median age of 59 years (IQR 47–66), and females represented 44%. Female sex was more frequent in the AntiHLA-NoDSA group (54/78, 69%) compared with the No Anti-HLA group (101/278, 36%). Donor types included HLA-identical siblings, matched unrelated donors (MUD), mismatched unrelated donors (mMUD), and haploidentical donors.
Disease characteristics were comparable across groups: 306/401 (76%) of patients had myeloid malignancies, and 251/385(65%) underwent transplantation in first complete remission or full remission with similar proportions in each subgroup. Pre-transplant transfusion burden was higher in the AntiHLA-NoDSA subgroup, with >20 RBC units in 30/78 (38%) and >20 platelet units in 31/78 (40%), compared with 82/278 (30%) and 73/278 (26%) in the No Anti-HLA group and 16/45 (36%) and 13/45 (29%) in the AntiHLA-DSA group. In the Cox model, >20 pre-transplant transfusions of RBCs (HR 1.81, 95% CI 1.24–2.64, p=0.01) and platelets (HR 1.65, 95% CI 1.13–2.42, p=0.01) were both independently associated with inferior overall survival. Platelet refractoriness was infrequent overall (3%) but more common in the AntiHLA-NoDSA subgroup (9%).[tab. 1]
Among AntiHLA-NoDSA patients, median maximal MFI was 5,649, with a cumulative MFI of 12,650. The median PRA was 21% for class I and 1% for class II.
At two years, overall survival was 69% in the No Anti-HLA group and 55% in the AntiHLA-NoDSA group (log-rank p = 0.14). [Fig. 1] In the Cox model, the presence of non–donor-specific antibodies was associated with a higher mortality risk, though without statistical significance (HR 1.36, 95% CI 0.90–2.05, p = 0.14). This association remained directionally consistent after adjustment for clinical covariates in the multivariate analysis (HR 1.44, 95%

CI 0.93–2.24, p = 0.11). No significant associations were observed between survival and antibody characteristics (maximum MFI, cumulative MFI, or PRA for class I and II).

Patients Characteristic	**Overall** N = 401[1]	**No anti-HLA antibodies** N = 278[1]	**AntiHLA-NoDSA** N = 78[1]	**DSA** N = 45[1]
Age	55 (14), 59 (47-66), 19, 75	55 (15), 59 (47-66), 19, 75	53 (14), 56 (45-64), 22, 74	58 (11), 61 (51-66), 28, 74
Main Diagnosis				
other	95 (24%)	74 (27%)	13 (17%)	8 (18%)
Myeloid malignancies	306 (76%)	204 (73%)	65 (83%)	37 (82%)
Disease status at treatment				
others	134 (35%)	89 (33%)	25 (34%)	20 (44%)
CR	251 (65%)	177 (67%)	49 (66%)	25 (56%)
Platelet refractoriness				
No	383 (97%)	271 (99%)	69 (91%)	43 (96%)
Yes	12 (3%)	3 (1.1%)	7 (9.2%)	2 (4.4%)
RBCs transfused before transplant				
< 10	182 (46%)	130 (47%)	33 (42%)	19 (42%)
> 20	128 (32%)	82 (30%)	30 (38%)	16 (36%)
>10 & <20	90 (23%)	65 (23%)	15 (19%)	10 (22%)
PLTs transfused before transplant				
< 10	197 (49%)	144 (52%)	34 (44%)	19 (42%)
>20	117 (29%)	73 (26%)	31 (40%)	13 (29%)
>10 & <20	86 (22%)	60 (22%)	13 (17%)	13 (29%)

[1]n (%); Mean (SD), Median (Q1-Q3), Min, Max, Complete remission (CR)



Conclusions: The alignment between survival curves and hazard ratio patterns reveals a consistent and clinically relevant signal implicating non–donor-specific anti-HLA antibodies as an unfavorable predictive factor in allogeneic HSCT in our multicenter cohort of 401 patients. These findings challenge the current paradigm that only donor-specific antibodies are clinically meaningful and position non-DSA as an overlooked immunologic variable warranting systematic and in-depth evaluation in future prospective studies.

Disclosure: No disclosure to declare

A116

V-DELTA-2 UNCONVENTIONAL T CELLS IN THE DONOR GRAFT ARE ASSOCIATED WITH IMPROVED OVERALL SURVIVAL AFTER UNRELATED DONOR ALLO-HCT FOR AML AND MDS

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Background: The DKMS (Germany) and the NMDP (USA) have embarked on a large collaborative project to characterize more than 2000 donor peripheral blood stem cell (PBSC) grafts in unprecedented detail. Here, we present an exploratory analysis focusing on microbiome-dependent mucosal-associated invariant T (MAIT) and Vδ2 populations, which have both been associated with favorable HCT outcomes in prior studies. We hypothesized that receiving a graft bearing higher 'doses' of these cell populations would be associated with favorable clinical outcomes.

Methods: PBSC graft samples were collected, processed, freshly stained (34-color panel for immunophenotyping of lymphocytes and hematopoietic stem cells), and analyzed using high dimensional full spectrum flow cytometry at the NMDP contract laboratory (n = 457; Roswell Park, Buffalo, NY) or the DKMS laboratory in Dresden, Germany (n = 270). Clinical data were collected via CIBMTR. We included patients who were transplanted for AML or MDS, with at least 1 year of follow-up data available. A Cox proportional hazard model was fitted to assess the relationship of MAIT and Vδ2 populations (dose/kg recipient weight in the graft) with transplant outcome and identify significant risk factors, including GVHD prophylaxis, cryopreservation status, patient and donor age, refined disease risk index, HCT-CI, conditioning intensity, and HLA matching.

Results: Patients with AML or MDS, receiving unrelated donor PBSC allografts were studied (n = 727). The median recipient age was 64.2 years. 404 (55.57%) received post-transplant cyclophosphamide (PT-Cy) as GVHD prophylaxis.
In multivariable analyses, recipients of grafts bearing a below-median number of Vδ2 cells was associated with significantly worse overall survival compared with equal to or below-median (HR=1.337, 95% CI 1.032-1.733, p = 0.0281; **Figure 1**). Additional clinical factors associated with worse overall survival are high/very high disease risk index (HR=1.637, 95% CI 1.234-2.172, p = 0.0006) compared to low/intermediate group and HCT-CI 3+ (HR=1.597, 95% CI 1.252-2.037, p = 0.0002) compared with the HCT-CI 0-2 group. There were no statistically significant differences in acute or chronic GVHD in patients who received above-median Vδ2 doses in our multivariable models. Multivariable analyses found no

associations between MAIT cell graft content and outcome (OS shown in **Figure 1**).
Given the OS finding among patients who received higher numbers of Vδ2 cells in their graft product, we next characterized the causes of death in the cohort. Notably, infection was reported as the cause of death in 3.9% in the above-median Vδ2 setting and 7.9% in the recipients of grafts containing below-median numbers of Vδ2 cells (p = 0.034; Fisher's exact test).

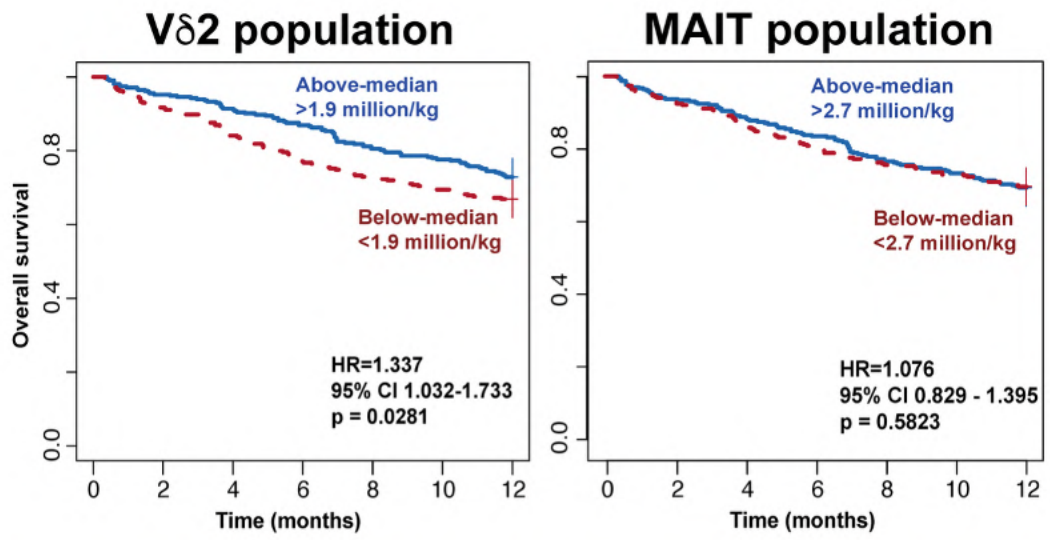

Figure 1: Kaplan-Meier curves comparing overall survival (OS) in the recipients of above- and below-median Vδ2 and MAIT cell-containing grafts. Data shown derived from 627 patients (a portion of participants had missing TNC data, thus absolute numbers could not be calculated). Statistics shown are derived from MV Cox proportional hazard model accounting for: GVHD prophylaxis (PT Cy vs others); Graft cryopreservation status (fresh vs frozen); patient age, donor age, disease risk, HCT-CI, conditioning intensity, HLA matching.

Conclusions: We report a novel association between the Vδ2 content of the donor graft and 1 year overall survival in the allo-HCT recipient. Vδ2 cells have previously been associated with lower rates of GVHD and improved OS when measured after HCT, however their number in the donor graft has not previously been correlated with outcome. Intriguingly, little is known regarding the functional capacity of these T cells after HCT, and further studies will focus on uncovering the mechanism by which they may contribute to improved overall survival.

Disclosure: The authors have no disclosures relevant to this presentation.

A117

DAN-CART 1901: PRELIMINARY RESULTS OF SAFE AND FEASIBLE ADMINISTRATION OF THE FRESH AUTOLOGOUS ANTI-CD19 CAR-T PRODUCT DK-CLIC-1901

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Background: Treatment with chimeric antigen receptor T-cells (CAR T) has demonstrated efficacy in patients with CD19-positive hematological malignancies and lower toxicity than other treatment options. We established an academic CAR-T cell program to broaden access for patients without other curative treatment options and to enable faster, more flexible local production.
We report preliminary results from the initial phase 1b/2 trial using the academic autologous 4-1BB anti-CD19 CAR-T product DK-CLIC-1901 (CTIS # 2024-515174-27-00). The primary objective was to evaluate the safety of DK-CLIC-1901. The secondary objectives were to assess feasibility, clinical efficacy, and immunological response after DK-CLIC-1901 infusion.

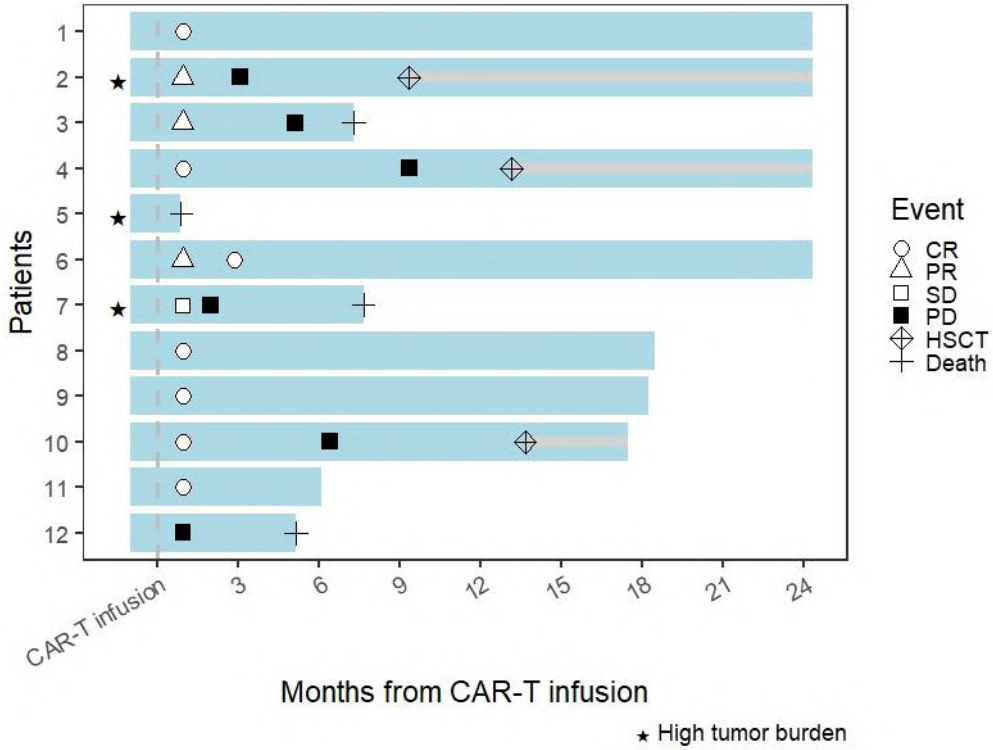
Methods: The main inclusion criteria were relapsed or refractory B-cell ALL or NHL, age between 1-70 years, adequate performance status and organ function (lung, heart, liver, and kidney), life expectancy ≥ 12 weeks, and written informed consent.
Patients received a single infusion of fresh-to-fresh autologous, *in vitro*-expanded DK-CLIC-1901 CAR T-cells at a minimum dose of $1x10^6$ CAR T-cells/kg, with a dose reduction to $2x10^7$CAR T-cells in total in case of high tumor burden. The DK-CLIC-1901 product was manufactured on the CliniMACS Prodigy platform (Miltenyi) using a lentiviral vector carrying a 4-1BB anti-CD19 CAR transgene [N. Kekre et al, Front Immunol 2022].

Results: Thirteen patients passed the initial screening for participation. One patient was excluded before apheresis due to rapid progression of hematological malignancy; 12 patients underwent apheresis and received CAR-T infusion (Table).

Clinical characteristics	**N=12**
Age (years), median (range)	54 (16-67)
Male sex, *n*. (%)	11 (92%)
Diagnosis, *n*. (%) B-ALL B-NHL DLBCL Transformed FL HGBL	 2 (17%) 10 (83%) 3 (25%) 4 (33%) 1 (8%)

Burkitt lymphoma Mantle cell lymphoma	1 (8%) 1 (8%)
High tumor load, *n*. (%) ALL: >20% blasts in BM NHL: ≥10 cm tumor mass or BM involvement	 0 (0%) 3 (25%)
LDH at the start of LDT (U/L), median (range)	229 (130-2200)
Prior lines of treatment, median (range)	3 (1-4)
CAR-T indication, *n*. (%) Primary refractory ≥2 relapse Relapse after autologous/allogeneic HSCT	 5 (42%) 4 (33%) 3 (25%)
LDT with FLU (30 mg/m^2 x4) and CY (500 mg/m^2 x2), *n*. (%)	12 (100%)
Time from enrollment to apheresis (days), median (range)	6 (2-16)
DK-CLIC-1901 production time (days from apheresis to CAR-T infusion), median (range)	13 (13-19)
Cellular composition of DK-CLIC-1901 product, median (range) CAR-T cell count (x10^6 CAR T-cells / kg bodyweight) CAR-T cell count (x10^8 CAR T-cells in total) CD4/CD8 T cell ratio	 2 (0.23-3.1) 200 (20-200) 0.63 (0.29-3.69)

CRS occurred in 9 patients (grade ≥3: n=3) and ICANS in 3 patients (grade ≥3: n=2), with a higher frequency in patients with high tumor burden (CRS grade ≥3: 67% vs. 11%; ICANS: 67% vs. 11%). One patient with a high tumor load died at day +26 from intracerebral hemorrhage following severe CRS/ICANS. Another patient developed HHV-6 encephalitis after CAR-T infusion with persistent neurological sequelae [NM Birk et al, Front Hematol 2025]. Late cytopenia was manageable, with grade ≥3 neutropenia (ICAHT), thrombocytopenia, and anemia occurring in 11%, 33%, and 0% of 9 evaluable patients at day 90 following CAR-T infusion.
Median follow-up time was 12 months (26 days to 2.0 years). Nine of 11 evaluable patients (82%) responded to CAR-T infusion, of which 5 remain in CR more than 6 months from CAR-T infusion (Figure). Two patients had loss of B-cell aplasia within the first year after CAR-T infusion (day +83 and +125), which was followed by a CD19-positive relapse in one patient. The estimated 1-year overall and progression-free survival were 65% (95%CI: 42-100) and 39% (95%CI: 19-82), and the 1-year cumulative incidence of non-relapse mortality was 8%. Three of the 6 patients with relapse or progressive disease were confirmed CD19 positive, and three patients (25%) were subsequently rescued with allogeneic HSCT.



Conclusions: This is the first trial of point-of-care manufactured CAR-T cells in Denmark and demonstrates that administering fresh CLIC-1901 product is safe, feasible and efficacious, especially in patients with low tumor burden. Our platform provides a feasible and rapid manufacturing procedure for future CAR-T products, which may also include targets outside commercial interests.

Clinical Trial Registry: CTIS no.: 2024-515174-27-00
https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en&EUCT=2024-515174-27-00

Disclosure: Nothing to declare

A118

OUTCOMES OF CRYOPRESERVED VERSUS NON-CRYOPRESERVED STEM CELL ALLOGRAFTS: A COMPARATIVE ANALYSIS

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Background: The use of fresh allogeneic stem cell grafts is traditionally preferred, to ensure optimal cell viability and functionality. However, the COVID-19 pandemic increased the use of cryopreserved stem cells due to logistical challenges in donor availability and allogeneic hematopoietic stem cell transplantation (alloSCT) scheduling. Cryopreservation offers greater flexibility but may impair cell viability, potentially delaying engraftment and reducing overall survival.

Methods: In this retrospective study, 394 consecutive alloSCT patients (170 females and 224 males, median age 58 years, (range 21-75) transplanted at the University Hospitals of Jena and Leipzig between January 2019 and December 2023 were analyzed. Of these, 97 patients received cryopreserved peripheral blood stem cell grafts, while 297 were transplanted with fresh allografts. The primary endpoints were time to neutrophil and platelet engraftment, defined according to EBMT-guidelines. Secondary endpoints included overall survival, relapse rate, non-relapse mortality, and incidence of acute and chronic graft-versus-host disease (GvHD).

Results: The majority of patients (n = 237, 60%) was diagnosed with acute myeloid leukemia (AML) with balanced disease risk index in both groups. The proportion of myeloablative (n = 37, 38.1% versus n = 100, 33.7%) and reduced intensity conditioning (n = 60, 61.9% versus 197, 66.3%) was similar between both cohorts. HLA-match, donor status, CMV-status of donor and recipient, age of donor, CMV-reactivation, and immunosuppression demonstrated no significant disparities.
No significant differences were observed between recipients of fresh or cryopreserved grafts in terms of neutrophil or platelet engraftment times, indicating comparable hematopoietic recovery kinetics. The median time to neutrophile engraftment was 17.5 days (range 8-32, IQR 8) in patients receiving cryopreserved grafts versus 18 days (range 8-139, IQR 6) in patients with fresh grafts ($p = 0.615$). Similarly, the median time to platelet recovery was 19 days (range 10-223, IQR 12) and 18 days (range 6-331, IQR 10), $p = 0.146$ in the two groups, respectively. Overall survival, number of patients with relapse, and time to relapse revealed no significant difference in patients with cryopreserved grafts versus fresh grafts. Acute GvHD and chronic GvHD did not differ significantly between groups. The only significant differences were found in infusion related adverse events (39.2% versus 17.2%, $p < 0.001$) and infections (75.3% versus 64%, $p = 0.047$).

Conclusions: The use of cryopreserved hematopoietic stem cells is safe in the alloSCT-setting without compromising neutrophil or platelet recovery, survival rate and risk of relapse, respectively. These data support the increased use of cryopreserved stem cells during logistical constraints such as those seen during the COVID-19 pandemic, expanding donor availability and transplant timing options without adverse effects on key clinical endpoints.

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Travel grants: J&J, Gilead Kite, Astra Zeneca
Honoraria: Abbvie, J&J, Gilead Kite, Roche, Novartis, Sobi, Astra Zeneca, Therakos/Malinckrodt, Elli Lilly, Amgen

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Research grants: Amgen

A119

COMPARISON OF OUTCOMES OF AUTOLOGOUS AND ALLOGENEIC STEM CELL TRANSPLANTATION FOR ALK-POSITIVE AND ALK-NEGATIVE ANAPLASTIC LARGE CELL LYMPHOMA: AN ANALYSIS OF THE EBMT LWP

Evgenii Shumilov[1], *Norbert Schmitz*[1], *Maud Ngoya*[2], *Shankara Paneesha*[3], *Kate Cwynarski*[4], *Flore Sicre de Fontbrune*[5], *Laura Magnano*[6], *Frank Kroschinsky*[7], *Johannes Clausen*[8], *Philipp Berning*[1], *Jose Antonio Perez-Simón*[9], *Lawrence Ng*[10], *Luca Castagna*[11], *Peter Dreger*[12], *Mohamad Mohty*[2], *Georg Lenz*[1], *Anna Sureda*[13], *Ghandi Damaj*[14], *Ali Bazarbachi*[15]
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Background: Autologous and allogeneic stem cell transplantation (auto-; allo-SCT) represent potentially curative approaches for patients (pts) with T-cell lymphoma. Large-scale outcome data on SCT in anaplastic large cell lymphoma (ALCL), particularly, a recent comparison of ALCL anaplastic lymphoma kinase (ALK)-positive vs. ALCL ALK-negative have not been reported. Several studies suggest younger age is the predominant factor for better outcomes of ALK-pos. pts. We aimed to compare the results of auto- and allo SCT in patients with ALK-pos. and ALK-neg. ALCL.

Methods: Pts registered with the EBMT registry between 2010 and 2022 and the following inclusion criteria were analyzed: age ≥18 years (yrs), diagnosis of ALK-pos. or neg. ALCL, auto-SCT as first/or salvage SCT or allo-SCT either as first SCT or after auto-SCT.

Results: 497 pts with ALK-neg. and 81 pts with ALK-pos. ALCL (median age 58 and 46 yrs, respectively) received up-front auto-SCT. At diagnosis, IPI ≥ 3 was 38% and 70%, respectively.
3-yr PFS and 3-yr OS rates after up-front auto-SCT were 68.5% and 75.1%, and 84.1% and 83.5 in ALK-neg. and ALK-pos. ALCLs, respectively. The 3-yr RI and NRM were 27.7% and 22.3%, and 3.9% and 2.6%. ALK-neg. and ALK-pos. pts transplanted in first CR (CR1) showed comparable outcomes [3-yr PFS 74.9% vs. 74.1%; 3-yr OS: 85.4% vs 83.5%] while

PR1 patients survived significantly better if having ALK-positivity [3-yr PFS 55.3% vs. 78.6%; 3-yr OS 68.4% vs 92.3%].
In r/r situation, 328 pts with ALK-neg. and 201 pts with ALK-pos. ALCL received salvage auto-SCT with a median age of 54 and 38 years. After a median of two therapies, 3-yr PFS and 3-yr OS after salvage auto-SCT were 62.4% and 57.1%, and 73.8% and 85.1% in ALK-neg. and ALK-pos. ALCLs, respectively. The 3-yr RI and NRM were 31.3% and 39.2%, and 6.3% and 3.6%, accordingly. Auto-SCT ALK-pos. and ALK-neg. pts transplanted in later CR (CR2+) showed comparable outcomes [3-yr PFS 65.5% vs. 55.7%; 3-yr OS: 78.8% vs 86.3%] while PR2+ pts with ALK-neg. status worse survival [3-yr PFS 55.1% vs. 61.5%; 3-yr OS: 73.3% vs 80.8%].
247 pts with ALK-neg and 100 pts with ALK-pos ALCL received salvage allo-SCT with a median age of 52 and 33 years. In the allo-SCT group (median of 3 therapies prior) with 49% and 23% undergoing prior auto-SCT in ALK-neg. and ALK-pos. pts, 3-yr outcomes were as follows: PFS: 49.5% vs. 62%; OS: 59.7% vs. 79%, RI 30.9% vs. 28%; and NRM 19.6% vs. 10%. In CR pts at allo-SCT, 3-yr outcomes were: PFS 63.1% vs. 67%; OS 72% vs. 85%. In PR pts at allo-SCT, 3-yr PFS and OS were 31% vs. 77%, and 51% vs. 77%, respectively.

Conclusions: In both, ALK-pos. and ALK-neg. ALCL, transplantation resulted in excellent survival after auto- or allo-SCT. Outcomes of auto-SCT performed in CR1/CR2+ were comparable between both entities while PR pts survived better if being ALK-positive. Outcomes post-allo-SCT were significantly better in the group of ALK-pos. pts probably reflecting a significantly younger age of these pts. A matched-pair analysis of ALK-pos. and ALK-neg. pts is ongoing.

Disclosure: K. Cwynarski: Consulting/Advisory Role: Abbvie, Roche, Autolus, Sobi, KITE, Takeda, BMS, Atara, Gilead, Janssen; Speakers' Bureau: Roche, Takeda, KITE, Gilead, BMS; Conferences/Travel support: Roche, Takeda, KITE, Janssen, BMS
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A120

TREATMENT OUTCOMES WITH OUT-OF-SPECIFICATION PRODUCTS AND REMANUFACTURING SUCCESS IN CAR T-CELL THERAPY FOR AGGRESSIVE B-CELL LYMPHOMAS: A MULTICENTRE REAL-WORLD STUDY GETH/GELTAMO

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Background: Out-of-specification (OOS) CAR-T products and manufacturing failure (MF) remains a major barrier for delivery of this treatment modality in aggressive B-cell non-Hodgkin lymphomas (B-NHL). Understanding MF patterns and OOS CAR-T outcomes, together with the rate of remanufacturing success is essential to improve access and clinical performance in real-world practice.

Methods: We conducted a multicentre, retrospective study of patients with aggressive B-NHL undergoing leukapheresis for commercial CAR-T therapy in Spain from 2019 to 2025. Manufacturing outcomes were categorised as first-attempt result (in-spec, OOS, or MF), remanufacturing attempt, and final product (OOS-infused, delayed-infused after in-spec remanufacturing, or non-infused), following previously published UK experience (Dulobdas et al., Blood Cancer J 2025). Survival was estimated using Kaplan-Meier curves. All CAR-T apheresis procedures performed at participating centres during the study period were

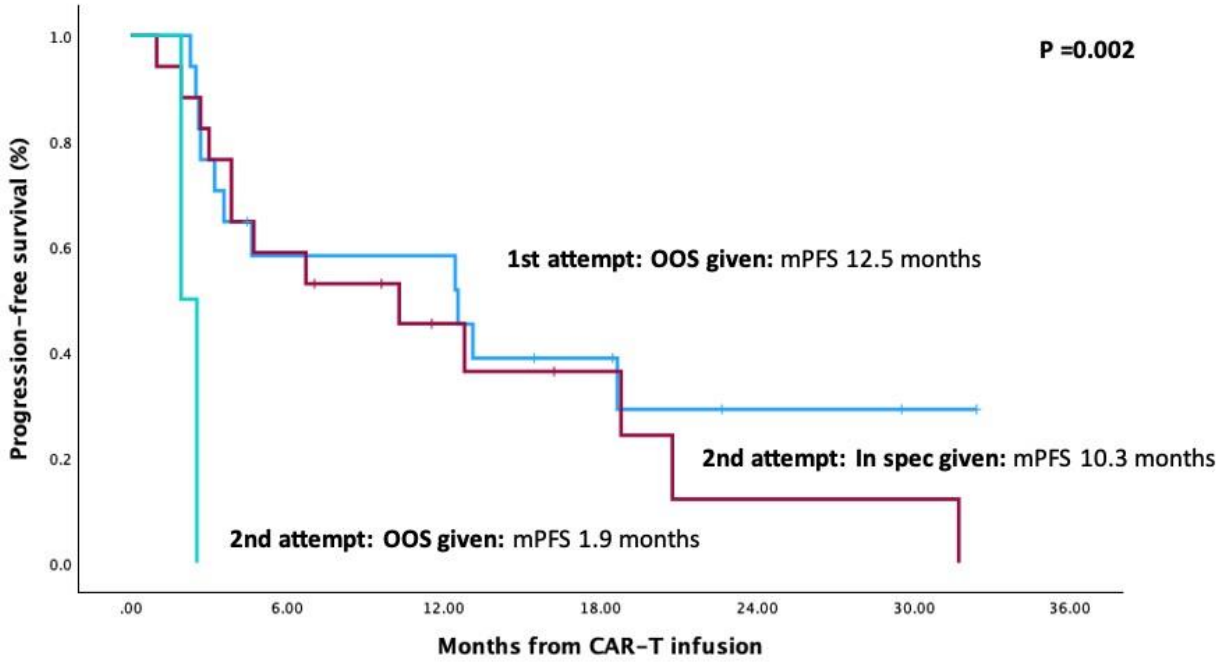
included. Manufacturing failure incidence was calculated overall and adjusted for product mix, accounting for the relative distribution of CAR-T products.

Results: A total of 1,210 apheresis procedures were analyzed, 79% corresponding to axicabtagene ciloleucel and 21% to tisagenlecleucel; 50 patients (4.13%) experienced manufacturing failure or out-of-specification products. Median age was 63 years (range: 41–78) and 60% were male. Subtypes included diffuse large B-cell lymphoma not otherwise specified (56%), transformed follicular lymphoma (18%), high-grade B-cell lymphoma (12%) and T-cell/histiocyte-rich large B-cell lymphoma (6%). Most patients (76%) underwent CAR-T in ≥3rd line and 78% were primary refractory. Based on product distribution, estimated MF incidence was 4.18% for axi-cel (40/956) and 3.94% for tisa-cel (10/254). Among MF cases, 56% had an OOS product available after the first attempt, of which 17 were infused, 3 proceeded to remanufacturing and 8 were not infused. When no OOS product was available, remanufacturing was attempted in 18 patients. Overall, 21 remanufacturing attempts yielded 17 in-spec products infused, 2 in-spec products not infused, and 2 OOS products infused. Final outcomes were OOS-infused (n=19), delayed-infused after remanufacturing (n=17) and non-infused (n=14).Among infused patients (n=36; axicabtagene ciloleucel 81%, tisagenlecleucel 19%), cytokine release syndrome occurred in 81% (grade ≥3: 3%) and ICANS in 55% (grade 3–4: 13%). The best overall response rate was 50% (CR 37%, PR 13%). Median OS was 12.5 months for infused versus 1.2 months for non-infused patients ($p<0.001$). Median PFS was 10.3 versus 0.7 months, respectively ($p<0.001$). Post-infusion PFS was comparable after first-attempt OOS infusion and second-attempt in-spec infusion, while inferior PFS was observed after second-attempt OOS infusion (Figure 1). Age >60 years ($p=0.04$), double-hit lymphoma ($p=0.028$), shorter time from diagnosis to apheresis ($p=0.014$), primary refractory disease ($p=0.008$) and prior bendamustine exposure (9/50; $p=0.049$) were associated with inferior PFS. Autoimmune disorders were present in 10% of patients.

IMPACT OF OOS STATUS AT INFUSION:

PFS from infusion:

Infusion group	Median PFS (95%CI)	p
1st attempt: OOS product given	12.5 (1.9-23.1)	0.002
2nd attempt. In spec product given	10.3 (1.5-19.1)	
2nd attempt. OOS product given	1.9 (NA)	



Conclusions: Manufacturing failure occurred in 4.13% of apheresis procedures, with nearly half of patients receiving CAR-T through OOS infusion or remanufacturing. Post-infusion outcomes were similar between OOS-infused and delayed-infused patients, while failure to reach infusion was associated with poor survival. These findings underscore the importance of optimized manufacturing pathways. Further analyses of OOS and manufacturing failure causes will be presented at the Congress.

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Kite/Gilead, Janssen, Miltenyi, Abbvie, MSD, Regeneron. Honoraria: Abbvie, AstraZeneca, BMS, Kite/Gilead, Miltenyi, Sobi, Roche, Lilly. Travel support: Abbvie, AstraZeneca, Kite/Gilead, Miltenyi, Roch. Leyre Bento: Honoraria and /or consulting fees: AbbVie, Incyte, Kite/Gilead, Roche, BMS. Research support: Roche Ana Jimenez-Ubieto: Honoraria and/or consulting fees: AbbVie, AstraZeneca, Bristol Myers Squibb (BMS), Incyte, Kite/Gilead, and Roche. Pere Barba: Honoraria and consulting: Gilead, Bristol Myers Squibb, Novartis. Mi Kwon: Honoraria and consulting: Kite/Gilead, Bristol Myers Squibb, Novartis Alejandro Martin García-Sancho: Honoraria and/or consulting fees: Abbvie, AstraZeneca, BeOne, BMS, Genmab, Gilead/Kite, GSK, Ideogen, Incyte, Janssen, Kyowa Kirin, Lilly, Miltenyi, Regeneron, Roche, Sobi, Takeda. The other authors have no conflict of interest to declare.

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INCIDENCE AND RISK FACTORS FOR POOR GRAFT FUNCTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE IN A MULTICENTER COHORT

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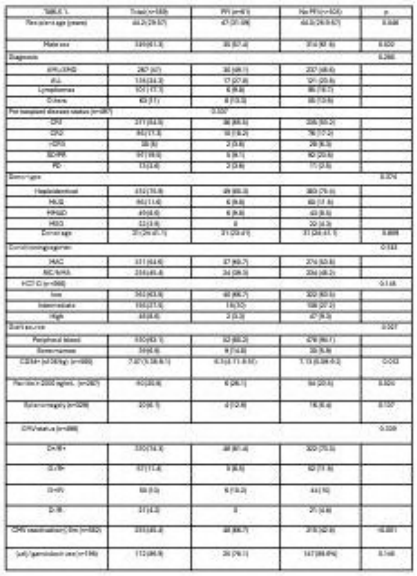
Background: Poor graft function (PGF) is a clinically relevant complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT) associated with substantial morbidity. Post-transplant cyclophosphamide (PTCy) has been proposed as a potential contributor to PGF development; however, data regarding its incidence and risk factors in this specific setting remain limited.
Objectives: To estimate the cumulative incidence of PGF within the first 6 months after allo-HSCT with PTCy, identify clinical factors associated with PGF development, and describe therapeutic strategies used for its management.

Methods: We conducted a multicenter retrospective study including ≥18-year patients with hematologic diseases undergoing allo-HSCT between 2016 and 2024 at 8 centers of the GATMO-TC. Donors included haploidentical, matched or mismatched unrelated, and HLA-identical related donors. GVHD prophylaxis consisted of PTCy plus mycophenolate mofetil and a calcineurin inhibitor, using peripheral blood or bone marrow as the graft source. PGF was defined as neutrophils <500/µL and/or platelets <20,000/µL from day +28 with donor chimerism >95%, without relapse or active GVHD. Six-month PGF cumulative incidence was estimated using cumulative incidence functions considering competing events: early

mortality (≤30 days), primary graft failure, and early relapse (≤180 days). Risk factors were assessed using Fine–Gray competing risks regression.

Results: A total of 569 patients were included (median age 44.2 years; 61.3% male). Diagnoses included AML/MDS (47%), ALL (24.3%), lymphomas (17.7%) and others. The 6-month cumulative incidence of PGF was 10.4% (95% CI 7.9–12.9), early mortality 4.7%, primary graft failure 2.0%, and early relapse 6.0%. Among patients with PGF (n=61), 84% had secondary PGF. Management included thrombopoietin receptor agonists (TPO-Ras) (n=21), TPO-Ras plus filgrastim and erythropoietin (n=7), filgrastim alone (n=13), or transfusional support; seven patients required second-line therapy ($CD34^+$ boost n=3, change of TPO-Ras n=3, second transplant n=1). Median time to response was 1.10 months (IQR 1–3), with no difference according to treatment strategy(p=0.388). Letermovir prophylaxis was used in 56/427 seropositive receptors. 44.8% had ≥1 CMV reactivation within 6 months. In univariate analysis, higher infused $CD34^+$ cell dose was associated with a reduced risk of PGF (HR 0.54 per 5×10^6/kg increase; 95% CI 0.32–0.90; p=0.017), while bone marrow graft source (HR 2.69; 95% CI 1.31–5.54; p=0.007) and CMV reactivation within 6 months (HR 2.42; 95% CI 1.41–4.14; p=0.001) were associated with increased PGF risk. The presence DSA showed a trend toward increased risk but did not reach statistical significance (HR 2.57; 95% CI 0.80–8.32; p=0.110). In multivariate analysis, bone marrow graft source (HR 2.46; 95% CI 1.10–5.49; p=0.028), CMV reactivation ≤6 months (HR 2.44; 95% CI 1.41–4.22; p=0.001), and presence of DSA (HR 2.93; 95% CI 1.05–8.20; p=0.040) remained independently associated with PGF.



Conclusions: In this multicenter cohort of allo-HSCT recipients receiving PTCy-based GVHD prophylaxis, the incidence of PGF was not higher than that reported in non-PTCy platforms. Bone marrow graft source, CMV reactivation within 6 months, and donor-specific anti-HLA

antibodies were the main independent risk factors for PGF. These findings support optimization of graft quality and intensified CMV monitoring and prophylaxis strategies in patients receiving PTCy.

Disclosure: No disclosures.

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ALLOGENEIC STEM CELL TRANSPLANTATION WITH 3-DAYS BUSULFAN PLUS FLUDARABINE AS CONDITIONING REGIMEN FOR PATIENTS WITH RELAPSED OR REFRACTORY T- AND NK/T-CELL LYMPHOMAS

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Background: Peripheral T-cell lymphomas (PTCL) and NK/T-cell lymphoma (NKTCL) are characterized by chemo-resistance, frequent relapses, and rapid progression. Allo-SCT can provide durable disease control, but optimal conditioning intensity/regimen remains uncertain. The objectives of this study is to prove the feasibility in terms of efficacy and safety of 3-days intravenous busulfan (Bu) in combination with fludarabine (Flu) in relapsed and refractory T- and NK/T-cell lymphomas.

Methods: This is a prospective phase II trial which plans to enroll 34 patients. Histologically confirmed relapsed and refractory T- and NK/T-cell lymphomas who relapsed after or were refractory to one or more of previous chemotherapy including auto-SCT and had achieved partial response (PR) or complete response (CR) after salvage chemotherapy were enrolled. Patients who had HLA full-match (8/8 in HLA-A, B, C, DR by DNA high-resolution technique) or one-locus mismatch (7/8) sibling, or unrelated bone marrow (BM) or peripheral blood (PB) or cord blood (CB) stem cell donors were enrolled. Conditioning therapy was started on day -8. Busulfan (Busulfex®; Patheon Manufacturing Services LLC, Greenville, NC 27834) was given 3.2 mg/kg intravenously once daily for 3 days (days -7 to -5) and fludarabine 30 mg/m^2 was infused once daily for 6 days (days -8 to -3) (Bu3Flu6). Primary endpoint of this study is 2-year progression-free survival (PFS). This is the preliminary result of 15 patients enrolled to the study.

Results: Twenty-three patients received Allo-SCT with Bu3Flu6 conditioning regimen for relapsed or refractory T- and NK/T-cell lymphomas. Median age was 55 years (range, 33–66 years), and the median number of prior lines of therapy was 2 (range, 1–4). Eleven patients (47.8%) had previously undergone autologous stem cell transplantation. Peripheral blood stem cells were used in 22 patients and cord blood in 1 patient; donor types included

matched sibling donors in 47.8%, matched unrelated donors in 43.5%, and one-locus mismatched donors in 8.7% of patients. After a median of 3 cycles of salvage chemotherapy, 15 patients (65.2%) achieved complete remission (CR) and 8 patients (34.8%) partial remission (PR) prior to Allo-SCT. Among the 8 patients in PR before transplantation, 5 patients achieved CR after Allo-SCT with Bu3Flu6 conditioning. With a median follow-up duration of 17.8 months (range, 0.67–96.30 months), the 2-year progression-free survival and overall survival rates were 58.3% (95% CI, 35.0–75.8%) and 53.6% (95% CI, 30.7–72.0%), respectively. All patients achieved neutrophil and platelet engraftment, with median times of 12 and 12 days, respectively. No unexpected regimen-related toxicities, including sinusoidal obstruction syndrome or hemorrhagic cystitis, were observed. Grade 3–4 acute graft-versus-host disease (GVHD) and moderate-to-severe chronic GVHD occurred in 39.1% and 56.5% of patients, respectively, and chronic GVHD complicated by severe infection led to death in two patients.

Conclusions: 3-days Bu and 6-days Flu combination as a conditioning regimen is effective with tolerable safety profile for relapsed or refractory T- and NK/T-cell lymphoma patients who are undergoing Allo-SCT after achieving CR or PR to salvage regimen.

Clinical Trial Registry: NCT02859402

Disclosure: Nothing to disclose.

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THE IMPACT OF HLA-DPB1 PERMISSIVE AND NON-PERMISSIVE MISMATCH ON OUTCOMES IN MATCHED RELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR THALASSEMIA

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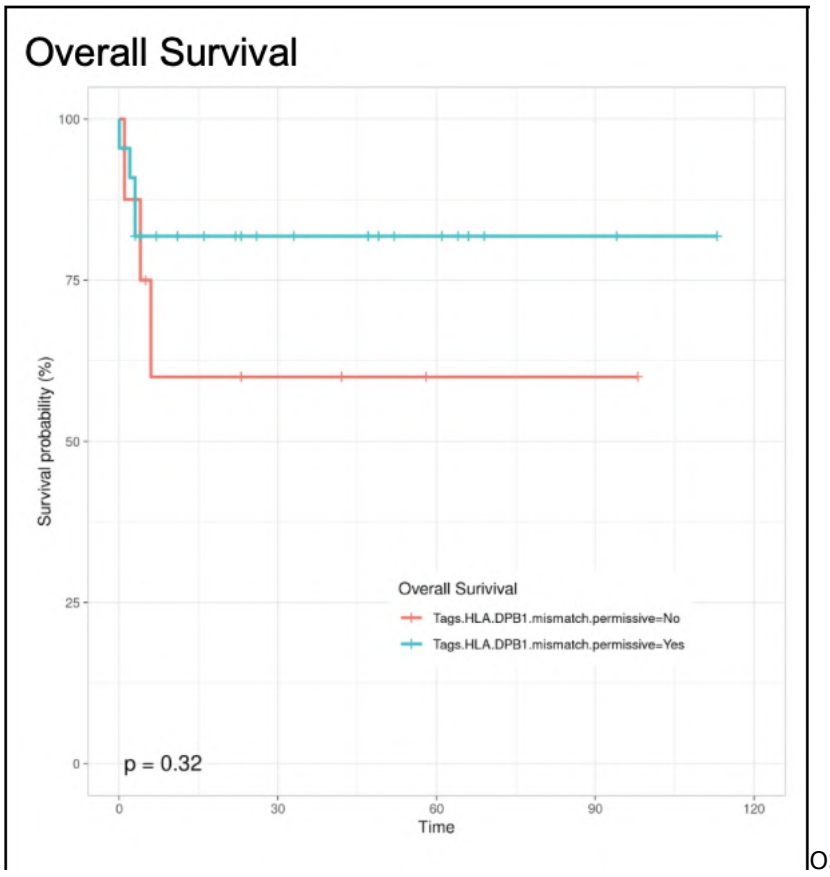
Background: Allogeneic HSCT remains the only definitive cure for transfusion-dependent thalassemia. While the permissive versus non-permissive HLA-DPB1 mismatch framework is well established as a determinant of GVHD and survival in unrelated donor transplantation, its significance in matched related donor HSCT-where DPB1 disparity is uncommon-has never been clearly defined. In this study, we systematically evaluate the clinical impact of DPB1 permissiveness in the matched related donor setting, addressing a long-standing evidence gap in thalassemia transplantation.

Methods: We conducted a retrospective analysis of 786 consecutive matched related donor HSCTs for transfusion-dependent thalassemia performed between 2017 and 2025 across

centres in Jaipur, Bangalore, Ahmedabad, Islamabad, and Vietnam. High-resolution DPB1 typing was available for 771 recipients. All transplants used a uniform platform consisting of Flu-ATG-Bu-Cy conditioning, cyclosporine–methotrexate–based GVHD prophylaxis, and G-CSF–primed bone marrow grafts, following our previously published protocol. The median patient age at transplant was 7.09 (IQR:4.11 - 11.03, Range: 1.01 - 21.07) years, with a median follow-up of 2.2 (IQR:0.8 - 4.4, Range: 0 - 9.4) years. DPB1 mismatches were assessed using the IPD-IMGT/HLA T-cell-epitope (TCE) algorithm and categorised as permissive or non-permissive. Clinical endpoints included overall survival (OS), disease-free survival (DFS), graft failure or rejection, GVHD-relapse-free survival (GRFS), transplant-related mortality (TRM), and grade 3–4 acute or moderate–severe chronic GVHD.

Results: Among 786 typed matched related donor transplants, 30 (3.8%) showed DPB1 mismatches - 22 permissive and 8 non-permissive-occurring across 15 sibling donors, 8 father, 6 mothers, and 1 cousin. Baseline characteristics, including age, sex, conditioning, and GVHD prophylaxis, were comparable between groups. There were no significant differences in overall survival (p=0.32), transplant-related mortality (p=0.75), disease-free survival (p=0.075), graft rejection (p=0.078), or GVHD-relapse-free survival (p=0.83). Grade 3 acute and moderate chronic GVHD occurred in one patient with a permissive mismatch, while no ≥ grade 3 GVHD events were observed in the non-permissive group. Across all variables assessed, DPB1 permissiveness showed no significant impact on outcomes.



OS

Conclusions: This large multi-centre series shows that DPB1 permissiveness is associated with meaningful differences in outcomes among matched related donor transplants for thalassemia. While acknowledging the limitations of the small number of mismatched cases, DPB1 disparities-permissive or non-permissive-do appear to influence prognosis in this setting.

Disclosure: The authors declare no competing financial interests.

A125

CLINICAL OUTCOMES OF FULLY HLA-MATCHED SIBLING VERSUS PARENTAL HSCT IN CHILDREN WITH HEMOGLOBINOPATHIES

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Background: Hematopoietic cell transplantation (HCT) is the only well-established long-term curative treatment. The highest success rates are achieved with HLA-matched sibling donors. However, in the absence of a matched sibling particularly in younger patients or those from smaller families, closely related family members, such as biological parents, are increasingly considered as potential donors. This study aims to evaluate the donor type, age, bone marrow cellularity, and donor–recipient sex mismatch on outcomes of fully HLA-matched pediatric HSCT.

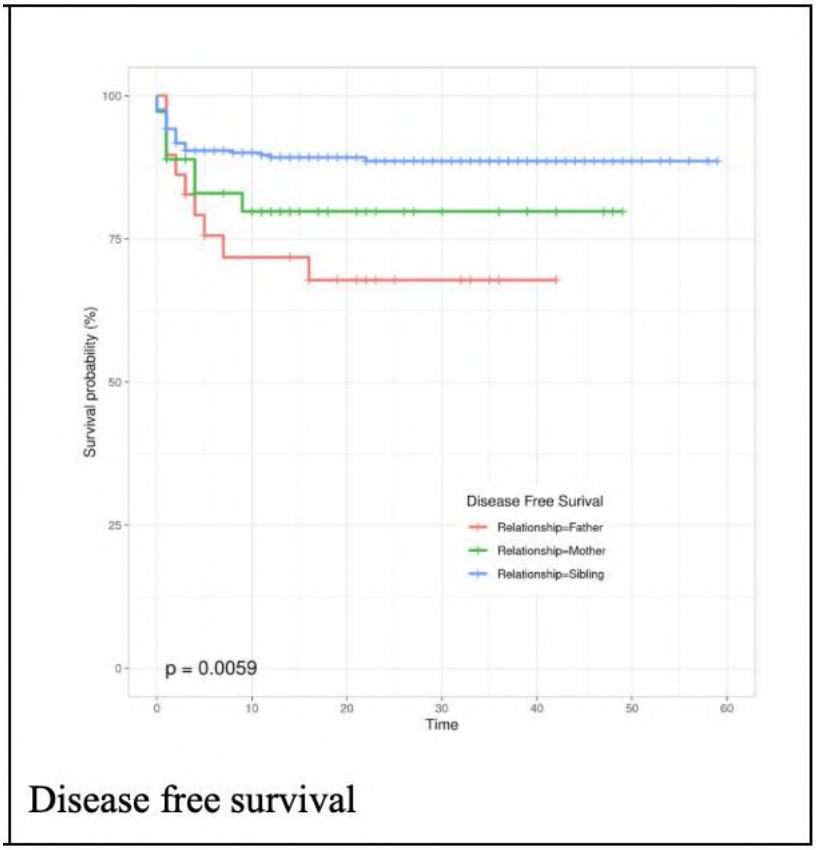
Methods: This is a multicenter study including pediatric patients with severe hemoglobinopathies who underwent hematopoietic stem cell transplantation (HSCT) from fully HLA-matched related donors between October 2020 and November 2025. All patients received granulocyte-colony stimulating factor (G-CSF)-primed unmanipulated bone marrow and myeloablative conditioning (fludarabine, busulfan, cyclophosphamide, and anti-thymocyte globulin (ATG), while ATG-free conditioning was used in the sibling cohort from May 2023. Graft-versus-host disease (GVHD) prophylaxis included cyclosporine and methotrexate, with supportive care administered according to individual institutional protocols.

Results:

A total of 404 paediatric patients underwent fully HLA-matched HSCT using matched siblings (n = 339) and matched parental donors (father, n = 30; mother, n = 35). The median follow-up was 15.8 months (IQR, 6.5–26.2 months). Overall survival (OS) was 92.9%, 91.7%, and 86.2% following sibling, maternal, and paternal donor transplants, respectively (p = 0.53). Disease-free survival (DFS) was 89.6 % in sibling donors, 80.6% maternal and 70% paternal donors (p = 0.0059).

The engraftment rate was 97.6% in sibling donor transplants (2.3% primary and 1.1% secondary graft failures), 93.3% in paternal donor transplants (6.6% primary and 10% secondary graft failures), and 91.4% in maternal donor transplants (8.5% primary and 2.8% secondary graft failure). Graft rejection was the highest in paternal donors (20.6%) and maternal donors (11.1%), and the lowest in sibling donors (3.9%) at p = 0.0041. Acute graft-versus-host disease (GVHD) grade ≥3 was observed in 2.4% siblings, 6.6% paternal, and 14.3% (5) maternal donor recipients (p < 0.0001).

The median donor age was 8.06 years (IQR, 5.05 -11 years) for sibling donors, 36.02 years (IQR, 32-40.7 years) for paternal donors, and 33.04 years (IQR, 28.7 - 36.2 years) for maternal donors. Donor recipient sex matching was observed in 44% (n = 177) of transplants, including male-to-male (24.2%) and female-to-female (19.5%) pairs. Sex mismatch was present in 56.1% (n = 227) of transplants, including male-to-female (20.7%) and female-to-male (35.4%) pairs. Overall survival did not differ between sex-matched and sex-mismatched transplants (92.1% vs 92.5%; p = 0.85). Disease-free survival was also comparable (88.1% vs 86.7%; p = 0.73). Similarly, graft rejection (5.1% vs 6.1%; p = 0.50) and GVHD (16.3% vs 17.1%; p = 0.81) did not differ by sex-matching status. Grade ≥3 acute GVHD occurred in approximately 4.5% of sex-matched and 5.7% of sex-mismatched transplants.



Disease free survival

Conclusions: In pediatric HSCT for severe hemoglobinopathies, fully HLA-matched sibling and parental donors achieve excellent overall survival, with disease-free survival and graft outcomes slightly higher with sibling donors, and donor–recipient sex mismatch does not significantly affect survival, graft rejection, or GVHD incidence

Disclosure: The authors declare no competing financial interests.

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PATIENTS WITH HIGH GRADE TRANSFORMATION OF WALDENSTRÖM'S MACROGLOBULINEMIA CAN BE RESCUED WITH TRANSPLANTATION. REPORT FROM THE LYMPHOMA WORKING PARTY OF THE EBMT

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Background: High Grade Transformation of Waldenstrom's Macroglobulinemia (tWM) although rare, is a serious complication. This retrospective EBMT registry study aimed to analyse the results of autologous (ASCT), allogeneic (Allo-SCT) stem cell transplantation and CAR T Cell therapy for patients with tWM.

Methods: EBMT centers submitted data for 310 tWM patients. ASCT was used in 217, Allo-SCT in 49 patients between 2010-2023, CAR T Cell therapy in 44 between 2023 -2024.

Results: Of the 217 ASCT patients, 122 were male with a median age of 53.9 years and Karnofsky performance status (KFS) ≥90 in 67%. Median time from diagnosis to ASCT was 8.1 (2.4-202) months. ASCT was performed post 1st treatment line in 37%, post 2nd line in 43%,following 3rd line in 20%. Disease status was CR in 118 patients (57%), Very Good Partial Response (VGPR) /Partial Response (PR) in 57 (27%), Primary Refractory (PRD) / Progressive Disease (PD) in 30 (14%) and in 12 (2%) it was not available (NA). 63% received BEAM based conditioning. The estimated Overall Survival (OS) was 68.9%, Progression Free Survival (PFS) 59.5%, Relapse Incidence (RI) 36.3%, Non-Relapse Mortality (NRM) 4.2% at 2 years respectively.
Of the 49 Allo-SCT patients, 33 were male with a median age of 47.6 years and KFS ≥90 in 60%. Median time from diagnosis to Allo-SCT was 13.6 (3.1-167) months. 43% had the Allo-SCT following 1st line, 33% post 2nd line, 24% following ≥3rd treatment lines. 39% had failed previous ASCT. Disease status was CR in 23 patients (47%), VGPR / PR in 14 (29%), PRD / PD in 9 (18%) and in 3 (6%) it was not available. Myeloablative conditioning (MAC) was used in 30 patients (61%), reduced intensity conditioning (RIC) in 19 (39%) and TBI was used for 14 (29%). Stem cell donor was sibling in 18 (37%), unrelated in 24 (49%) haploidentical in 7 (14%). 29 (63%) patients had in vivo T cell depletion. Median follow up was 7.8 years (3.1-8.2). The estimated OS was 43%, PFS 29%, RI 55%, NRM 17%, graft versus host disease (GVHD)-free/relapse-free survival (GRFS) 21% at 2 years respectively. The incidence of acute GVHD grade III/IV was 12% and chronic extended GVHD was 9%.
From the 44 CAR T Cell treated patients, 29 were male, median age was 61years, KFS ≥90 in 50%. Median time from diagnosis to CAR T Cell therapy was 12.8 (3.3- 198.2) months. 37% had CART following 1st treatment line, 43% after 2nd and 20% after ≥3rd prior treatment lines. The disease status was CR in 3 patients (7%), VGPR / PR in 6 (13.5%), PRD / PD in 33 (75%) and in 2 (4.5%) it was not available. Median follow up was 3 (0-6) months, OS 68.5%, PFS 35.8%, RI 59.7%, NRM 4.5% at 1 year respectively.

Conclusions: This EBMT analysis is the largest cohort of tWM patients to date, reporting satisfactory rescue survival outcomes of ASCT and CAR T cell therapy although longer follow up is required for this approach. Allo-SCT survival outcomes were low.

Disclosure: No conflict of interest to declare

A128

IMPACT OF PRE-APHERESIS HOLDING THERAPY ON EFFICACY AND HEMATOLOGIC TOXICITY AFTER CD19 CAR T-CELL THERAPY IN LARGE B-CELL LYMPHOMA

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Background: Patients with relapsed or refractory large B-cell lymphoma (LBCL) often require disease control while awaiting leukapheresis for CD19 CAR T-cell therapy. While bridging therapy administered between apheresis and lymphodepletion is well described, the clinical impact of therapy given after the CAR-T decision but before apheresis ("holding therapy") remains limited. We evaluated the association between pre-apheresis holding and outcomes after CD19-directed CAR T-cell therapy.

Methods: We performed a retrospective study of adults with LBCL who underwent leukapheresis for CD19 CAR-T (2022–2025) at our center. Holding therapy was defined as any systemic therapy or radiotherapy given after the decision to proceed with CAR-T therapy and before apheresis. Patients receiving holding plus bridging were compared with those receiving bridging alone. Primary endpoints were disease status at apheresis and day-28 response following CAR-T infusion. Secondary endpoints included best response within 1 year, progression-free survival (PFS), overall survival (OS), cumulative incidence of relapse and non-relapse mortality (NRM), and early and late hematologic toxicity (grade ≥3 neutropenia, anemia, thrombocytopenia, and N-ICAHT). Multivariable logistic, Cox, and competing-risk regression models were used.

Results: We included 147 adults with LBCL undergoing leukapheresis for CD19 CAR-T (59% lisocabtagene maraleucel, 37% axicabtagene ciloleucel and 5% tisagenlecleucel). Among these, 89 patients received holding plus bridging and 58 bridging alone. Median time from relapse to apheresis was longer with holding (54 vs 36 days), whereas apheresis-to-infusion intervals were similar between groups (**Table 1**).
Among patients who received holding plus bridging, 40 (45%) continued the same regimen

for bridging and 49 (55%) switched. Pre-apheresis CR/PR was more frequent after holding (40% vs 19%). However, day-28 response after CAR-T did not differ across holding strategies (p=0.80) (**Fig 1A-1B**); best 1-year response was also similar among groups (p=0.59). In multivariable models adjusting for KPS, primary refractory disease, pre-apheresis LDH and SUVmax, the hazard ratio for PFS for holding was 0.34 (95% CI 0.14–0.81; p=0.014) and for OS was 0.63 (95% CI 0.19–2.14; p=0.50). One-year cumulative incidence of relapse was 31% with holding versus 42% without (p=0.11), and 1-year CI of NRM was 4.8% versus 6.2% (p=0.50).
Early grade ≥3 cytopenias were common regardless of holding exposure (day-30 neutropenia 83% vs 82%; thrombocytopenia 32% vs 26%). Grade ≥3 anemia was more frequent with holding (40% vs 26%, p=0.074). Early N-ICAHT grade distribution differed, with more grade 4 events among patients receiving holding (9.2% vs 0%) (**Fig 1C**). In the day-30 landmark analysis, late grade ≥3 cytopenias and late N-ICAHT did not differ between groups.

Characteristic [1] n (%); Mean (SD)	**Received Holding** N = 89[1]	**Did Not Receive Holding** N = 58[1]	**Overall** N = 147[1]
CAR-T Product Received			
Lisocabtagene maraleucel	52 (58%)	34 (59%)	86 (59%)
Axicabtagene ciloleuce	31 (35%)	23 (40%)	54 (37%)
Tisagenlecleucel	6 (6.7%)	1 (1.7%)	7 (4.8%)
Karnofsky Performance Status pre-CAR-T			
< 90	65 (76%)	33 (57%)	98 (69%)
LBCL Subtype			
DLBCL NOS	68 (76%)	46 (79%)	114 (78%)
High-grade B-cell Ly.	13 (15%)	7 (12%)	20 (14%)
Disease stage at apheresis			

III-IV	60 (69%)	39 (67%)	99 (68%)
LDH range pre-lymphodepletion			
Elevated	29 (34%)	20 (37%)	49 (35%)
Primary refractory pre-apheresis	36 (41%)	35 (60%)	71 (49%)
Bulky disease pre-apheresis	9 (10%)	5 (8.6%)	14 (9.7%)
Pre-apheresis SUVmax	11 (14)	16 (11)	13 (13)
CAR-T Treatment Line ≤ 2	70 (79%)	51 (88%)	121 (82%)
Time(days) from apheresis to infusion			
Median (IQR), Range	39 (12), 35-47	40 (13), 33-46	39 (12), 34-46

Conclusions: In this real-world cohort, pre-apheresis holding therapy was associated with favorable PFS, without excess relapse or NRM, and did not worsen late hematologic toxicity. Early hematotoxicity was modestly higher with holding, but late cytopenias and N-ICAHT were not increased. Overall, these findings support the feasibility of pre-apheresis holding strategies to maintain disease control while patients await leukapheresis for CD19 CAR T-cell therapy.

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EFFECT OF DEFERASIROX INITIATED AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION ON OUTCOMES IN AML AND MDS: A PROSPECTIVE OBSERVATIONAL STUDY WITH PROPENSITY-SCORE MATCHED CONTROLS

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Background: In allo-HSCT setting, some studies have shown that iron overload was associated with lower overall survival (OS), and that deferasirox, an oral iron-chelating agent, may have possible antileukemia effect. On behalf of the SFGM-TC, we conducted a prospective, interventional study on iron chelation, matched with retrospective data of non-chelated patients from the SFGM-TC registry. The study aimed to evaluate the impact of iron chelation therapy on OS and progression free survival (PFS) from 6 months after allo-HSCT for AML and MDS.

Methods: Patients at inclusion were: (1) in CR at 6 months after allo-HSCT for AML or < 10% of blasts for MDS (2) with a ferritin level above 1,000 µg/L. All patients received deferasirox starting 6 months after allo-HSCT until a target ferritin level of 500 µg/L, unless intolerance. In parallel, we created a control group of allo-HSCT patients from the SFGM-TC registry and who did not receive iron chelation therapy. The control group was built using a propensity score matching (PSM) method, which balances between the two groups of patients potential confounding factors. A 1:2 ratio (chelated vs non-chelated) with a calliper <= 0.18 was set. The analysis period began 6 months after allo-HSCT and continued until the end of the data availability period or until death. Analyses employed exact matching, inverse probability of treatment weighting (IPTW), and multivariable Cox models, with adjustment for chronic GVHD and sensitivity analyses using E-values.

Results: A total of 41 AML/MDS patients treated by iron chelation were included between April 2015 and February 2022 from 7 allo-HSCT centres. The median age was 58 years (20-70), 66% were male, 85% had an AML, a majority of ELN 2010 intermediate-II score (76%), and a median ferritin level before and after allo-HSCT of 1529 (14-4157) and 1781 (1000-10 041) µg/L respectively. A control group of 82 patients from 950 AML/MDS allo-HSCT patients from SFGM-TC registry who did not receive iron chelation was built from PSM with a standard mean difference < 0.1 for each potential confounding factors. Across analytic methods, deferasirox was associated with improved PFS (HR 0.41–0.44) and favorable OS (HR 0.28–0.43). TRM was significantly reduced in PSM and Cox models (HR 0.21), with a trend in

IPTW. CIR did not differ significantly. The adverse events (AE) associated with iron chelation therapy were acceptable. Ferritin decreased under deferasirox, from 1,700 µg/L at baseline to <1,000 µg/L by 18 months.The median duration of iron chelation was 12.5 (0.8-24.3) months. A reduction in dosage occurred in 9.5% of cases. The permanent discontinuation in 33% of patients was predominantly related to acute renal failure (n=4) and altered of renal biomarkers (n=4).

Conclusions: In our study we evaluated the use of deferasirox after allo-HSCT for AML/MDS. We demonstrated a doubtful effect of iron chelation on OS but a clear benefit on PFS. The tolerance profile was acceptable, but special attention to renal function should be considered to modulate potentially the dose of desferasirox. This study reinforces the place of iron chelation in the therapeutic arsenal after-HSCT in AML/SMD patients.

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A130

HIGHER BODY MASS INDEX IS ASSOCIATED WITH IMPROVED OUTCOMES AFTER CAR-T CELL THERAPY IN PATIENTS WITH LARGE B-CELL LYMPHOMA

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Background: CAR-T cell therapy has revolutionized the treatment of Large B-Cell Lymphoma (LBCL); however, relapse remains frequent. Metabolic inflammation may modulate CAR-T expansion and relapse risk. The influence of body mass index (BMI) and metabolic status on CAR-T efficacy remains unclear. In this study, we evaluated the association between BMI, metabolic factors, and outcomes after CAR-T therapy in a bicentric real-world cohort.

Methods: We retrospectively analyzed patients with LBCL treated with commercial CAR-T products (axi-cel or tisa-cel) at the Bone Marrow Transplantation Units of Brescia and Verona,

Italy. Baseline BMI, lipid profile, glycemic status, and cardiovascular/metabolic comorbidities were collected prior to CAR-T. Patients were classified as BMI <25 kg/m² (Cohort 1) or BMI ≥25 kg/m² (Cohort 2).
A metabolic syndrome–like profile was defined by the presence of ≥3 factors among BMI >30 kg/m², diabetes or fasting glucose >100 mg/dL, hypertriglyceridemia, and hypertension. Event-free survival (EFS), cumulative incidence of relapse, and non-relapse mortality (NRM) were analyzed using univariate and multivariate Cox regression models and the Gray test, as appropriate.

Results: Sixty-five patients were analyzed (Brescia n=37, Verona n=28): 36 (55%) had BMI <25 (Cohort1), while 29 (45%) had BMI ≥25 (Cohort2). Baseline characteristics were comparable between cohorts, except for a higher prevalence of hypertension in Cohort 2 (58% vs 22%, p=0.01). Eight patients (12%) met criteria for a metabolic syndrome–like profile. Median follow-up was 17.4 months (IQR 11.7–26.5).
Patients with BMI ≥25 showed significantly superior EFS, with a 12-months EFS of 55% (95%CI 35–72) compared with 22% (95%CI 9–38) in patients with BMI <25 (p=0.04) (Figure 1). Median EFS was 18.1 months versus 3.8 months, respectively. The association between BMI and EFS remained consistent across CAR-T products and age groups (≥65 vs <65 years).
By contrast, patients with a metabolic syndrome–like profile had markedly inferior outcomes, with a median EFS of 1.4 months compared with 8.7 months in those without this profile (p=0.005). Bulky disease at leukapheresis showed a trend toward reduced EFS (p=0.07). In multivariate analysis, BMI ≥25 remained independently associated with improved EFS (HR 0.44, 95% CI 0.20–0.95; p=0.036), while a metabolic syndrome–like profile predicted inferior EFS (HR 7.66, p=0.01).
Patients with BMI ≥25 also exhibited a significantly lower cumulative incidence of relapse, with a 12-months incidence of 37.7% (95%CI 19.3-56.1) compared with 70.8% (95%CI 50.5-84.0) in Cohort 1 (p=0.02). No significant differences in NRM were observed between cohorts (24-month NRM: 6.5% vs 8.4%, p=0.90) (Figure 1). Conversely, patients with metabolic syndrome–like profile showed trend toward higher NRM (p 0.09).

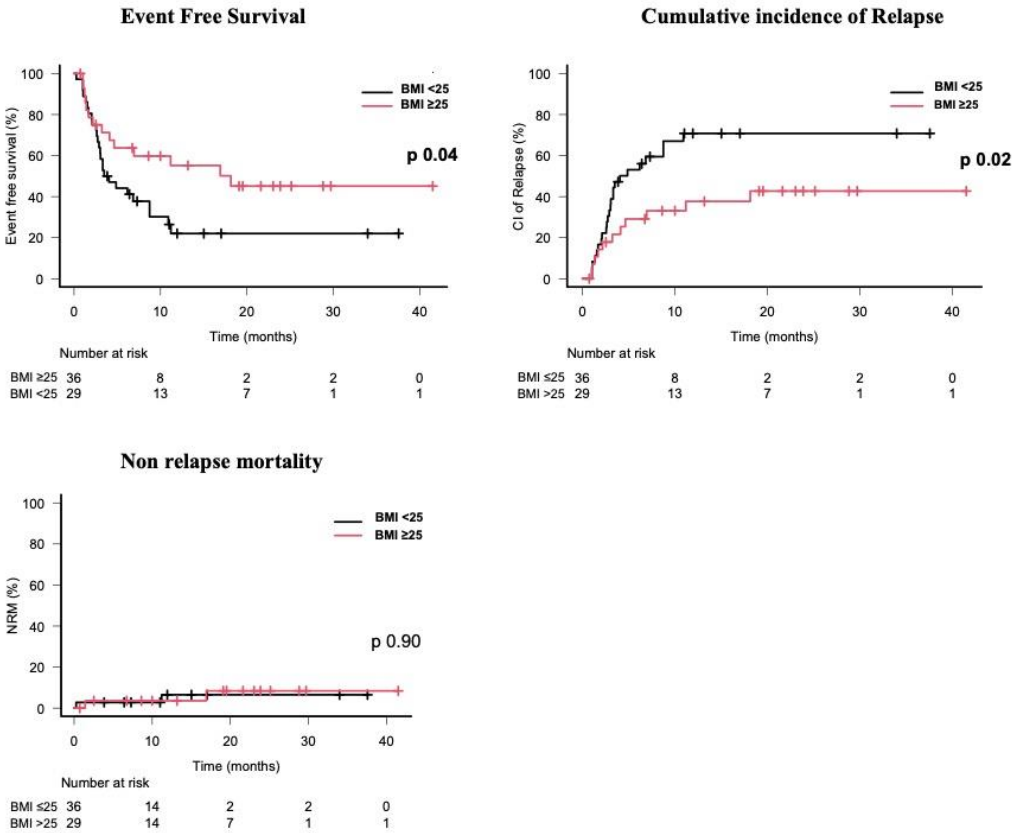

Figure 1: Impact of baseline body mass index (BMI) on outcomes after CAR-T cell therapy.

Conclusions: In this bicentric real-world cohort, elevated BMI (≥25) was independently associated with superior EFS after CAR-T cell therapy, driven by a significantly lower relapse risk and without increased NRM. This effect may be partially explained by the body weight–based dosing of CAR-T cells in LBCL. Conversely, the presence of a metabolic syndrome–like profile identified patients with inferior outcomes. Overall, these findings suggest that BMI and metabolic status are important modulators of CAR-T efficacy and warrant prospective validation.

Clinical Trial Registry: Not applicable.

Disclosure: Nothng to disclouse.

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POPULATION PHARMACOKINETICS AND OPTIMAL EXPOSURE OF ANTI-THYMOCYTE GLOBULIN IN MYELOABLATIVE HEMATOPOIETIC CELL TRANSPLANTATION

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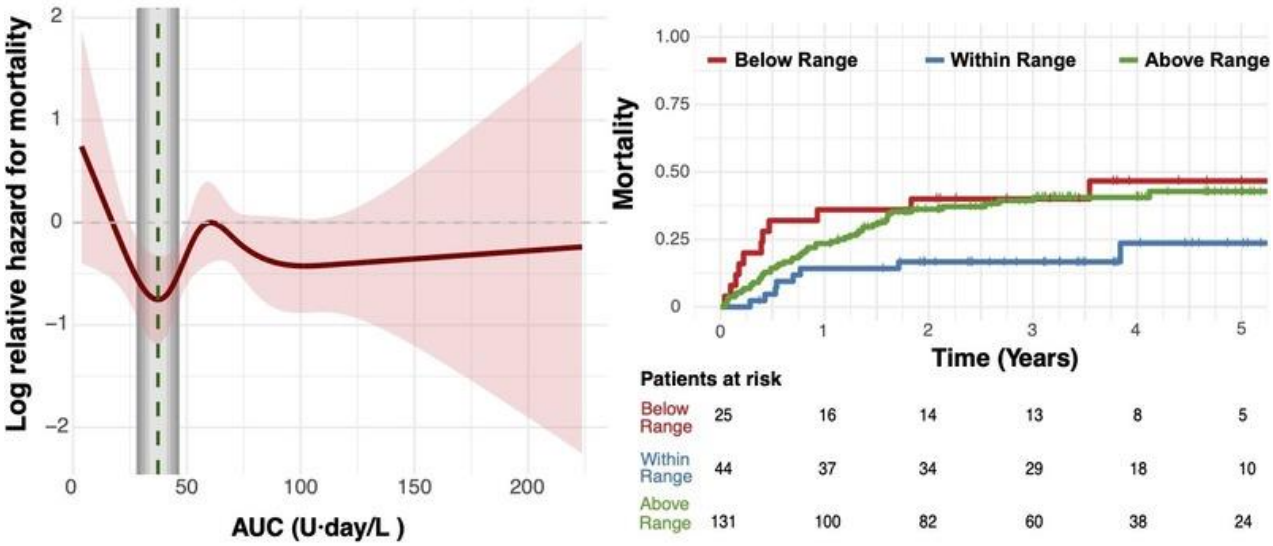
Background: Anti-thymocyte globulin (ATG) prevents graft-versus-host disease (GVHD) in allogeneic hematopoietic cell transplantation (HCT). However, variable ATG exposure impacts transplant outcomes. We aimed to develop a population pharmacokinetic (popPK) model for ATG in myeloablative HCT and evaluate the relationship between area under the time-concentration curve (AUC) and mortality to identify the optimal ATG AUC.

Methods: We studied 200 adult HCT recipients who received myeloablative conditioning (MAC) and a peripheral blood stem cell graft from 7/8 or 8/8 HLA-matched related or unrelated donors. ATG was given on days -2, -1, and 0. All patients received additional GVHD prophylaxis with methotrexate and cyclosporine. Serum concentration of lymphocyte-binding ATG was determined by flow cytometry in 2,140 samples. For the popPK modeling, the cohort was split into a model development cohort (n = 134) and a validation cohort (n = 66). The modeling was performed using Monolix Suite 2024R1. The relationship between model estimated AUCs and mortality was evaluated in all 200 patients (combined development and validation subcohorts) using a Cox proportional hazards model. The relationship between model estimated AUCs and cause-specific outcomes (e.g., relapse or acute graft-versus-host disease [aGVHD]) was evaluated using a competing risk analysis.

Results: A two-compartment model with parallel linear and target-mediated elimination best described ATG disposition (Abstract Figure 1). Population means and residual standard errors (RSE%) were 11.78 L (2.05%) for the central volume of distribution (V1), 0.20 L/h (4.36%) for linear clearance (CL), and 2.20 U/L (7.08%) for the initial ATG-binding capacity of lymphocytes in the central compartment (R0_initial). Lean body weight (LBW) positively correlated with V1, CL, and intercompartmental clearance, while pre-ATG absolute lymphocyte count (ALC) positively correlated with R0_initial. Internal and external validation (using the development and validation subcohorts, respectively) confirmed model stability and robustness. The optimal ATG AUC range was 30–45 U·day/L. In multivariate analysis, patients whose AUC was within this range had lower mortality than those whose AUC was outside this range (hazard ratio=0.46, p=0.03) (Abstract Figure 2). The low mortality of patients with AUC within the range of 30–45 U·day/L appeared to be due to both low incidence of grade III-IV aGVHD, which was high in patients with AUC <30 U·day/L, and low incidence of relapse, which was high in patients with AUC >45 U·day/L.



Conclusions: This novel model described the pharmacokinetics of ATG in adult HCT recipients following MAC. The model identified LBW and ALC as significant covariates for ATG disposition. Furthermore, we identified the optimal ATG AUC (associated with the lowest mortality). These findings provide the foundation for developing an individualized dosing strategy aimed at improving post-HCT survival.

Disclosure: Jan Storek received funding from Sanofi. None of the other authors declare a conflict of interest.

A132

EXPLORING BASELINE COGNITIVE FUNCTION ASSESSMENTS AS A PREDICTOR OF ICANS IN CAR-T CELL THERAPY PATIENTS

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Background: Chimeric antigen receptor T-cell (CAR-T) therapy has revolutionized the treatment of several haematological malignancies. However, immune effector cell-associated neurotoxicity syndrome (ICANS) remains a significant and potentially life-threatening complication. While tumour burden surrogate markers have shown some success in predicting ICANS risk, the utility of neurocognitive assessments, such as the Montreal Cognitive Assessment (MoCA), is not well-established.

Methods: We conducted a single-centre retrospective study of consecutive adults treated with commercial CAR-T therapy (May 2020–January 2025). Pre-infusion MoCA was analysed continuously, by standard cut-points (normal 26–30, mild 18–25, moderate 10–17, severe <10), and using validated ≤24 cut-point for low vs normal cognition. ICANS was graded per

ASTCT criteria. Multivariable analyses identified predictors of ICANS incidence/severity, ICANS-directed therapies, hospital/ICU stay. Domain-specific MoCA sub-scores (visuospatial/executive, naming, attention, language, abstraction, delayed recall, orientation) and longitudinal post-infusion assessments explored cognitive associations.

Results: Ninety-two patients were included (median age 63.5 years, range 16–84; 62% male). Median baseline MoCA score was 24 (range 15–30). At baseline, 48.8% of patients had normal cognition, 42.7% had mild cognitive impairment, and 8.5% had moderate or severe impairment.

Patients with low baseline MoCA had a significantly higher incidence of ICANS (any-grade ICANS: 65.5% vs 32%; p=0.005). High-grade ICANS (≥2) was also more frequent in the low MoCA group (41.4% vs 16%; p=0.017). Median ICANS duration was longer in patients with low MoCA (4 days [range 1–24] vs 2 days [1–14]; p=0.001). Rates of ICU admission (27% vs 16%; p=0.25), ICU duration, corticosteroid use, tocilizumab use, and other ICANS-directed therapies were numerically higher **i**n the low MoCA group but did not differ significantly.

On multivariable analysis, low baseline MoCA remained independently associated with ICANS (p=0.018), alongside CD28 costimulatory domain products (p=0.006) and CAR-T target (CD19 vs BCMA; p=0.003). Tocilizumab use showed a borderline association (p=0.059), while age was not significant (p=0.12). For high-grade ICANS, low MoCA (p=0.047) and CD28 costimulatory domain (p=0.016) remained independent predictors. Lower baseline language and naming scores predicted any-grade and high-grade ICANS, respectively (p=0.018 and p=0.033), with no associations for other cognitive domains.

Forty-nine patients underwent post-infusion MoCA assessments; 80% demonstrated stable or improved cognitive performance. Patients with low baseline MoCA showed significant improvement (median ΔMoCA +3 [−1 to +7], p<0.001), while those with normal baseline MoCA remained stable (median ΔMoCA 0 [−3 to +1]). Importantly, ICANS did not adversely affect longitudinal cognition: among patients who developed ICANS (n=20), 90% maintained or improved cognitive function at follow-up, with no difference compared with those without ICANS (median ΔMoCA +1 vs +1; p=0.76).

Conclusions: Baseline MoCA, a simple 10-minute assessment, independently predicts ICANS incidence and severity in CAR-T patients . ICANS appears to be a clinically significant but predominantly transient neuroinflammatory event and was not associated with measurable long-term global cognitive decline in most patients; notably, 90% of patients who developed ICANS maintained or improved cognitive function in this cohort. These findings are hypothesis-generating and warrant validation in larger, prospective, multicentre studies incorporating detailed neurocognitive profiling.

Disclosure: None.

A133

EASIX OUTPERFORMS EBMT AND CIBMTR RISK MODELS IN PREDICTING VOD/SOS DESPITE DEFIBROTIDE USE IN ALLOGENEIC HSCT

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Background: Hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) remains a severe and potentially fatal complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT), even in patients receiving defibrotide. Conventional clinical risk models such as EBMT and CIBMTR may inadequately capture early endothelial injury. The Endothelial Activation and Stress Index (EASIX) has emerged as a biomarker of endothelial stress and may improve risk prediction.
Objective: To determine whether EASIX outperforms EBMT and CIBMTR risk models in predicting VOD/SOS in allo-HSCT patients treated with defibrotide.

Methods: Adult patients (≥18 years) undergoing allo-HSCT at a single center between 2015 and 2025 who received defibrotide prophylactically or therapeutically were retrospectively analyzed. Patients with pre-existing liver cirrhosis, active infection, or dialysis dependence were excluded. EBMT, CIBMTR, and EASIX scores were calculated at the start of conditioning and compared between patients with and without VOD/SOS.

Results: Eighty-one patients were included; 19 (23.4%) developed VOD/SOS. Median EASIX scores were significantly higher in patients who developed VOD/SOS compared with those who did not (7.92 vs. 3.23, $p = 0.003$). EBMT risk scores were also higher in the VOD/SOS group ($p < 0.001$), whereas CIBMTR scores were not significantly different ($p = 0.06$). ABO incompatibility ($p = 0.005$) and hepatic steatosis (68.4% vs. 40.8%, $p = 0.02$) were additional factors associated with VOD/SOS. Exposure to busulfan or total body irradiation was not significantly associated with VOD/SOS development.

Conclusions: Despite defibrotide use, VOD/SOS remains a major complication after allo-HSCT. EASIX outperformed CIBMTR and complemented EBMT risk assessment in identifying patients at increased risk. Incorporating EASIX into the pretransplant evaluation may refine risk stratification and support targeted prophylactic strategies.

Disclosure: Nothing to declare.

A134

NON-CRYOPRESERVED HEMATOPOIETIC STEM CELLS FOR AUTOLOGOUS TRANSPLANTATION IN MULTIPLE MYELOMA: REDUCED TOXICITY AND DISTINCT INFLAMMATORY PROFILE AS COMPARED TO CRIOPRESERVED PRODUCTS

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Background: Autologous transplantation using non-cryopreserved hematopoietic stem cells (non-CRYO) has been proposed as a safe and effective alternative to cryopreservation (CRYO), potentially reducing toxicity and resource demands. However, the biological basis of this approach remain unclear.

Methods: We conducted a study including a retrospective cohort (2018–2023) and a prospective cohort (2023–2024) across two centers (Santiago, Chile; Seville, Spain). The retrospective phase analyzed outcomes in 283 CRYO and 148 non-CRYO recipients. The prospective phase evaluated 13 CRYO and 27 non-CRYO patients for clinical endpoints as well as biomarkers including plasma inflammatory markers (IL-2, IL-6, IL-8, IFN-γ, VEGF-D, MMP-1, IL-18, TNF-α) quantified by ELISA.

Results: Non-CRYO recipients achieved faster neutrophil recovery (11 vs 14–15 days, p=0.006) and had shorter hospital stay (13–14 vs 18–19 days, p=0.005). Platelet engraftment was slightly earlier in CRYO (11–12 vs 13 days). Toxicity profile was favourable to the non-CRYO cohort: febrile neutropenia (19–22% vs 45–50%, p=0.005), severe mucositis (19–20% vs 60–66%, p=0.001), and total parenteral nutrition requirement (4–8% vs 20–25%, p=0.001). Inflammatory profiling showed higher IFN-γ in non-CRYO, while CRYO grafts exhibited higher levels of IL-6, IL-8, and VEGF-D, consistent with endothelial activation and inflammatory stress. No early mortality occurred in either cohort. With a median follow up of 36 months, overall survival 89% and 88% in the non-CRYO vs CRYO (p= 0.92).

Table. Clinical outcomes and inflammatory markers in CRYO vs non-CRYO autografts

Outcome / Marker	CRYO	Non-CRYO	p-value
Neutrophil engraftment (days, median)	14–15	11	0.006
Platelet engraftment (days, median)	11–12	13	0.005

Outcome / Marker	CRYO	Non-CRYO	p-value
Febrile neutropenia (%)	45–50%	19–22%	0.005
Severe mucositis ≥G3 (%)	60–66%	19–20%	0.001
Total parenteral nutrition (%)	20–25%	4–8%	0.001
Hospital stay (days, median)	18–19	13–14	0.005
IFN-γ (Tx)	Lower	Higher	0.044
IL-8 (Tx)	3.60 mg/L	1.25 mg/L	0.017
IL-8 (Post)	Higher	Lower	0.048
VEGF-D (Tx)	5.47 pg/mL	1.22 pg/mL	0.004
VEGF-D (Post)	6.21 pg/mL	3.35 pg/mL	0.044
IL-6 (Tx/Post)	Higher (trend)	Lower (trend)	n.s.[1]
MMP-1 (Tx/Post)	Higher (trend)	Lower (trend)	n.s.[1]
IL-18 (Tx/Post)	Variable	Variable	n.s.[1]

Notes: Tx = transplant day; POST = post-transplant; n.s. = not significant. Values shown as reported medians where available; otherwise direction of difference is indicated. CRYO indicates cryopreserved; Non-CRYO indicates non-cryopreserved.

Conclusions: Non-cryopreserved autologous transplantation reduces early morbidity and favors a distinct, less inflammatory immune milieu compared with cryopreservation. This strategy may represent a safe, effective, and operationally efficient alternative, particularly in high-throughput or resource-limited settings.

Disclosure: Nothing to declare

A136

CLINICAL OUTCOMES OF LISOCABTAGENE MARALEUCEL (LISO-CEL) IN YOUNGER PATIENTS WITH RELAPSED OR REFRACTORY (R/R) LARGE B-CELL LYMPHOMA (LBCL)

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Background: Liso-cel is an autologous, CD19-directed, CAR T cell product with favorable efficacy and well-established safety profile across B-cell malignancies. Understanding outcomes of liso-cel treatment in younger patients remains an area of interest. In this study, we evaluated the effectiveness and safety of liso-cel in patients aged <50 years with R/R LBCL.

Methods: Patients in the United States with R/R LBCL who received commercial liso-cel as second-line (2L) or later treatment from 02/2021 to 05/2025 and had ≥1 postinfusion assessment reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) were included. Effectiveness outcomes were ORR, CR rate, duration of response (DOR), PFS, and OS. Safety outcomes were AEs of special interest and nonrelapse mortality rates; results are descriptive.

Results: Of 1144 total patients assessed, 74 (6%) were aged <50 years at infusion (median age, 42 years [range, 21.5–49.5]) and 62% were male. Among patients aged <50 years with data available, 73% had DLBCL, 9% had primary mediastinal B-cell lymphoma (PMBCL), and 9% had high-grade B-cell lymphoma; 83% had refractory disease; and 52% had elevated LDH preinfusion. Most patients had ≥1 comorbidity per Hematopoietic Cell Transplantation-Comorbidity Index criteria (80%) and ECOG PS of 0–1 (90%). Median number of prior lines of therapy (LOT) was 3 (range, 1–13), and 18% received liso-cel as 2L treatment; 61% received bridging therapy and 36% were reported as intended for outpatient infusion. Compared with the overall cohort, patients aged <50 years had higher prevalence of PMBCL, refractory disease, elevated LDH, and comorbidities, but similar ECOG PS, number of prior LOTs, and receipt of bridging therapy. Median follow-up in patients aged <50 years was 14.8 months (95% CI, 12.7–24).
In patients aged <50 years, responses were deep (ORR, 72%; CR rate, 68%) and durable, with median DOR not reached (NR) and 12-month DOR rate of 80%, consistent with outcomes in the overall cohort (**Table 1**). Survival outcomes were also consistent in patients aged <50 years and the overall cohort, with median PFS and OS NR and similar 12-month rates (**Figure 1**; **Table 1**).
Liso-cel safety profile in patients aged <50 years was consistent with the overall cohort and clinical trials. Any-grade cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome were reported in 58% and 28% of patients aged <50 years,

respectively, with low rates of grade ≥3 events (4% and 12%) (**Table 1**). Cytopenia at Day 30 was reported in 11% of patients and clinically significant infections at any time after infusion in 55%. Rates of second primary malignancies (1%), tumor lysis syndrome (3%), and grade 3/4 organ toxicity (7%) were low. In patients aged <50 years, 22 (30%) died, most commonly due to PD (n = 19/22 [86%]).

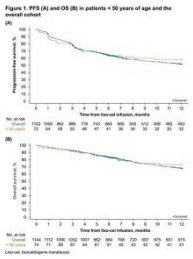
Conclusions: Consistent with clinical trials, these results reinforce that despite higher incidence of high-risk disease factors, younger patients with R/R LBCL experience clinically meaningful efficacy while the well-established safety profile of liso-cel is maintained, allowing potential outpatient use in the real-world setting.

Table 1. Summary of effectiveness and safety outcomes in patients < 50 years of age and the overall cohort

	Patients <50 years of age (n=74)	**Overall cohort (N=1144)**
ORR, % (95% CI)	72 (60–81.5)	81 (79–84)
CR rate, % (95% CI)	68 (56–78)	72 (69–75)
12-mo DOR rate, % (95% CI)	80 (65–89)	60.5 (57–64)
12-mo PFS rate, % (95% CI)	58 (45–69)	52 (49–55)
Cytokine release syndrome, n (%) Grade ≥3, n (%) Median (range) time to onset, days Median (range) time to resolution, days	 43 (58) 3 (4) 5 (2–495) 3.5 (1–14)	 586 (51) 28 (2) 4 (1–554) 4 (1–126)
Immune effector cell–associated neurotoxicity syndrome, n (%) Grade ≥3, n (%) Median (range) time to onset, days Median (range) time to resolution, days	 21 (28) 9 (12) 6 (1–14) 4 (2–375)	 305 (27) 106 (9) 7 (1–465) 5 (1–378)

Table 1. Summary of effectiveness and safety outcomes in patients < 50 years of age and the overall cohort

Cytopenia at Day 30,[a] n (%)	8 (11)	144 (13)
Clinically significant infections,[b] n (%)	41 (55)	545 (48)
Second primary malignancies, n (%)	1 (1)[c]	72 (6)
Tumor lysis syndrome, n (%)	2 (3)	8 (1)
Grade 3/4 organ toxicity, n (%)	5 (7)	63 (6)
Deaths, n (%)	22 (30)	424 (37)
All percentages are rounded to whole numbers except those with ".5%". [a]Defined as grade 4 thrombocytopenia and/or neutropenia at 30 days after infusion; [b]Any infection requiring treatment at any time on study; [c]Basal cell skin malignancy. DOR, duration of response.		



Clinical Trial Registry: Not applicable

Disclosure: **MAP:** research funding, honoraria, data safety monitoring board, and/or ownership interests from Allogene, Bristol Myers Squibb (BMS)/Celgene, Cidara Therapeutics, ExeVir, Genmab, ImmPACT Bio, Incyte Corporation, Kite/Gilead, Merck, Miltenyi Biotec, Nektar Therapeutics, Novartis, Omeros, Orca Bio, Pierre Fabre, Sanofi, Sellas Life Sciences, Syncopation, Takeda, Tr1x, VectivBio AG, Vor Biopharma; **INS:** none; **KP:** research funding and/or consulting from AbbVie, Adaptive Biotechnologies, Adicet Bio, Arcus Biosciences, Arvinas, AstraZeneca, AvenCell Therapeutics, BeOne Medicines, BMS, Caribou Biosciences, Century Therapeutics, CRISPR Therapeutics, Fate Therapeutics, Genentech, Kite Pharma, Indapta Therapeutics, Janssen, Lilly, Loxo Oncology, MEI Pharma, Merck, Nurix Therapeutics, Pfizer, Pharmacyclics, Sana Biotechnology, Sanofi, Xencor, Lyell Immunopharma; **RR:** research funding and/or consulting from AbbVie, Allogene, Arcellx, AstraZeneca, Atara Biotherapeutics, Autolus, Bayer, BMS, Cabaletta Bio, CareDx, Genentech, Gilead Sciences, Immatics, Imugene Limited, Incyte Corporation, Johnson & Johnson, Kinomica, Orca Bio, Pierre Fabre, Sail Biomedicines, Sana Biotechnology, Sanofi, Sonoma Biotherapeutics, Synthekine, Takeda, TScan Therapeutics, viTToria Biotherapeutics; **MF:** research funding, consulting, patents, and/or stock holding from BMS, CytoAgents, Gilead Sciences, ImmunoFree, Novartis, Sobi; **ML:** consulting and/or honoraria from Astellas Pharma, AbbVie, Acrotech Biopharma, ADC Therapeutics, AstraZeneca, BMS, Curis, CRISPR Therapeutics, Daiichi Sankyo, EUSA Pharma, Fate Therapeutics, Genentech, Genmab, Incyte Corporation, Instil Bio, Ipsen, Janssen, Kite Pharma, Lyell Immunopharma, Loxo Oncology, Pfizer, Recordati, Regeneron, Veeva, viTToria Biotherapeutics; **JLC:** research funding, consulting, and/or honoraria from AbbVie, ADC Therapeutics, Genentech, Genmab, Kite Pharma, Lilly, Merck, Novartis, Regeneron; **II:** consulting from BMS/Celgene; **MCP:** research funding, consulting, and/or honoraria from Amgen, BMS/Celgene, Gilead/Kite, Janssen, Medigene, Novartis, Pfizer; **DB, DR, PG:** employment and/or stock from BMS; **BDH:** research funding, consultancy, and/or honoraria from AbbVie, ADC Therapeutics, Astellas Pharma, BMS, Caribou Biosciences, Genentech, Genmab, IN8Bio, Johnson & Johnson, Kite Pharma, Notable Labs, Novartis, Poseida Therapeutics, Regeneron; **SA:** research funding and/or consultancy from ADC Therapeutics, BMS, Caribou Biosciences, Chimagen, Genmab, Gilead/Kite, Janssen, Merck, Nektar Therapeutics, Xencor.

A137

OUTCOMES OF ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN T-CELL NON-HODGKIN LYMPHOMA EXPERIENCE AT UNIVESITARY HOSPITAL OF SALAMANCA-SPAIN

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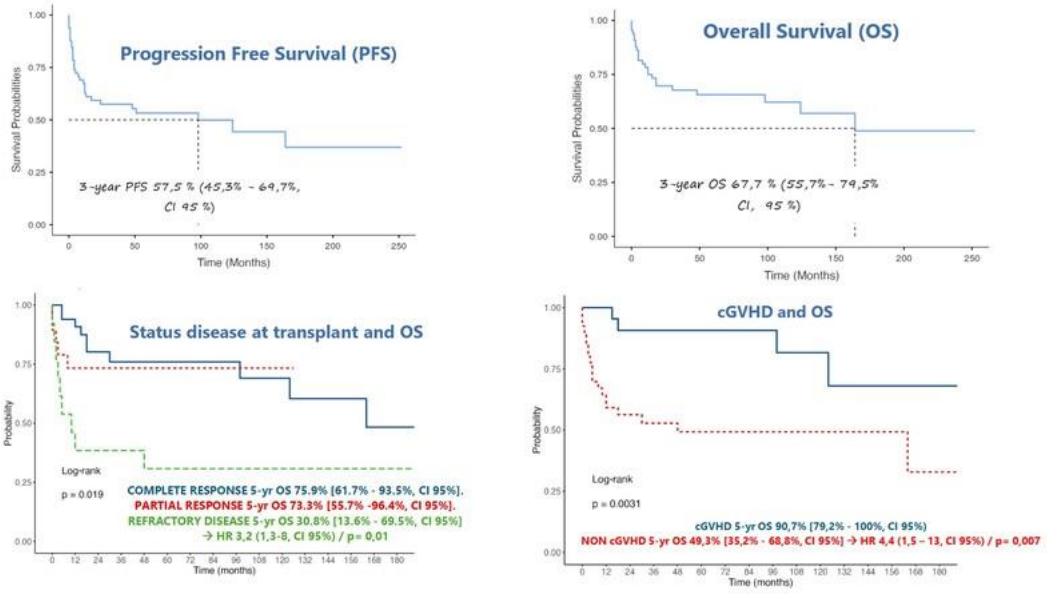
Background: T-cell non-Hodgkin lymphomas (T cell-NHL) are aggressive haematological neoplasms that, in most cases, have an adverse prognosis, with high chemorefractary rates. In these cases, allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is the only potencial curative treatment. The objective of the study is to analyze the efficacy of Allo-HSCT in T cell-NHL.

Methods: Single- center retrospective study of patients with T cell-NHL undergoing Allo-HSCT from 1997 to 2025.

Results:



65 patients undergoing Allo-HSCT. The median age was 51 years (18-70). Most of patients has a nodal T-NHL subtype (67,5%), 31% have previous autologous HSCT and 20% have a refractory disease to allo-HSCT (principal patients and Allo-HSCT characteristics are in Table).

At +100 day, 71% of patients were in complete response (CR). The incidence of relapse/progression was 24.5% (18.5% at one year) with a very low incidence (7%) in patients with nodal subtype and a high incidence in cutaneous subtypes (70%) (OR 42 (5,1-346,1 95% CI); p<0.001). Mortality was 37% and the first cause of death was infection (37.5% of deaths), followed by relapse/progression (25%). Mortality was higher in patients with high-risk HTC-CI (OR 7.6 (1.4-41.89 95% CI); p=0.02) and in patients with refractory disease at transplant (OR 6.5 (1.4-29.6 95% CI); p=0.02). Non relapsed mortality (NRM) was 9% at +100 day and 15.5% at one year. No other factor analyzed had an significant impact on relapse or mortality.

The rate of acute Graft Versus Host Disease (aGVHD) at day +100 was 50.5% (grade 3-4 33.5% (n=9)) and the rate of chronic GVHD at one year was 23% (moderate-severe 46.5% (n=7)); of them, 5 patients had a previous relapse with manipulation of immunosuppresor

treatment or an infusion donor lymphocyte (n=2) treatment.
With a median of follow-up in alive patients of 78 months (4-52), 5-year progression-free survival (PFS) and overall survival (OS) were 53.2% and 65.6%, respectively, with median PFS and OS of 8 and 13,5 years, respectively. T-cell NHL subtype, refractory disease at transplant, and high risk HCT-CI were associated with lower OS and PFS, while the development of cGVHD had a protective effect (Figure). So, median PFS and OS in nodal T-cell NHL was 164 months (5-year PFS and OS of 69%) versus only 7 and 10 months in extranodal T/NK subtype (PFS with HR 5.7 (1.3-25.7, 95% CI)/p=0.02 and OS with HR 5 (1.1-22.3, 95% CI)/p=0.03)); and median PFS of 2 months in Hepatosplenic (HR 5.2 (95% CI (1.5-18.2)/p=0.01)) and 4 months in Cutaneous subtypes (HR 4.6 (1.7-9.89 95% CI)/p<0.001)). In refractory disease at transplant, median PFS and OS were 4 and 10 months; in high-risk HCT-CI, 8 and 30 months; and in non cGVHD patients, 12 and 48 months, respectively. All these factors maintained their independent impact in the multivariate analysis.

		N (%)
Sex	Male	41 / (63)
OMS T-cell NHL subtype	Nodal T-cell lymphomas	44 / (67.5)
	Primary cutaneous T-cell lymphomas	10 / (15.5)
	Hepatosplenic T-cell lymphoma	4 / (6)
	Mature T-cell and NK-cell leukaemias	4 / (6)
	Extranodal NK/T-cell lymphoma	2 / (3)
	Intestinal T-cell lymphoma, NOS	1 / (1.5)
Lymphoma Stage (n=56)	III-IV	45 / (80,5)
DRI Score	High Risk	14 / (21,5)
HCT-CI	Low Risk (0)	43 / (66)
	Intermediate Risk (1-2)	13 / (20)
	High Risk (>3)	9 / (14)
	Identical sibling	29 / (44,5)

Donor	Haploidentical	16 / (24,5)
	Identical unrelated	14 / (21,5)
	Mismatch unrelated	6 / (9,5)
Conditioning	Reduced intensity	52 / (80)
	Myeloablative	13 / (20)

Conclusions: Allo-HSCT is an effective treatment for T-NHL and offers high PFS after long-term follow-up, especially in nodal subtypes. Disease status at transplant, High DRI, and HCT-CI are poor prognostic factors, whereas the beneficial effect of cGVHD demonstrates the curative potential of the graft-versus-lymphoma effect.

Disclosure: "Nothing to declare"

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"REAL WORLD" INCIDENCE AND CHARACTERISTICS OF IMMUNE EFFECTOR CELL–ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTICYTOSIS: A GOCART COALITION STUDY ON BEHALF OF THE EBMT ADWP, CTIWP AND TCWP

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Background: Hemophagocytic Lymphohistiocytosis (HLH) is an underestimated but potentially life-threatening CAR-T complication. Among anti-CD19 CAR-T cell recipients, secondary HLH (sHLH) incidence is reported around 3%. Secondary HLH is often misdiagnosed[CP1] , and the treatment is not standardized. This retrospective study aimed to assess the real-world sHLH incidence and characteristics after CAR-T administration.

Methods: We retrieved clinical data from the EBMT registry regarding patients treated with CAR-T cells from 2014 to 2022. We collected additional information about CAR-T cell indication and product, sHLH manifestations, outcome and treatment.

Results: We collected 815 patients (677 B-Lymphoma, 71 B-ALL, 67 Multiple Myeloma), among 21 EBMT centers with a median follow-up time of 2 years. Twenty-seven patients, (20 with B cell lymphoma and 7 with B-ALL), experienced sHLH after CAR-T cells with an incidence of 3.6% (95%CI: 2.5 - 5.1) at 90 days and a median onset time of 11 days (range 5-86). Two-years Overall Survival and Progression Free Survival were 54.3% and 38.6%, respectively. B-ALL patients showed a higher incidence of sHLH than B-Lymphoma ones (10% vs. 3%). No event occurred after 90 days. Secondary HLH frequency was higher in patients treated with tisagenlecleucel (40,7%), followed by axicabtagene ciloleucel (37%), brexucabtagene autoleucel (14.8%), and others (7.4%). Cytokine Release Syndrome was present in 93% of patients (34% grade 3-4), which resolved in 60% of them before sHLH onset.
Fever was the most prominent feature (n=18, 75% of patients), followed by liver (n=13, 54%), kidney (n=8, 32%), and lung toxicity (n=5, 22%). The median ferritin value was 10723 ng/ml (range 1558-50565). Increased liver enzymes, LDH, triglycerides and impaired coagulation test were common. Eleven patients underwent a bone marrow aspirate, with evidence of hemophagocytosis in 45% of cases.
Twenty patients (80%) received treatment, most commonly with a combination of steroids and anakinra. The median follow-up post-sHLH was 2 years. Four patients died in absence of sHLH resolution. Nine additional patients died after sHLH resolution: 7 following relapse (incl. 2 within 30 days post-resolution) and 2 without relapse within 30 days post sHLH resolution. The survival after sHLH was 81.5% at 90 days and 50.1% at 2 years.

Conclusions: This registry study characterizes CAR-related sHLH. Secondary HLH incidence differed between patients B-ALL and B-Lymphoma patients. Our study showed a better sHLH prognosis than what previously reported. These real-world data underscore the need for clinical awareness and provide a base to define standardized diagnostic criteria and treatment algorithms for this complication.

Disclosure: No relevant disclosures for this study

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RISK STRATIFICATION FOR HIGHER GRADE ICANS IN ANTI CD19 CAR T-CELL THERAPY TO GUIDE MANAGEMENT OF HIGH RISK PATIENTS

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Background: Effectiveness of CD19 CAR-T cell therapy is complicated by its inflammatory side effects: cytokine release syndrome (CRS) and immune effector cell associated neurotoxicity syndrome (ICANS). Some clinical features such as CAR product or high tumor burden are associated with increased incidence and severity of ICANS and CRS, but biomarkers such as glial fibrillary acidic protein (GFAP) or neurofilament light chain (Nfl) showed conflicting results for prediction of high grade ICANS.
A predictive score to identify patients at risk to develop high grade ICANS may guide to a preemptive or prophylactic intervention and improve outcomes.

Methods: We established a clinical score to identify patients at risk for high grade ICANS assessing the following criteria: CAR-T cell product (axi- or brexu-cel), tumor (B-ALL, DLBCL after >3 previous lines of therapy or high tumor burden) and patient factors (age >70y, CNS disease). Serum levels of Nfl and GFAP on d-5 were determined to assess their value in supplementing clinical risk scoring.
Patients that met at least 2 clinical criteria, were considered to be at risk for high grade ICANS. CRS and ICANS were graded using ASBMT consensus criteria.
In 04/23 we adapted the guidelines for the treatment of CRS & ICANS in our institution. Patients at high risk for ICANS received preemptive dexamethasone 1x10mg for CRS II° and dexamethasone 10mg qid already for ICANS I° (TOX 2). Low risk patients received dexamethasone 10 qid only for CRS III° and ICANS II° (TOX 1).

Results: Since 01/22 32 patients receiving CD19 CAR-T cell products met the criteria for high risk ICANS. 10 patients (9 axi-, 1 brexu-cel) treated between 01/22 and 04/23 were treated according to our former routine TOX 1 (Cohort 1). Since 04/23, 22 patients (15 axi-, 7 brexu-cel) followed our TOX 2 guidelines (Cohort 2).
The rate of ICANS was significantly higher in TOX2 patients (p=0.0139) and all ICANS ≥III° cases occurred in this cohort (negative predictive value=1). Rate of CRS did not differ between the two risk groups (p=0.7868).
Nfl levels on d-5 supplemented the clinical risk scoring and improved its predictive accuracy (AUC= 0.835 vs. 0.742 for the clinical score only). GFAP showed no significant correlation with occurrence of ICANS (p=0.62).
Intensified toxicity management significantly reduced the rate of high grade CRS (p=0.0361). Rate of higher grade ICANS also appeared lower.
The preemptive immunosuppressive approach did not have a negative impact on early lymphoma response by d+90 (p=0.1064).

Conclusions: Our risk assessment correctly identified patients at high risk for ICANS: In cohort 1 incidence of CRS (30%) and ICANS ≥III° (40%) was higher than reported for the

overall population within clinical trials. Inclusion of Nfl levels improved its positive predictive value by 10%.
Risk adapted toxicity management with early use of dexamethasone proved feasible in clinical routine and reduced the severity of both CRS and ICANS. This tailored approach may help to spare steroid exposure in contrast to a general prophylactic approach.
No negative impact on early response at day+90 was observed.

Disclosure: Jonas Wißkirchen: Pierre Fabre and Kite Gilead (travel expenses), Takeda (Honorarium).

A141

VENETOCLAX PLUS HIGH-DOSE CYTARABINE AND MITOXANTRONE (HAM-VEN) AS BRIDGE TO OR SALVAGE THERAPY AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN RELAPSED/REFRACTORY AML

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Background: High-dose cytarabine-based salvage regimens are commonly used for the treatment of relapsed/refractory acute myeloid leukemia (R/R AML), but response and survival remain suboptimal. Aiming to improve the outcome the BCL2 inhibitor Venetoclax (VEN) was included into chemotherapy-based salvage therapies. In a recent phase I/II trial (RELAX, EudraCT 2018-003025-28) the addition of VEN to high-dose AraC and mitoxantrone (HAM) showed high efficacy with a CR/CRi rate of 75% and a median overall survival (OS) of 25 months. However, pts in clinical trials often represent highly selected cohorts potentially impeding translation into clinical routine. Therefore, our analysis aimed to investigate response to and outcome after HMA-VEN-based salvage therapy with focus on transplant rate and post-transplant outcome in a real-world setting.

Methods: All pts receiving HAM-VEN as salvage therapy for R/R AML at two German centers between 2021 and 2024 were included. Treatment included cytarabine 1000-3000mg/m^2 IV BID (day 3-5), mitoxantrone 10mg/m^2 IV QD (day 5-7) and VEN 400mg PO QD (day 1-14). The study was approved by the local ethics committee (approval number: 22-10708-BO).

Results: Sixty-five pts with a median age of 54 (range, 18 to 72) received salvage therapy with HAM-VEN either for refractory (n=27, 42%) or relapsed disease (n=38, 58%). Pts had received a median of 1 (range, 1-3) therapy lines including 22 (34%) with allo-SCT and 11 (17%) with previous VEN exposure prior to HAM-VEN. ELN 2022 genetic risk was favorable, intermediate and adverse in 9 (14%), 22 (34%) and 34 (52%) pts. Patient-, disease- and treatment-related factors were comparable among those who received HMA-VEN for relapsed or refractory disease. Following HAM-VEN, 44 (68%) pts achieved CR/CRi and 49% of those evaluable for measurable residual disease (MRD) achieved MRD negativity (CR_{MRD-}). CR and

MRD-negativity rate were comparable among those receiving HMA-VEN for relapsed or refractory disease (relapsed, CR 70% vs. refractory, CR 67%, p=0.79; relapsed CR_{MRD-} 54% vs. refractory, CR_{MRD-} 41%, p=0.54). Furthermore, response was comparable among different ELN 2022 disease risk groups (CR favorable 89%, intermediate 68%, adverse 63%). Response rate did also not differ between pts without and with prior allo-SCT (74% vs. 59%, p=0.26). In contrast, those patients without previous VEN exposure showed significantly higher response rate compared to those who had already received VEN (75% vs. 36%, p=0.02). Day+30 mortality was 6% (n=4) and related to infections in all cases. After a median FU of 12 months (range, 1 to 38) the estimated 1-year OS and EFS rates were 56% and 40%, respectively.
Fifty-four (83%) pts proceeded to allo-SCT including 16 (30%), who had received previous allo-SCT. Median follow-up from allo-SCT was 9 months (range, 1 to 35). One-year OS, RFS, relapse incidence and NRM) were 57%, 53%, 36% and 6% respectively Posttransplant OS did not differ among patients receiving 1st or 2nd allo-SCT after HAM-Ven (1-yr OS 57% vs. 56%, p=0.56).

Conclusions: Our real-world analysis confirms HAM/VEN as save and efficient salvage treatment for R/R AML facilitating a bridge to transplant in a high rate of patients with an encouraging posttransplant outcome including patients after second transplantation.

Disclosure: Thomas Schroeder: lecture fees from abbvie; Christina Rautenberg: financial travel support and advisory board with honoraria from abbvie.

A142

SARCOPENIA ASSESSMENT BY BIOELECTRICAL IMPEDANCE AND FUNCTIONAL TESTS PREDICTS CLINICAL OUTCOMES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative therapy for various hematological diseases, yet its outcomes are strongly influenced by patients' nutritional and functional status, with sarcopenia—defined by reduced muscle mass, strength, and physical performance—being associated with increased treatment toxicity, longer hospitalization, poorer survival, and possibly predicting inferior Overall Survival (OS), lower Progression-Free Survival (PFS), and higher Non-Relapse Mortality (NRM), although its independent prognostic role in allo-HSCT remains insufficiently explored.

Methods: This retrospective study included patients who underwent allo-HSCT for any diagnosis at Spedali Civili di Brescia between November 2018 and February 2025. Data collection included demographics, transplant-related risk scores — Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), Clinical Frailty Scale (CFS), Disease Risk Index (DRI), and Transplant Conditioning Intensity (TCI) — functional tests (handgrip strength, chair stand test, gait speed), and body composition by Bioelectrical Impedance Analysis (BIA), including Phase Angle (PhA), Fat-Free Mass (FFM), Fat Mass (FM), Body Cell Mass (BCM), Total Muscle Mass (TMM), and Appendicular Skeletal Muscle Mass (ASMM). Sarcopenia was defined using European criteria: muscle mass (ASM, ASM/height²), strength (handgrip), and physical performance (gait speed, chair test), categorized as absent, mild, moderate, or severe. Outcomes included OS, mortality (relapse- or complication-related), and relapse incidence. Associations between sarcopenia indices and outcomes were assessed using descriptive statistics and univariate/multivariate analyses**.**

Results: 182 patients were included: 110 (60.4%) were alive and in complete remission, 38 (20.9%) relapsed, and 34 (18.7%) were deceased. Sarcopenia was absent in the majority of patients (67%), while 33% met at least one criterion. The estimated median overall survival of the studied population was 30 months (16–49). In univariate analysis (log-rank test), overall survival was significantly lower in patients meeting at least one criterion for sarcopenia (p=0.015), with a median estimated survival of 14 months (3–24) in sarcopenic patients compared to 30 months (16–43) in those without any sarcopenia criteria (Image 1). In univariate analyses, lower handgrip strength and ASM/height² were significantly associated with mortality (p=0.008), while relapse correlated with lower handgrip strength (p=0.008), percentage muscle mass (p=0.047), ASMM/height² (p=0.039), and BMI (p=0.043). Multivariate analysis (Table 1) showed that patients who relapsed or died had significantly lower lean, cellular, and muscle mass, with percentage BCM reaching statistical significance (p=0.020). Female sex was a protective factor, reducing risk by 76% (HR=0.21, p=0.013), as well as handgrip strength (HR=0.91, p=0.017), highlighting its role as an early, sensitive, and easily implementable prognostic marker. Overall, muscle strength, more than isolated anthropometric indices, appeared to drive post-transplant outcomes.

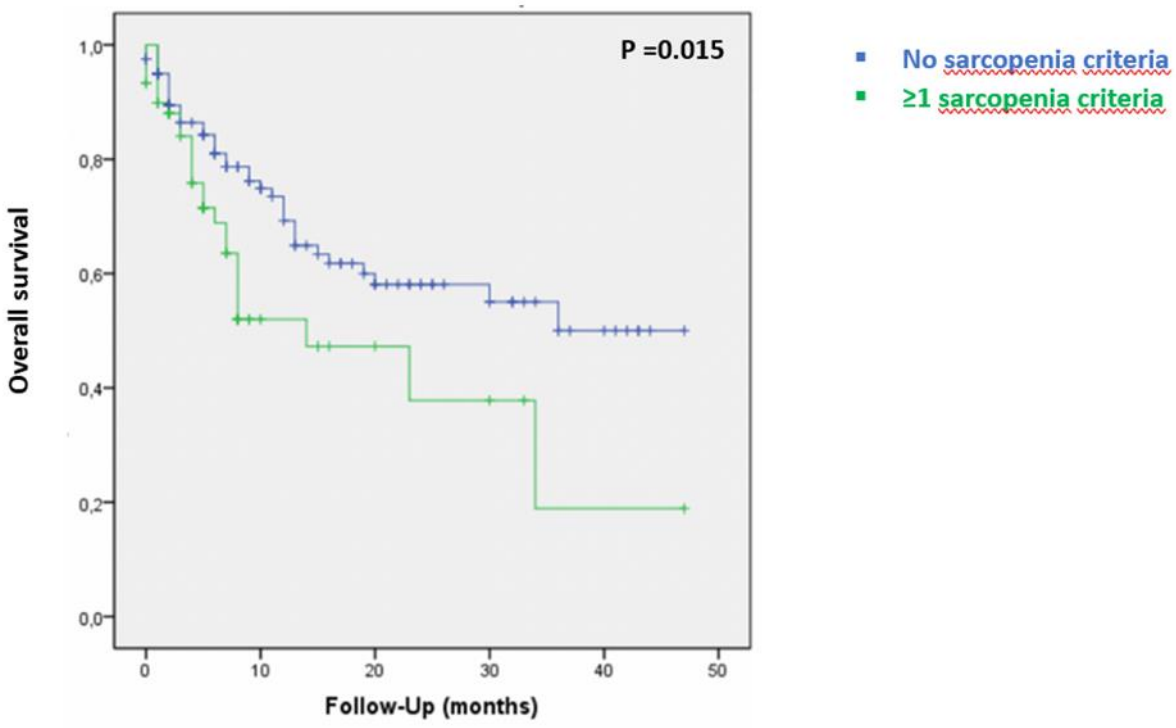

Image 1

Characteristics	HR	95% CI	p-value
Sex (female vs male)	0.24	0.08-0.73	**0.013**
Age	0.98	0.91-1.04	0.5
BMI (overweight vs normal)	0.60	0.21-1.66	0.3
Gait speed	3.04	0.32-29	0.3
Chair test	1.0	0.91-1.11	0.9
Handgrip	0.91	0.84-0.98	**0.017**
Clinical Frailty Scale	1.20	0.72-2.0	0.5
Disease Risk Index	1.09	0.50-2.39	0.8

Transplant Conditioning Intensity	0.66	0.37-1.17	0.2

Table 1

Conclusions: This study confirms the prognostic relevance of sarcopenia in allo-HSCT candidates, highlighting both functional and anatomical components. Handgrip strength is a practical, modifiable marker for routine assessment and risk stratification. Pre-frail and frail patients may benefit from tailored pre-habilitation combining exercise and nutritional support. A multidisciplinary approach with physiotherapists, nutritionists, and physicians enables individualized interventions, while ongoing monitoring with functional tests and BIA guides adaptive rehabilitation. Integrating sarcopenia assessment into pre-transplant protocols may improve survival, reduce complications, and enhance quality of life.

Disclosure: Nothing to declare.

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POOR GRAFT FUNCTION AND GRAFT FAILURE AFTER ALLOGENEIC HSCT: FOCUS ON CELLULAR THERAPY. A RETROSPECTIVE SINGLE-CENTER ANALYSIS

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Background: Poor graft function (PGF) and graft failure (GF) are life-threatening complications after allogeneic HSCT, and stem cell boost (SCB) represents a promising alternative to second transplantation. We performed a single-centre retrospective analysis of pediatric patients receiving SCB between 2014 and 2024 to evaluate patient (ptn) and treatment characteristics, SCB indications and responses according to EBMT criteria (Shapiro et al. 2023), overall survival (OS) by disease type, and the incidence of GvHD after SCB.

Methods: Among 328 allo-HSCT recipients, 18/328 pts (5%) developed PGF or primary/secondary GF requiring SCB. The median age was 11.3 years (range, 0.7–23), with a median observation time of 1.4 years (range, 0.1–8.8). Underlying diseases were malignant in 12/18 and non-malignant in 6/18 pts. HSCT/SCB were performed from a matched sibling donor in 5/18 pts, a matched unrelated in 10/18 and a haploidentical donor in 3/18 pts. GVHD prophylaxis post SCB was given in 9/18 pts, mainly those with non-malignant diseases. Response to SCB was classified as complete response (CR), partial response (PR), or no response (NR) according to EBMT consensus criteria. Overall survival (OS) was evaluated from the date of SCB.

Results: SCB was performed at a median of day +128 (range, 12–157) after allo-HSCT. PGF was diagnosed in 12/18 and primary or secondary GF in 6/18 pts. The main indications for SCB were viral infection in 12/18 and pending relapse in 4/18 pts. SCB products included

cryopreserved and non-cryopreserved CD34⁺-selected grafts (7/18 and 1/18 pts, respectively), as well as αβ-TCR–depleted or CD3/CD19–depleted grafts (10/18 pts). CD34⁺-selected grafts contained a median of 3.7 × 10^6 CD34⁺ cells/kg (range, 0.85–4.4) and 4 × 10^3 CD3⁺ cells/kg (range, 1–7); αβ TCR–depleted or CD3/CD19–depleted grafts contained a median of 5.3 × 10^6 CD34⁺ cells/kg (range, 1.9–8.4) and 3 × 10^5 CD3⁺ cells/kg (range, 0.01–5). Prior to SCB, 5/18 pts received plasma exchange and immune adsorption for B-cell dysregulation and antibody-production, with additional rituximab administered in 3 of these pts. After SCB, all patients receiving CD34⁺-selected SCB (8/8) achieved stable hematologic engraftment and became transfusion independent, whereas 70% (7/10) of patients receiving αβ TCR–depleted or CD3/CD19-depleted SCB achieved engraftment. Two-year OS was 100% in non-malignant diseases (6/6 pts) and 58% in malignant diseases (7/12 pts), with deaths in the malignant group primarily attributable to disease progression ($p > 0.05$).
SCB induced GvHD was rare with acute GvHD (I–II) in 2/18 pts, and no cases of severe acute and chronic GvHD, GvHD rates were comparable across different SCB product types.

Conclusions: SCB is a safe and effective treatment for PGF and GF after allo-HSCT, achieving high response rates and favourable survival without significant GvHD. Outcomes were excellent for non-malignant diseases, whereas OS was lower in malignant diseases, likely reflecting underlying disease risk. Despite the small cohort, these data support early consideration of SCB as a first-line cellular therapy for post-transplant graft dysfunction.

Disclosure: No conflict of interests.

A145

SCALABLE MANUFACTURING AND NATIONWIDE DISTRIBUTION OF ORCA-T: A PRECISION-ENGINEERED ALLOGENEIC IMMUNE CELL THERAPY

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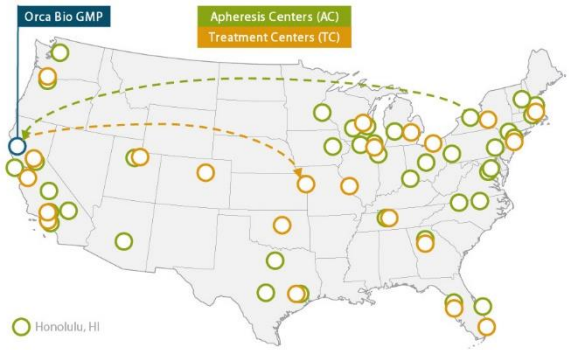
Background: Orca Bio is a clinical-stage biotechnology company advancing a pipeline of high-precision allogeneic cell therapies to replace diseased blood and immune systems. Our lead investigational candidate, Orca-T, is manufactured from mobilized apheresis collections of 8/8 HLA-matched donors and comprises purified regulatory T cells (Treg), hematopoietic stem and progenitor cells (HSPC), and conventional T cells (Tcon). Donor products are transported to a central GMP facility, where each cellular component is purified and formulated. Treg and HSPC are shipped as fresh infusions, while Tcon is cryopreserved. Final products are couriered under controlled conditions to treatment centers for administration. Logistics across apheresis sites, the central facility, and clinical centers are supported by OrcaPort, a proprietary supply chain platform, in partnership with the National Marrow Donor Program (NMDP).

Methods: We report manufacturing and distribution data from Orca-T in the Phase 1b (NCT4013685) and Phase 3 (NCT05316701) trials. Between December 2019 and September 2024, 243 products were manufactured, 215 from single-day collections and 28 from two-day collections. Time zero was defined as completion of the final collection. Apheresis centers and treatment centers were utilized widely across the US (Figure 1). Overall, 96% of products were delivered within 60 hours and 100% within 70 hours; 99% were infused within the 72-hour release window. Product quality was consistent: adjusted ideal body weight averaged 74 ± 13 kg (46–104); Treg dose was 2.7 ± 0.4 × 10^6/kg (1.3–3.7) with 92% ± 3% purity (78–97%); HSPC dose was 6.2 ± 3.0 × 10^6/kg (1.1–15.2); residual T cells were 17 ± 134 × 10^3/kg (0–1825); Tcon products were dosed at 3 × 10^6/kg.

Results: These results demonstrate that Orca-T can be reliably manufactured at scale, maintaining high purity, and distributed nationwide within a controlled logistics framework.

Conclusions: Collectively, these findings establish the feasibility of precision-engineered cell therapy manufacturing and distribution to enable multicenter clinical studies and lay the foundation for future commercial application.
Figure 1: Apheresis Centers and Transplant Centers participating in the Phase 1b (NCT4013685) and Phase 3 (NCT05316701) trials of Orca-T

Figure 1: Apheresis Centers and Transplant Centers participating in the Phase 1b (NCT4013685) and Phase 3 (NCT05316701) trials of Orca-T.



Clinical Trial Registry: NCT05316701 https://clinicaltrials.gov/study/NCT05316701, NCT4013685 https://clinicaltrials.gov/study/NCT04013685

Disclosure: Amy Putnam reports being employed by Orca Bio. Sandy Tang reports being employed by Orca Bio. Katie Chaddock reports being employed by Orca Bio. Marina R Becker reports being employed by Orca Bio. Jamie Goldman reports being employed by Orca Bio. Lauren Smith reports being an employee, officer, and equity holder at Orca Bio. Kate Bickett reports being employed by Orca Bio. Virginia Sullivan reports being employed by Orca Bio. James Scott McClellan, MD, PhD reports being an employee, officer, and equity holder at Orca Bio. Anna Pavlova, MD, PhD reports being an employee and equity holder at Orca Bio. Everett H. Meyer, MD, PhD reports Orca Biosystems clinical trial funding. Nathaniel B. Fernhoff, PhD reports being an employee, officer, and equity holder at Orca Bio. Jeroen Bekaert, PhD reports being an employee, officer, and equity holder at Orca Bio.

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OUTCOMES AFTER STANDARD- VS. REDUCED-DOSE TREOSULFAN IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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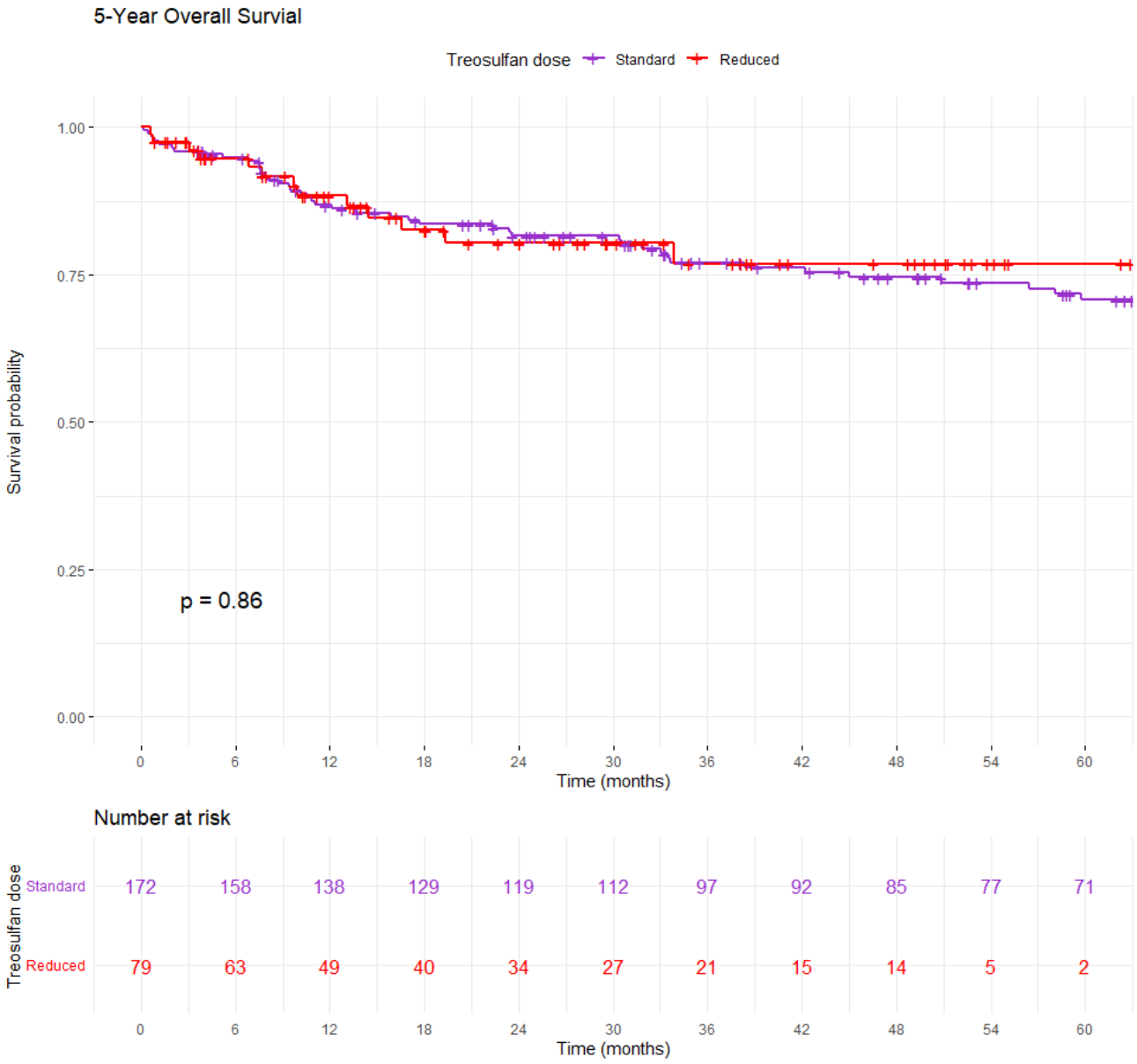
Background: Treosulfan-based conditioning is increasingly used in allogenic hematopoietic cell transplantation (allo-HCT) due to its myeloablative efficacy and reduced toxicity. However, evidence guiding optimal dosing remains limited and its clinical impact remains insufficiently defined. Conditioning with Fludarabine and Treosulfan (FluTreo) was implemented at Copenhagen University Hospital, Rigshospitalet, in 2014 with a standard dose of 42 g/m². In 2020, a dose-adjusted algorithm introduced 30 g/m² treosulfan for older patients or those with higher comorbidity. This study examines the impact of treosulfan dose on clinical outcomes, with the aim of improving understanding of dose optimization in FluTreo conditioning.

Methods: We performed a retrospective cohort study of all adults receiving FluTreo conditioning prior to allo-HCT for malignant disease at Rigshospitalet from 2014–2024. Diagnoses included myelodysplastic syndrome (MDS), high-risk acute myeloid leukemia (AML) and other myeloid malignancies. Patients received either standard-dose or reduced-dose treosulfan based on time of transplantation, age and comorbidity score (HCT-CI). Clinical data were extracted from electronic medical records. Statistical analyses included descriptive statistics, Kaplan–Meier survival analysis, and competing risks models.

Results: A total of 252 patients were included with 173 receiving standard-dose and 79 receiving reduced-dose Treosulfan. Reduced-dose recipients were older (median 64.5 years [inter quartile range (IQR) 52.6–67.8] vs. 57.7 years [IQR 52.1–62.2], p=0.00016), while comorbidity burden was comparable (median HCT-CI 2 [IQR 0–3] vs. 2 [IQR 0.5–3.5], respectively, p=0.27). Diagnostic distribution was similar between groups (around 70% MDS, 15% AML and 15% other diagnoses) (p=0.50), with a median IPSS-R for the MDS patients of 4.5 in both groups (p=0.59). Median follow-up was 5.9 and 2.2 years, in the standard and reduced dose groups respectively. For the entire cohort, overall survival (OS) was 87.2% [83.0–91.6%] at 1 year and 77.0% [71.4–83.0%] at 3 years. OS at 1 and 3 years was 86.7% [81.7–92.1%] and 77.0% [70.6–84.0%] in the standard-dose group, and 88.4% [81.1–96.3%] and 76.8% [65.8–89.7%] in the reduced-dose group (p=0.86). Cumulative incidence of relapse (CIR) for the whole cohort was 15.8% [11.1–20.5%] at 1 year and 21.4% [16.0–26.9%] at 3 years. CIR at 1 and 3 years was 14.0% [8.7–19.2%] and 18.5% [12.5–24.4%] with standard dose, and 19.3% [10.0–28.8%] and 29.3% [16.8–41.8%] with reduced dose (p=0.12). Non-relapse mortality (NRM) for the cohort was 6.8% [3.6–10.0%] at 1 year and 8.4% [4.8–12.1%] at 3 years. NRM at 1 and 3 years was 7.3% [3.4–11.4%] and 9.5% [4.9–14.0%] with standard dose, and 4.6% [0.0–9.4%] at both time points with reduced dose (p=0.35). Analyses of toxicity, chimerism, graft-versus-host disease, and

prognostic factors are ongoing.



Conclusions: Treosulfan dose adjustment was not associated with differences in overall survival, relapse, or non-relapse mortality. Despite significantly older age in the reduced-dose group, outcomes remained comparable, indicating that reduced-dose treosulfan may be a viable option for selected patients. Ongoing analyses of chimerism, graft-versus-host disease, and toxicity will help further define the clinical implications of treosulfan dosing and guide individualized conditioning strategies in allo-HCT.

Disclosure: IS attended the Costem congress 2023, supported by Medac. MH received a research grant from Medac. LSF attended Costem 2024 (Medac) and EBMT 2025 (Gilead) and participated in an advisory board with Immedica (October 2023). MN attended Costem 2024 and EBMT 2024, both supported by Medac. SP attended Costem in 2022 and 2023, supported by Medac. JS, EW, HS, BK, BM, NSA, and KG declare no conflicts of interest.

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REAL-WORLD EXPERIENCE WITH TABELECLEUCEL

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Background: Tabelecleucel (Tab-cel) is an allogeneic Epstein–Barr virus (EBV)-specific T-cell therapy approved in the European Union for relapsed or refractory (R/R) EBV-associated post-transplant lymphoproliferative disorder (PTLD) after failure of rituximab or immunochemotherapy. Despite its promise as the first approved therapeutic option, real-world evidence remains limited. The aim of this study was to evaluate the scope of use and outcomes of Tab-cel treatment in the real-world setting across Germany, Austria, and Switzerland (DACH countries).

Methods: Eleven patients with EBV-positive PTLD or other EBV-associated lymphoproliferative disorders (LPD) from nine academic centers were included for detailed analysis of their (disease) characteristics and survival parameters. The cohort analyzed includes all known Tab-cel–treated patients in DACH until July 2025.

Results: Eight patients with PTLD (six after solid organ transplantation, two after allogeneic hematopoietic cell transplantation) and three with EBV-associated LPD were treated with a median of two cycles Tab-cel (range 1-3). After a median follow-up of 15.1 months, 6/11 patients (55%) remain alive. Initially, 7/11 patients (64%) achieved an objective response and best response occurred after a median of 37 days after the first Tab-cel infusion (i. e. end of cycle one). Despite a high relapse and progression rate after Tab-cel affecting 7/11 patients (64%), estimated median overall survival was 10.7 months (CI 4.4-14.7) due to successful salvage treatments. Immunotherapy-related adverse events were rare.

Conclusions: Tab-cel demonstrates meaningful efficacy with a favorable safety profile in R/R PTLD/LPD within this highly vulnerable population of immunodeficient or transplanted patients. However, the durability of response depends on re-establishing effective immunosurveillance, and Tab-cel alone was not consistently sufficient to maintain long-term disease control. Future approaches should clarify how best to integrate Tab-cel into the therapeutic pathway for R/R LPD, potentially including optimized HLA matching to enhance antiviral activity and consideration of consolidation strategies following Tab-cel therapy. This study contributes to the early real-world experience with Tab-cel and highlights its potential for achieving remission induction.

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A148

MESENCHYMAL STEM CELLS DERIVED FROM DIFFERENT SOURCES AND THEIR SECRETOMES IN MULTIPLE SCLEROSIS THERAPY: A SINGLE CENTER EXPERIENCE

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Background: Multiple sclerosis (MS) is a chronic autoimmune, inflammatory, and demyelinating disease of the central nervous system (CNS), affecting young adults. While current treatments can improve symptoms, there remains a need for novel therapeutic approaches. Mesenchymal stem cell (MSC) therapy has emerged as a promising strategy for various neurodegenerative disorders due to its immunomodulatory properties and the therapeutic potential of its secretome. The MSC secretome comprises growth factors, cytokines, and extracellular vesicles that contribute to tissue repair and immune regulation.

Methods: This retrospective, experimental study conducted between 11/2023 and 11/2024, on an outpatient basis, involved 10 pts who were divided in 2 groups (each n = 5): Group A received bone marrow-derived MSCs and their secretome (BM-MSC + Secretome), while Group B received umbilical cord-derived MSCs and their secretome (UC-MSCs+Secretome). Median age was 53 yo (47-60). All pts were were refractory to the usual conventional treatments. Ten collections from BM and UC were made. BM aspirates were obtained by puncturing the iliac crest. UC units were collected from the unborn placenta of full-term deliveries in a multiple bag system containing 17 mL of citrate phosphate dextrose buffer (Cord Blood Collection System; Eltest, Bonn, Germany). Processing was performed within 24 h of collection. All MSCs were cultured with DMEM/F12 supplemented with 5% PSA at subconfluency. After 48h of incubation at 37 °C at a humidified atmosphere containing 5% CO2, the supernatant, containing all released cytokines and chemokines was collected. Two injection sessions were performed per patient on day 0 and 180; the number of cells were 10^8 diluted in 100 ml of secretome and cells were at passage three. The clinical outcome for evaluation was Kurtzke's expanded disability status scale (EDSS) and Symbol Digit Modalities Test (SDMT).

Results: Patients in Group B demonstrated greater improvement in the EDSS and SDMT compared to Group A. Additionally, we observed encouraging trends in cognitive and psychological parameters, as well as moderate improvements in neurological assessments, functional disability, and unaided mobility. Enhanced brain connectivity was also noted, alongside reduced dependency in daily activities such as eating, with patients maintaining clear communication. These findings suggest that UC-MSCs+Secretome may offer superior

therapeutic benefits in the treatment of MS compared to BM-MSCs+Secretome .In our study, we observed a reduction in CD20/CD19 expression on B lymphocytes following cell therapy, indicating a decrease in B cell population. This is noteworthy given the role of B cells in MS pathogenesis.

Conclusions: This trial suggests that BM-MSCs and UC-MSCs, along with their secretomes, may offer neuroprotective and clinical benefits in MS patients refractory to conventional treatments. However, due to the limited sample size and follow-up duration, further studies involving larger cohorts, repeated dosing, and objective biomarkers are essential to confirm these findings.
We propose that the timing of MSC administration is a critical factor in optimizing therapeutic outcomes. Administering high-dose MSCs during the early inflammatory phase of MS may enhance their effectiveness as a novel treatment strategy.

Clinical Trial Registry: N/A

Disclosure: No

A149

TREOSULFAN-FLUDARABINE AS A REDUCED INTENSITY CONDITIONING ALTERNATIVE TO BUSULFAN-FLUDARABINE FOR ADULT ALLOGENEIC STEM CELL TRANSPLANTATION: SINGLE-CENTER, EARLY REAL-LIFE CLINICAL AND ECONOMICAL COMPARATIVE OUTCOMES

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Background: Reduced-intensity conditioning (RIC) has substantially extended transplantation (allo-HCT) practices by balancing disease control with treatment-related toxicity. FB2 (Fludarabine 120 mg/m² + Busulfan 6.4 mg/kg) remains one of the most widely used RIC backbones. However, high-quality studies suggest that treosulfan-based regimens may reduce toxicity without compromising disease control. Based on this evidence, our center implemented FT10 (Fludarabine 120 mg/m² + Treosulfan 30 g/m²) in 2023 as an alternative RIC regimen. We report here our real-life comparative experience focusing on early post-transplant outcomes and economic indicators.

Methods: We retrospectively reviewed all allo-HCTs performed between 2021 and 2025 using FT10 or FB2 conditioning, both combined with anti-lymphocyte globulin ((ATG) Thymoglobulin 5 mg/kg or Grafalon 30 mg/kg), for adults with AML or MDS. Transplant practices were identical across the study period: peripheral blood stem cell grafts, ciclosporine + methotrexate for GVHD prophylaxis, letermovir prophylaxis, and unchanged center-level procedures and teams. Clinical variables and outcomes were extracted from electronic medical records. Due to shorter follow-up in the FT10 cohort, survival outcomes

were reported at a fixed 6-month (6m) landmark. Between-group imbalances were included in multivariable models. Fine-Gray competing risks models were used as appropriate. Costs were assessed from the French national health insurance perspective and reflect reimbursement-based hospital charges. The study was approved by the local ethics committee (IRB 2025-655).

Results: A total of 135 adults were included: FB2 (n = 100) and FT10 (n = 35). Baseline characteristics were comparable between FB2 and FT10 regarding age (median 63 vs 60 years), disease type (AML 70% vs 74%), remission status (CR1 69% vs 51%), disease risk, time from diagnosis to allo-HCT, donor type, ABO compatibility, comorbidity score, and subsequent injections of donor lymphocytes (DLI). The FT10 group had more secondary AML/MDS (43% vs 18%, p = 0.0061), second allo-HCT (23% vs 3%, p = 0.0009), and Grafalon use (69% vs 1%, p < 0.0001).
Median follow-up was 29.7 (FB2) and 8.3 months (FT10). The 6m overall survival (OS) and relapse-free survival (RFS) were similar in both groups. In multivariable analysis, CR1 status at allo-HCT significantly improved the RFS (HR=0.35, 95%CI 0.12 – 0.98, p= 0.04) independently of the conditioning group. The 6m incidence of relapse was 18% (FB2) vs 9% (FT10) and did not reach a statistical significance owing to limited power. The 6m TRM was similar (6% (FB2) vs 5% (FT10)). Day 100, grade ≥ II acute GVHD was comparable (11% (FB2) and 14% (FT10)). Engraftment rates, infectious complications and sinusoidal obstruction syndrome were similar between groups. FT10 was associated with higher upfront transplant-related costs (p=0.0036) but significantly lower secondary costs related to post-transplant unplanned care (p=0.0224) consistent with less severe or less resource-intensive complications. Detailed analysis of healthcare burden will be provided including a sensitivity analysis for ATG costs.

Conclusions: Despite being used in a substantially higher-risk population, FT10 achieved early post-transplant outcomes comparable to FB2, with a lower burden of early unplanned healthcare costs. These findings support the feasibility and cost effectiveness of FT10 as a reduced-toxicity RIC option for AML/MDS.

Disclosure: Nothing to declare

A150

CD72-GATED PRE-CAR-T MRD AS A NOVEL PREDICTOR OF POST-TRANSPLANT OUTCOMES IN R/R B-ALL ACHIEVING MRD-NEGATIVE REMISSION AFTER CD19 CAR-T THERAPY

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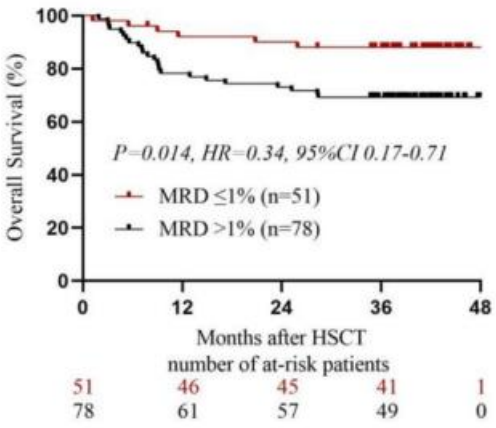
Background: Antigen loss limits MRD monitoring after CD19/CD22 CAR-T in r/r B-ALL. CD72, a B-lineage–restricted marker, offers a reliable alternative. We validated a CD72-gated

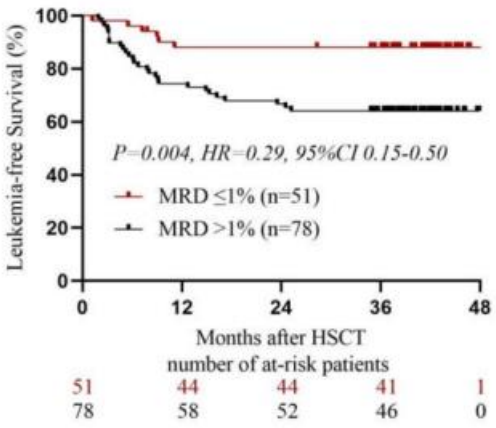
MFC strategy and assessed its prognostic value for post–HSCT outcomes in MRD-negative patients after CD19 CAR-T.

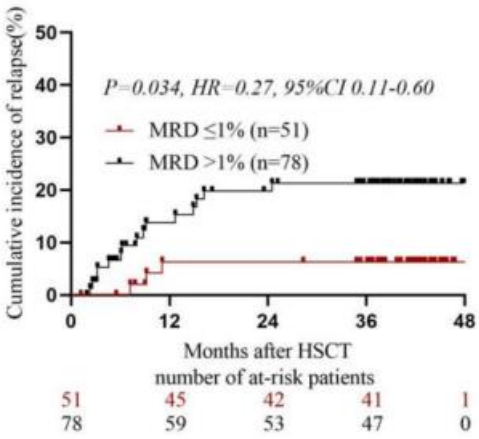
Methods: CD72-based MRD gating was validated in 66 B-ALL and assessed for lineage specificity in 129 acute leukemia samples. We retrospectively analyzed 129 r/r B-ALL patients achieving MRD-negative CR by day 28 post–CAR-T who underwent first allo-HSCT. Patients were stratified by CD72-gated pre–CAR-T MRD (≤1% vs. >1%). Outcomes included OS, LFS, CIR, and NRM; targeted sequencing profiled mutations.

Results: ***Validation of CD72-based gating***
CD72-based MRD detection showed near-perfect concordance with CD19-based gating (R^2 = 0.9936 in CR and 0.9993 in NR cases). CD72 was positive in 95.8% of B-ALL cases (vs. 29.3% AML, 23.5% T-ALL; $P < 0.001$), confirming strong B-lineage specificity.
Post–CAR-T and HSCT outcomes (Figure 1)
Among 129 patients (median age 13 years), all achieved MRD-negative CR and underwent allo-HSCT. Baseline characteristics were comparable between MRD groups. Among 114 genetically tested patients, 86.8% harbored mutations, most frequently in *IKZF1* (16.7%), *WT1* (9.6%), *ETV6* (9.6%), and RAS pathway genes (21.9%). Fusion positivity (36.4%) included *KMT2A-r* (8.5%) and *BCR::ABL1* (10.9%), with comparable distribution between MRD groups. After a median follow-up of 38.5 months, the 3-year OS and LFS were 76.6% and 72.3%, respectively. Patients with pre–CAR-T MRD ≤1% had significantly better outcomes (3-year OS 88.1% vs. 69.2%, $P = 0.014$; LFS 88.1% vs. 64.1%, $P = 0.004$) and lower relapse risk (CIR 6.0% vs. 19.2%, $P = 0.034$).
Multivariate Analysis (Table 1)
Patients harboring KMT2A rearrangement had significantly worse OS (HR = 3.57, 95% CI 1.11–11.50, $P = 0.033$). Similarly, IKZF1 mutation was associated with poorer OS (HR = 2.75, 95% CI 1.09–6.96, $P = 0.033$), and TP53 mutation predicted markedly inferior OS (HR = 5.31, 95% CI 1.85–15.28, $P = 0.002$), LFS (HR = 3.64, 95% CI 1.31–10.10, $P = 0.014$), and higher NRM (HR = 5.19, 95% CI 1.29–20.90, $P = 0.021$). Pre-CAR-T MRD > 1% was also an adverse factor for OS (HR = 2.83, 95% CI 1.12–7.15, $P = 0.028$), LFS (HR = 3.39, 95% CI 1.37–8.40, $P = 0.008$), and NRM (HR = 3.63, 95% CI 1.00–13.20, $P = 0.050$). Age, BCR::ABL1, complex cytogenetics, CAR-T cell dose, and the interval between CAR-T infusion and subsequent HSCT did not significantly impact OS, LFS, CIR, or NRM (*all* $P > 0.05$).

Figure 1. Outcomes of Allo-HSCT Following CAR-T Therapy between two pre–CAR-T MRD groups







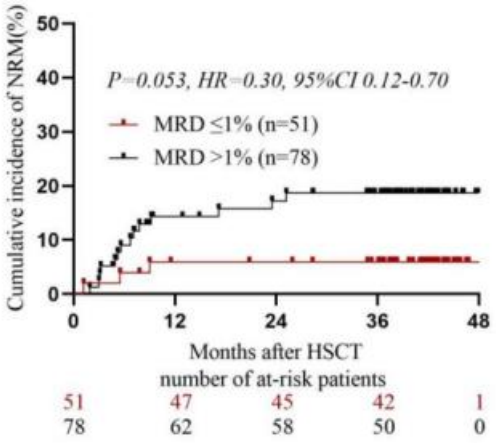


Table 1. Multivariate analysis results

Variable	OS		LFS		NRM		CIR	
	OR(95%CI)	*P-vaule*	OR(95%CI)	*P-vaule*	OR(95%CI)	*P-vaule*	OR(95%CI)	*P-vaule*
Age (0=≤14Y, 1=>14Y)	1.26 (0.58-2.72)	0.564	1.18 (0.58-2.41)	0.646	1.56 (0.65-3.74)	*0.320*	0.92 (0.35-2.40)	*0.860*
KMT2A_r (0=No, 1=Yes)	3.57 (1.11-11.50)	0.033	2.66 (0.86-8.22)	0.090	3.57 (0.75-16.9)	*0.110*	2.75 (0.67-11.2)	*0.160*
BCR::ABL1 (0=No, 1=Yes)	1.88 (0.60-5.87)	0.278	1.41 (0.47-4.30)	0.541	2.52 (0.69-9.17)	*0.160*	0.58 (0.06-5.11)	*0.620*

IKZF1 mut (0=No, 1=Yes)	2.75 (1.09-6.96)	0.033	2.26 (0.92-5.52)	0.075	5.08 (1.58-16.3)	*0.007*	0.45 (0.06-3.53)	*0.440*
TP53 mut (0=No, 1=Yes)	5.31 (1.85-15.28)	0.002	3.64 (1.31-10.1)	0.014	5.19 (1.29-20.9)	*0.021*	1.92 (0.49-7.55)	*0.350*
Complex_cytogenetics (0=No, 1=Yes)	1.24 (0.47-3.26)	0.663	1.33 (0.55-3.18)	0.527	0.81 (0.11-6.09)	*0.830*	1.57 (0.56-4.38)	*0.390*
MRD_level pre-CART (0=≤1%, 1=>1%)	2.83 (1.12-7.15)	0.028	3.39 (1.37-8.40)	0.008	3.63 (1.00-13.2)	*0.050*	2.93 (0.76-11.3)	*0.120*
Bridge HSCT after CART,>60d	reference							
≤45d	0.62 (0.20-1.89)	0.399	0.74 (0.26-2.13)	0.575	0.94 (0.17-5.04)	*0.940*	0.64 (0.17-2.37)	*0.510*
45-60d	0.57 (0.17-1.92)	0.362	0.66 (0.21-2.13)	0.491	0.89 (0.14-5.58)	*0.900*	0.68 (0.18-2.55)	*0.570*
CART_dose (0=≤5, 1=10)	1.12 (0.43-2.95)	0.816	1.19 (0.48-2.93)	0.707	0.88 (0.14-5.61)	*0.890*	1.42 (0.50-4.05)	*0.510*

Conclusions: CD72-gated MFC enables reliable, lineage-specific MRD monitoring in B-ALL and addresses the limitations of antigen-loss after CD19/CD22 CAR-T therapy. Importantly, CD72-gated pre–CAR-T MRD serves as a novel, independent biomarker predicting post-transplant survival and relapse. Integrating CD72-based MRD with molecular risk profiling (e.g., *KMT2A*, *TP53*, *IKZF1*) provides a powerful stratification tool to optimize transplant timing and post–CAR-T management in r/r B-ALL.

Disclosure: Nothing to declare

A151

NON-MYELOABLATIVE CONDITIONING FLUCYTBI WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE IS SAFE AND EFFECTIVE FOR BOTH HAPLOIDENTICAL AND UNRELATED DONOR ALLOGENEIC TRANSPLANTATION IN OLDER PATIENTS WITH AML OR MDS

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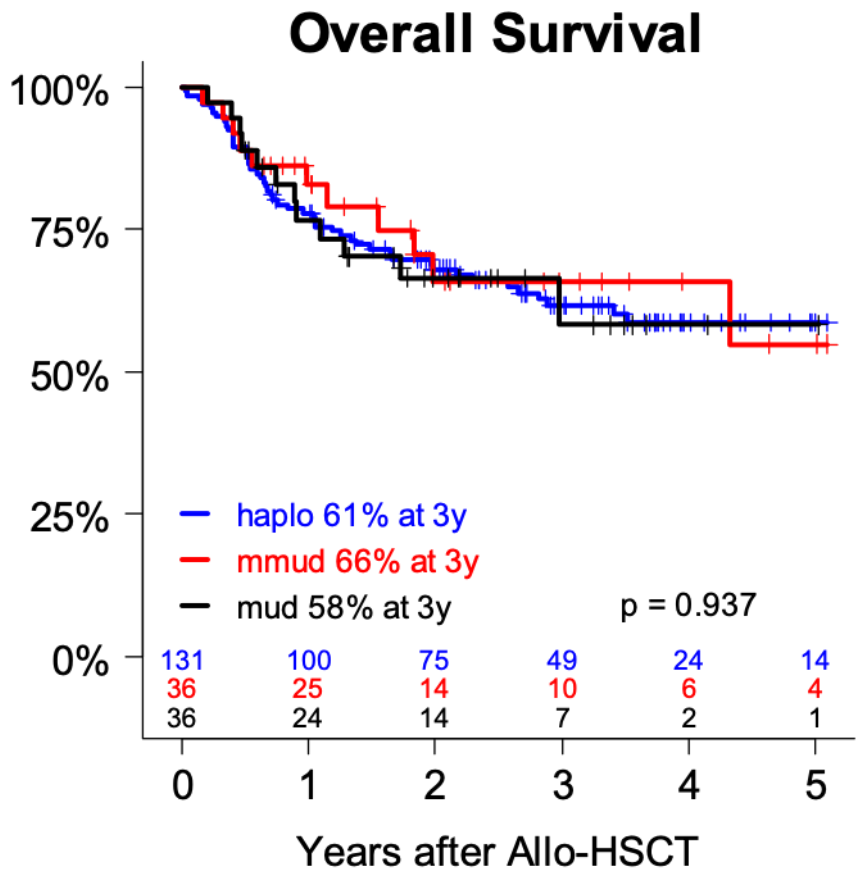
Background: The non-myeloablative conditioning regimen (NMAC) from Baltimore based on 2Gy TBI, fludarabine and cyclophosphamide (FluCyTBI) associated with post-transplant cyclophosphamide (PTCy) was initially developed in the context of haploidentical transplantation. We previously reported that this platform is well adapted to AML or MDS patients aged ≥70yo, with low incidence of GVHD and prolonged survival. In our center, this regimen was progressively implemented in the setting of mismatched unrelated donor (MMUD) and matched unrelated donor (MUD) for patients ≥60yo or younger in case of comorbidities. Here we report a large single-center retrospective study showing the feasibility and efficacy of FluCyTBI+PTCy as single platform for both haplo and unrelated donor (UD) allo-SCT in AML/MDS pts ≥60y or with comorbidities.

Methods: We included all consecutive patients with following criteria: age ≥60yo or younger if contraindicated to receive busulfan-based regimen; first allo-SCT for AML or high-risk MDS between 2015 and 2024; Haplo or UD allo-SCT; FluCyTBI regimen; PBSC as graft source; PT-Cy, CSA and MMF as GVHD prophylaxis. We evaluated acute and chronic GVHD, NRM, relapse, PFS and OS.

Results: 203 patients were included, with a median age of 69y (IQR 59-73). 94 patients were ≥70yo at the time of allo-SCT. 28 patients were younger than 60y and received NMAC because of comorbidities. Donors were haplo, MMUD and MUD in 131 (65%), 36 (18%) and 36 (18%) patients respectively. 145 and 58 patients had AML and MDS, respectively.
Out of 108 AML in first CR, CRi or MLFS at allo-SCT, ELN2022 risk stratification was favorable, intermediate and adverse in 9 (8%), 48 (44%) and 51 (47%) of cases respectively. Monosomal karyotype (MK) was found in 21 (10%) of the cohort. In the whole cohort, with a median follow-up of 38 months, median OS was not reached. Day+100 grade 2-4 acute, grade 3-4 acute and 3-y all grades chronic and moderate/severe chronic GVHD were 32%, 8%, 33% and 18%, respectively. 1-y and 3-y NRM were 9% and 15%, respectively. 3-y CIR rate was 27%. 3-y OS rates were 61%, 66% and 58% (P=0.937) and 3-y PFS rates were 59%, 63% and 40% (P=0.482) in the haplo, MMUD and MUD cohorts respectively. There was no difference in any endpoint between AML and MDS patients. Outcomes of patients ≥70y were not different from those of younger patients.
In multivariable analysis, MK predicted worse OS and PFS (HR 3.83, 95%CI 1.97-7.45, P<0.001 and HR 4.13, 95%CI 2.16-7.89, P<0.001, respectively). MK as well as MUD predicted increased relapse risk (HR 6.26, 95%CI 2.87-13.66, P<0.001 and HR 2.82, 95%CI 1.4-5.66, P=0.004 respectively). Donor age >35y predicted increased risk of aGVHD II-IV (HR 1.78, 95%CI 1-3.15, P=0.049). Female-to-male sex-mismatch predicted increased risk of moderate/severe chronic GVHD (HR 2.91, 95%CI 1.55-5.45, P=0.001).



Conclusions: We showed in a cohort of 203 homogeneously treated older AML/MDS patients that FluCyTBI NMAC associated with PTCy is safe and produces promising outcomes both in haplo and MMUD settings. Beyond HLA matching and donor type, non-HLA donor-related factors (age and sex) are critical for outcome.

Disclosure: Nothing to declare.

A152

HYPOMETHYLATING AGENTS PLUS VENETOCLAX VS INTENSIVE CHEMOTHERAPY PRIOR TO TRANSPLANT IN HIGH-RISK ACUTE MYELOID LEUKEMIA

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Luca Lanino[2], Eytan Stein[4], Amer Zeidan[2], Edouard Forcade[9], Thomas Cluzeau[10], Pierre-Yves Dumas[9], Mael Heiblig[11], Raynier Devillier[1], Shai Shimony[3], Aaron Goldberg[4], Maximilian Stahl[2], Sylvain Garciaz[1], ***Charlotte Nykolyszyn***[1]
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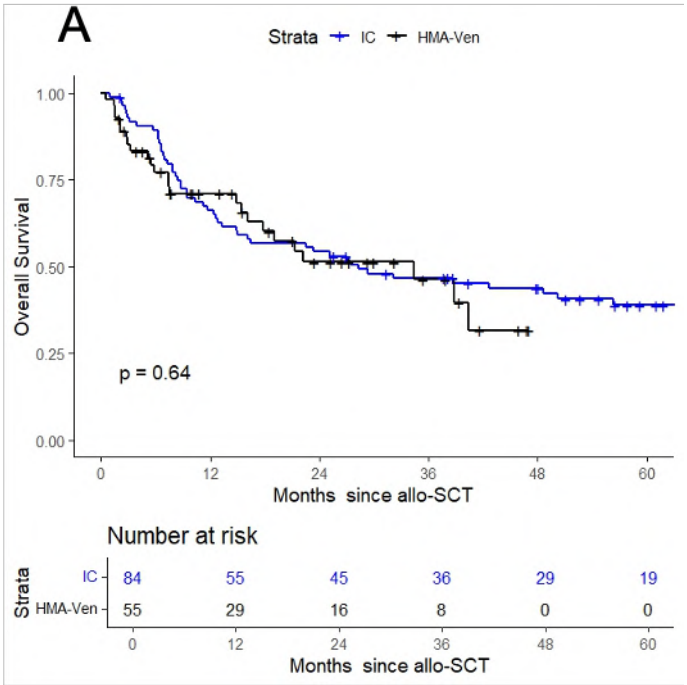
Background: High-risk AML has a poor prognosis and allo-SCT is the only curative therapy available. Older AML patients 60-74yo represent a high-risk population, with frequent high-risk AML characteristics predicting disease resistance to IC. Thus, there is a need for new therapeutic strategies in this population. The less-intensive regimen combining the hypomethylating agent (HMA) azacitidine (AZA) and the BCL-2 inhibitor venetoclax (VEN) has changed the treatment paradigm for older subjects with newly-diagnosed AML. Yet it still remains an open question whether HMA-VEN is equivalent to IC on post-transplant outcomes in high-risk AML patients.

Methods: We assembled a retrospective cohort of consecutive patients 60-74yo newly-diagnosed with ELN-2022 adverse-risk AML, treated with allo-SCT after prior intensive or less-intensive remission induction therapy. All patients were diagnosed between April 2014 and May 2024 at 3 United-States centers (DFCI, MSKCC, Yale Cancer Center) and 5 European centers (France: IPC Marseille; CHU Nice; HCL Lyon; CHU Bordeaux; Lithuania: Vilnius University Hospital Santaros Klinikos).

Results: We included 139 patients who consecutively underwent allo-SCT after first-line therapy. Median age at diagnosis was 66 years (60-74). Fifty-five patients (40%) had received HMA–VEN as induction treatment (AZA [n = 43] or DEC [n = 12]). Eighty-four patients (60%) had received IC as induction therapy (64 (76%) with 7+3; 20 (24%) with CPX-351).
In the HMA-VEN group, CR, CRi, and MLFS rates were 58.5%, 19%, and 13%, respectively. cCR and OR rates were 77% and 91%. In the IC group, CR, CRi, and MLFS rates were 66%, 5%, and 6%, respectively. cCR and OR rates were 71% and 77%.
Out of 68 patients with MRD status available at best response, 73% and 63% were MRD^- in the HMA-VEN and IC group, respectively.
A total of 31 patients were transplanted with active disease, 5 (9%) in the HMA-VEN group and 26 (31%) in the IC group (P=0.003).
With a median follow-up of 52.3 months, post allo-SCT OS was 34.4 (95%CI, 16.1-NA) and 28.3 months (95%CI, 14.9-56.3) in the HMA-VEN and IC groups, respectively (P=0.636, Figure). NRM and CIR were similar between both groups (NRM at 6 and 12 months: 8% and 11% in the HMA-VEN group vs 5% and 18% in the IC group, P=0.632; CIR at 6 and 12 months: 11% and 25% in the HMA-VEN group, 13% and 23% in the IC group, P=0.643). Multivariable analyses found that induction type (HMA-VEN vs IC) did not impact post allo-SCT OS (HR=0.95, 95%CI=0.54-1.68, P=0.864). The only factor associated with better survival was the achievement of cCR at allo-SCT (HR=0.43, 95%CI=0.26-0.69, P=0.001).

Monosomal karyotype was predictive of worse survival (HR=2.29, 95%CI=1.34-3.92, P=0.003). In subgroup analyses, patients with AML harboring del5q and *TP53*mutations had better OS with HMA-VEN + allo-SCT compared to IC (HR: 0.31; 95% CI: 0.12–0.88; P=0.027, and HR: 0.39; 95% CI: 0.16–0.98; P=0.044, respectively).



Conclusions: Our study provides evidence supporting the use of HMA-VEN as an alternative, less toxic remission induction strategy for patients with ELN-2022 adverse-risk AML who are intended to proceed to allo-SCT.

Disclosure: No COI.

A153

PROGNOSIS ANALYSIS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF MYELOID SARCOMA: A SINGLE-CENTER STUDY

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Background: Myeloid Sarcoma(MS) are solid tumors formed by (mature or immature) myeloid progenitor cells infiltrating extramedullary tissues and disrupting their original structure. MS exhibits heterogeneity, typically affecting a single site, though 30% of patients

experience multi-site involvement. Currently, the optimal treatment has not been established. Therapeutic options include radiotherapy, systemic chemotherapy, targeted therapy, surgical resection, and hematopoietic stem cell transplantation (HSCT). Multiple studies indicate that allogeneic HSCT holds therapeutic potential for MS.

Methods: A retrospective analysis was performed on patients diagnosed with MS and undergoing Allo-HSCT at our center between March 1, 2017 and September 1, 2023. The follow-up period was extended until June 1, 2025.

Results: This study included 25 patients , comprising 20 males (80%) and 5 females (20%). The median age at diagnosis was 27 years (range: 1-49), with 6 pediatric cases (24%). Disease types: The most common diagnosis was MS with AML (13 cases, 52%), followed by IMS (6 cases, 24%) and relapsed MS after AML treatment(6 cases, 24%). By MS involvement sites (Figure1):12 cases (48%) involved a single site, while 13 cases (52%) involved ≥2 sites. According to cytogenetic risk stratification (2025 NCCN guidelines): 12 cases (24%) were low-risk, 6 cases (24%) were intermediate-risk, and 7 cases (28%) were high-risk (Figure 2). Pre-transplant treatments: 15 cases (60%) received chemotherapy alone, while 10 cases (40%) received chemotherapy combined with other therapies (including targeted therapy and radiotherapy). The median time from diagnosis to transplantation was 24.8 months (range: 2-162 months). Disease status before transplantation: 13 cases (52%) achieved first complete remission (CR1),8 cases (32%) achieved ≥CR2, and 4 cases (16%) had no response (NR) or partial response (PR). The donors were classified as Haploidentcal donor (HID) in 19 cases (76%), Matched unrelated donor (MUD) in 4 cases (16%), and matched sibling donor (MSD) in 2 cases (8%). All patients received intensified myeloablative conditioning regimen (MAC). 15 cases (60%) MAC-based with busulfan (BU) and 10 cases (40%) based with total body irradiation (TBI). All patients achieved successful engraftment, with a median follow-up period of 24 months (range: 1-60 months)
The 5-years overall survival (OS) was 68%,5-years leukemia-free survival (LFS) was 60%,5-years cumulative incidence of relapse (CIR) was 18%, and 5-years non-relapse mortality (NRM) was 28%(Figure 3). Univariate analysis(Figure 4) revealed no significant prognostic influence of gender, age at diagnosis, multiple affected sites, cytogenetic status at initial diagnosis, coexisting fusion gene types, coexisting mutation types, pre-transplant therapy, pre-transplant complete remission (CR) status, or donor type. However, high-risk patients (5-years NRM rate: 57.14% vs 17.65%, p=0.0372) showed higher 5-years NRM rates, while children exhibited higher 5-year CIR rates (44.44% vs 0%, p=0.0314). The TBI-based conditioning regimen significantly affected prognosis (5-years OS: BU vs TBI: 46.6% vs 90.05%, p=0.0074; 5-years LFS: BU vs TBI: 40% vs 90%, p=0.0186; 5-years NRM: BU vs TBI: 44.94% vs 0%, p=0.0109).

Figure 1 Distribution of extramedullary involvement

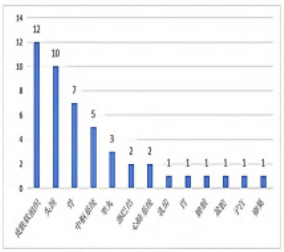


Figure2 Frequency of fusion genes and gene mutations

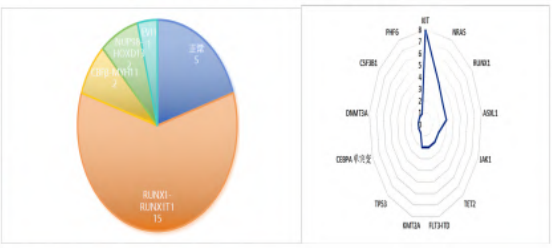


Figure 3 Survival curve

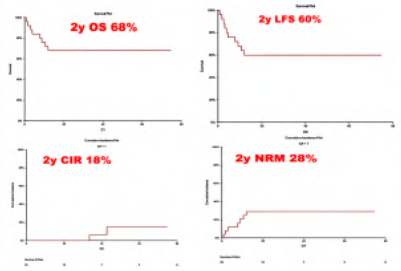
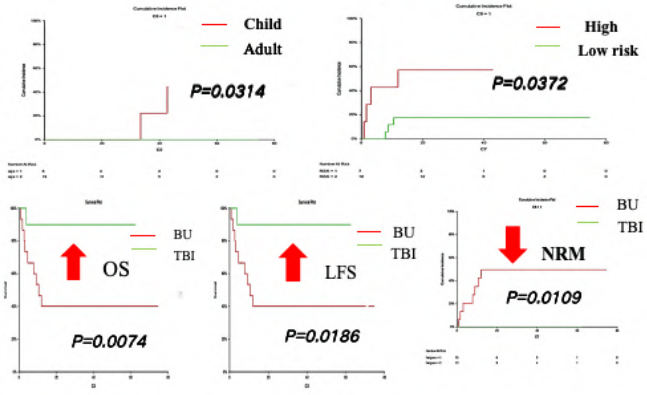


Figure 4 Single factor analysis of survival outcomes

	2y-OS	p	2y-LFS	p	2y-CIR	p	2y-NRM	p
Gender: (Male vs Female)	70%60%	0.7055	60%60%	0.9378	10.3%19%	0.5049	25.88%40%	0.5771
Age: (child vs adult)	66.6%68.4%	0.9711	33.33%68.42%	0.1781	44.44%0%	0.0314	33.33%27.3%	0.8507
Affecting sites: (single vs ≥2)	66.6%69.2%	0.735	58.33%61.54%	0.7122	3.6%2.34%	0.8286	33.33%25%	0.457
Risk stratification in cytogenetics (high vs. low risk)	42.86%77.78%	0.0541	42.86%66.67%	0.1951	0%5.66%	0.4857	57.14%17.65%	0.0372
fusion gene (AML-ETO vs others)	68.75%66.67%	0.7589	56.25%66.67%	0.8285	19.38%17.3%	0.9561	31.25%23.81%	0.8430
gene mutation (KIT vs others)	75%64.71%	0.5309	62.05%58.82%	0.707	10.33%6.85%	0.7071	25%30%	0.69
Treatment options (chemotherapy vs. others)	75%61.5%	0.4715	58.33%61.54%	0.9103	5.46%1.94%	0.2512	25%32.87%	0.68
State before transplantation (CR1 vs non-CR1)	64%72.7%	0.78	50%72.73%	0.3850	3.33%7,21%	0.1121	35.7%19.19%	0.46
Pre-treatment options (BU vs TBI)	46.6%90.5%	0.0074	40%90%	0.0186	13.1%10.2%	0.6715	49.44%0%	0.0109



Conclusions: Allogeneic hematopoietic stem cell transplantation is a safe and effective treatment for MS. The TBI-based iintensified MACcan reduce the NRM then improve the OS and LFS.

Clinical Trial Registry: NO

Disclosure: Nothing to declare.

A154

PATTERNS AND PREDICTORS OF HEMATOLOGIC TOXICITY AFTER BCMA- AND CD19-TARGETED CAR-T THERAPY

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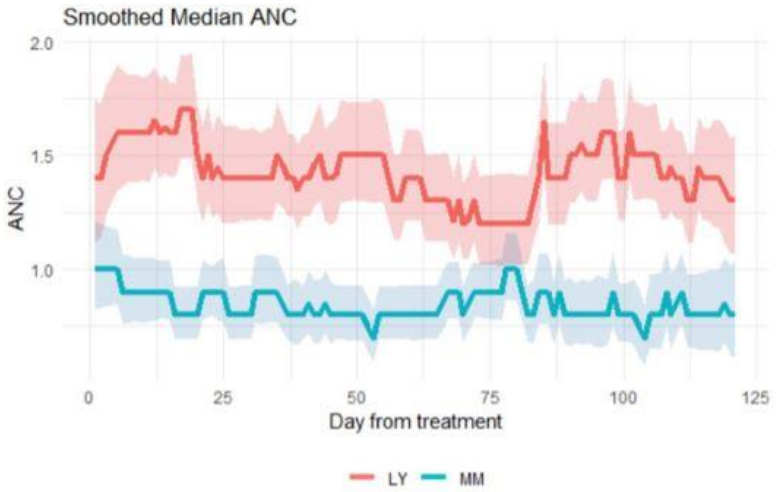
Background: Immune effector cell–associated hematotoxicity (ICAHT) is the most frequent complication following chimeric antigen receptor (CAR) T-cell therapy. Most available data derive from CD19-directed CAR T-cell products, whereas hematotoxicity following B-cell maturation antigen (BCMA)–directed CAR T-cell therapy remains poorly characterized.

Methods: We conducted a retrospective, single-center cohort study analyzed patients treated with CAR T-cell therapy at Hadassah Medical Center between December 2019 and January 2024. Patients were categorized into two cohorts according to underlying disease and CAR T-cell construct. The first cohort comprised patients with relapsed/refractory multiple myeloma (RRMM) (n=77) treated with a locally manufactured BCMA-directed CAR T-cell product (HBI0101). The second cohort included patients with relapsed/refractory (R/R) non-Hodgkin lymphoma (NHL) treated with commercially available CD19-directed CAR T cells (n=67).
In both cohorts, complete blood counts were analyzed at baseline, prior to lymphodepletion, and from day 0 (CAR T-cell infusion) through day 365 post-infusion or until progression, loss to follow-up, or death. Hematologic parameters were graded using CTCAE and ICAHT criteria, and the CAR-HEMATOTOX score was calculated. Grade ≥2 ICAHT was the primary endpoint. Blood count kinetics and associations with clinical and biological factors were analyzed.

Results: Among MM patients, early-stage (day 0 - 30) neutropenia of any grade occurred in 91% (ICAHT grade ≥2: 42.8%), with severe neutropenia (ANC <500/μL) in 87% and profound neutropenia (ANC <100/μL) in 20.7%. Late (day 31-60) neutropenia of any stage was observed in 66.6% (ICAHT grade ≥2: 48.5%), with severe neutropenia in 10.6% and profound neutropenia in 3%. In NHL patients, early-stage neutropenia occurred in 65.7% (ICAHT grade ≥2: 35.8%), with severe neutropenia in 61% and profound neutropenia in 24%; late neutropenia occurred in 56.8% (ICAHT grade ≥2: 40.9%), with severe neutropenia in 18.2% and profound neutropenia in 9%. A multiphasic neutrophil recovery pattern with multiple nadirs <1,000/μL predominated in MM, whereas quick recovery was most common in NHL.
Severe anemia (grade ≥3) occurred in 56% of MM and 36% of NHL patients early post-infusion, and 3% and 11.4% late, respectively. Severe thrombocytopenia (grade ≥3) occurred in 45% of MM and 28% of NHL patients early, and 22.7% and 18.2% late.
In univariate analysis early-phase neutropenia in MM was significantly associated with baseline hemoglobin, platelet count, absolute neutrophil count, ferritin, hematotoxicity index, plasma cell leukemia phenotype, and infusion of fresh CAR T cells. In NHL, early neutropenia correlated with baseline ANC and Jewish ethnicity. Late-phase neutropenia in MM remained associated with baseline ANC, while in NHL no variables reached significance.

Conclusions: Baseline neutropenia was the strongest predictor of post–CAR T-cell neutropenia, highlighting the importance of bone marrow reserve prior to infusion. Neutropenia was more frequent in the multiple myeloma patients treated with a BCMA-directed CAR T-cell construct compared with lymphoma patients, receiving CD19-directed products, likely reflecting differences in disease biology, prior treatment burden, and baseline cytopenias (as shown in supplementary figure baseline neutropenia was more severe in MM patients).

Supplementary figure



Supplementary figure. Showing smoothened median of absolute neutrophil count (ANC) for non-Hodgkin lymphoma (LY) and multiple myeloma (MM) cohorts.

Clinical Trial Registry: NCT07085676

Disclosure: Nothing to declare.

A156

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA: A RETROSPECTIVE STUDY ON PROGNOSTIC FACTORS AND A NOVEL SCORING SYSTEM

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Background: The efficacy of allogeneic hematopoietic stem cell transplantation (allo-HSCT) in patients with T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LBL) is not well

established, particularly regarding outcomes and prognostic factors. This study aimed to evaluate the efficacy of allo-HSCT for T-ALL/LBL and identify key factors influencing patient survival and relapse.

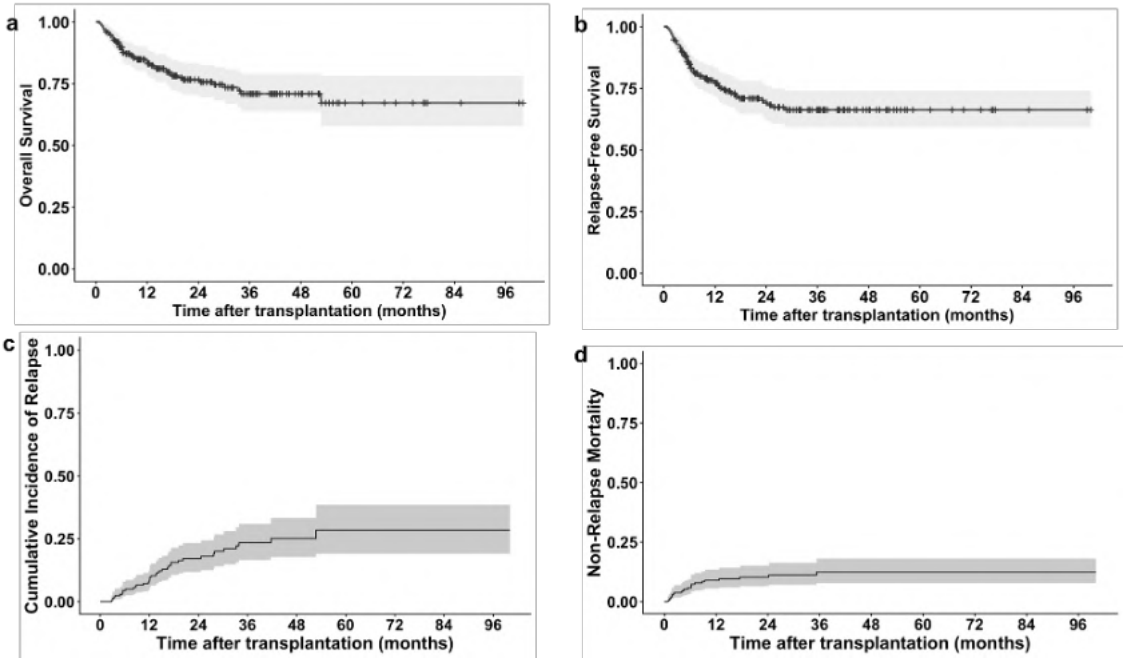
Methods: In this retrospective study, we included 211 patients with T-ALL/LBL who underwent allo-HSCT between March 2017 and June 2025. The median follow-up time for survival patients was 17.5 months (range, 0.8 – 100.1months). Patient characteristics, survival outcomes, and prognostic factors were analyzed.

Results: The estimated 2-year overall survival (OS) and relapse-free survival (RFS) rates were 75.7% ± 3.3% and 68.3% ± 3.6%, respectively. The 2-year cumulative incidence of relapse (CIR) and non-relapse mortality (NRM) were 17.1% ± 2.9% and 10.3% ± 2.2%, respectively. The estimated 2-year OS rates across four distinct cohorts were as follows: 85.7% ± 4.2% for patients in first complete remission with MRD negativity (CR1/MRD$^-$), 80.0% ± 3.7% for CR1/MRD$^+$, 70.5% ± 7.6% for patients not in CR1 but with MRD negativity, and 15.6% ± 14.2% for patients not in CR1 with MRD positivity (P < 0.001). The estimated 2-year CIR was significantly lower in patients with T-ALL compared to those with T-LBL (14.9% ± 3.9% vs. 19.2% ± 4.5%, P = 0.045). On multivariable Cox regression analysis, three factors were identified as independent protective factors associated with significantly improved OS and RFS: MRD negativity before transplantation (OS: HR = 0.35, 95% CI 0.18–0.68, P = 0.002; RFS: HR = 0.42, 95% CI 0.23–0.76, P = 0.004), transplantation during CR1 (OS: HR = 0.45, 95% CI 0.24–0.85, P = 0.013; RFS: HR = 0.50, 95% CI 0.28–0.89, P = 0.019), and the development of chronic graft-versus-host disease (cGVHD) (OS: HR = 0.31, 95% CI 0.15–0.65, P = 0.002; RFS: HR = 0.40, 95% CI 0.21–0.78, P = 0.007). Post-transplant maintenance therapy was an independent protective factor for OS (HR = 0.23, 95% CI 0.07–0.73, P = 0.022) but was not significantly associated with RFS in the multivariable model (HR = 0.49, 95% CI 0.21–1.15, P = 0.099).

Table 1 Characteristics of patients with T-ALL/LBL

Characteristics	All patients (n=211)
Age at transplantion, years, Median (range)	32 [24 - 40]
Gender, male, n (%)	145 (68.7%)
WBC ≥100×10^9, n (%)	14 (6.6%)
Subtype, n (%)	
T-ALL	112 (53.1%)
T-LBL	99 (46.9%)
WT1, n (%)	23 (10.9%)
TP53, n (%)	7 (3.3%)
TCR gene rearrangement, n (%)	11 (5.2%)

MRD negativity before transplantation, n (%)	192 (91.0%)
CR1 at transplantation, n (%)	163 (77.3%)
Stem cell source, n (%)	
MSD	24 (11.4%)
Haplo	149 (70.6%)
MUD	38 (18.0%)
Grade III-IV aGVHD, n (%)	21 (10.0%)
cGVHD, n (%)	94 (44.5%)
Time from diagnosis to transplantation, months, Median (range)	6.5 [2.8 - 146.5]
Maintenance after transplantation	61 (28.9%)



Conclusions: Allo-HSCT provides favorable survival and low relapse rates in patients with T-ALL/LBL. Pre-transplant MRD negativity, transplantation in CR1, development of cGVHD, and administration of maintenance therapy are associated with improved outcomes. This study supports allo-HSCT as a viable and effective consolidative treatment strategy for T-ALL/LBL, particularly in patients with favorable prognostic factors.

Disclosure: Nothing to declare.

A157

OUTCOME OF AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION (AHCT) AFTER PEMBROLIZUMAB IN RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA PATIENTS: A RETROSPECTIVE ANALYSIS OF THE KING HUSSEIN CANCER CENTER

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Background: Autologous Hematopoietic Cell Transplantation (AHCT) remains the standard of care for patients with relapsed refarctory classical Hodgkin lymphoma (rr cHL) with chemosensitive disease after salvage therapy. Historically, patients with refractory disease or multiple relapses have poor outecomes after AHCT. However, novel therapies, including checkpoint inhibitors (CPIs) and brentuximab vedotin (BV) have evolved treatment armamentarium, facilitating more patients to receive AHCT. The use of pembrolizumab can be as monotherapy or in combination regimens at different disease stages. The evidence suggests that pembrolizumab may enhance chemosensitivity and positively impact posttransplant outcomes, though long-term results remain uncertain. The aim of our study to assess survival outcomes of AHCT after pembrolizumab monotherapy in patients with rr cHL from KHCC.

Methods: This is a retrospective single center study from King Hussein cancer Center in Jordan included 48 out of 144 patients who received pembrolizumab as monotherapy for rr cHL and underwent AHCT between 2018–2024 after pembrolizumab. Overall survival (OS) and progression free survival (PFS) were estimated by Kaplan Meier method. Univariate analysis for survival outcomes was performed using log rank test. Patients who failed the first line and at least one salvage regimen before AHCT and received pembrolizumab monotherapy prior to AHCT were included. Patients who received combination of pembrolizumab and chemotherapy and lymphocyte-predominant HL patients were excluded.

Results: Median age was 23 years (IQR:19–32). 26 (54%) were females. 32 (74%) had advanced stage at diagnosis, 37(77%) B-symptoms, 28(58%) extranodal involvement and 15 (31.3%) had disease bulk. Chemo-refractory disease after first line therapy was frequent

(38;79%). Patients received a median of 3 lines (range: 2-8) of chemotherapy prior to pembrolizumab. 75% of patients received pembrolizumab as the last therapy prior to AHCT. 12 patients (25%) received intervening chemotherapy before AHCT. Patients received a median of 4 cycles (range: 3–13) of pembrolizumab.
Objective response (OR) after pembrolizumab was achieved in 31(64.5%) [17(35.4%) CR) and 14(29%) PR].CR was achieved after a median of 3 cycles (2-5). Disease status at AHCT was CR in 56%, and PR in 44%. The median time between last dose of pembrolizumab and AHCT was 6.6months (range:1.26-16).
After a median follow up of 14.6mo (1.1–77.7), 87.5% in CR and 12.5% had progression. 2-year OS and PFS were 83% (95% CI:60–93%) and 85% (95% CI: 65–94%), respectively. Cumulative relapse incidence at 2 years 4.7% (95% CI:0.0–13.8%), and non-relapse mortality (NRM) was 3% (95% CI:0.4-19%) at 1-year. At last encounter, 87.5% of patients still alive, and 12.5% died. In univariate analysis, disease status at AHCT did not impact OS or PFS (P ≥0.50). There was a trend toward relapse reduction in CR patients compared to no CR (P= 0.05). Number of lines of chemotherapy prior to pembrolizumab did not affect post-transplant outcomes(P=≥0.05).

Conclusions: This study demonstrates high PFS and OS outcomes in heavily pretreated rr cHL patients receiving pembrolizumab prior to AHCT compared to historical data. Disease status at the time of AHCT showed a trend toward reduced risk of relapse. Earlier integration of pembrolizumab in pre-AHCT setting is warranted.

Disclosure: Nothing to declare.

A158

A PILOT RANDOMIZED CLINICAL TRIAL OF A VIRTUAL REALITY SUPPORTIVE CARE INTERVENTION FOR PATIENTS UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Patients undergoing HCT experience substantial physical and psychological symptoms. Scalable supportive care interventions to reduce distress and improve quality of life are limited. Virtual reality (VR), with its three-dimensional capabilities, offers a novel, scalable, patient-centered modality to address these needs.

Methods: We randomized adult patients with hematologic malignancies undergoing autologous or allogeneic HCT to receive either a VR supportive care intervention (BMT-VR) or usual care during hospitalization. BMT-VR consists of six modules focused on: 1) psychoeducation and managing expectations; 2) psychosocial skill-building to promote

coping; and 3) strategies to facilitate acceptance while facing uncertainty. The primary endpoint was feasibility (≥60% enrollment and ≥60% completion of ≥4/6 modules). The secondary outcomes included quality of life (Functional-Assessment-of-Cancer-Therapy-BMT), depression and anxiety symptoms (Hospital-Anxiety-Depression Scale), and post-traumatic stress disorder symptoms (PTSD Checklist) at baseline, 4-, 12-, and 24- weeks post-HCT. The System Usability Scale (≥80 indicates excellent usability) was administered at 4 weeks post-HCT.

Results: We enrolled 59.6% (81/136) of eligible patients (mean age=57.9 (SD=14.7), 51.9% women, 70.4% allogeneic HCT). Among those assigned to BMT-VR, 74.4% completed ≥4/6 modules. After 4 weeks, patients randomized to BMT-VR reported improved quality of life (108.2 vs. 96.8, p=0.014) and anxiety symptoms (3.6 vs. 5.3, p=0.019) compared to usual care. No difference in depression or PTSD symptoms emerged between the groups at 4 weeks. In longitudinal analyses, BMT-VR participants showed greater improvements in quality of life (B=3.8, p=0.002), depression (B=-0.8, p<0.001), and PTSD symptoms (B=-1.7, p=0.006), but no improvement in anxiety symptoms over time, compared to usual care.

Conclusions: A virtual reality delivered supportive care intervention is feasible during hospitalization for autologous or allogeneic HCT and shows promising preliminary effects in improving quality of life and psychological outcomes. A future multi-site trial is needed to assess its efficacy for improving quality of life and psychological distress in HCT recipients.

Clinical Trial Registry: NCT05629676
https://clinicaltrials.gov/study/NCT05629676

Disclosure: Dr. El-Jawahri serves as a consultant for Incyte Corporation and Tuesday Health. All other authors report no conflict of interest.

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HARMONIZING HAPLOIDENTICAL STRATEGIES: A FOUR-YEAR COMPARATIVE ANALYSIS OF T-CELL–DEPLETED AND REPLETE PEDIATRIC TRANSPLANTS FROM A DEVELOPING COUNTRY

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is increasingly being used for children without matched donors, particularly in resource-limited settings. Advances such as TCRαβ/CD19 depletion (TCD) and post-transplant cyclophosphamide (PTCy)-based T-cell–replete (TCR) platforms have significantly reduced immunologic toxicity, yet comparative pediatric data from India remain sparse. This study presents a four-year single-center evaluation comparing TCD and TCR haplo-HSCT across malignant and benign pediatric disorders.

Methods: This retrospective cohort included all pediatric haplo-HSCT performed between 1 September 2021 and 31 August 2025. Sixty-one children (39 males, 22 females; mean age 8 years, range 1–17) underwent 62 transplants for benign (n=35) and malignant (n=27) disorders. Malignant indications comprised ALL (17), AML (5), MPAL (2), MDS (1), and JMML (1), while benign conditions included thalassemia major (26), primary immunodeficiency (4), severe aplastic anemia (3), sickle cell disease (1), and PNH (1). Transplant platforms included Tαβ-depleted (TCD) grafts (n=36; 58%) and TCR grafts with PTCy (n=26; 42%). All grafts consisted of peripheral blood stem cells. Although conditioning was disease-specific, most patients (57/62; 91%) received myeloablative regimens. Rabbit ATG was administered to all, with additional rituximab in TCD recipients. The median $CD34^+$ dose was 18×10^6/kg in TCD grafts and 8×10^6/kg in TCR grafts. TCD grafts targeted $<25\times10^3$/kg αβ T cells with scheduled $CD45RO^+$ add-back in dose escalated manner till day+120.

Results: Engraftment was achieved in 96% of patients with sustained full donor chimerism; median neutrophil and platelet recovery occurred at 13 days (11–21) and 14 days (10–39), respectively, with only two graft failures (one JMML, one thalassemia). Severe acute GVHD (grade III–IV) was lower in TCD (11%) than in TCR (23%). Overall chronic GVHD occurred in 5% (TCD) versus 11% (TCR). No GVHD-related deaths occurred in TCD recipients. TCR recipients had greater GVHD severity, with severe bacterial (30%) and fungal infections (12%) contributing to 10% toxic mortality. Viral reactivations were CMV (33%), BK (8%), adenovirus (9%), and EBV (3%); none caused mortality. Day-100 mean $CD4^+$ counts were higher in the TCD cohort (130 cells/μL) compared to TCR cohort (110 cells/μL). Overall survival (OS) was higher in TCD (89%) compared with TCR (62%), resulting in a combined OS of 79% at a median follow-up of 480 days. Outcomes in benign disorders predominantly in TCD cohort were excellent, with OS 97% and EFS 95% while in malignant indications, OS was 61%, with nine deaths (four toxic, five relapse). The 100-day Transplant-related mortality was low at 2% (0% in TCD), and overall TRM was significantly lower in TCD recipients (6%) compared with TCR recipients (21%). Relapse rates were similar (TCD 28% vs TCR 25%), indicating effective disease control despite profound T-cell depletion.

Conclusions: Pediatric haploidentical HSCT using either TCD or PTCy-based TCR approaches yields robust engraftment and acceptable toxicity. However, TCRαβ-depleted haplo-HSCT provides the most favorable profile, with markedly reduced GVHD, no significant increase in relapse rate, minimal TRM, and excellent survival. These results support broader adoption of TCD haplo-HSCT in resource-limited settings and warrant future comparative studies with matched unrelated donor transplants.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

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PERFORMANCE AND VALIDATION OF THE SIMPLIFIED COMORBIDITY INDEX IN PREDICTING NON-RELAPSE MORTALITY AFTER ALLOGENEIC HCT IN THE CURRENT ERA

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Background: The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), developed two decades ago to predict non-relapse mortality (NRM) and survival after allogeneic hematopoietic cell transplantation (alloHCT), has been widely validated, but recent studies have questioned its consistency in contemporary practice. AlloHCT has evolved substantially, with greater use of unrelated and haploidentical donors, new conditioning regimens, improvement of GVHD prophylaxis, and declining overall NRM. More recently, the Simplified Comorbidity Index (SCI) was developed to predict NRM in the setting of CD34-selected alloHCT and subsequently validated in unmanipulated reduced-intensity alloHCT. We performed a comparison of the performance of HCT-CI and the SCI to predict NRM in a modern adult alloHCT cohort.

Methods: We conducted a retrospective single-centre study of consecutive adults undergoing first alloHCT between July 2020 and December 2024. The primary endpoint was 24-month NRM, studied using competing-risk methods. Predictive performance of SCI and HCT-CI were evaluated by ROC analysis. Multivariable Fine-Gray models adjusted for Karnofsky Performance Status (KPS), Disease Risk Stratification System (DRSS), type of transplant (matched vs. mismatched), Transplant Conditioning Intensity (TCI) and age for HCT-CI.

Results: A total of 346 patients were included (median age 55 years; 42% female) (**Table 1**). Donors included MUD (51%), Haplo (17%), MSD (13%), CB (13%), and MMUD (6%). Most (66%) patients received ATG-based GvHD prophylaxis, while 20% received PTCy. By TCI, 22% received low intensity, 60% intermediate, and 18% high intensity conditioning. By DRSS, 14% of patients were low, 29% intermediate-1, 42% intermediate-2, 11% high, and 0.3% very high. Median follow-up was 29.4 months.
In univariate analyses, the HCT-CI was not associated with NRM, whether evaluated as individual scores or in grouped categories: NRM at 24 months for 0, 1-2 and ≥3 was 8.99% (95%CI: 4.17–16.10), 6.80% (95%CI: 3.45–11.70), and 9.96% (95%CI: 4.84–17.25), respectively. In contrast, the SCI showed a significant association with NRM both by individual values and grouped categories ($p<0.001$ for both), with 24-month NRM of 5.0% for SCI 0–2 (95%CI: 2.7–8.4), 10.8% for SCI 3 (95%CI: 4.4–20.7) and 29.9% for SCI ≥4 (95%CI 14.1–47.6) (**Figure 1**).
Concordance between HCT-CI and SCI was modest (correlation 0.40; 95%CI 0.30–0.48). For NRM prediction, the HCT-CI had an AUC of 50.6% ($p=0.919$), while the SCI achieved 64.1% ($p=0.015$).

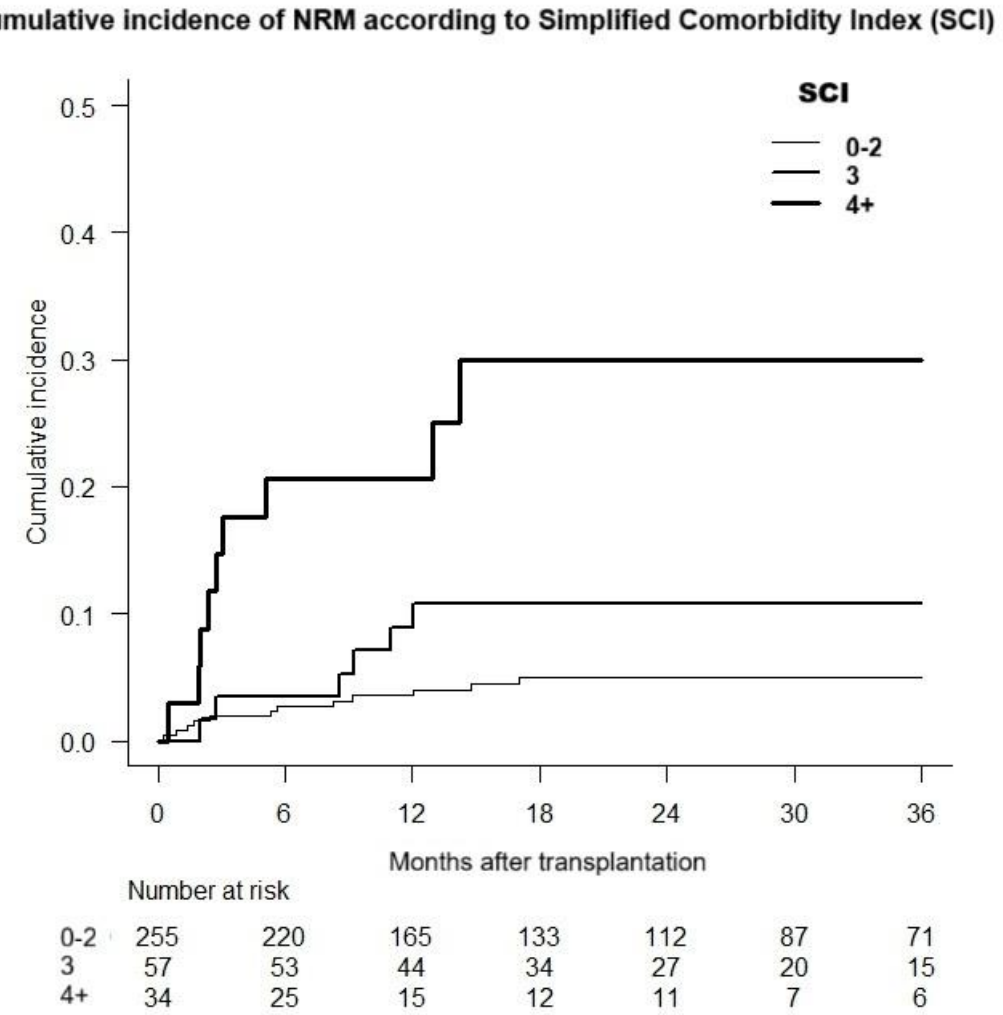
In multivariable analysis, the SCI remained independently associated with NRM (Wald X^2=20.7, p<0.001). Relative to SCI 0-2, patients with SCI=3 had an adjusted sHR of 2.4 (95%CI 0.8–7.1; p=0.100) and SCI ≥4 had an sHR of 7.0 (95%CI 3.0–16.3; p<0.001). HCT-CI categories were not independently associated with NRM (Wald test: X^2=0.51, p=0.78).

Table 1. Baseline subject characteristics

Variable	**Complete cohort n=346**
Age in years at HCT, median (IQR)	54.5 (43-62)
Diagnosis, n (%) Acute leukemia MDS/MPN Lymphoma Other	 175 (50.5) 80 (23.1) 64 (18.5) 27 (7.8)
Donor type, n (%) MSD MUD MMUD CB Haplo	 46 (13.3) 177 (51.2) 20 (5.8) 45 (13.0) 58 (16.8)
GvHD prophylaxis PTCy, n (%) ATG, n (%) Other, n (%)	 70 (20.2) 229 (66.2) 47 (13.6)
HCT-CI Score, % 0, 1, 2, 3, ≥4	 26.6, 28.0, 17.9, 14.5, 13.0
SCI score, % 0, 1, 2, 3, ≥4	 34.7, 22.5, 16.5, 16.5, 9.8

Figure 1 – Cumulative incidence of non-relapse mortality according to the Simplified

Comorbidity Index



Conclusions: In this modern alloHCT cohort, including varied donor sources, the SCI demonstrated superior predictive performance for NRM compared with the HCT-CI, and remained independently associated with NRM after multivariable adjustment. Prospective validation in larger cohorts and various alloHCT platforms is necessary to determine whether the SCI should replace the HCT-CI in current clinical practice.

Disclosure: No conflict of interest for all authors.

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GRAFT-VERSUS-HOST DISEASE, RELAPSE, AND A SIMPLE GRFS RISK GROUPING IN HAPLOIDENTICAL TRANSPLANTATION WITH PTCY

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Background: Haploidentical hematopoietic cell transplantation (haplo-HCT) with post-transplant cyclophosphamide (PTCy) is widely used, but data on graft-versus-host disease–free, relapse-free survival (GRFS) and simple bedside risk stratification remain limited. We aimed (1) to describe GVHD, relapse, non-relapse mortality (NRM) and GRFS in a homogeneous haplo-PTCy cohort, and (2) to derive and internally validate a simple pre-transplant GRFS risk grouping.

Methods: We retrospectively analyzed adults receiving a first Haplo-HCT with PTCy across three Argentinian centers (2017–2024). Median Follow up was 37.7 month. Underlying diseases included acute myeloid leukemia (30%), acute lymphoblastic leukemia (25%), non-Hodgkin lymphoma (15%), Hodgkin lymphoma (9%), myelodysplastic syndromes (8%), aplastic anemia (5%), myelodysplastic/myeloproliferative neoplasms (3%), myelofibrosis (2%), chronic myeloid leukemia (2%), multiple myeloma (0.5%) and hemoglobinopathies (1%). Disease Risk Index (DRI) and HCT-Comorbidity Index (HCT-CI) were assessed before transplant.
Cumulative incidence of acute GVHD (aGVHD) grade II–IV and III–IV by day 100, chronic GVHD (cGVHD), relapse and NRM was estimated using competing-risks methods. GRFS, was analyzed with Kaplan–Meier and Cox models. A binary GRFS risk grouping was built from two pre-transplant factors: DRI high/very high and HCT-CI >3. Patients with neither factor were classified as low risk, and those with ≥1 factor as high risk. Multivariable Cox models for GRFS adjusted for conditioning intensity. Internal validation of the GRFS grouping used 2000 bootstrap resamples; discrimination was assessed by the C-index. Findings were similar in malignant-only analyses.

Results: We included 193 patients (median age 45). DRI was low/intermediate in 63% and high/very high in 37%; HCT-CI >3 was present in 22%. Conditioning was reduced-intensity in 100 and myeloablative in 93; peripheral blood was the graft source in 98%. By day 100, cumulative aGVHD grade II–IV and III–IV incidence was ~17–18% and ~11%. At 3 years, the cumulative incidence of cGVHD, relapse and NRM was 19%, 21% and 23%. Median GRFS was 6.4 months; 1-, 2-, and 3-year GRFS 38.6%, 36.5% and 35.8%. By GRFS risk group, 89 patients (46%) were low risk and 104 (54%) high risk. Twelve-, 24- and 36-month GRFS were 48%, 46% and 46% in the low-risk group vs 31%, 29% and 27% in the high-risk group; median GRFS was 10.8 vs 3.3 months. On multivariable analysis, high vs low-risk status had a higher hazard of GRFS failure (HR 1.9; 95% CI 1.3–2.8), independent of

conditioning intensity (HR 1.6; 95% CI 1.1–2.4). The C-index for GRFS was 0.61. Bootstrap internal validation yielded a bias-corrected 95% CI for the log-HR consistent with a stable effect size.

COX GRFS	Comparison	HR for GRFS	95% CI	p-value
Sex match	Female→Male vs Female→Female	1.10	0.54–2.24	0.79
	Male→Female vs Female→Female	1.18	0.56–2.49	0.66
	Male→Male vs Female→Female	1.35	0.68–2.66	0.39
Conditioning	RIC vs MAC	**1.62**	1.12–2.33	**0.010**
DRI	Low/Intermediate vs High/Very high	**0.69**	0.47–0.96	**0.045**
HCT-CI	≤3 vs >3	**0.46**	0.31–0.69	**<0.001**

Conclusions: In this multicenter haplo-PTCy cohort, relapse incidence was relatively low, but NRM and GVHD remained substantial, resulting in GRFS below 50% at 3 years. A simple pre-transplant GRFS risk grouping based solely on DRI and HCT-CI identified a high-risk subgroup with nearly doubled risk of GRFS failure. This may provide a simple bedside framework to identify higher-risk patients, although its discriminative ability is modest and it should be considered hypothesis-generating pending external validation.

Disclosure: The authors report no conflicts of interest.

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CD45RA-DEPLETED T-CELL ADOPTIVE CELL THERAPY FOR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION RECIPIENTS WITH REFRACTORY/RESISTANT EBV INFECTIONS: A MULTICENTER, RETROSPECTIVE STUDY

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Background: Refractory/resistant (R/R) Epstein–Barr virus (EBV) infection after allogeneic hematopoietic cell transplant (allo-HCT) carries a poor prognosis. Survival is particularly low when EBV-driven disease does not respond to rituximab, with or without chemotherapy, underscoring the need for alternative treatments. Memory T cells, defined by expression of CD45RO and absence of CD45RA isoform, possess adaptive immunity against common virus infections, including EBV. CD45RA-depleted donor lymphocyte infusion shown a promising result of an effective antiviral boost after TCRαβ-depleted haploidentical (HID) HCT. However, limited data yet on therapeutic CD45RA-depleted ACT in broader allo-HCT populations, including adults, and transplant modalities except for HID HCT. In this multicenter study, we evaluated this novel approach for clearing EBV infection after allo-HCT across a mixed adult/paediatric cohort and multiple donor platforms.

Methods: This multicenter study was conducted at Shanghai Ruijin Hospital, Shanghai Children's Medical Center, and Liquan Hospital. Eligible participants were allo-HCT recipients diagnosed with R/R EBV infections who received at least one dose of CD45RA-depleted T-cell ACT.

Results: A total of 17 allo-HCT subjects with R/R EBV infections were enrolled between September 2023 and July 2025 (Figure 1A). The last follow-up was conducted on October 31, 2025. All CD45RA-depleted T-cell products were obtained from EBV-seropositive donors.The first CD45RA-depleted T-cell infusion was administered at a median of 117 days (range: 50–696) after allo-HCT, at a cumulative dose of 20×10^6 cells/kg (range: 8.09–51.13), and four patients also received intrathecal ACT concurrently. The overall response was similar for the adult (85.71%) and pediatric (90%) group. The median duration of response did not differ between two groups. The objective response rate was 100% for EBV DNAemia, 100% for EBV-related disease, and 80% for EBV-PTLD. The source of CD45RA donors did not influence the efficacy of the treatment. Objective response rates were comparable across subgroups. EBV DNA was detected in the cerebrospinal fluid of four patients with central nervous system (CNS) symptoms (one adult, three paediatric), two of whom were diagnosed with CNS PTLD. All these patients received intrathecal CD45RA-depleted T-cell infusions, with a median of 3 cycles (range: 1–4 cycles) at a cumulative dose of 4.16×10^6/kg (range: $1.5–7.86 \times 10^6$/kg). No additional adverse effects were observed. EBV DNA cleared in 3 patients, and 1 patient with CNS PTLD achieved CR.
At last follow-up, 13/17 (76.47%) patients were alive. The 1-year OS was 67.57% (95% CI: 30.89%–87.74%) (Figure 1B). One patient experienced relapse 91 days after ACT. The 1-year non-relapse mortality was 25.8% (95% CI: 4.04%–56.5%; 3 patients), with causes including severe infection related to PTLD in 2 patients and possible transplant-associated thrombotic microangiopathy secondary to GvHD in 1 patient. Univariable analyses of baseline characteristics and overall survival likewise showed no major differences in efficacy.

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Table 1. Baseline characteristics by age groups.

Variables	Adult group (n = 7)	Pediatric group (n = 10)	All (n = 17)
Sex, n (%)			
Male	4 (57.14%)	6 (60.00%)	10 (58.82%)
Female	3 (42.86%)	4 (40.00%)	7 (41.18%)
Age at allo-HCT (years), median (range)	46 (26–66)	10 (7-16)	15 (7–66)
Primary disease, n (%)			
ALL	3 (42.86%)	6 (60.00%)	9 (52.94%)
AML	3 (42.86%)	1 (10.00%)	4 (23.53%)
SAA	0 (0%)	2 (20.00%)	2 (11.76%)
Others	1 (14.29%)	1 (10.00%)	2 (11.76%)
CAR-T therapy before allo-HCT, n (%)			
No	6 (85.71%)	6 (60.00%)	12 (70.59%)
Yes	1 (14.29%)	4 (40.00%)	5 (29.41%)
Disease status before allo-HCT, n (%)			
CR1	4 (57.14%)	0 (0%)	4 (23.53%)
>CR1	2 (28.57%)	6 (60.00%)	8 (47.06%)
Others	1 (14.29%)	4 (40.00%)	5 (29.41%)
Karnofsky/Lansky score			
≥80	5 (71.43%)	3 (30.00%)	8 (47.06%)
50-70	2 (28.57%)	4 (40.00%)	6 (35.29%)
≤40	0 (0%)	3 (20.00%)	3 (17.65%)
HCT-CI scores before allo-HCT, n (%)			
0	5 (71.43%)	5 (50.00%)	10 (58.82%)
1-2	2 (28.57%)	4 (40.00%)	6 (35.29%)
≥3	0 (0%)	1 (10.00%)	1 (5.88%)
Conditioning intensity, n (%)			
MAC	6 (85.71%)	8 (80.00%)	14 (82.35%)
RIC	1 (14.29%)	2 (20.00%)	3 (17.65%)
Donor type, n (%)			
HID	7 (100%)	5 (50.00%)	12 (70.59%)
MUD/MMUD	0 (0%)	5 (50.00%)	5 (29.41%)
T-cell depleted, n (%)			
Ex vivo	1 (14.29%)	1 (10.00%)	2 (11.76%)
In vivo	6 (85.71%)	9 (90.00%)	15 (88.24%)
rATG-based	4 (57.14%)	9 (90.00%)	13 (76.47%)
PTCY-based	2 (28.57%)	0 (0%)	2 (11.76%)
Letermovir prophylaxis, n (%)			
No	1 (14.29%)	10 (100%)	11 (64.71%)
Yes	6 (85.71%)	0 (0%)	6 (35.29%)
DSA positivity before allo-HCT, n (%)			
MFI < 5000	7 (100%)	10 (100%)	17 (100%)
MFI ≥ 5000	0 (0%)	0 (0%)	0 (0%)
CD34+ cell counts in graft (×10⁶/kg), median (range)	7.30 (3.70–13.17)	7.12 (2.51–13.26)	7.30 (2.51–13.26)
MNC counts in graft (×10⁸/kg), median (range)	13.37 (3.20–15.54)	10.19 (5.02–15.80)	10.67 (3.20–15.80)
Neutrophil engraftment, n (%)			
Yes	7 (100%)	10 (100%)	17 (100%)
No	0 (0%)	0 (0%)	0 (0%)
Time from allo-HCT to neutrophil engraftment (days), median (range)	12 (9–15)	15 (12–25)	13 (9–25)
Platelet engraftment, n (%)			
No	0 (0%)	0 (0%)	0 (0%)
Yes	7 (100%)	10 (100%)	17 (100%)
Time from allo-HCT to platelet engraftment (days), median (range)	14 (8–20)	12 (9–77)	12 (8–77)
Anti-EBV treatment before CD45 RA+ depleted ACT, n (%)			
IS taper + Rituximab	3 (42.86%)	8 (80.00%)	11 (64.71%)
IS taper + Rituximab + chemotherapy	4 (57.14%)	2 (20.00%)	6 (35.29%)
Type of infusion, n (%)			
EBV-DNAemia	1 (14.29%)	5 (50.00%)	6 (35.29%)
EBV Related Disease	1 (14.29%)	0 (0%)	1 (5.88%)
EBV-PTLD	5 (71.43%)	5 (50.00%)	10 (58.82%)
CNS involvement, n (%)			
No	0 (0%)	7 (70.00%)	7 (41.18%)
Yes	1 (14.29%)	3 (30.00%)	4 (23.53%)
Missing	6 (85.71%)	0 (0%)	6 (35.29%)
Donor source of CD45 RA-depleted T cell ACT, n (%)			
Original transplant donor	6 (85.71%)	4 (40.00%)	10 (58.82%)
Third-party donor	1 (14.29%)	6 (60.00%)	7 (41.18%)
Time from graft infusion to first CD45RA-depleted T cell ACT (days), median (range)	93 (50–696)	122 (53–275)	117 (50–696)
<100 days	4 (57.14%)	4 (40.00%)	8 (47.06%)
≥100 days	3 (42.86%)	6 (60.00%)	9 (52.94%)
Viral load at initial infection (×10⁵ copies/mL), median (range)	1600 (2.12-205000)	53.10 (4.08-2250)	67.30 (2.12-205000)
Viral load before CD45 RA-depleted T cell ACT (×10⁵ copies/mL), median(range)	1950 (2.12-260000)	223.50 (16.24-11300)	253 (2.12-260000)
Cycles of CD45 RA-depleted T cell ACT, median(range)	2 (1–3)	3 (1–8)	2 (1–8)
Total dose of CD45 RA-depleted T cell ACT (×10⁶/kg), median (range)	20.35 (10.00–32.70)	18.81 (8.09–51.13)	20.00 (8.09–51.13)
Concomitant anti-EBV treatment, n (%)			
Rituximab	0 (0%)	1 (10.00%)	1 (5.88%)
Rituximab + Chemotherapy	0 (0%)	1 (10.00%)	1 (5.88%)
EBV-CTL	1 (14.29%)	0 (0%)	1 (5.88%)
Chemotherapy	1 (14.29%)	0 (0%)	1 (5.88%)
None	5 (71.43%)	8 (80.00%)	13 (76.47%)

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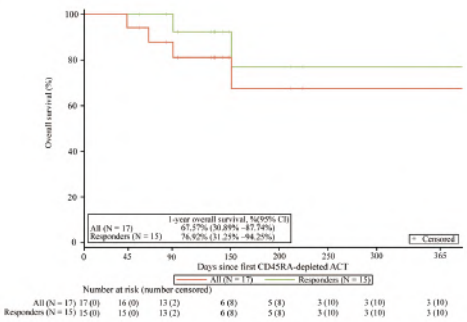

Abbreviation: allo-HCT, allogeneic hematopoietic cell transplant; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; ACT, adoptive cell therapy; rATG, rabbit anti-thymocyte globulin; CAR-T, chimeric antigen receptor T-cell therapy; CR1, first complete remission; CNS, central nervous system; CTL, cytotoxic T lymphocyte; DSA, donor-specific antibody; EBV, Epstein-Barr virus; HCT-CI, hematopoietic cell transplantation-comorbidity index; HID, haploidentical donor; IS, immunosuppressant; MUD, matched unrelated donor; MMUD, mismatched unrelated donor; MAC, myeloablative conditioning; MFI, mean fluorescence intensity; MNC, mononucleated cell; PTCy, post-transplant cyclophosphamide; PTLD, post-transplant lymphoproliferative disorder; RIC, reduced-intensity conditioning; SAA, severe aplastic anemia.

Figure 1. (A) **Baseline characteristics by age groups; (B)** Overall survival of total cohort. Abbreviation: ACT, adoptive cell therapy; CI, confidence interval.

Conclusions: CD45RA-depleted T-cell ACT thus provides clinical benefit in patients with R/R EBV infection after allo-HCT, without evidence of the safety concerns reported for other ACT approaches.

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HCT-CI FAILS TO PREDICT OUTCOMES OR TOXICITY IN A LARGE REAL-WORLD LBCL COHORT TREATED WITH AXICABTAGENE CILOLEUCEL: THE AUSTRALIAN CAR-T REAL-WORLD CONSORTIUM EXPERIENCE

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Background: The Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI) is a validated risk assessment tool for allogeneic stem cell transplantation. Its utility in predicting

outcomes and toxicity following Chimeric Antigen Receptor (CAR) T-cell therapy, particularly in large, real-world cohorts, remains uncertain. We assessed the prognostic value of HCT-CI in patients with relapsed/refractory Large B-cell Lymphoma (LBCL) treated with axicabtagene ciloleucel (axi-cel) as standard-of-care in Australia.

Methods: We conducted a retrospective, multicentre analysis of patients with LBCL infused with axi-cel between January 2020 and September 2025 at 6 sites participating in the Australian CAR-T Real World Consortium (AusCART). Comorbidity data were assessed at the time of T-cell collection and HCT-CI score was calculated as per Sorror *et al.* (2005). Patients were stratified by HCT-CI score into Low(0), Intermediate(1-2), and High(≥3) risk groups. Associations of HCT-CI risk categories with efficacy and toxicity outcomes were evaluated using Kaplan–Meier and chi-square tests.
The primary endpoints were progression-free survival (PFS) and overall survival (OS). Secondary endpoints included toxicity profiles (cytokine release syndrome [CRS], immune effector cell-associated neurotoxicity syndrome [ICANS], immune effector cell-associated hematotoxicity [ICAHT]) and response rates.

Results: From an intention-to-treat cohort of 404 apheresed patients, 384 (95%) proceeded to infusion, with no difference in infusion rates observed across HCT-CI risk categories (Low:96%, Intermediate:94%, High:95%; p=0.828). The 384 infused patients included for analysis were stratified into three HCT-CI groups: Low(n=192, 50%), Intermediate(n=110, 29%), and High(n=82, 21%). Baseline characteristics , prior therapies, and pre-lymphodepletion disease status were balanced across groups with a median age of 65 years (range 16-85), 52% with primary refractory disease and 90% needing bridging therapy.
With a median follow-up of 12.3 months, the overall complete response (CR) rate for the cohort was 69%, with comparable rates across HCT-CI groups: 69% in the Low , 67% in the Intermediate , and 71% in the High categories. No significant differences in survival outcomes were observed between groups. The overall 12-month progression-free survival (PFS) was 50% (Low 50%, Intermediate 50%, High 52%; p=0.94), and 12-month overall survival (OS) was 69%(Low 69%, Intermediate 70%, High 71%; p=0.80).
The incidence and severity of acute toxicities were comparable across HCT-CI categories. Neither cytokine release syndrome (CRS) nor immune effector cell-associated neurotoxicity syndrome (ICANS) correlated with HCT-CI burden (Grade ≥3 CRS:5%, p=0.614; Grade≥3 ICANS:22%, p=0.517). Rates of intensive care unit (ICU) admission(23%, p=0.913) and use of toxicity-directed interventions including tocilizumab (81%), corticosteroids (70%) and anakinra (20%) were likewise consistent across groups. Length of hospital stay also did not differ by HCT-CI (p = 0.830) .
The incidence of clinically significant early immune-effector cell-associated hematotoxicity (Grade≥3 ICAHT:31%) and the rates of prolonged cytopenias (>3 months) were also similar across HCT-CI groups.

Conclusions: In this large, multicentre Australian real-world cohort, the HCT-CI did not meaningfully stratify survival, response, or toxicity outcomes. Those findings suggest that transplant-era comorbidity indices may have limited discriminatory power for excluding otherwise appropriate CAR-T candidates and highlight the need for CAR-T specific tools that integrate comorbidity, frailty, and disease biology to refine patient selection and eligibility assessments.

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A169

SURVIVAL OUTCOMES FOLLOWING ALLOGENEIC TRANSPLANT FOR *TP53*-MUTATED MYELOID MALIGNANCY IN IRELAND

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Background: Mutations in the *TP53* tumour suppressor gene are a poor prognostic marker in myeloid malignancies. Retrospective series report suboptimal responses to conventional therapy and dismal outcomes following allogeneic transplant. However, prospective identification of *TP53* mutations at diagnosis facilitates tailored management of the peri-transplant period which may improve survival. We aimed to examine treatment practices and outcomes following allogeneic transplant in *TP53*-mutated myeloid malignancy since the incorporation of next-generation sequencing into myeloid diagnostics.

Methods: Patients undergoing allogeneic transplant for *TP53*-mutated myeloid malignancy at the National Adult Stem Cell Transplant Centre, St James' Hospital between 2021-2025 were evaluated. This cohort included referrals from 11 hospitals nationwide. Survival estimates were calculated using Kaplan–Meier and Cox proportional- hazards model was used for multivariable regression.

Results: Twenty-six patients (AML=17, MDS=8, MPN=1) were transplanted for *TP53*-mutated myeloid malignancy. Median age at time of transplant was 58 years (range 18-70), with 54% being female. *TP53* aberrations were biallelic in 62%, monoallelic in 27% and subclonal in 12%. Additional high risk features included complex karyotype (48%), therapy-related disease (15%) and prior myeloid malignancy (19%). Nineteen percent were refractory to first-line therapy.
Eight patients (31%) were treated with myeloablative and 18 (69%) with reduced-intensity conditioning (RIC). Busulfan was chosen as alkylation for 85%, with melphalan employed in 15%. Donor selection included 8 sibling, 14 matched-unrelated, 3 mismatched-unrelated, and 1 haploidentical graft. Twelve individuals (46%) received donor lymphocyte infusions (DLI; 1=prophylactic, 3=pre-emptive, 8=therapeutic) and 8 (31%) were treated with upfront maintenance azacitidine. Full donor chimerism was achieved in 85%, and 69% developed graft-versus-host disease (GVHD).
At a median follow up of 686 days, median overall survival was not reached. One and 2 year overall survival (OS) post-transplant were estimated at 69% (CI 0.53-0.91) and 55% (CI

0.37-0.81) respectively. Relapse free survival for the entire *TP53* mutated cohort was 54% (CI 0.37-0.80) and 48% (CI 0.31-0.76) at 1 and 2 years post-transplant.
Variable analysis was limited by sample size, however biallelic *TP53* mutations were not associated with excess mortality (HR 0.7, CI 0.2–2.5). RIC trended toward a lower rate of death than myeloablative conditioning (HR 0.67, CI 0.17-2.61). Two patients died from early transplant related mortality after myeloablation such that OS at 6 months in this group was estimated at 73% versus 100% in the RIC arm. Patients conditioned with melphalan (n=4, follow-up 223-844 days) had 2-year OS estimated at 100% versus 47% for those with busulfan (HR 0.67, CI 0.17-2.6).
While no significant association was identified between use of donor lymphocyte infusion (DLI) or development of GVHD, attainment of full donor chimerism was strongly associated with reduced mortality (HR 0.18, CI 0.05-0.71, p=0.015). Two-year OS was estimated at 63% for those with full chimerism versus 0% without.

Conclusions: Compared to published studies, these data demonstrate improved survival post-allogeneic transplant for *TP53*-mutated myeloid malignancy. Myeloablative conditioning conferred no advantage over RIC, however melphalan may offer superior anti-leukaemic effect to busulfan. Strategies that promote full donor chimerism, including early immunosuppression taper and DLI, appear critical to optimising outcomes in this high-risk population.

Disclosure: Nothing to declare.

A170

OUTCOME AND TOXICITY PROFILE OF CAR T-CELL THERAPY IN PEDIATRIC RELAPSED/REFRACTORY B ACUTE LYMPHOBLASTIC LEUKEMIA: SINGLE-CENTER EXPERIENCE FROM SAUDI ARABIA

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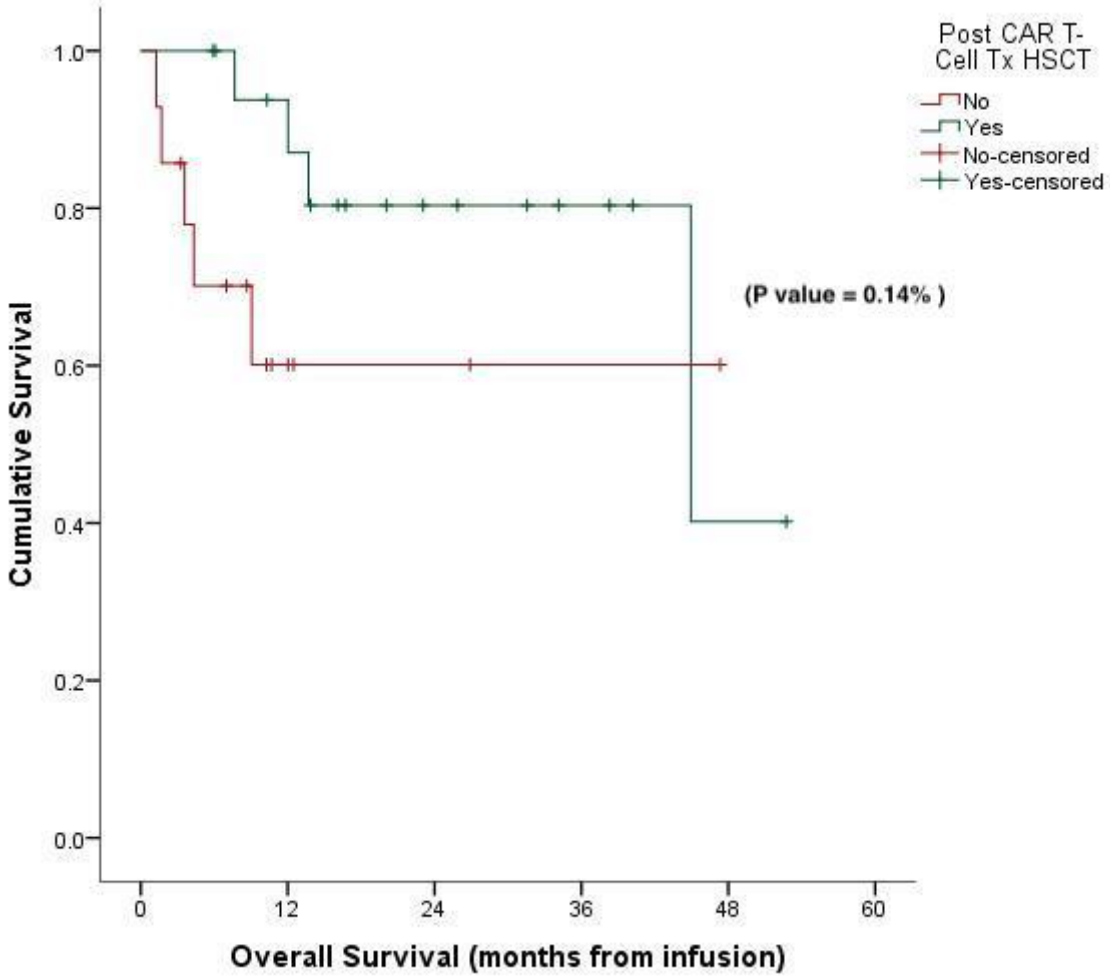
Background: Relapsed or Refractory B-cell ALL (R/R B-ALL) poses a significant treatment challenge. Tisagenlecleucel, an anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, has shown promising efficacy. However, real-world data, especially from Middle Eastern centers, remains limited. This study aims to evaluate outcomes and toxicities of tisagenlecleucel in pediatric B-ALL at a single center in Saudi Arabia.

Methods: This observational study included 32 pediatric patients (≤14 years) with (R/R B-ALL) treated with tisagenlecleucel between December 2020 and January 2025. We evaluated patient demographics, disease features, treatment parameters, toxicity profiles, cytokine release syndrome, and immune effector cell-associated neurotoxicity syndrome, response rates, survival outcomes, and post-infusion HSCT.

Results: The cohort had a median age of 8.2 years; 43.8% had undergone prior HSCT, and 43.8% had high disease burden (≥5% marrow blasts). CRS occurred in 75% of patients, with a median onset of 1.5 days post-infusion; 25% experienced severe (Grade 3–4) CRS events, which were managed successfully with tocilizumab and corticosteroids. ICANS was reported in 9.4%, with a median onset of 3 days after infusion. Post-infusion cytopenia (Grade 2–3) anemia was observed in all patients, with a median recovery time of 35.5 days. 87.5% had severe neutropenia, with a median recovery time of 17 days, and 28.1% had thrombocytopenia, with a median recovery time of 54 days. B-cell aplasia persisted for a median of 3.7 months; 33.3% exhibited early B-cell recovery within 6 months. All but three patients (90.6%) demon.strated a response to therapy, as determined by bone marrow MRD assessment at Day 28 following CAR T-cell infusion. Of the 29 responders, 10 (34.4%) had relapse disease, with a median follow-up of 16.7 months. Their 1-year and 2-year overall survival (OS) rates were 79.7% and 74%, respectively. Event-free survival (EFS) rates were 73.9% and 50% at one year and 2 years, respectively. Of the whole cohort including the refractory patients the 1-year and 2-year overall survival (OS) rates were 75.4% and 70.4%, respectively and the 1-year and 2-year overall survival (EFS) rates were 57% and 45.3%, respectively. Among the responding patients (n = 29), ten (34.4%) proceeded to HSCT consolidation while in remission. However, no statistically significant survival advantage was observed compared with patients who did not receive HSCT consolidation (EFS at 24 months: 72.9% vs. 37.8 %; p = 0.14).



Conclusions: Tisagenlecleucel is effective and feasible in heavily pretreated pediatric B-ALL in this regional cohort, with manageable toxicity profiles consistent with global experience. High rates of relapse and post-infusion cytopenias highlight the need for improved monitoring and consolidation strategies to optimize long-term outcomes.

Clinical Trial Registry: NA

Disclosure: The authors declare no conflicts of interest.

A171

INDIVIDUALIZED BUSULFAN COMPARED TO FIXED-DOSE IN HEMATOPOIETIC STEM CELL TRANSPLANT FOR AML/MDS: RESULTS FROM A SINGLE CENTER

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Background: Busulfan (Bu) exposure is a critical determinant of outcomes in allogeneic hematopoietic stem cell transplantation (HSCT). Fixed-dose strategies may lead to substantial intra and inter-patient variability, affecting toxicity and efficacy. Pharmacokinetics (PK) of Bu can maximize his antitumoral activity with an acceptable toxicity profile.

Methods: We conducted a retrospective single-center analysis of consecutive AML/MDS patients who underwent a myeloablative HSCT. Patient received either fixed-dose Bu (2010-2020) or individualized Bu dosing adjusted to achieve a predefined target area-under-the-curve (AUC) (2021-2025). PK was measured after the first fixed dose of BU (100 mg/m2) and after the 3rd dose. Two AUC levels were selected: AUC16 for patients aged 65-70 years and in patients with comorbidity index (HCT-CI) ≥3, and AUC20 for the remaining patients. GVHD prophylaxis was different, according to the donor type. Primary endpoints included overall survival (OS), progression-free survival (PFS). Secondary endpoints were incidence of sinusoidal obstruction syndrome (SOS), graft-versus-host disease (GvHD), non-relapse mortality (NRM) at day+100 and 1 year and cumulative incidence of relapse (CIR) at 1 year.

Results: From January 2010 to August 2025, 267 AML/MDS patients were included: 51in PK-BU cohort while 216 patients received fixed dose BU. Patient characteristics were reported in Table. The median follow-up was 18 months in the PK-BU cohort (2-35 months) and 72 months (2 -189 months) in fixed-BU.
In PK-BU cohort, 35 patients (69%) had AUC16 target and 16 (31%) AUC20 target. Median neutrophil engraftment was 17 (9-38) and 16 days (12-23) in the fixed dose and PK-BU cohort respectively, while platelet engraftment was 14 (8-72) and 13 days (10-46). The incidence of graft failure was 2% in the PK-BU cohort and 1% in the fixed-BU cohort (3/216). 100-day NRM was 12% and 18% in the fixed-BU cohort and PU-BK cohort, respectively (p value 0.79). 1-y NRM was 24 % and 21% in the fixed-BU cohort and PK-BUcohort, respectively (p value 0.79). The 1-year CIR was 28% in the fixed-dose cohort while 17% in the BU-PK (p value 0.21).
1 year OS and PFS were 65.2% and 55.2%,respectively.
In the fixed-BU cohort, the CI grade 3-4 aGVHD was 8.3% compared to 6% in the PK-BU cohort (p value 0.76). Cgvhd in the PK-BU cohort was 11% while 2% in the fixed-Bu cohort (p value 0.08).
In the PK-BU cohort, the incidence of grade 3-4 mucositis was 23% while 36.6% in the fixed-BU cohort (p value 0.0021). In the PK-BU cohort incidence of VOD/SOS was 8% (4/51) while 2.5% in the fixed-BU(5/216) (p value 0.14).

Patient characteristics	Patients N=267	BU_NO_PK N=216	BU_PK N=51	pvalue
Disease				0,3936
AML	234 (87.6%)	187 (86.6%)	47 (92.2%)	
MDS	33 (12.4%)	29 (13.4%)	4 (7.8%)	
HCT-CI				0,4019
<=2	53 (58.9%)	26 (65%)	27 (54%)	
>2	37 (41.1%)	14 (35%)	23 (46%)	
Disease status				0,1992
CR	216 (80.9%)	171 (79.2%)	45 (88.2%)	
NO CR	51 (19.1%)	45 (20.8%)	6 (11.8%)	
Donor				0,1977
APLO	54 (20.3%)	40 (18.6%)	14 (27.5%)	
HLAid	104 (39.1%)	90 (41.9%)	14 (27.5%)	
mMUD	35 (13.2%)	29 (13.5%)	6 (11.8%)	
MUD	73 (27.4%)	56 (26%)	17 (33.3%)	
TCI				<0,0001
high	89 (33.3%)	89 (41.2%)	0 (0%)	
int	178 (66.7%)	127 (58.8%)	51 (100%)	
low	0 (0%)	0 (0%)	0 (0%)	

Conclusions: A PK-guided BU-based conditioning regimen is safe and effective for AML/MDS patients undergoing allo-SCT. We observed a trend towards a lower CIR and better OS and PFS in PK-BU compared to fixed dose BU. Mucosal toxicity was reduced with PK-BU.

Disclosure: No disclosure.

A172

IMMUNE EFFECTOR CELL ASSOCIATED NEUROTOXICITY (ICANS) IN PAEDIATRIC PATIENTS FOLLOWING CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY: EXPERIENCE FROM A TERTIARY CARE CENTER

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Background: ICANS is a serious complication of CAR T-cell therapy. Diagnostic and treatment approaches rely mainly on expert consensus, with limited paediatric data. This study describes clinical features and management of ICANS in a paediatric cohort receiving 4-1BB CAR-T19 therapy at a single center.

Methods: Patients aged 1–25 years with R/R B-cell ALL treated between April 2016 to September 2025 were included. ICANS severity was graded according to ASTCT criteria. All patients underwent baseline brain MRI and neurological evaluation, with post-infusion follow-up. Individuals with prior neurological symptoms, CNS involvement, or abnormal imaging received prophylactic antiepileptics initiated 5 days before infusion. From March 2021, patients deemed at high risk for neurotoxicity additionally received intravenous prophylactic anakinra (2mg/kg/day) starting on infusion day. Demographic and clinical data were retrospectively collected.

Results:

Variables	Overall cohort n=37	Non-ICANS neurotoxicity n=13	ICANS grade 1-2 n=11	ICANS grade 3-4 n=13
Male, n(%)	24 (64.9%)	9 (69.2%)	7 (63.6%)	8 (61.5%)
Median age at infusion, years (range); IQR	9.4; (2.1-24.2); 6.1	10.8 (5.9-18); 5.9	8.2 (2.3-24.2); 10.8	11.1 (5.8-16.5); 4.4
Baseline disease status: • 1st refractory relapse, n(%) • ≥2nd relapse, n(%)	 14 (37.8%) 23 (62.8%)	 5 (38.4%) 8 (61.6%)	 5 (45.5%) 6 (54.5%)	 4 (30.8%) 9 (69.2%)

CNS infiltration in the past, n(%)	17 (45.9%)	6 (46%)	5 (45%)	6 (46%)
Neurologic history • None • Methotrexate neurotoxicity • Seizure • Prior structural injury (stroke, PRES, ICH, infection)	 27 (73%) 5 (13.5%) 4 (10.8%) 1 (2.7%)	 10 (77%) 2 (15%) 0 (0%) 1 (8%)	 8 (73%) 2 (18%) 1 (9%) 0 (0%)	 9 (69.2%) 1 (7.7%) 3 (23%) 0 (0%)
Previous lines, median (range) • Prior HSCT, n(%) • Prior Blinatumomab, n(%) • Prior inotuzumab, n(%)	 3 (1-5) 10 (27%) 0 (0%) 2 (5.4%)	 3 (2-5) 3 (23%) 0 (0%) 0 (0%)	 3 (1-3) 4 (36%) 0 (0%) 2 (18%)	 2 (2-4) 3 (23.1%) 0 (0%) 0 (0%)
Radiation history • No • Yes	 28 9	 9 4 (1TBI/3Cranial)	 7 4 (2TBI/2Cranial)	 12 1 (Cranial)
% BM Blasts pre-lymphodepletion: • <5%blasts, n(%) • ≥5% blasts, n(%)	 14 (37.8%) 23 (62.2%)	 5 (38.4%) 8 (61.6%)	 3 (27.3%) 8 (72.7%)	 3 (23.1%) 10 (76.9%)
CAR-T construct: • Tisagenleucleucel, n(%) • ARI-0001, n(%)	 32 (86.5%) 5 (13.5%)	 10 (76.9%) 3 (23.1%)	 10 (91%) 1 (9%)	 12 (93.2%) 1 (7.7%)
Dose of CART19(x10^6CART/Kg), median (range); IQR	3.06 (0.9-5); 1.6	3.7 (0.9-5); 1.8	3.3 (1.0-4.2); 1.9	3 (1.0-4.4); 0.54

CRS present, n(%) • CRS onset median (days) (range); IQR • CRS severity 1. Grade 1-2 2. Grade 3-4 - Tocilizumab treatment (number of doses)	34 (91.9%) 1(0-18);3 20 (38.8%) 24 (70.6%)	11 (84.6%) 1(0-3); 3 6 (46%) 5 (38.4%) 6 (2 doses in 4 cases)	11 (100%) 2(0-9); 2 5 (45.5%) 6 (54.5%) 8 (2 doses in 4 cases)	12 (92.3%) 1(0-18);2.5 9 (75%) 10 (83.3%) 10 (2 doses in 7 cases)
Neurotoxicity onset median (days) (Range); IQR	6(1-16); 4	4(1-16); 3	6(1-12); 5	7(3-11); 4

Among 111 patients treated with 4-1BB CAR-T19 therapy (Tisa-cel=88; ARI-0001=23), 37(33%) developed neurotoxicity (Tisa-cel=32; ARI-0001=5). Twenty-four (65%) presented ICANS (grade 1–2=11; grade 3–4=13), while 13 experienced isolated tremor.
Among patients who developed neurotoxicity, almost half (17/37;45.9%) had a previous history of CNS-3 without involvement in the 30 days prior to infusion, and 10(27%) had neurological symptoms related to prior treatments. Most ICANS patients (18/24;75%) had high tumor burden (≥5% blasts) before infusion. CRS occurred in 23/24 ICANS cases,12 (50%) severe, requiring prolonged PICU stays.
Neurological manifestations included seizures (n=7), decreased consciousness (n=6), speech impairment (n=4), hallucinations (n=5), cranial nerve deficits (n=3), and PRES (n=1). Median onset was 6 days post-infusion (range 1–16), and all cases resolved within 4 days (range 1–296), except one patient with persistent facial paralysis refractory to treatment.
Diagnostic tests during neurotoxicity included EEG in 11 patients (8 diffuse slowing; 1 epileptiform discharges; 2 normal), brain MRI in 12 (1 cerebral oedema;1 PRES;6 stable pre-existing white matter changes; 4 normal), and CSF analysis in 5 (hyperproteinorachy in all; HHV-6 in two).
Prophylactic antiepileptics were administered to 11 patients, four also receiving anakinra. ICANS treatment included intravenous anakinra 10mg/kg/8hours (16/24;67%), siltuximab (9/24;38%), and corticosteroids (10/24;42%), mainly methylprednisolone (2mg/kg/day), except for two cases with dexamethasone. Twelve patients received antiviral therapy: two for HHV-6 and two empirically until CSF herpes studies were negative. The OS at 2 years of patients with ICANS compared to those without was 46.1%(95%CI 24.8-65.1) and 68.8%(95%CI 57.3-77.8) (p=0.046) and the EFS was 32.3%(95%CI 14.0-52.1) and 53.1%(95%CI 41.5-63.4) (p=0.09), respectively.

Conclusions: The incidence of severe ICANS (grade ≥3) was 11.7%, comparable to real-world paediatric cohorts and lower than rates reported in adults treated with CD28-based constructs. Except for one case, severe ICANS did not occur with ARI-0001, suggesting a lower neurotoxicity profile compared with tisa-cel. Neurotoxicity resolved without sequelae in all but one patient. Brain MRI was the primary diagnostic tool both at baseline and during

neurotoxicity, while CSF analysis was reserved for atypical presentations due to coagulopathy risk. Management primarily involved corticosteroids and anti-cytokine agents (anakinra, siltuximab). OS at 2 years was lower in patients with ICANS; however, larger paediatric series are required to better elucidate risk factors and prognostic indicators.

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A SINGLE CENTRE RETROSPECTIVE REVIEW OF DONOR LYMPHOCYTE INFUSION - INDICATIONS, OUTCOMES AND TOXICITY

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Background: The use of donor lymphocyte infusions (DLI) post allogeneic stem cell transplant remains common with DLI being given prophylactically to improve mixed T cell chimerism (pDLI), or therapeutically to treat relapsed disease (tDLI). Whilst its efficacy is established DLI is associated with toxicity, particularly Graft versus host disease (GVHD), and there remains a need to optimise its use to improve patient outcomes.

Methods: This retrospective single centre study reviewed outcomes of patients undergoing allogeneic stem cell transplantation at our institution between 2019-2024 who subsequently received DLI. DLI dose was dependent on the donor and the indication with further infusions given at escalated doses as per local policy.

Results: 456 patients underwent allogeneic transplantation with 11 patients receiving 2 transplants and 467 transplants being performed in total.
As of 19/11/2025 (Median follow up 973 days) DLI has been administered following 142/467 (30.4%) transplants and to 141/456 (30.9%) patients with 257 infusions being administered in total.
The median age of patients receiving DLI was 61 years (16-73). 68.3% were male. 35.3% of patients receiving reduced intensity conditioning regimes required DLI compared to 13.3% myeloablative. 83.1% of DLI was given in the context of Fludarabine/Melphalan/Alemtuzumab (FMC) conditioning with 45.7% of all FMC conditioned transplants requiring DLI.

105 patients received pDLI. The median T Cell chimerism pre infusion was 41% donor (1-91) and the median number of days between transplant and first infusion was 217 (125-576). The median number of infusions given was 1 (1-6) with a median total dose received of 5x10^5 CD3/kg (5x10^5 –1.35x10^8 CD3/kg). Overall survival (OS) in this cohort was 78.1% (Median follow up 866 days) (Figure 1). The median T cell chimerism at first reassessment (2-3 months post DLI) was 70% donor (3-100). 51 (48.6%) of patients reverted to full donor chimerism (T Cell chimerism >95%) following 1 infusion with 71 (68.3%) achieving full donor chimerism in total. 9 (8.7%) of patients relapsed despite DLI. 37 patients received tDLI either alone or in combination with other therapy. The median number of days between transplant and first infusion was 653 (157-1465). The median number of infusions given was 2 (1-4) and the median total dose was 4x10^6 CD3/kg (1x10^6-4.4x10^7). 19 patients (51.3%) received DLI for relapsed AML and the remainder for other indications. OS was 62.2% (Median follow up 1260 days). 12 patients (32.4%) achieved disease control and remain in remission, 11 (29.7%) remain alive with active disease and 14 (37.8%) have died.
38 (27%) of all patients receiving DLI suffered from GVHD with 12 (8.5%) having confirmed grade III/IV GVHD. 14 (9.9%) patients died with GVHD felt to be a contributing factor in their death. 92.1% cases of GVHD occurred in patients receiving pDLI with 7.9% receiving tDLI.

Figure 1: Kaplan-Meier curve of overall survival (OS) in patients receiving pDLI

Conclusions: This study demonstrated high rates of DLI use particularly in the context of reduced intensity conditioning regimes. We provide further evidence of the of efficacy of DLI particularly in preventing disease relapse however GVHD remains a significant complication. Further strategies to reduce DLI use in future and to manage its toxicity are required.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

A174

REAL-WORLD OUTCOMES OF AUTOLOGOUS BONE MARROW TRANSPLANTATION IN RELAPSED/REFRACTORY HODGKIN LYMPHOMA: A MULTICENTER RETROSPECTIVE ANALYSIS FROM THE UKRAINIAN NATIONAL BMT REGISTRY

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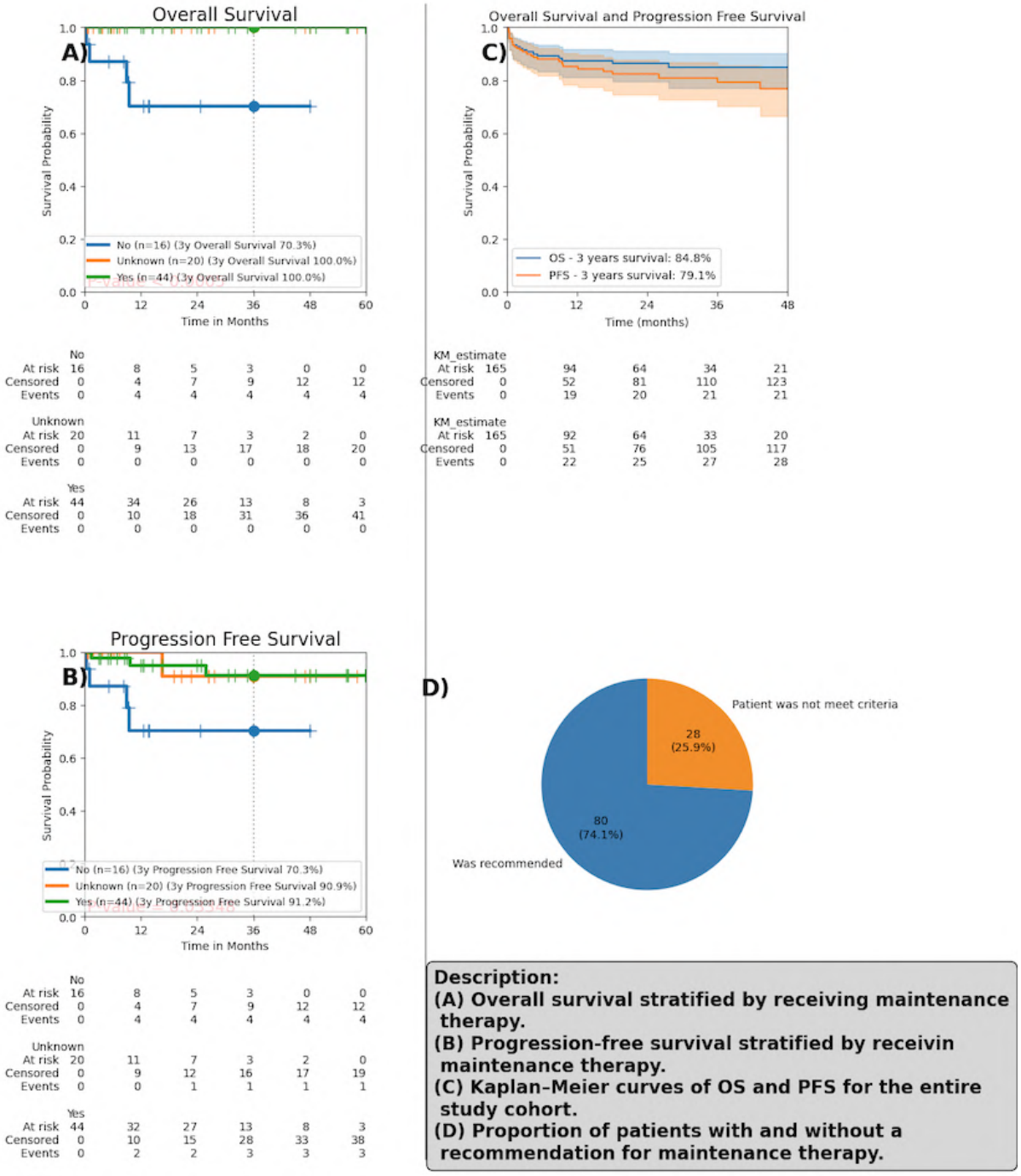
Background: The Hodgkin lymphoma (HL) is a potentially curable lymphoma with a cure rate in first line around 85- 90%. In relapsed cases, autologous stem cell transplantation (ASCT) offers a 60% chance of long-term remission. In 2024-2025, ASCT was performed for 747 patients in 11 centers across Ukraine. Real-world data from transplant registries provides region-specific insights into treatment practices and outcomes, reflecting variations in healthcare infrastructure, drug availability, and clinical decision-making across different geographic settings.

Methods: Restrospective analysis of 179 cases that underwent ASCT from the National Bone Marrow Transplantation Registry, coordinated by the Ukrainian Bone Marrow Transplantation Association. Data were collected from 6 Ukrainian transplant centers using REDCap software from 2016 - 2025. We provide descriptive analysis of clinical characteristics, estimate 3-year OS and PFS using the Kaplan-Meier Curve.

Results: Ninety-one patients (51.4%) were male; median age at ASCT was 30 years (range 14–60). At diagnosis, 89 patients (53.6%) had advanced disease (stage III–IV). In 83 of 123 evaluable cases (67.5%), the indication for ASCT was relapse; the median time from initial diagnosis to relapse was 4.1 years (range 0.7–19).
Salvage therapy data were available for 124 patients. The median number of treatment lines

prior to ASCT (including first line) was three (range 1–6). The most frequently used salvage regimens were IGEV (63 patients, 50.8%) and DHAP (57 patients, 46.0%); 17 patients (14.0%) received both regimens sequentially. Brentuximab vedotin (BV) was administered in 44 patients (35.5%), including 26 (21.0%) as monotherapy. Complete remission prior to ASCT was achieved in 99 of 124 evaluable patients (79.8%).
Conditioning data were available for 131 patients. LEAM was the most commonly used regimen (108 patients, 82.4%), followed by BuCyE (15 patients, 11.5%). Although 80 of 108 patients fulfilled criteria for BV maintenance after ASCT, only 44 received maintenance therapy. Follow-up data were available for 169 patients (94.4%), with a median follow-up of 2.1 years (range 0.1–6.9) from ASCT.
Twenty-two patients died after ASCT, and eight experienced relapse. Transplant-related mortality was observed in 14 patients (8.7%). Three-year OS and PFS were 84.8% (95% CI 66–89) and 79.1% (95% CI 66–88), respectively. BV maintenance was associated with superior 2-year OS and PFS (100% and 91.2%) compared with no maintenance (70.3% and 70.3%).

Figure 1



Description:
(A) Overall survival stratified by receiving maintenance therapy.
(B) Progression-free survival stratified by receivin maintenance therapy.
(C) Kaplan-Meier curves of OS and PFS for the entire study cohort.
(D) Proportion of patients with and without a recommendation for maintenance therapy.

Conclusions: This first multicenter analysis from the Ukrainian National Bone Marrow Transplantation Registry confirms that ASCT remains an effective strategy for

relapsed/refractory HL in a real-world setting, with encouraging three-year survival outcomes. At the same time, the registry highlights important gaps in care, including limited access to novel agents and inconsistent use of post-transplant maintenance therapy. These findings underscore the value of a national registry for identifying country-specific barriers to optimal care and for guiding future efforts to improve access to evidence-based treatments.

Disclosure: Nothing to disclosure.

A175

TREOSULFAN COMPARED WITH BUSULFAN-BASED CONDITIONING FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HEMATOLOGICAL MALIGNANCIES

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Background: The randomized MC-FludT.14/L Trial II demonstrated that conditioning with fludarabine plus treosulfan (total dose 30 g/m²), compared with reduced-intensity busulfan (total dose 6.4 mg/kg), improved transplantation outcomes in older patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). However, data directly comparing treosulfan-based conditioning with higher-dose busulfan regimens (total dose 9.6 mg/kg) remain limited. We therefore performed a single-center retrospective analysis comparing treosulfan- and busulfan-based conditioning in patients with hematological malignancies undergoing allogeneic hematopoietic stem cell transplantation (alloHCT).

Methods:

Between 2018 and 2025, 121 consecutive patients (median age 65 years, IQR 56–65) underwent alloHCT for acute leukemia, myelodysplastic or myeloproliferative neoplasms, or lymphoma. Disease Risk Index (DRI) was low in 10, intermediate in 71, and high or very high in 40 patients. Donors included matched sibling (n = 16), matched unrelated (n = 97), and haploidentical donors (n = 8).

Conditioning consisted of fludarabine (total dose 150 mg/m²) combined with busulfan 9.6 mg/kg (FluBu3; n = 36) or treosulfan 36 g/m² (FluTreo12; n = 40) or 30 g/m² (FluTreo10; n = 45). Patients receiving FluBu3 were younger than those treated with FluTreo12 and FluTreo10 (median 56, 62, and 66 years, respectively; p = 0.014). Other baseline characteristics, including diagnosis, DRI, donor type, CMV serostatus, and graft-versus-host disease (GvHD) prophylaxis, were comparable across groups.

Results:

With a median follow-up of 26 months (range 1–93), 3-year overall survival (OS) for the entire cohort was 65.7% (95% CI 56.0–75.4), and 3-year progression-free survival (PFS) was 63.0% (95% CI 53.2–72.8). OS and PFS did not differ significantly between conditioning

regimens. Three-year OS was 72.7% for FluBu3, 73.1% for FluTreo12, and 56.4% for FluTreo10 (p = 0.95), while corresponding PFS rates were 69.7%, 70.6%, and 56.6%, respectively (p = 0.84).

The 3-year cumulative incidence of relapse (RI) was 25.9% (95% CI 18.3–36.7) and non-relapse mortality (NRM) was 11.1% (95% CI 6.5–18.9). RI did not differ between conditioning regimens (p = 0.87), with rates of 24.4% (FluBu3), 16.6% (FluTreo12), and 34.9% (FluTreo10). Similarly, NRM was comparable across groups (p = 0.55), at 6.2%, 12.2%, and 13.9%, respectively.

Rates of severe infectious complications, acute GvHD grade II–IV, and extensive chronic GvHD were similar across groups. In contrast, severe non-infectious complications (grade 3–4) occurred more frequently after FluBu3 (36.1%) than after FluTreo12 (12.5%) or FluTreo10 (13.3%), mainly due to severe mucositis (p = 0.014).

Conclusions: Treosulfan-based conditioning provides comparable survival and disease control to FluBu3 in patients not eligible for fully myeloablative busulfan dosing, with significantly lower rates of severe non-infectious toxicity. Importantly, both OS and PFS were satisfactory when interpreted in the context of the DRI distribution of this cohort, which included a substantial proportion of patients with intermediate- and high-risk disease.

Disclosure: Nothing to declare.

A176

UTILIZING GVHD BIOMARKERS TO PREDICT POOR ENGRAFTMENT: THE GOLDILOCKS PHENOMENON OF ALLOREACTIVE T CELLS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION

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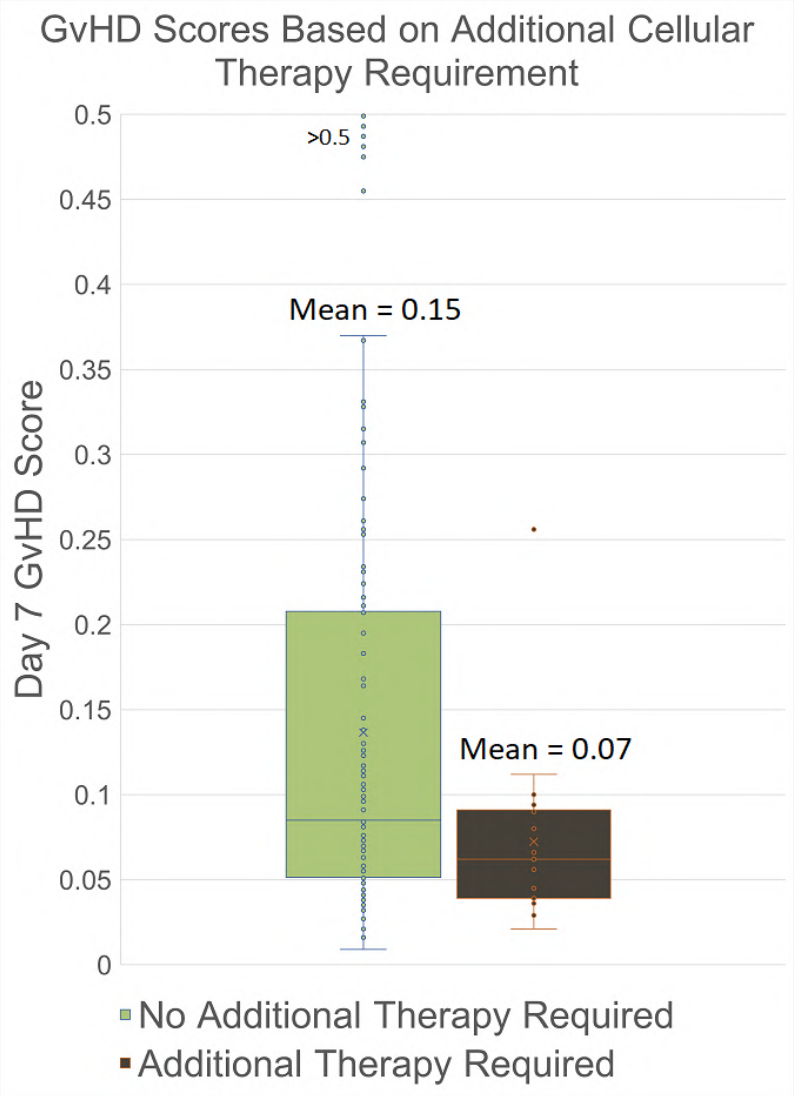
Background: T cells play a critical role in hematopoietic stem cell transplant (HSCT). They assist with engraftment but are also directly related to graft-versus-host disease (GvHD). Attempts have been made to decrease GvHD through the reduction of alloreactive T cells in stem cell products prior to transplant, processes that also result in higher rates of graft failure. Biomarker assays have been utilized to predict therapy resistant GvHD when obtained at day +7 after HSCT. High biomarker scores predict an increased risk of developing therapy resistant acute GvHD. Our objective was to evaluate the association of low day +7 GvHD biomarker scores with rates of graft failure requiring additional cellular therapy after initial HSCT in pediatric patients. We hypothesized that a low day +7 GvHD score would be associated with an increased risk of graft failure, though this has not been previously studied.

Methods: We performed a retrospective review of all pediatric patients who underwent allogeneic HSCT at Phoenix Children's Hospital over a 5-year period (1/1/2018 - 12/31/2023). Patients were included if they survived to day +30 and had both a day +7 GvHD biomarker assay and day +30 T-cell chimerism available. Of 160 transplants performed, 137 patients were included in analysis. Day +7 biomarker values were compared between patients who did or did not require additional cellular therapy after initial transplant. Statistical analysis included Mann-Whitney U tests and odds ratios.

Results: Of the 137 patients, 116 did not require additional cellular therapy, while 21 did. Of the 21 patients, 5 required additional therapy due to relapse of malignant disease. Of these 5 patients, 3 had falling chimerisms prior to relapse and were included in the analysis while 2 patients documented 100% T cell chimerism at the time of relapse and were excluded from analyses. Mean day +7 biomarker values were significantly lower in patients requiring additional therapy with a value of 0.07 (95% CI 0.05 – 0.09) compared to those who did not with a value of 0.15 (95% CI 0.12 – 0.18). The Mann-Whitney U test demonstrated statistical difference ($z = 2.29$, $p = 0.02$). Patients with very low GvHD biomarker scores (≤0.1) had an odds ratio of 7.4 (95% CI 1.6–33.5) for graft failure requiring additional cellular therapy.



Conclusions: Our study demonstrates that very low day +7 GvHD biomarker assays (≤0.1) are significantly associated with an increased risk of graft failure requiring additional cellular therapy in pediatric HSCT recipients. While prior studies have focused on the predictive value of these assays relating to acute GvHD, our findings suggest they may also have utility in identifying patients at risk for poor engraftment outcomes.
These results highlight the need to refine biomarker cutoff thresholds and to incorporate additional variables into predictive models. Larger, multi-institutional studies are warranted to validate these findings and determine how biomarker-guided risk stratification may inform early intervention strategies to improve transplant outcomes.

Disclosure: No conflicts of interest to disclose.

A177

IMMUNE EFFECTOR CELL ASSOCIATED HAEMATOTOXICITY (ICAHT) AND CORRELATION WITH CLINICAL OUTCOMES POST CD19 CAR-T; A SINGLE CENTRE RETROSPECTIVE EXPERIENCE FROM THE ROYAL MARSDEN HOSPITAL

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Background: There is increasing recognition of immune effector cell-associated haematotoxicity (ICAHT) as a distinct CAR-T toxicity with important consequences on patient survival outcomes and quality of life. Rejeski et al. proposed a grading system for thrombocytopenia[SF1] [NS2] , referred to as T-ICAHT and described prognostic implications of this score, building on their previously described N-ICAHT grading system. We applied both grading systems to a large real-world cohort and explored associations with clinical outcomes.

Methods: We retrospectively analysed 102 adult patients treated with CAR-T at our centre for B-Non-Hodgkin lymphoma (B-NHL) between 2019-2025. Data was collected from patient's electronic record. Early ICAHT day 0–30 post-infusion; late >30 days.

Results: Patient characteristics including CAR-T product and disease status prior to infusion are described in table 1. For early N-ICAHT there was 86% concordance with T-ICAHT. For late ICAHT, 60% of patients with grade 3-4 T-ICAHT had a corresponding lower N-ICAHT grade of 0-2(figure 1).Significant bleeding complications were observed in two patients, Gastrointestinal/intracranial bleed due to ICANS; early T-ICAHT score 2, Rectal bleeding;ICAHT grade 4. Within 30 days following CAR-T infusion, 41 patients (40.19%) received red cell transfusions, 37 patients (36.27%) platelet transfusions. Patients requiring transfusions had worse OS, red cell transfusion HR 0.37 (95% CI 0.20–0.68; p = 0.00128) and platelet transfusion HR 0.57 (95% CI 0.31–1.04; p = 0.069). One patient with grade 4 early T-ICAHT was commenced on TPO agonist. Univariable analysis showed significant correlation between early N-ICAHT and PFS (P = 0.009) (Figure 1). There was no significant correlation between T-ICAHT or late N-ICAHT and OS/PFS.There was a strong correlation between OS and pre-lymphodepletion Hb (HR 0.51 (95% CI 0.28–0.92; p = 0.0266), LDH (HR 0.35 (95% CI 0.19–0.65; p = 0.00095), albumin(HR 0.41 (95% CI 0.21–0.83; p = 0.0124), CRP (HR 0.52 (95% CI 0.25–1.05; p = 0.0674) and alkaline phosphatase(HR 0.55 (95% CI 0.29–1.03; p = 0.0616).EASIX score demonstrated moderate correlations with T-ICAHT grade, with strongest association for EASIX Day 3 and early T-ICAHT. For late T-ICAHT, the highest correlation was seen with EASIX Day -5[SF1].Modified EASIX (M-EASIX) showed weaker associations overall, particularly for Day 3 and late T-ICAHT(Figure1d).ICAHT grade did not correlate with the use of steroids for toxicities;(p=0.214 for early N-ICAHT, p=0.448 for late N-ICAHT, early T-ICAHT (p = 0.133) and late T-ICAHT (p = 0.621).

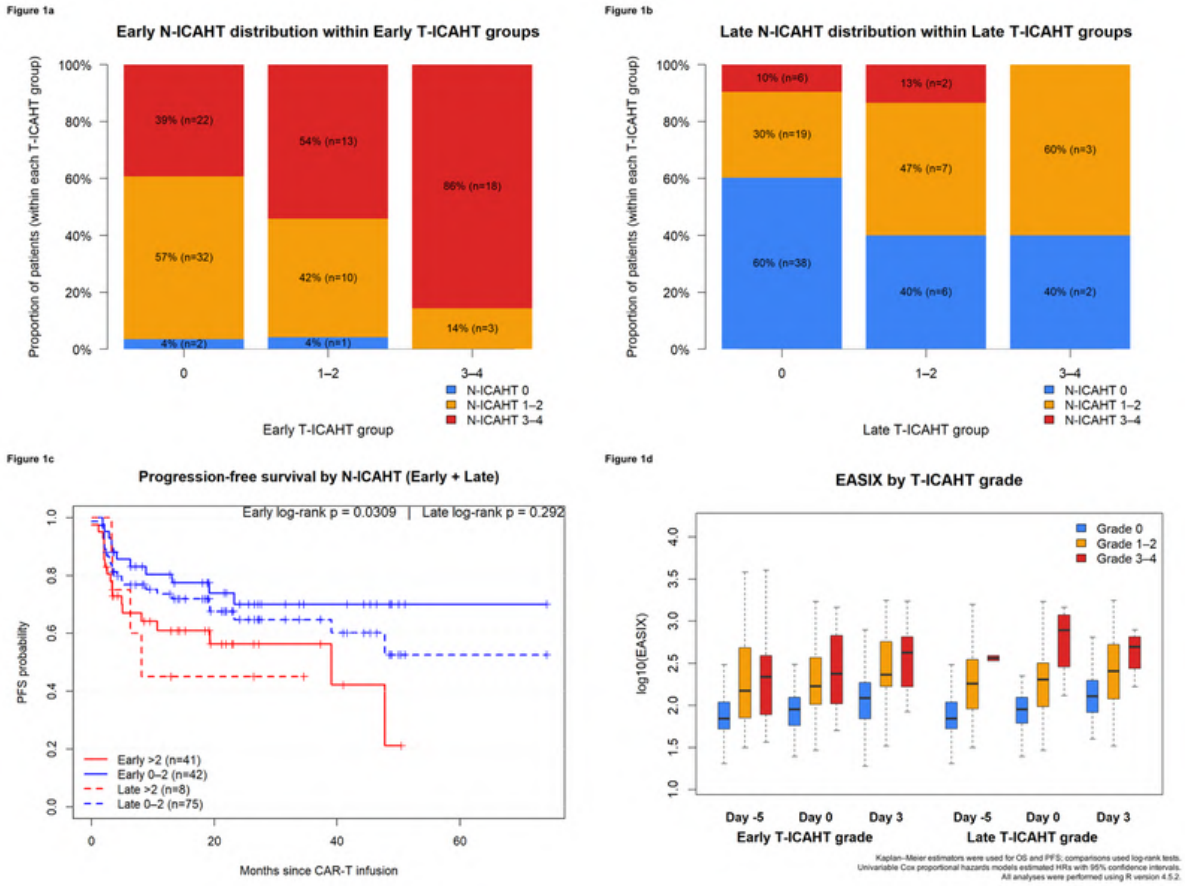

Table 1

Characteristics	NHL, N(%)
Sex	
Male	62(60.78)
Female	40(39.21)
Age	
Median	64
IQR	16.75
Diagnosis	
DLBCL	69(67.64)
FL	1(0.985)
tFL	21 (20.58)
PMBCL	3(2.94)
SLL with Richter's transformation	1(0.98)

Characteristics	NHL, N(%)
T cell/histiocytic rich large B cell lymphoma	1(0.98)
MCL	6 (5.88)
Status Pre CAR-T	
CR	34(33.33)
PR	45(44.11)
SD/PD	23(22.54)
CAR-T Product	
Kymriah	3(2.94)
Yescarta	93(91.17)
Tecartus	6(5.88)
CAR Domain	
CD28	99(97.05)
41BB	3(2.94)
CAR Haematotox Score	
≥2	36(35.29)
0-1	66(64.70)
Prior lines of treatment	
Median	2
Minimum	1
Maximum	9
IQR	1
CRS	
Any Grade	98(96.07)
G≥3	8(7.84)
ICANS	
Any Grade	50(49.01)
G≥3	(20.58%)
Day 28 response	
CR	62(60.78)
PR	26(25.49)
PD/relapse	10(9.80)
SD	2(1.96)
Not available	2(1.96)
Day 100 response	
CR	69(67.64)
PR	5(4.90)

Characteristics	NHL, N(%)
PD/relapse SD Not available	17(16.66) 0(0) 11(10.78)
Blood transfusions within 30 days post CAR-T infusion Yes No PRBC Platelet	 46(45.09) 56(54.90) 41/46(40) 37/46(36.27)
Grades of early T-ICAHT Grade 0-2 Grade 3-4	 55(53.92) 47(46.07)
Grades of late T-ICAHT Grade 0-2 Grade 3-4 Unknown	 74(72.54) 9(8.73) 19(18.44)
Grades of early N-ICAHT Grade 0-2 Grade 3-4 Unknown	 48(47.05) 53(51.96) 1(0.98)
Grades of late N-ICAHT Grade 0-2 Grade 3-4 Unknown	 75(73.52) 8(7.84) 19(18.62)

Conclusions: ICAHT grading systems are feasible to use in practice. We show there is concordance between severe grade 3-4 early T-ICAHT and N-ICAHT, however severe late T-ICAHT correlated with milder grade 1-2 N-ICAHT, emphasising that late T-ICAHT may identify a separate risk-group; however, interpretation is limited by small numbers.EASIX correlates with T-ICAHT severity as a dynamic biomarker of inflammation and warrants further evaluation in predictive modelling of toxicity.M-EASIX provides limited additional value. Baseline LDH and cytopenia's were significantly associated with OS. There is need to investigate optimal management of ICAHT including the timing of GCSF, TPO agonists and stem cell rescue.

Clinical Trial Registry: None

Disclosure: Francesca Sillito(Honoraria Kite Gilead, Honoraria BMS, International sponsorship MEDAC/Miltenyi Biotec).

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DUAL T-CELL DEPLETION WITH ANTITHYMOCYTE GLOBULIN AND POST-TRANSPLANT CYCLOPHOSPHAMIDE IN PERIPHERAL BLOOD ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR ACUTE LEUKEMIA AND MYELODYSPLASTIC SYNDROME

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Background: This study evaluates the efficacy of a dual T-cell depletion strategy in peripheral blood hematopoietic cell transplantation (PBSCT) for acute leukemia and myelodysplastic syndrome (MDS), compared with standard post-transplant cyclophosphamide (PTCy)-based graft-versus-host disease (GVHD) prophylaxis using propensity score matching.

Methods: This retrospective study included adult patients with acute leukemia or MDS who underwent PBSCT at Seoul National University Hospital between 2017 and 2025. Patients conditioned with busulfan and fludarabine and receiving either PTCy alone or antithymocyte globulin (ATG)/PTCy as in vivo T-cell depletion were eligible. In the ATG/PTCy group, ATG was administered at a total dose of 3.0–4.0 mg/kg according to the absolute lymphocyte count on day −3, and PTCy was given at 50 mg/kg on day +3 and 30 mg/kg on day +4. A 1:1 nearest-neighbor matching method using propensity scores was performed based on key covariates, including recipient age, disease type, DRI, donor type, donor sex, conditioning intensity, and infused $CD34^+$ cell dose.

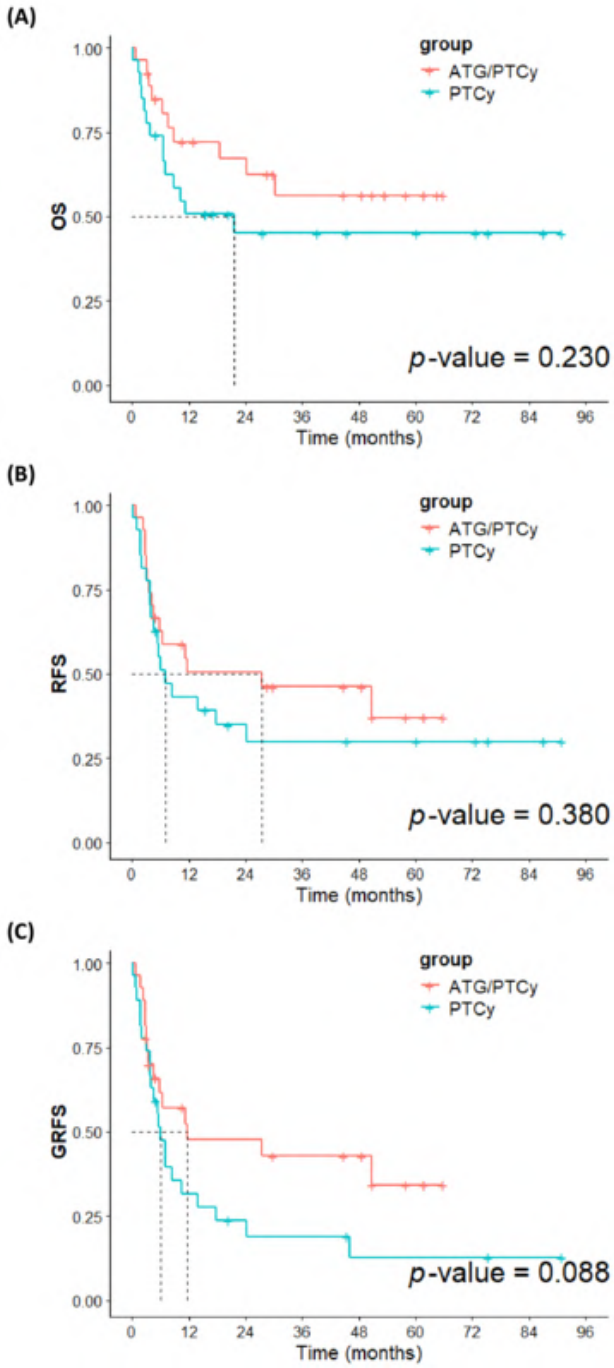
Results: A total of 97 patients were analyzed (54 ATG/PTCy, 43 PTCy). In the overall cohort, the ATG/PTCy group was older (median, 59 vs. 52 years) and had higher proportions of MDS (40.7% vs. 11.6%) and high/very high disease risk index (DRI) (55.6% vs. 30.2%) (Table 1). After propensity score matching (n = 27 per group), baseline characteristics were well balanced.

Variable	Overall cohort			Propensity score matching cohort		
	ATG/PTCy (N=54)	PTCy (N=43)	P-value	ATG/PTCy (N=27)	PTCy (N=27)	P-value
Median age at HCT, years (range)	59 (19 - 75)	52 (19 - 69)	0.017	51 (23 - 69)	55 (19 - 69)	0.938

Variable	Overall cohort			Propensity score matching cohort		
	ATG/PTCy (N=54)	PTCy (N=43)	P-value	ATG/PTCy (N=27)	PTCy (N=27)	P-value
Sex, n (%) Male Female	36 (66.7) 18 (33.3)	29 (67.4) 14 (32.6)	0.999	17 (63.0) 10 (37.0)	18 (66.7) 9 (33.3)	0.999
Diagnosis, n (%) AML ALL MDS	19 (35.2) 13 (24.1) 22 (40.7)	27 (62.8) 11 (25.6) 5 (11.6)	0.004	13 (48.1) 6 (22.2) 8 (29.6)	14 (51.9) 8 (29.6) 5 (18.5)	0.602
Disease risk index, n (%) Low/Intermediate High/Very high	24 (44.4) 30 (55.6)	30 (69.8) 13 (30.2)	0.022	12 (44.4) 15 (55.6)	14 (51.9) 13 (48.1)	0.785
Donor type, n (%) Matched donor Haploidentical donor	12 (22.2) 42 (77.8)	15 (34.9) 28 (65.1)	0.248	4 (14.8) 23 (85.2)	6 (22.2) 21 (77.8)	0.726
Donor age, years (range)	33 (13 - 64)	33 (11 - 65)	0.999	31 (13 - 64)	37 (11 - 65)	0.251
Donor sex, n (%) Female donor to male recipient Others	6 (11.1) 48 (88.9)	11 (25.6) 32 (74.4)	0.111	3 (11.1) 24 (88.9)	2 (7.4) 25 (92.6)	0.999
Conditioning intensity, n (%) MAC RIC	13 (24.1) 41 (75.9)	13 (30.2) 30 (69.8)	0.653	9 (33.3) 18 (66.7)	7 (25.9) 20 (74.1)	0.766
CD34+ cell dose, median (range)	5.12 (3.07 - 8.36)	5.00 (1.42 - 7.58)	0.170	5.00 (3.07 - 6.96)	5.15 (2.95 - 7.58)	0.771

In the overall cohort, there were no significant differences in overall survival (OS), relapse-free survival (RFS), and GVHD-free, relapse-free survival (GRFS). In the propensity score matched cohort, the median OS, RFS, and GRFS were not reached, 27.5 months, and 11.6 months, respectively, in the ATG/PTCy group. Corresponding values in the PTCy group were

21.5, 7.0, and 6.0 months. Four-year OS was similar between the ATG/PTCy and PTCy groups (56.3% [95% CI, 38.6–82.0] vs. 45.1% [95% CI, 28.9–70.2]; *P* = 0.230), as was 4-year RFS (46.2% [95% CI, 30.4–70.3] vs. 30.0% [95% CI, 16.3–55.2]; *P* = 0.380). A trend toward higher 4-year GRFS was observed with ATG/PTCy (42.8% [95% CI, 26.7–68.6] vs. 12.6% [95% CI, 4.0–39.8]; *P* = 0.088) (Table 1).
In the overall cohort, multivariate Cox analysis demonstrated that low/intermediate DRI, MDS, and use of reduced-intensity conditioning were significantly associated with improved GRFS. ATG/PTCy showed a trend toward superior GRFS compared with PTCy (HR 0.60; 95% CI, 0.33–1.05; *P* = 0.074). After propensity score matching, the favorable impact of low/intermediate DRI (HR 0.18; 95% CI, 0.07–0.42; *P* < 0.001) and MDS (HR 0.22; 95% CI, 0.06–0.79; *P* = 0.021) on GRFS remained significant. Notably, ATG/PTCy emerged as an independent predictor of superior GRFS (HR 0.45; 95% CI, 0.21–0.93; *P*= 0.031).



Conclusions: Dual T-cell depletion with low-dose ATG plus attenuated-dose PTCy may offer enhanced protection against clinically significant GVHD without compromising relapse control, thereby improving GRFS in PBSCT for acute leukemia and MDS. Given the central

role of PTCy in current practice, these findings support continued exploration of the potential added value of incorporating ATG as part of combination GVHD prophylaxis.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

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IMPACT OF HLA B LEADER GENOTYPE ON SINGLE HLA MISMATCHED ALLOGENEIC STEM CELL TRANSPLANTATION: A MULTICENTER COHORT STUDY

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Background: The HLA-B leader polymorphism encodes either methionine (M) or threonine (T) at position -21, generating the MM, MT, or TT genotypes. This study aimed to evaluate the impact of this dimorphism on transplant outcomes in unrelated allogeneic stem cell transplant (ASCT) patients with single locus mismatch.

Methods: This was an observational, retrospective, multicenter cohort study. Adult patients (n = 276) with newly diagnosed acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), or acute lymphoblastic leukemia (ALL) in first complete remission (CR1) and

undergoing single HLA-mismatched unrelated ASCT (national/international: 95%/5%) between January 2021 and August 2025 were included in the study. B-leader genotypes were determined using the HLA-B Leader Assessment Tool (BLEAT), and their impact on clinical outcomes was evaluated using multivariate Cox proportional hazards regression.

Results: Data from 276 individuals (138 patients and 138 donors) from 20 transplant centers were analyzed. The median ages of patients and donors were 47.5 (range, 18-74) and 31 (range, 19-52), years respectively. Of the patients 69 (50%), and donors 113 (82%) were male; ASCT indications were AML, ALL and MDS 82 (60%), 39 (28%), 17 (12%), respectively. Hematopoietic Cell Transplantation–Comorbidity Index (HCT-CI) scores were low in 70 patients (51%), moderate in 43 (31%), and high in 25 (18%). Disease Risk Index (DRI) of the cohort were low in 2 (2%), intermediate in 71 (51%), and high/very high in 65 (47%). Conditioning regimens included myeloablative in 84 patients (61%), reduced intensity in 49 (35%), and non-myeloablative in 5 (4%). The median follow-up was 8.8 months (range, 0.2–50.9).Single HLA mismatches involved HLA-A (55%), HLA-B (15%), HLA-C (10%), HLA-DRB1 (13%), and HLA-DQB1 (7%). TT, MT, and MM B-leader genotypes were observed in 66%, 30%, and 4% of patients, respectively. Allele-level mismatches occurred in 22% and antigen-level mismatches in 78% of the cohort.
Table 1 summarizes the results of the multivariable Cox proportional hazards regression models evaluating the association between HLA-B leader genotypes and key clinical outcomes, including overall survival (OS), progression-free survival (PFS), and transplant-related mortality (TRM) (Figure 1).
Patients <60 years carrying the MM genotype had significantly lower PFS and OS than those with TT or MT genotypes (PFS: p = 0.016 and p = 0.023; OS: p = 0.001 and p = 0.002, respectively). The prognostic effect of the HLA-B leader genotype was more evident in this younger group. Among patients with a single HLA-A, -C, -DRB1, or -DQB1 mismatch (n=117), MM carriers showed higher TRM100 and overall TRM, a difference confined to patients <60 years (p<0.05).
GVHD prophylaxis was categorized as ATG alone, PTCy alone, or combined ATG+PTCy, with the reference group defined as TT-genotype patients receiving ATG only. Compared with ATG, PTCy was associated with lower mortality (p = 0.009; HR 0.38; 95% CI, 0.18–0.78). Additionally, among MT-genotype patients, PTCy use was associated with an increased risk of acute GVHD compared with the reference group (p = 0.007; HR 5.1; 95% CI, 1.5–17).

Table 1: Impact of B-Leader Genotypes on Clinical Outcomes: Multivariable Cox Regression Analysis

Outcome	Variable	HR	**95% CI**	P-value*
OS[&]	MM vs TT	4.3	1.2-15.7	**0.025**
PFS**	MM vs TT	48	1.2-128	**0.02**
TRM100[&]	MM vs MT	6.1	1-37	**0.046**
aGVHD G3-4[&]	Donor MM vs TT	5.5	1.1–27.1	**0.035**

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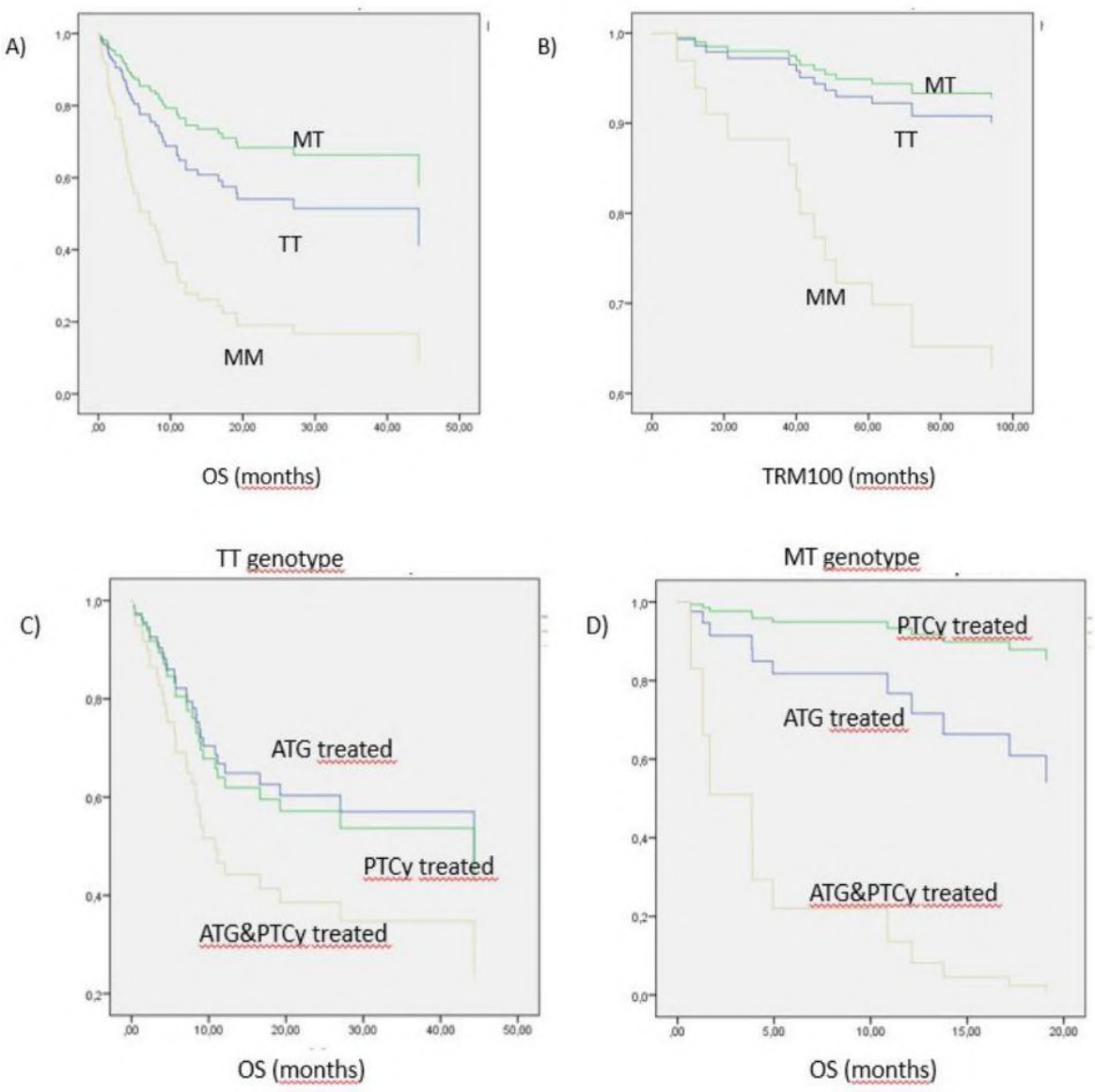
[&]In the entire cohort

** In single HLA-B–mismatched transplants (n = 21) PFS was significantly lower in patients with the **MM** genotype compared with those with the **TT** genotype



Conclusions: In ASCT with single-locus mismatches, HLA-B leader genotypes provide additional guidance for donor selection and GVHD prophylaxis decisions

Disclosure: Nothing to declare

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION USING DECEASED DONOR DERIVED CRYOPRESERVED BONE MARROW: A FIRST-IN-HUMAN REPORT OF SUCCESSFUL ENGRAFTMENT IN PRESERVE 1

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Background: Allogeneic hematopoietic cell transplantation (alloHCT) is a potentially curative therapy for many hematologic diseases. Historically, outcomes reflect the degree of HLA-matching between the donor and recipient, with worse survival associated with higher degrees of HLA-mismatch. Ethnically diverse patients often lack a suitable HLA-matched donor and require HLA-mismatched donor options. PRESERVE 1 (NCT05589896) is a first-in-human clinical trial studying safety and efficacy of 4-8/8 HLA-matched cryopreserved hematopoietic progenitor cells (HPC) obtained from bone marrow (BM) of vertebral bodies harvested from deceased, solid organ donors (age 7-55 years). Here we report results of the first enrolled patient in the PRESERVE study infused with Ossium HPC Marrow.

Methods: PRESERVE 1 is a multicenter, open-label clinical trial sponsored by Ossium Health and conducted by the CIBMTR. This is a 52 year old Hispanic patient with T-cell ALL in CR1 who lacked a suitable donor. The patient's baseline organ function was normal, Karnofsky performance status was 90%, and HCT-CI was 2. The patient received myeloablative conditioning with fludarabine 30 mg/m^2 (days -6 through -2) and TBI 200 cGy BID (days -3 through -1) and graft-versus-host disease (GvHD) prophylaxis with tacrolimus, mycophenolate mofetil, and post-transplant cyclophosphamide (days +3 and +4). On day 0, the patient received 4/8 HLA loci (HLA-A, B, C and DRB1) cryopreserved BM allograft from a deceased donor. The patient received 5.63 million CD34 cells/kg (TNC 2.03 x10e8) Ossium HPC Marrow (5% DMSO). G-CSF (5 µg/kg/day) started on day +1 and continued until first day of neutrophil engraftment.

Results: BM product was thawed at bedside and no infusion-related adverse events occurred. Transplant-related complications included grade 3 mucositis and culture-negative neutropenic fever. The first day of neutrophil engraftment (ANC >500/µL for 3 consecutive days) occurred on day +15 post-alloHCT with an ANC of 500, an ANC of 1100 on day +16, and by day +17 an ANC of 4200. The first day of platelet engraftment (transfusion-independent platelet >20,000/µL for 7 consecutive days) occurred on day +16. Day +90 bone marrow biopsy showed 100% donor chimerism in both unsorted and sorted T cell compartments. The patient completed 1 year follow up, post-Ossium HPC Marrow infusion with no acute or chronic GvHD, serious infection, end-organ injury, or disease relapse have occurred in the patient who maintains hematopoietic engraftment without need for cytokine

augmentation or transfusion.

Fig 1: Patient safety journey

Conclusions: The patient demonstrated robust engraftment with no major safety issues or complications. These early results confirm the proof of concept of building an off-the-shelf bank of allogeneic marrow grafts to expedite time to transplant and provide a source of stem cells for recipients who lack access to suitable living donors. The clinical trial is actively recruiting patients to further characterize the efficacy and safety of these novel grafts.

Clinical Trial Registry: NCT05589896

Disclosure:

1. Sagar S. Patel, MD – Nothing to declare
2. Sagar Munjal, MD, MS is an employee of Ossium Health
3. Brian McClune DO – Nothing to declare
4. Lauren Lee, MD – Nothing to declare
5. Preethi Prasad MS is an employee of Ossium Health
6. Vicki L Graves MS is an employee of Ossium Health

7. Erik Woods PhD is an employee of Ossium Health
8. W. Scott Goebel, MD, PhD is a consultant to Ossium Health
9. Daniel Couriel, MD, MBA – Nothing to declare

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EFFICACY OF UNRELATED ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SEVERE APLASTIC ANEMIA: A SINGLE-CENTER RETROSPECTIVE STUDY OF 206 PATIENTS

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Background: Unrelated allogeneic hematopoietic stem cell transplantation (URD-HSCT) is an important treatment modality for aplastic anemia.

Methods: To evaluate its efficacy, this study retrospectively analyzed the clinical data of 206 patients with severe aplastic anemia (SAA) who underwent URD-HSCT at a single center between November 2012 and December 2024.

Results: The results showed that the median age was 28 years (range: 5–64 years), 57.3% were male, and 13.6% had received immunosuppressive therapy (IST) prior to transplantation. The median time to neutrophil and platelet engraftment was 12 days (range: 9–22 days / 8–55 days), respectively, and the graft failure rate was 3.4%. CD8+ T lymphocytes returned to normal levels by 2 months post-transplantation, CD19+ B cells by 6 months, and CD4+ T lymphocytes approached normal levels by 1 year. The cumulative incidence of grade II–IV acute graft-versus-host disease (aGVHD) was 21.7% (95% CI: 16.6%–27.8%), and that of chronic GVHD (cGVHD) was 20.4% (95% CI: 15.4%–26.6%). The primary cause of death was infection (64.7%, 11/17). Survival analysis revealed a 4-year overall survival (OS) rate of 91% for the entire cohort. Notably, the 4-year OS rate was significantly higher in the donor age ≤30 years group compared to the >30 years group (97% vs 85%, $P = 0.0028$), and in the HLA 10/10 matched group compared to the 9/10 matched group (95% vs 86%, $P = 0.023$). The optimal donor profile was defined as a donor aged ≤30 years with HLA 10/10 matching, which was associated with a 4-year OS of 98% compared to 88% in other groups ($P = 0.023$). Multivariate analysis identified male sex, donor age >30 years, and HLA 9/10 matching as independent risk factors for inferior OS, while donor age >30 years and HLA 9/10 matching were also independent risk factors for worse graft-versus-host disease-free, relapse-free survival (GRFS).

Conclusions: In conclusion, URD-HSCT is an effective treatment for SAA, and selecting an appropriate donor can significantly improve therapeutic outcomes.

Disclosure: Nothing to declare

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UMBILICAL CORD BLOOD MICROTRANSPLANTATION PLUS CHEMOTHERAPY FOR AML AND HIGH-RISK MDS POST-CR1

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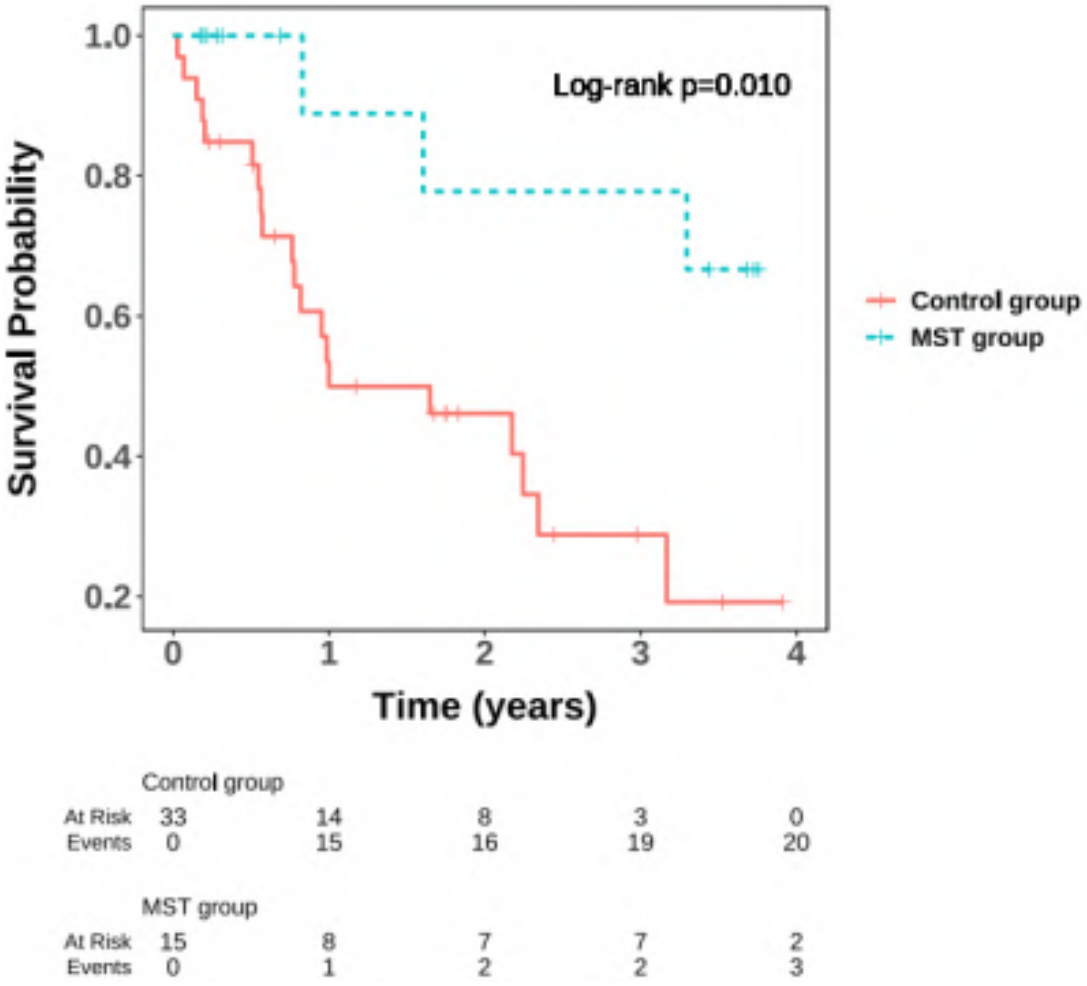
Background: Acute myeloid leukemia (AML) and high-risk myelodysplastic syndrome (HR-MDS) patients face high relapse risk after first induction complete remission.

Methods: This was a single-center retrospective study. A total of 48 patients with AML and HR-MDS who achieved first complete remission after induction therapy were enrolled and divided into MST combined with chemotherapy group (MST group, n=15) and chemotherapy alone group (control group, n=33). The primary endpoints were DFS and OS. Kaplan-Meier method was used for survival analysis, log-rank test was applied to compare differences between groups, and multivariate Cox regression model was employed to control for potential confounding factors.

Results: The MST group demonstrated significantly superior DFS: 1-year, 2-year, and 3-year DFS rates were 88.9%, 77.8%, and 77.8% respectively, compared to 50.0%, 46.1%, and 28.8% in the control group (p=0.010). Median DFS was not reached in the MST group versus 1.0 years in controls. Multivariate Cox analysis confirmed MST independently improved DFS (adjusted HR=0.24, 95% CI: 0.07-0.85, p=0.027). OS showed an improving trend: 3-year OS rates were 71.8% (MST) versus 34.9% (control), with median OS 3.9 years versus 1.9 years (p=0.064). Subgroup analysis revealed pronounced DFS benefit in patients ≥60 years (adjusted HR=0.11, p=0.039). No severe acute GVHD occurred; cord blood infusion was well tolerated with no serious adverse events.



Conclusions: Umbilical cord blood stem cell microtransplantation combined with chemotherapy significantly prolongs disease-free survival in AML and HR-MDS patients post-first complete remission, with a clear trend toward improved overall survival, particularly benefiting elderly patients. This strategy provides a safe, effective treatment option for patients ineligible for traditional allogeneic transplantation, supported by robust evidence for clinical practice.

Disclosure: **No declaration required**

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CLINICAL IMPACT OF IN-SILICO HISTOCOMPATIBILITY ALGORITHMS IN 9/10 MISMATCHED DONOR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATIO

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Background: Donor selection in 9/10 HLA-mismatched donor (MMD) allo-HCT remains challenging due to higher risks of GVHD and non-relapse mortality (NRM). In-silico histocompatibility models, including PIRCHE, HLA-B leader status, and immunopeptidome-based approaches, aim to refine donor–recipient matching beyond conventional HLA typing. However, comparative real-world evaluations integrating these tools in the MMD setting are limited.

Methods: We conducted a retrospective single-center study of 93 adults undergoing 9/10 MMD allo-HCT (2014–2024). Median age at transplant was 53 years. Median follow-up was 41.7 months (IQR 93.47) PIRCHE scores (class I/II, GVH/HVG directions), donor and recipient B-leader genotypes, and immunopeptidome mismatch categories were calculated for each pair. Outcomes included grade 3–4 aGVHD, cGVHD (overall and moderate–severe), incidence of relapse, NRM, PFS, GVHD-relapse-free survival (GRFS), and OS. Variables with $p<0.10$ in univariate analysis were evaluated in multivariable Cox or Fine-Gray models.

Results: Cumulative incidence of G3-4 aGVHD was 21.5% at 100 days. No clinical or immunogenetic variables predicted grade 3–4 acute GVHD. HCT-CI≥3 showed a trend toward increased risk (HR 1.86, 95% CI 0.86–4.06, p=0.12), while higher infused mononuclear cell dose (>9×10⁸/kg) showed a nonsignificant protective trend (SHR 0.35, 95% CI 0.11–1.14, p=0.081).
cGVHD developed in 36.6% of patients. In multivariable analysis, only recipient age >60 years remained independently associated with chronic GVHD (HR 2.73, 95% CI 1.19–6.31, p=0.018). When focusing on moderate–severe chronic GVHD, independent predictors included HLA-B allelic mismatch (HR 2.64, 95% CI 1.13–6.15, p=0.025), recipient HLA-B leader MM genotype (HR 5.66, 95% CI 1.31–24.41, p=0.020), and age>60 years (HR 3.70, 95% CI 1.22–11.19, p=0.021). PIRCHE-C score in the GvH direction>4.5 showed a borderline association (HR 2.46, 95% CI 0.89–6.78, p=0.082).
The cumulative incidence of relapse and NRM at last follow-up was 38.1% and 23.6%, respectively. In multivariable analysis, relapse was independently predicted by PIRCHE-B≥4.5 in GvH direction (HR 6.57, 95% CI 1.76–24.50, p=0.005) and PIRCHE-II≥17.5 in HvG direction (HR 3.22, 95% CI 1.34–7.70, p=0.0087). A higher infused mononuclear cell dose (>9×10⁸/kg) showed an unexpected association with relapse (HR 2.65, 95% CI 1.05–6.70, p=0.04).
None of the algorithm-derived parameters predicted NRM.
PFS was adversely impacted by DRI-very high risk (HR 6.80, 95% CI 2.18–21.28,

p=0.0009). GRFS was similarly impaired by DRI-very high risk (HR 4.29, 95% CI 1.44–12.81, p=0.009), while higher donor age also exerted an independent negative effect (HR 1.03 per year, 95% CI 1.00–1.05, p=0.025). OS was independently influenced by DRI-very high risk (HR 5.94, 95% CI 1.66–21.23, p=0.006), HCT-CI≥3 (HR 2.57, 95% CI 1.22–5.44, p=0.013), and donor age>35 years (HR 3.28, 95% CI 1.57–6.86, p=0.001), whereas no in-silico algorithm retained independent prognostic significance for OS.

Conclusions: In this 9/10 MMD cohort, in-silico histocompatibility algorithms provided outcome-specific prognostic information. PIRCHE-derived metrics independently predicted relapse, while HLA-B leader status was associated with chronic GVHD severity. NRM and survival outcomes were driven by established clinical factors. These findings support selective integration of immunogenetic algorithms into MMUD donor-selection strategies.

Disclosure: No

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INTRARENAL ARTERIAL INFUSION OF MESENCHYMAL STEM CELLS FOR THE TREATMENT OF TRANSPLANTATION-ASSOCIATED ACUTE RENAL FAILURE: A CASE REPORT

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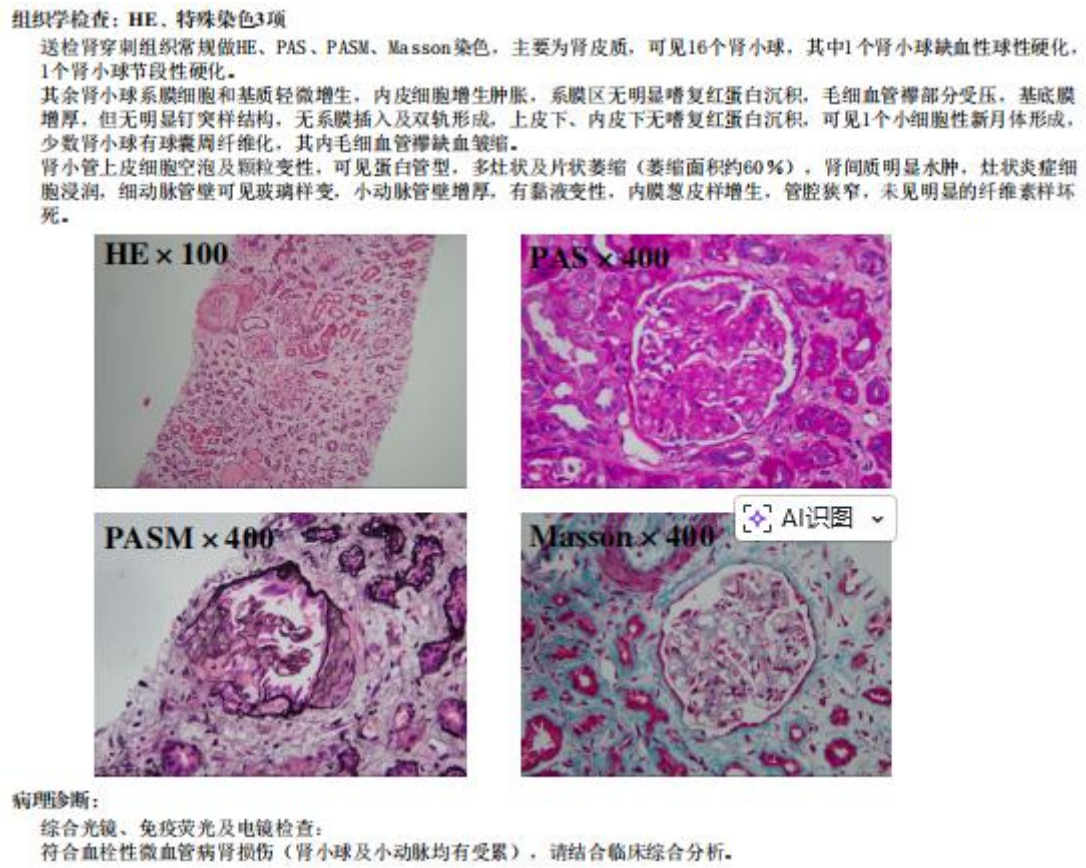
Background: Acute renal failure (ARF) is a severe complication of allo-HSCT. Its pathophysiology involves the necrosis of renal proximal tubular epithelial cells due to ischemic or toxic injury. This subsequently triggers a cascade of events including loss of autoregulation, tubular obstruction, and exacerbated renal vasoconstriction, ultimately resulting in a sudden decline in the glomerular filtration rate (GFR).Currently available treatments primarily consist of renal replacement therapy (e.g., dialysis) and kidney transplantation. However, these approaches are expensive, require ongoing maintenance, and the procurement of donor organs is challenging. Consequently, there is an urgent clinical need to identify novel, safe, and effective therapies for ARF.

Methods: A 14-year-old boy was diagnosed with chronic active Epstein-Barr virus disease. Genetic testing revealed multiple germline mutations (TCS2, ATM, BAX, CASP10, IRF7, FAT4, LCK). Following immunochemotherapy and chemotherapy (CHOP and ESCAP), he underwent allogeneic hematopoietic stem cell transplantation from a 9/10 HLA-matched unrelated Chinese donor on June 16, 2023. EBV-DNA turned negative by day +3 post-transplantation, and neutrophil and platelet engraftment were achieved by day +20. However, around day +50, the patient developed pancytopenia (WBC 2.57×10^9/L, HGB 78 g/L, PLT 51×10^9/L), followed by hypertension, proteinuria, and an increase in schistocytes (6%-9%). With progressive elevation of LDH, transplantation-associated thrombotic microangiopathy (TA-TMA) was diagnosed according to the Harmonization Panel Consensus criteria. Despite

treatment with defibrotide and plasma exchange, his condition deteriorated rapidly, progressing to acute renal failure. Concurrently, he experienced transient blindness, and magnetic resonance imaging of the head led to a diagnosis of posterior reversible encephalopathy syndrome. Hemodialysis was initiated on day +98 due to anuria, initially performed every other day. After two months of dialysis, some experts considered renal transplantation necessary.
Given the regenerative and immunomodulatory properties of mesenchymal stem cells (MSCs) and the limitation that intravenous infusion leads to significant pulmonary sequestration with minimal renal delivery, we proposed intrarenal arterial infusion of MSCs. After detailed discussion, the patient and his family provided informed consent. Consequently, on day +130, umbilical cord blood-derived MSCs were administered via renal artery interventional radiology, once every other week for a total of four infusions(one course). Following the third infusion, urine output began, initially at 30 mL/day and gradually increasing. After completing the four infusions, urine output exceeded 300 mL/day. We then progressively extended the dialysis intervals: to twice weekly, then once weekly as urine output continued to increase, to twice monthly after two months, and once monthly after four months when urine output reached approximately 2000 mL/day. Dialysis was completely discontinued eight months post-MSC therapy. No other major treatment adjustments were made during this period. We believe that if the TA-TMA was not self-limiting, the renal recovery observed in this patient is likely associated with the intrarenal arterial MSC infusion.

Results: Kidney biopsy 3 months after intrarenal arterial infusion of MSC



Conclusions: Currently, the patient is 2.5 years post-transplantation, continues to take antihypertensive medication orally, and has returned to school. Although his renal function has not fully normalized, it has not impacted his daily life or studies.

Disclosure: Nothing to declare.

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CLINICAL STUDY OF AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION PLUS UMBILICAL CORD BLOOD STEM CELL TRANSPLANTATION FOR THE RELAPSED AND REFRACTORY DIFFUSE LARGE B-CELL LYMPHOMA

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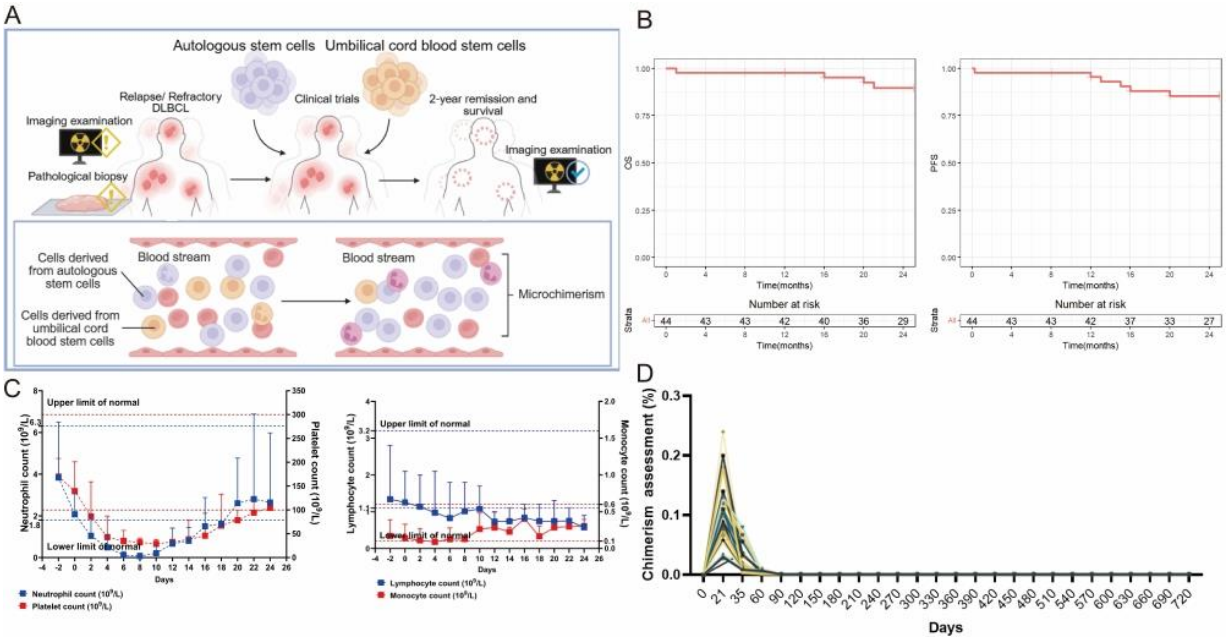
Background: Autologous hematopoietic stem cell transplantation (auto-HSCT) depends on conditioning for the maximal elimination of lymphoma cells to attain long-term survival. In the absence of the graft-versus-tumor (GVT) of allogeneic hematopoietic stem cell transplantation (allo-HSCT), auto-HSCT results in a 50–60% recurrence rate for MRD-positive or chemotherapy-resistant relapsed/refractory diffuse large B-cell lymphoma (R/R DLBCL). Is it possible to establish a new transplantation model to achieve the dual efficacy of auto-HSCT and allo-HSCT? Human umbilical cord blood stem cells (hUCBSCs) are a potential option for exerting the GVT effect with low immunogenicity, robust immune reconstitution and good biosafety. This study aims to evaluate the efficacy and safety of auto-HSCT combined with unrelated hUCBSCs infusion in the treatment of R/R DLBCL.

Methods: This single-center, single-arm prospective clinical trial recruited patients with R/R DLBCL confirmed in tertiary grade A hospitals in China. Participants received unrelated hUCBSCs infusion on Day 2 after auto-HSCT. The unrelated hUCBSCs units must satisfy the requirement of HLA matching ≥ 5/10 loci and blood type-compatible units will be prioritized for selection. Unrelated hUCBSCs was infused as a single dose, with the total nucleated cell (TNC) count ranging from 5 - 15 × 10^8 and $CD34^+$ cell count from 1.5 - 3.5 × 10^6. The BEAM conditioning included carmustine (300 mg/m^2), etoposide (200 mg/m^2), cytarabine (300 mg/m^2), and melphalan (140 mg/m^2). Primary endpoints were 2-year overall survival (OS), relapse-free survival (RFS) and progression-free survival (PFS); secondary endpoints included neutrophil and platelet engraftment times.

Results: A total of 44 patients were enrolled in this study from September 27, 2023 to November 27, 2023. The median age was 37 years (range, 18–65 years), including 20 males and 24 females. Among these patients, 23 cases (55.6%) were relapsed and 21 cases (44.4%) were refractory. The percentage of cells derived from unrelated hUCBSCs in peripheral blood remained below 0.01% after 90 days. The 2-year overall survival (OS) rate was 90.9%, and the 2-year progression free survival (PFS) rate was 86.3%, with the median survival time not reached. The median time to neutrophil engraftment was 11 days (range, 10–21 days), and the median time to platelet engraftment was 14 days (range, 12–31 days).



Conclusions: The findings of this study suggest that auto-HSCT combined with unrelated hUCBSCs infusion markedly enhances patients' quality of life. Further validation of the regimen's feasibility will rely on an expanded patient cohort and prolonged follow-up for in-depth assessment.

Disclosure: Nothing to declare.

A188

POST-TRANSPLANT MONITORING OF NGS-BASED MINIMAL RESIDUAL DISEASE AND DONOR CHIMERISM AS A PROGNOSTIC TOOL IN OLDERLY PATIENTS WITH AML/MDS

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Background: Next-generation sequencing (NGS)-based monitoring of minimal residual disease (MRD) and complete donor chimerism status plays a critical role in predicting post-transplant survival outcomes in patients with acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Compared to traditional techniques such as flow cytometry or quantitative PCR, NGS offers superior sensitivity in detecting MRD, enabling earlier identification of residual leukemic cells. The prognostic accuracy can be further

enhanced by integrating donor chimerism analysis, allowing for early risk stratification and timely intervention.

Methods: This retrospective study analyzed clinical outcomes of 113 patients with AML or MDS who underwent reduced-intensity conditioning (RIC) allogeneic hematopoietic stem cell transplantation (allo-HSCT) between January 2018 and May 2025. Eligible patients were aged ≥60 years, or ≥55 years if considered ineligible for standard-intensity SCT. Post-transplant monitoring included NGS-based MRD testing and assessment of donor chimerism at 2–3 months post-transplant.

Results: A total of 31 patients (27.4%) had MRD-positive results after transplantation. MRD positivity was significantly associated with reduced overall survival (OS) (hazard ratio [HR], 4.705; P < .001). Full donor chimerism (FDC) was observed in 82 patients (72.6%), and these patients had improved OS compared to those with mixed donor chimerism (HR, 0.361; P = .002). Based on MRD and chimerism status during post-transplant follow-up, patients were stratified into four groups: (1) MRD(−)/FDC(+), (2) MRD(−)/FDC(-), (3) MRD(+)/FDC(+), (4) MRD(+)/FDC(-).
Disease status before hematopoietic stem cell transplantation (HSCT) differed significantly (P < 0.001), with fewer patients in the MRD(+) groups achieving complete remission prior to transplantation. High-risk HCT-CI scores were more common in the MRD(+) groups (P < .001). MRD positivity prior to HSCT seemed to be more frequently observed among patients who remained MRD-positive post-transplant (P=0.169). There were no significant differences in the incidence of major post-transplant complications among the groups. In survival analysis, non-relapse mortality (NRM) at 100 days was significantly higher in the MRD(−)/FDC(+) group (P=0.004). Relapse rates differed markedly among the groups (P<0.001), as did overall mortality (P<0.001). The MRD(+)/FDC(-) group had the poorest prognosis, characterized by the highest relapse rate and lowest OS. In multivariate Cox regression analysis, both MRD positivity and incomplete donor chimerism at 3 months post-transplant were independently associated with inferior survival outcomes.

Conclusions: Integrated post-transplant monitoring of NGS-based MRD and donor chimerism is a critical prognostic tool in elderly AML/MDS patients undergoing RIC allo-HSCT. Early identification of MRD positivity or mixed chimerism can facilitate timely risk-adapted interventions. In patients with high-risk post-transplant molecular profiles, preemptive strategies such as donor lymphocyte infusion (DLI) may be considered to reduce relapse risk and improve long-term outcomes.

Clinical Trial Registry: None.

Disclosure: All presenting authors declare that we have no conflicts of interest, including specific financial interests and relationships and affiliations.

A189

PTCY VERSUS ATLG IN ALLOGENEIC HSCT FOR ACUTE LEUKEMIA WITH HIGH DISEASE BURDEN: A REAL-WORLD STUDY

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the primary curative treatment for relapsed or refractory acute leukemia. However, patients with non-remission still face high post-transplant relapse rates and transplant-related mortality. For graft-versus-host disease (GVHD) prophylaxis, the PTCY (Baltimore protocol) and Beijing protocol (G-ATG-based combination regimen) are commonly used, but systematic studies comparing the efficacy of ATLG and PTCY are lacking.

Methods: We retrospectively analyzed patients with non-remission acute leukemia who underwent allo-HSCT at Peking University Aerospace Clinical Medical College between 2020 and 2024. A total of 275 patients were included, with 229 in the ATLG group (83.3%) and 46 in the PTCY group (16.7%). Baseline imbalances were adjusted using inverse probability of treatment weighting (IPTW), and a multivariate model was further applied to account for residual confounding. Outcome measures included overall survival (OS), disease-free survival (DFS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM), and acute/chronic GVHD (aGVHD/cGVHD).

Results: Compared with the ATLG group, the PTCY group had significantly shorter 5-year OS (HR=1.88, 95% CI: 1.02–3.46, P=0.043) and a trend toward shorter 5-year DFS (HR=1.66, 95% CI: 0.98–2.82, P=0.059). Competing risk analysis showed that the PTCY group had significantly higher 5-year CIR (SHR=1.49, 95% CI: 1.04–2.14, P=0.031) and NRM (SHR=1.55, 95% CI: 1.03–2.34, P=0.035). There were no significant differences in the incidence of aGVHD (SHR=1.23, 95% CI: 0.77–1.95, P=0.38) or 5-year cGVHD (SHR=0.51, 95% CI: 0.20–1.32, P=0.17) between the two groups.

Conclusions: For GVHD prophylaxis, PTCY and ATLG have comparable efficacy in reducing GVHD risk. However, the PTCY group was associated with lower OS and DFS, as well as higher CIR and NRM. Due to the small sample size of the PTCY group, these findings require further validation.

Disclosure: Nothing to declare.

A190

ADMISSION TO INTENSIVE CARE UNIT (ICU) OF ADULT HEMATOPOIETIC TRANSPLANT RECIPIENTS: SINGLE CENTER EXPERIENCE

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Background: Hematopoietic stem cell transplantation (HSCT) can entail significant morbidity during the procedure. Published series in HSCT report a range of ICU admission rates from 24-25% of transplant patients and is associated with poor prognosis (75% mortality rate). Most frequent reasons involve respiratory failure, septic shock, and veno-occlusive disease. The aim of this study was to analyze outcome of HSCT patients requiring ICU admission in our center.

Methods: We retrospectively analysed outcomes of 903 patients who underwent HSCT in our centre from January/2008 to June/2025. Data were collected from patients' clinical records.

Results:

Median age (range)	52 (20 – 70)
Sex: male/female	79 (60%) / 53 (40%)
Underlying disease: - AML /ALL / MDS **-** Myeloma / NHL / HL/ Other	48 (36%) / 16 (12%) / 23 (17%) 9 (7%) / 13 (10%) / 6 (5%) / 17 (13%)
Type of HSCT: **- Allogeneic:** Sibling donor / Unrelated donor / Haploidentical **- Autologous**	**111 (84%)** 40 (30%) / 49 (37%) / 22 (17%) **21 (16%)**
Conditioning regimen: Myeloablative / RIC	98 (74%) / 34 (26%)
GVHD: acute/chronic	40 (30%) / 6 (5%)

Table 1. Patients' basal characteristics.

Of the 903 HSCT recipients, 122 (14%) required ICU admission (baseline and HSCT characteristics on table). Median time to ICU admission was 46 days (–2-1765). Ten of these patients required two ICU admissions, resulting in a total of 132 ICU admissions available for analysis.

Main reason for ICU admission was respiratory distress (86; 65%), mainly due to pneumonia (51%) (43% caused by gram-negative bacteria and only 3% by COVID-19), pulmonary edema (26%) and pulmonary hemorrhage (8%). Septic shock was second most common cause of ICU admission (37; 28%), attributed to gram-negative bacilli (52%), fungal (16%), gram-positive (15%), virus (10%), and others/idiopathic (17%).

Other less frequent causes included veno-occlusive disease (11; 8%), hemorrhagic complications (8; 6%), encephalopathy (7; 5%), cardiogenic shock (4%), graft-versus-host disease (2%), and one case of cardiorespiratory arrest due to vasospastic angina.

During the 132 ICU admissions, 78 patients (59%) died in the ICU, of these, 27 had received unrelated donor HSCT, 26 sibling donor, 12 haploidentical and 13 autologous. Median ICU length of stay was 9 days (1–82). In addition, 54 patients (41%) required hemofiltration and 92 (70%) required endotracheal intubation; 43 patients (33%) required both interventions,

of whom only 6 survived the ICU admission.
Of the 132 admissions, 76 (58%) occurred during the pre-engraftment period, with the remainder taking place post-engraftment. These admissions had a median ICU stay of 13 days (1–76) and a mortality rate of 64% (49/76). Mortality was higher among allogeneic HSCT recipients (82%). The cause of death was the same reason for ICU admission. Eight patients (10.5%) were discharged from the ICU but died before hospital discharge, whereas 19 were ultimately discharged home; among these, 11 patients (15%) remain alive, while the remaining 8 (10.5%) died due to disease progression or complications post-HSCT.

Conclusions: In our study, 14% of hematopoietic stem cell transplant recipients were admitted to the ICU, a low percentage compared to the literature and associated with higher survival rates, with an in-ICU mortality rate of 59%. Higher death rate was observed in allogeneic transplantation and those requiring aggressive ICU treatments such as mechanical ventilation or haemodialysis. The most common cause of admission was respiratory failure, similar to published series. Therefore, although admission to the ICU after HSCT is associated with a poor prognosis, it should be considered, as it may improve survival.

Disclosure: Nothing to declare.

A191

DETERMINANTS OF GVHD AND SURVIVAL AFTER HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA: A SINGLE-CENTER ANALYSIS OF 169 PATIENTS

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) , including haploidentical transplantation combined with third-party unrelated cord blood (haplo-cord HSCT) and intensified BU+MEL/TT-based conditioning, is a widely used curative approach for acute myeloid leukemia (AML), yet post-transplant outcomes remain heterogeneous. Identifying independent determinants of GVHD, viral reactivation, and long-term survival is critical for optimizing transplant strategies.

Methods: We retrospectively analyzed 169 consecutive AML patients undergoing first haplo-HSCT at our center, all treated with a uniform Bu/Cy–based myeloablative conditioning and standardized GVHD prophylaxis. Multivariable Cox and competing-risk analyses were used to identify independent predictors of survival, GVHD, relapse, and viral reactivation.

Results: The median age was 14 years (IQR, 3–34), and 55.0% were male. Haplo-cord transplantation was performed in 76.3% of patients, while 23.7% received haplo-HSCT alone. HLA matching was 5/10 in 64.5% and ≥6/10 in 35.5%. BU+MEL/TT-based intense conditioning was used in 84.0%, and 60.4% received anti-CD25 monoclonal antibody. Pre-

transplant MRD positivity was observed in 41.4%. At transplantation, 68.1% were in CR1, 16.0% in ≥CR2, and 16.0% in NR/PR. Median infused cell doses were 16.01×10⁸/kg for MNCs, 9.27×10⁶/kg for CD34⁺ cells, and 3.37×10⁸/kg for CD3⁺ cells. Median neutrophil and platelet engraftment occurred at 14 and 11 days, respectively.

With a median follow-up of 3.4(0.1- 10.9）years, multivariable analyses demonstrated that disease status at transplantation was the dominant determinant of post-transplant outcomes. Compared with CR1, patients transplanted in NR/PR had significantly inferior OS (HR 5.58, 95% CI 2.17–14.3; P<0.001) and LFS (HR 5.45, 95% CI 2.12–13.9; P<0.001), along with a markedly increased risk of NRM (HR 4.67, 95% CI 1.53–14.3; P=0.007). HLA matching, donor source, and age showed no independent impact on long-term survival. Haplo-cord transplantation showed a trend toward improved OS and LFS after adjustment, although statistical significance was not reached (Figure 1).

For GVHD, BU+MEL/TT-based intense conditioning was independently associated with a reduced incidence of grade II–IV (HR 0.32, 95% CI 0.14–0.74; P=0.008) and grade III–IV aGVHD (HR 0.26, 95% CI 0.08–0.82; P=0.022). NR/PR status significantly increased the risk of grade III–IV aGVHD (HR 5.11, P=0.039). Use of unrelated cord blood grafts and higher infused CD34⁺ cell dose (>9×10⁶/kg) were associated with a lower incidence of grade II–IV aGVHD. No transplant-related variables were independently associated with CMV or EBV DNAemia (Figure 1).

Figure 1. Multivariable Cox and competing-risk analyses results to identify independent predictors of survival, GVHD, relapse, and viral reactivation.

Variables	*3-4 aGVHD*		*2-4 aGVHD*		*CMV*		*EBV*	
	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*
CR1(reference)								
≥CR2	1.09(0.30-3.89)	*0.900*	0.46(0.14-1.58)	*0.220*	0.78(0.42-1.45)	*0.440*	1.29(0.34-4.84)	*0.710*
NR/PR	5.11(1.08-24.0)	*0.039*	2.74(0.97-7.78)	*0.058*	1.20(0.62-2.32)	*0.580*	0.36(0.04-2.84)	*0.330*
MRD(Neg vs. Pos)	0.35(0.08-1.52)	*0.160*	0.74(0.29-1.87)	*0.530*	0.96(0.59-1.57)	*0.880*	1.16(0.35-3.88)	*0.810*
age(≤14 vs.＞14)	0.62(0.23-1.65)	*0.340*	0.66(0.33-1.32)	*0.240*	1.04(0.61-1.77)	*0.890*	0.58(0.14-2.48)	*0.460*
BU+MEL/TT(No vs.Yes)	0.26(0.08-0.82)	*0.022*	0.32(0.14-0.74)	*0.008*	0.90(0.51-1.59)	*0.700*	2.41(0.28-20.5)	*0.420*
CD25(No vs.Yes)	1.07(0.40-2.84)	*0.900*	0.96(0.43-2.16)	*0.920*	1.42(0.86-2.34)	*0.170*	0.67(0.18-2.48)	*0.540*
HLA(5/10 vs.≥6/10)	0.37(0.12-1.16)	*0.089*	0.37(0.15-0.89)	*0.026*	0.84(0.53-1.33)	*0.450*	0.96(0.34-2.67)	*0.930*
UCB (No vs.Yes)	0.35(0.11-1.10)	*0.072*	0.38(0.16-0.92)	*0.031*	0.92(0.52-1.62)	*0.780*	1.52(0.31-7.33)	*0.600*
CD34(≤9 vs.＞9)	0.88(0.37-2.11)	*0.780*	0.52(0.28-0.97)	*0.038*	1.00(0.65-1.53)	*1.000*	1.11(0.39-3.17)	*0.840*
CD3(≤3.5 vs.＞3.5)	0.79(0.30-2.07)	*0.630*	0.93(0.49-1.80)	*0.840*	0.96(0.59-1.56)	*0.850*	0.69(0.21-2.30)	*0.550*

Variables	*OS*		*LFS*		*RI*		*NRM*	
	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*	HR(95% CI)	*p-value*
CR1(reference)								
≥CR2	0.62(0.20-1.88)	*0.397*	0.62(0.20-1.88)	*0.398*	0.80(0.05-13.4)	*0.880*	0.49(0.13-1.86)	*0.300*
NR/PR	5.58(2.17-14.3)	*0.000*	5.45(2.12-13.9)	*0.000*	1.17(0.21-6.42)	*0.850*	4.67(1.53-14.3)	*0.007*
MRD(Neg vs. Pos)	0.95(0.40-2.26)	*0.899*	0.96(0.40-2.29)	*0.931*	5.36(0.90-31.9)	*0.066*	0.89(0.32-2.45)	*0.820*
age(≤14 vs.＞14)	1.26(0.60-2.67)	*0.543*	1.23(0.58-2.60)	*0.585*	0.29(0.06-1.46)	*0.130*	1.37(0.68-2.75)	*0.380*
BU+MEL/TT(No vs.Yes)	0.61(0.26-1.40)	*0.245*	0.61(0.26-1.40)	*0.244*	0.65(0.03-14.8)	*0.790*	0.69(0.30-1.59)	*0.380*
CD25(No vs.Yes)	0.65(0.31-1.35)	*0.248*	0.65(0.31-1.35)	*0.246*	0.26(0.03-2.42)	*0.240*	0.69(0.32-1.49)	*0.350*
HLA(5/10 vs.≥6/10)	1.20(0.65-2.20)	*0.567*	1.19(0.65-2.19)	*0.579*	1.32(0.40-4.40)	*0.650*	1.17(0.60-2.28)	*0.660*
UCB (No vs.Yes)	0.63(0.29-1.37)	*0.243*	0.61(0.28-1.33)	*0.217*	0.79(0.13-4.95)	*0.800*	0.72(0.29-1.79)	*0.480*
CD34(≤9 vs.＞9)	0.84(0.41-1.69)	*0.618*	0.85(0.42-1.71)	*0.641*	7.20(1.54-33.7)	*0.012*	0.69(0.32-1.49)	*0.340*
CD3(≤3.5 vs.＞3.5)	0.68(0.33-1.42)	*0.308*	0.67(0.32-1.39)	*0.284*	0.50(0.11-2.24)	*0.360*	0.69(0.32-1.49)	*0.340*

Conclusions: Haplo-HSCT in CR remains the most critical determinant of survival in AML. BU+MEL/TT-based intense conditioning, higher CD34⁺ cell dose, and haplo-cord transplantation confer protective effects against aGVHD, with a favorable trend toward

improved survival. These findings provide clinically relevant evidence for risk-adapted transplant optimization in AML patients undergoing haplo-HSCT.

Disclosure: Nothing to declare.

A193

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR THERAPY-RELATED MYELOID NEOPLASMS: LONG-TERM OUTCOMES AND PROGNOSTIC DETERMINANTS FROM A SINGLE-CENTER COHORT

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Background: Therapy-related acute myeloid leukemia or myelodysplastic syndromes (t-AML/MDS) arise after exposure to cytotoxic chemotherapy and/or radiation therapy, and represent a biologically and clinically distinct entity from de novo AML/MDS. Although allogeneic hematopoietic cell transplantation (HCT) has expanded in this population over the past decade, data on post-HCT outcomes and prognostic factors remain limited. We aimed to evaluate HCT outcomes and identify prognostic factors in patients with t-AML/MDS.

Methods: We retrospectively analyzed 1,626 patients with AML or MDS who underwent HCT at Asan Medical Center between 2005 and 2024, including 86 patients with t-AML/MDS. Clinical data were obtained from the Asan Medical Center HCT registry and medical records.

Results: The t-AML/MDS cohort consisted of 53 patients with t-AML and 33 patients with t-MDS. Patients with t-AML/MDS were younger than those with de novo AML/MDS (median age, 50 vs. 54 years, P=0.024), but had a higher HCT-comorbidity index score (median, 4 vs. 3; P<0.001), and a higher frequency of adverse-risk cytogenetics at diagnosis (59.4% vs. 35.3%, P=0.039). The median latency from prior cancer and t-AML/MDS diagnosis was 50.5 months (range, 4.0-299.6 months).
5-year event-free survival (EFS) rate post HCT was significantly inferior in t-AML/MDS compared with de novo AML/MDS (31.8% vs 42.7%, P=0.033), whereas overall survival (OS) did not differ between the two groups (46.2% vs. 41.1% at 5 years, P=0.255). Within the t-MDS/AML cohort, OS and EFS were comparable between t-MDS and t-AML (P=0.631 and P=0.743, respectively).
In univariate analysis, a lower mutational burden (0-1 mutations) on targeted next generation sequencing was associated with superior OS (P=0.027) and showed a trend toward improved EFS (P=0.086). In multivariate analysis, prior cancer types was independent prognostic factor; antecedent AML or lymphoma was associated with significantly superior OS and EFS (hazard ratio [HR], 0.364, P=0.007; HR 0.338, P=0.003, respectively), and prior breast cancer with improved OS (HR, 0.479, P=0.036), compared with other solid cancers showed significantly better survival. Poor performance status (Karnofsky score ≤ 80, HR for OS, 4.401, P=0.021), high-risk disease status at HCT (HR for

OS, 1.949, P=0.929; HR for EFS, 1.851, P=0.033, respectively), and older age (≥ 60 years, HR for EFS, 1.926, P=0.023) were independently associated with inferior post-HCT outcomes.

Conclusions: Allogeneic HCT provides comparable long-term OS in patients with t-AML/MDS and denovo AML/MDS despite inferior EFS in the t-AML/MDS setting. Post-HCT outcomes in t-AML/MDS are strongly influenced by antecedent cancer type, performance status, disease risk at HCT, and age. These findings support refined risk stratification and individualized HCT strategies for patients with t-AML/MDS.

Disclosure: Nothing to disclose.

A194

EFFICACY AND SAFETY OF COMBINING BCL-2 INHIBITORS WITH HYPOMETHYLATING AGENTS IN PATIENTS WITH ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROME AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a cornerstone treatment for patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). However, disease relapse occurs in approximately 50% of AML patients in the post-transplant period. With current salvage therapies, long-term overall survival rates remain poor, ranging from 10% to 20%. Consequently, relapse is now one of the leading causes of treatment failure in AML and MDS patients after allo-HSCT. This has prompted active investigation into both maintenance therapy for patients who are minimal residual disease (MRD)-negative after allo-HSCT and preemptive therapy upon MRD detection. Additionally, efforts are ongoing to identify the most rational and effective treatment strategies to reduce relapse risk in high-risk AML patients following allo-HSCT.
Aim: To evaluate the efficacy and safety of maintenance and preemptive therapy using selective BCL-2 inhibitors in combination with hypomethylating agents in high-risk patients with AML or MDS after allo-HSCT.

Methods: This study included 37 patients who had undergone allo-HSCT: 32 with AML and 5 with MDS. Patient characteristics are summarized in Table 1.

Table 1. Clinical and demographic characteristics of patients (n=37)

Parameter	Characteristics

Sex, n (%)	
Male/Female	8 (21.6)/29 (78,4)
Age, years	
Median (range)	47 (21-66)
Diagnosis, n	
AML/MDS	32/5
Disease status of AML at allo-HSCT, n	
First complete remission (CR1)/Second complete remission (CR2)	22/10
Pre-transplant MRD status in AML, n	
MRD-positive/MRD-negative	15/17
Post-transplant MRD status in AML (pre-therapy), n	
MRD-positive/MRD-negative	7/25
Time from allo-HSCT to therapy initiation, days	
Median (range)	98 (34–264)
Number of therapy cycles	
Median (range)	6 (1–17)
Follow-up from therapy initiation, days	
Median (range)	205 (20-675)

After allo-HSCT (median time to therapy initiation, 98 days) patients received a BCL-2 inhibitor (venetoclax 200 mg/day) on days 1–5 of each cycle in combination with a hypomethylating agent — either azacitidine (32 mg/m²) or decitabine (10 mg/m²) — on days 1–3. Donor lymphocyte infusion (DLI) was additionally administered in 9 patients (1–2 infusions).

Results:

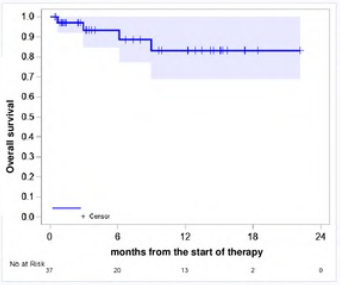

Fig. 1. Overall survival of patients with AML and MDS after allo-HSCT during therapy with selective BCL-2 inhibitors in combination with hypomethylating agents

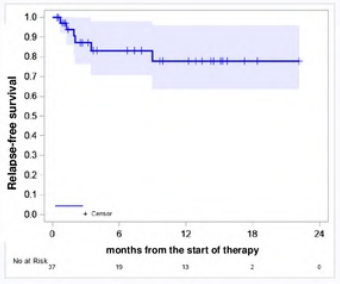

Fig. 2. Relapse-free survival of patients with AML and MDS after allo-HSCT during therapy with selective BCL-2 inhibitors in combination with hypomethylating agents

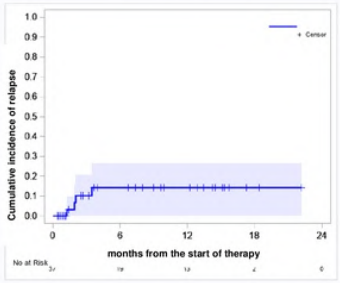

Fig. 3. Cumulative incidence of relapse in patients with AML and MDS after allo-HSCT during therapy with selective BCL-2 inhibitors in combination with hypomethylating agents

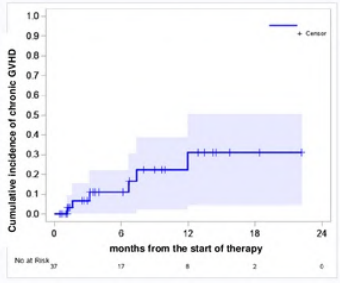

Fig. 4. Cumulative incidence of chronic GVHD in patients with AML and MDS after allo-HSCT during therapy with selective BCL-2 inhibitors in combination with hypomethylating agents

At the time of analysis, 33 patients remained alive. Disease relapse occurred in four AML patients: the median time to relapse after allo-HSCT was 125 days (range: 84–219 days), and from initiation of therapy it was 60 days (range: 38–106 days). Two patients died due to infectious complications. No cases of acute graft-versus-host disease (GvHD) of grade II–IV were observed following the start of maintenance therapy. Chronic GvHD developed in five patients, with a 12-month cumulative incidence of 31% after allo-HSCT. Hematologic toxicity (grade II–IV) was observed in four patients. The 12-month relapse-free survival rate after allo-HSCT was 78%, and the cumulative incidence of relapse was 14%.

Conclusions: Preliminary results suggest that maintenance and preemptive therapy with selective BCL-2 inhibitors combined with hypomethylating agents is both effective and well-

tolerated in high-risk patients with AML or MDS following allogeneic hematopoietic stem cell transplantation.

Clinical Trial Registry: -

Disclosure: Nothing to declare.

A195

SECONDARY MYELODYSPLASTIC SYNDROME AFTER CAR-T THERAPY: AN EMERGING LATE TOXICITY

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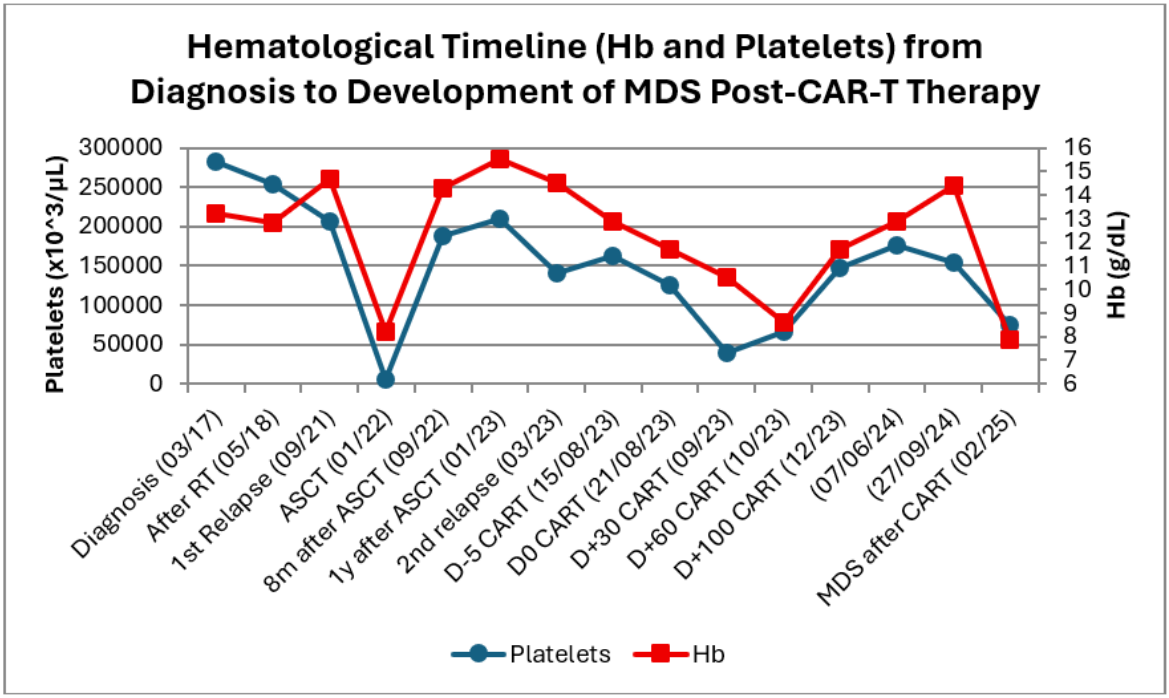
Background: Persistent cytopenias and secondary myeloid neoplasms are increasingly recognized as late complications following chimeric antigen receptor T-cell(CAR-T) therapy. However, available evidence remains limited and largely derived from isolated case reports and small series.

Methods: We performed a structured literature review of myelodysplastic syndromes(MDS) occurring after CAR-T therapy, searching publications from 2016 to 2025 in PubMed/MEDLINE, Scopus, and Embase. A total of 48 cases describing new-onset myeloid neoplasms following CAR-T therapy were included. Clinical, epidemiological, cytogenetic/molecular, and outcome data were extracted, including demographics, underlying malignancy, prior therapies, CAR-T product/target, latency to diagnosis, cytogenetic and next-generation sequencing findings, and clinical outcomes. In addition, we report a case from our institution of a patient diagnosed with high-risk MDS following CAR-T therapy.

Results: Among reported cases, 56.5%(13/23) were male, with a median age of 57 years (range, 6–78). The most common underlying malignancy was diffuse large B-cell lymphoma or high-grade B-cell lymphoma (63.2%, 24/38), followed by acute lymphoblastic leukemia (15.8%, 6/38), multiple myeloma (13.2%, 5/38), follicular lymphoma (5.3%, 2/38), and mantle cell lymphoma (2.6%, 1/38). Prior autologous HSCT was reported in 55.0%(22/48) and allogeneic HSCT in 12.5%(6/48) of patients. Anti-CD19 CAR-T products predominated (82.1%, 32/39). The median time to cytopenia onset was 8 months (range, 1–78). MDS was developed in 79.5%(35/44), acute myeloid leukemia (AML) in 9.1% (4/44), MDS/AML overlap in 4.5%(2/44), clonal cytopenia of undetermined significance (CCUS) in 4.5%(2/44), and myeloid sarcoma in 2.3% (1/44). Cytogenetic and/or molecular data were available in 47.9%(23/48). The most frequent non–mutually exclusive alterations included TP53 mutations (53.6%, 15/28), complex karyotype (42.9%, 12/28), chromosome 7 abnormalities [−7/del(7q)](28.6%, 8/28), and DNMT3A mutations(25.0%, 7/28). Among cases with available risk stratification, high or very high-risk disease predominated (69.2%, 9/13). Reported mortality reached 59.1%.
We report a 70-year-old male with follicular lymphoma grade 3B, relapsed after three prior lines of therapy including autologous HSCT, who achieved a complete metabolic response

after CAR-T therapy (tisagenlecleucel) despite developing grade 1 cytokine release syndrome(CRS) and grade 4 immune effector cell–associated neurotoxicity syndrome(ICANS). Eighteen months after CAR-T, he developed progressive cytopenias and was diagnosed with high-risk therapy-related myelodysplastic syndrome(t-MDS). Bone marrow evaluation revealed marked hypoplasia, dysmegakaryopoiesis, 7q deletions, and a TP53 mutation. The patient was initiated on azacitidine, with treatment delays due to intercurrent clinical complications, and after three cycles, follow-up molecular assessment demonstrated clonal evolution, including clearance of the initial TP53 mutation and the emergence of additional TP53 variants, as well as NF1 and PPM1D mutations, consistent with treatment-related selective pressure. He remains on azacitidine without evidence of AML transformation as of November 2025.



Conclusions: Secondary myeloid neoplasms after CAR-T therapy, although rare, are frequently associated with high-risk biological features, particularly TP53 alterations, as demonstrated in our review and illustrated by our case of high-risk TP53-mutated MDS. These findings underscore the importance of close and long-term hematologic monitoring following CAR-T therapy. In the future, pre–CAR-T clonal hematopoiesis screening and risk assessment tools integrating clinical and molecular variables may represent strategies to identify patients at higher risk and guide surveillance.

Disclosure: Nothing to declare.

A196

EARLY CYCLOSPORINE TAPERING AND PROPHYLACTIC DONOR LYMPHOCYTE INFUSION FOR POST-TRANSPLANT IMMUNOMODULATION IN HIGH-RISK HEMATOLOGIC MALIGNANCIES: A SINGLE-CENTER FEASIBILITY STUDY

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Background: Relapse remains the principal cause of treatment failure after allogeneic hematopoietic stem cell transplantation (allo-HSCT) in patients with high-risk hematologic malignancies. Early post-transplant immunomodulation (IM), based on accelerated cyclosporine tapering and prophylactic donor lymphocyte infusion (DLI), has been proposed as a strategy to enhance graft-versus-leukemia (GVL) effects, although its adoption in routine clinical practice is challenging due to concerns regarding feasibility and toxicity. Evaluating the feasibility of IM strategies and their potential impact on relapse and survival outcomes is clinically relevant.

Methods: We retrospectively analyzed two high-risk allo-HSCT cohorts treated at a single center (Table 1). Group A (IM cohort, n=35; 2022–2025) underwent cyclosporine tapering starting around day +60 followed by scheduled prophylactic DLIs from approximately from day +120. Group B (historical non-IM cohort, n=33; 2017–2021) received standard immunosuppressive management. Median follow-up was 1010 days. High-risk criteria included MRD-positive AML/ALL, ELN high-risk AML, active MDS/MPN, or lymphoma in partial remission. The primary endpoint was the feasibility of the IM program; secondary endpoints included the cumulative incidence (CI) of relapse at 6 months, overall survival (OS), and progression-free survival (PFS) at 1 year in both cohorts.

Variable	All patients (N=68)	Group A (N=35)	Group B (N=33)	pvalue
Sex				0,0923
f	31 (45.6%)	12 (34.3%)	19 (57.6%)	
m	37 (54.4%)	23 (65.7%)	14 (42.4%)	
Age	55 (19-71)	60 (19-71)	53 (25-69)	0,0028
Disease				0,2021
ALL	9 (13.2%)	6 (17.1%)	3 (9.1%)	
AML	40 (58.8%)	17 (48.6%)	23 (69.7%)	
Lymphoma	5 (7.4%)	2 (5.7%)	3 (9.1%)	
MDS/MPN	14 (20.6%)	10 (28.6%)	4 (12.1%)	
Donor type				0,0233
APLO	25 (37.3%)	17 (48.6%)	8 (25%)	
HLAid sib	22 (32.8%)	7 (20%)	15 (46.9%)	
mMUD	5 (7.5%)	1 (2.9%)	4 (12.5%)	
MUD	15 (22.4%)	10 (28.6%)	5 (15.6%)	
TCI				0,0007
high	18 (26.5%)	3 (8.6%)	15 (45.5%)	
int	31 (45.6%)	17 (48.6%)	14 (42.4%)	
low	19 (27.9%)	15 (42.9%)	4 (12.1%)	

Results: In Group A, IM was initiated in 22/35 patients (63%), with cyclosporine tapering starting at a median of day +61 (range 57–84). IM was not initiated in 13/35 (37%) due to early complications, including acute GVHD (n=6,) infection (n=1), relapse (n=1), death (n=2,) other causes (n=3). Among patients in whom IM was initiated only 7/22 patients (31%) subsequently received prophylactic DLI and completed the full IM program. IM discontinuation in the other 15 patients was due to GVHD (n=6), relapse (n=3), death (n=1), or donor-related issues in MUD transplants (n=5). The 6-month CI for relapse was 8.5% in Group A compared with 33% in Group B (p=0.35). At 1 year, no statistically significant difference was observed between Group A and Group B in OS (73% vs 57%) or PFS (61% vs 42%).

Conclusions: In this single center retrospective study, early immunomodulation showed limited in feasibility, primarily due to early post-transplant complications. A lower relapse incidence was observed in immunomodulate patients, suggesting a potential antileukemic effect, although no statistically significant differences in survival outcomes were observed. These findings support the need to optimize immunomodulation strategies, in terms of timing, patient selection, and personalized strategy to improve feasibility while preserving antileukemic efficacy.

Disclosure: Nothing to declare.

A198

LONG-TERM OUTCOMES OF ADULT PH+ ALL TREATED WITH DASATINIB OR IMATINIB BEFORE THE BLINATUMOMAB ERA: A RETROSPECTIVE ANALYSIS OF 250 PATIENTS FROM THE PALG REGISTRY

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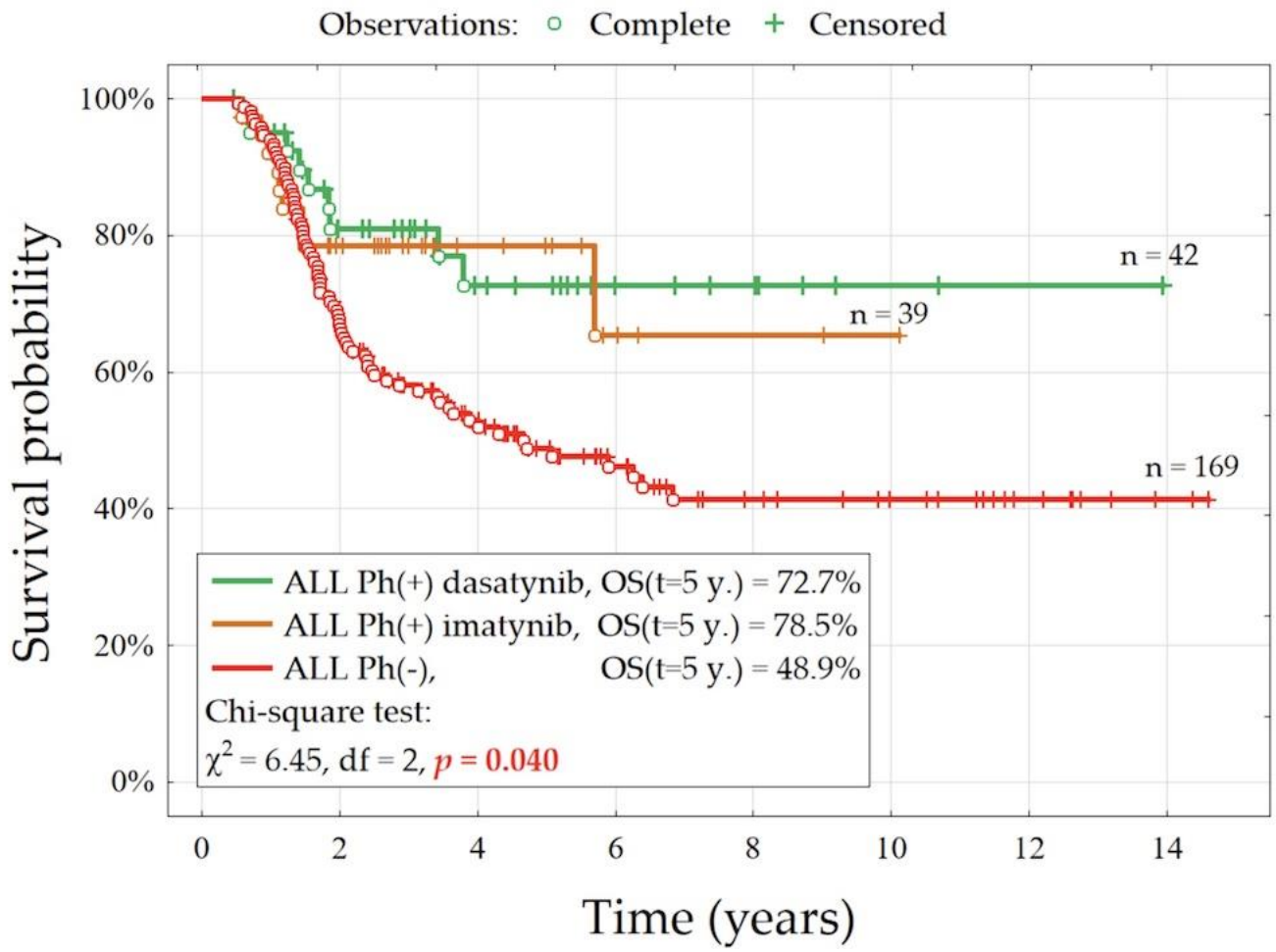
[1]*Wroclaw Clinical Hospital, Wroclaw, Poland,* [2]*Lower Silesian Center of Oncology, Pulmonology and Hematology, Wroclaw, Poland,* [3]*University Clinical Center, Medical University of Gdańsk, Gdańsk, Poland,* [4]*Poznań University of Medical Sciences, Poznań, Poland,* [5]*Maria Skłodowska-Curie National Research Institute of Oncology (MSCNRIO), Gliwice, Poland,* [6]*Wroclaw University of Science and Technology, Wroclaw, Poland*

Background: The prognosis of Philadelphia chromosome–positive acute lymphoblastic leukemia (Ph+ ALL) has improved substantially with the introduction of tyrosine kinase inhibitors (TKIs). Modern chemotherapy-free and stem cell transplantation (SCT)-free regimens, such as ponatinib combined with blinatumomab as first line therapy, provide excellent survival outcomes. However, before the widespread use of blinatumomab, many high-risk patients proceeded to allogeneic hematopoietic SCT (allo-HSCT). We present a retrospective analysis of transplanted adults with Ph+ ALL treated with either imatinib or dasatinib, compared with a Ph-negative cohort, presenting long-term survival outcomes and transplant-related complications in the pre-blinatumomab era.

Methods: We analyzed 250 adult ALL patients undergoing allo-HSCT between 2010 and 2022, including 42 with Ph+ ALL treated with dasatinib, 39 with Ph+ ALL treated with imatinib, and 169 with Ph-negative ALL. Baseline characteristics, conditioning intensity, donor features, and graft-versus-host disease (GvHD) incidence and severity were compared using chi-square or Fisher exact tests. Overall survival was assessed using Kaplan–Meier estimates. Ten-year OS probabilities were estimated for all three groups. Causes of death were evaluated using separate 2×2 independence tests for each category.

Results: Patients receiving dasatinib or imatinib were older than those with Ph-negative ALL, and most Ph+ ALL patients suffered from B-cell phenotype ALL. Conditioning intensity and donor characteristics were mostly comparable. The overall incidence of acute GvHD differed significantly among groups (31.0%, 61.5%, and 41.4% for the dasatinib, imatinib and Ph− cohorts, respectively; p=0.040). Skin aGvhD was more frequent in the imatinib group, whereas gastrointestinal and hepatic involvement showed no statistically significant differences. Chronic GvHD rates and severity were similar across all groups. At a median follow-up of 3.9 years, OS differed between groups. The dasatinib group demonstrated significantly higher OS than the Ph-negative cohort (p=0.010). The comparison between imatinib and Ph-negative patients did not yield statistical significance (p=0.059). Similarly, OS did not differ between dasatinib and imatinib recipients (p=0.735). Ten-year OS probabilities were 72.7% for dasatinib, 65.4% for imatinib, and 41.4% for Ph-negative ALL.

No substantial discrepancies in causes of death were observed among the three groups.



Conclusions: In this pre-blinatumomab era subgroup analysis, adults with Ph+ ALL undergoing allo-HSCT achieved favorable long-term outcomes. Despite being part of a clinically high-risk subgroup (imatinib resistance or central nervous system involvement), patients receiving dasatinib demonstrated promising 10-year OS probability, exceeding that of imatinib and yielding statistical significance compared to that the Ph-negative ALL group. Rates, grades and involved sites of aGvHD, cGvHD, and causes of death did not differ significantly between groups, suggesting that survival differences may be driven mainly by disease control rather than transplant-related toxicity. Compared with modern chemotherapy-free regimens using ponatinib plus blinatumomab with 3-year OS yielding 91%1, the high-risk dasatinib cohort patients also achieved positive survival outcomes, underscoring the effectiveness of TKI-based strategies in Ph+ ALL prior to the immunotherapy era.

Disclosure: Nothing to declare.

A199

OVERCOMING ULTIMATE RESISTANCE: EFFICACY AND SAFETY OF RECIPIENT-DERIVED (DONOR-CHIMERIC) CAR-T THERAPY COMBINED WITH MULTIMODAL STRATEGIES FOR EARLY RELAPSE POST-ALLO-HSCT: A SINGLE-CENTER CASE SERIES

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Background: Early relapse within 12 months after allogeneic hematopoietic stem cell transplantation (allo-HSCT), especially with extramedullary disease (EMD), confers a dismal prognosis. Salvage options are limited by toxicity and the risk of exacerbating Graft-versus-Host Disease (GvHD). Chimeric antigen receptor (CAR) T-cell therapy is a promising modality, but its application in the post-allo-HSCT setting remains underexplored. This series assesses the feasibility and efficacy of using CAR-T cells derived from two distinct donor sources to overcome resistance and serve as a bridge to curative second transplantation.

Methods: Four patients (2 MM, 1 T-LBL, 1 AML; median age 37 years) with early relapse (6-12 months post-HSCT) and EMD were enrolled. At relapse, all patients had >98% donor chimerism and no history of severe GvHD. Three patients received CAR-T cells manufactured from their post-transplant peripheral blood (functionally "host-environment-educated" donor-origin cells): two MM patients received BCMA-targeted (n=1) or sequential BCMA/GPRC5D-targeted (n=1) CAR-T, and the T-LBL patient received CD7-targeted CAR-T. The fourth patient (AML with aberrant CD7 expression) received CD7 CAR-T manufactured from the original healthy haploidentical donor. Pre-infusion lymphodepletion was fludarabine/cyclophosphamide. Responses were assessed by IMWG/ELN criteria. The study was approved by the institutional ethics committee (ChiCTR1900025419).

Results: All four patients achieved rapid, MRD-negative remissions with manageable toxicity. Remarkably, the T-LBL patient, who had previously failed both autologous CD7 CAR-T and a subsequent allo-HSCT, achieved a second systemic remission with the donor-origin CD7 CAR-T. Both MM patients with EMD achieved stringent complete response; the patient treated with sequential BCMA/GPRC5D therapy remains in CR >8 months. The other MM patient died of septic shock at 5 months while in CR. Safety was favorable: Cytokine Release Syndrome was Grade 1 (n=4) , with no ICANS. Critically, no GvHD was induced or exacerbated by CAR-T therapy. The T-LBL and AML patients were successfully bridged to a second Haploidentical allo-HSCT and remain in continuous remission.

Table 1. Patient Characteristics and Outcomes

	Patient	Diagnosis	Age/Sex	EM Sites	CAR-T Type/Source	Dose (×10^6/kg)	Response (IMWG/ELN)	MRD Status	Follow-up (m)	Outcome	Toxicity

	1	MM	45/M	Bone marrow/ soft tissue	BCMA/Recipient PB	2	CR	Negative (flow)	5	Death while in CR(sepsis)	CRS G1, infection 5m post CART
	2	MM	42/M	Liver/lymph nodes/Bone marrow	Sequential BCMA+GPRC5D/ Recipient PB	2+2	CR	Negative (flow)	8	Ongoing CR; bridged HSCT	CRS G1
	3	T-LBL	32/F	CNS/multi-site EMD	CD7/Recipient PB	1	CR	Negative (flow)	2	Ongoing CR; bridged HSCT	CRS G1
	4	AML (CD7+)	32/M	bone marrow/ no EMD	CD7/Donor-derived	1	CR	Negative (flow)	4	Ongoing CR	CRS G1, infection gr2

Conclusions: This series provides powerful proof-of-concept that donor-origin CAR-T therapy is a feasible and highly effective strategy for patients at the frontier of treatment failure. We demonstrate that potent CAR-T cells can be generated from both "host-educated" and "pristine" donor lymphocytes, effectively eradicating EMD and overcoming serial resistance to both CAR-T and allo-HSCT. This "bridge-to-cure" approach transforms a terminal scenario into a potential planned, curative pathway. Limited by small sample size, short follow-up, and single-center design, these findings warrant prospective studies to optimize patient selection, timing, chimerism monitoring, and integration with consolidation therapies. While follow-up is ongoing, these findings offer a tangible new therapeutic paradigm for the most challenging post-transplant relapses and warrant validation in larger, prospective trials.

Clinical Trial Registry: ChiCTR1900025419（https://www.chictr.org.cn/）

Disclosure: Nothing to declare

A200

GEMTUZUMAB OZOGAMICIN ENABLES BRIDGING TO 2ND/3RD ALLO-HSCT WITH FAVORABLE OUTCOMES IN CD33-HIGH RELAPSED/REFRACTORY AML WITH POST–ALLO-HSCT RELAPSE

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Background: Post-transplant relapse of CD33-high AML is associated with extremely poor outcomes, particularly in patients(pts) refractory to salvage therapy. Gemtuzumab ozogamicin (GO), a CD33-directed antibody–drug conjugate, may provide disease control and enable subsequent transplantation. We evaluated GO in heavily pretreated CD33-high R/R AML relapsing after allo-HSCT, focusing on response, safety, and feasibility as a bridge to 2nd/3rd allo-HSCT.

Methods: We retrospectively analyzed R/R AML pts treated between September 2021 and March 2025 at Yanda and Beijing Lu Daopei Hospitals. All pts relapsed after allo-HSCT, had CD33 expression ≥80%, and failed conventional chemotherapy. Patients received GO monotherapy (3 mg/m² on days 1, 4, and 7) or GO combined with chemotherapy or targeted agents. Responses were assessed within 30 days, and responders were bridged to 2nd/3rd allo-HSCT. Follow-up was censored on October 1, 2025.

Results: Thirty-six pts were enrolled, and 34 were evaluable for analysis, median age was 38 years (range, 7–68), and 24 were male (70.6%). First HSCT was predominantly haplo (64.7%), with median time to relapse of 6.2 months (range, 1.7–25.9). Before GO, pts had received a median of 7 prior chemotherapy lines; 65% had complex karyotypes, and TP53 (n=5) 、FLT3-ITD (n=8) mutations , MLL rearrangements (n=7). Median BM blasts and MFC-MRD were 20.5% (5–79.5) and 16.9% (0.12–84.9), respectively. GO was administered in combination in 27 pts (79.4%) and as monotherapy in 7 (20.6%).
The overall response rate(ORR) was 61.8%(21/34), including CR in 20 pts (95.2%) and PR in 1 (4.8%), while 13 pts (38.2%) had no response. Among CR patients, 9/20 (45%) achieved MRD-negative CR. No moderate or severe GO-related adverse events were observed.
With a median follow-up of 4.8 months (0.2–31.4) after GO, 16 of 20 CR pts (80.0%) proceeded to 2nd/3nd allo-HSCT within 7–29 days (haplo n=13, MUD n=3). After HSCT, median follow-up was 11.8 months (0.4–30.5), with 1-year OS and LFS both 60.9% (95% CI, 36.4–85.47) (Figure 1A) and a 100-day incidence of grade III–IV aGVHD of 18.75% (95% CI, 6.76–52). Pts achieving MRD-negative CR had significantly superior 1-year OS/LFS compared with MRD-positive CR (87.5% [95% CI, 64.58–100] vs. 30% [95% CI, 0–64.37], p=0.041) (Figure 1B). Six post-transplant deaths occurred due to CD33-positive relapse (n=2), severe pneumonia or diffuse alveolar hemorrhage (n=3), and veno-occlusive disease (n=1).
Among 4 CR pts not bridged to HSCT, three relapsed and died at 1 and 7.5 months, while one survived 2.6 months and lost to follow-up (Figure 1A). Among 14 pts with NR/PR after GO, 12 received conventional therapy, and 11 died of CD33-positive relapse within 100 days;

the remaining two underwent salvage 2nd allo-HSCT at days 10 and 11 after GO and remain disease-free at 3.7 and 27.5 months.

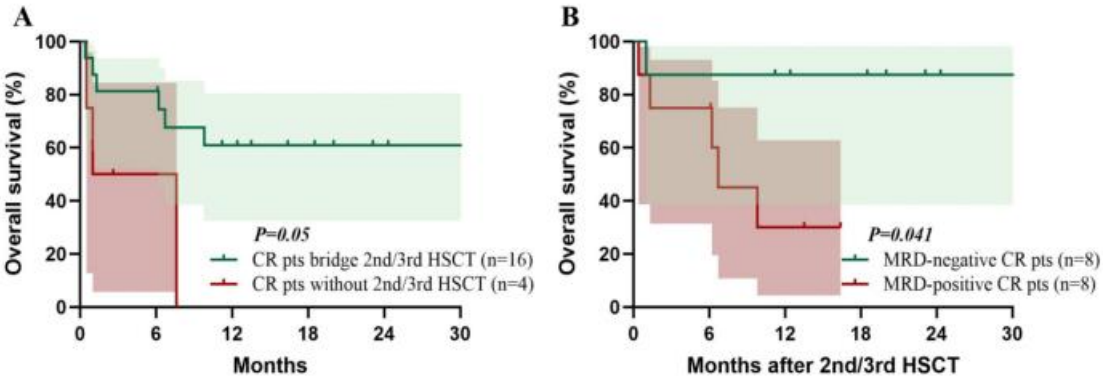

Figure 1. Survival of GO-induced CR patients stratified by bridging to 2nd/3rd allo-HSCT (A) and by MRD status (MRD-negative vs MRD-positive CR) among those undergoing 2nd/3rd allo-HSCT (B).

Conclusions: In heavily pretreated CD33-positive R/R AML pts relapsing after allo-HSCT, GO is an effective and well-tolerated therapy, achieving a high CR rate.Early bridging to second/third allo-HSCT in CR markedly improves survival, particularly in those with MRD-negative.The role of salvage second/third allo-HSCT in GO-refractory pts warrants further evaluation in larger cohorts.

Disclosure: Nothing to declare.

A201

LONGITUDINAL IMPROVEMENT IN SURVIVAL AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A 15-YEAR SINGLE-CENTRE EVALUATION OF QUALITY INITIATIVES

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Background: Outcomes following allogeneic haematopoietic stem cell transplantation (allo-HSCT) have improved over time, although the relative contribution of evolving clinical practice and structured quality initiatives remains unclear. At our centre, several major practice changes were implemented sequentially over a 15-year period, including relocation to a new hospital site(2015), introduction of intravenous busulfan with pharmacokinetic dose adjustment(2016), FACT accreditation(2018), and adoption of antithymocyte globulin (ATG) for unrelated donor transplantation(2020). We examined longitudinal survival outcomes to evaluate temporal trends and their association with these changes.

Methods: We included consecutive adult patients undergoing first allo-HSCT between 2008 and 2023 . Patient, transplant, and outcome data were obtained from the CIBMTR registry and supplemented by a FACT-validated local quality database. Survival analyses were performed using Kaplan–Meier methods and multivariable Cox regression. To explore temporal effects, the cohort was analysed both as a continuous function of transplant year and across four sequential eras: 2008–2014, 2015–2017, 2018–2020, and 2021–2023.

Results: Among 581 consecutive adult patients undergoing first allogeneic stem cell transplantation between 2008 and 2023 , the median follow-up was 74.2 months (range 15–277), and the median age at transplant was 49 years (range 16–71). Patients stratified into the four transplant eras were approximately equal in size : 2008–2014 (n=187), 2015–2017 (n=112), 2018–2020 (n=130), and 2021–2023 (n=153).
Recipient age and comorbidity burden increased progressively over time (median age by era: 45, 51, 50, and 53 years; p<0.001), alongside a marked shift toward reduced-intensity conditioning, which increased from 9% to 45% of transplants across eras (p<0.001).
Overall survival (OS) improved significantly over calendar time, corresponding to a 4.7% relative reduction in mortality per transplant year (HR 0.953, 95% CI 0.928–0.979; p=0.0004). In multivariable analysis, later year of transplant remained independently associated with improved survival, even after adjustment for increasing age, which was itself an independent risk factor for higher mortality (HR 1.014 per year, 95% CI 1.004–1.023; p = 0.004). Disease risk index (rDRI), donor type, and HCT-CI were not significantly associated with OS.

One-year OS for the entire cohort was 74% and increased sequentially by era: 71% in 2008–2014, 72% in 2015–2017, 76% in 2018–2020, and 77% in 2021–2023 (p=0.037), with the most pronounced improvement observed after 2018 coinciding with the period following FACT accreditation . NRM remained low across eras (3.8% vs 2.9% at day100; 9.7% vs 7.0% at 1year), while the later period was characterised by significantly reduced relapse incidence (sHR 0.51; p<0.001) and numerically lower rates of moderate-to-severe chronic GVHD (15% vs 24%,p=0.057).
Conclusions: Survival outcomes improved sequentially over time at our program despite an increasingly older and more comorbid transplant population, demonstrating that sustained systematic evolution can offset rising patient-related risk. Interestingly, the most pronounced improvement occurred after 2018, coinciding temporally with the period following FACT accreditation, while other major practice changes were not associated with effects of similar magnitude. These findings suggest that structured quality management frameworks may contribute to improved allogeneic transplant outcomes.
Disclosure: None to disclose.

A202

THROMBOTIC MICROANGIOPATHY FOLLOWING CAR T-CELL THERAPY: A CASE SERIES FROM THE EBMT TRANSPLANT COMPLICATIONS WORKING PARTY

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Moiseev[8], Helene Schoemans[9], Alberto Mussetti[10], Zinaida Peric[11], Lars Klingen Gjaerde[12], Charlotte Graham[13], Olaf Penack[14]
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Background: Endothelial activation plays a key role in CAR T-cell therapy-related complications, such as CRS, ICANS and HLH. CAR-T patients are potentially at increased risk for thrombotic microangiopathy (TMA) and we here present the first case series from EBMT centres, collected by the Transplant Complications Working Party (TCWP).

Methods: EBMT CAR-T centres were contacted by e-mail to identify cases. A retrospective collection of detailed data was subsequently carried out with a study specific form. TMA was defined according to diagnostic criteria described by Schoettler et al (Transplant Cell Ther 2023).

Results: We identified six cases of CAR T-cell associated TMA: one patient with B-ALL and five with malignant B-cell lymphoma: large B-cell lymphomas (n=3), follicular lymphoma (n=1), mantle cell lymphoma (n=1). Overall, 215 EBMT CAR-T centres were contacted, and 90 responded indicating that they had no eligible patients.
Among lymphoma patients, CAR T-cell products included axi-cel (n=3), brexu-cel (n=1) and tisa-cel (n=1). Median age at CAR-T infusion was 63 years (range, 41–75). Median time from lymphoma diagnosis to infusion was 25.6 months. No patients had previous autologous HCT, median ECOG at CAR-T was 2, and only one patient was in CR at infusion. Three patients received two prior lines of therapy, 1 received three and 1 received five or more. TMA developed after a median of 8 days after CAR-T infusion (range, 6–237). Diagnostic features included anemia (60%), elevated LDH above threshold (100%), thrombocytopenia (100%), proteinuria (60%), hypertension (80%) and elevated schistocytes (40%), C5b-9 was assessed in four of the five patients and none showed elevated levels. One case was biopsy-proven. Four patients met high-risk criteria with peak LDH >2×ULN. Clinically significant renal involvement with proteinuria ≥30 mg/dL occurred in two patients and pulmonary involvement in two. Three were given treatment for their TMA (corticosteroids, antihypertensive therapy, or ravulizumab). Before TMA onset, all patients had experienced CRS (mostly grade II), which overlapped temporally with TMA; four patients also developed ICANS (grade 1–4). All patients developed infectious complications post-CAR T, though only one had a clinically active infection at TMA onset.
Two patients achieved complete remission (CR) of their lymphoma. Three patients died from disease progression at 20, 31 and 203 days post CAR-T. The two remaining patients were still

alive at last follow up.
The identified case of B-ALL was a 42-year-old woman who had undergone allogeneic HCT 33 months prior to brexu-cel infusion. She developed TMA 442 days after CAR-T infusion, with anemia, thrombocytopenia, elevated LDH, schistocytes, elevated C5b9, biopsy confirmation, and LDH >2× ULN. Multisystem involvement (cardiovascular, serosal, gastrointestinal, CNS) was observed. Treatment included corticosteroids, plasma exchange, tocilizumab, and long-term eculizumab. She remains in CR of her B-ALL, 699 days after CAR-T.

Conclusions: This case-series suggests that TMA after CAR T-cell therapy, although rare, is clinically significant and frequently requires management. All patients exhibited preceding CRS and most ICANS, hinting that inflammatory triggers may play a relevant role. Continued vigilance and dedicated prospective data collection are needed to characterise incidence and treatment strategies of TMA after CAR-T-cell therapy.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare.

A203

THE IMPACT OF PRE-TRANSPLANT ISOAGGLUTININ REDUCTION IN MAJOR AND BIDIRECTIONAL ABO-MISMATCHED ALLOGENEIC STEM CELL TRANSPLANTATION – A TWO CENTRE COMPARISON

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Background: ABO incompatibility occurs in 40-50% of allogeneic haematopoietic stem cell transplants (alloHSCT). In major/bidirectional ABO mismatch, high recipient isoagglutinin titres are associated with increased risk of pure red cell aplasia (PRCA) and delayed erythroid engraftment. Pre-transplant interventions to reduce titres are widely used; however, their efficacy remains uncertain, and no consensus exists regarding the optimal approach.

Methods: We conducted a retrospective study of all major and bidirectional ABO-mismatched alloHSCTs performed at two centres in Australia to evaluate whether pre-transplant isoagglutinin reduction is effective in reducing PRCA incidence and red blood cell (RBC) transfusion requirement. The two centres are Royal Adelaide Hospital (RAH), South Australia, which routinely performed isoagglutinin reduction using donor secretor plasma and/or plasma exchange in patients with high baseline titres (defined as ≥32), and Fiona Stanley Hospital (FSH), Western Australia, which did not. Transplants performed between 2012-2021 at RAH and 2016-2023 at FSH were included. Data collected included baseline characteristics, ABO blood groups, recipient isoagglutinin titres, pre-alloHSCT interventions, day-60 haemoglobin level, cumulative RBC transfusions (total units transfused at 6 months post-transplant, censored at death/relapse) and incidence of PRCA (defined as persistent

anaemia with reticulocytopenia beyond day 60, transfusion dependence beyond day 60 and bone marrow erythroblasts <5%). Umbilical cord blood transplants and patients with deaths before day-60 were excluded.

Results:
A total of 148 major/bidirectional ABO-mismatched alloHSCTs were performed during the study period (61 at RAH and 87 at FSH). The median baseline isoagglutinin titre were 64 (IQR 16-256) at RAH and 64 (IQR 16-128) at FSH (figure 1A). There were 97 patients with high titres (≥32) and 35 (36%) of them received pre-transplant interventions. PRCA occurred less frequently in those who received intervention compared to the non-intervention group but this was not statistically significant (5.7% vs 16.1%, p=0.135). At day 60, the median haemoglobin level was significantly lower in patients who developed PRCA compared to non-PRCA patients (69g/L vs 95g/L, p<0.0001, figure 1B) and significant higher in the low titre group compared to the high titre group (99g/L vs 92g/L, p=0.023, figure 1C). There was a trend towards higher haemoglobin level at day 60 in the intervention group compared to the non-intervention group (96g/L vs 89g/L, p=0.054, figure 1D). Patients who developed PRCA had significantly higher RBC transfusion requirement compared to non-PRCA patients (median 19 vs 10 units, p=0.003, figure 1E). There was no statistically significant difference in RBC transfusion requirement between the intervention and non-intervention group (median 9 vs 14 units, p=0.633, figure 1F).

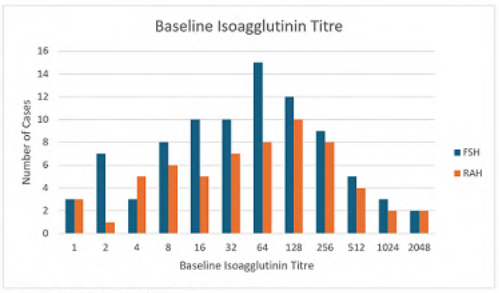

Figure 1A: Baseline isoagglutinin titre

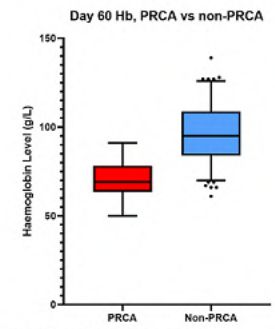

Figure 1B: Day 60 Hb, PRCA vs non-PRCA

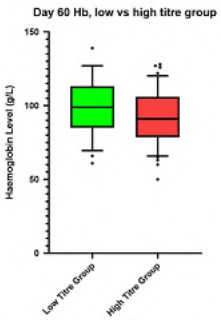

Figure 1C: Day 60 Hb, low titre vs high titre group

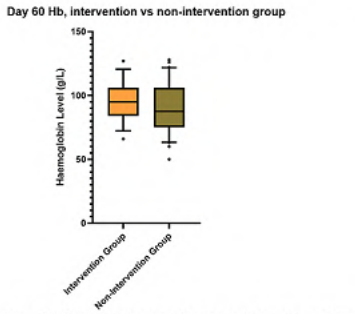

Figure 1D: Day 60 Hb, intervention vs non-intervention group

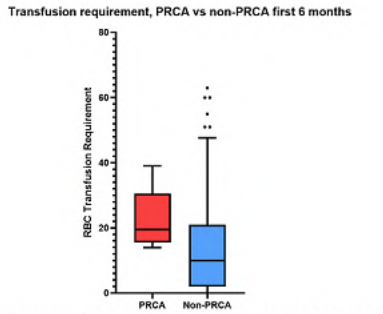

Figure 1E: RBC transfusion requirement, PRCA vs non-PRCA

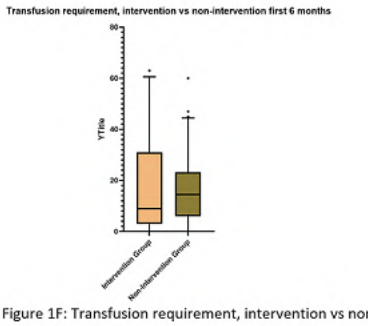

Figure 1F: Transfusion requirement, intervention vs non-intervention group

Conclusions: Pre-transplant isoagglutinin reduction was not associated with a statistically significant reduction in PRCA incidence or cumulative RBC transfusion requirement following major/bidirectional ABO mismatched alloHSCT due to the relative small sample size of our study. High baseline isoagglutinin titres and development of PRCA were associated with lower

day-60 haemoglobin level and higher RBC transfusion requirement. These findings, although limited by the study's retrospective design and sample size, highlight the need for larger prospective randomised trials to definitively assess the utility of titre-reduction strategies.

Disclosure: Nothing to declare

A204

SAFETY AND EMERGING CLINICAL IMPACT OF CD19 CAR T-CELL THERAPY IN SEVERE AUTOIMMUNE RHEUMATIC DISEASES: A SINGLE-CENTRE CASE SERIES

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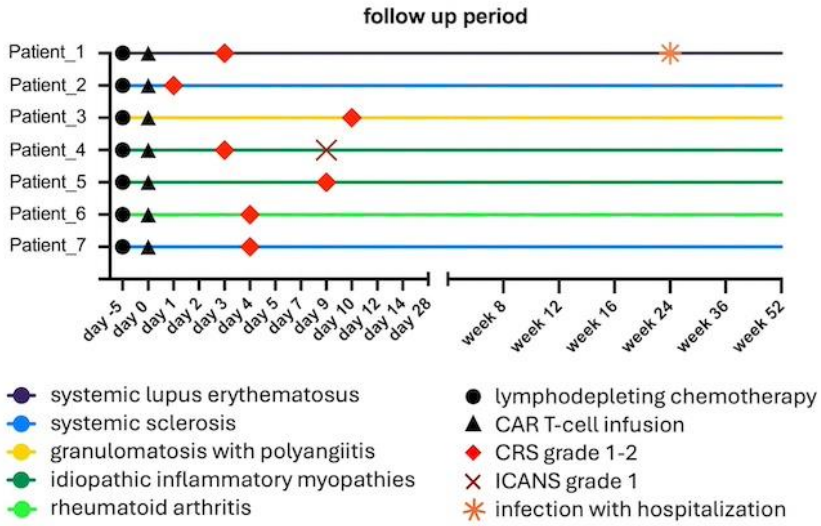
Background: Autoimmune rheumatic diseases (ARDs) can cause progressive organ damage and substantial disability despite modern immunosuppression, partly due to persistent pathogenic B-cell activity. Current B-cell-directed therapies often achieve incomplete depletion, allowing autoreactivity to recur. CD19-directed CAR T-cells enable deeper B-cell depletion with the potential for an immune "reset", yet clinical data in ARDs remain very limited. This study reports feasibility, immune-cell dynamics, toxicity, and emerging clinical impact following autologous CD19 CAR T-cell therapy with KYV-101, a fully human, anti-CD19 CAR T-cell with CD28 costimulation, in a cohort with severe, refractory ARDs.

Methods: Seven adult patients (age 32–71 years; 4/7 female) with severe, treatment-refractory ARDs, including idiopathic inflammatory myopathies (n=2), systemic sclerosis (n=2), rheumatoid arthritis (n=1), systemic lupus erythematosus (n=1), and granulomatosis with polyangiitis (n=1) were treated under a named-patient (individual therapeutic use) approach after multidisciplinary review and informed consent. All patients received lymphodepletion (mainly fludarabine/cyclophosphamide; dose-adjusted fludarabine for renal impairment; bendamustine as alternative in severe renal dysfunction) followed by a single KYV-101 infusion. Inpatient monitoring was performed for at least 10 days, followed by outpatient longitudinal follow-up for ≥12 months.

Results: CAR T-cell expansion peaked at a median of day 10 (IQR 10–12), reaching a median peak of 366.7 CAR T-cells/µL (IQR 136.6–384.4) and a median of 31.5% of circulating T cells at peak. $CD19^+$ B cells became undetectable in all patients within 24 hours after infusion followed by B-cell reconstitution occurring in 4/7 between weeks 8–24. All patients experienced a clinical response and are currently off background medications. Cytokine Release Syndrome (CRS) was observed in all patients but remained uniformly mild, limited to grade 1 (4/7) or grade 2 (3/7), with a median onset on day 4 (IQR 3–9). All cases

responded promptly to tocilizumab, and four patients received additional dexamethasone. No intensive care support was required. Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS) was infrequent and mild (1/7, grade 1, ICE 9/10) and resolved within 24 hours following dexamethasone. Anticipated early (within 30 days) Grade 3-4 neutropenia occurred in 5/7, infections were observed in 2/7 and responded to antibiotics. Late-onset severe neutropenia (immune effector cell-associated haematotoxicity grade 3) occurred in 2/7 (weeks 8 and 24) and recovered after G-CSF, including one episode complicated by neutropenic pneumonia. Additionally, some patients experienced transient, localised, disease-site specific inflammation likely connected to CAR T-cell activity. These events were self-limiting or manageable with supportive care.

Figure 1:
Timeline of patients with ARDs treated with CD19 CAR T-cells



Conclusions: In this cohort of patients with severe, treatment-refractory ARDs, KYV-101 induced rapid, profound B-cell depletion, leading to a durable, drug-free response with a manageable safety profile over ≥12 months. CRS events were uniformly low grade and controllable with early, protocolised intervention. Haematotoxicity, particularly neutropenia, including delayed episodes, represented a relevant component of the adverse event spectrum and responded to supportive care. Overall, these findings support the feasibility of CD19 CAR T-cell therapy in ARDs, provided it is administered in centres with established expertise in cell therapy.

Disclosure: OP has no COIs directly related to this work. OP has received honoraria or travel support from Alexion, Gilead, Jazz, MSD, Neovii, Novartis, Pfizer and Therakos. He has received research support from Incyte, Gilead and Priothera. He is member of advisory boards to Apogepha, Alexion, Equillium Bio, Jazz, Gilead, Novartis, MSD, Omeros, Orca Bio, Priothera, Sanofi, Shionogi and SOBI.

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A205

SINGLE CENTRE EXPERIENCE OF USING A THERAPEUTIC PLATELET REGIME DURING AUTOLOGOUS STEM CELL TRANSPLANT

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Background: Historically, our centre administered prophylactic platelet transfusions during autologous transplantation when counts fell below 10 $\times 10^9$/L. However, updated guidance from the BSH, EBMT, and JCO has questioned the necessity of routine prophylaxis in this setting. Following the UK national platelet shortage in 2022, we implemented a therapeutic platelet transfusion strategy for a carefully selected cohort of patients undergoing autologous stem cell transplantation. Under this approach, platelet transfusions are reserved for episodes of bleeding (WHO grade ≥1) or for pre-procedural optimisation.

Methods: Beginning in 2022, eligible patients were identified prior to admission for transplant based on the following criteria: first high-dose procedure, age <65 years, absence of CNS disease, no increased risk of falls, and no additional bleeding risk factors as determined by the treating physician. Under the therapeutic protocol, platelet transfusions were administered only for bleeding or for pre-procedural optimisation to achieve guideline recommended target values. Patients admitted to the intensive care unit were automatically removed from the therapeutic strategy, due to the high prevalence of sepsis and frequent need for procedures. Bleeding events were captured retrospectively from patient records. The therapeutic platelet cohort was compared with a demographically matched historical cohort meeting identical inclusion criteria and managed with prophylactic platelets. Statistical comparisons were performed using a t-test for parametric values and a Mann-Whitney test for non-parametric values.

Results: A total of 50 patients were included in each cohort. Most underwent high-dose melphalan-conditioned autologous transplantation (41/50 in the prophylactic group and 43/50 in the therapeutic group). Mean age was 52 in both cohorts. Median platelet engraftment was similar: 12 days (IQR [11-14]) in the prophylactic group versus 13 days (IQR [13–15]) in the therapeutic group. Median platelet nadir was lower in the therapeutic group (5 $\times 10^9$/L, IQR [2–8]) than in the prophylactic group (8$\times 10^9$/L, IQR [5–11]) ($p = 0.003$). Patients in the prophylactic group spent a median of 1 day (IQR [0-1]) with platelet counts <10 $\times 10^9$/L versus 2 days (IQR [1–4]) in the therapeutic group ($p < 0.0001$). Bleeding events were low in both groups: five patients in the prophylactic group experienced WHO grade 1 bleeding versus seven in the therapeutic group, with an additional two WHO grade 2 events in the therapeutic cohort. No grade 3 or 4 bleeding episodes were observed.

Significantly fewer platelet transfusions were used in the therapeutic cohort (14 vs. 66; $p < 0.001$), with 13 patients receiving at least one transfusion versus 42 in the prophylactic group. The therapeutic approach resulted in £11,500 less spent on platelet provision for the 50 patients based on NHSBT component pricing alone.

Conclusions: A therapeutic platelet transfusion strategy is feasible in selected patients undergoing autologous stem cell transplantation. This approach significantly reduces platelet usage and associated costs, without increasing clinically significant bleeding. Limitations of this study include the low number of severe bleeding events, which may limit statistical power. Our centre has now stopped the use of prophylactic platelets in autologous transplantation when the above criteria are met.

Disclosure: Nothing to declare

A206

ALLOGENEIC HSCT FOR ADVANCED STAGE AND RELAPSED/REFRACTORY EXTRANODAL NK/T CELL LYMPHOMA (ENKTCL): A SINGLE INSTITUTION EXPERIENCE IN L-ASPARAGINASE ERA

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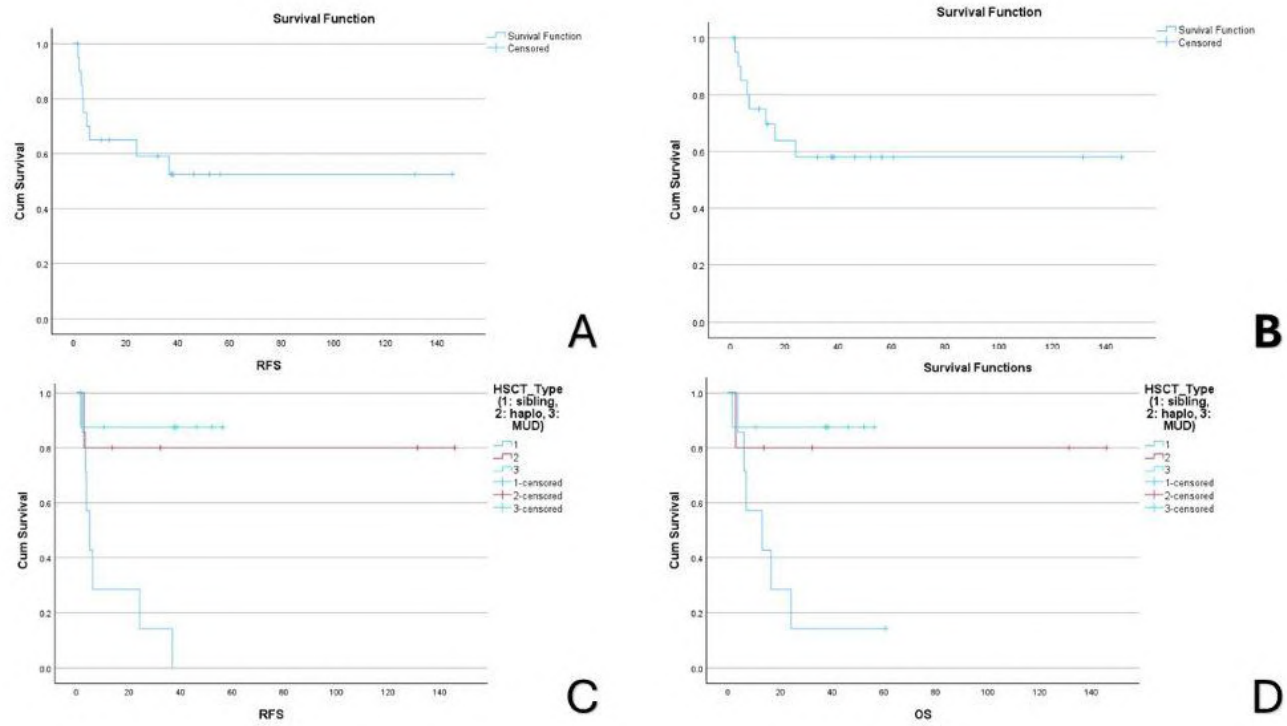
Background: Extranodal NK/T-cell lymphoma (NKTCL) is an aggressive lymphoma with poor prognosis, especially in advanced or relapsed/refractory cases. L-asparaginase–based regimens have improved outcomes in newly-diagnosed cases. For relapsed/refractory cases, use of immune checkpoint inhibitors induces high response rates. Hence, although allogeneic hematopoietic stem cell transplantation (allo-HSCT) offers the potential to achieve durable remission through a graft-versus-lymphoma effect, it is infrequently needed. Recent international data of allo-HSCT in NKTCL showed 3-year progression-free-survival and overall-survival (OS) of 48% and 55%. However, factors influencing allo-HSCT outcome, including donor types and prior exposure to immune checkpoint inhibitors, remain undefined. We conducted a retrospective single-center analysis to address these issues.

Methods: Consecutive NKTCL patients undergoing allo-HSCT in an 18-yer period were analyzed. There were no exclusion criteria. Analyzed outcomes included incidence and severity of acute and chronic graft-versus-host disease (GVHD), non-relapse mortality (NRM), relapse-free-survival (RFS) and OS.

Results:



From 2007 to 2025, twenty-one patients underwent allo-HSCT for ENKTCL. There were fourteen men and seven women, at a median age of 41(Table 1). Five patients had previously been reported. Indications for allo-HSCT included high-risk disease in first complete remission (CR1) (N=11, 52%), relapsed disease in CR2 (N=7, 33%), and refactory disease (N=3, 14%). Donors were voluntary unrelated (N=9, 43%), matched sibling (N=7, 33%) and haploidentical (N=5, 24%). In the majority of cases, peripheral blood HSC (N=17, 81%) and myeloablative conditioning (N=14, 67%) were used. GVHD prophylaxis were summarized in table 1.

Prognostic factors including pre-transplant disease status (CR1 vs. CR2; CR vs. <CR), PINK-E risk categories and circulating EBV DNA load did not significantly predict survival. However, recipients of matched sibling donor grafts demonstrated inferior RFS and OS compared with unrelated or haploidentical donor recipients ($P < 0.01$ and $P = 0.03$, respectively) (Figure 1). Regarding toxicity, the 1-year non-relapse mortality (NRM) was 20%. Grade 3–4 acute GVHD occurred in three patients (14.3%), while moderate-to-severe chronic GVHD occurred in five patients (24%) by one year. Eight patients had received a PD-1 inhibitor as part of their last regimen prior to HSCT. Our standard practice mandates discontinuing PD-1 inhibitors at least four weeks before stem cell infusion to mitigate GVHD risk; the median washout period in this cohort was 114 days. Prior exposure to PD-1 inhibitors did not increase the risk of grade 3–4 acute GVHD or moderate-to-severe chronic GVHD.

Parameters	Value	

Age	Median 41 (range: 25-66)	
Sex	M: 14 (67%), F: 7 (33%)	
Stage at HSCT	Stage II: 1 (5%), stage IV: 20 (95%)	
Bone marrow involvement	Yes: 12 (57%), No: 9 (43%)	
Primary site	Nasal: 16 (76%), non-nasal: 5 (24%)	
PINK-E score risk group	Low (0-1): 4 (19%) Intermediate (2): 8 (38%) High (< or =3): 9 (43%)	
L-asparaginase based therapy	Yes: 21 (100%)	
Regimens:	First line regimens	SMILE: 7 (33%) SIMPLE: 7 (33%) SMILE + PD-1 inhibitor: 1 (5%) SIMPLE + PD-1 inhibitor: 1 (5%) GDP + L-asparaginase: 1 (5%) Non-asparaginase based: 4 (19%)
	Second line regimens	SMILE: 4 (29%) PD-1 inhibitor alone: 3 (21%) GDP: 2 (15%) PD-1 inhibitor + chemotherapy: 4 (29%)
	Third line regimens	PD-1 inhibitor + chemotherapy: 2 (40%) SIMPLE: 1 (20%) SMILE: 1 (20%) Daratumomab: 1 (20%)
	Fourth line regimens	ESHAP: 1 (50%) PD-1 inhibitor: 1 (50%)

PD-1 inhibitors prior to HSCT	Yes:11 (52%) No: 10 (48%)	
Disease status prior to HSCT	CR1: 11 (52%) CR2: 7 (33%) PR: 1 (5%) PD: 2 (10%	
Conditioning regimens	Flu-TBI-PTCY: 7 (33%) Cy-TBI: 7 (33%) TBF-PTCY: 3 (14%) Flu-Bu: 3(14%) Big CBV: 1 (5%)	
GVHD prophylaxis	PTCY, CsA, MMF: 10 (48%) ShMTX, CsA, MMF: 5 (24%) ShMTX, CsA: 6 (28%)	
Table 1		

Conclusions: Allogeneic HSCT remains a potentially curative option for advanced stage ENKTCL, achieving durable survival in over half of the cohort. While pre-transplant disease depth did not statistically stratify outcomes in this series, donor selection emerged as a significant prognostic factor, with unrelated and haploidentical grafts yielding superior RFS and OS compared to matched sibling transplants. Furthermore, prior exposure to PD-1 inhibitors did not significantly increase the risk of severe GVHD, supporting the safety of sequencing checkpoint inhibition before transplantation when an appropriate washout period is observed.

Disclosure: None

A207

EFFICACY AND SAFETY OF CD20XCD3 BISPECIFIC ANTIBODIES IN RELAPSED OR REFRACTORY INDOLENT B-CELL NON-HODGKIN LYMPHOMAS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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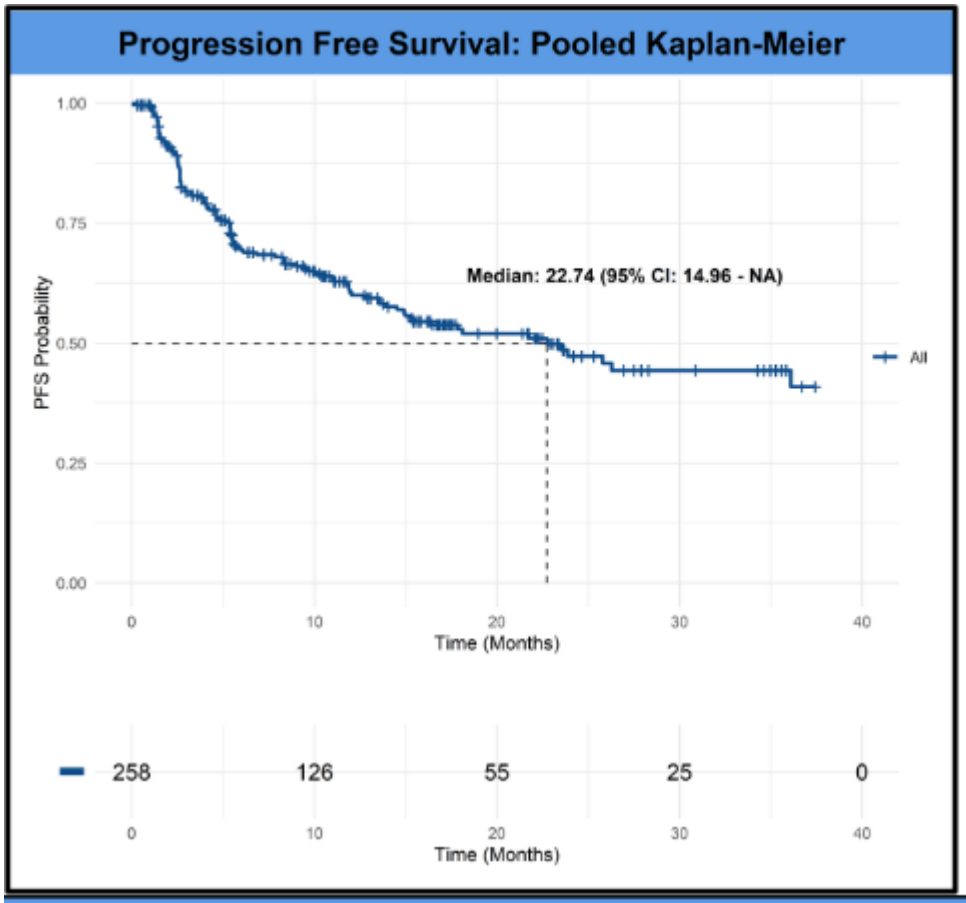
Background: Patients with relapsed/refractory (R/R) indolent non-Hodgkin lymphoma (iNHL) have limited therapeutic options and progressively shorter durations of response with subsequent therapies. CD20xCD3 T-cell engaging bispecific antibodies (BsAbs) are a novel therapeutic class designed to redirect T-cells to eliminate malignant B-cells.

Methods: We conducted a systematic review and meta-analysis to evaluate efficacy and safety of CD20xCD3 BsAbs (mosunetuzumab, epcoritamab, odronextamab, and glofitamab) in patients with R/R iNHL. Following a pre-registered protocol (PROSPERO CRD420251158501), we systematically searched PubMed, Cochrane, and Embase for studies evaluating CD20xCD3 BsAbs in R/R iNHL. Binary outcomes were pooled using random-effects proportional meta-analyses with Freeman-Tukey double arcsine transformation. We reconstructed individual patient data (IPD) from published Kaplan-Meier (KM) curves to synthesize time-to-event outcomes, generating pooled KM estimates.

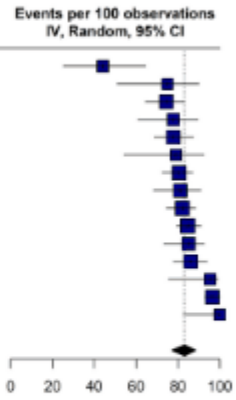
Results:



Overall Response Rate

Study	Event	Total	Weight	Prevalence	95% CI
Budde 2024 (Mosunetuzumab / MCL)	11	25	5.5%	44.00	[25.17; 64.62]
Wang 2023 (Mosunetuzumab / MCL)	15	20	5.0%	75.00	[50.86; 89.95]
Bartlett 2024 (Mosunetuzumab / FL)	70	94	7.6%	74.47	[64.44; 82.92]
Bannerji 2020 (Odronextamab/ FL cohort)	28	36	6.2%	77.78	[60.73; 89.48]
Sehn 2025 (Mosunetuzumab / FL)	70	90	7.6%	77.78	[68.49; 87.25]
Goto 2025 (Mosunetuzumab / FL)	15	19	4.9%	78.95	[54.26; 92.30]
Kim 2024 (Odronextamab/ FL)	103	128	7.9%	80.47	[72.53; 86.94]
Morschhauser 2021 (Glofitamab / FL) - Monotherapy cohort	43	53	6.9%	81.13	[68.18; 90.90]
Linton 2024 (Epcoritamab / FL) - Pivotal cohort	105	128	7.9%	82.03	[74.34; 88.36]
Iacoboni 2024 (CD20/CD3-targeted BsAbs / FL)	143	169	8.1%	84.62	[79.20; 90.96]
Phillips 2024 (Glofitamab / MCL)	51	60	7.0%	85.00	[73.18; 92.47]
Linton 2024 (Epcoritamab / FL) - Optimisation cohort	74	86	7.5%	86.05	[77.81; 93.94]
Izutsu 2025 (Epcoritamab / FL)	20	21	5.1%	95.24	[75.49; 99.20]
Falchi 2024 (Epcoritamab / FL)	107	111	7.8%	96.40	[92.65; 99.99]
Morschhauser 2021 (Glofitamab / FL) - Combination therapy cohort	19	19	4.9%	100.00	[82.28; 100.00]
Total (95% CI)	**874**	**1059**	**100.0%**	**83.06**	**[76.95; 88.44]**

Heterogeneity: $Tau^2 = 0.0160$; $Chi^2 = 60.18$, $df = 14$ ($P < 0.0001$); $I^2 = 76.7\%$



We included 13 studies with a total of 1059 patients. The pooled overall response rate (ORR) for the entire cohort was 83.06% (95% CI: 76.95-88.44), and the complete response rate (CRR) was 67.43% (95% CI: 60.63-73.90). ORR in high-risk groups was 77.08% (95% CI: 69.88-83.65) in double-refractory patients and 81.57% (95% CI: 74.45-87.83) in the POD24 population. No significant difference was found between treatment-to-progression (83.15%) and fixed-duration (81.90%) strategies (p=0.7870). Reconstructed time-to-event data showed a pooled median progression-free survival (PFS) of 22.74 months (95% CI: 14.96 – NA; n=258), with a 36-month PFS rate of 44.3%. For 156 responders, the median duration of response (DOR) was 34.48 months (95% CI: 16.52 – NA). The median overall survival (OS) was not reached (95% CI: Not Estimable; n=239), with a 36-month OS rate of 74.1%. Key safety findings included an incidence of any-grade cytokine release syndrome (CRS) of 56.55% (95% CI: 48.41-64.53) and any-grade ICANS of 2.30% (95% CI: 0.66-4.61). Treatment discontinuation due to adverse events occurred in 9.98% (95% CI: 5.81-15.00) of patients.

Conclusions: CD20xCD3 bispecific antibodies demonstrate substantial clinical activity and induce high, durable complete response rates in heavily pretreated patients with R/R iNHL, including those with high-risk features. The safety profile is manageable, with CRS being the most common adverse event of special interest, although predominantly low-grade. These findings support BsAbs as a new, effective therapeutic class for indolent lymphomas.

Disclosure: Nothing to declare.

A208

ACCESS TO CAR-T CELL THERAPY IN CENTRAL AND EASTERN EUROPE (CEE) – PERSISTENT DISPARITIES

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Background: CAR-T therapy represents a major advancement in the treatment of hematological malignancies. Despite improved access and introduction of new commercial

products, significant disparities in availability persist across the Central and Eastern European region.

Methods: We surveyed representatives from 15 countries in the region. Participation in the survey was voluntary. Ethics approval was considered unnecessary due to the use of non-identifiable institutional data. Respondents provided information current as of October/November 2025. No response was received from Bulgaria. Lithuania withdrew from participation, but basic data were found in open access sources. Respondents answered six questions regarding access to CAR-T therapy in both adult and pediatric patients in their countries.

Results: The findings reveal substantial inequality in access to CAR-T therapy across the region. The earliest accreditation for adult *tisagenlecleucel* therapy in the region was granted in Czech Republic in 2019, while the first pediatric accreditation was issued in Poland the same year. These two countries were the first to administer CAR-T cells to adult patients in 2019, followed by the first pediatric infusions in 2020. Both countries have since established national CAR-T programs, performing hundreds of infusions across multiple certified centers. Slovenia and Croatia began treating both adult and pediatric patients in 2020. Belarus reported its first adult treatment in 2020. Russia initiated CAR-T cell therapy in pediatric patients in 2018 and in adults in 2022. Romania reported the simultaneous initiation of adult and pediatric treatments in 2022. Hungary began treating adults in 2022 and children in 2024. Slovakia treated its first adult patient in 2023, with the first pediatric infusion conducted in November 2025. Several countries in the region have not yet received accreditation for any commercial CAR-T products. Ukraine, Latvia, Estonia and Serbia, currently lack access to CAR-T therapies. Belarus and Lithuania report using domestically produced, academic, point of care CAR-T cells. The majority of countries provide reimbursement for CAR-T therapy. In Belarus, access to CAR-T cell treatment is provided through state-funded academic programs. Russia reported region-specific reimbursement since 2025, with full government reimbursement expected in 2026. The most commonly reported barriers of limited availability and difficulty in introducing CAR-T therapy to the market include insufficient funding, regulatory obstacles and lack of commercial incentives for pharmaceutical companies in smaller markets. In Ukraine, the ongoing war and reimbursement challenges significantly impede implementation. Notably, access for pediatric patients remains more restricted than for adults, both in terms of the number of accredited centers and the availability of commercial products.

Number of patients treated with CAR-T cell therapy							
Country	No of adult infusions	No of adult infusions per 5 mln people	No of pediatric infusions	No of pediatric infusions per 1 mln children	No of CAR-T centers	No of CAR-T Centers per capita	*Availability of commercial products*
Poland	451	59.15	51	8.90	13A+2P	0.39	*tisagenlecleucel, axicabtagene ciloleucel*

							brexucabtagene autoleucel academic CAR-T cells
Czech Republic	330	153.50	24	11.70	8A+2P	0.93	*tisagenlecleucel axicabtagene ciloleucel brexucabtagene autoleucel idecabtagene vicleucel lisocabtagene maraleucel* clinical trials: *ciltacabtagene autoleucel arlocabtagene autoleucel*
Belarus	124	69.00	17	9.90	3A+1P	0.45	academic CAR-T cells
Slovakia	72	66.30	1	1.14	2A+1P	0.55	*tisagenlecleucel*
Russia	68	2.35	76	2.28	5	0.04	*tisagenlecleucel*
Croatia	57	74.05	3	4.10	1	0.26	*tisagenlecleucel*
Romania	29	7.65	7	1.90	1AP+1A	0.11	*tisagenlecleucel*
Slovenia	15	35.70	6	19.20	1A+1P	0.95	*tisagenlecleucel*
Hungary	4	2.10	2	1.43	1	0.11	*tisagenlecleucel*
Ukraine	0	0	0	0	0	0	-
Lithuania	n/a	n/a	n/a	n/a	n/a	n/a	point of care CAR-T cells
Latvia	0	0	0	0	0	0	-
Estonia	0	0	0	0	0	0	-
Serbia	0	0	0	0	0	0	-

Table 1: Number of adult and pediatric patients treated with CAR-T cells in the Central and Eastern European region
Legend: A – adult, P – pediatric; n/a – data not available

Conclusions: Our results highlight an urgent need for coordinated regional efforts to reduce disparities in access to CAR-T therapy across the region. Development of national reimbursement systems, investment in healthcare infrastructure, optimizing of referral pathways and strengthened international collaboration are essential. Supporting the development of both commercial and academic CAR-T programs is necessary. Sustained efforts in data collection, outcome monitoring and sharing of best practice are crucial for shaping effective policies and ensuring equitable access to CAR-T therapies for residents of CEE countries.

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Juergen Kuball - inventor on multiple patents dealing with genetically engineered immune cells and receives grant support from Miltenyi Biotech and Novartis
Krzysztof Kałwak - speakers bureau Novartis
The other authors declare no conflicts of interest.

A211

HYPOFIBRINOGENEMIA AND SYSTEMIC INFLAMMATION FOLLOWING BCMA-DIRECTED CAR-T THERAPY: A RETROSPECTIVE STUDY

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Background: Hypofibrinogenemia is a common complication following CAR-T therapy and has been linked to systemic inflammation, CRS/ICANS, and other hemostatic disturbances. Reported bleeding rates range from 10–30%, but early fibrinogen replacement often makes it difficult to assess its natural course. Data on anti-BCMA CAR-T products remain limited. This study aims to evaluate the incidence, risk factors, and clinical impact of hypofibrinogenemia in patients receiving BCMA-directed CAR-T therapy.

Methods: In this single-center, retrospective study, 71 adult multiple myeloma patients treated with Cilta-cel, Ide-cel, or ARI-0002h between 2020 and 2025 were analyzed. Patients were stratified by fibrinogen nadir, with clinically relevant hypofibrinogenemia defined as a fibrinogen level ≤150 mg/dL and hemorrhagic events defined as events grade ≥2.

Results: Hypofibrinogenemia occurred in 46.5% (n=33) of patients, with 42.4% (n=14) presenting fibrinogen levels <100 mg/dL and 6.1% (n=2) <50 mg/dL. The incidence of hypofibrinogenemia did not differ significantly between CAR T-cell products (cilta-cel 40%, ide-cel 50%, ARI-0002h 61.1%; p = 0.3). The median duration of hypofibrinogenemia was 13 days (IQR 8–20). Prolonged hypofibrinogenemia (≥14 days) was observed in 42% of affected patients (n=14). The median time to onset was 13 days (IQR 10–18), nadir at day +15 (IQR 13–21), and recovery by day +25 (IQR 18–38). Prophylactic fibrinogen supplementation was administered in 15.5% of cases, at a median fibrinogen level of 84 mg/dL at supplementation. Bleeding events occurred in 9.1% (n=3), all in the setting of concurrent hypofibrinogenemia, with no significant association between fibrinogen nadir and bleeding (p=0.109) (Table 1).

Table 1: Demographic and clinical characteristics of study population

	Total (n=71)[1]	Fibrinogen ≥150 mg/dL (n=38)[1]	Fibrinogen <150 mg/dL (n=33)[1]	p-value[2]
Age at infusion	62 (51-69)	62 (51-69)	62 (50-68)	0.7
Female sex	33 (46%)	17 (45%)	16 (48%)	0.8
CART product				0.3
Cilta-cel	45 (63%)	27 (71%)	18 (55%)	
ARI-0002h	18 (25%)	7 (18%)	11 (33%)	
Ide-cel	8 (11%)	4 (11%)	4 (12%)	
CRS	64 (90%)	31 (82%)	33 (100%)	0.004
Grade 1	46 (72%)	25 (81%)	21 (67%)	
Grade 2	9 (14%)	5 (16%)	4 (12%)	
Grade 3	9 (14%)	1 (3%)	8 (24%)	
CRS onset	6 (5-8)	6 (5-7)	6 (4-8)	0.123
Duration (days)	2 (1-3)	2 (1-3)	2 (1-4)	0.047
ICANS	8 (11%)	4 (10%)	4 (12%)	0.8
Grade ≥3	0	0	0	
Anti-IL6 treatment	60 (84%)	27 (71%)	33 (100%)	<0.001
Cummulative dose	1 (1-2)	1 (0-2)	2 (1-3)	<0.001
Fibrinogen nadir (mg/dL)	150 (118-268)	264 (176-368)	114 (82-132)	
Bleeding grade ≥2	3 (4%)	0	3 (9%)	0.109

[1] Median (IQR); n (%).
[2] Fisher's exact test; Chi-squared test; Wilcoxon rank sum test

Any-grade CRS increased the risk of hypofibrinogenemia (OR 2.17; 95% CI 1.66–2.84; p = 0.011) and was associated with lower nadir levels (160 vs 150.5 mg/dL; p = 0.001). Greater CRS severity correlated with higher incidence (OR 2.43; 95% CI 1.06–5.56; p = 0.035) and

deeper fibrinogen depletion (p = 0.002) (Figure 1). Longer CRS duration and cumulative anti–IL-6 therapy were also linked to increased incidence (OR 1.67; 95% CI 1.05–2.64; p = 0.03; and OR 3.08; 95% CI 1.70–5.56; p < 0.001 respectively) and lower fibrinogen levels (rho -0.39, p = 0.001; rho -0.62, p < 0.001). No significant association was observed between ICANS and hypofibrinogenemia. Hypofibrinogenemia did not impact overall survival (median follow-up 7 months).

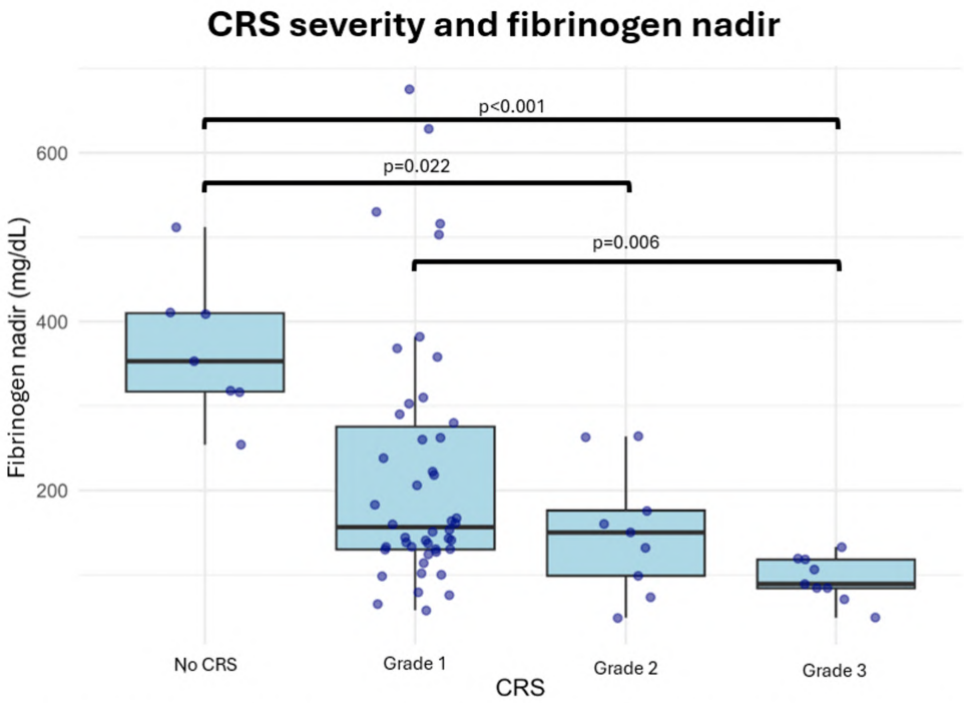

Figure 1: Fibrinogen nadir according to CRS severity. Increasing CRS grade is associated with progressively lower fibrinogen levels.

Conclusions: Hypofibrinogenemia is frequent after BCMA-directed CAR-T therapy and reflects the systemic inflammatory response rather than isolated hemostatic dysfunction. Its severity is moderately inversely correlated with CRS grade, CRS duration, and cumulative anti–IL-6 therapy, without significantly increasing bleeding risk. These results support the concept of a unified inflammatory syndrome in CAR-T recipients, with fibrinogen serving as a measurable marker of inflammatory burden. Routine monitoring may aid in early detection and assessment of systemic inflammation.

Disclosure: Nothing to declare.

A212

SURVIVAL AND OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN OLDER ADULTS WITH ACUTE MYELOID LEUKEMIA: A SINGLE-CENTER, DECADE-LONG ANALYSIS

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Background: The median age at diagnosis for acute myeloid leukemia (AML) is in the seventh decade, and yet little progress has been made in improving outcomes for older adults undergoing allogeneic hematopoietic stem cell transplantation (alloHSCT). Herein, we report the clinical outcomes and associated factors for older AML patients undergoing alloHSCT.

Methods: Patients with AML (n=279) who underwent alloHSCT between January 2014 and August 2024 at our institution were identified. Patients were analyzed in two subgroups based on age (years): younger (age <65) vs older (age ≥65). Overall survival (OS), defined as the time from date of alloHSCT to death or last follow-up (FU), was estimated using the Kaplan-Meier method. Cox proportional-hazards models were used to identify prognostic factors for OS. Cumulative incidence of non-relapse mortality (NRM) was reported using competing-risk analysis, accounting for relapse or relapse-related mortality (RRM). Fine and Gray regression models were used to analyze NRM.

Results: Median age at HSCT was 55 years (interquartile range (IQR): 45-64), 51% were male, 66% with HCT-CI≥3, and 54% with KPS ≥90%. 61% underwent MAC, 40% with MUD, and GVHD prophylaxis was Tac/MTX in 27%, Tac/MTX/ATG in 47%, and PTCy in 26%. When comparing younger (n=211) and older (n=68) cohorts, baseline demographics were similar except for a higher proportion of men in the older cohort: 44.1% vs 72.1%(P<.0001).
With a median FU of 27 months (IQR: 9.4-59.6), median OS was not estimable (NE) for younger vs 20.1 months for older. Univariable Cox models identified age ≥65 (HR=1.86, 95%CI:1.26-2.73, P=0.002), RIC HSCT (HR=1.56, 95%CI:1.07-2.20, P=0.019), HCT-CI≥3 (HR=1.78, 95%CI:1.17-2.70, P=0.007), and KPS<80 (HR=2.24, 95%CI:1.38-3.63, P=0.001) as significantly associated with worse OS (P<.05). These associations remain significant in the multivariable model except for RIC HSCT (P=0.646). In age-stratified analyses, HCT-CI≥3 predicted poorer OS in the younger cohort (HR=1.95, 95%CI: 1.18-3.23, P=0.009) but this association did not hold for older patients (P=0.769).
OS at 2 years was 64.3% (95%CI:58.2-69.7%), with 55% of deaths due to RRM. In contrast, among older patients, NRM accounted for 68% of deaths. The cumulative incidence of NRM at 2-years was more than double in older vs younger cohort: 33.7% (95%CI:22.4-45.3%) vs 11.1% (95%CI:7.3-15.8%). Univariable Fine and Gray models showed that older age (HR=3.44, 95%CI:2.03-5.82, P<.0001), male sex (HR=1.80, 95%CI:1.04-3.11, P=0.035), RIC (HR=2.77, 95%CI:1.63-4.71, P=0.0002), and HCT-CI≥3 (HR=1.91,

95%CI:1.01-3.63, P=0.048) associated with higher NRM. On multivariable analysis, only age ≥65 years remained significantly associated with NRM (HR=2.35, 95%CI:1.01-5.45, P=0.047).
The cumulative incidence rate of relapse at 2-years was 24.7%, with no difference between older and younger groups (P=0.146). Within the older cohort, no significant difference in OS was observed between patients aged 65-69 and ≥70 years (P=0.319).

Conclusions: Older adults with AML (≥65 years) have inferior post-transplant OS and higher NRM than their younger counterparts. HCT-CI≥3 is not associated with NRM or OS in those age ≥65, suggesting that conventional comorbidity indices may have limited discriminatory ability in carefully selected older adults and highlighting the need for improved frailty-based risk assessment in older patients undergoing alloHSCT.

Disclosure: Nothing to declare.

A213

AGE AT TRANSPLANT DETERMINES OUTCOME FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MITOCHONDRIAL NEURO-GASTROINTESTINAL ENCEPHALOPATHY (MNGIE)

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Background: Mitochondrial neuro-gastrointestinal encephalopathy (MNGIE) is a rare autosomal recessive disorder caused by pathogenic variants in the *TYMP* gene, leading to thymidine phosphorylase (TP) enzyme deficiency resulting in the accumulation of toxic nucleosides (dThd and dUrd). Hematopoietic stem cell transplantation (HSCT) is effective in MNGIE to restore TP enzyme activity via engrafted donor-derived leukocytes, enabling detoxification of accumulated metabolites but outcomes vary significantly due to factors like patient age at transplant, disease severity, and donor characteristics, with treatment-related risks remaining substantial.
Here, we describe our experience of HSCT in four siblings having same mutation transplanted with the same donor but at different stages in disease course, to more exactly determine the influence of age on disease response.

Methods: Four siblings diagnosed with MNGIE disease, from a single family with consanguineous parentage (first-degree cousins) were referred for allogeneic-HSCT. These siblings shared the same donor - a fifth, wild-type (non-carrier) but HLA-matched sibling. The four affected siblings, representing a spectrum of disease severity—from asymptomatic to severely affected—underwent HSCT from this unaffected matched sibling donor, offering a unique opportunity to observe differential disease responses to transplantation within a

genetically and environmentally similar cohort. Data collected included demographic information, symptomatology, serum dUrd/dThd levels, TYMP mutations, pre-transplant characteristics, conditioning regimen, chimerism, post-transplant survival, long term follow-up and outcomes.

Results: Pre-transplant nutritional status was poor in all four patients. Severe neurological disease was seen in two patients whilst the youngest sibling was asymptomatic and had normal MRI and NCS. Two patients received fludarabine, treosulfan, and thiotepa (FTT) whilst two received busulfan and fludarabine conditioning. All had alemtuzumab as part of the institutional protocol for non-malignant disease. All patients engrafted successfully, with mean neutrophil engraftment on day +11.5±1.3 and platelet engraftment by day +15.3±5.9. At median follow-up of 6.75 years,we report 100% survival. No significant GvHD was seen. Notably, the second sibling had developed a severe acute stroke like-episode resembling those in MELAS. She eventually made remarkably recovery with minimal residual right hemiparesis. No other patient has demonstrated such progressive neurological decline post-HSCT. Pre-existing neurological deficits have remained largely unchanged. Two older siblings developed intestinal failure requiring prolonged TPN. One of them has been transitioned to enteral feeding, but both continue to experience GI symptoms and difficulty gaining weight. Third sibling also continues to struggle with GI symptoms but manages on high calorie enteral feeds. The youngest has not required nutritional support. Biochemically these 4 siblings have shown a dramatic decrease in disease related metabolites.

Transplant characteristics	**Patient A**	**Patient B**	**Patient C**	**Patient D**
Age at HSCT	16	15	13	5
Donor	10/10 HLA MSD	10/10 HLA MSD	10/10 HLA MSD	10/10 HLA MSD
Conditioning regimen	F - 40 mg/m2 T – 10 mg/Kg T – 14000 mg/m2 Alemtuzumab – 0.1 mg/Kg	F - 40 mg/m2 T – 10 mg/Kg T – 14000 mg/m2 Alemtuzumab – 0.1 mg/Kg	Bu – 1.9 mg/Kg (AUC – 80 mg/L/h) Flu – 40mg/m2 Alemtuzumab – 0.1 mg/Kg	Bu – 2.4 mg/Kg (AUC – 80 mg/L/h) Flu – 40mg/m2 Alemtuzumab – 0.1 mg/Kg
HSC source	PB	PB	PB	PB
TNC (x10^8/Kg)	4.18	4.18	6.25	6.35
CD34+ cell count (x106/Kg)	4.87	4.86	5.24	5.33
GVHD prophylaxis	CsA/MMF	CsA/MMF	CsA/MMF	CsA/MMF

Neutrophil engraftment	D+11	D+10	D+12	D+13
Platelet engraftment	D+12	D+13	D+12	D+24
Most recent chimerism	100%	100%	100%	100%
Outcomes	Post-Tx intestinal failure but currently on high calorie enteral feeds. Nil neurological progression.	Intestinal failure on TPN, Stroke like episode	Ovarian failure on HRT, Vitiligo, Nil neurological progression.	Ovarian failure on HRT, Vitiligo, Nil neurological progression. Gastrostomy in-situ to help with nutrition. Nil neurological progression.

Conclusions: Our unique experience highlights the critical importance of timing of HSCT in MNGIE in determining outcome. Those without disease manifestations do not develop them, but those with them do not improve. This persistent morbidity underscores the importance of considering MNGIE for inclusion in newborn screening programs to enable the earliest possible therapeutic intervention. This observation includes the GI manifestations, related to autonomic neuropathy, and there remains persistent nutritional difficulties and this long-term morbidity must form part of pre-transplant patient planning for the affected child.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

A214

LONG-TERM OUTCOMES OF HAPLOIDENTICAL AND MATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN COMPLETE REMISSION NON-DS-AMKL: A SINGLE-CENTER COHORT STUDY

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Background: Acute megakaryoblastic leukemia without Down syndrome (non-DS-AMKL) is a rare subtype of pediatric AML with limited evidence guiding optimal transplantation

strategies. This study aimed to compare the efficacy and safety of haplo-HSCT versus MUD-HSCT in non-DS-AMKL patients in complete remission (CR).

Methods: We retrospectively analyzed 63 pediatric non-DS-AMKL patients who underwent allo-HSCT in CR at our center between July 2016 and January 2025. Fifty-one patients received haplo-HSCT and 12 underwent MUD-HSCT. Clinical characteristics, engraftment kinetics, graft-versus-host disease (GVHD) incidence, viral reactivation, relapse, transplant-related mortality (TRM), and survival outcomes were compared. To identify independent prognostic determinants, multivariate Cox proportional hazards models were applied for OS and LFS, while Fine–Gray competing-risk models were used to evaluate relapse and NRM in the full cohort of 63 patients.

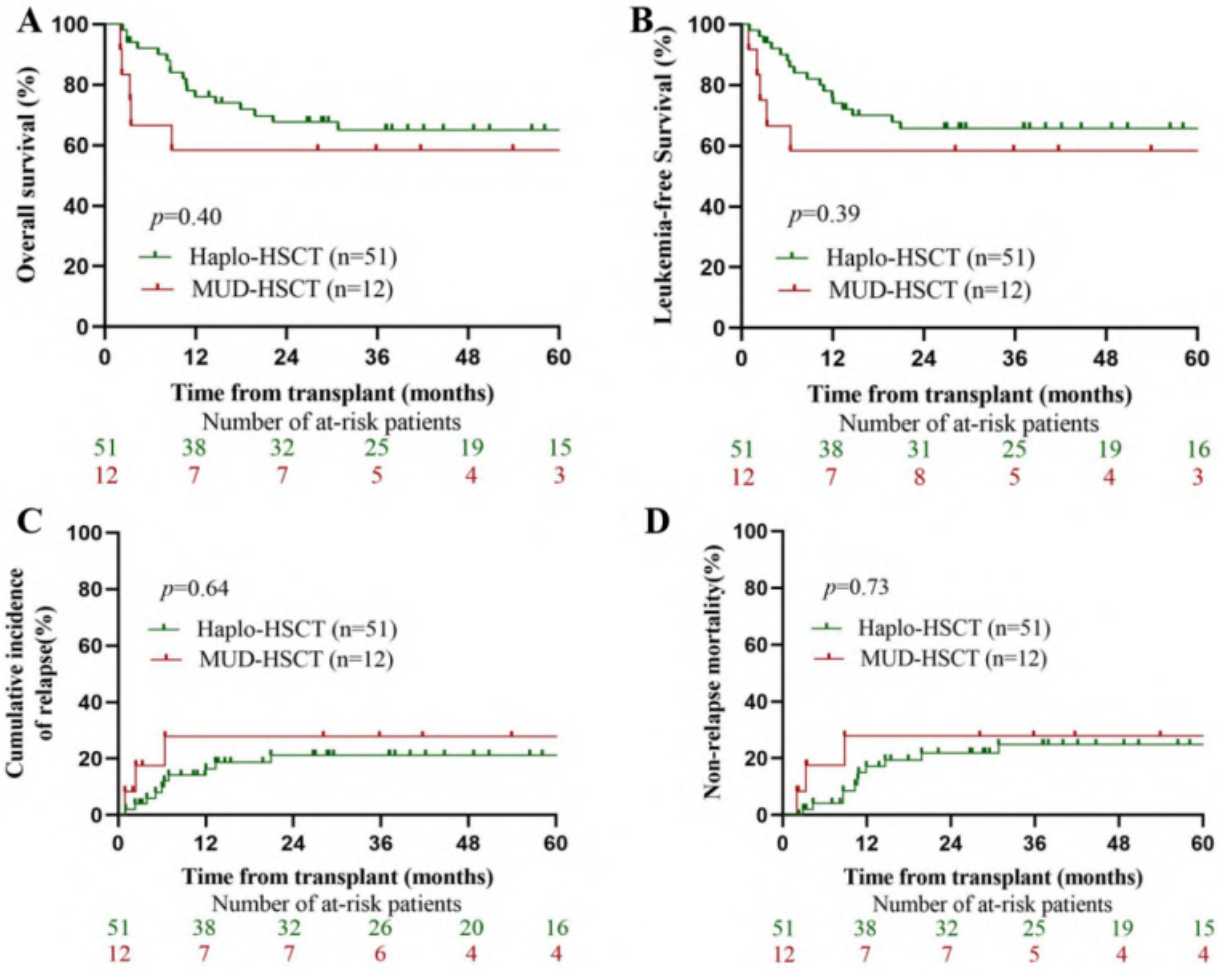
Results: Baseline characteristics of the 63 children with non-DS-AMKL undergoing allo-HSCT (51 haplo-HSCT; 12 MUD-HSCT) were overall comparable . All patients (100%) achieved WBC engraftment by day 28 post-HSCT. Platelet engraftment by day 28 occurred in 94.1% (48/51) of patients in the haplo-HSCT group and in 100% (12/12) of the MUD-HSCT group (P = 1.00). With the median follow-up 30.8 months (range, 2.0–105.3), the 5-year overall survival (OS) was 65.8% in the haplo-HSCT group versus 58.3% in the MUD-HSCT group (P = 0.40) (Figure 1A); 5-year leukemia-free survival (LFS) was 65.1% versus 58.3% (P = 0.40) (Figure 1B), respectively. 5-year Cumulative incidence of relapse was 20.1% in the haplo-HSCT group and 25.0% in the MUD-HSCT group (P = 0.64), while 5-year non-relapse mortality (NRM) was 22.8% and 25.0% (P = 0.73) (Figure 1 C/D), respectively. The incidence of grade III–IV aGVHD and severe chronic GVHD was higher in the haplo-HSCT group, but without statistical significance (all P>0.05).
Multivariate Cox and Fine–Gray analyses (Table 1) identified complex cytogenetics as the only consistent adverse prognostic factor, significantly worsening OS (HR 2.79; 95% CI, 1.14–6.87; P = 0.03), LFS (HR 2.88; 95% CI, 1.18–7.08; P = 0.02), and RI (HR 4.05; 95% CI, 1.03–15.99; P = 0.05). A higher MNC dose (>15 $\times 10^8$/kg) showed a trend toward improved survival, though without statistical significance for OS (HR 0.19; P = 0.07) or LFS (HR 0.17; P = 0.06). Notably, a higher $CD34^+$ cell dose (>8 $\times 10^6$/kg) was associated with better OS and LFS (both P = 0.05), but this observation requires further validation given the CI width. Use of a MEL+BU–based conditioning regimen significantly reduced relapse risk (HR 0.27; 95% CI, 0.08–0.96; P = 0.04). In contrast, donor type (MUD vs haplo), fusion gene status, $CD3^+$ T-cell dose, and age showed no measurable impact on OS, LFS, RI, or NRM.

Table 1. Multivariate analysis Results

Variables	**OS**		**LFS**		**RI**		**NRM**	
	HR (95% CI)	*P-vaule*	HR (95% CI)	*P-vaule*	HR (95% CI)	*P-vaule*	HR (95% CI)	*P-vaule*
Age (≤ 2Y vs. > 2Y)	0.58 (0.24-1.42)	*0.23*	0.55 (0.22-1.37)	*0.20*	0.38 (0.09-1.69)	*0.20*	1.01 (0.33-3.08)	*0.98*

Conditioning regimen (BU vs. BU+MEL)	0.85 (0.25-2.85)	*0.79*	0.83 (0.25-2.80)	*0.77*	0.27 (0.08-0.96)	*0.04*	1.12 (0.29-4.30)	*0.87*
HSCT(MUD vs. Haplo)	0.94 (0.24-3.70)	*0.93*	0.98 (0.25-3.77)	*0.97*	1.32 (0.32-5.48)	*0.70*	0.82 (0.10-6.82)	*0.85*
Complex cytogenetics (No vs. Yes)	2.79 (1.14-6.87)	*0.03*	2.88 (1.18-7.08)	*0.02*	4.05 (1.03-15.99)	*0.05*	1.84 (0.71-4.80)	*0.21*
Fusion_gene (Neg vs. Pos)	0.38 (0.11-1.30)	*0.12*	0.36 (0.11-1.22)	*0.10*	0.19 (0.03-1.25)	*0.08*	0.35 (0.06-1.89)	*0.22*
MNC (≤ 15 vs. > 15)	0.19 (0.03-1.11)	*0.07*	0.17 (0.03-1.04)	*0.06*	0.05 (0.003-0.70)	*0.03*	0.44 (0.06-2.97)	*0.40*
CD34+ (≤ 8 vs. > 8)	3.31 (0.99-11.05)	*0.05*	3.51 (1.02-12.03)	*0.05*	4.66 (0.70-30.93)	*0.11*	2.97 (0.47-18.98)	*0.25*
CD3+ (≤ 3 vs. > 3)	1.22 (0.29-5.25)	*0.79*	1.18 (0.27-5.11)	*0.83*	0.44 (0.04-5.10)	*0.51*	1.80 (0.27-11.83)	*0.54*

Figure 1. Long-term outcomes in 63 patients with non-DS-AMKL



Conclusions: In pediatric non–DS-AMKL patients undergoing allogeneic HSCT in complete remission, haplo-HSCT yielded long-term outcomes comparable to MUD-HSCT, with similar relapse risks and survival. These findings support haplo-HSCT as an effective and practical alternative when a matched unrelated donor is unavailable or when timely transplantation is essential.

Disclosure: Nothing to declare

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IMPACT OF HEPATITIS E VIRUS INFECTION ON ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CURRENT TREATMENT STATUS

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Background: Hepatitis E virus (HEV) is a single-stranded RNA virus. Besides its hepatotropism, it may also cause extrahepatic damage to systems such as the nervous, urinary, and hematological systems. In patients undergoing allo-HSCT, the inability to spontaneously clear the virus predisposes them to chronic infection upon exposure. Reports on its impact on allo-HSCT are scarce.

Methods: A retrospective analysis was conducted on clinical cases of HEV infection among allo-HSCT patients at Hebei Yanda Lu Daopei Hospital and Beijing Lu Daopei Hospital from January 2023 to November 2025. HEV infection was diagnosed via NGS and/or PCR. Clinical manifestations and outcomes of HEV infection in transplant patients were analyzed.

Results: Among 3,393 transplant patients, four were diagnosed with hepatitis E virus infection, comprising one male and three females, with a median age of 33.5 years(8~52years). Diagnoses included AML (n=3) and B-ALL(n=1). All patients received myeloablative conditioning regimens and underwent haploidentical hematopoietic stem cell transplantation. The GVHD prophylaxis regimen consisted of CSA, sMTX, and MMF. HEV was detected at a median time of −5.5 days relative to transplantation (−17~+69d). Specimen types included blood (n=2), cerebrospinal fluid (n=1), and bronchoalveolar lavage fluid (n=1). Clinical presentations included asymptomatic HEV viremia (n=2), HEV-associated encephalitis (n=1), and HEV-associated pneumonia (n=1). The median NGS read count was 316.5 (4~73,311), and the median PCR viral load was 3.8E+07copies/mL (1.2E+07~6.4 E+07copies/mL). Serology showed HEV IgM-positive and IgG-negative in one patient; IgM-negative and IgG-negative in one patient ;two patients were not tested. Two patients received ribavirin with or without interferon therapy, while two did not. The median treatment duration was 50 days (30~60d). The median time to viral clearance by PCR was 341days (259~423d). Clinical features of HEV infection included elevated transaminase and bilirubin levels, pneumonia, encephalitis, and symptoms such as limb weakness and dysphagia. Imaging of HEV encephalitis typically revealed multiple brain lesions, predominantly in the white matter. All four patients with HEV infection achieved successful engraftment of granulocytes and platelets. Complications included CMV reactivation (n=1), EBV reactivation (n=1), HHV-6 reactivation (n=1), and pancytopenia (n=1). No ADV reactivation was observed. aGVHD occurred in three cases, and cGVHD occurred in two. One patient died from cerebral hemorrhage, and one patient was lost to follow-up due to limb weakness.

Conclusions: Hepatitis E virus infection is not exclusively hepatotropic and can involve multiple organ systems. Time to viral clearance is prolonged in allo-HSCT patients, and HEV may exert a non-negligibie impact on transplantation outcomes. Further studies with larger

sample sizes are warranted to clarify its clinical significance and optimize management strategies.

Disclosure: Nothing to declare.

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IMPACT OF THERAPEUTIC PLASMA EXCHANGE ON PAN-REACTIVE HLA ANTIBODY TITRES IN PATIENTS WITH TRANSFUSION-DEPENDENT THALASSEMIA UNDERGOING MATCHED RELATED DONOR HSCT: A SINGLE-CENTRE STUDY

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Background: Donor non-specific HLA antibodies or pan-reactive antibodies (PRA) in paediatric transfusion-dependent thalassemia (TDT) patients may impact the outcomes of HSCT by increasing the blood-product transfusion requirement, graft-failure, and post-transplant complications. Therapeutic plasma-exchange (TPE) prior to transplant might assist in optimising outcomes in PRA positive patients.

Methods: Children with TDT undergoing HSCT with fully-matched related donors were included in this study (period:January-December,2024). All patients were screened for class I and II PRA using Immunoassay on Luminex solid-phase technology. Pre-transplant PRA levels were evaluated and PRA-positive (n = 22) children were included in the study. Patient characteristics: age, gender and stem-cell source, were analyzed. Depending upon the MFI value, they were planned for TPE prior to conditioning chemotherapy. MFI value >1200 was considered positive and those with MFI>3000 warranted TPE. TPE cycles were done at approximately 1.2-1.5 times blood-volume. For MFI of upto 5000, 5000 to 10000, 10000 to 15000, 15000 to 20000, and >20000, the TPE cycles done were respectively 1,2,3,4 and 5. PRA were repeated thereafter and compared. Transplant outcomes, including engraftment and graft failure were compared with the data available from previous studies.

Results: Out of 49 total HSCT in 2024, 22children(males=11, females=11), who underwent HSCT for TDT in the age-group 2-12 years with PRApositive status, were included in the study. Out of this,15 were from PBSC(68%), rest bone-marrow(32%). All these patients had positive HLA class I antibody level(100%), however 15 out of 22 had class II positive antibody titre(68%). There was reduction in antibody-titres of class I panel in 78% (17) patients; no reduction in 22% (5) patients, reduction in antibody-titres of class II panel in 94%(14) patients; no reduction in 6% (1)patient. Engraftment occurred in 20 patients out of 22 (90%); 1 had primary graft failure due to CMV reactivation and 1 died of gram-negative sepsis pre-engraftment. Median platelet engraftment occurred on day +19.

Parameter	Result
Total Patients Included	22 PRA-positive pediatric thalassemia
Gender Distribution	11 Male (50%), 11 Female (50%)
Stem Cell Source	68% PBSC, 32% Bone Marrow
Class I PRA Reduction	17 / 22 patients (77%)
Class II PRA Reduction	14 / 15 patients (93%)
TPE Cycles per Patient	1–6, based on MFI levels
Neutrophil Engraftment	20 / 22 patients (91%), Day +14
Platelet Engraftment	20 / 22 patients (91%), Day +19
Graft Failure	1 patient (4.5%) — CMV reactivation
Pre-Engraftment Mortality	1 patient (4.5%) — Sepsis
Comparison with Literature	Engraftment timelines comparable (WBC: 11–21d, Platelets: 14–24d)

Conclusions: Patients with TDT need repeated red-cell transfusions leading to alloimmunization with PRA, which hamper HSCT by increasing the transfusion requirement, delayed platelet engraftment and causing primary graft failure. By doing TPE to reduce PRA positivity, 90%patients engrafted and none had delay in platelet-engraftment, thereby improving the overall transplant outcomes. Although, TPE is well-studied in solid organ transplantation to reduce anti-HLA antibodies, including DSAs and PRA, there is no direct evidence that specifically evaluates TPE to lower anti-HLA antibody levels before HSCT in matched related donor patients. As per our experience, TPE might be an effective technique in reducing PRA and thereby decreasing the chances of primary graft failure and delay in platelet engraftment.

Disclosure: Nothing to declare.

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RISK FACTORS FOR REFRACTORY CYTOMEGALOVIRUS INFECTION IN HEMATOPOIETIC STEM CELL AND SOLID ORGAN TRANSPLANT RECIPIENTS

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Background: Refractory cytomegalovirus (CMV viral load <1 $\log_{10}$ reduction after 2 weeks' antiviral therapy) and resistant CMV (with specific genotypic mutations in refractory CMV) could portend poor outcomes including increased mortality, end-organ disease, and graft failure. Meanwhile, patients with refractory CMV infection face prolonged antiviral treatment. A thorough understanding of the risk factors for refractory CMV is important for improving disease management and prognosis. This scoping review identifies key risk factors to guide clinical decision.

Methods: This study employed a scoping review framework (PRISMA-ScR guidelines) to systematically search PubMed, EMBASE, the Cochrane Library, Web of science, CNKI, Wanfang, VIP and CBM (2010-2023) for literature on risk factors for refractory CMV infection after transplantation.

Results: A total of 13 studies were included (hematopoietic stem cell transplantation (HSCT): 10 studies involving 946 patients; solid organ transplantation (SOT): 3 studies involving 101 patients). Based on the 13 studies, 15 risk factors for refractory CMV infection were identified and stratified as follows: 1) There were 14 HSCT-specific factors, including 4 host-related factors [acute graft-versus-host disease, Epstein-Barr virus viremia, NKG2C del/del genotype, platelet count at 90 days after transplant <= 86×10^9/L], 8 transplant-related factors [CMV serological status of donor$^{(-)}$ and recipient$^{(+)}$ (vs donor$^{(+)}$ and recipient$^{(+)}$), ATG used in conditioning therapy total body irradiation/mycophenolate mofetil used in prophylactic immunosuppression (vs busulfan/mycophenolate mofetil used in prophylactic immunosuppression), mycophenolate mofetil used in Prophylactic immunosuppression (vs mizoribine), steroid use >=1 (vs <1) mg/kg/day, umbilical cord blood/bone marrow transplantation, haploidentical/mismatched transplantation, white blood cell at 14 day after transplant < 4×10^9/L], and 2 viral-related factors [highest CMV load > 10^4 copies/mL, CMV-specific $CD8^+$ TcM at day 30 <0.032 μL)] factors . Moreover, 2) 5 SOT-specific risk factors for refractory and resistance CMV included 2 anti-CMV drug-related factors [history of Valganciclovir underdosing or low plasma concentration, breakthrough infection during the use of valganciclovir], 2 host-related factors [persistent clinical disease and younger recipient age], and 1 transplant-related factor [CMV serological status of donor$^{(+)}$ and recipient$^{(-)}$ (vs others)].

Transplant type	Factor category	Factors	Number of refractory reference	Number of resistance reference
Haematology transplant (n=10)	Host-related factors	aGVHD (grade II-IV vs. grade 0-I)	4	
		aGVHD (yes vs. no)	2	
		EB viremia (yes vs. no)	1	
		NKG2C (del/del vs. wt/del)	1	
		NKG2C (del/del vs. wt/wt)	1	
		Platelet count at day 90 after transplant ($\times 10^9$/L) (≤86 vs. >86)	1	
	Transplantation-related factors	ATG used in conditioning therapy (yes vs. no)	1	
		CMV serostatus (D-/R+ vs. D+/R+)	1	
		Conditioning regimen (TBI/Cy vs. Bu/Cy)	1	
		Donor type (cord blood vs. non-cord blood)	1	
		Donor type (Haplo or MUD vs. MSD)	1	
		Donor type (HBMT vs. MSD)	1	
		Donor type (mismatched family vs. MSD)	1	
		Prophylactic immunosuppression (MMF vs. MZR)	1	
		Stem cell source (BM or CB vs. PB or PB+BM)	1	
		Steroid use (MP, mg/kg/day) (≥1 vs. <1)	1	
		WBC at 14 day after transplant ($\times 10^9$/L) (<4 vs. ≥4)	1	
	Viral-related factors	CMV-specific CD8+ TcM at day 30 (μL) (<0.032 vs. ≥0.032)	1	
		Highest CMV viral load ($\times 10^4$ copies/mL) (>1 vs. ≤1)	2	
Organ transplant (n=3)	Anti-CMV drug-related factors	History of VGCV underdosing or low plasma concentration (yes vs. no)		1
		VGCV prophylaxis at infection onset (yes vs. no)		1
	Host-related factors	Persistent clinical disease (yes vs. no)		1
		Younger recipient age		1
	Transplantation-related factors	CMV serostatus (D+/R- vs. others)	1	1

Figure 1. Hot map of risk factors for refractory or resistance CMV infection.
Notes: The numbers in the hot map indicate the number of articles corresponding to the factors.
Abbreviations: aGVHD, acute graft-versus-host disease; ATG, anti-thymocyte globulin; CMV: cytomegalovirus; BM: bone marrow; BU: busulfan; CB: cord blood; Cy: cyclophosphamide; EB, Epstein-Bar; MMF: mycophenolate mofetil; MP: methylprednisolone; MSD: matched sibling donor; MUD: matched unrelated donor; MZR: mizoribine; PB: peripheral blood; TBI: total body irradiation; VGCV: valganciclovir; WBC: white blood cell.

Conclusions: The HSCT-specific risk factors for refractory CMV infection included host immune status, transplantation regimens and viral load, genotypes and blood parameters, while, CMV serological status of donor and recipient, anti-CMV drug exposure, and persistent disease were SOT-specific risk factors for refractory and resistance CMV. Early identification of patients at risk of refractory CMV infection can help guide the selection of drugs that can quickly achieve CMV clearance and have better tolerance when CMV infection occurs, thereby improving the clinical prognosis of patients.

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PROGNOSTIC AND SAFETY PREDICTIVE VALUE OF THE SYSTEMIC IMMUNE-INFLAMMATION INDEX IN R/R B-CELL LYMPHOMA PATIENTS UNDERGOING CAR-T CELL THERAPY

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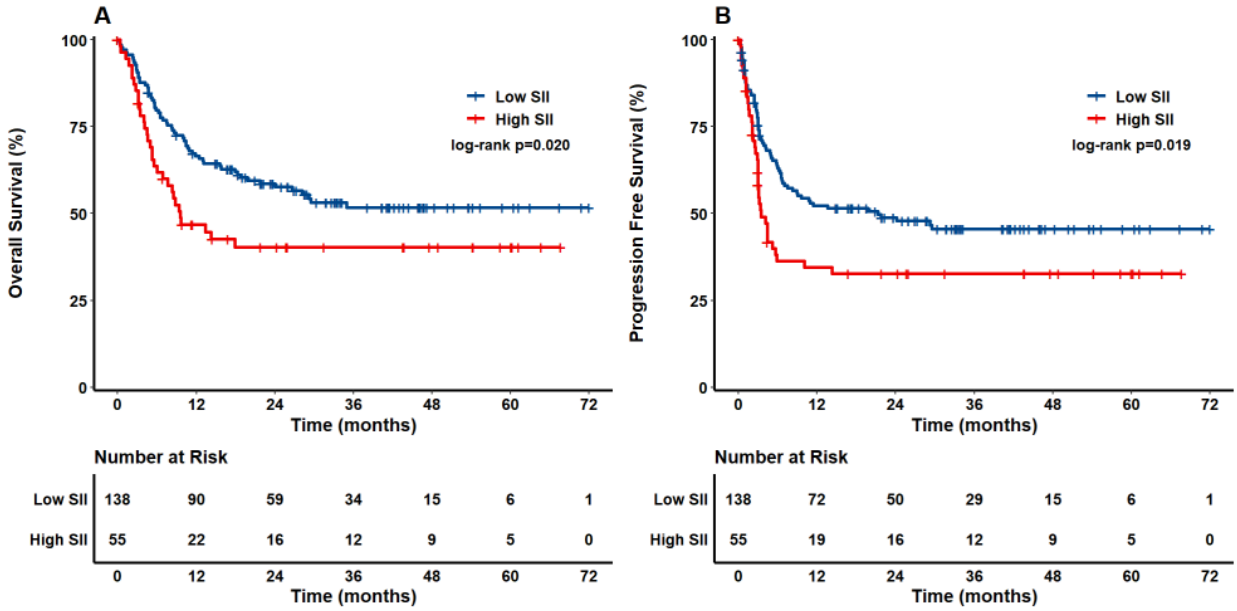
Background: Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as an effective treatment option for relapsed or refractory (R/R) lymphomas. However, simple and reliable biomarkers capable of predicting survival outcomes and treatment-related toxicities remain lacking. The systemic immune-inflammation index (SII), which reflects a patient's inflammatory and immune status, has been recognized as a prognostic marker in various malignancies. This study aimed to evaluate the predictive value of pre-lymphodepletion SII levels for survival and safety outcomes in R/R B-cell lymphoma patients receiving CAR-T therapy.

Methods: We retrospectively analyzed 504 patients who underwent CAR-T therapy in our department from December 2018 to January 2024. The SII was calculated before lymphodepletion chemotherapy using the formula: platelet count × neutrophil count / lymphocyte count. The optimal cutoff value for overall survival (OS) was determined using a Cox regression model. To minimize baseline imbalances, patients were divided into Low-SII and High-SII groups using propensity score matching (PSM). Adverse events, treatment response, and survival outcomes were analyzed using Kaplan–Meier curves, log-rank tests, and Cox proportional hazards models.

Results: A total of 193 patients were included (median age 50; 75.6% male; median BMI 22.7 kg/m²). Disease subtypes were predominantly DLBCL (n=144). ECOG ≥2, IPI ≥3, and stage ≥III were observed in 34.2%, 46.6%, and 92.2% of patients, respectively.The optimal SII cutoff for OS was 1499.65, resulting in 138 patients in the Low-SII group and 55 in the High-SII group after PSM.
CRS occurred in 78.8% of patients, including 14.5% with grade ≥2 events. ICANS occurred in 2.6% (all grade ≥3). Grade ≥3 hematologic toxicities were common: neutropenia 92.7%, thrombocytopenia 66.3%, anemia 64.2%.
High SII was associated with a significantly higher incidence of grade ≥2 ICANS (7.3% vs. 0.7%; P=0.0239; OR=10.746), while rates of CRS and hematologic toxicity were comparable between groups.
The ORR was 62.7%, with a CR rate of 46.6%. High-SII patients had lower ORR (50.9% vs. 67.4%; P=0.0472) and CR rates (34.5% vs. 51.4%; P=0.0384).
At a median follow-up of 34.29 months, median PFS was 9.04 months and median OS was 29.52 months; 5-year PFS and OS rates were 42.03% and 48.39%. Low-SII patients showed significantly better survival (5-year PFS 45.56% vs. 32.73%; P=0.019; 5-year OS 51.65%

vs. 40.25%; P=0.020). High SII remained an independent predictor of inferior PFS (HR=1.599) and OS.



Conclusions: High pre-treatment SII is an independent and powerful biomarker for predicting inferior survival (shorter OS and PFS) and reduced treatment response in R/R B-cell lymphoma patients undergoing CAR-T therapy. In addition, elevated SII is significantly associated with a higher risk of severe neurotoxicity (ICANS). As a readily obtainable inflammatory marker, SII may facilitate risk stratification prior to CAR-T therapy and support individualized decision-making in clinical practice.

Disclosure: Nothing to Disclosure

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BONE MARROW TRANSPLANTATION IN SICKLE, ACCORDING TO DONOR STATUS: COMPARISON AND DIFFERENCES IN CLINICAL OUTCOMES

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Background: The primary objective of allogeneic hematopoietic stem cell transplantation (HSCT) in sickle cell disease (SCD) patients is to prevent irreversible organ damage that occur during the natural progression of the disease. The donor's status (AA vs. AS carrier) directly influences the proportion of haemoglobin S and A after HSCT. With AS donors, HbS final proportion is around 35-40%, so to correct haemolysis, >50% chimerism is required. Currently, there are no descriptive studies comparing the impact of donor status (AA vs AS) on HSCT outcomes and chimerism.

Methods: A single retrospective center study conducted in SCD children, who underwent allogeneic HSCT of HLA-identical sibling donor, between may 2010 and October 2025 in the Pediatric Oncohematology area of Hospital Gregorio Marañon. We excluded haploidentical donor transplants, in order to homogenize the results.
Clinical characteristics pre-HSCT and complications after the transplant were analyzed, differentiating between AA or AS carrier donors. Epidemiological and clinical parameters were collected.

Results: 69 HSCT were performed. Excluding haploidentical transplants, 63 allo-HSCT were included in 62 SCD patients (54.4% males, 45.6% females), median age 7.63 years (p25 3.23; p75 10.47). All were HLA-identical 10/10 sibling donor. The source of stem cells were bone marrow in all cases, median $CD34^{+}$ number infused $6.52^{x10e6/Kg}$. Regarding donor status (AA or AS carrier), 57.6% were AA donors and 42.4% were AS donors.

- In the HSCT of carrier AS donors cohort (30 HSCT): median time for neutrophil engraftment was 18.5 days (p25 16.75; p75 22), and the median time for platelets engraftment was 21 days (p25 18; p75 28,75). 71.4% developed reactivation CMV, 71.4% mucositis, 46.4% acute GvHD, 22.2% neurologic complications and 21.4% AKI renal complications. 2 patients developed graft rejection, currently asymptomatic. 1 patient of this cohort died, due to refractory grade IV GvHD and multiorgan failure at day +51.
- In the HSCT of AA donors cohort (33 HSCT): median time for neutrophil engraftment was 19 days (p25 17; p75 22.74), and the median time for platelets engraftment was 24.5 days (p25 20; p75 28,75). 61.5% developed reactivation CMV, 38.5% mucositis, 33.5% acute GvHD, 17.9% neurologic complications and 17.9% AKI renal complications. 3 patients (9%) developed chronic GvHD. 1 patient developed graft rejection, with recurrence of vasoocclusive crisis on day +180, so we did a second HSCT from the same donor. 1 patient of this cohort died, due to refractory hemophagocytic lymphohistiocytosis on +2 years after HSCT, secondary to VEB infection and cholestatic liver disease.
- Regarding chimerism, in the cohort of AS donors: 4 patients (14%) had mixed chimerism at +1 year posHSCT, and 8 patients (28.6%) at the time of last appointment. In the cohort of AA donors: 11 patients (29.7%) had mixed chimerism at +1 year posHSCT, and 10 patients (26.5%) at the time of last appointment. No statistically significant evidence was found between the percentage of patients with mixed chimerism or time of engraftment, and AA vs. AS donors.

Conclusions: The need for prospective comparative studies or randomised controlled trials, directly comparing transplants according to AA or AS donors, is emphasised.

Disclosure: Nothing to declare.

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THE PROGNOSTIC IMPACT OF CEBPA MUTATIONS IN ACUTE MYELOID LEUKEMIA PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Myelodysplasia-related gene mutations and cytogenetic abnormalities in acute myeloid leukemia (AML) patients are strongly associated with clinical outcomes and play a pivotal role in guiding therapeutic strategies. The presence of mutations in the basic leucine zipper (bZIP) region of the CEBPA gene in patients with AML is defined as a favorable risk marker according to the guidelines. However, the value of allogeneic hematopoietic stem cell transplantation (allo-HSCT) in AML patients with CEBPA mutations remains to be clarified.

Methods: We retrospectively enrolled 173 patients with de novo AML who had undergone their first allo-HSCT between January, 2014 and March, 2025 in the IHCAMS (Institute of Hematology and Blood Diseases Hospital, Peking Union Medical College). Moreover, we enrolled 345 patients with newly diagnosed AML without CEBPA mutations, who received first allo-HSCT as the control group. Genomic DNA of all patients was extracted from BM cells for next-generation sequencing (NGS).

Results: In total, 204 (12.57%) of the 1600 patients with AML receiving allo-HSCT were detected CEBPA mutations. After excluding ineligible patients, 173 de novo AML patients with $CEBPA^{mut}$ detected before induce chemotherapy were enrolled in our study compared with 345 $CEBPA^{wt}$. The median follow-up time was 37.9 months (95% CI, 31.6-43.9 months) from transplantation. Patients carrying $CEBPA^{mut}$ had a significantly higher complete remission (CR) rate after first induction chemotherapy (80% vs. 68%, $P < 0.006$) and had a better 5-year PFS than $CEBPA^{wt}$ group (60.8% vs. 55.0%, $P = 0.016$). Failure to achieve remission after first induction chemotherapy as well as before transplantation, the presence of CEBPA mutation before allo-HSCT and the absence of maintenance therapy were proven to be statistically significant factors for worse overall survival (all $P < 0.001$). Univariate and multivariate Cox proportional hazards models were applied to evaluate risk factors and confirmed that $CEBPA^{mut}$ was an independent prognostic factors associated with improved PFS after allo-HSCT (HR, 0.68; 95% CI, 0.48 - 0.96, $P = 0.03$). Surprisingly, survival analysis revealed that patients with nontypical in-frame bZIP mutations had a favorable outcome of PFS than typical bZIP mutations ($CEBPA^{no\ in\text{-}frame\ bZIP}$ 63.3% vs. $CEBPA^{in\text{-}frame\ bZIP}$ 59.9% vs. $CEBPA^{wt}$ 55.0%, $P = 0.045$). Furthermore, the most common frequently co-mutated genes were WT1 (48 of 173, 28%), GATA2 (35 of 173, 20%), NRAS (33 of 173, 20%), FLT3-ITD (32 of 173, 19%), TET2 (28 of 173, 16%), NPM1 (21 of 173, 12%), and KIT (19 of 173, 11%). Interestingly, patients harboring both FLT3-ITD and CEBPA mutations had a significantly longer 5-year PFS than other groups ($CEBPA^{mut}$/$FLT3\text{-}ITD^{mut}$ 75.9% vs. $CEBPA^{mut}$/$FLT3\text{-}ITD^{wt}$ 57.3% vs. $CEBPA^{wt}$ 55.0%, $P = 0.02$). Conversely, the presence of GATA2 mutations (PFS: $CEBPA^{mut}$/$GATA2^{mut}$ 43.2% vs. $CEBPA^{mut}$/$GATA2^{wt}$ 63.8% vs. $CEBPA^{wt}$

55.0%, *P* = 0.04) showed no benefit.

Figure 1

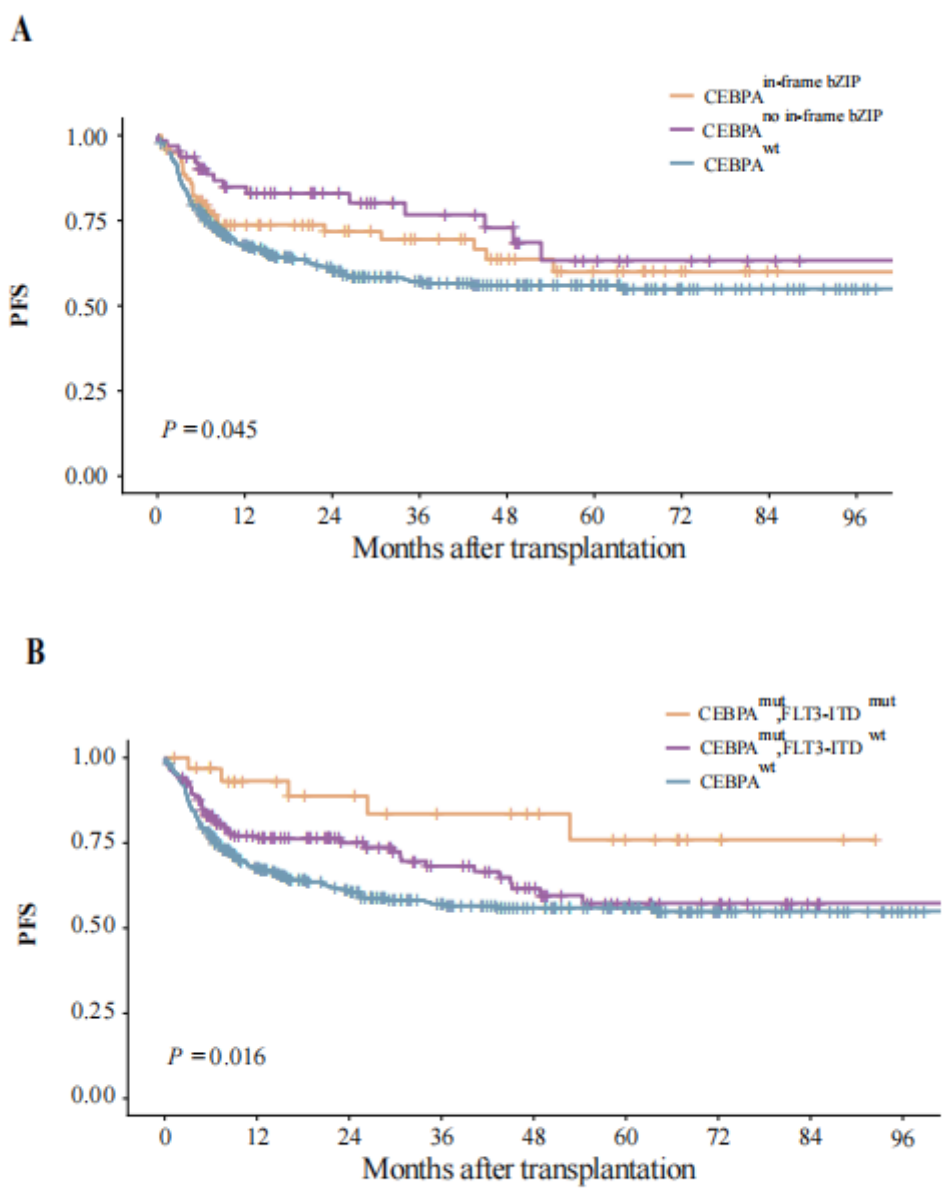

Fig 1. PFS in patients stratified by CEBPA mutation status and frequent concurrent co-mutations.
A.CEBPA in-frame bZIP vs. CEBPA no in-frame bZIP
B.CEBPAmut with or without the co-mutation of FLT3-ITD

Conclusions: CEBPA^{mut} patients achieving CR after initial therapy and before transplantation, without the presence of mutations and receiving maintenance therapy three

months after allo-HSCT had a superior probability of longer survival. Our findings suggest that CEBPA^{mut} patients with nontypical in-frame shift in bZIP region or with the co-mutation of FLT3-ITD could benefit from allo-HSCT.

Disclosure: Nothing to declare.

A221

MESENCHYMAL STEM CELL TRANSPLANTATION IN PATIENTS WITH GRAFT HYPOFUNCTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Graft hypofunction (GH) with preserved donor chimerism, the absence of drug toxicity, disease recurrence, or severe infectious complications poses a challenge in post-transplant patient management. Causes of GH may include HLA incompatibility or haploHSCT, toxicity of conditioning regimens, patient status, graft cellularity by CD34, graft source, and others. Treatment of GH: use of growth factors, transfusion of donor red blood cells and platelets, re-transplantation, correction of immunosuppressive therapy. At the Minsk Scientific Practical Center for Surgery, Transplantology, and Hematology, we use mesenchymal stem cell (MSCs) transplantation to treat various autoimmune diseases, GVHD, and GH therapy. MSCs exert a immunosuppressive effect, inhibit the proliferation of T- and B-lymphocytes, and activate anti-inflammatory pathways in vitro and in vivo. Their immunomodulatory properties offer clinical advantages in the treatment and prevention of GVHD, and they promote tissue repair and graft engraftment afterg hematopoietic stem cell transplantation (HSCT).

Methods: We used TMSC obtained from adipose tissue of an unrelated donor in 13 patients with HFT: 6 women, 7 men, aged from 24 to 51 years (Me 37). Diagnoses, patients : myelofibrosis - 2, chronic myelogenous leukemia - 2, severe aplastic anemia - 3, myelodysplastic syndrome - 2, acute myeloid leukemia - 4. Conditioning regimens: MAC in 6 patients, RIC - in 7, post-transplant cyclophosphamide were used in 6 patients, in 5 patients the HSC transplantation was from a 9/10, in one - haploSCTl (6/10), Mediana CD34+ was 6.02x106/kg (from 3.2 to 13.99), BM -1 patients (1.16 x106/kg). ABO incompatibility - in 8 patients (major 2, minor -3, major+minor -3), the donor was female in 6 patients.
Three patients had 3-lineage GH, five patients had 2-line GH (neutrophils and platelets), and five patients had 2-line GH (platelets only).
Was performed from 1 to 20 (Me 3) MSCs transplantation.
We considered a complete response (CR) to treatment as a neutrophil level greater than 1x109\l without the use of CSF, a hemoglobin level greater than 90 g\l, a platelet level greater than 50x109\l, improvement - neutrophils 0.5-1x109\l without the use of CSF, no need for blood or platelets transfusion, no response (NR) - no changes in laboratory tests.

Results: In the 3-line GH group, there was no response: 2 patients died from infection, and 1 patient underwent haploHSCT.
In the 2-line GH group: 2 patients were improved, and 3 patients achieved CR.
In the 1-line GH group, all 5 patients achieved CR.

Conclusions: Allo-MSC may be used to improve graft function in patients with GH after allogenic HSCT.
The best result was observed in patients with 1-line and 2-line GH.

Disclosure: No conflict

A222

REFINING HLA-DPB1 MISMATCH (PERMISSIVENESS/NON PERMISSIVENESS) ASSESSMENT IN ALLOGENEIC STEM CELL TRANSPLANTATION

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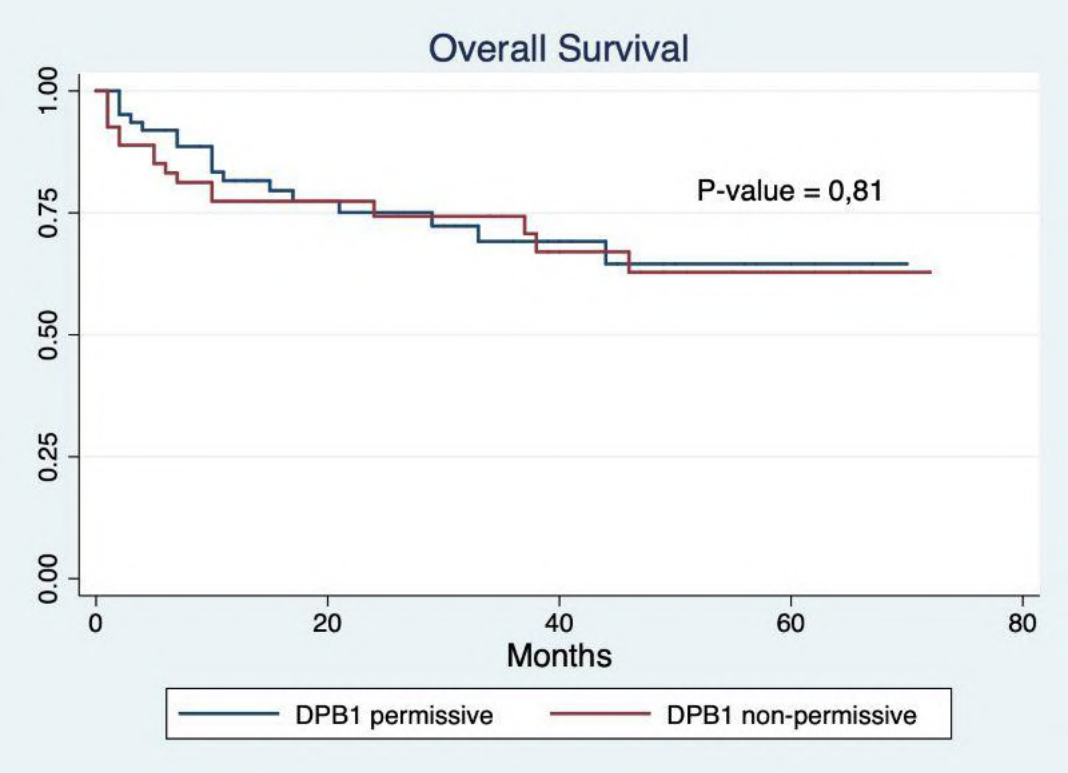
Background: While high-resolution compatibility across HLA Class I and II loci (HLA-A, -B, -C, -DRB1, -DQB1) is a priority criterion for MUD donor selection, HLA-DPB1 locus is highly polymorphic and frequently mismatched. DPB1 disparities are conventionally classified as permissive or non-permissive, based on T-Cell Epitope (TCE) grouping, aiming to predict the risk of acute Graft-versus-Host Disease (aGvHD) and relapse. However, the clinical utility of this binary classification remains controversial, prompting the need for quantitative molecular assessment methods to accurately predict alloreactivity and clinical outcomes.

Methods: This retrospective study evaluates the influence of non-permissive HLA-DPB1 mismatch, as defined by the T-cell Epitope (TCE) Algorithm version 2.0 and 3.0, on clinical outcomes especially in GvH in a cohort of UD allo-HSCT patients. We analyzed retrospectively data from 122 consecutive patients who underwent UD allo-HSCT at our Center between 2020 and 2025. All patients received grafts from highly matched unrelated donors: 98 patients with HLA 10/10 match and 24 patients with HLA 7/8 match. High-resolution HLA typing was performed by next-generation sequencing (NGS) with AlloSeq Tx17 (CareDx) or AllType FASTplex (OneLambda) assay. We divided patients into two conventional groups, based on TCE Algorithms: permissive versus non-permissive mismatch. Primary endpoints included overall survival (OS), relapse, the incidence of acute GvHD (grade II-IV) and chronic GvHD (moderate/severe). Statistical analysis was performed using the Kaplan-Meier method.

Results: The patient cohort had a median age of 54 years (21-71).
HLA-DPB1 mismatch permissive was present in 65 patients (53%), while 56 (47%) were classified as non-permissive.

- Survival: our analysis showed that the presence of a non-permissive HLA-DPB1 mismatch was associated with a no difference in OS (CI=95%; p-value=0.81) [Fig. 1]. The 5-year overall survival was 69% in the non-permissive group compared to 68% in the permissive group.
- Relapse: the data point out not statistically significant difference between relapsed patients who received non-permissive HLA-DPB1 mismatch (23%) and patients who received permissive HLA-DPB1 mismatch (21%).
- Acute GvHD (II-IV): the 100-day incidence of acute GvHD (grade II-IV) was respectively in HLA 10/10 12% and in HLA 7/8 16%. It was found to be not significantly different in patients with non-permissive HLA-DPB1 mismatch compared to those with permissive mismatch (14% vs 9%).
- Chronic GvHD (Moderate/Severe): incidence of chronic GvHD was 34% in patients who received 10/10 donor; 44% in patients who received 7/8 donor. Similarly, no difference emerged in non-permissive versus permissive HLA-DPB1 mismatch (27% vs 35%).



Conclusions: In our analysis based on conventional TCE grouping, there were no statistically significant differences between the permissive and non-permissive mismatch groups regarding OS, relapse or the incidence of acute or chronic GvHD. This failure to differentiate clinical outcomes highlights the limitations of the binary TCE classification. Although our study is limited for its retrospective design and small cohort size, these findings underscore the necessity to move beyond the traditional definition and adopt quantitative molecular approaches to potentially reveal clinically relevant differences in alloreactivity, enabling better prediction of outcome, risk stratification, maintaining potential GvL effect, and personalized prophylactic regimen adjustments for UD-HSCT recipients.

Disclosure: Nothing to declare.

A223

DYNAMIC CHANGES IN PHASE ANGLE ASSESSED BY BIOELECTRICAL IMPEDANCE ANALYSIS AS A MARKER OF TOXICITY IN PATIENTS UNDERGOING CAR-T CELL THERAPY

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Background: Chimeric Antigen Receptor T-cell (CAR-T) therapies are highly effective treatments for several hematologic malignancies, but their use is frequently complicated by acute immune-mediated toxicities, mainly cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS). Early identification of these events is critical, as prompt intervention can optimize clinical management. The phase angle (PhA), derived from bioelectrical impedance analysis (BIA), reflects cellular integrity and body composition, and has emerging value as a biomarker of inflammation. Prospective data on PhA behavior during CAR-T cell therapy are lacking. We investigated whether serial PhA measurements correlate with the onset and course of CRS/ICANS.

Methods: Patients older than 18 years treated since July 2023 with commercial anti-CD19 CAR-T products (axi-cel, tisa-cel, or brexu-cel) were included. Bioelectrical impedance analysis (BIA) and phase angle (PhA) were prospectively measured at pre-lymphodepleting conditioning, on the day of infusion, twice weekly until discharge, and at the onset of CRS/ICANS. An additional assessment was performed on day +30. CRS and ICANS were graded according to ASTCT criteria. Changes in PhA were analyzed in relation to toxicity onset, severity, and subsequent clinical recovery.

Results: Thirty patients were included: 19 (63%) had Diffuse Large B-Cell Lymphoma (10 treated in second line), 5 (17%) Follicular Lymphoma, 3 (10%) Mantle Cell Lymphoma, 2 (7%) Acute Lymphoblastic Leukemia and 1 (3%) Primary Mediastinal B-cell Lymphoma. Products infused were axi-cel (n=18; 60%), tisa-cel (n=7; 23%), and brexu-cel (n=5; 17%). The median age was 62 years (IQR 51-70), and 20 (66%) were male.
Twenty-five patients (83%) developed CRS and/or ICANS (severe CRS 1/30 [3%], severe ICANS 1/30 [3%]), while 5 (17%) experienced no acute toxicity.
A consistent and statistically significant PhA decline was observed in all patients who

developed CRS/ICANS, temporally coinciding with toxicity onset. The median PhA reduction was –1.0° (IQR -0.6° to –1.4°), whereas patients without toxicity showed no PhA decline (median change +0.1°; IQR 0.08°–0.48°; p<0.001) (Figure 1). Patients with severe acute toxicities had higher PhA variation (ΔPhA). During active toxicity, PhA values remained diminished. Following CRS/ICANS resolution, PhA values returned toward or above baseline, reflecting restoration of cellular homeostasis (Figure 1). The PhA decline was associated with CAR-T-related acute toxicities, regardless of the CAR-T product used, the underlying disease, response status at infusion, or any other clinical characteristic analyzed.
No association was found between baseline BMI or nutritional status and either PhA values or ΔPhA, indicating that the observed PhA decline was not driven by differences in body composition.

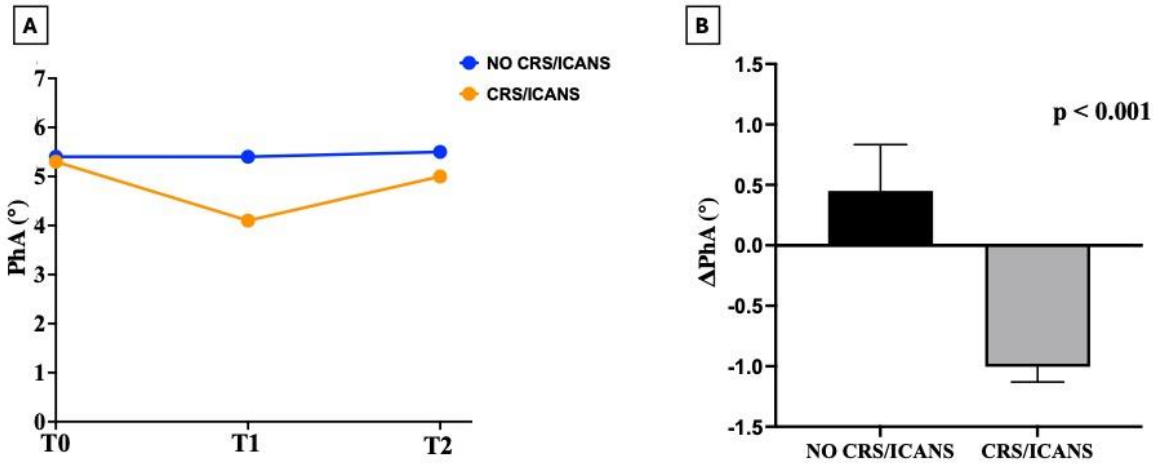

Figure 1. Serial PhA assessment via BIA in patients receiving CAR-T cells.
(A) Variation in phase angle (°) in patients who developed CRS/ICANS (orange) versus those who did not (blue). T0 = lymphodepleting therapy; T1 = onset of CRS/ICANS or day +3 after infusion; T2 = CRS/ICANS resolution or day +6/+9.
(B) Change in phase angle (ΔPhA, °) between day 0 and toxicity onset, or between day 0 and days +3/+6 in patients without toxicity.

Conclusions: Serial PhA assessment via BIA provides a non-invasive, rapid, and sensitive biomarker of immune activation and cellular homeostasis in patients undergoing CAR-T cell therapy. A PhA decrease has been specifically associated with CRS/ICANS and normalizes after recovery, while remaining stable in toxicity-free patients. These findings support integrating PhA monitoring into routine post-CAR-T assessment and suggest its potential utility for early prediction and real-time monitoring of acute toxicities, especially in the growing outpatient CAR-T setting.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to disclose.

A224

HYPOMETHYLATING AGENTS AND VENETOCLAX FOR RELAPSE PREVENTION IN PATIENTS WITH HIGH-RISK MYELOID MALIGNANCIES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Allogeneic stem cell transplantation is an effective modality for hematological malignancies. However, disease relapse is still the major barrier for high-risk patients. It was reported that the 1 year recurrence rate was 22.2%，1 year leukemia free survival was 41.5%. The overall survival was less than 10% if patients had disease relapse after transplant. Hypomethylating Agents (azacytidine or decitabine) and venetoclax were effective in myeloid malignancies.

Methods: This is a prospective single arm study. Patients with high-risk AML or MDS aged between 18-70 years old and underwent allogeneic stem cell transplantation will be included if they fulfill the following criteria: adverse risk group of AML by European LeukemiaNet；MDS with high-risk or very high-risk IPSS-R scores or Presence of TP53 mutation；Presence of measurable residual disease at the time of HSCT, requirement of more than 2 courses of induction chemotherapy to reach complete remission (CR), Extramedullary myeloid malignancy, ≥CR2. All patients will be given hypomethylating agents (azacytidine 32mg/m2 or decitabine 5mg/m2) for 5 days and venetoclax 400mg/d for 7 days after allogeneic hematopoietic stem cell transplantation，when their CBC reach the following criteria: ANC ≥ 1.0 × 10e9/L, Hb ≥ 80g/L, and PLT ≥ 50 × 10e9/L；Patients will be excluded if they have concurrent use of target drugs, such as FLT-ITD inhibitor, active aGVHD or chronic GVHD, diseases recurrence, donor chimerism of bone marrow <90% or graft rejection, or active uncontrolled systemic fungal, bacterial, or viral infection. The maintenance therapy will start from 60th days posttransplant, repeated every 28 days until up to 1-year posttransplant. The 1-year leukemia-free survival rate，1-year cumulative recurrence rate and 1-year overall survival will be analyzed.

Results: A total of 39 patients enrolled the study, male: female=20:19, the median age was 48 (18~66) years old. Thirty-two patients were diagnosed with AML, the other 7 patients were diagnosed with MDS. after a median follow-up of 15.6 months, 10 patients relapsed; 5 patients died, 4 of them died of disease relapse, 1 patient died of hepatic failure. The 1-year and 2-year leukemia free survival was 77.24% and 69.51% respectively, the 1-year overall survival was 91.74%. the 1-year cumulative recurrence rate was 22.70%. The most common side effects were cytopenia. Leucopenia developed in 29 (74.35%) patients, 3 of them had grade 3 leucopenia, 1 patient had grade 4 leucopenia, the other 25 patients had grad 1 or 2 leucopenia. Thrombocytopenia developed in 20(51.28%) patients, 3 patients had grad 3 thrombocytopenia, no one with grade 4 thrombocytopenia.

Conclusions: Maintenance therapy with low dose hypomethylating Agents (azacytidine or decitabine) and venetoclax was effective and well-tolerated in relapse prevention for high-risk myeloid malignancies after allogeneic hematopoietic stem cell transplantation. The majority of adverse events were reversible and manageable.

Clinical Trial Registry: The study was approved by the institutional review committee of the ethics committee of Shanghai General Hospital, and registered at clinicaltrials. gov (NCT 05841771)

Disclosure: No.

A225

A SIMPLIFIED APPROACH TO GENERATE TREG-ENRICHED GRAFT: TECHNICAL AND EARLY CLINICAL DEVELOPMENT OF CD3-DEPLETION AND CD25-SELECTION

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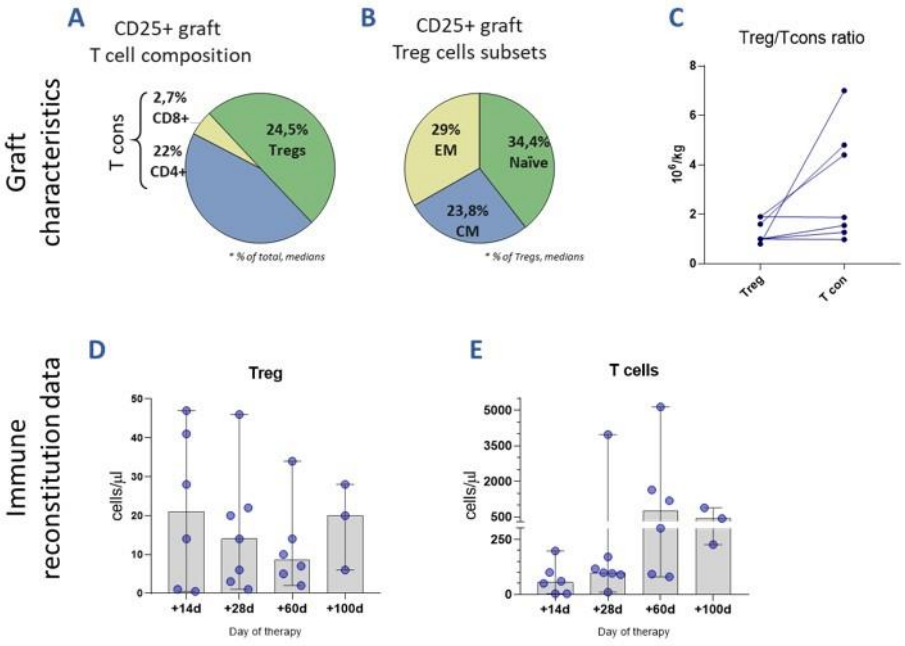
Background: The primary challenge in allo-HSCT graft engineering is balancing GVHD prevention against immune reconstitution and infection control. Engineering Treg: Tcon composition of the graft is a novel approach to achieve this balance, reducing dependence on pharmacological immunosuppression and its associated toxicity (DiIanni 2011, Marteli 2014, Pierini 2021). We propose a simplified approach to engineer Treg-enriched graft by combining a CD3-depleted graft with a concurrent CD25-enriched product containing T-memory cells and Tregs, designed to promote tolerance while supporting antiviral immunity.

Methods: A clinical-grade protocol for manufacturing two-component haploidentical grafts (CD3-depleted/CD25-enriched) was developed. Following six validation runs, the protocol received approval from the local independent ethics committee and was applied for seven ALL-patients.
Grafts were manufactured from a single stimulated donor apheresis product using the CliniMACS Plus system. The CD3-depleted grafts were generated using CD3 Nanobeads (*CytoSinct*). The CD25-enriched grafts were isolated as the non-target cell fraction from a CD25-depletion procedure (*CliniMACS CD25 Reagent GMP, Miltenyi Biotec)*. The cellular composition of both graft components was assessed by FC. All manufactured grafts met the established release criteria. Patients were monitored for engraftment, immune reconstitution, GVHD, viral infections and virus-specific T cells response (IFNγ ELISpot assay).

Results: Graft characteristic: CD3+ T cells were depleted by *lg* 3,34 (2,9–3,8), a median dose was 0.15×10⁶/kg (0.05-0.64). CD34⁺ stem cells median administrated dose was 9,9×10⁶/kg (7-11,8). Treg recovery was 50.4% (42.3–64.8%) across all CD25+products (including validation). The median administered Treg dose was 1×10⁶/kg (0.8-2). The median total dose of T-cons was 1,8×10⁶/kg (0,84-7,03) for both-component grafts. Tcon composition: Naïve 16.3% (3-27%), Memory 83.7% (72-97%).
No infusion-related toxicities, aGVHD, or early inflammatory or neurotoxic events were observed. All patients achieved primary engraftment, with medians of day 10 (8-14) for neutrophils/platelets and day 15 (11-20) for WBC.
By day +14 marked expansion of Tregs was detected of a median of 28 cells/μL (1-47) (34% among CD4+ T-cells 29-74%)), and by day +28 to a median of 14 cells/μL (1-46) (13% among CD4+ T-cells 5-26%)) in patient's peripheral blood. The median total T-cell count was 100 cells/μL (10-3900) by day +28 (*fig.1*). By day 60, virus-specific T cells were detected in 3/7 patients.



Conclusions: These early results demonstrate the safety and feasibility of a combined CD3-depleted + CD25+enriched graft, which was well-tolerated, supported prompt engraftment, and induced Treg expansion. This approach may provide antiviral protection through a preserved memory T-cell compartment. A prospective trial testing this approach is ongoing.

Disclosure: Nothing to declare.

A226

REAL-WORLD OVERALL SURVIVAL OUTCOMES AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE LYMPHOBLASTIC LEUKEMIA: EXPERIENCE FROM A MEXICAN CENTER

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Background: In Mexico, ALL ranks tenth in cancer frequency, with 7,457 new cases and 5,126 deaths reported by Globocan 2022, and an annual incidence of 4.2 cases per 100,000 people. HSCT remains a potentially curative strategy for adults with ALL; however, real-world outcomes and access to transplantation remain variable.

Methods: We conducted a retrospective study focused on patients diagnosed with ALL, using the historical registry of the National Cancer Institute, covering the period from January 2018 to December 2024, reviewing 303 medical records. A total of 261 adult patients with ALL were included in the analysis.

Results:

The median age at diagnosis was 32 years. Gender distribution was balanced, with 50.6% females and 49.4% males. Most patients were younger than 40 years (68.6%). B-cell ALL was observed in 93.9% of cases, while 6.1% had T-cell ALL. High-risk disease was present in 82.8% of patients.

Regarding cytogenetics, 38.3% had a normal karyotype and 32.6% showed hypodiploidy. KMT2A/MLL rearrangements were identified in 10.7%. Complex karyotype was observed in 5.0%, and other very high-risk abnormalities were infrequent. BCR-ABL positivity was documented in 17.2% of patients.

Induction therapy most commonly consisted of CALGB 10403 (45.6%), followed by Hyper-CVAD (31.0%) and BFM (10.7%). CALGB 10403 achieved the highest complete remission (CR) rate (76.2%), followed by BFM (75.0%) and Hyper-CVAD (66.2%).

A total of 58 patients (22.2%) underwent HSCT. Haploidentical transplantation was the most frequent modality (55.2%), followed by matched related donor (MRD) transplantation (39.7%); only two patients received matched unrelated donor transplants. Myeloablative conditioning was used in 89.5% of cases. The most commonly used conditioning regimens were FluBuCy (56.1%) and FluBu (29.8%).

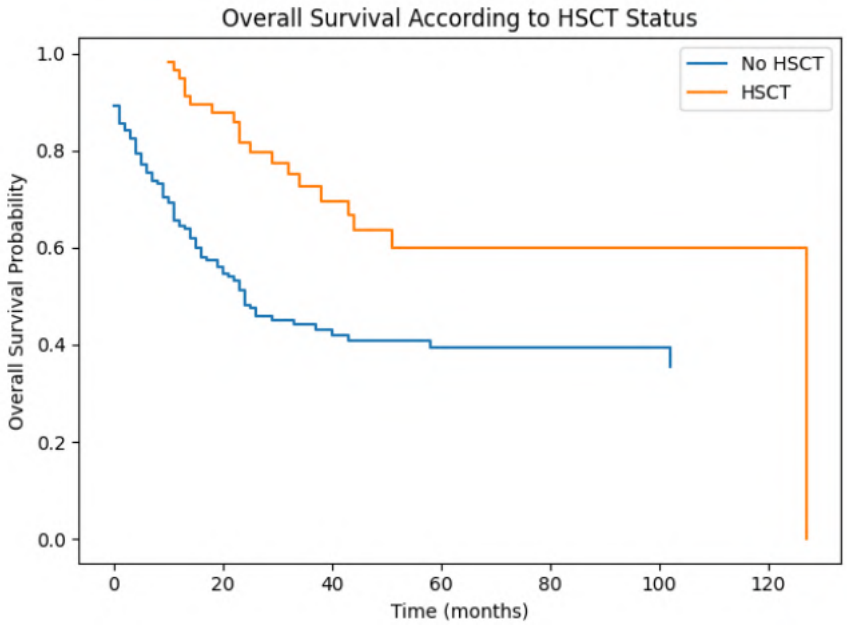
Post-transplant complications were frequent. Graft-versus-host disease (GVHD) accounted for 61% of reported complications, followed by mucositis (30%) and infections (9%).

In the overall cohort (n = 261), median overall survival was 24 months. When stratified by transplant status, patients undergoing allogeneic HSCT demonstrated significantly improved

survival compared with non-transplanted patients (median OS 35 vs 14 months; HR 0.42, 95% CI 0.26–0.69; log-rank p < 0.001).

When stratified by transplant subtype, median OS was 36.5 months for MRD and 36 months for haploidentical transplantation, with no significant difference between groups (log-rank p = 0.696). Conditioning intensity did not significantly impact OS, with median OS of 34 months for myeloablative conditioning and 44.5 months for RIC (p = 0.650). The number of prior treatment lines before HSCT was also not associated with significant differences in OS (p = 0.84).

The most frequent causes of death were infection (19.6%) and disease progression (18.1%). Mortality increased over the study period, peaking in 2023 and remaining high in 2024.



Variable	No HSCT(n)	Median OS no HSCT(mo)	HSCT(n)	Median OS HSCT (mo)	HR HSCT vs No(95% CI)	p value
Overall	203	14	58	35	0.42(0.26-0.69)	<0.001
Lines of therapy ≤2	165	22	42	35	0.41 (0.23–0.73)	0.002
Lines of therapy ≥ 3	38	23	16	41	0.44 (0.20–0.98)	0.039

Standard risk	43	16	2	75	0.50 (0.07–3.88)	0.490
High risk	159	14	56	34	0.44 (0.26–0.73)	0.001
MRD (-) post induction	110	NR	36	35	0.68 (0.35–1.33)	0.255
MRD(+) post induction	57	9	22	35	0.32 (0.15–0.69)	0.002
Conditioning MAC	-	-	52	35	0.41 (0.25–0.69)	<0.001
Conditioning RIC	-	-	6	NR	0.55 (0.18–1.66)	0.280

Table.1 Overall survival according to HSCT status across clinical subgroups. NR=Not Reached

Conclusions:

In this real-world cohort of adult patients with ALL, allogeneic HSCT was associated with improved overall survival, confirming its key role in high-risk disease. Comparable outcomes between haploidentical and matched related donor HSCT support alternative donor strategies to expand timely access and improve outcomes in resource-limited healthcare systems.

Disclosure: Nothing to declare.

A227

EFFICACY AND SAFETY OF GRANULOCYTE COLONY STIMULATING FACTOR (GCSF) USE FOLLOWING CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY (CAR-T): A SYSTEMATIC REVIEW

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Background: CAR-T therapy, effective for hematologic malignancies, can cause complications like hematologic toxicities, cytokine release syndrome (CRS), and immune

effector cell-associated neurotoxicity syndrome (ICANS). Early use of granulocyte colony-stimulating factor (G-CSF) for neutropenia post-CAR-T is controversial due to CRS and ICANS risks, with limited and conflicting clinical data.

Methods: Our systematic review aims to review the literature of early G-CSF administration post CAR-T therapy on the duration and severity of neutropenia, prevalence of early infections and risks of CRS and ICANS.

A systematic literature search from the inception of each database to August 2025 identified 515 studies from Medline, Embase, and the Cochrane Library. After review, 10 studies (involving 1203 participants) were included. All studies on CAR-T in approved indications, evaluating the safety and efficacy of G-CSF use on clinical outcomes compared to its omission, were included.

Results: Among the 10 retrospective studies, 3 were multicentre and 7 single centre, primarily in the USA (n=5) or China (n=3). All examined GCSF use post-CD19 CAR-T, with 6 focusing on B-NHL, 3 on B-ALL, and 1 on both. GCSF timing varied significantly amongst studies. 7 studies used it pre-emptively for neutropenia, 2 as primary prophylaxis, and 1 without a defined rationale. CAR-T types included axi-cel, tisa-cel, brexa-cel, and lisocel.

All studies assessed the impact of GCSF on CRS, ICANs, and neutropenia duration, with 8 also reporting on neutropenia severity. Infectious complications were noted in all studies, but outcomes varied, with some reporting febrile neutropenia rates, others severe infection rates, or specific infection types.

For CRS, 5 studies showed increased incidence of all grades (14-43%) or severe CRS (>G2) (33-36%) with GCSF, 1 showed increased CRS duration (4.5 vs 8 days), and 4 showed no impact, including one using propensity score matching. For ICANS, only 1 study showed increased incidence (17% vs 0%) with GCSF.

Regarding neutropenia duration, 4 studies showed improvement, 4 no benefit, and 2 prolonged neutropenia with GCSF. Among 8 studies on neutropenia severity, only 1 showed reduced G3/4 rates with GCSF. Infection impact analysis showed 1 study with improved FN rates (56% vs 81%, p =0.018) in the GCSF group, and another with higher severe infection rates (61 vs 27%, p=0.007). These findings were likely limited by heterogeneity in GCSF timing and patient populations, affecting conclusions on its efficacy regarding infective risks.

Conclusions: Our findings demonstrated that GCSF use may potentially exacerbate the rates and severity of CRS rates associated with CAR-T cell therapy. Given above, the routine use GCSF to reduce infection risks post CAR T cell therapy should be avoided while awaiting randomized, prospective data confirming the efficacy of growth factors in preventing infections without exacerbating CRS.

Disclosure: Nothing to declare.

A228

COMPUTED TOMOGRAPHY-DERIVED MUSCLE QUALITY PREDICTS LENGTH OF HOSPITALIZATION AFTER STEM CELL TRANSPLANTATION

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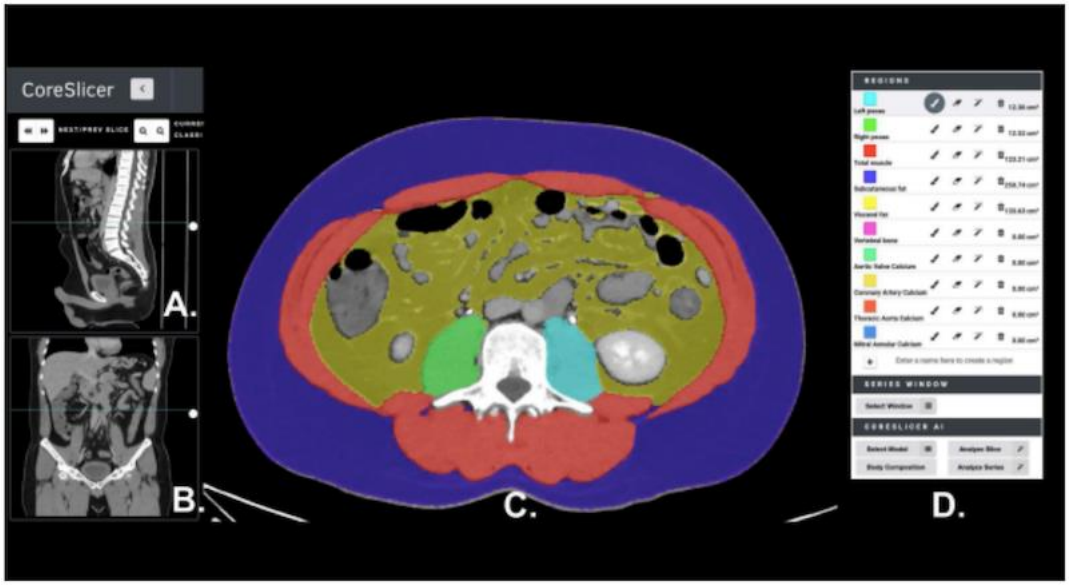
Background: Poor muscle quality, reflected by low skeletal muscle attenuation (SMA) on computed tomography (CT), has emerged as a potential marker of adverse outcomes across hemato-oncological populations. However, its association with post-transplant recovery remains unclear. We aimed to evaluate the relationship between CT-derived muscle quality and length of hospitalization (LOH) in patients undergoing hematopoietic stem cell transplantation (HSCT).

Methods: We retrospectively analyzed a cohort of 49 patients from Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), a tertiary referral center in Mexico, who underwent HSCT from 2015 to 2025. We included patients who underwent autologous or allogeneic HSCT and had a CT scan available for body composition analysis from 30 days before to 7 days after conditioning. Body composition was assessed at the third lumbar vertebra (L3) to derive lean body mass (LBM), skeletal muscle index (SMI), and adipose tissue indices. All CT datasets were processed using the CoreSlicer platform following a standardized segmentation workflow (Figure 1). Muscle quality was evaluated using mean SMA expressed in Hounsfield units (HU). Sarcopenia was defined a priori using sex-specific SMI cut-offs (SMI <52.4 cm^2/m^2 in men and <38.5 cm^2/m^2 in women). Length of hospitalization was analyzed as a continuous variable and stratified into tertiles. Continuous variables are presented as median (Q1–Q3), and categorical variables as counts and percentages. Associations were assessed using non-parametric tests and Spearman correlation.



Results: Median age was 46 years (IQR: 29–52), 51% were male, and 59% underwent allogeneic HSCT (Table 1). Median hospitalization duration was 28 days (IQR: 21–37). CT-defined sarcopenia was present in 37% of patients. SMA decreased progressively across increasing tertiles of hospitalization (38 [33–43], 34 [29–39], and 30 [20–34] HU; p = 0.029), and correlated inversely with hospitalization length (Spearman ρ = −0.33; p = 0.021). In contrast, SMI, LBM, and FFMI showed no significant associations with hospitalization duration (p > 0.5). Subcutaneous adipose tissue index (SATI) differed across tertiles (p = 0.032) but lacked a consistent trend. As expected, hospitalization was longer among allogeneic vs autologous transplant recipients (p < 0.001).

Table 1. Distribution of clinical and body composition variables across tertiles of length of hospitalization

	T1 (Shorter LOH) n= 17	**T2 (Intermediate LOH) n= 16**	**T3 (Longer LOH) n= 16**	**p value***
Type of BMT, n(%) Autologous Allogeneic	4 (24) 13 (76)	9 (56) 7 (44)	16 (100) 0 (0)	< 0.001
Sex, n(%) Female Male	7 (41) 10 (59)	10 (62) 6 (38)	7 (44) 9 (56)	0.5

	T1 (Shorter LOH) n= 17	T2 (Intermediate LOH) n= 16	T3 (Longer LOH) n= 16	p value*
Age, years (IQR)	51 (38, 58)	41 (25, 51)	43 (33, 47)	0.12
BMI, kg/m² (IQR)	26.4 (22.4, 27.8)	29.5 (23.4, 32.5)	27.8 (23.8, 29.9)	0.2
LBM, kg (IQR)	43 (34, 48)	40 (37, 47)	45 (38, 51)	0.7
FFMI, kg/m² (IQR)	16.7 (14.4, 18.5)	16.1 (14.2, 17)	16.4 (14.9, 18.7)	0.6
SMI, cm²/m² (IQR)	49 (41, 53)	46 (40, 49)	47 (41, 55)	0.6
SATI, cm²/m² (IQR)	54 (44, 77)	98 (72, 153)	80 (57, 124)	0.032
VATI, cm²/m² (IQR)	37 (24, 58)	56 (23, 68)	53 (40, 66)	0.3
VAT to SAT Ratio	0.62 (0.39, 1.04)	0.46 (0.26, 0.69)	0.65 (0.48, 0.90)	0.2
Mean SMA, HU (IQR)	38 (33, 43)	34 (29, 39)	30 (20, 34)	0.029
Sarcopenia, n(%) Non-sarcopenic Sarcopenic	9 (53) 8 (47)	10 (62) 6 (38)	12 (75) 4 (25)	0.5

*Fisher's exact test; Kruskal-Wallis rank sum test. Abbreviations: BMI = body mass index; LBM = lean body mass; FFMI = fat-free mass index; SMI = skeletal muscle index; SATI = subcutaneous adipose tissue index; VATI = visceral adipose tissue index; SMA = skeletal muscle attenuation; HU = Hounsfield units.

Conclusions: In this HSCT cohort, lower skeletal muscle quality—but not muscle mass—was significantly associated with prolonged hospitalization. These findings suggest that SMA may serve as a more sensitive imaging biomarker of functional reserve than traditional measures of muscle quantity. Lower skeletal muscle attenuation was consistently linked to longer inpatient stay, suggesting that muscle quality may better capture early post-transplant vulnerability. Larger and multivariate studies are warranted to validate these findings and to explore whether CT-derived body composition phenotypes such as myosteatosis, lean mass depletion, or combined phenotypic patterns independently predict inpatient utilization and early transplant morbidity.

Disclosure: Nothing to declare.

A229

THE ROLE OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH CHRONIC MYELOMONOCYTIC LEUKEMIA

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Background: Chronic myelomonocytic leukemia (CMML) is a myeloid neoplasm characterized by persistent monocytosis and morphological features of both myelodysplastic and myeloproliferative syndromes. The median overall survival for high-risk CMML patients receiving conventional therapy is 18-22 months [Tremblay D. et. al., Leukemia, 2025]. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only potentially curative treatment modality for CMML, offering a chance for long-term remission and improved overall survival (OS).

Methods: A retrospective study included 112 patients with a confirmed diagnosis of CMML who were managed at the RM Gorbacheva Research Institute, Pavlov University from 2011 to 2025. OS was analyzed using the Kaplan-Meier method, and factors affecting OS were assessed by Cox regression analysis. The median age at diagnosis was 56 years (range: 18-88), with males comprising 66% (n=74) and females 34% (n=38). According to the 2016 World Health Organization classification, 38 (34%) patients were classified as CMML-0, 31 (28%) as CMML-1, and 43 (38%) as CMML-2 at diagnosis. During the follow-up period, transformation to acute myeloid leukemia (AML) was documented in 33 (29%) patients. The median follow-up was 16.5 months.

Results: The 2-year OS for the entire cohort was 57% (95% CI 47.0-68.5%), with a median OS of 44 months. The median time to transformation to AML from diagnosis was 6.5 months. The presence of constitutional symptoms was identified as a factor significantly associated with worse OS (HR = 2.38, p = 0.009). The following factors showed a trend towards statistical significance: documented transformation to AML (HR = 1.84, p = 0.052), bone marrow blast count (HR = 1.02, p = 0.079), and absolute monocyte count in peripheral blood (HR = 1.03, p = 0.088)at disease onset. The 2-year OS for CMML patients with and without blast transformation was 38.8% (95% CI 26.0-48.0%) and 59.9% (95% CI 48.5-69.0%), respectively (p=0.05). The highest number of complete responses was observed with hypomethylating agent-based therapy; however, this difference did not reach statistical significance (p=0.31).
Allo-HSCT was performed in 24 (21%) patients, all of whom were classified as intermediate-2 or high-risk according to the CMML-specific prognostic scoring system (CPSS). At the time of transplant, 15 (62%) patients had a bone marrow blast count exceeding 10%. 9 (38%) patients underwent allo-HSCT in the chronic phase (CP), including those who achieved CP

after blast transformation, with a bone marrow blast count of <5% at the time of transplantation; the 2-year OS in this group was 100%. In contrast, the 2-year OS for patients with a blast count >10% at the time of allo-HSCT was 34.4% (95% CI 17.0-67.5%, p=0.014). The causes of death after allo-HSCT were: disease relapse in 6 (46%) patients, primary graft failure in 1 (8%), and infectious complications in 6 (46%) patients.

Conclusions: Allo-HSCT remains the only potentially curative treatment for patients with CMML. A bone marrow blast count of less than 5% is associated with superior post-transplantation survival. To further improve transplant outcomes, future efforts should focus on determining the optimal timing for the procedure and selecting the most effective pre-transplantation therapy.

Disclosure: Nothing to declare.

A230

TRANSITIONING CAR-T CELL THERAPY FOR MYELOMA TO THE OUTPATIENT SETTING: FIRST EXPERIENCE FROM A GERMAN CENTER

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Background: The BCMA-targeting CAR-T cell product ciltacabtagene autoleucel (cilta-cel) is increasingly used as standard-of-care therapy in relapsed or refractory multiple myeloma (MM). Due to safety concerns, treatment is usually administered with inpatient monitoring for 14 to 20 days. With growing experience in risk stratification and management of acute toxicities, outpatient treatment is emerging as a potential alternative.

Methods: At a tertiary care center in Germany treating approximately 100 CAR-T cell patients annually, we identified patients suitable for outpatient treatment based on predefined criteria: reliable adherence, good performance status, adequate organ function, absence of relevant comorbidities (e.g. cardiovascular or neurologic disease), low tumor burden (assessed by paraprotein levels and PET/CT) or response to bridging therapy, travel time of less than 60 minutes to the center, availability of a caregiver in the same household. Patients received standard lymphodepleting chemotherapy in the outpatient setting. Cilta-cel was infused on day 0 at our center, followed by a 6-hour observation. Post-infusion monitoring consisted of outpatient visits 3 times/week including clinical assessment and laboratory testing, daily telephone contact by trained medical staff, and patient-performed monitoring of vital signs and ICE scores at home.
Round-the-clock availability of CAR-T–experienced physicians as well as immediate access to emergency and intensive care facilities, including tocilizumab, was ensured. Dexamethasone 10 mg and oral standby antibiotics were prescribed as standby medication and used only after medical consultation. Data was retrospectively analyzed, CRS and ICANS grading per ASBMT consensus criteria.

Results: Between 08/2023 and 06/2025, 11 myeloma patients were treated in the outpatient setting. Median age was 61 years (range 47–73), median ECOG was 0 (range 0–1), median number of prior therapy lines before apheresis was 2 (range 1–9), median vein-to-vein time 88 days (range 55–123).
Acute toxicity was generally mild. Nine patients developed CRS, which was grade 1 in eight cases and grade 2 in one case with no ICANS observed. Within the first 30 days after infusion, four patients (36.4%) required hospitalization, with a median length of stay of 3 days (range 1–5). Two patients presented to the emergency department due to fever and were admitted at their own request, while two patients were after a second consecutive day of fever during scheduled outpatient follow-up. Reasons for hospitalization were grade 2 CRS in one patient and persistent fever with neutropenia in three patients. Tocilizumab was administered in all readmitted patients, leading to rapid symptom resolution after a single dose in each case. Antibiotic therapy for neutropenic fever was initiated in one outpatient and three inpatients with no infection documented in any of those.
Median absolute lymphocyte count on day 10 post-infusion was 0.58 $\times 10^9$/L (range 0.09–3.71). Best overall response was complete response in 10 patients and stable disease in one patient. No deaths occurred within the first 6 months after infusion.

Patient Characteristic	**Value (n = 11)**		
Age at infusion, years	61 (47–73)		
Sex, n (%)	Male 9 (82%)	Female 2 (18%)	
ECOG performance status at CAR-T, n (%)	0: 8 (73%)	1: 3 (27%)	
ISS stage at diagnosis, n (%)	I: 3 (27%)	II: 4 (36%)	III: 4 (36%)
High-risk cytogenetics, n (%)	6 (55%)		
Median number of prior therapy lines	2 (1–9)		
Triple- or penta-refractory disease, n (%)	8 (73%)		
Prior BCMA-directed therapy, n (%)	2 (18%)		
Bridging therapy administered, n (%)	10 (91%)		
Response to bridging therapy, n (%)	≥PR: 8 (73%)	SD/PD: 3 (27%)	
Vein-to-vein time, days	88 (55–123)		
Baseline creatinine at CAR-T, mg/dL	0.86 (0.59–1.19)		
Baseline albumin at CAR-T, g/L	42 (33–46)		
CRS occurrence, n (%)	9 (82%)		
CRS grade ≥2, n (%)	1 (9%)		

ICANS, n (%)	0		
Hospitalization within 30 days, n (%)	4 (36%)		
Length of inpatient stay, days	3 (1–5)	12 days in total	
Best overall response, n (%)	CR 10 (91%)	SD 1 (9%)	

Conclusions: In a selected patient population within an experienced center, outpatient administration of cilta-cel appears safe and feasible. This approach may reduce unnecessary hospital stays while preserving patient quality of life and conserving medical and financial resources.

Disclosure: Nothing to declare.

A231

THE PRACTICAL DIFFICULTIES OF DLI THERAPY: A SINGLE-CENTRE AUDIT OF DLI COLLECTION AND USE

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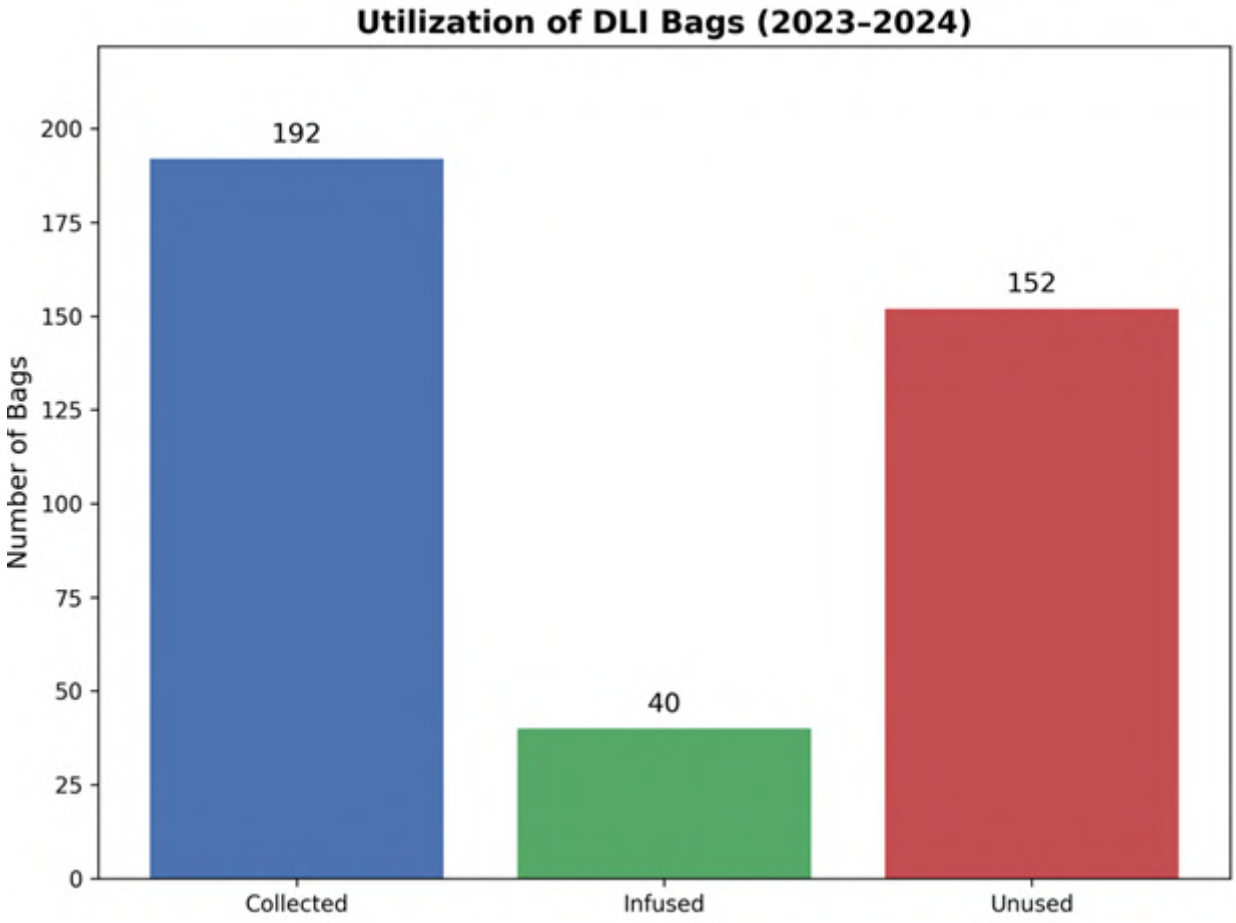
Background: Donor lymphocyte infusion (DLI) is an important strategy after haematopoietic cell transplantation (HCT), particularly following T-cell–depleted conditioning where mixed or falling chimerism may occur. DLI can be administered prophylactically, pre-emptively (falling chimerism or MRD positivity), or therapeutically (frank relapse). At our centre, bulk DLI are harvested at a second collection and then cryopreserved in aliquots. However the clinical picture is dynamic, and anticipating the timing of requesting a new donor apheresis can be difficult to predict e.g. if chimerism or MRD improves as a result of immune suppression wean, or a patient is too unwell after chemotherapy to receive DLI. This present an ethical issue around requesting second donations and we wished to audit our practice.

Methods: We retrospectively analysed all DLI collections over a 2-year period in adult patients undergoing HCT at King’s College Hospital.

Results: Between January 2023 and December 2024, DLI were requested for 49 patients (AML, n=26 or MDS, n=12). Of 49 requests, 43 were collected and 24 (55.8%) infused (15 pre-emptive, 9 therapeutic); 6 were cancelled due to T-cell Chimerism recovery, relapse, or donor issues. Of the 19 DLIs not infused, reasons included death (n=7), chimerism recovery (n=5), GVHD (n=4), MRD negativity (n=2), and relapse (n=1). Within the pre-emptive group, 11 patients (73.3%) had falling chimerism, while 4 (26.6%) were MRD positive before infusion.Median time from transplant to request was 116 days (33–5230). Eight (16%)

patients were on immunosuppression at request, only one at collection. Timing after transplant that the new collection was organized (<100 vs >100 days) showed no correlation with the likelihood of infusion or mortality. Median time from request to collection was 45 days (20–231) and from collection to infusion 33.5 days (4–219). A total of 192 bags were prepared (median 4.8 per patient), but only 40 were used (median 2 doses per patient), leaving 152 unused.
Regarding patient outcomes, 8 patients relapsed after pre-emptive DLI, 5 of whom had falling chimerism; only one MRD-positive patient relapsed and died. Among these, 4 achieved remission with full donor chimerism. Overall, higher or full donor chimerism was achieved in 7 patients (63.6%), with a median time to best response of 171 days (IQR 125–241). In the therapeutic group, 5 patients died due to relapse. The remaining 4 achieved disease control when DLI was combined with additional therapies (Gilteritinib, n=1; Venetoclax + Azacitidine, n=3).



Category	Total number and/or Median	Notes
Patient with DLI requested	49	AML (N=26) MDS(n=12)

Collection performed	43	6 cancelled (recovery, relapse, donor issues)
Infusions performed	24 (55.8%)	Pre-emptive (n=15), Therapeutic (n=9)
Not infused	19 (44.2%)	Death (N=7), Recovery (N=5), GVHD (N=4), MRD- (N=2), Relapse (N=1)
Median Time: • Transplant to request • Request to collection • Collection to infusion	• 116 days (33-5230) • 45 days(20-231) • 33.5 days(4-219)	8 patients on immunosuppression at request No correlation with <100 or >100 days post-transplant
Pre-emptive DLI subgroup	11 falling chimerism, 4 MRD+	
Therapeutic DLI subgroup	9 infused	

Conclusions: DLI planning is complex. Nearly half of collected DLIs were never used, mainly due to chimerism recovery or clinical deterioration, causing major resource waste (152 unused bags) and risk to the donor. Delays and repeated donor collections further complicate care. To reduce waste and improve efficiency, we propose requesting fewer bags, infusing the first dose fresh when feasible, and freezing only the remaining doses. For patients who relapse, there may be scope to assess response to first cycle of salvage before requesting new donor lymphocyte collection, although this must be balanced by donor/procedural availability. These changes could simplify logistics, minimize donor burden, and optimize DLI utilization.

Disclosure: Nothing to declare.

A232

EARLY STEROID PROPHYLAXIS AS A STRATEGY TO REDUCE CAR T-CELL TOXICITIES WITHOUT AFFECTING EFFICACY

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Background: CD19-directed chimeric antigen receptor T-cell (CAR T-cell) therapy is associated with potentially life-threatening toxicities, primarily cytokine release syndrome (CRS) and immune-effector-cell–associated neurotoxicity syndrome (ICANS). Higher-grade CRS and ICANS occur more frequently in patients with high disease burden and poor response to bridging. The prophylactic use of corticosteroids before CAR T-cell infusion has been proposed to mitigate these toxicities, but supporting evidence remains limited to the ZUMA-1 study (cohort 6) and real-world evidence is lacking.

Methods: We performed a retrospective analysis of 23 consecutive adult patients with lymphoproliferative disorders who received CD19-directed CAR T-cell therapy (axicel and brexucel) at our institution between June 2023 and May 2025. Per institutional guidelines, prophylactic steroids were administered according to the ZUMA-6 schedule following axicel and brexucel, in case of less than complete response to bridging therapy, residual bulky masses and elevated LDH at the time of CAR-T cell infusion. Early use of anakinra for grade 1 ICANS was implemented as well, in order to further reduce the incidence of severe neurotoxicity.

Results: After a median of 15 months from diagnosis (range 4–143), all patients (N=23) underwent lymphodepleting therapy with fludarabine and cyclophosphamide, followed by autologous CD19-directed CAR T-cell infusion. In line with approved indications, 18 patients (78%) with relapsed/refractory (r/r) diffuse large B-cell lymphoma (DLBCL, n = 13), r/r primary mediastinal large B-cell lymphoma (PMBCL, n = 2) or r/r follicular lymphoma (FL, n = 3) received axicabtagene ciloleucel (Yescarta), whereas 5 patients (22%) with r/r mantle cell lymphoma (MCL, n = 4) and r/r B-cell acute lymphoblastic leukemia (B-ALL, n = 1) received brexucabtagene autoleucel (Tecartus). 18 patients (78 %) received histology-specific bridging therapy. According to our institutional policy, 21 (91%) patients received prophylactic corticosteroids (11 DLBCL, 3 FL, 2 PMBCL, 4 MCL, 1 B-ALL). At the time of CAR T-cell therapy, the median age was 53 years (range 24–69) and 2 patients (9%) achieved a complete response (CR). Prophylactic steroid therapy consisted in dexamethasone 10 mg per day on days 0, +1, and +2 following CAR T-cell infusion. After a median of 4 days (range, 1–7), 23 patients (100 %) developed grade ≤2 CRS. For persistent fever >72 hours or grade 2 CRS, all patients received a maximum of two 8-mg/kg IV doses of tocilizumab. 14 patients (61%) were also treated with dexamethasone 10 mg every 6 hours for refractory CRS until symptoms resolution. On day +7, 2 patient (9%) experienced grade 1 ICANS (ICE score 7–9) and received dexamethasone 10 mg every 6 hours and required anakinra 100 mg SC every 6 hours until resolution. All patients (100%) were discharged with no recurrent CRS or ICANS. After a median follow-up of 13 months (range 3–26) from day 0, 16 patients (69%) showed a complete response to CAR T-cell therapy.

Conclusions: Prophylactic dexamethasone before CAR T-cell infusion appears to be feasible and may reduce the incidence of severe CRS and ICANS without compromising clinical efficacy in the world practice. Larger prospective studies are warranted to confirm these findings.

Disclosure: ED: Research funding from ADC-Therapeutics, Takeda; advisory board for Beigene, Astra Zeneca, Abbvie, Roche. The remaining authors declare no competing financial interests.

A233

SEQUENTIAL IMMUNOMODULATION WITH PRE-APHERESIS PRIMING AND POST-INFUSION BOOST TO RESTORE T-CELL FITNESS AND IMPROVE ANTI-CD19 CAR-T EXPANSION IN BENDAMUSTINE-EXPOSED R/R B-NHL: A PILOT STUDY

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Background: Bendamustine exposure in relapsed/refractory (R/R) B-cell non-Hodgkin lymphoma (B-NHL) is associated with prolonged T-cell dysfunction, which may compromise autologous CAR-T manufacturing and in vivo expansion. We explored a sequential immunomodulatory approach incorporating pre-apheresis priming to improve T-cell fitness prior to leukapheresis and an early post-infusion boost to support CAR-T expansion and response depth.

Methods: This investigator-initiated, single-center pilot study enrolled 7 adults (median age 59; range 48-76) with bendamustine-exposed within the previous 3 months R/R B-NHL (DLBCL n=4; tFL n=1; MCL n=1; Richter transformation n=1) treated between March 2024 and December 2025. Pre-apheresis priming consisted of ibrutinib (420-560 mg/d) plus camrelizumab (200 mg IV q21d) for 1–2 cycles, followed by leukapheresis. Patients received standard lymphodepletion and autologous anti-CD19 CAR-T infusion (0.7–1.6×10^6 CAR+ cells/kg). Pomalidomide (2-4 mg PO daily, 14 days) was planned from day +3 as a post-infusion boost if clinically tolerated. CD3+ T cells subsets were assessed by flow cytometry before priming and immediately pre-apheresis (TN: CD45RA+CCR7+; TCM: CD45RO+CCR7+; TSCM: CD45RA+CCR7+CD95+). CAR transgene levels were monitored by qPCR performed at prespecified time points (e.g., days 0, 4 , 7 , 11, 15, 21, 28).

Results: Leukapheresis and manufacturing were successful in 7/7 patients. Pre-apheresis priming was associated with increases in less-differentiated T-cell compartments (TN, TCM, and TSCM) compared with baseline (Table 1). Post-infusion CAR-T expansion median peaked at day +11, with Cmax ranging from 38,101 to 108,661 copies/μg gDNA. The best overall response rate was 86% (6/7) with best CR 71% (5/7). With a median follow-up of 9 months (range 4–19), 6-month PFS was 57%. CRS occurred in 5/7 patients (all grade 1–2), with no grade ≥3 CRS and no ICANS. Grade 3–4 neutropenia occurred in 4/7 (57%); no treatment-related mortality .

Table 1: Impact of Sequential Immunomodulation on T-Cell Fitness and Clinical Outcomes (N=7)

Category	Parameter	Baseline (Median)	Post-Priming / Outcome	P Value / Note
T-Cell Fitness	Naïve T-cells (TN, %)	0.08 (0.03-0.12)	5.95 (3.78-8.12)	< 0.001
	Central Memory (TCM, %)	0.90 (0.26 - 1.53)	7.92 (5.07 - 10.78)	0.002
Exhaustion	PD-1+ T-cells (%)	65.51 (48.62 - 80.79)	19.80(14.71 - 24.95)	0.008
Expansion	Cmax (copies/µg gDNA)	-	64,500 (38,101–108,661)	-
Efficacy	Best ORR	-	85.7% (6/7)	-
	Best CR	-	71.4% (5/7)	-
Survival	Median follow-up, months		9	
	6-month PFS	-	57%	-
Safety	CRS (Grade ≥≥3)	-	0%	-
	ICANS (Any Grade)	-	0%	-
	Grade 3–4 neutropenia		57% (4/7)	
	Treatment-related mortality		0%	

Conclusions: This sequential strategy of pre-apheresis T-cell priming and post-infusion boosting appears feasible and demonstrates a manageable safety profile in heavily pre-treated, bendamustine-exposed R/R B-NHL patients. The intervention was associated with favorable changes in T-cell subsets and encouraging CAR-T expansion kinetics. These biological effects translated into a high initial response rate in a population with an otherwise poor prognosis. These preliminary findings provide a compelling rationale for this approach and warrant further validation in a larger, prospective study to confirm its potential to improve outcomes in this high-risk setting.

Clinical Trial Registry: ChiCTR1900025419(https://www.chictr.org.cn)

Disclosure: Nothing to declare.

A234

REDEFINING CURATIVE HORIZONS IN THALASSEMIA MAJOR: 100% SURVIVAL FOLLOWING ALTERNATIVE DONOR HSCT IN A RESOURCE-LIMITED SETTING

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Background: β-thalassemia major remains a significant global health challenge, particularly in regions with limited transfusion and chelation support. Hematopoietic stem cell transplantation (HSCT) is the only curative option, and broader use of matched unrelated (MUD) and haploidentical donors has expanded access. However, graft failure, graft-versus-host disease (GVHD), infection, and treatment-related mortality remain major concerns in this non-malignant setting. This report summarizes a four-year real-world pediatric experience using alternative donor HSCT—employing MUD and haploidentical grafts with modern TCRαβ depletion, PBSC grafts, Treosulfan-based conditioning, and structured immune-reconstitution approaches—to improve safety and curative outcomes.

Methods: This retrospective cohort study evaluated 33 consecutive children (20 males, 13 females; median age 8 years, range 1–16) with transfusion-dependent β-thalassemia major who underwent alternative-donor HSCT between September 2021 and August 2025. Donor types included TCRαβ-depleted (TCD) haploidentical donors (n=24, 72%), T-cell–replete (TCR) haploidentical donors (n=2, 6%), and MUD (n=7, 22%). All patients received peripheral blood stem cell grafts. Conditioning was standardized with thiotepa, treosulfan, fludarabine, and antithymocyte globulin (administered distally in TCD/TCR grafts and proximally in MUD transplants). GVHD prophylaxis comprised of cyclosporine alone in TCD recipients, post-transplant cyclophosphamide, cyclosporine with mycophenolate mofetil (MMF) in TCR recipients and cyclosporine with MMF in MUD recipients; TCD patients additionally received rituximab on day −1. Median $CD34^+$ doses were 18×10^6/kg (TCD) and 10×10^6/kg (MUD). TCRαβ depletion targeted $<25\times10^3$/kg αβ T cells, supported by a structured $CD45RO^+$ add-back strategy from day 0 to +120.

Results: Engraftment occurred in 94% of patients, with sustained full donor chimerism at last follow-up. Median neutrophil and platelet recovery occurred by day +13 (range 11–21) and day +16 (range 12–31), respectively. Two secondary graft failures were observed—one in a TCR haploidentical transplant and one in a MUD recipient, both salvaged by autologous stem cell back-up. The incidence of severe acute GVHD (grade III–IV) was 18%, lowest in the TCRαβ-depleted haploidentical cohort (12%) compared with MUD transplants (28%). Notably, no patient developed clinically significant chronic GVHD, and no GVHD-related mortality occurred. Infectious complications comprised bacterial (18%) and invasive fungal infections (12%), viral reactivations were frequent (CMV 45%, adenovirus 18%, EBV 3%) but uniformly manageable, with no associated deaths. Immune reconstitution was robust, with day-100 $CD4^+$ counts of 110/μL, 140/μL and 120/μL respectively in TCD, TCR and MUD transplants. Transplant-related mortality was 0%, overall survival reached 100%, and event-free survival was 100% in the TCD cohort, 50% in TCR cohort and 85% among MUD

recipients with median follow up of 441 days. All except two survivors achieved and continue to maintain complete transfusion independence.

Conclusions: This study shows that alternative donor HSCT, especially TCRαβ-depleted haploidentical and matched unrelated donor transplantation, achieves outcomes in thalassemia major comparable to matched sibling donor HSCT, even in resource-limited settings. Complete survival, near-universal engraftment, and absence of chronic GVHD highlight the effectiveness of modern graft-engineering with optimal supportive care. These robust real-world data strongly support wider adoption of alternative donor HSCT in transfusion-dependent β-thalassemia major patients to overcome donor availability limitations.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

A235

EXPERIENCE OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH *GATA2* MUTATION

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Background: The *GATA2* gene, located on the long arm of chromosome 3, follows an autosomal dominant inheritance pattern. *GATA2* deficiency is associated with immunodeficiency, cytopenias, severe infections, and a high risk of hematologic malignancies. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative option. However, these patients pose a significant therapeutic challenge due to the high prevalence of comorbidities and infectious complications.

Methods: We retrospectively analyzed data from five patients diagnosed with myelodysplastic syndrome (MDS) and confirmed *GATA2* mutations. Clinical presentations were diverse and included prolonged trilineage cytopenia, isolated thrombocytopenia, non-tuberculous mycobacterial infection (*Mycobacterium avium*), interstitial lung disease, primary lymphedema, sensorineural hearing loss, clinodactyly, thrombotic events, renal abscess, and salpingo-oophoritis. Two patients had additional hematologic malignancies (CML and hepatosplenic T-cell lymphoma), and one developed secondary AML. Three patients exhibited high-risk cytogenetic abnormalities, specifically monosomy 7. Patient characteristics are summarized in Table 1.

Results: All patients underwent allo-HSCT; four received reduced-intensity conditioning, one reduced-toxicity conditioning. Donors included three haploidentical relatives (after genetic screening), one matched unrelated donor (MUD), and one partially matched unrelated donor (MMUD). All potential related donors underwent genetic screening for *GATA2* mutations. In

two cases, no pathogenic variants were detected, and the relatives were used as donors. In one case, the *GATA2* mutation was identified in both the patient's father and brother; consequently, they were excluded as donors, and an alternative donor source was utilized. In one case, related donors were excluded after identification of the familial *GATA2* mutation. Acute GVHD occurred in 2 patients, chronic GVHD in 3. One patient died due to septic shock at 11 months post-transplant. Four patients remain alive in remission with follow-up ranging from 1 to >10 years. Transplant outcomes are detailed in Table 1.

Table 1. Clinical characteristics of patients and outcomes of allo-HSCT.

Parameter	Patient №1 Ts, 27 y.o.	Patient №2 S, 45 y.o.	Patient №3 I, 27 y.o.	Patient №4 L, 41 y.o.	Patient №5 B, 19 y.o.
History	Since 2015	Since 1998	Since 2022	Since 2006	Since 2012
Clinical manifestations	Trilineage cytopenia	Trilineage cytopenia, mycobacterial infection	Recurrent infections	Lymphedema, hearing loss, clinodactyly, cytopenia, thromboses	Thrombocytopenia, left kidney abscess, salpingo-oophoritis
Family history	Father, brother – *GATA2* mutation	None	None	Grandmother – lymphedema, clinodactyly	None
Diagnosis	AML (transformed from MDS)	MDS	CML, MDS	MDS, hepatosplenic T-cell lymphoma	MDS
GATA2 mutation	Heterozygous, c.1187G>A, missense	-	Heterozygous, c.1168A>G, missense	-	-
Cytogenetics	Monosomy 7, trisomy 8	Tetrasomy 1, deletion 3	Monosomy 7	Trisomy 8	Monosomy 7
Conditioning / Donor	Flu180+Bu8 Haploidentical (mother)	Flu180+Bu8 Haploidentical (son)	Flu180+Bu8 Haploidentical (brother)	Flu150+Treo36 Matched unrelated donor (MUD)	FLAMSA-RIC Partially matched unrelated donor (MMUD)
GVHD	Chronic GVHD	Acute GVHD	Chronic GVHD	Chronic GVHD	Acute GVHD

Follow-up / Outcome	11 months Death (sepsis)	16 months Remission	1 year Remission	4 years Remission	>10 years Remission

Conclusions: *GATA2* mutations confer a high risk of hematologic malignancies, profound immunodeficiency, and life-threatening infectious complications throughout the disease course and during treatment. In patients presenting with a suggestive clinical phenotype, genetic testing for *GATA2* deficiency syndrome is strongly recommended. Allo-HSCT can be curative in *GATA2* deficiency, but requires careful donor selection, including genetic testing of related donors.

Disclosure: Nothing to declare.

A236

ALLOGENEIC HSCT WITH MYELOABLATIVE CONDITIONING IN SICKLE CELL DISEASE: A SINGLE-CENTER EXPERIENCE

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Background: Sickle cell disease (SCD) is associated with substantial morbidity, including recurrent vaso-occlusive crises, progressive organ damage, and reduced quality of life despite advances in supportive and disease-modifying therapies. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents the only curative treatment option; however, transplant-related toxicity, graft failure, and graft-versus-host disease (GVHD) remain significant concerns. In recent years, reduced-toxicity conditioning regimens and improved GVHD prophylaxis strategies have enhanced the safety of allo-HSCT in children, underscoring the importance of real-world, single-center outcome data.

Methods: We performed a single-center, retrospective analysis of pediatric patients with SCD who underwent allo-HSCT between 2011 and 2025, evaluating clinical characteristics, transplant-related variables, and post-transplant outcomes.

Results: A total of 15 pediatric patients were included, of whom 9 (60%) were female. The median age at transplantation was 8.2 years (range, 1–20 years). Indications for transplantation primarily included transfusion dependency (60%) and recurrent painful vaso-occlusive crises (27%). Donors consisted of matched sibling donors in 8 patients (53.3%), matched unrelated donors in 3 patients, and related donors in 4 patients (2 matched related and 2 haploidentical). Bone marrow was the predominant stem cell source (n=10, 66.6%). At last follow-up, 12 patients (80%) remained disease-free, while graft rejection occurred in 3 patients. Only one had the chance to undergo second transplant which resulted in aplasia. Therefore, a backup transplant utilized to him. The median post-transplant follow-up was 40 months (range, 3–91 months). BU/Treo based myeloablative conditioning, also including

ATG, was used in all patients. For GVHD prophylaxis PTCy was given for haploidentical donors and the other patients received MTX+CsA or Tacrolimus. Grade II-IV acute GVHD occurred in 4 patients with gastrointestinal, cutaneous, or hepatic involvement, all of whom responded to intensified immunosuppressive therapy.No cGVHD was observed.

Conclusions: In this single-center pediatric cohort, using myeloablative conditioning, allo-HSCT demonstrated favorable long-term disease control with low transplant-related morbidity in children with SCD. The absence of chronic GVHD and the manageable incidence of acute GVHD highlight the feasibility and safety of allo-HSCT. Larger prospective studies are warranted to optimize conditioning strategies and donor selection to further improve outcomes.

Disclosure: None.

A238

SHOULD FRAILTY SCORES BE CONSIDERED WHEN ASSESSING ELIGIBILITY FOR ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION? THE EXPERIENCE OF THE SOUTH WALES BLOOD AND MARROW TRANSPLANT PROGRAMME

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Background: Frailty and haematological malignancy both increase with age and increased frailty is associated with poorer health outcomes. All patients undergoing haematopoietic stem cell transplantation (HSCT) at the SWBMT Programme are assessed for frailty as part of prehabilitation. The aim of this study was to assess whether frailty predicted for outcome following allogeneic HSCT and whether it should be routinely incorporated into eligibility criteria.

Methods: 87 patients, undergoing allogeneic HSCT, for a variety of indications, between June 2022 and December 2024, were assessed prior to undergoing prehabilitation, using the clinical frailty scale (CFS) and short physical performance battery (SPPB) alongside traditional widely accepted and validated assessment methods, including HCT-comorbidity index (HCT-CI). Admission and discharge CFS and SPPB scores were also recorded.
We assessed HCT-CI scores of 0-2 v 3+, SPPB scores of ≤9 v 10+ and CFS of ≤3 v 4+, with the outcome measures length of stay (LOS), number of readmission days within one year of HSCT, overall survival, 1y relapse rate and 1y NRM.

Results: Our study confirmed the known statistically significant relationship between HCT-CI and LOS, with higher HCT-CI scores correlating to longer LOS (p=0.0314). There was no statistical difference seen according to CFS or SPPB scores, but those with higher admission

SPPB scores were more likely to have a longer stay (p=0.1901). For prehab scores this was a median of 24 days for SPPB 10+ versus 28 days for SPPB of ≤9.
14/87 (16%) patients relapsed within the first year. This was evenly distributed between HCT-CI scores of 3+ and 0-2. For the SPPB, 7/14 had a score of 10+, 6/14 a score of ≤9 and 1 was unrecorded. 5/14 were over the age of 60.
23/87 (26%) patients died within 1 year, 6 of these due to relapse. No difference was found between either NRM or OS and CFS or SPPB, possibly because of small patient numbers.
There was a trend towards discharge frailty scores predicting readmission within 1 year: 8.5 v 1 day for SPPB of ≤9 v 10+, respectively (p=NS).

N	**87 (%)**
Gender Male Female	 54 (62) 33 (38)
Age <60 60 and above	 48 (55) 39 (45)
Diagnosis AML (including tAML/sAML) MDS (including tMDS/sMDS) MF ALL CMML/sMPN CML (one with concurrent CLL) SAA Other- Histiocytic sarcoma (1), HL (1), NHL (2), CLL (1)	 40 (46) 13 (15) 9 (10) 8 (9) 7 (8) 2 (2) 2 (2) 6 (7)
Baseline SPPB 9 or below 10+ Missing data	 36 (41) 48 (55) 3 (3)
Baseline CFS 3 or below 4+ Missing data	 46 (53) 40 (46) 1 (1)
HCT-CI 0-2 3+	 48 (55) 39 (45)

Baseline patient characteristics are shown in the table.

Conclusions: Our data did not show any statistically significant association between prehab frailty measures and relapse, NRM or LOS. However, discharge SPPB may predict for risk of readmission within 1 year. Whilst our study was probably not large enough to show a significant correlation, it is also possible that SPPB and CFS are not sensitive enough as frailty measures in the allogeneic HSCT population. Note that the EBMT recommends use of the Electronic Frailty Index in MDS. We have since added the HCT frailty score and it will be interesting to compare this with existing measures prospectively in a larger dataset.

Disclosure: Nothing to declare

A240

IS HLA MISMATCHING BECOMING A HISTORY IN THE ERA OF POST-TRANSPLANT CYCLOPHOSPHAMIDE?

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Background: Post-transplant cyclophosphamide (PTCy) represents a paradigm shift in the prevention of graft-versus-host disease (GVHD) following allogeneic hematopoietic stem cell transplantation (HSCT). PTCy offers a unique mechanism to facilitate graft tolerance, mitigate GVHD, and preserve graft-versus-leukemia (GVL) effects. The beneficial effects of PTCy on GVHD appear to be independent of donor type, graft source, or conditioning regimen intensity. The aim of this study was to determine the effect of HLA mismatching on transplant outcomes in patients receiving PTCy.

Methods: We retrospectively analyzed 61 adult patients who underwent HSCT at our transplantation center between May 2024 and October. Patients who received PTCy as GVHD prophylaxis were included in the study. Stem cell source was peripheral blood (PBSCs). All patients received PTCy at 50 mg/kg/day on days +3 and +4, with cyclosporine on days +5 after transplant. In the haploidentical setting, mycophenolate mofetil (MMF) was combined with cyclosporine. The analysis assessed the impact of HLA mismatching on the period of PTCy using multivariable Cox regression and competing risks models supplemented with Kaplan-Meier survival estimates.

Results: Patients were grouped according to HLA matching status as 10/10 (n=30), 9/10 (n=20), and haploidentical (n=11). Median follow up time was 4.7 (2.2-20.5) months. Demographic features of the patients presented in Table 1. The underlying disease profile was predominantly acute myeloid leukemia (AML) in all groups (n=55). No significant difference was found between the groups in terms of conditioning regimen intensity, with myeloablative conditioning (MAC) being the most frequently used regimen. Donor-recipient age and the frequency of female-to-male transplants were also similar between the groups. The only variable differing significantly between HLA matching groups was the total

nucleated cell dose infused, which was higher in the haploidentical cohort (p=0.008) (Table 1).

No significant differences were observed in survival outcomes or the incidence of acute GVHD among the transplant groups. When 61 patients undergoing HSCT were stratified by HLA match status, progression-free survival (PFS), overall survival (OS), GVHD-free relapse-free survival (GRFS), and relapse-free survival (RFS) did not differ significantly ($p > 0.05$). According to donor HLA compatibility (9/10 matched, 10/10 matched, and haploidentical), median OS was 5.1, 4.2, and 4.2 months, respectively; median GRFS was 2.2, 2.4, and 2.4 months; median PFS was 5.1, 3.6, and 4.0 months; and median RFS was 2.6, 2.4, and 3.9 months, respectively.

In the entire cohort, 25 (41%) patients were administered ant thymocyte globulin (ATG) with PTCY. When patients who received ATG and those who did not were compared based on HLA mismatch status, no significant association was found between the occurrence of GVHD and relapse (p=0.78).

When patients were stratified by conditioning intensity (MAC vs RIC/NMA), no statistically significant differences were observed in PFS, OS, GVHD, GRFS, RFS, or non-relapse mortality (NRM) ($p > 0.05$; Figure 1). Similarly, the incidence of acute and chronic GVHD did not differ significantly between the groups ($p > 0.05$).

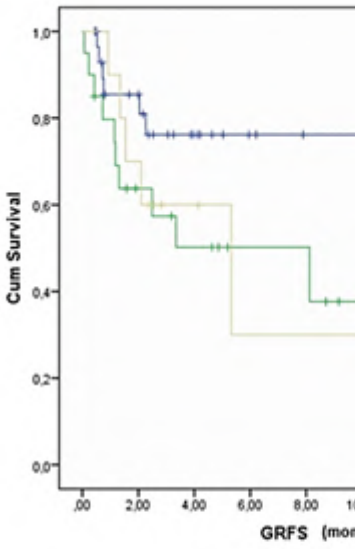
Table 1: Patient/donor and transplant characteristics according to HLA mismatch groups

Variable	All patients N=61	10/10 MRUD N=30	9/10 MRUD N=20	Haploidentical N=11	P value
Recipient age, median (range), years	45 (20-69)	41 (20-69)	45 (20-69)	48 (34-69)	0.392
Male, N	35 (57%)	18 (60%)	10 (50%)	7 (64%)	0.706
Diagnosis, N					
AML	55 (90%)	28 (93%)	18 (90%)	9 (82%)	
Others*	6 (10%)	2 (7%)	2 (10%)	2 (8%)	
HCT-CI risk groups, N					
Low	12 (19.7%)	9 (30%)	1 (5%)	2 (18.2%)	0.278
Intermediate	40 (65.5%)	17 (56.7%)	15 (75%)	8 (72.7%)	
High	9 (14.8%)	4 (13.3%)	4 (20%)	1 (9.1%)	
Diasease Risk Index, N					
Low	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0.447
Intermediate	42 (68.9%)	21 (70%)	12 (60%)	9 (81.8%)	
High	19 (31.1%)	9 (30%)	8 (40%)	2 (18.2%)	
Conditioning regimen					
RIC/NMA	13(21.3%)	4(13.3%)	7(35%)	2(18.2%)	0.199
MAC	48(78.7%)	26(86.7%)	13(65%)	9(81.8%)	
GVHD					
ATG naive/ ATG treated (n)	36/25	22/8	8/12	6/5	0.068
Recipient /Donor CMV serostatus, N,% (+/+)	58 (95.1%)	28 (93.3%)	19 (95%)	11 (100%)	
Donor age, median (range), years	33 (12-53)	31 (12-53)	37 (20-52)	35 (19-52)	0.808
Female donor to male recipient, N	10 (16.4%)	6 (20%)	2 (20%)	2 (18.2%)	0.771
Total nucleatedcelldose infused x10^8/kg, median (range)	7.7 (4.3-10.81)	7.5 (4.3-10.73)	7.5 (5.2-9.80)	8.4 (7.6-10.81)	0.008*

N: Number; MRUD: Matched related-unrelated donor; AML: Acute myeloma leukemia, RCT: reduced-intensity stem cell transplantation; HCT-CI: Hematopoietic cell transplant co-morbidity index; MAC: myeloablative; GVHD: graft versus host disease; NMA: Non- myeloablative conditioning; RIC: Reduced-intensity conditioning

*Others: Myelofibrosis (n=1); acute lymphoblastic leukemia (n=2); non-Hodgkın lymphoma (n=1); aplastic anemia (n=1)

Figure 1: Kaplan-Meier probalities of graft-versus-ho
overall HLA matching (p=0.738).



Conclusions: This study suggests that the adverse effects of HLA incompatibility may be reduced by PTCY in patients undergoing HSCT. Further multicenter studies are warranted to confirm these findings.

Clinical Trial Registry: None

Disclosure: Nothing to declare

A241

INDUCING KETOSIS WITH B-HYDROXYBUTYRATE SUPPLEMENTATION DURING CHIMERIC ANTIGEN RECEPTOR T CELL THERAPY IN RELAPSED/REFRACTORY INFANT ACUTE LYMPHOBLASTIC LEUKEMIA

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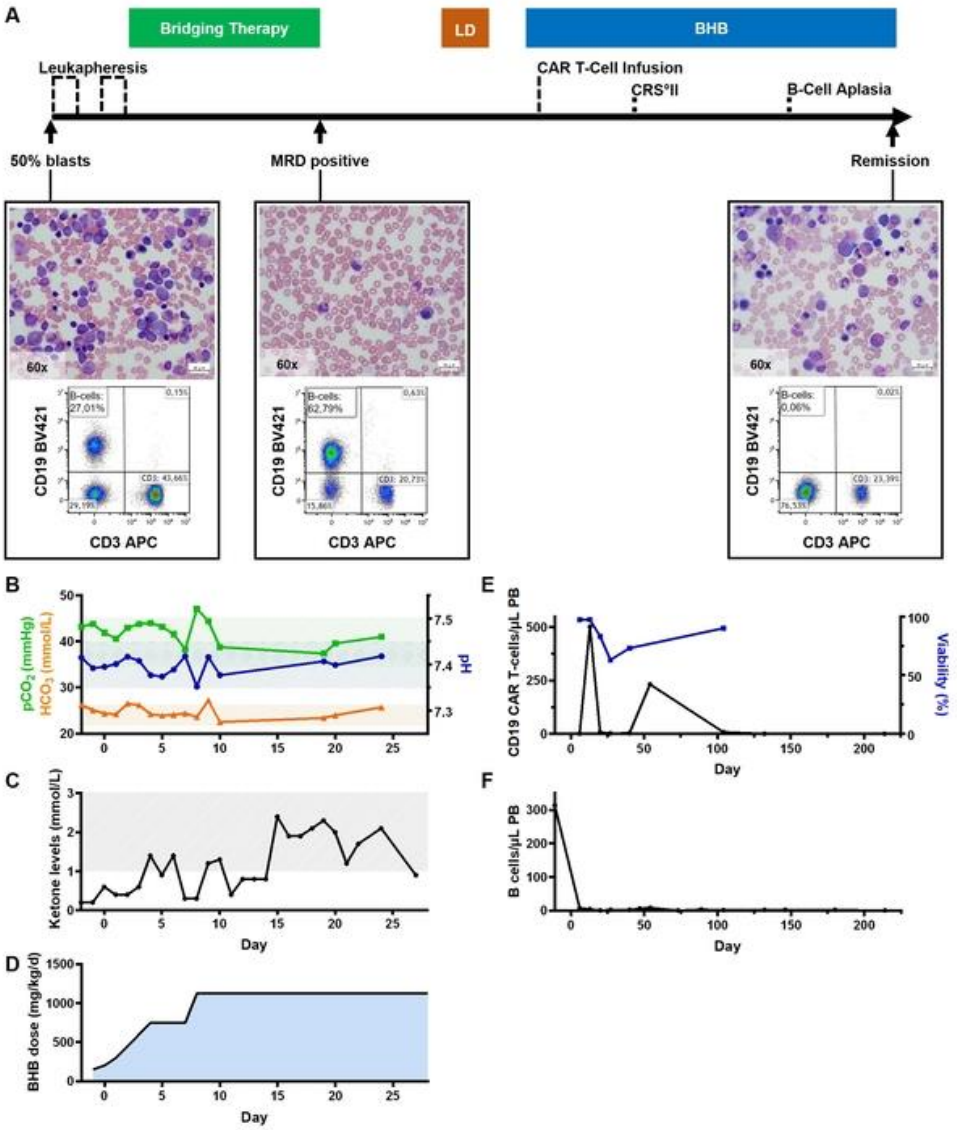
Background: *KMT2A*-rearranged acute lymphoblastic leukemia (ALL) is an aggressive subtype with poor prognosis despite intensive therapy, though outcomes have improved with CD19-directed chimeric antigen receptor (CAR) T-cell treatment. Metabolic modulation, particularly through β-hydroxybutyrate (BHB) supplementation, has been proposed as a strategy to enhance CAR T-cell efficacy, with murine studies showing that BHB augments CAR T-cell function and clinical data suggesting associations between elevated BHB levels and improved outcomes.

Methods: We report the case of *KMT2A*-rearranged infant leukemia with early isolated bone marrow relapse after hematopoietic stem cell transplantation. The patient subsequently received CAR T-cell therapy with tisagenlecleucel. We developed a strategy for managing ketosis with BHB supplementation, focusing on feasibility, dosing, monitoring, and safety in a pediatric setting. BHB was initiated on day -2 before CAR T-cell infusion and continued until day +28 (A). Ketone levels were measured in venous blood. Blood gas analyses, including acid-base status and electrolyte profiles, were performed daily during the first two weeks to assess potential metabolic complications of BHB supplementation. Following CAR T-cell administration, CAR T-cell expansion kinetics, CAR T-cell viability, B-cell count, and remission status were assessed.

Results: BHB supplementation was well tolerated and achieved target ketone levels on nearly half of treatment days (C+D). No supplementation-related adverse effects were observed. Blood gas analysis revealed no notable changes and serum creatinine levels remained within the normal range (B). CAR T-cells demonstrated robust expansion, peaking two weeks post-infusion with subsequent transient re-expansion. From day +132 onwards, CAR T-cells were no longer detectable in peripheral blood. Viability was initially high, declined over time, and showed a secondary peak (E). B-cell aplasia occurred rapidly after CAR T-cell infusion, with near-complete depletion by day +14 (F). Importantly, B-cell aplasia persisted despite undetectable circulating CAR T-cells, consistent with continued CAR T-cell activity. The patient remains in complete morphological and molecular remission with sustained full donor chimerism, as confirmed by bone marrow assessment at day +278 post CAR T-cell infusion. Same day peripheral blood analysis demonstrated ongoing B-cell aplasia.



Conclusions: This is the first reported case of BHB supplementation in a young child undergoing CAR T-cell therapy. Treatment was safe, feasible, and associated with favorable CAR T-cell kinetics and durable remission in an infant with very high-risk *KMT2A*-rearranged ALL. These observations may assist clinicians in considering BHB as a low-risk adjunct to CAR T-cell therapy for pediatric patients, with the potential to improve outcomes in high-risk cases.

Disclosure: Nothing to declare

A243

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PRIMARY IMMUNODEFICIENCY IN ADOLESCENTS AND YOUNG ADULTS: A SINGLE-CENTRE EXPERIENCE

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Background: Primary immunodeficiencies (PID) represent a diverse group of inherited immune disorders that predispose affected individuals to severe infections, immune dysregulation, organ dysfunction, and premature mortality. Allogeneic hematopoietic stem cell transplantation (HSCT) offers a definitive curative strategy for many PID subtypes by restoring normal immune function. While outcomes of HSCT in pediatric populations are increasingly well characterised, data evaluating outcomes in adolescents and young adults remain limited.
This study presents a comprehensive single-centre analysis of survival, graft stability, immune reconstitution, infectious complications, and graft-versus-host disease (GVHD) in a consecutively transplanted cohort of young adult PID patients at King Faisal Specialist Hospital and Research Centre in Saudi Arabia

Methods: We retrospectively reviewed 21 patients with genetically or clinically defined PID who underwent allogeneic HSCT at our institution during the last two decades. The median age at transplant was 17 years (range 15-28). Underlying diagnoses where classified according to the International Union of Immunological Societies Expert Committee which included phagocytic/innate defects(n=10), combined immunodeficiency (n=10) and humoral/B-cell disorders (n=2). Donor sources included matched sibling donors (MSD, n=17), matched unrelated donors (MUD, n=2) and haploidentical donors (n=2). Stem cell source consisted of bone marrow (n=14) or peripheral blood stem cells (n=7). All patients received myeloablative conditioning regimens with Busulfan based regimen. Clinical outcomes assessed included overall survival (OS), acute and chronic GVHD, CMV viremia, need for IVIG post transplant, and donor chimerism.

Results: after a median follow up of 4.8 years, 20 out of 21 patients (95%) were alive, with a single transplant-related death. Cumulative incidence of Acute GVHD at 100 days was (39.8%), while cumulative incidence of chronic GVHD was (23.6%), all with mild to moderate severity and good responsiveness to immunosuppression. CMV viremia was documented in 47% of patients , with all episodes controlled using antiviral therapy without CMV-related mortality, 4 patients devloped invasive fungal infection and 2 patients had Veno-occlusive disease. During the finalassessment, 52% required immunoglobulin replacement at

a certain point of time. Donor chimerism showed full chimerism in 12 patients (57%) and mixed chimerism in 9 patients (43%). The single death was related to secondary graft failure and development of sever infection and ARDS. Kaplan-Meier survival curves demonstrated stable long-term OS following early post-transplant recovery.

Conclusions: Our single-centre experience shows that adolescents and young adults with PID can achieve HSCT outcomes comparable to pediatric populations, with 95% survival, acceptable GVHD rates, stable donor chimerism and immune reconstitution profiles similar to those reported in large pediatric cohorts.These findings support the effectiveness of HSCT as curative therapy in young adults with PID while emphasising the ongoing need for structured long-term follow-up to optimise immuno-recovery, manage infections, and monitor donor chimerism dynamics

Disclosure: I have no conflicts of interest to disclose

A244

CD34⁺ CELL DOSE ABOVE 10 MILLION PER KILOGRAM ON THE OUTCOMES OF ALLOGENEIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE

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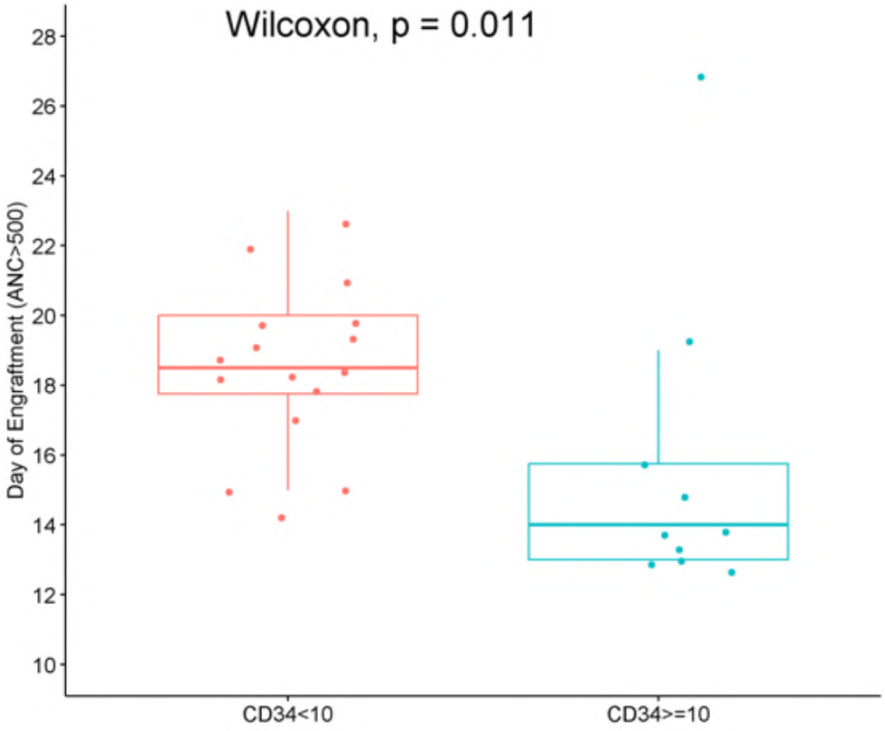
Background: For patients with high-risk malignant hematologic diseases or aplastic anemia, HLA-haploidentical related donors have become an acceptable stem cell source when matched sibling or unrelated donors are unavailable. Between October 2014 and March 2021, 26 patients underwent 27 haploidentical transplantations with post-transplant cyclophosphamide (PTCy) at Koo-Foundation Sun Yat-Sen Cancer Center. The objective of this study is to review our series and evaluate the impact of CD34+ stem cell doses greater than 10×10^6/kg on clinical outcomes in this cohort.

Methods: Retrospectively, we retrieved consecutive data from the hematopoietic stem cell transplantation database, reviewed medical charts, and made the analysis. We used a boxplot and the Wilcoxon rank-sum test to analyze the impact of $CD34^+$ dose above and below 10 million per kilogram on the median engraftment day. We divided cohorts into three groups based on disease risk at transplantation and used the Kaplan-Meier method to plot disease-free and overall survival curves for each group. We used a bar chart to record and grade graft-versus-host disease based on $CD34^+$ dose to analyze the association.

Results: Twenty-six patients, aged 7 to 64 years, were included. Thirteen were female. The cohort exhibited heterogeneous diagnoses, including AML (n=8), ALL (n=4), ATLL (n=1), HL (n=3), DLBCL (n=3), CLL with Richter's transformation (n=1), and sAA (n=6). At the time of transplantation, among the 20 patients with malignant diseases, 6 had active disease, 4 had minimal residual disease, and 10 were in complete remission (CR1–CR2). Six patients with sAA underwent a total of seven transplantations.

Survival ranged from 17 to 3,530 days. At 5 years, 70% of patients in CR1–CR2 and 100% of patients with sAA remained alive. Neutrophil engraftment was achieved in 96.3% of patients between days +13 and +27, and 88.8% reached platelet counts >20,000/μL with sustained transfusion independence between days +5 and +223. Median neutrophil engraftment occurred on day +14 for patients receiving CD34+ cell doses ≥10 × 10^6/kg and on day +18.5 for those receiving <10 × 10^6/kg (P=0.011).
The incidence of all-grade aGvHD was 70% and 68.8% in patients receiving CD34+ cell doses ≥10 × 10^6/kg and <10 × 10^6/kg, respectively. The incidence of cGvHD was 16.7% (n=6) and 42.8% (n=14) in the respective dose groups.



Conclusions: Haploidentical transplantation with PTCy for malignant hematologic diseases is a feasible therapeutic approach. In our cohort, remission status was the primary determinant of survival probability. A higher CD34+ cell dose (>10 × 10^6/kg) resulted in more rapid ANC engraftment—by approximately 4.5 days—compared with lower doses, without an associated increase in the incidence of aGvHD or cGvHD. The limitations of this study include its retrospective design and the relatively small sample size. Larger prospective studies will be required to validate these findings.

Disclosure: No conflict on interest

A245

OUTCOME OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT IN ACUTE LEUKEMIAS IN ECUADOR

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Background: Allogeneic stem cell transplantation remains the most appropriate consolidation strategy and the only curative option for high-risk acute myeloid leukemia (AML) and acute lymphoblastic leukemias (ALL). Worldwide, most transplants are performed in North America and Europe; in Latin America, they are carried out in only 13 countries, with SOLCA Guayaquil being the only center accredited to perform them in Ecuador.

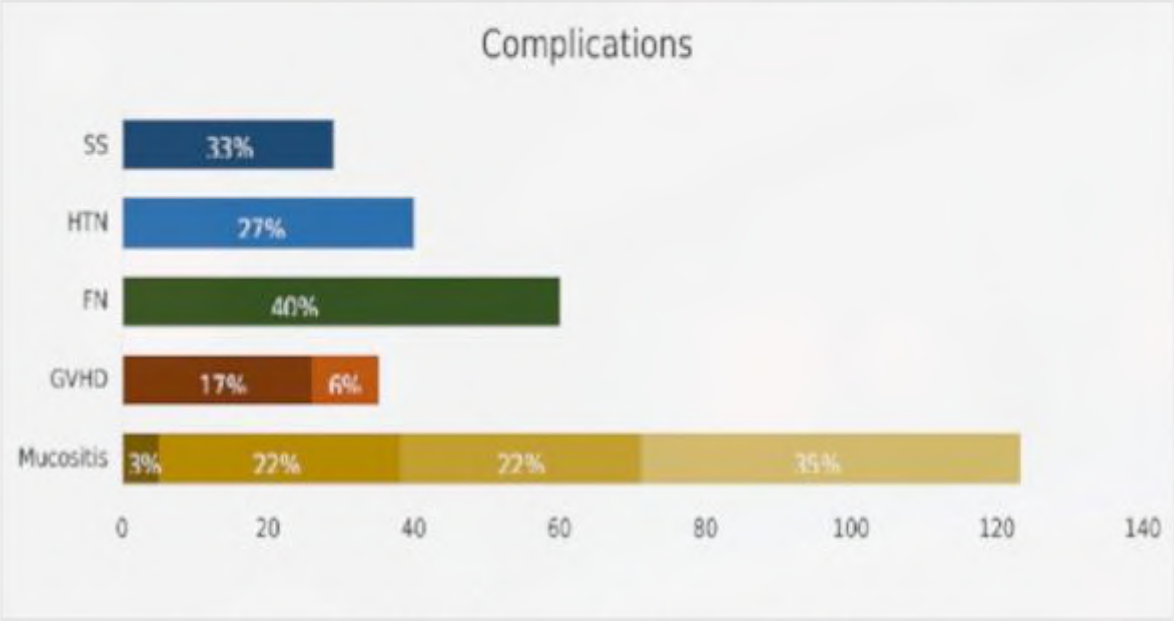
Methods: Retrospective and analytical study of patients treated between June 2006 and June 2025, evaluating the main clinical complications. Ten-year-disease-free survival was estimated using Kaplan-Meier within a 19-year observation window. Data analysis and visualization were performed using RStudio and Power BI.

Results:

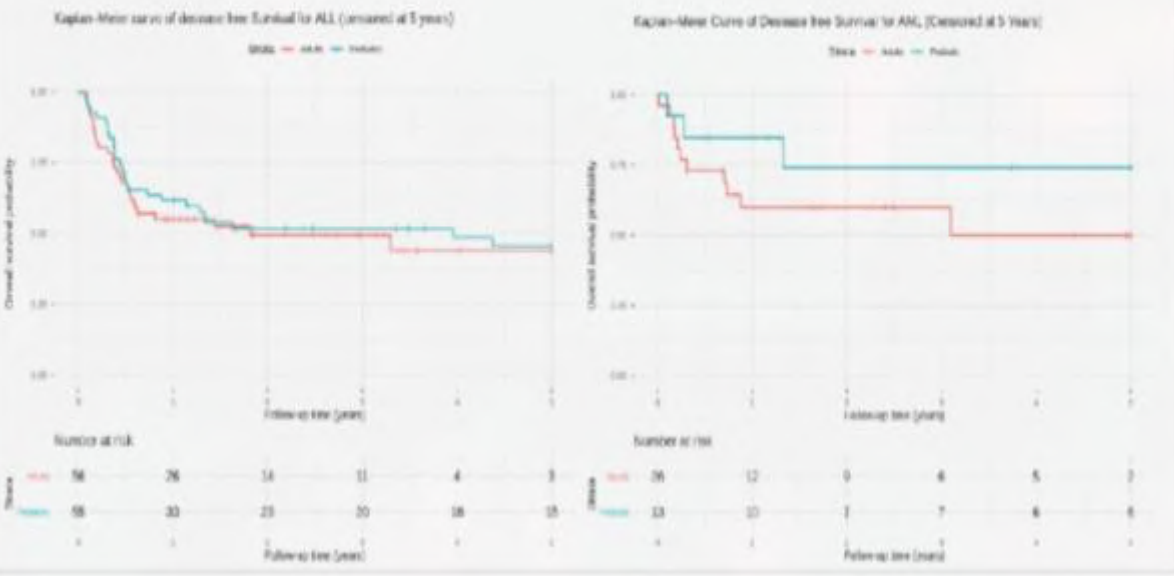
Figure 1. Complications related with Allogeneic HSCT and Disease Free Survival in Acute Leukemia

N= 150 patients

ALL 111: Pediatric 49,5% Adults 50,5%
AML 39 : Pediatric 33,3% Adults 66.7%



Kaplan–Meier Estimates of 5-Year Disease-Free Survival



We included 150 allogeneic transplant patients (111 ALL, 39 AML). All conditioned with Busulfan-Cyclophosphamide and given Cyclosporine-Methotrexate for graft vs host disease (GVHD) prophylaxis. Stem cell sources were bone marrow (5.3%), umbilical cord blood (9.3%), and peripheral blood (85.3%). The most frequent complications were mucositis, febrile neutropenia (FN), septic shock (SS), GVHD and calcineurin inhibitor induced-hypertension (HTN). The 5-year disease-free overall survival within 19-year follow-up was 49.50% for ALL and 61.5% for AML and was compared between pediatric and adult patients, as shown in Figure 1.
Mucositis occurred predominantly as Grade IV (35%). Markedly severe mucositis was associated with febrile episodes from an intestinal infectious source. Among 150 allogeneic transplant recipients with acute leukemia, febrile neutropenia occurred in 40% of patients, with 19.3% developing septic shock, while afebrile neutropenia occurred in 90 patients, with a shock rate of 20%. Most febrile episodes were non-infectious inflammatory events, whereas 1 in 5 afebrile patients developed severe infection. Fever was not a reliable discriminator of septic complications in this cohort. Graft-versus-host disease (GVHD) was observed in 23.3%; 17.3% were acute and 6% were chronic. No association was found between infectious febrile episodes and the occurrence of GVHD. Treatments available for GVHD management include calcineurin inhibitors (cyclosporine and tacrolimus), corticosteroids, and ruxolitinib. Additionally, 26.6% of patients receiving cyclosporine developed arterial hypertension during intravenous administration.

Conclusions: The 5-year disease-free survival in our 19-year cohort aligns with international benchmarks reported by EBMT and CIBMTR, confirming that our center's long-term outcomes are comparable to global standards. AML showed stronger disease control, while ALL demonstrated survival rates within expected ranges for allogeneic transplantation. Higher severity mucositis is a predisposing factor for intestinal infections. Septic shock occurred at similar rates in febrile and afebrile neutropenia, indicating that fever is not a reliable indicator of severe infection in post-transplant patients. A notable proportion of afebrile patients developed septic shock, reflecting profound immunosuppression and blunted inflammatory response, while nearly half of febrile episodes were non-infectious. These findings emphasize the need for early screening, biomarker-guided evaluation, and rapid initiation of sepsis management protocols regardless of fever. Continuous vigilance is essential to prevent delayed recognition of life-threatening infections. Although graft-versus-host disease represents a state of profound immune dysregulation, it was not associated with an increase of infectious complications. However, patients treated with ruxolitinib showed CMV reactivation. Arterial hypertension was exclusively associated with intravenous cyclosporine use, and occurred despite maintaining therapeutic serum cyclosporine levels.

Disclosure: Nothing to declare

A246

EVALUATING THE ROLE OF ELTROMBOPAG IN POST-HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS WITH HEMATOLOGIC DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Thrombocytopenia contributes to transfusion dependence, bleeding risk, and inferior survival after hematopoietic stem cell transplantation (HSCT). Eltrombopag, a thrombopoietin-receptor agonist, is increasingly used to enhance post-transplant platelet recovery.

Methods: A comprehensive search identified 577 citations from six databases with ten single-arm retrospective studies included in the analysis. Outcomes extracted included platelet recovery (≥50,000/μL), platelet transfusion independence, and time from eltrombopag initiation to response. Dichotomous outcomes (platelet recovery and platelet transfusion independence) were pooled as proportions and continuous outcomes (time from eltrombopag initiation to response) were pooled as means, with 95% CIs using a random-effects model. Subgroup analyses were conducted to compare platelet recovery between autologous and allogeneic HSCT.

Results:

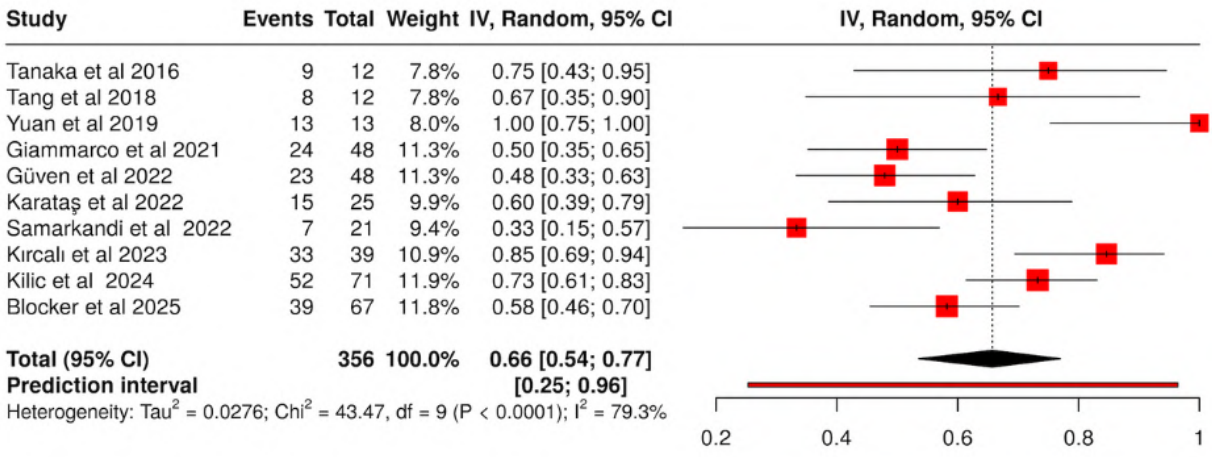

Figure 1. Forest plot of eltrombopag treatment outcomes following hematopoietic stem cell transplantation depicting pooled platelet recovery rate (≥50,000/μL) for all patients (n = 356).

Table 1. Summary of included studies reporting outcomes following eltrombopag treatment in post-hematopoietic stem cell transplantation patients.

Study (Year)	Platelet count recovery (≥50,000/μL)		Platelet Transfusion Independence		Time to Response (Platelet Recovery)		
	n	e	n	e	n	mean	SD
Tanaka et al (2016)	2	9	11	8	12	163.00	26.00
Tang et al (2018)	12	8	--	--	--	--	--
Yuan et al (2019)	13	13	13	8	13	29.25	9.75
Giammarco et al (2021)	48	24	--	--	48	33.00	9.50
Güven et al (2022)	48 (Auto 20; Allo 28)	23 (Auto 13; Allo 10)	--	--	48	60.00	47.70
Karataş et al (2022)	25 (Auto 15; Allo 10)	15 (Auto 10; Allo 5)	--	--	25	63.25	41.25
Samarkandi et al (2022)	21	7	16	12	21	107.75	83.75
Kırcalı et al (2023)	39	33	39	33	--	--	--
Kilic et al (2024)	71 (Auto 37; Allo 36)	52 (Auto 29; Allo 23)	--	--	73	32.00	42.00
Blocker et al (2025)	67	39	67	32	67	23.00	43.17

Across 356 total patients started on eltrombopag after hematopoietic stem cell transplantation, 66% (0.66; 95% CI 0.54-0.77) attained platelet recovery ≥50,000/μL for at least seven consecutive days without needing transfusion. Substantial heterogeneity was observed (I^2 = 79.3%, $p < 0.0001$), with individual study estimates ranging from 33% to 100%. The prediction interval (25%–96%) reflects variability in anticipated outcomes across

various clinical environments. In subgroup analyses involving three studies, the pooled platelet recovery rate was 0.69 (95% CI, 0.57–0.80) in autologous HSCT (82 patients) and 0.50 (95% CI, 0.32–0.69) in allogeneic HSCT (74 patients). Five studies including 146 patients contributed to the analysis of platelet transfusion independence, yielding a pooled proportion of 0.68 (95% CI, 0.50–0.83). Finally, eight cohorts comprising 307 patients were analyzed for time to platelet recovery, with a pooled mean of 61.7 days (95% CI, 41.4–82.0).

Conclusions: Eltrombopag treatment after hematopoietic stem cell transplantation is associated with a substantial rate of platelet recovery and transfusion independence in patients with thrombocytopenia. Two-thirds of patients reach platelet counts ≥50,000/μL without needing transfusions though notable variation occurs across different clinical contexts. There is substantial heterogeneity which is expected in retrospective, single-arm studies due to timing of platelet counts, disease severity, treatment protocols and center differences. Recovery rates are generally greater in autologous than in allogeneic HSCT recipients. Time to platelet recovery averages around two months but varies widely among patients. These findings support eltrombopag as an effective therapeutic option for post-transplant thrombocytopenia, while highlighting the need to consider patient and treatment heterogeneity when interpreting outcomes. Larger randomized trials are needed to confirm the magnitude of benefit.

Disclosure: Nothing to declare.

A247

TREATMENT OF RELAPSED/REFRACTORY HIGH-GRADE B-CELL LYMPHOMAS WITH POINT-OF-CARE MANUFACTURED ANTI-CD-MB-19.1 - CART-CELLS: A SINGLE CENTER, INTERIM ANALYSIS OF A PHASE 2 TRIAL FROM JORDAN

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Background: Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy is the standard of care for patients with relapsed refractory high-grade B-cell lymphomas. However, industry-driven-CART-cells manufacturing complexity, financial toxicity, and manufacturing time represent barriers to widespread implementation. Study applicability, safety, and efficacy of a point-of-care manufacturing of autologous MB-19.1-CD19-directed CAR T-cell product, using lentiviral vector (Miltenyi-Biotec, Germany), were studied in a low-resourced country.

Methods: This is an interim analysis of a phase 2 trial, prospective single center, open label, single arm, single dose, optimal 2-stage Simon design, clinical trial. Patients aged >18-years-old with confirmed CD19+ve relapsed refractory diffuse large B-cell (DLBCL) and transformed follicular lymphomas (tFL), were included. Patients received a fresh single dose of MB-19.1-CD19-CART, will be followed for 12 months and evaluated for safety and efficacy. The primary endpoint was overall response rate (ORR), defined as complete response (CR) plus partial response (PR) within 3 months post-infusion. Secondary endpoints included duration of response, cumulative incidence of relapse-progression, CART-cell persistence, progression free survival (PFS) and overall survival (OS). Safety endpoints evaluated the incidence of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Thirteen products were manufactured on site. Validation run data (n-3) demonstrated a successful anti-CD-MB-19.1 CART- cells production with robust transduction efficiency.

Results: As of December 5, 2025, 10 patients with high grade B-cell lymphoma relapsed or refractory to 2 lines of therapy were enrolled and 9 patients are included in this analysis. Among evaluable patients, 80% had DLBCL and 20% tFL to DLBCL, 70% received ≥ 3 lines of chemoimmunotherapy including, 60% had prior auto-SCT and none had prior CART therapy. The median age 43 yr (Interquartile range (IQR 41–58), and 50% male. Of subjects enrolled, all had progressive disease prior to apheresis, and none received bridging therapy prior to CART-cell infusion.
At a median follow-up of 148.5 days (IQR:108.75-238.25), the best ORR was 78%, with 56% of patients achieved CR and 22% achieved PR. The ORR at 3 months was 66.6%. Three patients progressed at a median of 31 day(range:30-91). The median duration of response was 77 days (range:28-180). The median PFS is 149 days (range:78–313 days) and all patients are alive at last encounter. There were no cases of manufacturing failure. MB-CD19.1-CART-cells peaked at a median of 13 days (range 12-14). CRS occurred in 22% and no patient had ICANS. No grade 3 CRS were observed. The median duration of grade 2 CRS was one day. One patient developed late pancytopenia fully recovered and has no serious sequalae.

Conclusions: In this pilot single institution study in a limited-resource setting, anti-MB-CD19.1-CART-cells were successfully manufactured. The construct demonstrated high objective responses despite high burden refractory diseases. Response rates were comparable to historic responses reported in pivotal trial using Tisagenlecleucel (JULIET trail, NCT02445248). Low incidence of immune toxicities were observed in our cohort. These promising results warrant a longer follow up and validation in a multicenter trial.

Clinical Trial Registry: NCT0271121

Disclosure: Nothing to declare.

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FEASIBILITY OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ELDERLY PATIENTS WITH MYELOID NEOPLASMS: SINGLE-CENTER EXPERIENCE

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Background: Older adults have traditionally faced higher morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT), which has limited its use in this age group. As transplant strategies have become more individualized, this therapy is increasingly offered to older patients. This shift underscores the need to better understand how advanced age affects clinical outcomes following allo-HSCT in patients with myeloid neoplasms.

Methods: We performed a retrospective observational study of patients aged ≥60 years with myeloid neoplasms who underwent their first allo-HSCT at a tertiary care center between January 2018 and May 2025. Outcomes assessed included overall survival (OS), relapse-free survival (RFS), non-relapse mortality (NRM), and graft-versus-host disease–free/relapse-free survival (GRFS), analyzed with Kaplan–Meier curves and compared with a cohort aged 40–59 years.

Results:

The study included 146 patients (55.5% aged 40-59; 45.5% aged ≥60), with a median age of 58 years (IQR 52 - 58) and balanced sex distribution. At transplant, 57.2% were in first complete remission. Donor types were: HLA-identical siblings (38.4%), haploidentical (43.2%), 10/10 matched unrelated (15.8%), and 9/10 matched unrelated (2.7%). Myeloablative conditioning (MAC) was used in 67.8% of the cohort and in 91.4% of patients aged 40-59. Additional characteristics are shown in Table 1. All patients received GVHD prophylaxis with post-transplant cyclophosphamide, tacrolimus, and mycophenolate.

With a median follow-up of 16.4 months (IQR 6.9 - 33.9), the overall cohort showed: OS of 70.2% (62.7 - 77.8) at 12 months and 59.4% (50.4 - 68.5) at 36 months; RFS of 63.9% (55.9 - 71.9) at 12 months and 51.3% (41.9 - 60.7) at 36 months; NRM of 23.5% (16.3 - 30.7) at 12 months and 27.4% (19.2 - 35.6) at 36 months; and GRFS of 56.4% (48.2 - 64.6) at 12 months and 39% (29.7 - 48.3) at 36 months.

When outcomes were compared by age group (Figure 1), OS was similar between patients aged 40–59 and those ≥60 (76.1% vs. 62.8%, log-rank=0.3). RFS (67.3% vs. 59.4%, log-rank=0.6) and GRFS (57.5% vs. 54.9%, log-rank=0.8) were also comparable. However, NRM was higher in the ≥60 group (33.1% vs. 15.5%, log-rank=0.04), driven mainly by infections (60.87%, 85.7% bacterial), followed by GVHD (17.3%). Within the older cohort,

NRM did not differ significantly by conditioning intensity (MAC 32% vs. RIC 35%, p=0.91). Among the patients aged ≥60, eight were ≥70 years old; in this subgroup, OS was 75% (45 - 100), RFS 75% (45 - 100), NMR 25% (0.0 - 55), and GRFS 72.9% (40.6 - 100).

Table 1. Clinical and demographic characteristics of patients with myeloid neoplasms undergoing allo-HSCT

		TOTAL n=146	40-59 years GROUP n=81 (55.5%)	≥60 years GROUP n=65 (44.5%)	*p*
Age		58 (52-58)	53 (46-56)	64 (62-68)	0.00
Sex	*Male, n (%)*	69 (47.3%)	32 (39.5%)	37 (56.9%)	0.04
	Female, n (%)	77 (52.7%)	49 (60.5%)	28 (43.1%)	
Disease	*AML, n (%)*	96 (65.8%)	59 (72.8%)	37 (56.9%)	0.04
	MDS, n (%)	50 (34.2%)	22 (27.2%)	28 (43.1%)	
Disease status	*Complete remission, n (%)*	90 (62%)	53 (66.2%)	37 (56.9%)	0.68
	Active disease, n (%)	55 (38%)	27 (33.8%)	28 (43.1%)	
ECOG	*0, n (%)*	110 (80.9%)	62 (80.5%)	48 (81.4%)	0.90
	1, n (%)	23 (16.9%)	13 (16.9%)	10 (16.9%)	0.99
	≥2, n (%)	3 (2.1%)	2 (2.5%)	1 (1.5%)	0.73
HCT-CI	*Intermediate risk (1-2), n (%)*	96 (67.6%)	57 (72.2%)	39 (61.9%)	0.19
	High risk (≥3), n (%)	46 (32.4%)	22 (27.8%)	24 (38.1%)	
Donor type	*HLA-identical sibling, n (%)*	56 (38.4%)	34 (42.0%)	22 (33.8%)	0.32
	Haploidentical, n (%)	63 (43.2%)	40 (49.4%)	23 (35.4%)	0.10

Table 1. Clinical and demographic characteristics of patients with myeloid neoplasms undergoing allo-HSCT

	MUD 10/10, n (%)	23 (15.8%)	5 (6.2%)	18 (27.7%)	0.00
	MMUD 9/10, n (%)	4 (2.7%)	2 (2.5%)	2 (3.1%)	0.82
Conditioning regimen	*MAC, n (%)*	99 (67.8%)	74 (91.4%)	25 (38.5%)	0.00
	RIC, n (%)	47 (32.2%)	7 (8.6%)	40 (61.5%)	

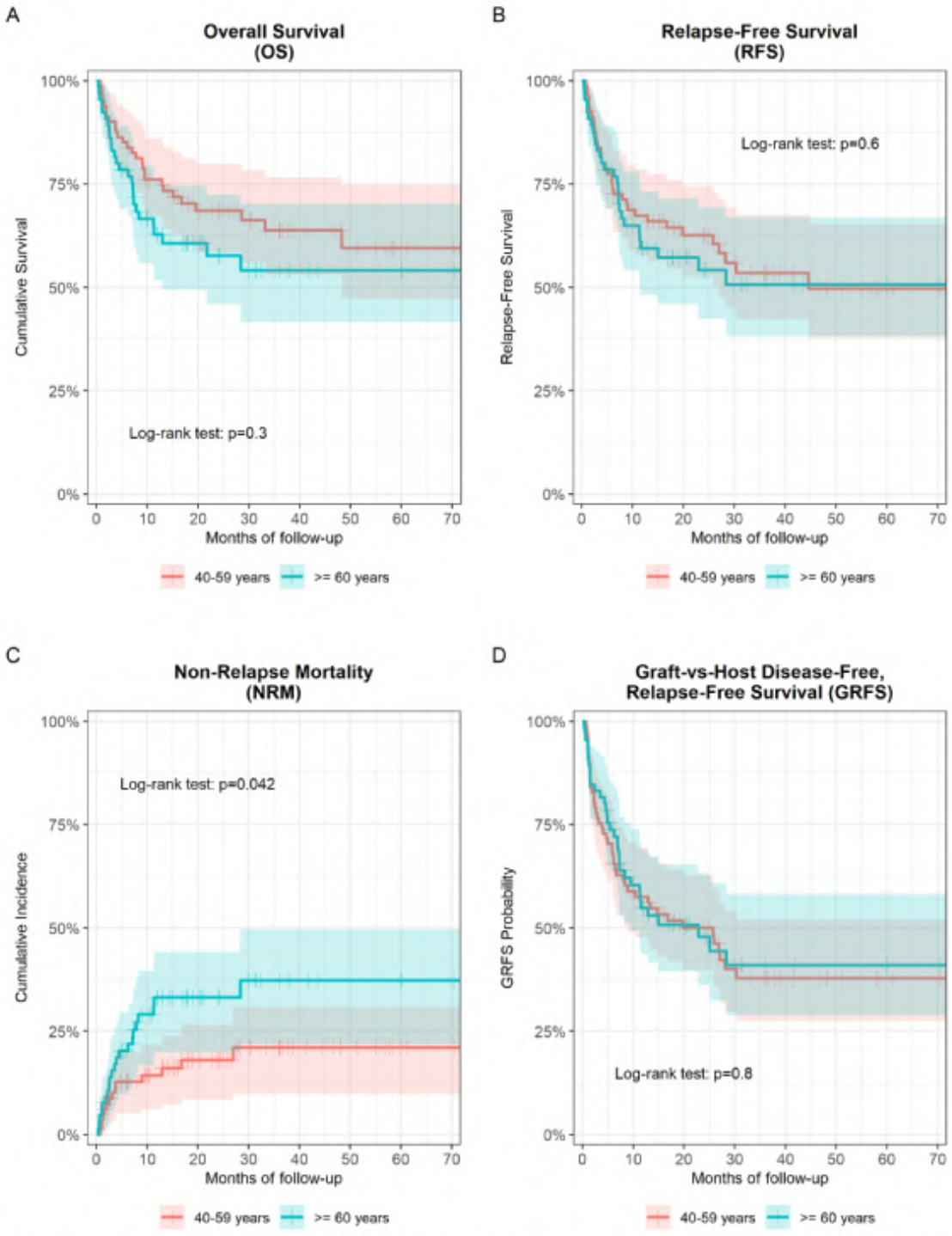

Figure 1. Impact of Age on Transplant Outcomes. Comparison of (A) Overall Survival (OS), (B) Relapse-Free Survival (RFS), (C) Non-Relapse Mortality (NRM), and (D) Graft-versus-Host Disease-Free, Relapse-Free Survival (GRFS) between patients aged 40-59 years (red) and >=60 years (blue).

Conclusions: Advanced age alone should not preclude allo-HSCT in patients with myeloid neoplasms. Data from patients aged ≥60 years, and particularly those ≥70 years, demonstrate that with appropriate selection, this approach is clinically feasible. Individualization of the conditioning regimen, prehabilitation, and specialized supportive care are key determinants for optimizing outcomes. Nevertheless, the risk of non-relapse mortality persists and requires a rigorous, case-by-case assessment.

Disclosure: Nothing to declare.

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OUTCOMES OF CORD BLOOD TRANSPLANTATION FOR AML-MR: PROGRESS AND REMAINING CHALLENGES

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is the only potentially curative option for AML-MR. Cord blood transplantation (CBT) offers rapid donor availability and has been used as an alternative donor source. However, concerns regarding non-relapse mortality after CBT have been raised, and prognostic factors as well as the optimal patient population for CBT in AML-MR remain poorly defined.

Methods: We retrospectively analyzed patients with AML-MR who underwent first single-unit CBT at our institution between 2010 and 2024, excluding those with an ECOG performance status (PS) ≥3 or those with AML-MR arising from antecedent MDS/MPN. Survival and competing-risk outcomes were analyzed using Kaplan–Meier and Fine–Gray methods. Prognostic factors were assessed using multivariable regression models.

Results: A total of 333 patients were included, with a median follow-up time of 62 months. 230 patients (69.1%) were male. The cohort included a substantial proportion of older patients, with a median age at CBT of 63 (range 19-79), and 275 (82.6%) patients were in non-remission status. The median infused CD34-positive cell dose was 0.84 $\times 10^5$/kg. Complex (≥3) and monosomal karyotype were observed in 117 (35.1%) and 103 (30.9%) patients, respectively; adverse cytogenetics were present in 151 patients (45.3%). Other baseline characteristics are shown in Table1.
The 3-year OS and LFS were 37.6% (95%CI: 32.3-43.0%) and 34.7% (29.5-40.0%). The 3-year CIR and NRM were 23.9% (95%CI: 19.4-28.8%) and 41.3% (95%CI: 35.9-46.7%), as shown in Figure1. Neutrophil engraftment was achieved in 85.0% of patients at day 28 and in 92.5% overall.

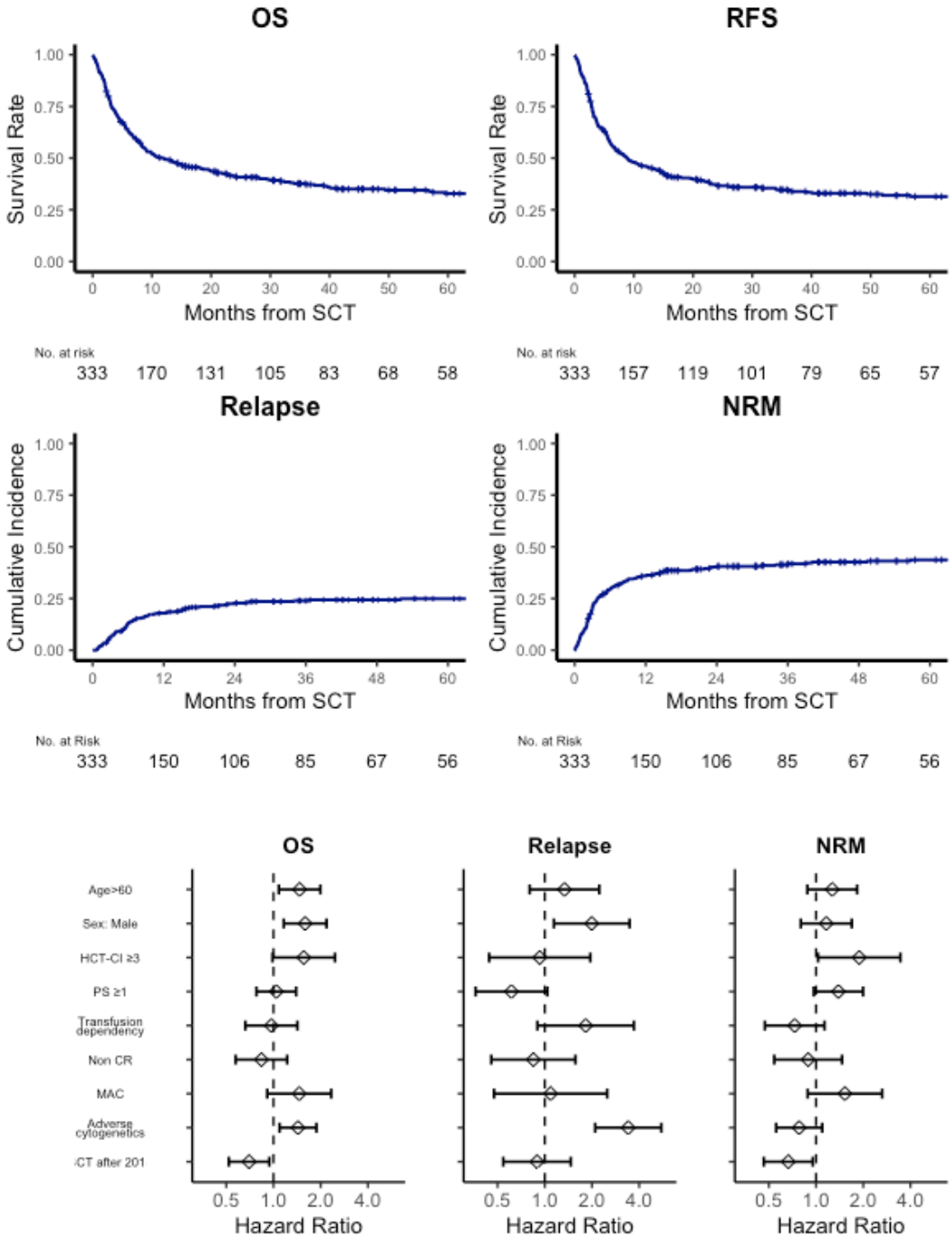
Characteristic	N = 333	Characteristic

Age (range, years)	63 (19-79)	Monosomal karyotype
<60	130 (39%)	Complex karyotype (≥3)
≥60	203 (61%)	Adverse cytogenetics
Sex		Disease Status
Female	103 (31%)	CR
Male	230 (69%)	Non CR
Neutropenia (<500)	198 (60%)	CMV antibody status in recipient
Transfusion dependency (RBC)	231 (69%)	HCT-CI
Transfusion dependency (PLT)	201 (60%)	0-2
ECOG Performance Status		≥3
0	51 (15%)	HLA mismatch
1	224 (67%)	≤1 mismatch
2	58 (17%)	≥2 mismatch
anti-HLA antibody	135 (41%)	
1Median (IQR); n (%)		

Univariate analysis showed age >60, male sex, transfusion dependency, non-remission status, impaired PS (≥1), adverse cytogenetics, transplant era were associated with inferior OS, and the same with LFS. For relapse, male sex, transfusion dependency, and adverse cytogenetics were significant, while age >60, PS≥1, high HCT-CI (≥3), transplant era were associated with NRM.
In multivariate Cox analysis, age>60 (HR 1.47, p=0.01), male sex (HR 1.59, p<0.01), adverse cytogenetics (HR 1.43, p<0.01), transplantation era (HR 0.70, p=0.02) were identified as independent prognostic factors with inferior OS. PS≥1 and non-remission status showed a trend toward an association with OS and LFS, although this did not reach statistical significance. For relapse, male sex (HR 1.99, p=0.01), adverse cytogenetics (HR 3.41, p<0.01) were independently associated, while PS≥1 and transplantation era were prognostic factors for NRM (HR 1.88 and 0.67, respectively).
Notably, a substantial reduction in NRM of more than 10 percentage points was observed in the more recent transplant era (2-year NRM, 46.3% vs 35.1%). In contrast, the relapse rate remained high in patients with adverse cytogenetic features, with a particularly high

incidence of early relapse, affecting 32.1% of patients within a year after CBT.

Figure.1 Transplant Outcomes and Multivariate analysis



Conclusions: CBT represents a viable option for allogeneic HSCT in patients with AML-MR, even in a clinically challenging population characterized by advanced age and a high proportion of non-remission status. While non-relapse mortality has substantially decreased over time, likely reflecting advances in transplant-related care, the high incidence of relapse in patients with adverse cytogenetic features remains a significant unmet challenge.

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HAPLOIDENTICAL VERSUS FULLY MATCHED RELATED DONOR STEM CELL TRANSPLANTATION IN PEDIATRIC AND YOUNG ADULTS WITH SEVERE APLASTIC ANEMIA: A SINGLE-CENTER EXPERIENCE FROM A RESOURCE-LIMITED SETTING

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Background:

In pediatric severe aplastic anemia, matched related donor transplantation is the preferred first-line treatment. In the absence of a matched related donor, immunosuppressive therapy is commonly used, while matched unrelated donor transplantation may be pursued when feasible. Given the financial and logistical barriers to matched unrelated donor transplantation in many regions, haploidentical transplantation with post-transplant cyclophosphamide (PTCy) has emerged as an accessible alternative, though pediatric data remain limited.

We present our single-center experience comparing haploidentical and fully matched related donor transplantation in children and young adults with severe aplastic anemia.

Methods: We retrospectively analyzed all pediatric patients and one young adult with SAA undergoing SCT from 2013 to 2025 at the American University of Beirut Medical Center. Outcomes included engraftment, chimerism, GvHD, complications, hospitalization, and early survival.

Results:

Fourteen patients were diagnosed with SAA, and one had DDX41-associated marrow failure. All but one were naïve to immunosuppressive therapy. The single patient previously treated with rabbit ATG and cyclosporine developed posterior reversible encephalopathy syndrome (PRES), which resolved with supportive management and treatment adjustment.

Sixteen transplants were performed in 15 patients (median age 7 years; range 3–20; males n=8). Eight patients received haploidentical related donor transplants, including one second transplant following delayed graft failure after matched-sibling SCT. Conditioning consisted of fludarabine (150 mg/m²), cyclophosphamide (29 mg/kg), antithymocyte globulin (2.5 mg/kg), and TBI (4 Gy) for haploidentical transplants, while fully matched related donor transplants received reduced-dose TBI. GVHD prophylaxis included a calcineurin inhibitor and methotrexate for matched related donors, and post-transplant cyclophosphamide with a calcineurin inhibitor and mycophenolate mofetil for haploidentical donors. T-cell–replete bone marrow was used in all cases.

The median infused $CD34^+$ cell dose was 4.93×10^6 cells/kg.

All 11 evaluable transplants achieved hematologic recovery (median neutrophil engraftment 15 days; platelet engraftment 17 days), with comparable engraftment between haploidentical and fully matched groups. Day +30 chimerism (n=12) demonstrated high donor fractions (median ~99%).

Acute GVHD occurred in two haploidentical recipients: one with hyperacute steroid-refractory gastrointestinal GVHD successfully treated with etanercept and ruxolitinib, and one with mild cutaneous GVHD versus trimethoprim-sulfamethoxazole hypersensitivity. No acute GVHD occurred in the fully matched group, and no chronic GVHD was observed.

Infectious complications included CMV viremia (n=2), EBV viremia (n=1), BK virus–associated cystitis (n=1), and isolated mild bacterial or viral infections. Median hospitalization duration was 43 days (range 28–136). All patients were alive at the last follow-up (median 22.6 months). Follow-up dates were available for 12 patients; duration data were incomplete for the others.

Conclusions: In pediatric patients with severe aplastic anemia, of whom only one patient had received prior IST**,** haploidentical stem cell transplantation using the Baltimore protocol achieved reliable engraftment, high donor chimerism, a comparable toxicity profile, and excellent early survival, comparable to outcomes observed with fully matched related donor transplantation.
Given the financial and logistical barriers to matched unrelated donor transplantation in many regions, haploidentical transplantation should be strongly considered as a curative and readily accessible alternative for children with severe aplastic anemia when a matched related donor is unavailable.

Disclosure: Nothing to declare.

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PROGNOSTIC FACTORS FOR CYTOKINE RELEASE SYNDROME (CRS) AND IMMUNE EFFECTOR CELL–ASSOCIATED NEUROTOXICITY SYNDROME (ICANS) AFTER CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) THERAPY: A SINGLE-CENTER EXPERIENCE

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Background: The present study aims to identify clinical and laboratory prognostic factors associated with the incidence and severity of CRS and ICANS following CAR-T therapy.

Methods: Fifty-one consecutive patients treated with CAR-T therapy for B-cell lymphomas between October 2022 and July 2025 were retrospectively analyzed. Patient characteristics

are summarized in the table. Grading and management of CRS and ICANS were performed according to EHA/EBMT guidelines. The appropriate non-parametric tests were applied for statistical analysis.

Results: A. For ICANS:

1. Performance status (PS) at referral and at lymphodepletion was associated with ICANS but not CRS. ICANS grade 2–4 occurred more frequently in patients with poor PS both at referral (PS 2–3: 55% vs 10%, p=0.004) and at lymphodepletion (PS 3–4: 63% vs 12%, p=0.004). Overall, PS>1 was associated with a higher risk of ICANS of any grade at referral (72% vs 13%, p=0.001) and at lymphodepletion (75% vs 16%, p=0.007).
2. Bulky disease at LDP was associated with higher rates of ICANS grade 2–4 (43% vs 11%, p=0.018), while only a non-significant trend was observed for CRS (CRS yes/no: 33% vs 12%, p=0.07).
3. C-reactive protein (CRP) levels on the day of CAR-T infusion were strongly associated with increased incidence and severity of ICANS. ICANS occurred in 8/16 patients with CRP >30 mg/L compared to 5/35 with CRP ≤30 mg/L (p=0.013). Similar results were observed using a CRP cutoff of 20 mg/L (ICANS yes vs no: 47% vs 12%, p=0.009). CRP levels >30 mg/L and >20 mg/L were also associated with a higher incidence of ICANS grade 2–4 (44% vs 9%, p=0.006 and 42% vs 6%, p=0.003, respectively).
4. Combined elevated CRP [(>20 mg/L), (*normal CRP (0-5 mg/L)]* and poor PS (>2) markedly increased the risk and severity of ICANS. ICANS occurred in 4/31 (13%) with CRP ≤20 mg/L and PS 0–2 (Group A), 3/13 (23%) with CRP >20 mg/L and/or PS 3–4 (Group B), and 6/7 (86%) with CRP >20 mg/L and PS 3–4 (Group C) (p=0.0001). ICANS grade 2–4 occurred in 6%, 23%, and 71% of Groups A–C, respectively (p=0.0001).

B. For CRS

1. Primary refractory disease was associated with higher rates of CRS grade 2–4 (10/17 vs 4/20, p=0.015).

C.Both for CRS and ICANS:

1. Ferritin levels at LDP were predictive of both toxicities. Patents with ferritin >650 ng/mL developed CRS grade 2–4 more frequently than those with lower levels (53% vs 25%, p=0.046) and also showed a higher incidence of ICANS (42% vs 15.6%, p=0.05).

Finally, ICANS grade 2–4 was associated with inferior overall survival. Two-year overall survival was 57% in patients with ICANS grade 0–1 versus 40% in those with ICANS grade 2–4 (p=0.05).

Patient's Characteristics	Number
Total patients	51
Median age, years (range)	62 (35-77)

Sex	Number / N (%)
Male - Female	29 (57%) - 22 (43%)
Indication for CAR-T therapy	
DLBCL[1] – 2nd line	26 (51%)
DLBCL [1] - ≥3rd line	11 (21.6%)
MCL[2]	8 (15.7%)
Follicular lymphoma (FL)	6 (11.8%)
Prophylactic treatment	
Levetiracetam	51 (100%)
Corticosteroids	19 (37.3%)
CRS	Number / N (%)
Grade 1, Grade 2, Grade 3, Grade 4	30 (58.8), 15 (29.4), 3 (5.9), 0
No	3 (5.9)
ICANS	
Grade 1, Grade 2, Grade 3, Grade 4	3 (5.9), 5 (9.8), 2 (3.9), 3 (5.9)
No	38 (75)
[1]DLBCL: Diffuse Large B-cell lymphoma, [2]MCL: Mantle cell lymphoma	

Conclusions: Poor performance status, primary refractory disease, and bulky disease represent important clinical risk factors for CRS and ICANS following CAR-T therapy. Ferritin levels at lymphodepletion and CRP levels at infusion are significant predictive biomarkers for these severe toxicities, enabling early identification of patients at increased risk and potentially supporting pre-emptive management strategies.

Disclosure: Nothing to declare.

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WHEN COMBINING ATG WITH PTCY, HIGHER ATG EXPOSURE MAY RESULT IN HIGHER SURVIVAL

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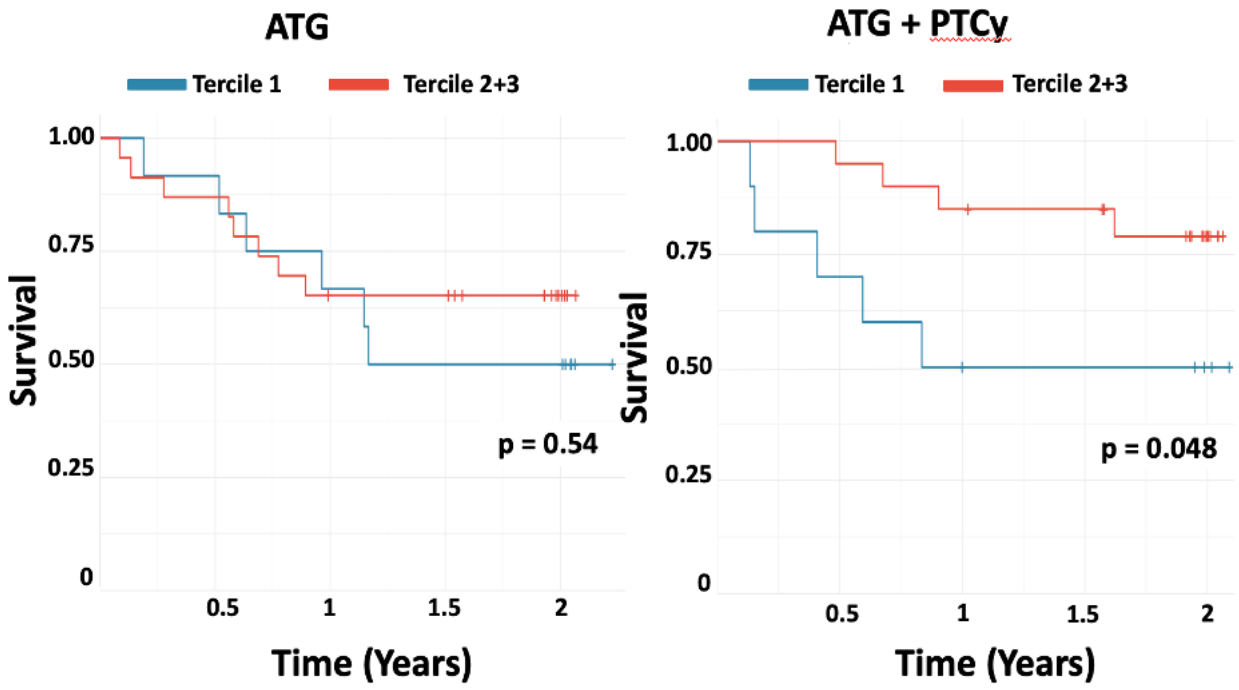
Background: Anti-thymocyte globulin (ATG)-based GVHD prophylaxis as well as posttransplant cyclophosphamide (PTCy) based GVHD prophylaxis are commonly used because of their superiority to previously used GVHD prophylaxis (an antimetabolite and a calcineurin inhibitor). It is unclear whether the combination of ATG and PTCy in GVHD prophylaxis is even better. In a randomized study, ATG-based GVHD prophylaxis was compared to a combination of ATG and PTCy-based GVHD prophylaxis (Walker I.: ASH 2024 Abstract No. 3519, https://ash.confex.com/ash/2024/webprogram/Paper198798.html). Acute GVHD appeared to be reduced in the ATG+PTCy arm but, surprisingly, overall survival (OS) was not. Here we studied whether this surprising finding could be related to ATG exposure.

Methods: ATG was given as 0.5 mg/kg on day -2, 2.0 mg/kg on day -1, and 2.0 mg/kg on day +1 (total 4.5 mg/kg). PTCy was given as 50 mg/kg on day 3 and 4 (total 100 mg/kg). We studied 30 patients from the ATG arm and 35 patients from the ATG+PTCy arm, who consented to blood drawing for ATG pharmacokinetics (PK) (at the start and the end of each ATG infusion, before and after graft infusion, and on day 3, 7, 14, and 28 posttransplant). Serum concentration of ATG capable of binding to lymphocytes was measured using flow cytometry. A validated PK model estimated the AUC (surrogate for ATG exposure) for each patient. Patients were stratified into AUC terciles: T1 <40, T2 40-54, and T3 >54 U·day/L. Per preliminary analysis, in the ATG+PTCy arm, OS appeared higher for patients with T2 and T3 AUC than T1 AUC. Thus, for further analyses we used a combined group of patients with T2 and T3 AUC and compared their OS to the T1 AUC group, using Cox regression.

Results: In the ATG+PTCy arm, OS was higher in the T2+3 patients than the T1 patients (hazard ratio (HR)=3.4, p=0.048). In the ATG arm, no OS difference was observed between the T2+3 and the T1 patients.



Conclusions: Higher ATG exposure, which could be achieved by a higher than the 4.5 mg/kg ATG dose, appeared beneficial when combined with PTCy. We hypothesize that PTCy's attenuation of graft-versus-leukemia effect may increase reliance on ATG's direct antileukemic properties (Dabas et al 2019, DOI 10.1182/bloodadvances.2018030247) . Larger studies are needed to confirm these our findings.

Clinical Trial Registry: NCT04202835

Disclosure: Jan Storek received funding from Sanofi. None of the other authors declare a conflict of interest.

A253

IMPACT OF CORTICOSTEROID THERAPY ON CLINICAL OUTCOMES, TOXICITY, AND CAR T-CELL KINETICS IN PATIENTS TREATED WITH ACADEMIC ANTI-BCMA CAR T CELLS (HBI0101)

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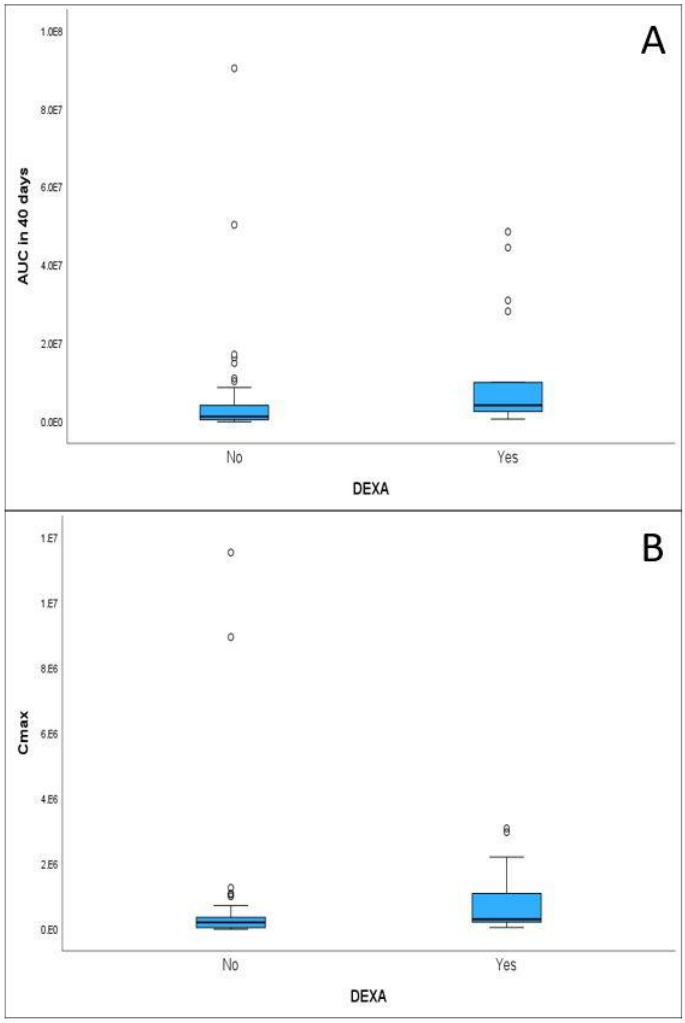
Background: Cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) are the principal acute toxicities of CAR T-cell therapy. Corticosteroids are commonly used to treat higher-grade CRS and ICANS, yet concerns persist regarding potential negative effects on CAR T-cell expansion and durability. While these effects have been studied in commercial anti-CD19 CAR T products, data regarding anti-BCMA CAR T therapies, remain limited. This study evaluates the clinical, laboratory, and kinetic impact of corticosteroid exposure in patients treated with HBI0101, a locally manufactured academic anti-BCMA CAR T product.

Methods: This analysis included patients enrolled in the HBI0101 phase Ia/b clinical trial who received BCMA-targeted CAR T therapy. Patients were grouped according to corticosteroid exposure after infusion. Clinical outcomes, adverse events , response depth, progression-free survival (PFS), overall survival (OS), laboratory parameters, cytokine levels (IFN-γ, TNF-α, granzyme B), and CAR T-cell kinetics (40-day AUC - Area under the curve of CAR+ T cells concentrations, as a measure of CAR T overall expansion over a 40-days period and Cmax - Peak concentration of CAR+ T cells in the blood), were compared between groups. Statistical analyses included Mann–Whitney U tests, χ^2 tests, and Kaplan–Meier survival analyses.

Results: Eighty-four patients with relapsed/refractory multiple myeloma received BCMA-targeted CAR T therapy between October 2021 and March 2024; 17 (20.2%) received corticosteroids and 67 (79.8%) did not. Baseline characteristics were largely comparable, although steroid-treated patients were older (median 71 vs. 63 years; p=0.035) and had higher bone marrow plasma cell burden (≥10% in 70.6% vs. 36.5%; p=0.012).CAR T-cell expansion was greater in the steroid group, with higher 40-day AUC (median 4,231,953 vs. 1,318,310 cells/mL; p=0.007) and higher Cmax (median 307,433 vs. 209,899 cells/mL; p=0.016; Figure 1). Cytokine levels did not differ between groups.
CRS occurred in 95.2% of patients, with grade 3 CRS more frequent in the steroid group (64.7% vs. 6.0%; p<0.001), consistent with steroid indication. ICANS was uncommon (3.6%) but occurred more frequently among steroid-treated patients (17.6% vs. 0%; p=0.007). Infection rates were similar between groups, while febrile neutropenia was more frequent with steroid use (76.5% vs. 46.3%; p=0.026). Treatment responses are summarized in Table 1, with no significant differences between groups. Though steroid exposure was not associated with PFS (p=0.909), it was associated with borderline inferior OS (p=0.050, HR38.521, 95% CI 31.990-44.592). However, in a multivariable analysis for OS, only ECOG performance status > 0 retained statistical significance (p=0.038, HR 9.362, 95% CI 1.138 - 77.036), while steroid exposure did not (p=0.067).

Figure 1:



A:
Box plot comparing 40-days AUC (Area Under the Curve) CAR positive T cells/mL between the Corticosteroid and the control groups, with a statistically significant difference observed between the two groups (Mann-Whitney Test, p=0.007).

B:
Box plot comparing Cmax (Peak concentration) of CAR positive T cells/mL in the blood between the Corticosteroid and the control groups, with a statistically significant difference observed between the two groups (Mann-Whitney Test, p=0.016).

Table 1:
Best response by corticosteroid administration

Variable	Overall N=84	Corticosteroids		p-value[1]
		No N=67	Yes N=17	
Best response[1]				0.826[2]
sCR – No. (%)	57 (67.9%)	46 (68.7%)	11 (64.7%)	
VGPR – No. (%)	14 (16.7%)	11 (16.4%)	3 (17.6%)	

Variable	Overall N=84	Corticosteroids		p-value[1]
PR – No. (%)	6 (7.1%)	4 (6.0%)	2 (11.8%)	
PD – No. (%)	7 (8.3%)	6 (9.0%)	1 (5.9%)	
MRD status				1.000[2]
Negative – No. (valid%)	62 (73.8%)	49 (79.0%)	13 (76.5%)	
Positive – No. (valid%)	17 (20.2%)	13 (21.0%)	4 (23.5%)	
Missing	5			

[1]Best response, as defined in the International Myeloma Working Group (IMWG) consensus criteria for response and minimal residual disease assessment in multiple myeloma.
[2]Fisher-Freeman-Halton Exact Test

Conclusions: Among patients receiving the anti-BCMA CAR T product HBI0101, corticosteroid administration for CRS/ICANS did not negatively impact CAR T-cell expansion or depth of response. Although an association with inferior OS was observed in univariate analysis, this effect was attenuated and did not reach statistical significance in multivariable modeling. These findings support the safety of clinically indicated corticosteroid use in managing CAR T-related toxicities, while underscoring the need for larger cohorts to confirm these results and refine toxicity management strategies for anti-BCMA CAR T therapies.

Disclosure: "Nothing to declare".

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ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION POST–CAR-T THERAPY IN CHILDREN WITH PRE-B ACUTE LYMPHOBLASTIC LEUKAEMIA: NATIONAL POLISH EXPERIENCE

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Background: CAR-T therapy represents an innovative treatment option for hematologic malignancies resistant to conventional therapies. However, in selected patients, hematopoietic stem cell transplantation (HSCT) may still be required following CAR-T therapy. The decision to proceed with HSCT depends on multiple factors, including relapse risk, biological and genetic characteristics of the malignancy, and the response to CAR-T therapy. A timely decision to perform HSCT may improve the likelihood of achieving long-term disease control.

Methods: Among 51 patients treated with CAR-T therapy in Poland, 12 children subsequently required allogeneic HSCT. HSCT procedures were performed at three pediatric centers: Wrocław, Bydgoszcz, and Kraków. We conducted a retrospective analysis that included demographic data, clinical history, CAR-T therapy characteristics, and details of the HSCT course. Seven children were treated for relapsed acute lymphoblastic leukemia (ALL), including one with a CD19-negative relapse. In one patient, the indication for HSCT was severe and prolonged hematologic toxicity after CAR-T therapy (ICAHT). One patient failed to achieve molecular remission, while in three children, CAR-T therapy served as a bridge to transplantation.
During the interval between CAR-T infusion and HSCT, two patients required a CD34+ stem cell boost.
The median time between CAR-T infusion and HSCT was 340 days (range, 64–908 days). Conditioning regimens included total body irradiation with etoposide in nine patients; treosulfan, fludarabine, and thiotepa in two patients; and fludarabine with cyclophosphamide in one patient.

Results: Post-transplant complications included one patient developing severe veno-occlusive disease, treated with defibrotide. Four children developed acute skin graft-versus-host disease (GVHD): three responded to steroid therapy, while one had steroid-resistant GVHD requiring etanercept. One child experienced graft rejection and required a second HSCT.
Two patients were treated with cidofovir for adenovirus reactivation, and one subsequently developed chronic bone marrow failure. No cases of chronic GVHD were observed.
The median duration of follow-up after HSCT was 8 months (range, 1-62 months). 1-year overall survival was 79%, while disease-free and event-free survival rates were 79% and 68%, respectively. Two patients died from disease recurrence, one at 5 months and the other at 8 months after the procedure.

Conclusions: Hematopoietic stem cell transplantation remains an important therapeutic strategy in selected patients following CAR-T therapy. The primary indication for HSCT in this setting is disease relapse; however, second CAR-T infusions are increasingly considered. Allogeneic HSCT after CAR-T is also recommended as remission consolidation in patients at very high risk of relapse—based on biological or genetic features—or in those who fail to achieve minimal residual disease (MRD) negativity after CAR-T therapy. In addition, severe or prolonged hematologic toxicity following CAR-T may necessitate HSCT. In these clinical scenarios, transplantation can provide more durable disease control and reduce the risk of subsequent relapse.

Disclosure: Nothing to declare.

A256

MULTICENTER PILOT CLINICAL TRIAL OF OLUTASIDENIB AS MAINTENANCE THERAPY AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN PATIENTS WITH AML/MDS CARRYING IDH1 MUTATIONS

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Background: Somatic mutations in isocitrate dehydrogenase *(IDH1)* is seen in ~10% AML and 3-5% MDS patients. We and others have previously reported higher relapse with IDH mutation post allogeneic hematopoietic cell transplantation (alloHCT). Olutasidenb is a small molecule inhibitor of mutant *IDH1* (*mIDH1*) and has shown efficacy in phase 2 trial [ORR of 48% and response duration 26 months in patients who achieve Cr/CRh]. Here, we report on results of our multicenter pilot trial of Olutasidenib as maintenance after alloHCT in *IDH1* mutated AML/MDS patients (NCT06543381).

Methods: Patients were eligible if they were in complete remission (CR) on day +30 and had adequate marrow function. Olutasidenib was given at FDA approved dose of 150 mg twice daily between days +50-120 post-HCT for 2 years (Fig 1). The primary objective was to evaluate safety and tolerability, and secondary objectives were to assess survival outcomes. Sample size of 15 was determined based on modified rule of continuous monitoring for toxicity using Pocock-boundary with desired probability of early stopping of 0.75 if the unacceptable toxicity rate was ≥33%.

Results: Between 2024-2025, we enrolled 6 patients (n=5 AML; 83%) and MDS (n=1;16%) on study. The median age was 68 years (range:42-71) and majority of patients were Caucasian (83%). All patients with AML (n=5) were in CR1 pre HCT with majority (80%) being MRD negative. Based on ELN 2022, majority of AML patients had adverse risk (n=4; 80%), one patient was intermediate risk and MDS patient had IPSS high risk. Majority of patients received reduced intensity conditioning (n=5; 83%) and all patients received PBSC graft from 8/8 HLA matched donor (=4;66%) or 7/8 mismatched MUD (n=2;33%). GVHD prophylaxis was with post-transplant cyclophosphamide in majority of patients (n=5;83%) At the data cutoff of December 2025, 4 patients are currently on study with median follow-up of 140 days (range: 112-293). One pt died on day +131 (fungal pneumonia unrelated to study drug) and 1 withdrew on day +7. Median start time of protocol therapy is 119 days(range:77-138). All patients currently on treatment have completed >5 cycles of maintenance therapy and one patient has completed 12 maintenance cycles. We collected all grades of adverse effects (AEs) during the first 2 cycles, and grade ≥3 AEs for subsequent

cycles (Table 2). In the first 2 cycles, grade ≥3 AEs were mainly due to hematologic toxicity including: anemia (n=1), lymphopenia (n=1), dyspnea(n=1) and upper respiratory infection (n=1), one patient had grade 2 AE of URI. Most common grade 1 AEs included fatigue (n=2) and transaminitis (n=2), anemia, lymphopenia, nausea, diarrhea, and edema were other common AEs. Table 1 shows AEs for all cycles for the 5 patients treated on study. One patient passed away from fungal pneumonia (unrelated to study drug). No relapse of primary hematologic malignancy has been seen.

Conclusions: In conclusion, post-HCT maintenance therapy with Olutasidenib was safe and feasible with favorable survival outcomes in AML/MDS patients carrying *IDH1* mutations. No unusual toxicity or safety signal was noted in patients treated so far, the trial continues to accrue patients in multicenter setting.

Clinical Trial Registry: NCT06543381; https://clinicaltrials.gov/study/NCT06543381

Disclosure: AS has received funding from Rigel Pharma for conduct of this trial. No COI for all other authors.

A257

A SINGLE CENTRE EXPERIENCE OF ALLOGENEIC STEM CELL TRANSPLANT IN PATIENTS OVER 70

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Background: Incidence of haematological disorders increases with age. Yet use of allogeneic stem cell transplantation (alloSCT)—the only curative option for many such disorders—remains limited in elderly patients due to concerns about complications and comorbidity. Measures such as reduced-intensity conditioning regimens and improved supportive care have broadened eligibility, but outcome data in this age group remain scarce.

Methods: This retrospective single-centre study reviewed outcomes of patients aged ≥70 years undergoing alloSCT between 2015 and February 2024 at Addenbrookes Hospital (UK). Outcomes included: overall survival (OS), relapse-free survival (RFS), GVHD-free relapse-free survival (GRFS), relapse incidence, GVHD incidence/severity, chimerism, donor lymphocyte infusion (DLI) requirement, infection, and mortality incidence/cause.
Survival was estimated using Kaplan–Meier method. Cumulative incidences were calculated using competing-risks methods.

Results: Twenty-two patients (mean age 70.5, 72.7% male) were identified. Characteristics in Table 1. All received reduced-intensity conditioning (fludarabine/melphalan/alemtuzumab). 90.9% (20/22) had fully HLA-matched donors.
Median OS was 699.5 days. Survival at 1,2,3, and 5 years was 77.3%, 45.5%, 45.5%, and

39.8%, respectively. Median RFS was 667 days, with corresponding rates of 68.2%, 45.5%, 40.9%, and 35.8%. Median GRFS was 621.5 days. GRFS at 1,2,3, and 5 years was 63.6%, 45.5%, 40.9%, and 35.8%. (Figure 1)
Relapse occurred in 31.8% (7/22) patients. Median time to relapse was 203 days. Relapse incidence at 1 and 3 years was 18% and 27%. Survival probability 1-year post-relapse was 43%.
Acute GVHD occurred in 45.5% (10/22), with only one grade 3-4 case. Chronic GVHD affected 31.8% (9/22) including two severe cases, but no admission was required for either.
At analysis (June 2025), 13/22 patients had died. Transplant-related mortality (day-100 mortality) was 0%. 46.5% (6/13) of deaths were relapse-related. Incidence of relapse-related mortality was 9.1% at 1 year, 23% at 2 years, and 28% at 5 years. Incidence of non-relapse mortality was 14% at 1 year and 32% at 2 and 5 years, with infection as the leading cause contributing to 30.7% (4/13) of all deaths.
Clinically significant infections occurred in 86.4% (19/22) patients.
Complete whole-blood chimerism was achieved in all patients by day 30. Complete T-cell donor chimerism was 36.4% by day 30, decreasing to 31.8% by day 90. DLI was required in 45.5% (10/22) patients, for mixed chimerism (n=7), relapse (n=1), or both (n=2).

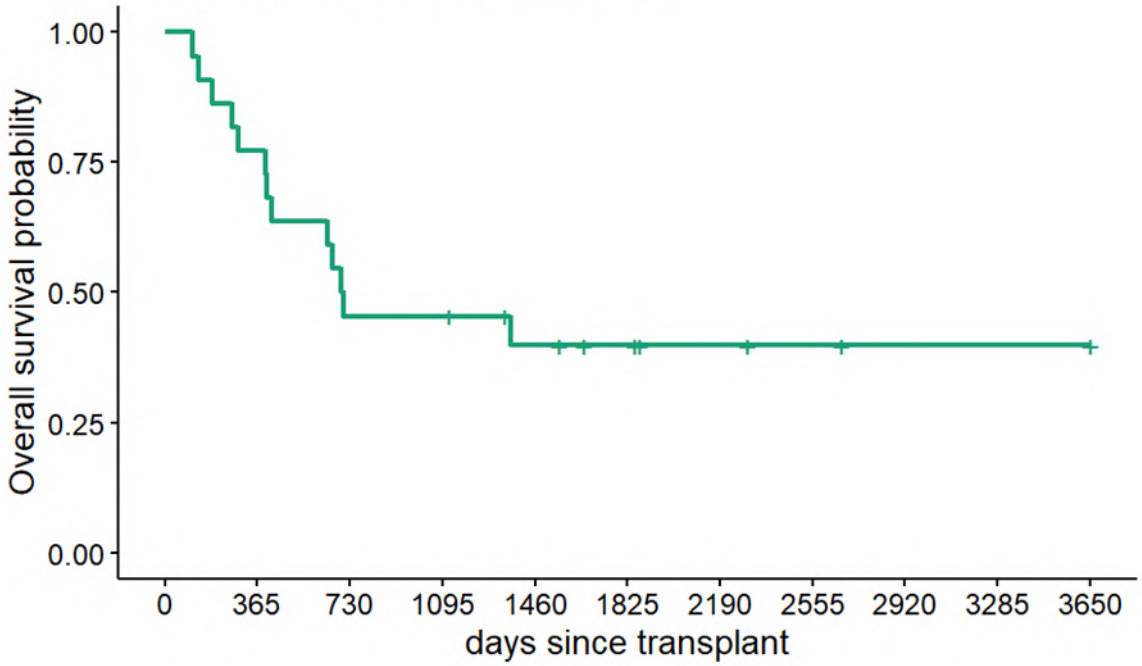
Table 1: Patient characteristics

Characteristic		**Number of patients**	**% of patients**
Diagnosis	MDS	7	31.8
	AML	13	59.1
	CML	1	4.6
	Diffuse large B-cell lymphoma	1	4.6
Donor type	VUD	20	90.9
	Sibling	2	9.1
HLA match	Full match	20	90.9
	9/10	2	9.1
HSCT-CI score	0	5	22.7
	1	7	31.8
	2	4	18.2
	3	2	9.1
	4	2	9.1

	5	2	9.1
ECOG	0	17	77.3
	1	5	22.7

Abbreviations: MDS, myelodysplastic syndromes; AML, acute myeloid leukaemia; CML, chronic myeloid leukaemia; DLBCL, diffuse large B-cell lymphoma; VUD, volunteer unrelated donor; HLA, human leukocyte antigen; HSCT-CI, Haematopoietic Cell Transplantation–Comorbidity Index; ECOG, Eastern Cooperative Oncology Group performance status

Figure 1: Overall Survival (OS)



Conclusions: AlloSCT in patients ≥70 years showed acceptable outcomes with good survival outcomes and zero transplant-related mortality. High rates of GVHD and infections highlight the need for improved post-transplant care, particularly in optimising GVHD prophylaxis/treatment and infection prevention.

Disclosure: Nothing to declare.

A258

LOW-LEVEL PRETRANSPLANT CMV DNAEMIA IS ALREADY A RISK FACTOR FOR POSTTRANSPLANT CMV INFECTION AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Clinically-significant CMV infections (csCMVi) still occur in allogeneic hematopoietic cell transplant recipients (allo-HCTr), even on letermovir prophylaxis. We recently reported that allo-HCTr with a positive pre-HCT CMV DNAemia were at higher risk of post-HCT csCMVi compared to allo-HCTr with undetectable CMV PCR (59.3% vs 26.3% at 180 days (d) post-HCT, respectively). Herein, we further explore the impact of pre-HCT CMV viral load (VL) on the incidence of post-HCT csCMVi and hematological outcomes.

Methods: This was a retrospective cohort study including consecutive adult allo-HCTr (16.11.2015-31.12.2023) with ≥1 CMV positive PCR (detectable (DT) or quantifiable (QT)) up to 90d prior to HCT. Plasma CMV PCR was performed with COBAS CMV test with limit of detection and quantification of 21 and 26 IU/mL, respectively, since 16.05.2018, and previously of 56 and 137 IU/mL, respectively. Since 01.05.2019, letermovir prophylaxis was administered to CMV-seropositive patients for 100d post-HCT. Pre-HCT CMV PCR was performed at pre-HCT consultation, HCT admission, day of HCT, and as clinically indicated. Post-HCT CMV PCR was performed weekly for 90d post-HCT and as clinically indicated thereafter. CsCMVi was defined as CMV PCR ≥ 500IU/mL during letermovir administration and ≥ 150 IU/mL without letermovir.

Results: Among 505 allo-HCT, a median of 3 CMV PCR tests (range 1-14) were performed within 90d pre-HCT. 63/505 allo-HCTr (12.5%) had ≥ 1 positive pre-HCT CMV PCR: 38/63 (60.3%) with DT PCRs and 25/63 (39.7%) ≥ 1 QT PCR. Among the latter, the median VL was 118 IU/mL (range: 38.2-95,600) and mean VL 4,221 IU/mL. Incidence of csCMVi at 180d post-HCT was similar between patients with DT (24/38, 63.2%) or QT (17/25, 68.0%, p=0.69) pre-HCT CMV DNAemia. Similarly, incidence of acute GvHD (60.5% vs 60.0%), relapse (50.0% vs 60.0%) and all-cause mortality (47.4% vs 44.0%) at 1-year post-HCT were similar between the 2 groups (all p > 0.05). There was no significant association between a higher pre-HCT CMV DNAemia and csCMVi, acute GvHD, relapse or death in logistic regressions.

Conclusions: Whereas pre-HCT CMV DNAemia was strongly associated with increased post-HCT csCMVi incidence, the magnitude of the VL is not associated with an increased risk. This suggests that any DT pre-HCT CMV DNAemia may represent an activity of CMV reservoir and could be considered as a relevant risk factor for csCMVi, regardless of the VL.

Disclosure: Nothing to declare.

A259

ASSESSMENT OF COMPLEMENT PATHWAY DYNAMICS AFTER ALLOGENIC HEMATOPOIETIC CELL TRANSPLANT: RESULTS FROM A MONOCENTRIC LONGITUDINAL MONITORING PROGRAM

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Background: Systemic complement activation is a well-established pathophysiological mechanism involved in endothelial complications, particularly post-transplant microangiopathy (TMA), following allogeneic hematopoietic cell transplantation (allo-HCT). We previously demonstrated its impact on post-transplant outcomes in a prospective study involving patients who received a myeloablative conditioning (MAC) regimen (*Notarantonio et al. AJH 2024*). Here, we aimed to investigate the role of complement activation in the clinical course of a cohort of patients prospectively enrolled in a monitoring program between 2022 and 2024.

Methods: The cohort included patients who received either MAC or reduced-intensity conditioning (RIC) regimens. Complement monitoring was performed weekly from baseline through week 12 post-transplant, assessing CH50 activity and C3/C4 levels. Activation profiles were defined by a drop in one or more of these markers below the lower limit of normal.

Results:
A total of 125 patients were included in this study, with a male-to-female ratio of 2.3 and a median age of 59.4 years (interquartile range [IQR] 45.6–65.5). The cohort comprised 67 patients (54%) with acute myeloid leukemia, 13 (11%) acute lymphoblastic leukemia, 11 (8%) myelofibrosis, 6 (5%) other myeloproliferative neoplasms, 18 (14%) lymphoproliferative neoplasms or lymphoma, 9 (7%) myelodysplastic syndromes and 1 (1%) bone marrow failure. Donor types included matched related donors (n=20, 16%), matched unrelated donors (n=65, 53%), mismatched unrelated donors (n=24, 19%), and haploidentical donors (n=16, 12%). Most patients received grafts from mobilized peripheral blood (n=117, 94%), bone marrow (n=6, 5%) and umbilical cord blood (n=2, 1%). RIC regimens were mainly represented (n=107, 86%).

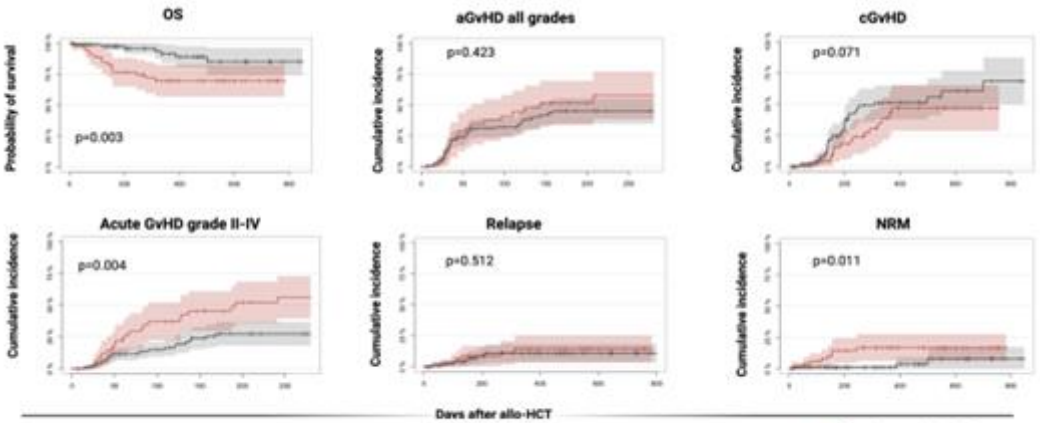

Figure 1. Different outcomes after allo-HCT in patients showing complement activation (red) or not (grey).

The complement profile at baseline showed that a substantial number of patients (n=20, 16%) exhibited isolated C3 activation, suggesting a possible selective activation of the alternative pathway prior to the initiation of the conditioning regimen. After allo-HCT, 52 patients (41%) developed a complement activation profile during follow-up between week 1 and 12. Among them, 16 patients had already exhibited an activated profile at baseline. We found that complement activation was associated with significantly worse overall survival (HR 3.84, 95% CI 1.55–9.49, p=0.0035) and higher non-relapse mortality (NRM, HR 5.44, 95% CI 1.49–20.16, p=0.0112), driven by an increased risk of grade II–IV acute graft-versus-host disease (GvHD) (HR 2.25, 95% CI 1.28–3.95, p=0.0046). The limited number of endothelial events (veno-occlusive disease [VOD] n=7, post-transplant TMA n=6, capillary leak syndrome n=1) precluded firm conclusions, although most affected patients exhibited complement activation. In the TMA group, 4 of 6 patients showed persistent, isolated C3 consumption suggestive of sustained alternative pathway activation. In the VOD group, 3 patients had isolated C3 decline and one showed global complement consumption consistent with systemic classical or lectin pathway activation.

Conclusions: These findings underscore the importance of monitoring complement activity after allo-HCT, since dynamic complement activation was associated with inferior survival and higher NRM, primarily driven by an increased risk of acute GvHD. Incorporating complement monitoring into routine post-transplant follow-up may help identify patients at risk and may open new avenues for the prevention of alloreactive complications.

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Pagliuca: Novartis, Consultancy; Jazz Pharmaceutics, Consultancy; Alexion, Consultancy; Astellas, Consultancy; Sobi, Consultancy.

A260

HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE FOR MALIGNANT AND NON-MALIGNANT HEMATOLOGIC DISORDERS: A REAL-WORLD EXPERIENCE FROM QATAR

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Background: Haploidentical hematopoietic cell transplantation (Haplo-HCT) using post-transplant cyclophosphamide (PTCy) is a readily available alternative for patients without HLA-matched donors. This is an attractive approach in countries that lack donor registries and/or cannot afford the costs of an unrelated donor search. Accumulated experience shows that outcomes of haplo-HCT for hematological diseases are similar to those of matched related and unrelated transplants. We report our 5-years' experience of Haplo-HCT in hematologic malignancies and bone marrow failure syndromes at the National Center for Cancer Care and Research in Qatar.

Methods: Forty-three patients with a median age of 39 years (range 14–59) received haplo-HCT at our center. Majority with hematological malignancies; 28 (65.1%) with myeloid malignancies (AML, MDS, CML-BP), 11(25.6%) with lymphoid malignancies (ALL, NHL) and 4 (9.3%) with aplastic anemia and PNH. Donors were siblings in 69.8%. Donor-specific antibodies were negative in 38 (88.4%), while 5 (11.6%) were positive, 3 (7.0%) of whom required desensitization before transplant. At the time of transplantation, 38 patients of the hematological malignancy patients were in CR1/CR2, and 3 had relapsed/refractory disease. Most patients (90.7%) received a myeloablative conditioning (MAC) (90.7%), whereas 4 patients (9.3%) received a reduced-intensity conditioning (RIC). TBI-based conditioning with fludarabine 160 mg/m² and TBI 1200 cGy were administered to 30 patients (69.8%), whereas 13 patients (30.2%) received non-TBI conditioning. GVHD prophylaxis consisted of PTCy on days +3 and +4, CSA starting from day -1 and MMF from day +1. The median CD34 cell dose was 7.9 x 10^6/kg. Median CD34 dose 7.9 (range, 4.0–12.0), and the CD3 cell dose was 154.3 × 10^6/kg (range, 46.5-283.1).

Results: The median follow-up for surviving patients was 16 months (3 – 52 months). All patients engrafted, median chimerism at the time of engraftment was 99.8% (range, 95-100). The median time for neutrophil and platelets engraftment was 14 days (range, 11.0-42.0) and 18 days (range 9.0 -50), respectively. 2-year and 3-year OS: 90.2%, and OS: 84.2%, respectively (Figure 1). 2-year DFS and GRFS were 76.9% and 67.3%, respectively,

(Figures 2 and 3). The incidence of grade II-IV acute GVHD was 28%, (Figure 4). The 2 - year incidence of cGVHD (all grades) was 36.8% while the moderate to severe cGVHD was 23 % (Figures 5 and 6). 2-year CIR and NRM were 20.8% and 2.3% (Figure 7 and 8), respectively. The incidence of grade 1 and 2 CRS was 20.9%. Three patients (7%) had grade 3 CRS and required tocilizumab. Clinically significant CMV infection was significantly higher in patients who did not receive letermovir prophylaxis (92%) than in those who did (11.6%). One patient developed VOD that was treated with defibrotide. Three patients (7%) developed grade 3 BK-virus-associated hemorrhagic cystitis, and two developed TA-TMA.

Patients, n	**43**
Median patient, age (range)	39 (12-59)
Male gender, n (%)	37 (86%)
Disease, n (%)	
AML/MDS	25 (58.1%)
B-cell ALL/ETP-ALL	9 (20.9%)
CML/CMML	3 (7%)
Non-Hodgkin lymphoma	3 (7%)
Severe aplastic anemia	2 (4.7%)
MPAL	1 (2.3%)
Disease status at transplantation, n (%)	
CR1/CRi1/CR2	38 (88.4%)
Relapsed/refractory	3 (7%)
HCT-CI, n (%)	
0	20 (46.5%)
1-2	15 (34.9%)
≥3	8 (18.6%)
Patient/Donor CMV serostatus, n (%)	
Positive	41 (95.3%)
Any negative	2 (4.7%)
Donor specific antibodies, n (%)	
Positive	38 (88.4%)
Negative	5 (11.6%)
Conditioning, n (%)	
TBI-based	30 (69.8%)
Chemotherapy-based	13 (30.2%)
Conditioning intensity, n (%)	
MAC	39 (90.7%)
RIC	4 (9.3 %)

GVHD prophylaxis, n (%) CSA/MMF/PTCy TAC/MMF/PTCy	 41 (95.3%) 2 (4.7%)
Graft source, n (%) PBSC BM	 42 (97.7%) 1 (2.3%)
Median CD34+ dose, x10^6/kg, n (%) **Median CD3+ dose, x10^6/kg, n (%)**	7.9 (4-12) 154.3 (46.5-283.1)
Engraftment, days (range) Median ANC > 0.5 x10^3 /µL *Median PLTs > 20 x10^3 /µL	 14 (11-42.8) 18 (9-50)
Chimerism, % (range)	99.8 (95-100)
Median follow-up, months (range)	16 (3-52)

* Platelet count was never below 20 for 2 patients

Figure 1

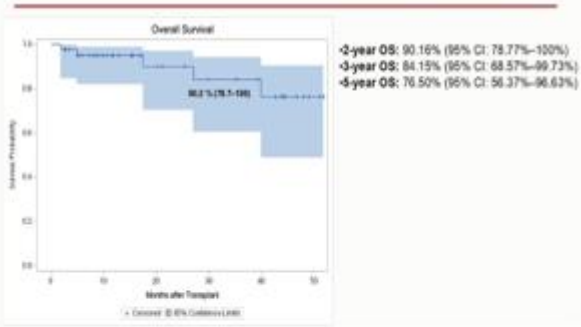


Figure 2

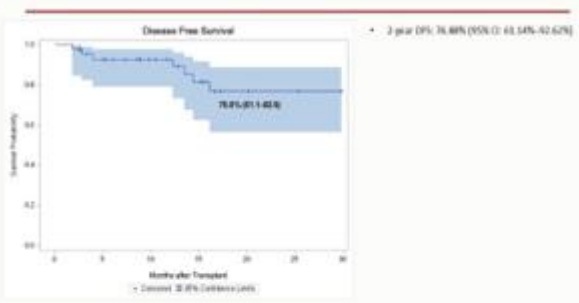


Figure 3

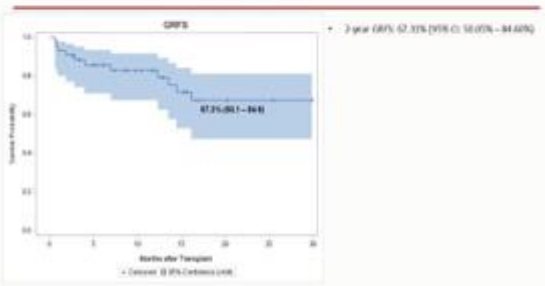


Figure 4

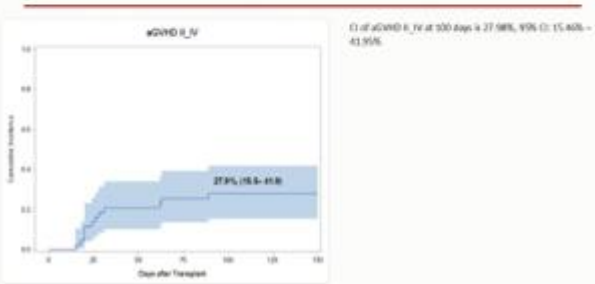


Figure 5

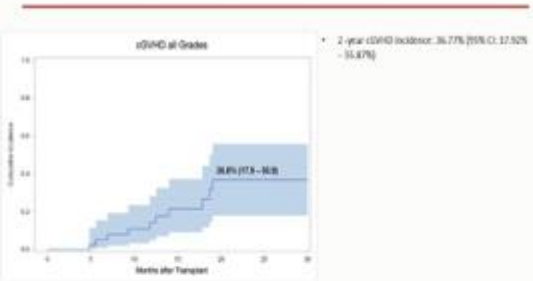


Figure 6

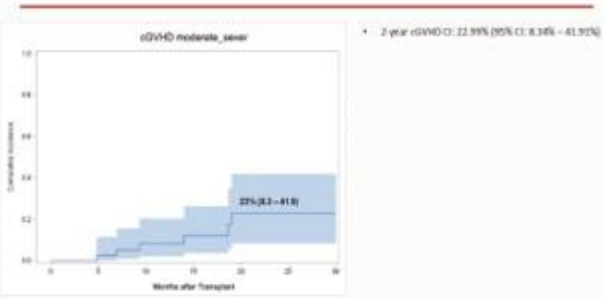


Figure 7

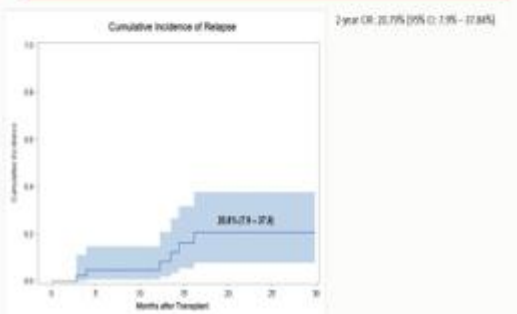
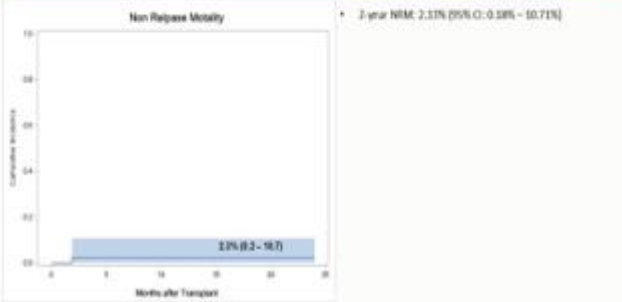


Figure 8



Conclusions: Haplo-HCT with PTCy leads to excellent survival for patients who lack HLA-matched donors or access to an unrelated donor. Our results revealed universal engraftment, higher rates of disease-free survival and an improved graft-versus-host disease-free-relapse-free survival. Finally, in our cohort, both chemo and radiotherapy-based conditioning haploidentical cell transplantation resulted in low rates of relapse, non-relapse mortality and chronic GVHD.

Disclosure: The authors have no Conflict of Interest to disclose

A261

OUTCOMES OF HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHRONIC MYELOID LEUKEMIA IN TYROSINE KINASE INHIBITORS ERA: A SINGLE CENTRE STUDY FROM PAKISTAN

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Background: Chronic Myelogenous Leukemia (CML), a myeloproliferative stem cell cancer driven by the BCR-ABL1 gene, has seen a treatment revolution with tyrosine kinase inhibitors (TKIs). TKIs have enabled high survival rates in the chronic phase, superseding hematopoietic stem cell transplantation (HSCT) as the primary therapy. Nonetheless, factors such as TKI resistance, drug intolerance, the high expenses associated with ongoing treatment and molecular monitoring, and limited TKI access mean that HSCT continues to be an important option in resource-limited environments.

Methods: **Objectives:** To analyse OS, DFS and GRFS in CML patients undergoing allogeneic HSCT.
Methods: This retrospective study was carried out at AFBMTC from 1 Jan 2001 to 31 Aug 25. IRB approval was obtained and anonymized data was analyzed.

Results: A total of 104 CML patients underwent HSCT. The median age of patients was 27 years. (range: 5-50, IQR:21-34). 82 patients were males (76.6%) and 25 were females (23.3%). 72 patients in chronic phase (CP) underwent HSCT due to TKI resistance /intolerance, 19 were transplanted in accelerated phase and 16 in blast crises (BC). Out of BC, 7 patients had lymphoid BC and 9 had myeloid BC. There were 69 male and 38 female donors (median age:24). Myeloablative conditioning (MAC) (Bu, Cy with or without TG/ATG) was given to 103 patients and (Flu, Bu, TG/ATG) was given to 4 patients. Total body irradiation (TBI) was not given due to non-availability of TBI facility. CSA + MTX was the most common GVHD prophylaxis given to 106 patients who underwent fully HLA matched Allogeneic HSCT and PT/Cy was given to 1 patient who underwent haploidentical HSCT. Stem cell source was bone marrow harvest (BMH) in 40, peripheral blood stem cells (PBSC) in 64 and both BMH + PBSC in 3 patients. The median CD 34 dose was 3.94×10^6 /Kg and TNC dose was 3.79×10^8/Kg . Median days to neutrophil and platelets engraftment were +13 and

+18 post HSCT respectively. The most common infectious complication was neutropenic fever followed by hemorrhagic cystitis and gut toxicity. Acute GVHD was experienced in 27% patients and chronic GVHD was experienced in 30% patients. OS was 71.7%, DFS was 63% and GRFS was 37.4%.

Conclusions: Allogeneic hematopoietic stem cell transplantation (HSCT) remains a critical treatment for Chronic Myeloid Leukemia (CML) in low- and middle-income countries (LMICs), especially in cases of TKI resistance or advanced disease. While requiring a major initial investment and complex infrastructure, HSCT provides the possibility of a durable, treatment-free cure. This outcome can ultimately be more cost-effective than lifelong TKI therapy, offering significant long-term survival benefits for eligible patients in resource-limited settings.

Disclosure: No conflict of interest, No disclosures

A262

ABT/CD19 DEPLETED HAPLOIDENTICAL STEM CELL TRANSPLANTATION IS A SAFE AND EFFECTIVE SALVAGE THERAPY IN HEAVILY PRETREATED RELAPSED/REFRACTORY PATIENTS WITH HODGKIN LYMPHOMA

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Background: Hodgkin lymphoma (HL) represents only about 10% of all lymphomas, but has become a paradigm of successful cancer treatment, with cure rates now exceeding 80% in most patient populations. The prognosis of HL has dramatically improved over the past several decades through multiple therapeutic advances. Allogenic transplantation (HSCT) is now reserved only for a small number of patients who fail immunotherapy or experience early relapse. Due to the considerably high Transplant related mortality, above all GVHD, its role in HL has evolved considerably. In the last years haplo transplantation with PTCy has shown high efficacy, with a reported toxicity.

Methods: Ten patients, median age 27 years old (20-39) entered the study. Characteristics are shown in Tab 1. All but two patients had active disease at moment of transplantation. Median number of previous therapies was 6 (range 3-9). All but one patient has already received an autologous transplantation. One patient had received also an HSCT from matched unrelated donor. Only 2 patients were in CR (more than 2) at HSCT. Conditioning consisted of ATG 1,5 mg/kg from day -13 to day -10, Treosulfan 12gr/sqm from -9 to –7, Fludarabine 30mg/sqm from -6 to -2 and Thiotepa 5mg/Kg on days -5 and -4. Ten µg/kg G-CSF was used to mobilize PBPCs from one-haplotype mismatched donors (3 mothers, 5 brothers, 1 sister and 1 uncle; median age 45; range 21-62). T depletion was the only GVHD

prophylaxis. Any additional GVHD prophylaxis was used. Six patients had an unfavorable CMV sierology.

	#1	#2	#3	#4	#5	#6	#7
Age	28	27	20	26	39	23	26
HL type	LYMPHOCYTE DEPLETION	NODULAR SCLEROSIS	NODULAR SCLEROSIS	NODULAR SCLEROSIS	NODULAR SCLEROSIS	NODULAR SCLEROSIS	MIXED CELLULARIT
stage	IV B	II A	III A	II B	IV B	III A	IV
Diagnosis date	01/06/13	01/07/12	14/06/12	01/03/13	01/01/10	01/07/14	18/05/17
Numb Previous lines	4	6	8	9	8	5	5
Previous CT	ABVD +RT	ABVD+RT; IGEV; ABMT; BV; ANTIPD1; DHAP	OEPA; DVCP; COP +RT; ABVD + RT; IEP; DHAP;Dauno Lipo; ABMT; BV	ABVD; BV; BEACOP; Benda; DHAP; ABMT; NIVO; Dauno Lipo; BV Benda	ABVD; IGEV; ABMT; BV; BENDA; BEACOP; HSCT; Doxo Lipo; Lena; Dauno Lipo; NIVO	ABVD; IGEV ; ABMT; BV; NIVO	ABVD; BEACOPP; EDX; BV; ABMT
Previous RT	YES	YES	YES	NO	NO	NO	NO
Previous ABMT	YES	YES	YES	YES	YES	YES	YES
status HSCT	CR	NOT CR	NOT CR	NOT CR	NOT CR	NOT CR	CR

Results: Grafts contained a median of $10x10^6$/kg (range 6-17) CD34+cells, $9x10^6$ $CD3^+$Tcells/kg (range 2-21) with $4x10^4$/kg $\alpha\beta^+$T cells (range 1 – 7.5) and 9 $x10^6$ $\gamma\delta^+$Tcells/kg (range 2-20), $3x10^4$ B cells/kg(range 1,2-6.2) and $22.6x10^8$ $CD56^+$NKcells/kg (range 1-48). All patients engrafted. Median time to reach 500 neutrophils and 20.000 platelets was 12 days and 11 days, respectively. At a median follow up of 7.5 years (range 0.2-9.65) the overall survival was 80%. One patient died because of recurrent CMV reactivation in patient with an unfavorable sierology R POS/D NEG in pre letermovir era and the other one due to GVHD post Donor lymphocyte Infusion. No other cases of GVHD were seen. Interestingly, no relapses occurred. The most frequent infections were of viral origin, especially in the first 100 days post HSCT, but without leading to organ disease. CMV reactivation occurred, in 5 patients, with one experiencing organ disease, and EBV reactivation in three, that completely

responded to 2 cycles of Rituximab. No other long term life-threatening complications occurred. No patients have so far developed chronic GVHD.

Conclusions: Allogenic transplantation with ab T cell depletion is an effective and safe approach in relapsed/refractory Hodgkin lymphoma heavily pretreated, with a rapid donor hematopoietic engraftment and very promising outcome, with a very low transplant related mortality in patients heavily pretreated before HSCT.

Disclosure: No disclosure

A264

FACTORS AFFECTING QUALITY OF BONE MARROW HARVESTING: AN ANALYSIS OF ANTHONY NOLAN DONORS FROM 2019-2024

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Background: Peripheral blood stem cell (PBSC) harvesting has changed the landscape of stem cell collection. However bone marrow harvesting (BMH) remains an important collection method. The total nucleated cell (TNC) dose administered is essential for successful engraftment with consensus of a minimum dose defined as $2x10^8$ cells/kg recipient body weight (RBW) and an "adequate" TNC dose 4 $x10^8$cells/kg RBW. Previous studies have shown higher infused TNC doses correlate with improved clinical outcomes including engraftment and overall survival .Factors impacting BMH yield include donor-recipient weight discrepancy and duration of harvest. We retrospectively examined procedural and donor variables at the Anthony Nolan unrelated donor registry in a contemporary donor cohort to confirm our previous findings and explore any additional factors influencing BMH yield.

Methods: 253 bone marrow donations from 2019-2024 were identified using our electronic database. Several variables were selected for analysis including:

- Collection centre
- Donor sex, age, weight, height, blood parameters (haemoglobin pre/post donation, platelets, ferritin)
- Patient weight and nucleated cells/kg ($x10^8$) requested
- Total Duration, TNC $x10^8$ Collected, TNC Density, CD3+, CD34+, Volume

Variables were analysed using the statsmodels package in python. A p value <0.05 was considered significant. All linear regressions are not adjusted.

Results:

Procedural/ Donor Factor	Categories	n	Outcome (unit)	Result	Statistical Test	Statistical Test result
Donor-recipient weight discrepancy *n=251 as patient weight unavailable in 2 cases	Donor heavier (>5kg)	199	Number of donors achieving adequate TNC yield (>4x10^8/kg)	127 (63%)	Fisher–Freeman–Halton exact test	p < 0.0001
	Weight matched (+/- 5kg)	22		1 (5%)		
	Patient heavier (>5kg)	30		1 (3%)		
Collection centre	5 collection centres	253	Average TNC yield (x10^8/kg RBW)	5.53	Kruskal-Wallis	H=10.336 p=0.035
	A	3		1.59		
	B	16		5.43		
	C	18		6.96		
	D	206		5.46		
	E	10		5.54		
Donor Age	> 40 years	9	Number of donors achieving adequate TNC yield (>4x10^8/kg)	0 (0%)	Fisher's test	p=0.001
	< 40 years	244		131 (54%)		
Duration of harvest	Minutes	253	Average TNC yield (x10^8/kg RBW)	Longer harvest duration associated with lower TNC yield	Linear regression	Coef = -0.063 p <0.001

52% BMHs collected an 'adequate' TNC yield > 4x10^8/kg. Donor-recipient weight discrepancy was strongly associated with the likelihood of achieving TNC > 4x10^8/kg RBW. 63% of donors heavier than their recipients achieved an adequate harvest compared with 5% and 3% of those who were a similar or lower weight respectively (p<0.0001).
Donors >40 collected significantly lower TNC dose than younger donors - median 4.4x10^8/kg

(95% CI: 3.85-4.97) vs 3.0x10^8/kg (95% CI: 1.83-3.29) (Mann Whitney U p=0.008). Small sample size is a limitation in other subcategory analyses. We found a significant difference in TNC yield between 2 collection centres, but one of the sites only performed 3 BMHs, so this should be cautiously interpreted.
Our data confirmed TNC yield per kg decreases as the duration of harvests increases, suggesting longer procedures lead to poorer efficiency harvests (Coef = -0.063, p< 0.001).

Conclusions: These findings support our previous analysis and that of others regarding the importance of the donor/recipient weight in achieving adequate BM harvest, as well as the impact of harvest duration. It also provides new insight to the impact of age in the efficacy of BMH donations in addition to other adverse outcomes from older donors.

Disclosure: Nothing to declare.

A265

FOR CAR T CELL, SIZE DOES SEEM TO MATTER!

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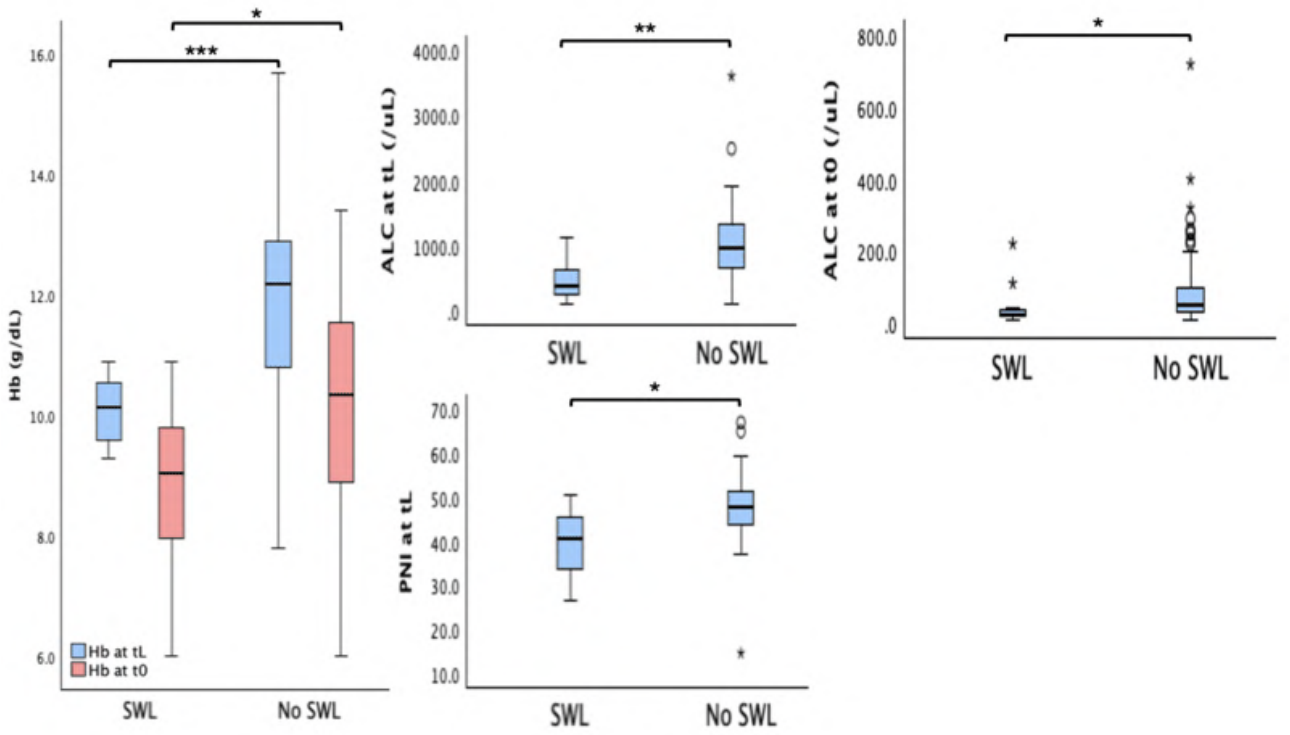
Background: Chimeric antigen receptor (CAR) T-cell therapy has reshaped treatment of lymphoproliferative disorders. As with other T cell–based immunotherapies, nutritional status may influence outcomes. However, as a putative prognostic marker, its clinical significance remains unclear. This study aims to evaluate the impact of significant weight loss (SWL) prior to anti-CD19 CAR T-cell therapy on clinical outcomes and analytical markers of malnutrition.

Methods: This single-center retrospective cohort included adults treated with CAR T between 2019 and 2025. Key timepoints were the first CAR T evaluation (tC), apheresis (tA), pre-lymphodepletion (tL), and infusion (t0). SWL was defined as >5% weight loss, assessed between tC–tL (ΔC–L) and tA–tL (ΔA–L). The prognostic nutritional index (PNI) was calculated from serum albumin and absolute lymphocyte count (ALC). Endpoints included overall survival (OS), progression-free survival (PFS), duration of response (DoR), complete response (CR), overall response rate (ORR), plus laboratory differences by SWL. Associations were tested using chi-square/Fisher and Mann–Whitney/Student's t-test for univariate analysis, and Cox proportional hazards and logistic regression models for multivariate analysis.

Results: Ninety-eight patients (median age 57; male:female 1.4:1) were included, mostly with diffuse large B-cell lymphoma. Thirty patients had ≥3 prior treatment lines, and 76% were refractory to the last therapy. Within the prior month to infusion, 10% had been hospitalized and 11% had received anaerobe-spectrum antibiotics. Tisa-cel was the most frequently used product (61%), associated with lower neurotoxicity risk compared with axi-cel (OR 7.4). CR and ORR were 64% and 70%, respectively. Two-year OS, PFS, and DoR

were 56%, 71%, and 54% (median follow-up 7 months). Several analytical markers of malnutrition were associated with OS, PFS and DoR in univariate analysis; however, in multivariate models, only ALC at t0 and C-reactive protein at tL remained independent predictors of PFS (p=0.032; HR 1.01, 95% CI 1.001-1.020) and DoR (p=0.015; HR 1.005, 95% CI 1.001-1.010), respectively.
SWL occurred in 17% of patients during ΔC–L (median 81 days), and 14% during ΔA–L (median 46 days). SWL was not associated with baseline variables or clinical outcomes. Nonetheless, SWL in ΔC–L correlated with lower hemoglobin, ALC, and PNI at tL (p<0.001, 0.017, 0.049) and with lower hemoglobin at t0 (p=0.042). In ΔA–L, only ALC at t0 was reduced in the SWL group (p=0.019) (Figure 1). In multivariate analysis, no significant differences in laboratory parameters were observed between both groups.



Conclusions: Although not sustained in multivariate models, SWL showed a trend toward an association with adverse hematologic parameters, which in turn may constitute independent predictors of relapse. Nevertheless, the study stresses the pertinence of a more tailored multidisciplinary management for patients presenting with SWL at CAR T referral. Despite sample-size limitations, findings highlight the importance of systematic SWL awareness and the need for a targeted characterisation of nutritional status in CAR T programs.

Disclosure: Nothing to declare.

A267

IMPACT OF SOCIODEMOGRAPHIC AND CLINICAL FACTORS ON ACCESS TO HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACUTE LYMPHOBLASTIC LEUKEMIA: A STUDY FROM MEXICO

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Background:

Acute lymphoblastic leukemia (ALL) is one of the most aggressive hematologic malignancies in adults. Although survival has improved in high-income countries, substantial barriers persist in low- and middle-income settings such as Mexico, limiting timely diagnosis, treatment continuity, and access to highly specialized therapies. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the most effective curative strategy for patients with high-risk, relapsed, or refractory ALL; however, indication for transplantation does not necessarily translate into access.

In Mexico, structural constraints including limited availability of specialized diagnostic tests, prolonged turnaround times, workforce shortages, and centralization of transplant centers contribute to delays that adversely affect outcomes. Additionally, social determinants such as socioeconomic status, travel distance, and indirect treatment costs further restrict access to HSCT in a disease characterized by rapid progression.

Methods: We conducted a retrospective, descriptive observational study of consecutive patients aged ≥16 years with confirmed B- or T-lineage ALL treated at the Instituto Nacional de Cancerología (INCan), Mexico, between January 1, 2018 and December 31, 2024.

Results:

Of 303 records reviewed, 261 adult patients with ALL were included. Median age was 32 years, and 50.6% were female. Most patients were <40 years old (68.6%). B-ALL accounted for 93.9%, and 82.8% were classified as high risk.

Socioeconomically, 36.0% of patients lived in poverty and 41.0% had low socioeconomic status; mean monthly household income was approximately USD 400. 48.7% patients originated with a median travel time of 3 hours. Most lived in urban areas (79.3%), and family support was present in 97.7%. Educational attainment was low, with only 17.6% completing higher education. Unemployment affected 52.5% of patients.

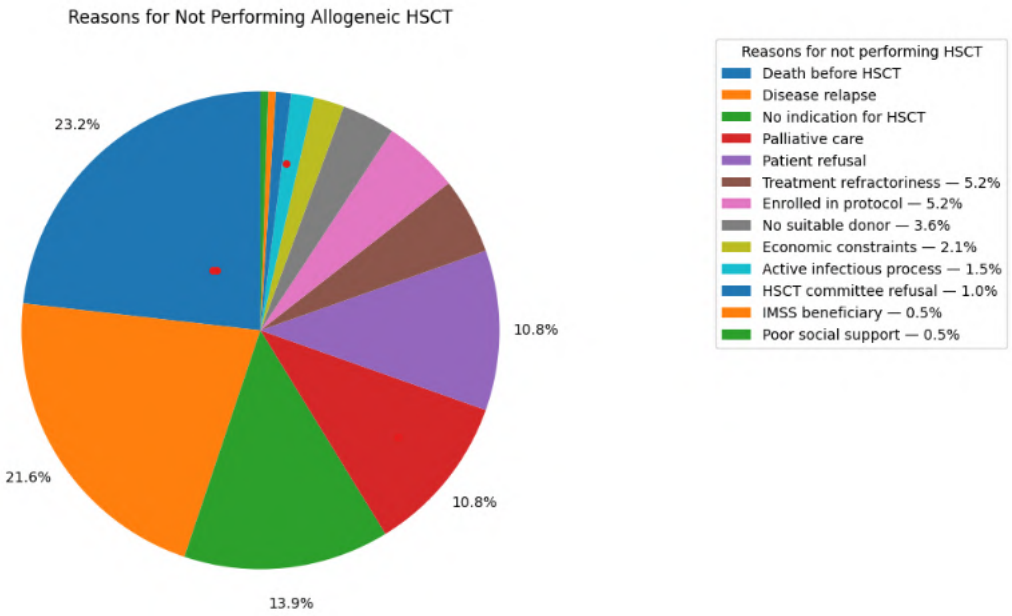
Overall, 237 patients (90.8%) had an indication for allogeneic HSCT, but only 58 (22.2%) underwent transplantation. Donor availability was identified in 47.9%. The most frequent reasons for not proceeding to HSCT were death prior to transplant (24.1%) and disease relapse (22.7%).

Among transplanted patients, haploidentical HSCT was the most common modality (55.2%), followed by matched related donor HSCT (39.7%). Myeloablative conditioning was used in 89.5% of cases. GvHD was the most frequent complication (61.3%).

Transplanted patients experienced prolonged pre-HSCT timelines, with a median of 160 days from diagnosis to transplant referral and 316 days from evaluation to HSCT, mainly driven by delays related to dentistry, psychology, and infectious disease assessments.
In multivariable analysis, marital status (OR 1.42, 95% CI 1.01–1.99; p=0.044) and lack of donor availability (OR 0.016, 95% CI 0.0035–0.076; p<0.001) were independently associated with failure to undergo HSCT. Median OS was longer in transplanted versus non-transplanted patients (35 vs 14 months; p=0.00037), with no OS difference between haploidentical and MRD HSCT (36 vs 36.5 months).

Characteristic	Overall (n=261)	No HSCT (n=203)	HSCT (n=58)	P value
Age at diagnosis	32(21-43)	33(21-44)	27(19-28)	0.040
Male sex,n(%)	129(49.4)	95(46.8)	34(58.6)	0.150
B-lineage ALL,n(%)	245(93.9)	187(92.1)	58(100)	0.027
CNS involmvement at diagnosis,n(%)	74(28.4)	56(27.6)	18(31)	0.727
High clinical risk, n(%)	215(82.4)	159(78.3)	56(96.6)	<0.001
Ph +, n(%)	45(17.2)	36(17.7)	9(15.5)	0.844
MRD positive post-induction, n(%)	79(34.1)	57(34.1)	22(37.9)	0.717
Relapse,n(%)	77(31.2)	58(30.5)	19(33.3)	0.812
HLA availability,n(%)	125(47.9)	69(34)`	56(96.6)	<0.001

Table1. Baseline clinical and demographic characteristics of adult patients with LLA



Conclusions:

In adult patients with ALL in Mexico, a significant gap persists between transplant indication and access to allogeneic HSCT. Delayed referral and limited donor availability often related to restricted access to timely HLA typing, donor identification, and prolonged pre-transplant evaluation pathways are key determinants of HSCT access, particularly in rapidly progressive disease, beyond socioeconomic or geographic factors.

Disclosure: Nothing to declare.

A268

SINGLE-CENTER RETROSPECTIVE CLINICAL STUDY ON THE CONDITIONING REGIMEN OF DECITABINE, THIOTEPA, BUSULFAN, AND FLUDARABINE (DTBF) COMBINED WITH ATG/PTCY FOR ALTERNATIVE DONOR TRANSPLANTATION IN MYELODYSPLASTIC NEOPLASMS

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Background: Allogeneic hematopoietic stem cell transplantation (allo - HSCT) is the only curative treatment for high-risk myelodysplastic neoplasms (MDS). Thiotepa has been

demonstrated favorable safety and efficacy in conditioning regimens for transplantation.However, no research data have been reported yet on the DTBF conditioning regimen combined with anti-thymocyte globulin (ATG)/post-transplantation cyclophosphamide (PTCy) in alternative donor HSCT for adult MDS. We conducted a retrospective single-center study focusing on adult MDS patients with DTBF conditioning regimen.

Methods: This study retrospectively analyzed a total of 11 adult MDS patients from October 2024 to August 2025. All patients provided written informed consent. The DTBF regimen consisted of decitabine (100 mg/m²), thiotepa (10 mg/kg), busulfan (9.6 mg/kg), and fludarabine (160 mg/m²). The GVHD prophylaxis regimen was based on ATG (7.5 mg/kg) combined with low-dose PTCy (29mg/kg), supplemented with cyclosporine, mycophenolate mofetil, and short-course methotrexate. All grafts were derived from donor peripheral blood stem cells.

Results: Among the 11 patients , the median age was 56 years (range: 24-65 years), and males accounted for 54.5% (6/11). All patients had an ECOG performance status of 0-1. Risk stratification included 3 cases of IPSS-M high risk and 8 cases of very high risk. Before transplantation, 27.3% (3/11) of patients achieved MRD negativity. One patient with MDS - biTP53 underwent a second transplantation due to primary graft failure after the first haploidentical transplantation. The second transplant succeeded involving 9/10 mismatched unrelated donor. Among the remaining 10 patients, 9 received haploidentical transplants, and 1 received 10/10 matched unrelated donor transplant. 10 patients achieved complete donor chimerism after HSCT. The median mononuclear cell dose was 9.56×10^8/kg (range: 7.12–15.03 × 10^8/kg), and the median $CD34^+$cell dose was 7.92×10^6/kg (range: 4.12–11.04 × 10^6/kg).The median time to neutrophil engraftment was 12 days (range: 11–14 days), and the median time to platelet engraftment was 13 days (range: 13–18 days).
As of December 12, 2025, the median follow - up duration was 242 days (range: 41–422 days). Six patients developed grade I acute GVHD.Two patients developed grade II acute GVHD (one with skin and gastrointestinal involvement due to self - discontinuation of immunosuppressive medication). Two patients developed chronic GVHD, one with moderate cGVHD and one with mild cGVHD. All GVHD were controlled well.
Other complications included infections in 9 cases(3 with pulmonary and 6 with intestinal), grade 3 oral mucositis in 3 cases, grade II hemorrhagic cystitis in 1 case, and renal impairment in 3 cases. All patients received letermovir for cytomegalovirus (CMV) infection prophylaxis. Among them, CMV reactivation occurred in 5 cases, and Epstein - Barr virus (EBV) reactivation occurred in 7 cases. One patient(MDS derived AML) relapsed after 5 months of HSCT . All patients remained alive at the time of reporting.

Characteristic	**DTBF (N=11)**	**Outcomes**	**DTBF (N=11)**
Median age, year (range)	56(24～65)	Neutrophil engraftment, day, median (range)	12(11～14)

Gender, *n* (%)		Platelet engraftment, day, median (range)	13(13～18)
Male/Female	6(54.5%)/5(45.5%)	Complete engraftment,n (%)	10(90.9%)
Disease subtype, n (%)		aGVHD, n (%)	
MDS-IB1	4(36.4%)	Grade I/ Grade II	6(54.5%)/2(18.2%)
MDS-IB2	4(36.4%)	Grade III-IV	0(0%)
MDS-LB	2(18.2%)	cGVHD, n (%)	
MDS-AML	1(9.0%)	Mild/Moderate/Severe	1(9.0%)/1(9.0%)/0(0%)
Risk stratification, n (%)		Invasion pulmonary mycosis	3(27.3%)
IPSS-M High risk/Very high risk	3(27.3%)/8(72.7%)	Oral mucositis	3(27.3%)
IPSS-R Intermediate risk/High risk/Very high risk	1(9.0%)/6(54.5%)/4(36.4%)	Sepsis	2(18.2%)
MRD at allo-HSCT, n (%)		Intestinal infection	6(54.5%)
Positive /Negative	8(72.7%)/3(27.3%)	Hemorrhagic cystitis	1(9.0%)
Donor source		Renal function impairment.	3(27.3%)
Haploidentical	10(83.3%)	Cytomegalovirus reactivation	5(45.5%)
Unrelated	2(16.7%)	EBV reactivation	7(63.6%)

Mononuclear cells, $\times 10^8$ /L, median (range)	9.56(7.12～15.03)	Relapse, n (%)	1(9.0%)
CD34+ cells, $\times 10^6$ /L, median (range)	7.92(4.12～11.04)	Death, n (%)	0(0%)

Conclusions: The preliminary data indicate that the DTBF + ATG/PTCy conditioning regimen demonstrates favorable efficacy and safety for alternative donor-HSCT in adult MDS patients.Future evaluations will involve expanding the patient cohort and extending the follow - up periods.

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A269

CONDITIONING MATTERS: A RETROSPECTIVE COMPARISON OF BUCY AND FLUBU IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: BuCy has historically been used as a standard myeloablative conditioning regimen for allo-HSCT. FluBu has increasingly been adopted. Comparative outcome data between these regimens in real-world clinical practice remain limited.

Methods: This was a retrospective single-center study conducted at the National Cancer Institute, including 50 adult patients with a diagnosis of ALL or AML who underwent allo-HSCT.

Results:

A total of 50 patients were included, 25 conditioned with BuCy and 25 with FluBu. Patients in the BuCy group had a median age of 27 years (IQR 23–37), whereas those receiving FluBu were older (38 years, IQR 28–48; p=0.06). Male sex accounted for 48.0% of BuCy and 60.0% of FluBu patients (p=0.39). Diagnosis distribution was comparable, with ALL in 64.0% vs 56.0% and AML in 36.0% vs 44.0% of BuCy and FluBu patients, respectively (p=0.57).

Regarding conditioning intensity, MAC was more frequently used in the BuCy group (80.0%) compared with FluBu (56.0%), whereas RIC was more common in the FluBu group (44.0% vs 20.0%; p=0.07). Post-transplant relapse occurred in 12 patients overall, with a higher incidence in the BuCy group (28.0%) than in the FluBu group (20.0%), although this difference was not statistically significant (p=0.53). Transplant-related mortality at day +100 was identical in both cohorts (12.0% each; p=1.00).

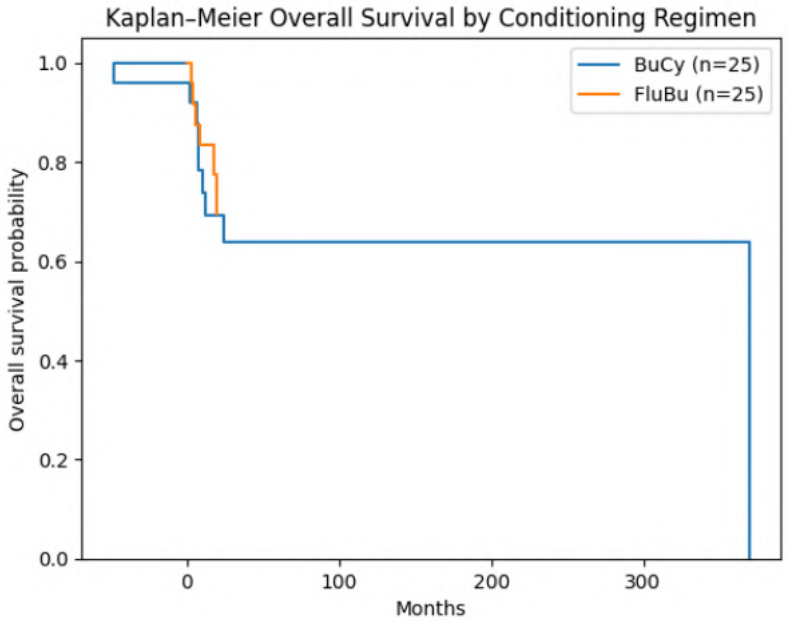
Early toxicities were analyzed by conditioning regimen and stratified by severity (≥ Grade II). Hepatic toxicity ≥ Grade II occurred exclusively in the FluBu group (16.7% vs 0%; p=0.04). Renal toxicity ≥ Grade II was uncommon and comparable between groups (4.0% vs 4.2%; p=1.00). Gastrointestinal toxicity ≥ Grade II occurred in 28.0% of BuCy and 20.8% of FluBu patients (p=0.54), while oral mucositis ≥ Grade II was frequent and similar in both cohorts (36.0% vs 37.5%; p=0.91). SOS was observed only in the BuCy group (8.0% vs 0%), without reaching statistical significance (p=0.15).

Median time to neutrophil engraftment was 13 days (IQR 10–13.5) in the BuCy group and 14 days (IQR 13.3–15.8) in the FluBu group (p=0.18). Median time to platelet engraftment was 15 days in both groups (BuCy IQR 11–17.5 vs FluBu IQR 14.3–16.8; p=0.74). Median hospital length of stay was 30 days (IQR 26–34) for BuCy and 29.5 days (IQR 29–31.8) for FluBu (p=0.81).

Overall mortality was 36.0% (9/25) in the BuCy group and 28.0% (7/25) in the FluBu group (p=0.55). FluBu was associated with fewer death events (25.0% vs 33.3%) and EFS tended to be higher compared with BuCy. Survival curves were comparable between conditioning regimens and between RIC and MAC approaches.

Variable	OS-HR(95% CI)	p value	EFS-HR(95% CI)	p value
Conditioning regimen (FluBu vs BuCy)	0.45 (0.10–2.01)	0.29	0.42 (0.12–1.49)	0.18
Conditioning intensity (RIC vs MAC)	0.33 (0.07–1.57)	0.16	0.60 (0.18–2.00)	0.40
Age	1.08 (0.99–1.18)	0.09	1.06 (0.99–1.15)	0.11
Sex (Female vs Male)	0.32 (0.08–1.35)	0.12	0.43 (0.12–1.48)	0.18
Diagnosis (ALL vs AML)	1.75 (0.41–7.46)	0.45	2.33 (0.65–8.36)	0.19

Table 1. Multivariable Cox proportional hazards analysis for OS and EFS



Conclusions: In this real-world cohort of patients with ALL and AML undergoing allo-HSCT, FluBu demonstrated comparable overall survival and a trend toward improved event-free survival compared with BuCy. Early transplant-related mortality, engraftment kinetics, and hospital length of stay were similar between regimens. These findings support FluBu as a safe and effective alternative to BuCy, although larger studies are needed to confirm potential differences in event-free survival.

Disclosure: Nothing to declare.

A270

MULTI-VIRUS SPECIFIC MEMORY T CELLS TARGETING CMV, BKV, AND EBV IN POST-HSCT VIRAL INFECTIONS

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Background: Reactivation of cytomegalovirus (CMV), BK virus (BKV), and Epstein–Barr virus (EBV) is a serious and potentially life-threatening complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). While antiviral therapies are available for CMV, no approved treatments exist for BKV or EBV, and current antiviral approaches are often limited by toxicity and drug resistance. Virus-specific T cell (VST) therapy represents a promising strategy to address these unmet clinical needs. Notably, our group has previously

established and clinically applied a SARS-CoV-2–specific VST platform, demonstrating complete resolution of COVID-19–associated pneumonia in immunocompromised patients with refractory disease, thereby providing a strong translational foundation for the development of multi-virus VSTs (Lee et al., *Clin Infect Dis*, 2025).

Methods: An off-the-shelf, partially HLA-matched, multi-virus-specific memory T cell platform targeting CMV, BKV, and EBV was established using peripheral blood mononuclear cells (PBMCs) from healthy donors. Virus-specific T cells were generated through peptide-based stimulation with immunodominant viral antigens, followed by ex vivo expansion. Product characterization focused on antigen-specific functional activity and safety. In vivo functional performance was evaluated in virus-relevant experimental models to support clinical translation. In parallel, this platform is currently being evaluated in an ongoing Phase I/II clinical trial enrolling allo-HSCT recipients with antiviral-refractory or -resistant viral infections.

Results: The final VST products demonstrated robust, multi-virus–specific functional activity, including antigen-specific IFN-γ and TNF-α secretion and cytotoxic responses, without evidence of alloreactivity. Across multiple virus-specific in vivo models, administration of VSTs resulted in effective target-specific control accompanied by sustained expansion and persistence of human T cells. Consistent antiviral activity was observed against CMV-, EBV-, and BKV-associated targets, along with enhanced infiltration of virus-reactive $CD8^+$ T cells at sites of viral challenge. Collectively, these findings demonstrate the functional potency and in vivo persistence of multi-virus-specific memory T cells, supporting their translational relevance for post-HSCT viral infections.

Conclusions: Our off-the-shelf, multi-virus-specific memory T cells demonstrate consistent functional activity and in vivo persistence against CMV, EBV, and BKV. Collectively, these findings support their potential as a clinically applicable immunotherapeutic strategy for managing viral complications following allo-HSCT and provide a foundation for ongoing clinical investigation in patients with antiviral-refractory or -resistant viral infections.

Clinical Trial Registry: This study was registered with the Clinical Research Information Service, Republic of Korea, as part of the World Health Organization (WHO) Registry Network (no. KCT0011031).

Disclosure: Seok-Goo Cho is the Chief Executive Officer and shareholder of LucasBio Co, Ltd. Nayoun Kim, Keon-Il Im, Junseok Lee are employed by LucasBio Co, Ltd.

A271

LONG-TERM OUTCOMES OF HAPLOIDENTICAL, MATCHED SIBLING, AND MATCHED UNRELATED DONOR HSCT IN 133 ELDERLY PATIENTS WITH HEMATOLOGIC MALIGNANCIES: A SINGLE-CENTER COMPARATIVE STUDY

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Background: In patients aged ≥60, allogeneic HSCT remains high-risk, with increased toxicity, NRM, and GVHD concerns. Yet evidence from large cohorts directly comparing donor platforms is limited. Robust comparison of haplo, MUD, and MSD outcomes in this population is therefore needed to inform optimal donor choice.

Methods: We retrospectively analyzed 133 patients aged ≥60 who underwent first allogeneic HSCT between December 2023 and January 2015, stratified by donor type into haploidentical (haplo, n=99), matched unrelated (URD, n=16), and matched sibling (MSD, n=18) groups. Clinical characteristics, engraftment kinetics, GVHD incidence, viral reactivation, relapse, transplant-related mortality (TRM), and long-term survival outcomes were compared across the three donor platforms.

Results: Among 133 elderly patients (≥60 years) undergoing first allo-HSCT, 99 received haploidentical, 16 URD, and 18 MSD grafts. Median age differed slightly across groups (haplo 63, URD 62, MSD 61 years, P = 0.010). Diagnosis distribution was similar (AML 60.9%, MDS 25.6%, ALL 7.5%,CMML 6%), and most patients were transplanted in CR1 (57.9%) or ≥CR2 (9.8%), with comparable pre-HSCT MFC-MRD positivity (~22%). Conditioning was predominantly BU-based (92.5%), and ATG use varied significantly by donor type (100% haplo and URD vs. 44.4% MSD, P < 0.001). Haplo-HSCT grafts were largely BM+PB (98%), URD grafts were 100% PB, and MSD BM+PB (66.7%) and PB (33%, P < 0.001). Haplo recipients received higher MNC doses (median 9.10 $\times 10^8$/kg) compared with URD (5.97 $\times 10^8$/kg) and MSD (7.20 $\times 10^8$/kg, P < 0.001), while $CD34^+$ and $CD3^+$ cell doses were similar. Median neutrophil (15–16 days) and platelet (13–15 days) engraftment times were comparable across groups.
Detailed prognostic results for different types of transplants see Table 1. With a median follow-up of 20.8 months across all transplant types, URD group demonstrated the best OS outcomes of 68.75%. This was followed by MSD (OS 55%;), while haplo transplants the lower rates (OS 46.96%). The 3-year CIR was not significantly different among the MSD, haplo, and URD groups. NRM was highest in the haplo group (44.20%). The incidences of Day 100 grade 2-4 and grade 3-4 aGVHD were 30.08% and 15.79%, respectively. The cumulative incidence of cGVHD was 11.71%. In the 90 CR patients, the MSD group had the highest 3-year OS(72.73%). The URD group showed intermediate outcomes(66.67%), and the haplo group had the lowest survival(53.90%). NRM was lowest in the MSD group and highest in the URD group for this cohort, while CIR remained low across all groups. Among the 43 NR patients, the URD group exhibited superior 2-year OS compared to the haplo and MSD groups. The CIR was 0% in the URD group, while the haplo group had the highest CIR. NRM was highest in the MSD group for NR patients.

Table 1. Detailed Prognostic Results for Different Types of Transplants

Characteristic	all pts(n=133)	MSD (n = 18)	Haplo (n = 99)	URD (n = 16)	p-value

Day 100 grade2-4 aGVHD	30.08%(95%CI,23.21-38.97)	38.89%(95%CI,21.79-69.40)	32.32%(95%CI,24.31-42.98)	12.50%(95%CI,3.42-45.70)	0.178
Day 100 grade3-4 aGVHD	15.79%(95%CI,10.66-23.38)	16.67%(95%CI,5.93-46.82)	18.18%(95%CI,11.97-27.61)	0%(95%CI,0-0)	0.148
Cumulative incidence of cGVHD	11.71%(95%CI,7.27-18.85)	16.67%(95%CI,5.93-46.82)	12.64%(95%CI,7.44-21.46)	0%(95%CI,0-0)	0.245
Day 180 CMV reactivation	38.35%(95%CI,30.91-47.57)	22.22%(95%CI,9.36-52.74)	44.44%(95%CI,35.66-55.39)	25%(95%CI,10.7-58.41)	0.076
Day 180 EBV reactivation	19.55%(95%CI,13.85-27.60)	16.67%(95%CI,5.93-46.82)	18.18%(95%CI,11.97-27.61)	31.25%(95%CI,15.11-64.64)	0.468
3-year-CIR	11.67%(95%CI,7.24-18.82)	11.62%(95%CI,3.15-42.84)	13.60%(95%CI,8.19-55.29)	0%(95%CI,0-0)	0.307
3-year-NRM	42.32%(95%CI,34.44-52.01)	33.89%(95%CI,17.64-65.12)	44.20%(95%CI,35.13-55.61)	39.84%(95%CI,21.08-75.30)	0.669
3-year-LFS	50.10%(95%CI,41.45-58.75)	54.55%(95%CI,31.13-77.96)	46.26%(95%CI,36.23-56.29)	68.75%(95%CI,46.04-91.46)	0.37
3-year-OS	50.66%(95%CI,41.98-59.34)	55%(95%CI,31.76-78.24)	46.96%(95%CI,36.88-57.05)	68.75%(95%CI,46.04-91.46)	0.413
Characteristic	CR pts(n=90)	MSD (n = 11)	Haplo (n = 70)	URD (n = 9)	p-value
3-year-CIR	11.67%(95%CI,7.24-18.82)	10.23%(95%CI,1.6-65.33)	8.81%(95%CI,4.10-18.94)	0%(95%CI,0-0)	0.646
3-year-NRM	40.30%(95%CI,30.88-52.58)	18.18%(95%CI,5.19-63.69)	42.30%(95%CI,31.74-56.38)	46.67%(95%CI,22.54-96.62)	0.351
3-year-LFS	56.45%(95%CI,45.98-66.93)	71.59%(95%CI,44.22-98.96)	52.83%(95%CI,40.85-64.81)	66.67%(95%CI,35.87-97.46)	0.436
3-year-OS	57.33%(95%CI,46.83-67.82)	72.73%(95%CI,46.41-99.05)	53.90%(95%CI,41.86-65.93)	66.67%(95%CI,35.87-97.46)	0.487

Characteristic	NR/PR pts(n=43)	MSD (n = 7)	Haplo (n = 29)	URD (n = 7)	p-value
2-year-CIR	16.28%(95%CI,8.27-32.06)	14.29%(95%CI,2.33-87.69)	20.69%(95%CI,10.15-42.19)	0%(95%CI,0-0)	0.362
2-year-NRM	44.19%(95%CI,31.58-61.83)	57.14%(95%CI,30.08-100)	44.83%(95%CI,29.94-67.13)	28.57%(95%CI,8.86-92.18)	0.551
2-year-LFS	39.53%(95%CI,24.92-54.15)	28.57%(95%CI,0-62.04)	34.48%(95%CI,17.18-51.78)	71.43%(95%CI,37.96-100)	0.195
2-year-OS	39.53%(95%CI,24.92-54.15)	28.57%(95%CI,0-62.04)	34.48%(95%CI,17.18-51.78)	71.43%(95%CI,37.96-100)	0.195

Conclusions: For CR patients, MSD transplantation remains the preferred choice due to its optimal survival and safety profile. For NR patients, URD transplantation demonstrates superior outcomes. Haploidentical transplantation is an effective alternative when a fully matched related or unrelated donor is unavailable.

Disclosure: Nothing to declare.

A272

ALEMTUZUMAB PROVIDES DURABLE DEPLETION OF CIRCULATING CAR-T CELLS IN A PATIENT WITH HYPOKINETIC MOVEMENT DISORDERS AFTER BCMA-TARGETING CAR-T CELL THERAPY

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Background: Movement and neurocognitive disorders (MNTs) are a rare but severe complication of BCMA-targeting CAR-T cell therapy (Cohen et al., Blood Cancer Journal (2022)). Thus far, "on-target/off-tumor" effects involving BCMA-expressing neurons and astrocytes in the basal ganglia have been discussed as the pathomechanism driving MNTs (Oekelen et al., Nature Medicine (2021)). Several studies have identified the massive expansion of CAR-T cells as a major risk factor in the development of MNTs. Therefore, effective treatment strategies to manage uncontrolled CAR-T cell expansion in these patients are urgently needed.

Methods: The patient, a 49-year-old male diagnosed with IgA lambda multiple myeloma in April 2024, received cilta-cel following three prior lines of therapy. Apart from cytokine release syndrome (CRS °II), which was successfully managed with tocilizumab and anakinra, the patient experienced no other adverse events in the first days following cilta-cel infusion. Nineteen days after CAR-T cell infusion, the patient presented with cranial nerve palsies and

a hypokinetic movement disorder displaying features of parkinsonism. Symptom onset was preceded by a massive expansion of circulating CAR-T cells, despite prophylactic administration of glucocorticoids. Based on previous reports, treatment attempts were made with cyclophosphamide, venetoclax, and ruxolitinib, complemented by intrathecal triple therapy after detection of CAR-T cells in the cerebrospinal fluid (CSF). Circulating CAR-T cells were characterized by multicolor flow cytometry at various time points throughout CAR-T expansion and disease progression. From day 26 onwards, the patient was treated with alemtuzumab intravenously and intrathecally following the identification of strong CD52 expression on both circulating and CSF CAR-T cells.

Results: CAR-T cell expansion in the peripheral blood peaked within the second week after cilta-cel infusion, reaching 40.000 CAR-T cells/µl. However, peak infiltration of the CSF occurred significantly later, on day 39 at a concentration of 157 CAR-T cells/µl, despite multiple cycles of intrathecal chemotherapy with dexamethasone, methotrexate and cytarabine. Longitudinal flow cytometric analysis revealed a dominance of $CD4^+$ CAR-T cells (CD4/CD8 ratio ~ 12) without evidence of clonal T-cell expansion as assessed by TRBC1 staining. Panel-sequencing of peripheral blood cells did not identify any mutations associated with clonal hematopoiesis. Strikingly, CAR-T cell expansion persisted despite multimodal chemotherapy. Flow cytometric analysis of potential immunotherapy targets revealed low expression of CD194 (mogalizumab) and CD30 (brentuximab vedotin) on circulating CAR-T cells, while strong expression of CD52 (alemtuzumab) was observed. Shortly after administration of alemtuzumab, a significant decline in CAR-T cells in the peripheral blood could be observed. Durable repression of CAR-T cells was achieved after four treatment cycles.

Conclusions: Non-ICANS neurotoxicities (NINTs), including MNTs are associated with uncontrolled expansion of CAR-T cells in the peripheral blood and CSF. In our case study, alemtuzumab successfully suppressed CAR-T cells in the peripheral blood and CSF after failure of systemic and intrathecal chemotherapy. Therefore, administration of alemtuzumab could be an effective rescue therapy for patients at risk of NINTs due to uncontrolled expansion of BCMA-targeting CAR T cells following cilta-cel therapy.

Disclosure: Nothing to declare.

P008

IMPACT OF ATG DOSE ON OUTCOMES FOLLOWING MATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE COMPARISON OF 5 MG/KG VERSUS 10 MG/KG

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Background: Anti-thymocyte globulin (ATG) is commonly used for graft-versus-host disease (GVHD) prophylaxis in matched unrelated donor (MUD) allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, the optimal ATG dose remains controversial,

particularly regarding the balance between infection risk, GVHD prevention, and relapse control.

Methods: We retrospectively analyzed patients who underwent MUD allo-HSCT at Ajou University Hospital between 2014 and 2024, receiving a total of either 5 mg/kg or 10 mg/kg of rabbit anti-thymocyte globulin (ATG). Key clinical outcomes included 2-year overall survival (OS), relapse, acute and chronic GVHD, cytomegalovirus (CMV) reactivation, and infection events. Fisher's exact test was used to compare the incidence of these events between groups, while overall survival was analyzed using the Kaplan–Meier method.

Results: A total of 59 patients were included (5 mg group: n = 33; 10 mg group: n = 26). The most common underlying disease was acute myeloid leukemia (AML, 35.6%), followed by acute lymphoblastic leukemia (ALL, 22.0%) and myelodysplastic syndrome (MDS, 18.6%). The most frequently used GVHD prophylaxis regimen was cyclosporine combined with methotrexate (MTX), administered in 47 patients (79.7%). The incidence of relapse was comparable between groups (30.3% vs. 30.8%, p = 1.00). Acute GVHD occurred in 21.2% of the 5 mg group and 26.9% of the 10 mg group (p = 0.76), while chronic GVHD developed in 24.2% and 30.8%, respectively (p = 0.77). At 2 years after transplantation, the estimated overall survival was 62.6% in the 10 mg ATG group and 53.8% in the 5 mg ATG group (p = 0.41), with no statistically significant difference between the two groups. Notably, CMV reactivation was significantly more frequent in the 10 mg group (61.5% vs. 27.3%, p = 0.016). The incidence of infection events was slightly higher in the 10 mg group (73.1% vs. 66.7%, p = 0.78), though not statistically significant.

Conclusions: Although not statistically significant, the overall incidence of infection events tended to be lower in the 5 mg group compared with the 10 mg group. The 2-year overall survival did not differ significantly between the two groups. Our findings suggest that a total ATG dose of 5 mg/kg may reduce the risk of CMV reactivation without increasing the incidence of GVHD. These results support the potential feasibility of dose-reduced ATG in MUD transplantation settings, and prospective validation is warranted.
This abstract was previously presented at the 2025 ICBMT meeting. The current version includes updated 2-year overall survival data with extended follow-up.

Disclosure: Nothing to declare

P009

BONE MARROW TRANSPLANTATION IN TELOMERE BIOLOGY DISORDERS, THE EXPERIENCE OF PEDIATRIC BONE MARROW TRANSPLANT UNIT OF BRESCIA

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Background: Telomere Biology Disorders (TBD) are a group of a rare hereditary diseases with the classic Dyskeratosis Congenita (DC) occurring predominantly in males and manifests clinically as the classic triad of reticulate hyperpigmentation, nail dystrophy and leukoplakia. These conditions are characterized by a predisposition to develop hematologic and non-hematologic malignancies, according to increased susceptibility of this subjects to chemo-radiation agents. Hematopoietic cell transplantation (HCT) represents the only possible cure for the hematologic features, though the risk of graft failure and toxicities are higher in this group of patients.

Methods: We report three recents cases of children affected by TBD. Patient A is a 5-years-old boy, affected with Revesz syndrome, treated with haploidentical HCT (TINF2 gene defect). Patient B is a 12-years-old girl (TERT gene defect), patient C is a 5-years-old girl (RTEL1 gene defect).

Results: Patient A presented bilinear pancytopenia and was candidated for allogenic hematopoietic stem cell transplantation and the father was selected as donor. Unfortunately during the work-up phase anti-HLA class I antibodies were detected (DSA HLA B27 1961 MFI, NDSA 1227-3336 MFI), for this reason he performed three plasma exchange sessions, infusion of Rituximab 375 mg/m2 and an infusion of high-dose IgEV. Conditioning therapy was: Alemtuzumab, Fludarabine Cyclophosphamide, TBI 200 cGy. Depleted TcR alpha/beta/CD19+ CD34+ 12.59 x10^6/kg, 0,612 x10^5/kg TcR alfabeta+. Unfortunately the patient developed a primary graft failure and second transplant was needed urgently. Second haploidentical transplant from a sibling donor with bone marrow stem cell collection was soon organized. During aplasia, the patient presented appendicitis, initially treated with broad-spectrum antibiotic therapy. Laparoscopic appendectomy was necessary on D-8. Antibiotic therapy was continued throughout the period, even during second conditioning started at D-5: ATG, fludarabine, TBI monofraction 200 cGy, Cyclophosphamide. Bone marrow stem cells were infused, 11.04 x10^6/kg. From D+10 patient showed an increased in white blood cells with clinical improvement and reduction of inflammation indices.
Patient B presented trilinear pancytopenia and bone marrow transplant was planned with the brother selected as donor. Conditioning regiment was: ATG, Fludarabine, Cyclophosphamide, TBI 200 cGy, Rituximab, GvHD prophylaxis with Tacrolimus and MMF. HPC-A: CD34+ 6,66 x 10^6/kg, CD3+ 30,52 x 10^6/kg. Platelet engraftment D+18, Neutrophil engraftment D+13.
Patient C presented a history of recurrent infections, trilinear cytopenia, hypogammaglobulinemia. Haploidentical transplant was performed using PBSC from his father (WBC 1.73x10^8cell/kg, CD34+ 14.19x10^6cell/kg, CD3+ 42.01 x 10^6 cell/kg). Unfortunately the patient developed a primary graft failure and second transplant was planned urgently using MUD donor 10/10, conditioning regimen: Alemtuzumab, Fludarabine, Cyclophosphamide, TBI200cGy, Rituximab 200 mg, GvHD with Tacrolimus. Platelet engraftment take D+14, neutrophil engraftment D+18.

Conclusions: Patients with TBD may benefit from allogenic HCT, though with higher risk of graft failure and toxicity. Multidisciplinary considerations must be taken into account to decide the best transplant strategy for this patients.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare.

P010

OUTCOME OF SECOND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HEMATOLOGIC MALIGNANCIES

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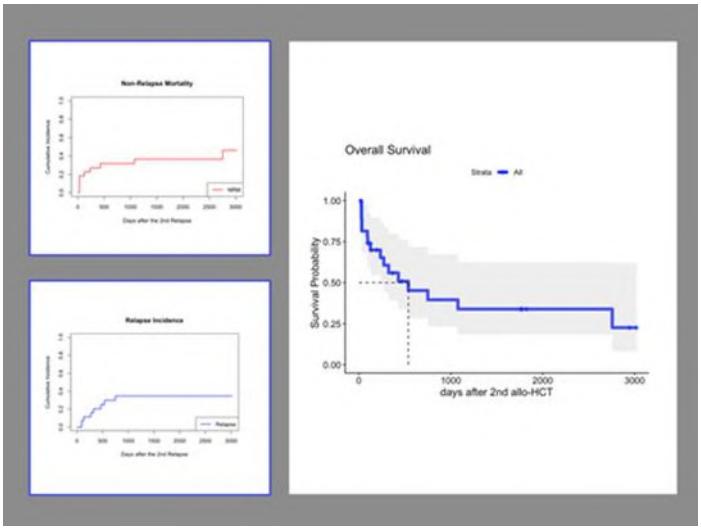
Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only potentially curative approach for various hematologic malignancies, largely due to its graft-versus-leukemia effect. However, relapse after allo-HSCT continues to be the leading cause of treatment failure and is associated with extremely poor prognosis. Therapeutic options for post-transplant relapse include salvage chemotherapy, targeted agents, immunotherapy, donor lymphocyte infusions, and in carefully selected patients, a second allo-HSCT. Evidence on outcomes of second allo-HSCT remains limited. This study aimed to evaluate real-world outcomes of adult patients undergoing a second allo-HSCT in two transplant centers in Greece.

Methods: We conducted a retrospective analysis of consecutive patients with hematologic malignancies who underwent a second allo-HSCT for relapsed hematological malignancies, between October 2006 and June 2025 in two bone marrow transplantation centers in Greece. Demographic, clinical, disease-related, and transplant-related characteristics were extracted from institutional databases. Statistical analyses were performed with R software (R Development Core Team, Vienna, Austria) packages. Competing risk was taken into consideration when estimating the cumulative incidence rates of Graft vs Host Disease (GvHD), NRM and relapse rate.

Results: Twenty-seven patients were included (15 women, 12 men), with a median age of 38 years (range 20–66). Underlying diagnoses were acute myeloid leukemia (AML, n=14), acute lymphoblastic leukemia (ALL, n=8), myelodysplastic syndrome (MDS, n=4), and Hodgkin lymphoma (HL, n=1). The median time to relapse after the first allo-HSCT was 373 days (range 27–1215), and the median interval between the two transplants was 647 days (35–2583). At the time of the second allo-HSCT, 20 patients were in complete remission, 4 in partial remission, and 3 had refractory disease.
Donor type differed between the two procedures in all but one patient (26/27). For the second transplant, 3 patients received grafts from matched related donors, 19 from unrelated donors (11 WMUD, 8 MMUD), and 5 from haploidentical donors. Peripheral blood

stem cells were used in 24 cases, and bone marrow in 3. Engraftment was achieved in all but two patients who died early from transplant-related complications (on days +27 and +32). Median neutrophil recovery (WBC ≥1000/mm³) occurred on day 14 and median platelet engraftment (PLT≥20,000/mm³) on day 14.5.
The cumulative incidence of acute GvHD grades II-IV and III-IV at 100 days post 2nd allo-HSCT were 31% and 9%, respectively. The cumulative incidence of overall and severe chronic GvHD were 12.4% and 3.9%, respectively. OS at 12 and 24 months was 60.63% and 49%, respectively. Cumulative relapse incidence at 12 and 24 months was 26.73% and 37.51%, with median time to relapse of 199.5 days (160–448). NRM reached 22.59% at 12 months and 26.94% at 24 months.



Patients Characteristics			
Number of patients	27	Time to relapse (range)	373 (27-1215)
Median Age (range)	38 (20-66)	Time to 2nd allo (range)	647 (35-2583)
Sex – M/F	12/15		
Disease AML MDS HL B-ALL	 14 4 1 8	Donor Sibling WMUD MMUD Haplo	 3 11 8 5
Disease Stage before allo-HCT Refractory Disease Partial Response Complete Response	 3 4 20	Engraftment WBC≥1000/mmc, day (range) PLT≥ 20.000/mmc, day (range)	 +14 (8-20) +14.5 (8-134)

Conclusions: This real-world study demonstrates that a second allo-HSCT can offer meaningful long-term survival for selected patients with relapsed hematologic malignancies,

particularly those achieving remission before. Despite notable risks, including significant transplant-related mortality, outcomes compare favorably with other salvage strategies. These findings highlight the importance of careful patient selection, optimal timing of transplant, and tailored donor choice to maximize benefit while minimizing toxicity.

Disclosure: No conflict of interest to declare

P011

THE USEFULNESS OF CULTURING APHERESIS PRODUCTS IN HEMATOPOIETIC STEM CELL AUTOTRANSPLANTS

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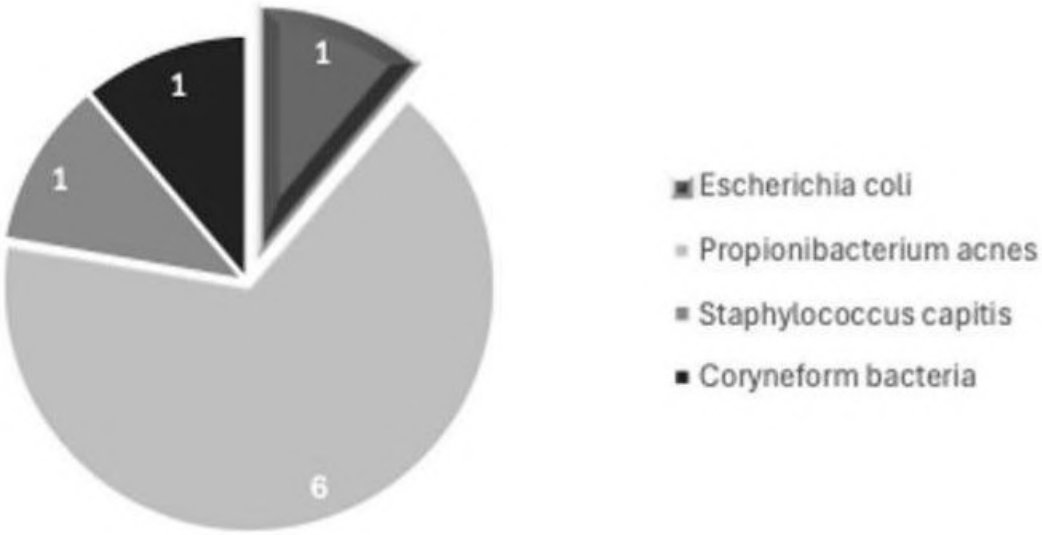
Background: Bacterial cultures of apheresis products are mandated by FACT– JACIE standards as a safety measure in autologous hematopoietic stem cell transplantation (aHSCT), yet their clinical utility remains uncertain when fresh, noncryopreserved grafts are used.

Methods: We prospectively analyzed 629 apheresis products administered to 586 patients with multiple sclerosis or chronic inflammatory demyelinating polyneuropathy who underwent outpatient aHSCT between July 2021 and March 2025. Cultures were performed using the BACTEC system, and positive isolates underwent antimicrobial susceptibility testing.

Results: Bacterial contamination was identified in 8 products (1.3%). One culture yielded Escherichia coli within 24 hours, corresponding to a urinary tract infection and fatal sepsis in the donor; this product was discarded. The remaining seven cultures became positive 2–11 days after infusion and grew Cutibacterium acnes, Staphylococcus capitis, or Coryneform bacteria, all consistent with handling contaminants. None of the corresponding patients developed infectious complications within 28 days of follow-up.



Conclusions: Routine bacterial cultures provided clinically relevant information in only 1 of 629 cases, while most positive results represented contamination rather than true infection. Thus, the diagnostic yield of routine bacterial cultures in fresh, non-cryopreserved aHSCT grafts for autoimmune diseases is low, and their necessity should be reconsidered.

Disclosure: Nothing to declare.

P012

OUTCOME OF AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANT IN RELAPSE/REFRACTORY DIFFUSE LARGE B CELL LYMPHOMA: A MULTI-CENTRE RETROSPECTIVE COHORT STUDY

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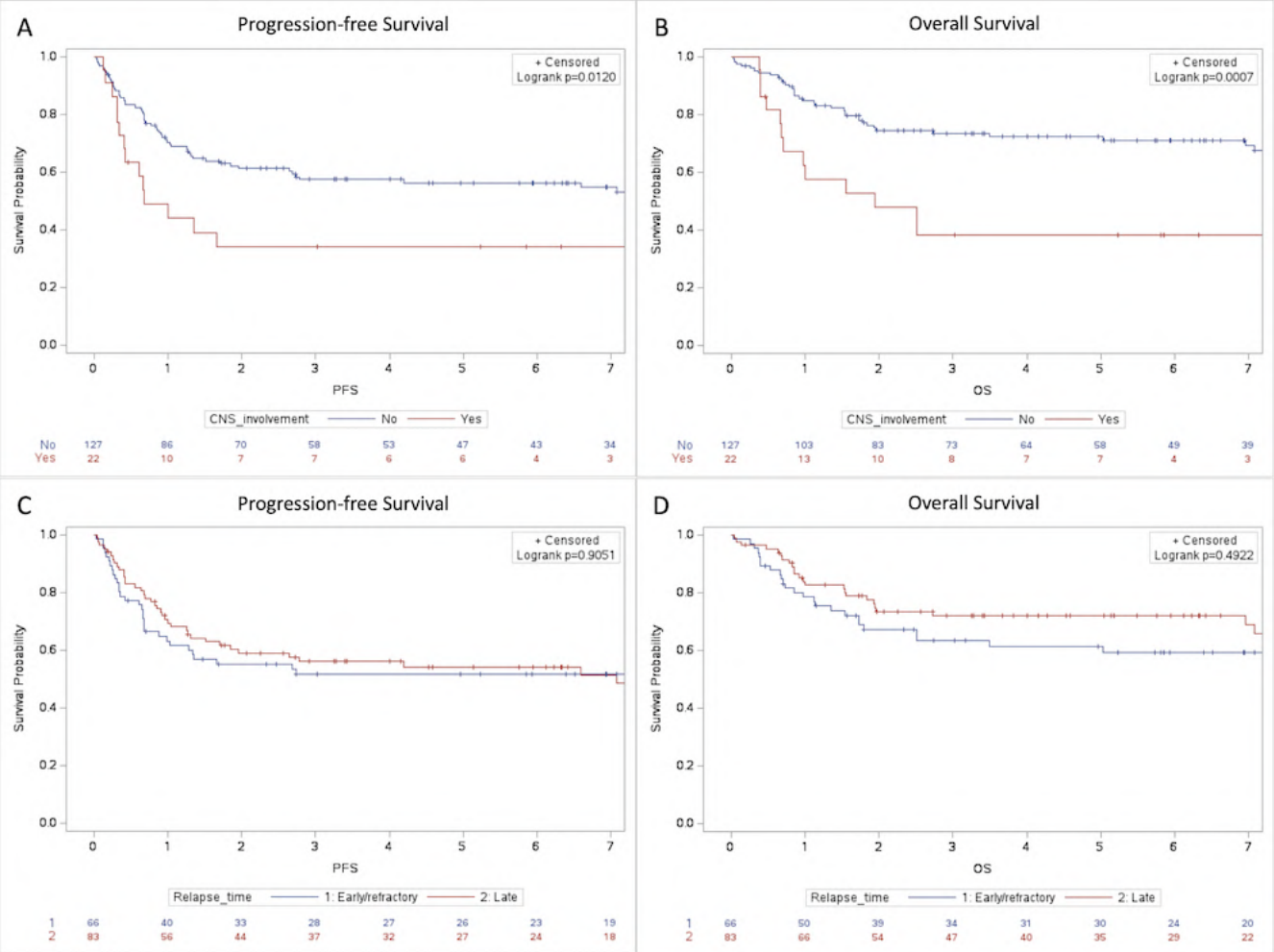
Background: Emerging novel treatments offer increasing therapeutic options for relapse/refractory diffuse large B cell lymphoma (R/R DLBCL). Despite this, intensive immunochemotherapy followed by autologous haematopoietic stem cell transplant (ASCT) consolidation remains an important treatment modality. This study examined the outcome of ASCT in R/R DLBCL and evaluated factors associated with the outcome.

Methods: R/R DLBCL cases that underwent second line immunochemotherapy followed by ASCT consolidation at Haematology Department, Singapore General Hospital and Division of Haematology, National University Hospital Singapore, between 2010 to 2024 were included. Demographics, disease characteristics and survival data were collected. Survival analyses were performed using Kaplan-Meier and Cox regression models.

Results:



149 R/R DLBCL cases were identified. Median follow up was 5.7 years (0.2 - 13.1 years). Average age was 53.6 years old at time of ASCT and 58.4% were male.
44.3% cases were early relapse (relapsed less than 1 year from end of first line treatment) or primary refractory, while the rest were late relapse. 14.8% (22 cases) of the cohort had central nervous system (CNS) involvement at relapse. Prior to ASCT, complete response was achieved in 73.4% of the cohort, partial response was achieved in 25.2%, and 2 cases (1.4%) were stable disease/progressive disease.
The overall 5-year progression-free survival (PFS) and overall survival (OS) post-ASCT were 53.1% [95%CI: 44.5 - 60.9] and 67.3% [95%CI: 58.8 - 74.4] respectively. 5-year non-

relapse mortality rate was 5.5% [95%CI: 2.6 – 10.1].
Between cases with and without CNS involvement, there was no significant difference in age, gender, relapse time, or pre-ASCT disease status, except in conditioning regimens (CNS involved group had more thiotepa-containing regimens: 81.8% vs. 4.7%, p<0.001). Compared with CNS non-involved group, CNS involved group had significantly inferior PFS (5-year PFS 34.2% vs. 56.3%, p = 0.01) and OS (5-year OS 38.6% vs. 72.5%, p < 0.001). The inferior PFS and OS of CNS involved group remained significant after adjusting for age, pre-ASCT disease status, and relapse time (PFS: HR 2.11 [95%CI 1.16 – 3.83], p = 0.01; OS: HR 2.74 [95%CI 1.44 – 5.21], p < 0.01). Between early relapse/primary refractory group and late relapse group, there was no significant difference in term of PFS and OS.

Conclusions: For R/R DLBCL that are chemo-sensitive, ASCT provides meaningful survival outcomes in both early relapse/primary refractory and late relapse cases. CNS involvement at relapse is associated with inferior survival post ASCT. Alternative salvaging treatments should be considered for this group.

Disclosure: Nothing to declare

P013

IMPACT OF CYCLOSPORINE A BLOOD LEVELS EARLY AFTER ALLOGENEIC STEM CELL TRANSPLANTATION FOR MYELOFIBROSIS ON OUTCOME

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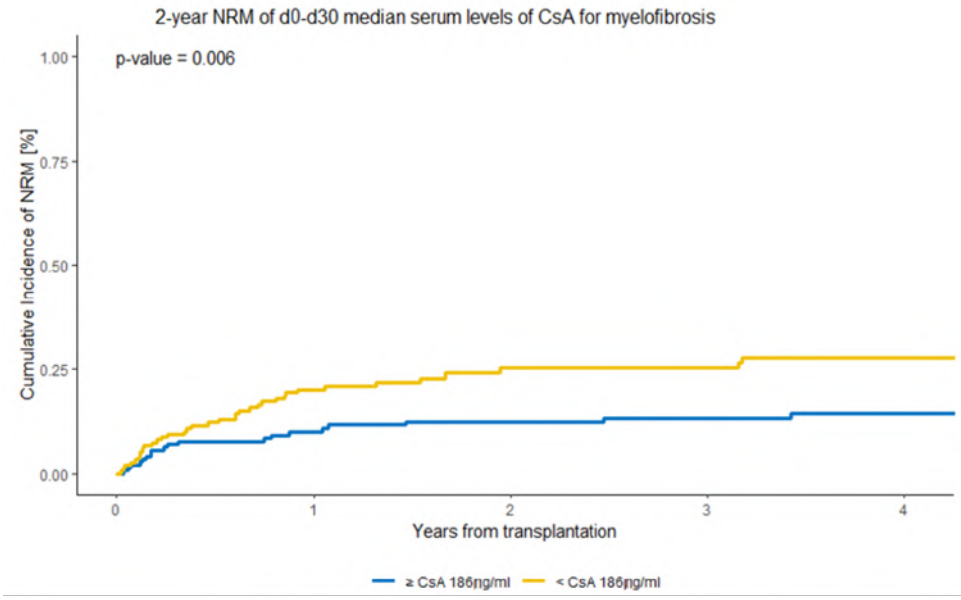
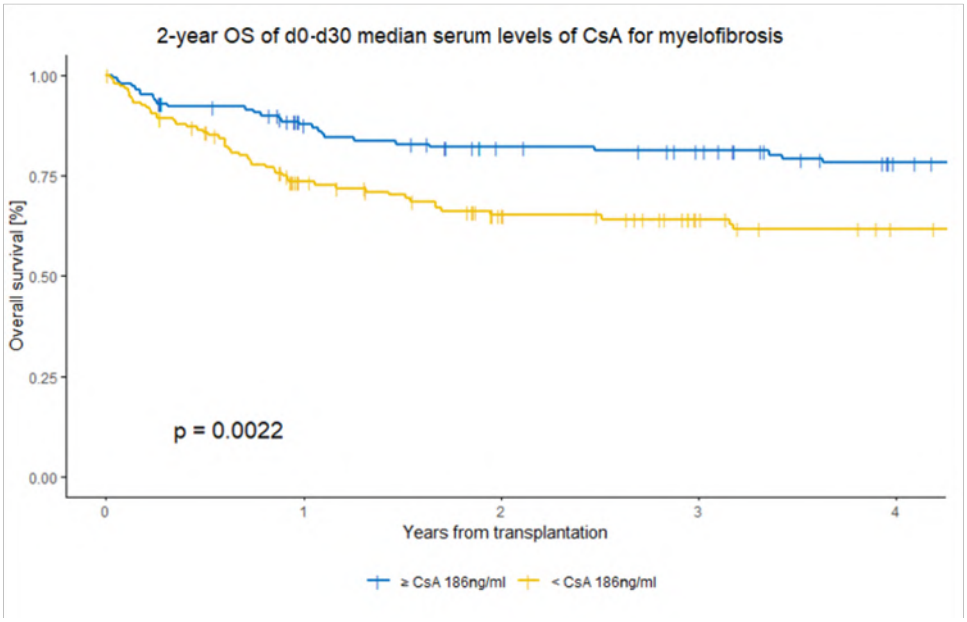
Background: In patients with myelofibrosis who undergo allogeneic stem cell transplantation (allo-HCT), the optimal level of post-transplant immunosuppression requires balancing between preventing graft-versus-host disease (GvHD) on the one hand and allowing graft-versus-malignancy effects as well as reducing drug toxicity on the other. The early days after transplantation may play a particularly decisive role in the development of GvHD. Therefore, we aimed to evaluate the association between early post-transplant Cyclosporine A (CSA) exposure and clinical outcomes following allo-HCT.

Methods: In this retrospective single-center study, we included patients with myelofibrosis who underwent allo-HCT between 2013 and 2025 at our clinic. Relevant patient characteristics, transplant-related variables, and CSA blood trough levels from day 0 to day 30 post-HCT were collected and median CSA blood level calculated. Patients were stratified into two groups above vs. below median level and compared regarding the cumulative incidence of non-relapse mortality (NRM), overall survival (OS), relapse and acute GvHD.

Results: The analysis included a total of 293 patients. The cumulative incidence of NRM at 2 years was significantly lower in patients above (12.4%) vs. below (25.2%) the median (p = 0.006; Figure 1). Consistently, overall survival at 2 years was higher in patients with CSA levels above the median (82.1%) compared with those below the median (65.2%; p = 0.002; Figure 1). The cumulative incidence for relapse was 11.2% and 15.5% for patients above and below the median, respectively (p = 0.77). Acute GvHD (grade 2 and higher) and severe acute GvHD (grade 3 and higher) on day 100 occurred more frequently in patients below (>°II: 39.4%, >°III 15.8%) vs. above (>°II: 25.9%, >°III 12.7%) the median (>II° p: 0.018; >III° p: 0.214). In univariate analysis, CSA levels below the median were associated with higher NRM (HR: 1.97, 95% CI 1.2-3.2, p = 0.008). Other factors significantly associated with NRM, were: Total body irradiation (TBI), Donor-type (matched related vs. other), recipient CMV serostatus, recipient age, and ECOG performance status. In multivariate analysis (n=133), CSA exposure above the median was not an independent predictor of NRM (HR 1.56, 95% CI 0.7-3.7, p = 0.32). Independent predictors of NRM were a high-risk MTSS score (HR 13.28, p = 0.027) and TBI (HR <0.001, p <0.001).





Conclusions: In this exploratory analysis, lower CSA exposure during the first 30 days after allo-HCT for myelofibrosis was associated with increased non-relapse mortality and inferior overall survival in the univariate analysis. These findings warrant further investigation in larger patient cohorts.

Disclosure: Neovii Biotech GmbH (D-82166 Gräfeling) has provided the following support:

- Reimbursement of travel expenses

- Coverage of congress registration fees
- Payment of accommodation during the congress
- Invitation to and coverage of a company-sponsored dinner held in the context of the meeting

P016

UTILITY OF IL-6, FERRITIN AND CRP LEVELS IN PREDICTING CAR T-CELL TOXICITIES IN PATIENTS TREATED WITH TISA-CEL FOR B CELL LYMPHOMA AND B-ALL

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Background: Chimeric antigen receptor T cell (CAR-T) is a major breakthrough treatment for B cell malignancies. However, it is frequently associated with life threatening toxicities such as cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS). Identifying proinflammatory markers that can predict at high-risk patients for sever toxicities is critical for patients monitoring and management.

Methods: A retrospective analysis was conducted on 45 patients who received tisagenlecleucel (Tisa-cel) (25 patients with B-cell lymphoma and 20 patients with B-cell acute lymphoblastic leukemia (B-ALL). Patient demographics and inflammatory biomarkers levels (IL-6, ferritin, and C-reactive protein (CRP)) were collected from pre-infusion Day −1 to Day +28 post-infusion. The incidence and grades of CRS and ICANS were collected. Peak concentration, area under the curve (AUC), and duration of biomarker elevation were assessed for each patient. Associations between biomarker features and toxicity severity were evaluated using Spearman correlation analysis.

Results: The median age was 48 years (IQR 36–60) and 22 years (IQR 18.5–26) for patients with lymphoma and B-ALL, respectively. CRS was observed in 88% of B-cell lymphoma patients (Grade 1: 56%, Grade 2: 20%, Grade 3: 4%, Grade 4: 8%) and in 95% of B-ALL patients (Grade 1: 70%, Grade 2: 25%, Grade ≥3: 0%). ICANS occurred in 24% of B-cell lymphoma patients (Grade 2: 4%, Grade 3: 20%) and in all B-ALL patients (Grade 1: 15%, Grade 2: 85%). IL-6 AUC showed a strong correlation with CRS severity in both B-cell lymphoma (Spearman ρ=0.67, P=0.00025) and B-ALL patients (Spearman ρ=−0.67, P=0.0011). IL-6 peak concentration was also significantly associated with CRS severity in both cohorts (B-cell lymphoma: Spearman ρ=0.57, P=0.0029; B-ALL: Spearman ρ=0.64, P=0.0023). In contrast, duration of IL-6 elevation demonstrated a significant association with

CRS severity in B-cell lymphoma patients (Spearman ρ=0.62, P=0.00093) but not in B-ALL patients (Spearman ρ=−0.35, P=0.13). Ferritin and CRP levels showed no significant association with CRS severity in either cohort. IL-6, ferritin, and CRP were not associated with ICANS occurrence or severity in B-cell lymphoma patients (P>0.2). However, in B-ALL patients, IL-6 AUC and IL-6 peak concentration were significantly associated with ICANS grade (P=0.018), while IL-6 elevation duration, ferritin, and CRP showed no significant associations.

Conclusions: IL-6, primarily AUC and peak concentration, is a reliable predictive marker for CAR-T toxicity severity and may be utilized for early identification of patients at risk for severe CAR-T toxicities, whereas ferritin and CRP provide limited utility. In B-ALL patients receiving Tisa-Cel, IL-6 AUC and peak concentrations also predict ICANS severity and may guide preemptive interventions. Further prospective studies are required to confirm these findings.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

P018

THE JOURNEY TO ALLOGENEIC STEM CELL TRANSPLANTATION OF PATIENTS TREATED WITH BCL2 INHIBITOR THERAPY IN MYELODYSPLASTIC SYNDROME AND ACUTE MYELOID LEUKEMIA IN MIDDLE INCOME COUNTRY

Gustavo Mesquita de Oliveira[1], Emanuelly Thays Muniz Figueiredo Silva Vasconcelos[1], Maria Laura Fontoura Chagas Rocha[1], Felipe de Menezes Cunha[1], Hercules Amorim Mota Segundo[1], ***Fernando Barroso Duarte***[1]
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Background: Acute myeloid leukemia (AML) and high-risk myelodysplastic syndromes (MDS) disproportionately affect elderly and frail patients, particularly in low- and middle-income countries, where access to intensive chemotherapy, transplantation, and novel agents remains limited. The introduction of BCL2 inhibitors, especially venetoclax, combined with hypomethylating agents or low-dose cytarabine (LDAC), has expanded treatment options for patients deemed unfit for intensive therapy. This study aimed to describe the clinical characteristics, treatment patterns, and outcomes of patients with AML and high-risk MDS treated with venetoclax-based regimens in a public university hospital in Northeastern Brazil, with emphasis on barriers to allogeneic hematopoietic stem cell transplantation (allo-HSCT) in an middle-income country setting.

Methods: Retrospective, descriptive study including patients aged ≥18 years diagnosed with AML and high-risk MDS treated with a BCL2 inhibitor combination between January 2020 and October 2025.

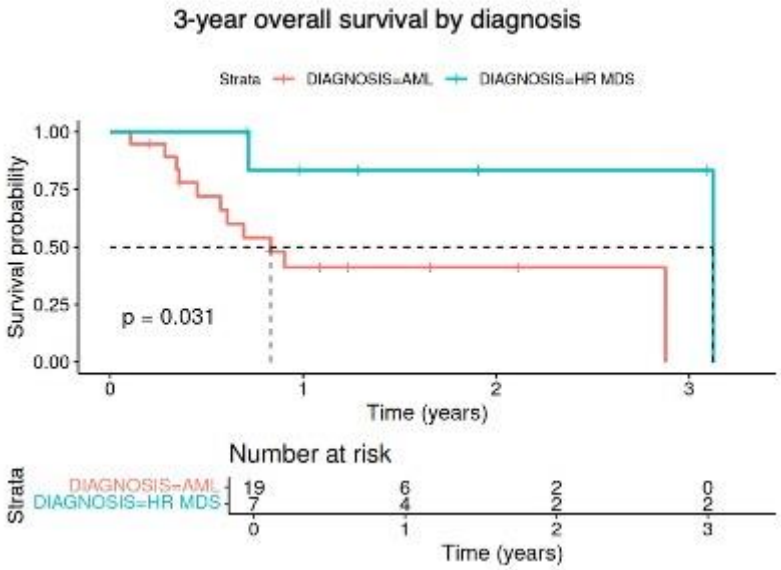
Results: Twenty-six patients were included (19 AML and 7 MDS), with a median age of 65 years (range: 37–81). Among AML cases, 57.9% were secondary, mostly evolving from prior MDS, reflecting delayed diagnosis and limited access to early disease-modifying therapies. Overall, 46.1% achieved complete remission and 3.8% partial remission, with a median time to best response of one treatment cycle. In AML, patients had a median overall survival of 304 days, whereas MDS patients had a median OS of 1141 days. Hematologic toxicity was universal, and febrile neutropenia occurred in 78.3% of patients. Despite many patients achieving remission, only three (11.5%) proceeded to allo-HSCT, all of them high-risk MDS patients. Major barriers to transplantation included advanced age, frailty, relapse and infectious complications.

Clinical and demographic characteristics

Characteristics	Cohort (N = 26)
Median age (range)	65 (37-81)
Female (%)	15 (57,6%)
AML (%) De novo Secondary	19 (73%) 8/19 (42,1%) 11/19 (57,9%)
Secondary AML (%) MDS CMML PV/PMF	 7/11 (63,6,%) 2/11 (18,2%) 2/11 (18,2%)
MDS (%) LB IB1 IB2	7 (27%) 2/7 (28,6%) 1/7 (14,3%) 4/7 (57,1%)
ECOG 0-1 2	 13/26 (50%) 13/26 (50%)
Risk stratification (AML) Favorable Intermediate Adverse	 1/19 (5,3%) 16/19 (84,2%) 2/19 (10,5%)
R-IPSS (MDS)	6 (5-10)
CBC at diagnosis Hemoglobin (g/dL)	7,01 (4,23-11,3) 1130 (50-40.960)

Clinical and demographic characteristics

Neutrophils (n/mm^3)	574 (0-300.675)
Blasts (n/mm^3)	35070 (14.330-383.000)
Platelets (n/mm^3)	



Conclusions: In this real-world middle-income country cohort, venetoclax-based regimens achieved response rates comparable to those reported in high-income countries. However, structural limitations, clinical frailty, treatment-related toxicities and relapse significantly restricted access to allo-HSCT, even among responding patients. These findings highlight the critical need to expand access to targeted therapies, optimize supportive care, and improve transplant referral pathways in public healthcare systems across low- and middle-income countries.

Disclosure: Nothing to declare.

P019

OUTCOME OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN INFANT LEUKEMIA: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Infant leukemia (IL) refers to leukemia diagnosed initially in patients under one year of age, with an extremely low incidence rate, and tends to present with aggressive clinical features and unique biology. The event-free survival of infants with leukemia is poor due to the vulnerability to complications and toxicity of the treatments and high relapse rate despite the use of intensive chemotherapy with or without hematopoietic stem cell transplantation. This study aims to evaluate the outcome and early complications of infants who underwent HSCT.

Methods: Infant leukemia (IL) refers to leukemia diagnosed initially in patients under one year of age, with an extremely low incidence rate, and tends to present with aggressive clinical features and unique biology. The event-free survival of infants with leukemia is poor due to the vulnerability to complications and toxicity of the treatments and high relapse rate despite the use of intensive chemotherapy with or without hematopoietic stem cell transplantation. This study aims to evaluate the outcome and early complications of infants who underwent HSCT.

Results: This study analyzed data from 32 infant leukemia who underwent HSCT. Patient and transplant characteristics are shown in Table 1. Nineteen males and thirteen females were enrolled, with a male-to-female ratio of 1.46:1. Median age at diagnosis was 8 (0, 12) months, and median age at transplantation was 15 (8, 49) months. There were 17(53%) infant acute lymphoblastic leukemia (IALL), 12(38%) infant acute myeloid leukemia (IAML), and 3(9%) infant mixed phenotype acute leukemia (IMPAL). MLL gene rearrangement occurs in 23 patients(72%). There were 23 CR1 patients(72%), 8 CR2 patients(25%), and 1 PR patient(3%). All of the 8 patients with CR2 achieved molecular remission in which 7 patients were treated with autologous CAR-T, including CD19 and CD19/CD22, and 1 patient was treated with Blinatumomab.All patients were treated with the MAC regimen, and with tacrolimus and low-dose MTX to prevent active GVHD. Donors included Cord Blood (n=19), Haploidentical (n=5), Matched Unrelated Donor (n=3), Matched Sibling Donor (n=3), and Mismatched Unrelated Donor (n=2). All patients achieved hematopoietic reconstitution. Median follow-up was 36 (2, 74) months. The overall survival (OS) during the follow-up period were 90.1%. The cumulative incidence relapse rate was 9.48%.The OS was 100% for MPAL group, 94% for ALL group, and 80% for AML group respectively(p=0.5%). The OS was 93% for patients with negative fusion genes prior to transplantation, compared to 0% for those with positive fusion genes ($p<0.001$).Three patients died due to relapse. Among them, one received second HSCT from father but relapse again after 3 month.The incidence rates of sepsis were 44%. Major complications included veno–occlusive disease (VOD) in 9% of patients which resolved by supportive measures and defibrotide.The incidence of grade II-IV acute GVHD was 31%, and the incidence of chronic GVHD was 15% respectively. 34% patients were diagnosed CMV viremia but only one patient suffered cytomegalovirus ophthalmia.

Conclusions: Infants with leukemia shows a low long-term survival. Hematopoietic stem cell transplantation is safe and effective in the treatment of infant leukemia. It is the most importance to make MRD negative before transplantation.

Disclosure: Nothing to declare.

P021

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN APLASTIC ANAEMIA: EXPERIENCE FROM A TERTIARY CARE REFERRAL HOSPITAL

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Background: Aplastic anemia (AA) is associated with high morbidity and mortality, contributing significantly to both disease and economic burden. This study aimed to assess the clinical characteristics, survival rates, and treatment costs of patients who underwent hematopoietic stem cell transplantation (HSCT) for AA to support future research.

Methods: This retrospective study was conducted on patients who underwent HSCT for AA at a tertiary care referral hospital in India from January 2020 to June 2025. This study included patient demographic details, human leukocyte antigen (HLA) matching status, conditioning regimens, graft-versus-host disease (GVHD) prophylaxis, stem cell source and dose, transplant-related complications (infections, GVHD, and graft rejection or relapse), and survival outcomes. Transplant types comprised of matched sibling donor (MSD), matched unrelated donor (MUD), and haploidentical transplants. The stem cell dose ranged between 2.5×10^6 and 8.6×10^6 cells/kg body weight.

Results: A total of 29 patients with acquired AA who underwent HSCT were included in the study. The majority of patients (79.3%) were 18-40 years of age. Most patients (69.0%) were male, and 31.0% were female. Most patients (72.4%) presented with severe AA, whereas 27.6% had very severe AA. Paroxysmal nocturnal hemoglobinuria (PNH) clone was absent in most patients (69.0%), whereas 31.0% demonstrated a positive PNH clone. Hematopoietic cell transplantation Comorbidity Index score 0 was observed in 93% of patients. A majority of patients (83.0%) underwent transplantation with MSD, followed by haploidentical donors (10.0%) and MUD (7.0%). Sex-matched transplants were performed in 68.0% of patients, while 32.0% received transplants from sex-mismatched donors. 90.0% of patients received HLA-matched transplants, while only 10.0% received transplants from HLA-mismatched donors. Peripheral blood stem cells accounted for 79.0% of the stem cell harvest, followed by bone marrow stem cells (21.0%). First-line treatment was initiated in a significant proportion of patients (96.6%), while only 3.4% received second-line treatment. A triple combination of fludarabine, cyclophosphamide, and antithymocyte globulin (ATG) was administered in 79.0% of patients, whereas 17.0% received cyclophosphamide and ATG, and 3.0% received fludarabine and cyclophosphamide. Engraftment occurred on days 9-11 for MSD transplants and on days 18-21 for haploidentical transplants. Pre and peri-engraftment infections were the most common cause of mortality (44.0%), followed by graft rejection (22.0%), transfusion-related acute lung injury (11.0%), GVHD (11.0%), and life-threatening internal bleeding (11.0%). At 3 months, patient survival was 86.2%, while 1-year survival was 76.0%. The highest cost of allogenic bone marrow transplantation (BMT) was approximately 24.0 lakhs rupees, while the lowest cost was 7.2 lakhs rupees, indicating a wide range of expense, and all the transplants were covered under government sponsored schemes.

Conclusions: Allogeneic HSCT offers a curative option for AA, especially in younger patients with MSDs, with an overall survival rate of 76 % at 1 year at our institution**.** However, infection-related complications remain a major challenge, requiring enhanced supportive care. Government-sponsored allogenic BMT schemes are a boon for patients from low socioeconomic backgrounds.

Disclosure: Nothing to declare.

P022

A RARE CASE OF AUTOSOMAL DOMINANT OSTEOPETROSIS WITH CONCOMITANT CMML 1 TREATED WITH ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Osteopetrosis is a rare hereditary bone disorder with genetic and clinical heterogeneity. While allogeneic haematopoietic stem cell transplantation (allo-HSCT) is an established curative treatment for the severe autosomal recessive infantile form (ARO). Its use in patients with benign autosomal dominant osteopetrosis is rarely reported, as it is generally not recommended due to the typically mild clinical course and the increased risk of transplantation related complications with advancing age. We present a rare case of a young adult patient with ADO and concomitant chronic myelomonocytic leukaemia (CMML-1), both represent conditions potentially amenable to allogeneic haematopoietic stem cell transplantation.

Methods: A 33-year-old woman with confirmed diagnosis of ADO presented with leukocytosis, macrocytic anaemia, elevated LDH, hepatosplenomegaly, extramedullary haematopoiesis and EBV reactivation. A comprehensive diagnostic evaluation to exclude lymphoma, incorporating PET/CT imaging, bone marrow biopsy, and lymph node histopathology, ultimately revealed an MDS/MPN overlap consistent with CMML-1. Molecular analysis identified pathogenic *ASXL1* and *RUNX1*mutations, as well as a heterozygous *CLCN7* variant in Exon 11 associated with osteopetrosis. Due to intermediate 2 risk (CPSS Mol Score), the patient was referred for allo-HSCT.
She received reduced-intensity conditioning with treosulfan, fludarabine, and ATG, followed by peripheral blood stem cells from a 10/10 HLA-matched, unrelated donor. GvHD prophylaxis consisted of MMF/tacrolimus. Engraftment occurred on days +14 (neutrophilic), and +19 (platelet), while erythropoiesis was not yet self-sustaining. No acute graft-versus-host disease (GVHD) was observed by day +25.

Results: The patient tolerated allo-HSCT without major complications and demonstrated timely engraftment with dose-reduced conditioning. A gradual decline in risk of bone fracture and splenomegaly is anticipated.

Conclusions: This case highlights the feasibility of allo-HSCT in a young adult patient with ADO — an exceedingly rare scenario with limited published experience. Longer follow-up will be essential to assess long-term engraftment stability, GvHD risk, and osteopetrosis-related outcomes.

Disclosure: Nothing to declare.

P023

HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANT FOR JUVENILE MYELOMONOCYTIC LEUKAEMIA

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Background: Allogenic haematopoietic stem cell transplantation (HSCT) remains the only curative option for most children with Juvenile Myelomonocytic Leukaemia (JMML). While a subset of JMML patients with mainly germline CBL mutations can be long-term survivors with minimal therapy, the majority progress within a year if untreated. Predictors of aggressive JMML include age more than 2 at presentation, high Haemoglobin F levels, refractory thrombocytopenia and non CBL somatic gene mutations. We share our experience in managing this rare paediatric haematological malignancy using pre-transplant strategies for the 'best" disease control followed by haploidentical stem cell transplant with the "best" available donor and then post-transplant decitabine as a pre-emptive strategy to prevent relapse.

Methods: We transplanted 6 JMML patients over the last 10 years, with all >2 years old at diagnosis except 1 patient who was 1 month of age. One patient had previously received a matched sibling cord blood transplant but relapsed. All patients received chemotherapy consisting of Azacitidine, Cytarabine and etoposide prior to stem cell transplant. All patients received a peripheral blood haploidentical stem cell transplant with either parent as the donor. 5 out of the 6 patients (all PTPN11) underwent a splenectomy prior to HSCT. Choice of parent was predominantly dependent on gender (father preferred), or the parent with better NK alloreactivity. None of the patients had GVHD prophylaxis as these were all ex-vivo T cell depleted grafts using CD3/CD45 RA T- cell depletion technique. Transplant conditioning was Fludarabine Thiotepa and melphalan based, without radiation. 4 out of the 6 patients received Decitabine pre-emptive therapy, with a minimum of 6 cycles given monthly.

Results: All 6 patients are alive and remain in remission with a median follow-up of 6.6 years (range 1 year to 10.2 years) post HSCT. One out of the 6 patients required a second transplant as he failed to engraft the first time and his course was complicated by disease relapse and sepsis (klebsiella, sternotrophomonas maltophilia, disseminated mycobacterium). Five of the other patients all engrafted by D20 post HSCT and no patient had more than grade 2 acute graft versus host disease (aGVHD). Only 1 patient had chronic GVHD.

Patient	Age at transplant (y)/ Gender (M/F)	Genetics	Bone marrow blast % (time of transplant)	Haplo PBSCT conditioning	Engraftment	Complications	aGVHD	cGVHD	Outcome
1	8.4y/ M	PTPN11	49%	FluCyTTMel	100% Donor D+9	Engraftment fever, Infections (Adenovirus)	Grade 2 (skin/liver/gut)	Extensive (oral, skin, joins)	Alive
2	1.2y/ M	NRAS	Not done	FluTreoTTMel	100% Donor D+9	Engraftment fever, Infections (CMV reactivation)	Grade 2 (gut)	Nil	Alive
3	5.1y/ M	PTPN11	10%	FluTreoTTMel	98% Donor D+20	Engraftment fever, Infections (C.difficile, Mycobacterium abscessus, fortuitum)	Nil	Nil	Alive
4a	6.8/M	PTPN11	1.3%	FluBuTTMel	86% Donor D+10, 2% Donor D+18	Rejection, Infections (Klebsiella, Stenotrophomonas)	NA	NA	Rejection/Relapse
4b	6.9y/ M	PTPN11	27.5%	FluTreoTTMel	98% D+11	Infections (CMV reactivation, BK hemorrhagic cystitis, Stenotrophomonas,	Nil	Nil	Alive

						disseminated mycobacterium)			
5	7.2y/F	PTPN11	0.01%	FluTreoTTMel	96% Donor D+24	Engraftment fever, Infections (Ecoli)	Nil	Nil	Alive
6	3.4y/F	PTPN11	0.014%	FluTreoTTMel	98% Donor D+9	Engraftment fever	Nil	Nil	Alive

Conclusions: High risk PTPN11 JMML is associated with high morbidity and mortality. In our 6 patients, 5 had PTPN11 mutations and 1 infant with NRAS. These patients with PTPN11 mutations also had abnormal cytogenetics, high blast percentage, HbF (>10%) at diagnosis and also severe thrombocytopenia. Although there is no robust clinical evidence in using azacytidine in combination with chemotherapy in JMML, however it is efficacious in cytoreduction and generally safe as a bridging therapy prior to HSCT. In summary, haploidentical HSCT has proven to be effective in the long-term treatment of our group of high risk JMML by providing a source of stem cells quickly and allowing rapid engraftment and immune recovery. Together with post-transplant Decitabine, we have achieved 100% overall survival in this high risk group of patients. Splenectomy before HSCT has not shown to reduce relapse and as it may increase infection risks, its use remains unclear.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

P024

OPTIMIZING PAEDIATRIC LYMPHAPHERESIS: KEY FACTORS FOR SAFE AND EFFECTIVE PROCEDURES

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Background: Current literature provides limited details on technical and procedural approach to paediatric lymphapheresis with the Spectra Optia system, highlighting the need

for harmonized practices. Our aim is to describe our experience and share practical insights to help other centres optimise paediatric lymphapheresis safely.

Methods: We performed a retrospective study at a single paediatric centre (2019–2025) using the Spectra Optia® machine (Terumo BCT) with the cMNC programme. We analysed patient demographic characteristics, peripheral blood values, and lymphapheresis-related parameters. Results are reported as median [minimum–maximum].

Results: We analysed 26 lymphapheresis performed in 25 subjects (10 months-17 years), of whom 23 had B-cell acute lymphoblastic leukaemia and 2 were healthy lymphocyte donors. Patients aged 8 years or younger accounted for 52% of the cohort. Other baseline characteristics are shown in Table 1.
Central venous catheters (CVCs) were employed in 23 lymphaperesis, whereas peripheral venous access was used in 3 adolescent subjects (aged ≥ 12 years). CVCs were located in the jugular vein (left n=12, right n=9, non-available n=2). French (Fr) size and weight of the subjects were: Fr 6.5, n=2, 7.3 kg [7.3–7.3]; Fr 8, n=11, 27.0 kg [15.0–37.0], Fr 11.5 (n=10, 47.5 kg [21–61]).
Regarding machine set up, blood priming was required for 13 processes (50%) and collection preference remained stable across 10 procedures, while it was modified during lymphapheresis in the remaining 61.5% of cases. Other technical aspects are described in Table 1.
Acid Citrate Dextrose solution A (ACD-A) was used in 7 procedures (26.92%), and ACD-A+heparin in 19 (73.08%). Prophylactic calcium was given in 21 runs (80.8%), 1 subject experienced tingling and received calcium post-procedure. Procedures using ACD-A alone resulted in higher citrate infusion volumes (625 [518–1178] mL) compared to ACD-A+heparin (291 [105–772] mL). Citrate volumes positively correlated with patient's weight ($p<0.001$, $r=0.63$).
Maximum flow rate (mL/min) varied by CVC Fr: 10.8 (Fr 6.5), 45 (Fr 8), and 65 (Fr 11.5); and correlated with patient weight ($p<0.001$, $r=0.72$). Minimum and maximum ACD-A infusion rates were 0.4 and 1.1, with ACD-A ratios ranging 1:14–1:10 (ACD-A alone) and 1:28–1:16 (ACD-A+heparin).
Subjects had a 22.96% [2.90–69.88] of peripheral blood CD3+ lymphocytes and 630 cells/µL [60–2350]. This peripheral blood CD3+ cell count correlated with product CD3+ cell yield ($p<0.001$, $r=0.73$). Collection efficiency for CD3+ was 70.04% [29.87–107.5]. Lymphapheresis product was 11.54-fold (1.15–29.61) more concentrated than peripheral blood. Yields are shown in Table 1. Lymphaperesis caused drops in platelets counts (-29.73% [-62.07 – 1.00), while haematocrit and haemoglobin changes were not relevant.
Target criteria for CAR T-cells (1-1.5x10^9 $CD3^+$ T-cells) were met in 22/23 patients, although CAR T-cells could be manufactured in all cases. No serious side-effects associated with the lymphapheresis process were observed.

Table. 1	Parameter	Values
Subject Characteristics (N=25)	**Age** (years)	8.0 [0.83–17.00]

	Sex - Female / Male n (%)	10 (40%) / 15 (60%)
	Weight (Kg)	33.0 [7.30-64.0]
	Diagnosis (B-ALL / Healthy donor)	23 / 2
	Subjects undergoing T-cell lymphapheresis (Once / Twice)	23 / 2[a]
Patients Receiving CAR T cells (N=23)	**CAR-T infused / non-infused** (n patients)	22 / 1[b]
	Exitus within the 1st year after infusion (yes / no)	5 / 17[c]
Lymphapheresis Process Parameters (N=26)	**Patient's total blood volume** (mL)	2342 [660.6–4404]
	Time of the process (min)	242 [112–403]
	Total blood volume processed	3.12 [1.46–6.00]
	AC in the patient (mL)	434 [105–1178]
	Collection volume (mL)	203 [105–370]
	Total AC in lymphapheresis product (%)	10.22 [4.67–17.06]

	Maximum flow rate (mL/min)	38 [10–65]
Lymphapheresis Collection Yields (N=26)	**Total Nucleated Cells** (x 10^9)	5.53 [0.36–101.00]
	Mononuclear Cells (x 10^9 / %)	4.77 [0.32–99.95] / 95.54 [38–100]
	Lymphocytes (x 10^9 / %)	3.99 [0.24-32.12] / 69.67 [4.00-98.62]
	CD3+ Lymphocytes (x 10^9 / %)	3.15 [0.22-8.75] / 53.99 [3.5-92.9]

[a]A patient underwent a failed lymphapheresis due to venous access issues (excluded from this analysis). Another patient underwent 2 consecutive successful lymphapheresis to obtain a single product.
[b]The CAR-T was not infused because disease relapsed.
[c]Three patients have not yet reached one year since lymphapheresis but are currently alive.

Conclusions: Paediatric lymphapheresis is safe and effective even in very young and low-weight patients. Weight is crucial for selecting venous access and setting up the procedure. Our study outlines relevant aspects that may help optimise practice and guide future research, offering practical parameters for other centres, although further studies are needed.

Disclosure: Nothing to declare

P026

CLINICAL CHARACTERISTICS AND OUTCOMES OF HODGKIN LYMPHOMA PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: A REAL-WORLD EXPERIENCE FROM A NATIONAL REFERRAL CENTER

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Background: High-dose chemotherapy followed by hematopoietic stem cell transplantation (HSCT) remains a cornerstone therapeutic strategy for patients with relapsed or refractory classical Hodgkin lymphoma (cHL). However, much of the evidence supporting transplant-based approaches originates from clinical trials conducted in highly selected populations, which limits their applicability to routine clinical practice. In Latin America, real-world data remain particularly scarce despite notable differences in epidemiology, access to healthcare, tumor burden at diagnosis, and availability of novel therapies. These factors highlight the need to generate context-specific evidence to better inform therapeutic decision-making in the region.

Methods: This was a retrospective, observational study including adult patients diagnosed with Hodgkin lymphoma who underwent HSCT between 2014 and 2024. Clinical, laboratory, and treatment-related variables were collected from institutional medical records. Outcomes of interest included overall survival (OS), progression-free survival (PFS), relapse, and transplant-related mortality. Survival curves were estimated using the Kaplan–Meier method. Statistical analysis was performed using SPSS version 2.2.

Results: A total of 73 patients were included, with a mean age at diagnosis of 27 years (range 18–62), and a predominance of males (60.3%). Most had good functional status (ECOG 0–1 in 93%) and low comorbidity burden (HCT-CI = 0 in 72.6%). At diagnosis, 69.9% presented with advanced-stage disease (Ann Arbor III–IV) and 79.5% had B symptoms. Extranodal involvement occurred in 49.3%, mainly in the mediastinum/lung and bone marrow. Nodular sclerosis was the predominant histological subtype (54.8%). The mean time from diagnosis to transplant was 30.3 months.
The most common frontline regimen was ABVD (79.5%); however, high rates of primary refractory disease (60.3%) and early relapse (<12 months) were observed (69.3%). Prior to transplant, 53.4% received brentuximab vedotin (BV) as bridging therapy, and 52.1% received BV as post-transplant consolidation, with an average of 10 total cycles.
Most patients underwent autologous transplantation (89.0%), with myeloablative conditioning in 91.8%. At day +100 post-transplant, 71.2% achieved complete metabolic response. During follow-up, 87.7% remained in complete remission. Five deaths (6.8%) were documented, mainly due to disease progression or leukemic transformation. With approximately 10 years of follow-up, the mean OS was 9.94 years (95% CI: 9.13–10.75), and the mean PFS was 9.18 years (95% CI: 8.33–10.03); the median was not reached for either outcome.

Conclusions:

Figure 1.

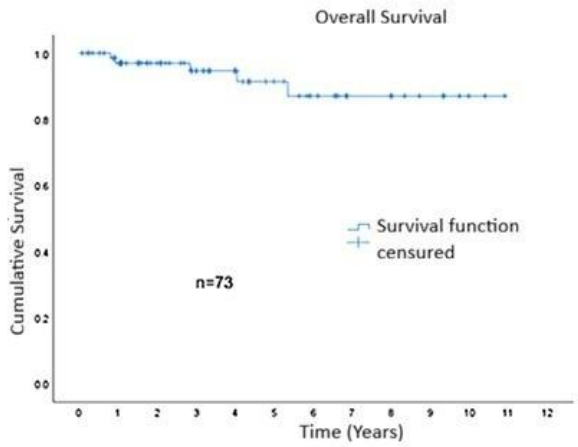
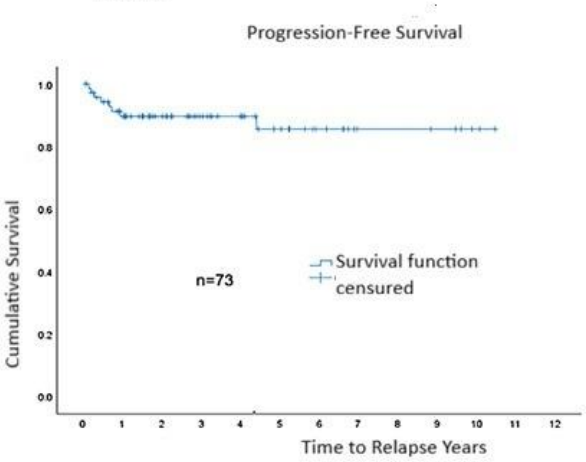


Figure 2.



Despite a high proportion of advanced-stage disease, extranodal involvement, and early refractoriness, patients with Hodgkin lymphoma undergoing HSCT in this real-world cohort achieved highly favorable post-transplant outcomes. The incorporation of brentuximab vedotin as both bridging and consolidation therapy, along with appropriate patient selection, resulted in survival outcomes comparable to—or even superior to—those reported in international series. These findings reinforce the role of HSCT as an effective therapeutic strategy and underscore the importance of generating real-world evidence in Latin America'.

Disclosure: Nothing to declare.

P028

CD19 CAR-T THERAPY OUTCOMES IN OLDER ADULTS: A SINGLE-CENTER REAL-WORLD EXPERIENCE FROM ASIA

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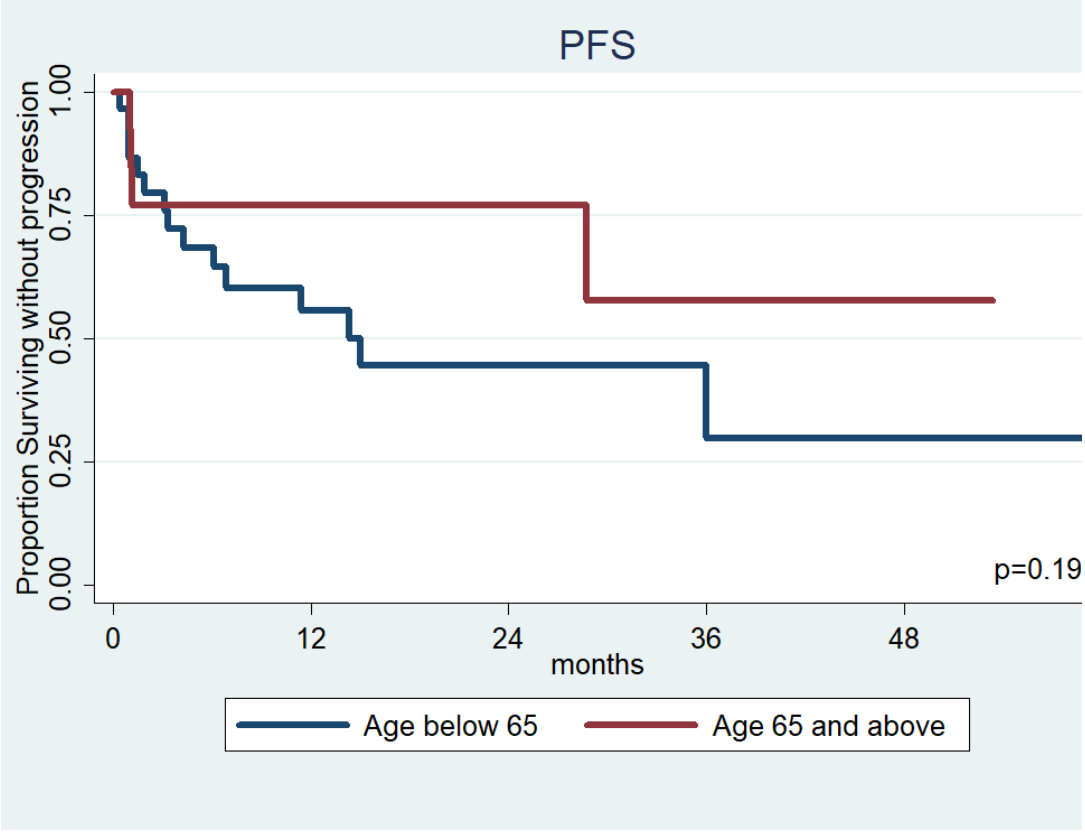
Background: CD19 CAR-T therapy shown promising results in patients with relapsed or refractory B-cell lymphoma, demonstrating durable responses and potential for cure. However, unique toxicities—including cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), and an increased risk of infection—may limit its use in older adults. Several studies have highlighted the importance of geriatric and comorbidity assessments when managing CAR-T therapy in this population. In this retrospective study, we compared the outcomes of CAR-T therapy in patients aged 65 and older with those of patients younger than 65.

Methods: We retrospectively analyse data of patients underwent CD19 CAR-T therapy for lymphoma from the Singapore General Hospital CAR-T registry (2020-2025). Demographic data and CAR-T outcome from medical records were collected. Chi-squared and Fisher's exact two-sided tests were used to compare the categorical variables. Two-sided P-values of <0.05 were statistically significant. The survival probabilities, progression-free survival (PFS), and overall survival (OS) were calculated using the Kaplan-Meier estimator. Log-rank analysis was used to compare the different groups.

Results: A total of 43 patients were included in the analysis: 30 were aged <65 years, and 13 were aged ≥65 years. Baseline functional and comorbidity characteristics—including ECOG performance status, Karnofsky Performance Score (KPS), and Cumulative Illness Rating Scale (CIRS)—were similar between the two groups. All four mantle cell lymphoma patients who received Brexu-cel were age ≥65 years. The median number of prior lines of therapy was three in the younger cohort and two in the older cohort. Before CAR-T infusion, 67% of older adults and 69% of younger adults had stable or progressive disease.Regarding toxicities, there was a trend toward higher rates of ≥ grade 3 CRS and ICANS in younger adults compared with older adults (CRS: 10% vs 0%; ICANS: 23% vs 8%). Correspondingly, younger adults had a longer median hospitalization duration (22 days) than older adults (16 days). Grade ≥3 N-ICAHT occurred in 67% of younger adults and 46% of older adults, while ≥ grade 3 T-ICAHT was similar in both groups (31% vs 30%). Grade ≥3 infections occurred in 30% of younger adults and 46% of older adults. The 30-day readmission rates were similar between groups (13% vs 15%). Non-relapse mortality occurred in three younger adults (10%) and one older adult (8%).
With median follow-up of 12 months, younger adults had similar overall response (77%) and complete response (57%) rates compared with older adults (ORR 77%, CR 69%). The 12-month PFS were 55% in younger patients and 77% in older patients (p=0.19), whereas 12-months OS were 86% and 77% for younger adults and older adults, respectively (p=0.49).

Outcome of CAR-T		< 65-year-old (N=30)	%	≥ 65-year-old (N=13)	%	p-value
Median duration of hospitalization		22 days (16-53)		17 days (14-34)		
CRS	None	4	13	1		0.62
	Grade 1-2	23	77	12	92	
	Grade 3-4	3	10	0		
ICANS	None	18	60	10	77	0.60
	Grade 1-2	8	27	2	15	
	Grade 3-4	4	23	1	8	
No. of patients required anakinra		5	17	2	15	0.91

N-ICAHT	≥ Grade 3	20	67	6	46	0.21
T-ICAHT	≥ Grade 3	9	30	4	31	0.96
Infection (including CMV reactivation)	≥ Grade 3	9	30	6	46	0.31
Readmission within 30days		4	13	2	15	0.86



Conclusions: Patients with age 65 years and older experienced toxicity and efficacy outcomes comparable to those of younger patients, suggesting that age alone should not preclude access to CD19 CAR-T therapy. Geriatric assessment, comorbidity indices, and disease-burden biomarkers remain important considerations during patient selection. A prospective study incorporating geriatric assessment is currently underway at our institution to further elucidate the complex relationship between age-related risk and CAR-T outcomes.

Disclosure: No disclosure

P029

DECEASED DONOR BONE MARROW TRANSPLANT: FIRST EVER HUMAN CASE REPORT OF SUCCESSFUL ENGRAFTMENT AFTER INFUSION OF A CRYOPRESERVED DECEASED DONOR BONE MARROW IN A PATIENT WITH AML

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Background: Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for a variety of hematologic diseases. Clinical data now confirm that T-cells contained within the donor graft exert a "graft- versus-malignancy" effect. Use of HLA-mismatched unrelated donors (MMUD) would greatly increase treatment options for all patients, but particularly for those who are ethnically diverse. Cryopreserved hematopoietic progenitor cell (HPC) marrow from deceased organ donors provides an "on-demand" HPC graft for patients without available living donors. Here we report the first human to be treated with unrelated, minimally manipulated allogeneic cryopreserved HPC marrow for hematopoietic reconstitution after reduced intensity conditioning. This marrow is processed through proprietary means from vertebral bodies of deceased organ donors.

Methods: A 68-year-old African American female patient with acute myeloid leukemia in CR1 was transplanted using cryopreserved HPC marrow from a cadaveric donor at Henry Ford Health, Detroit, MI. Prior to transplant the patient received fludarabine 30 mg/m^2 (Day -6 to Day -2), melphalan 140 mg/m^2 (Day -6) and TBI 2Gy in one fraction, as part of reduced intensity conditioning regimen. The transplant was approved by the local IRB. High resolution HLA matching between donor and recipient was 4/8. All organ function were reported to be in normal range and KPS score was 80%. Patient received 5.27x10^6 cryopreserved CD34$^+$ cells/kg. The infusion lasted for approximately 76 minutes. The HPC, marrow product infusion was uneventful. Graft-versus-host disease (GVHD) prophylaxis consisted of tacrolimus, mycophenolate mofetil and two doses of post-transplant cyclophosphamide (PTCy) at a dose of 50 mg/kg administered on Days +3 and +4.

Results: Neutrophil engraftment was reported on Day +16 (neutrophil count D+16- 570, D+17-1500, D+18-3690 cells/L) and platelet engraftment was reported on Day+ 21 (platelet count Day + 21-20,000, D+22-22,000, D+23-34,000 cells/L) post-transplant. Full blood donor chimerism was reported on Day +30. Bone marrow on Day +60 showed 100% donor chimerism.
Based on clinical suspicion, on Day +54 acute upper GI GVHD (Grade II, stage 1) was diagnosed. The acute GVHD is being treated with budesonide 3 mg by mouth daily and tacrolimus 2.5 mg twice daily, and her GVHD was well controlled. The patient subsequently

died on Day 282 from non-relapse causes, determined not to be related to HPC-marrow.

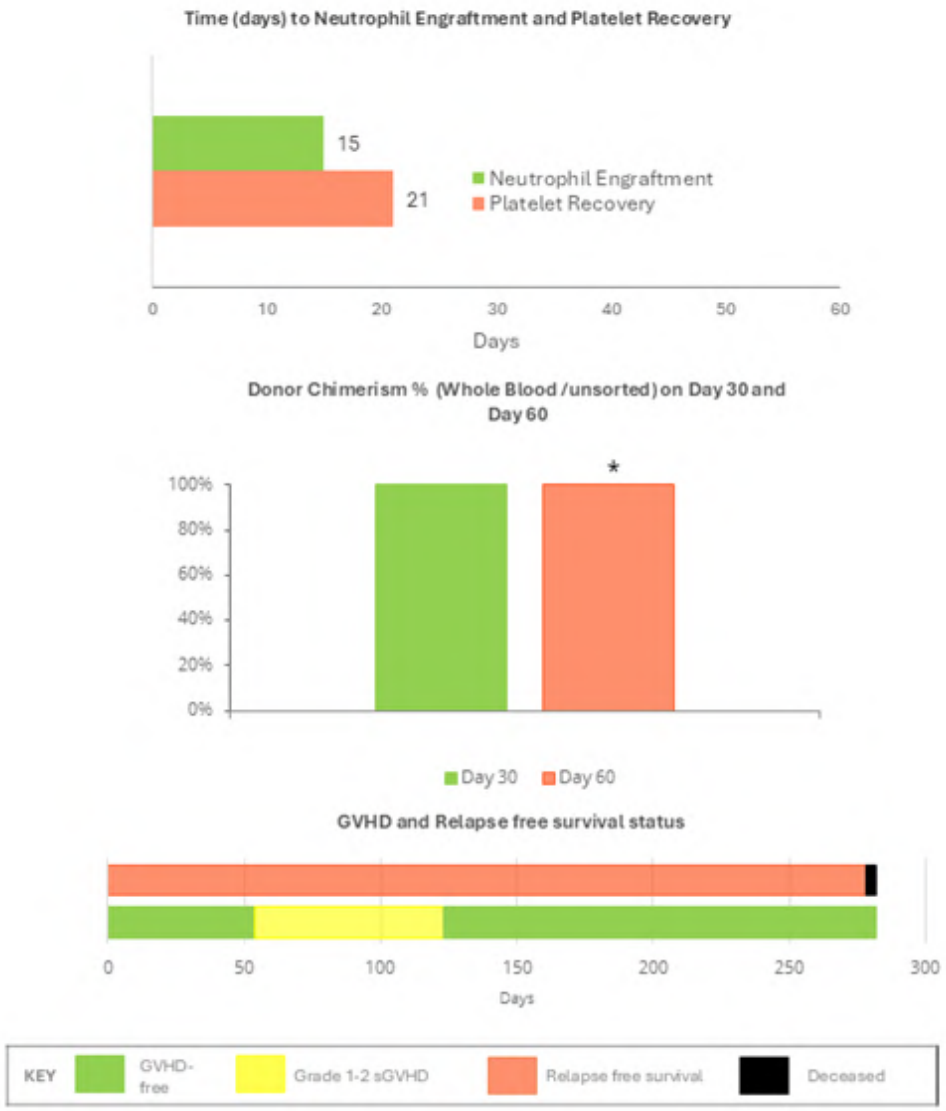

Fig 1: Patient safety journey, * Bone marrow chimerism

Conclusions: The successful engraftment in this case demonstrates the potential of cryopreserved HPC marrow from mismatched deceased organ donors as a viable option for HCT. HCT with a MMUD cryopreserved HPC marrow from a deceased organ donor can play a significant role in expanding access to HCT for patients who have unmet needs, and it can be made available "on demand". Clinical studies are currently being conducted to further evaluate the safety and effectiveness of a cryopreserved HPC marrow product.

Disclosure:

1. Muneer H. Abidi MD – Nothing to declare
2. Josephine Emole MD – Nothing to declare
3. Shatha Farhan MD – Nothing to declare
4. Edward Peres MD – Nothing to declare
5. Asif Alavi MD – Nothing to declare
6. Nancy Mikulandric PharmD, BCOP – Nothing to declare
7. Klodiana Neme PharmD, BCOP – Nothing to declare
8. Preethi Prasad MS is an employee of Ossium Health
9. Vicki L Graves MS is an employee of Ossium Health
10. Erik Woods PhD is an employee of Ossium Health
11. W. Scott Goebel, MD, PhD is a consultant to Ossium Health
12. Sagar Munjal MD, MS is an employee of Ossium Health

P030

COMPARATIVE EFFECTIVENESS OF RATG, PTCY, AND CNI/MTX FOR GVHD PROPHYLAXIS IN MATCHED SIBLING AND UNRELATED DONOR TRANSPLANTATION

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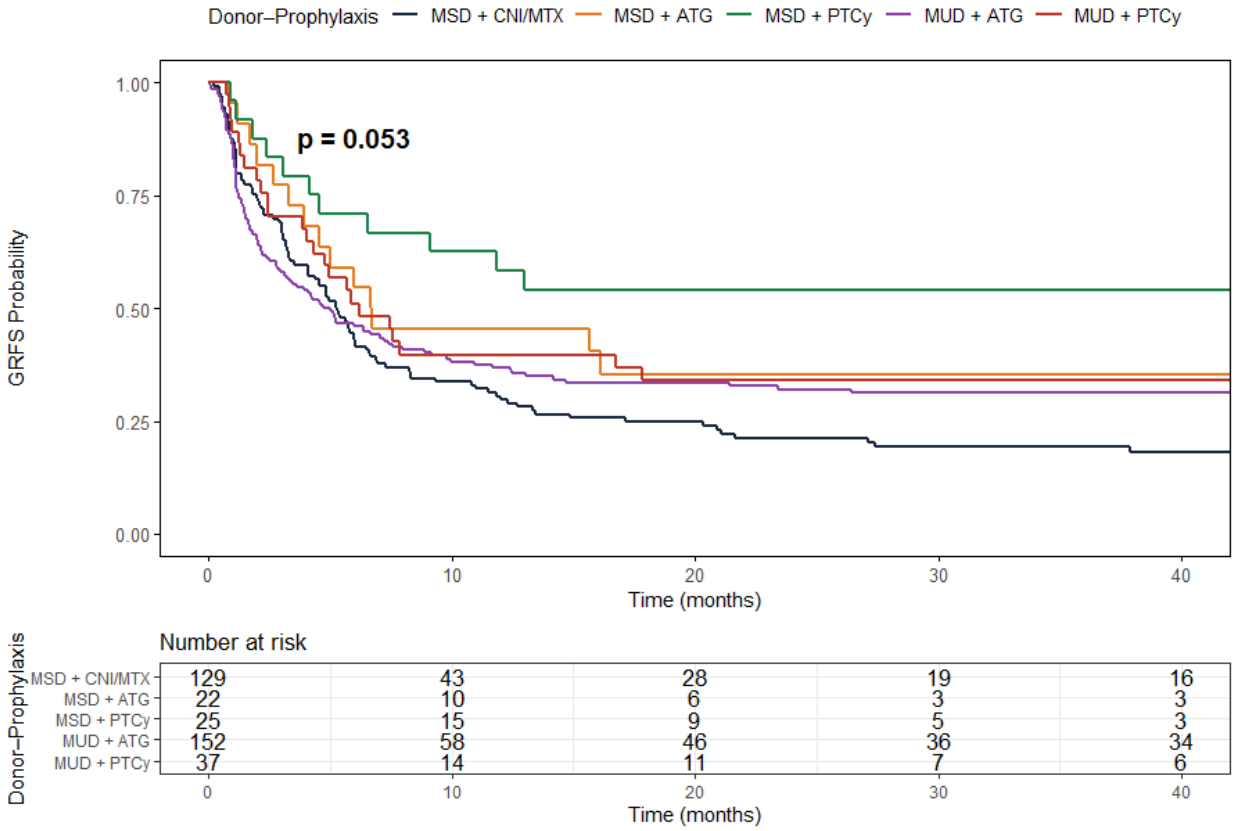
Background: Graft-versus-host disease–free, relapse-free survival (GRFS) provides an integrated measure of post-transplant tolerance in hematologic malignant diseases. Although several GVHD-prophylaxis strategies are widely used, their comparative effectiveness across donor types remains uncertain. We aimed to determine whether CNI/MTX, PTCy, or rATG differentially influence GRFS and major transplant outcomes in matched sibling (MSD) and unrelated donors (MUD).

Methods: We conducted a multicenter cohort study of adults undergoing first allogeneic transplantation between 2017–2024 across three Argentine centers (n=365; median follow-up 44 months). Five donor–prophylaxis strategies were evaluated: MSD–CNI/MTX, MSD–rATG, MSD–PTCy, MUD–rATG, and MUD–PTCy. The primary endpoint was GRFS. Secondary endpoints included relapse, non-relapse mortality (NRM), acute and chronic GVHD, and the proportion of patients achieving ≥90 consecutive days free of systemic immunosuppression (IS-free ≥90d). Multivariable Cox and Fine–Gray models adjusted for age, DRI, HCT-CI, conditioning intensity, donor age/sex, graft source, and CD34 dose.

Results:

Marked heterogeneity was observed among MSD cohorts: MSD–ATG was enriched for myelofibrosis, MSD–PTCy included younger recipients with diverse malignancies, and MSD–CNI/MTX showed the broadest diagnostic distribution. Conversely, MUD–rATG and MUD–PTCy were clinically comparable.
GRFS did not differ significantly across strategies (log-rank p=0.053). MSD–PTCy was the only regimen independently associated with improved GRFS (HR 0.47 vs MSD–CNI/MTX). Age ≥60 years (HR 1.51) and high/very-high DRI (HR 1.43) were adverse predictors.
No prophylaxis strategy was independently associated with NRM in multivariable Fine–Gray models. Relapse differences across strategies were also non-significant, although MSD–CNI/MTX and MUD–PTCy exhibited numerically higher hazards. High/very-high DRI remained the only independent predictor of relapse (HR 1.59; p=0.035).
In a pooled comparison of rATG versus PTCy, ATG showed a non-significant trend toward higher NRM (HR 2.20; p=0.11) but was associated with significantly lower relapse (HR 0.53; p=0.03). In this subanalysis, relapse risk further increased among patients with high/very-high DRI (p=0.0013) and with HCT-CI ≥3 (p=0.0093).
Acute GVHD II–IV occurred in 16–38%, with no independent association with prophylaxis strategy or sex-match category. Moderate-to-severe chronic GVHD showed a non-significant reduction with MSD–PTCy (sHR 0.14; p=0.052) and MSD–rATG (sHR 0.20; p=0.11). Female donor grafts were strong independent predictors of moderate-to-severe cGVHD (female→female: sHR 2.81; p=0.018; female→male: sHR 2.68; p=0.014).
IS-free ≥90d was more frequent in MSD–PTCy and MSD–rATG (27–40%) compared with MSD–CNI/MTX and both MUD strategies (6–24%).



Conclusions: Profound baseline imbalance among MSD cohorts limits direct comparison of prophylaxis strategies and likely underlies the variability in GRFS, relapse, NRM, and IS-free outcomes. In contrast, the close clinical alignment of MUD–rATG and MUD–PTCy yielded virtually indistinguishable results across all endpoints, suggesting functional equivalence in unrelated donor transplantation. Across analyses, disease-risk level and comorbidity burden—not prophylaxis choice—were the dominant determinants of relapse and GVHD-related morbidity.

Disclosure: Nothing to declare for all authors.

P031

EFFICACY OF ROMIPLOSTIM ON HASTENING PLATELET COUNT RECOVERY IN POST-TRANSPLANT PATIENTS: A SINGLE-CENTER EXPERIENCE

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Background: Prolonged thrombocytopenia following hematopoietic stem cell transplantation (HSCT) increases bleeding risk and healthcare burden. Romiplostim, a thrombopoietin receptor agonist, has shown potential in accelerating platelet recovery. However, data on its efficacy in the post-transplant setting remains limited. To evaluate the efficacy of romiplostim in shortening the duration of thrombocytopenia in patients undergoing peripheral blood stem cell transplantation.

Methods: We conducted a retrospective cohort study comparing 33 consecutive patients who received romiplostim (2-3 mcg/kg between D+5 to D+10) following HSCT at our center (March 2023–October 2025) with 23 historical controls transplanted prior to March 2023 without romiplostim. The cohort included 21 autologous and 12 allogenic transplants in cases, and 13 autologous and 10 allogenic in controls. We excluded patients at high risk of veno-occlusive disease. Primary endpoint was platelet engraftment (first of two consecutive platelet counts >20,000/μL, unsupported). Subgroup analyses were performed by disease category (plasma cell dyscrasia, lymphoma), conditioning intensity (MAC, RIC), and donor status (matched, haploidentical). Statistical analysis used Mann-Whitney U test with significance at $p<0.05$.

Results: Baseline characteristics were comparable between groups (age: 47.3±14.3 vs 43.1±12.9 years, p=0.261; male sex: 57.6% vs 69.6%, p=0.412). Median time to platelet engraftment was 11.5 days (IQR 11.0–13.2) in the romiplostim group versus 12.0 days (IQR 10.0–15.0) in controls (p=0.630). Mean engraftment time was 12.75±3.70 vs 13.17±4.00 days (mean difference: 0.42 days, 95% CI: -1.65 to 2.50). Subgroup analyses showed no significant differences in plasma cell dyscrasias (11.0±1.2 vs 10.4±2.0 days, p=0.328), lymphoma (13.5±2.4 vs 15.8±1.5 days, p=0.180), autologous (11.5±1.8 vs 12.1±3.1 days,

p=0.801), or allogenic transplants (15.2±5.1 vs 14.6±4.7 days, p=0.697). Notably, later engraftment (>14 days) occurred in 15.6% of romiplostim patients versus 30.4% of controls (OR=0.42, p=0.208).

Study Population Characteristics

Variable	Romiplostim (n=33)	Control (n=23)	p-Value	Test
Age (years)	47.3±14.3 / 49 (21-75)	43.1±12.9/45(19-67)	0.261	Mann-Whitney U
Sex (M/F)	19 (57.6%) / 14 (42.4%)	16(69.6%)/7(30.4%)	0.412	Fisher's Exact
Transplant Type	Auto:21(63.6%)/Allo:12(36.4%)	Auto:13(56.5%)/Allo:10(43.5%)	0.796	Chi-square
Plasma Cell Dyscrasia	17 (51.5%)	9 (39.1%)	----	----
Lymphoma	4 (12.1%)	4 (17.4%)	----	----
Other (AML/MDS/CML)	12 (36.4%)	10 (43.5%)	----	----
Conditioning (Allo only)	MAC: 7(58.3%)/RIC:5(41.7%)	MAC:3 (30.0%)/RIC:7(70.0%)	0.231	Fisher's Exact
Donor: Matched	5 (41.7%)	8 (80.0%)	---	-----
Donor: Haploidentical	7 (58.3%)	2 (20.0%)	---	-----

Age shown as Mean ± SD / Median (Range); Auto=Autologous, Allo=Allogenic, MAC=Myeloablative, RIC=Reduced Intensity

Conclusions: Romiplostim administration (2-3 mcg/kg, D+5 to D+10) did not significantly hasten platelet engraftment in this cohort. None of the patients experienced any adverse effects from romiplostim. However, amongst patients who had a later engraftment, there was a trend toward benefit from romiplostim. Given that romiplostim appears safe in the immediate post-transplant period, we propose larger, prospective ,randomized trials to assess its utility and define its role in this setting.

Disclosure: Nothing to declare

P034

ANALYSIS OF GRAFT-VERSUS-HOST DISEASE–FREE, RELAPSE-FREE SURVIVAL (GRFS) IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MYELOID MALIGNANCIES

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a standard curative treatment for myeloid malignancies, although its effectiveness may be limited by relapse-related and treatment-associated morbidity and mortality. Severe graft-versus-host disease (GVHD) significantly impairs long-term quality of life in survivors, a dimension not adequately captured by overall survival (OS). In this context, graft-versus-host disease–free, relapse-free survival (GRFS), as a composite endpoint integrating treatment-related mortality, relapse, and severe GVHD, provides a comprehensive assessment of clinical benefit and a reliable criterion for risk estimation and long-term quality of life in transplant candidates. The aim of this study was to assess the clinical benefit of allo-HSCT using GRFS, thereby evaluating transplant success in terms of long-term quality of life.

Methods: A retrospective observational analysis was conducted in patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML) who underwent a first allo-HSCT at a tertiary-care center between January 2018 and May 2025. GRFS events were defined as grade ≥3 acute GVHD, severe chronic GVHD, disease relapse, or death from any cause. Descriptive statistics were summarized using measures of central tendency; risk associations were evaluated using the χ^2 test; and event-free survival was assessed using Kaplan–Meier methodology

Results:

Table 1: Cohort Characteristics

Sex	*Male n (%)*	80 (46.8%)	**Conditioning Regimen**	*Non-myeloablative n (%)*	47 (28%)
	Female n (%)	91 (53.2%)		*Myeloablative n (%)*	121 (72%)

Diagnosis	*AML n (%)*	116 (67.8%)	**EBMT Risk Score**	*Low n (%)*	104 (66.7%)
	MDS n (%)	55 (32.2%)		*Intermediate n (%)*	22 (14.1%)
Disease Status Pre-HSCT	*Persistent disease n (%)*	54 (32.9%)		*High n (%)*	30 (19.2%)
	Complete response n (%)	110 (67.1%)			
AML Disease Status Pre-HSCT	*First complete remission n (%)*	93 (90.3%)	**ECOG**	*0 n (%)*	130 (81.3%)
	Second or subsequent remission n (%)	10 (9.7%)			
Transplant Type	*HLA-identical related donor n (%)*	66 (38.6%)		*1 n (%)*	26 (16.2%)
	Matched unrelated donor (10/10) n (%)	27 (15.8%)		*≥ 2 n (%)*	4 (2.5%)
	Matched unrelated donor (9/10) *n (%)*	5 (2.9%)	**Karyotype**	*No complex (%)*	125 (87.4%)
	Haploidentical n (%)	73 (42.7%)		*Complex (%)*	18 (12.6%)
Stem Cell Source	*Peripheral blood n (%)*	169 (99.4%	**Transplant-related complications**	*Hemorrhagic cystitis n (%)*	18 (10.6%)
	Bone marrow	1 (0.6%)		*VOD n (%)*	13 (7.6%)

A total of 171 allo-HSCT recipients were analyzed; 67.8% had AML and 32.2% had MDS. The median follow-up was 18.2 months (IQR, 7.2–38.2). The median age was 56 years (19–73). Donor types included haploidentical (42.7%), HLA-identical related (38.6%), 10/10 matched unrelated donor (15.8%), and 9/10 matched unrelated donor (2.9%). All patients received GVHD prophylaxis with post-transplant cyclophosphamide, tacrolimus, and mycophenolate. Clinical and transplant characteristics are detailed in Table 1.

At the median follow-up, GRFS was 65.4%, with death representing the most frequent cause of GRFS failure (45.7%) (Figure 1). GRFS declined to 63.1% at 24 months, coinciding with a 6.3% absolute increase in relapse, and further decreased to 59.1% at 30 months; although death remained the most frequent cause of GRFS failure, this additional decline was associated with a 3.2% absolute increase in severe GVHD.
GRFS differed significantly between AML and MDS in the overall analysis ($p = 0.02$) (Figure 1); however, the marked differences in age distribution between both groups suggest a potential influence of age on GRFS outcomes.
In the overall cohort, at the median follow-up, GRFS was 70.6% in AML and 56.3% in MDS, with treatment-related mortality being the most prevalent event in both groups (38.2% and 54.1%, respectively). At 24 months, treatment-related mortality remained predominant in MDS (56%), whereas relapse increased in AML (35.1%). At 30 months, higher mortality persisted in MDS (55.5%), while relapse and severe GVHD were more frequent in AML (35.7% and 33.3%, respectively).

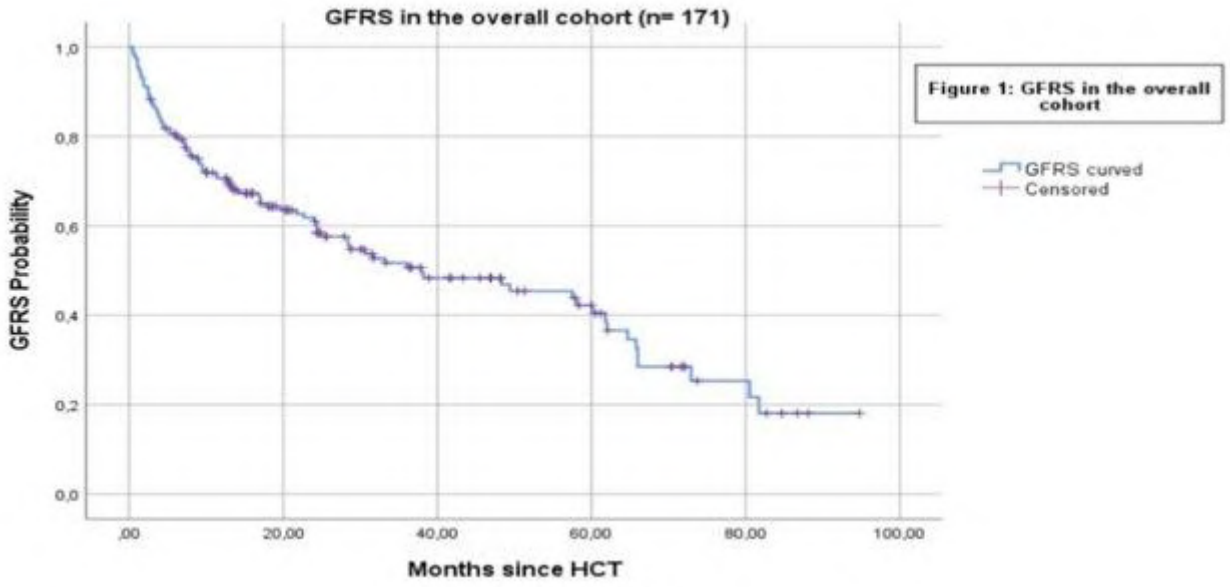

Figure 1: GFRS in the overall cohort

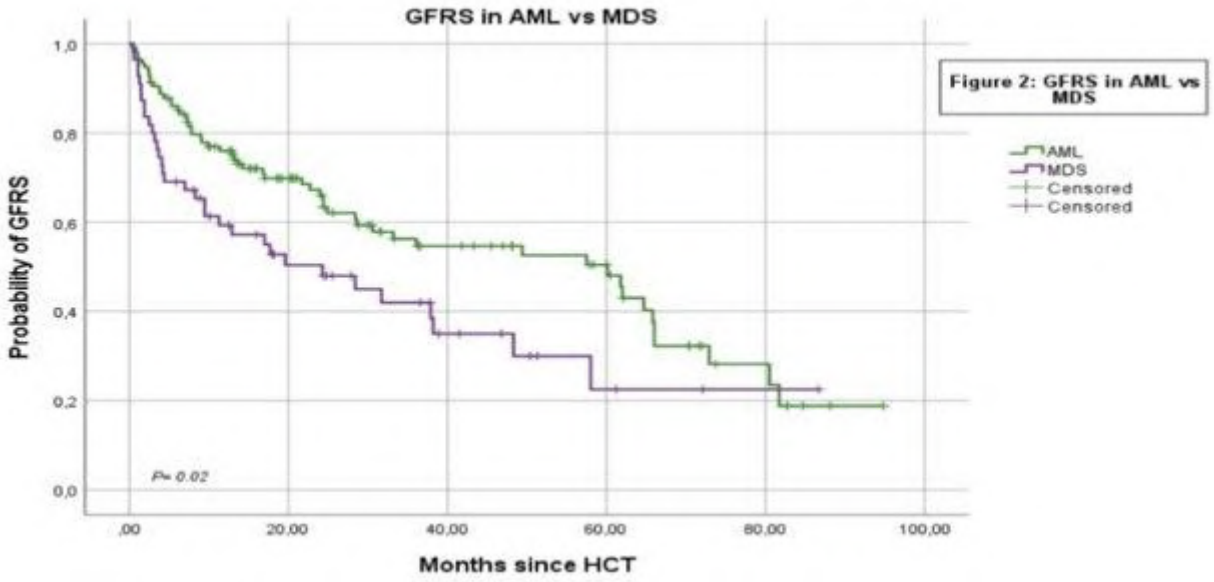

Figure 2: GFRS in AML vs MDS

Conclusions: GRFS declined progressively during follow-up, with treatment-related mortality remaining the leading cause of failure and an increasing late contribution of relapse and severe GVHD. Although overall GRFS differences between AML and MDS may be influenced by age, GRFS enabled an integrated assessment of post-transplant events, reaffirming its value as a clinically relevant endpoint in allo-HSCT.

Disclosure: Nothing to declare.

P035

CRYOPRESERVED LEUKAPHERESIS FOR CAR-T MANUFACTURING IN SPAIN: A NATIONAL SURVEY FROM THE SPANISH SOCIETY FOR BLOOD TRANSFUSION AND CELLULAR THERAPY (SETS)

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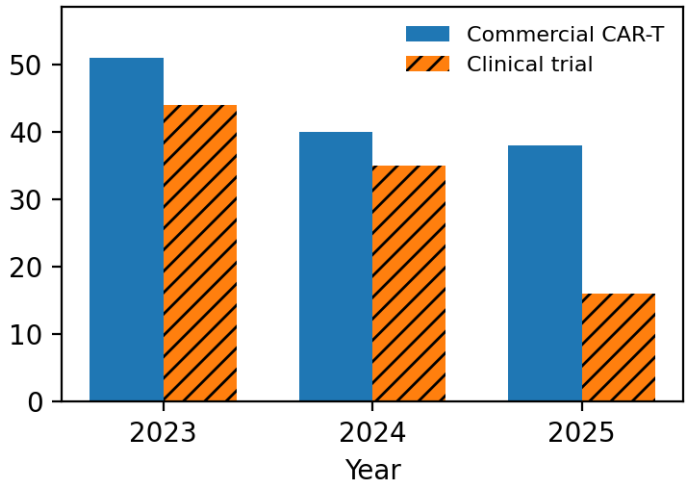
Background: Cryopreserved leukapheresis has become an established option for modern CAR-T cell manufacturing, ensuring product stability and enabling flexible logistics without compromising clinical outcomes. In Spain, Kymriah® (tisagenlecleucel) and Novartis clinical-trial platforms mandate cryopreservation at hospital-based cell-processing laboratories. Despite its widespread use, national real-world data describing the magnitude and temporal evolution of this activity are lacking.

Methods: The Spanish Society for Blood Transfusion and Cellular Therapy (SETS) Working Group on Cellular Processing and Advanced Therapies conducted a nationwide survey assessing cryopreserved leukapheresis activity for both commercial (Kymriah®) and clinical-trial CAR-T manufacturing over the last three years. The study included all authorized cell-processing centers in Spain, ensuring comprehensive national coverage.

Results: Nineteen centers responded to the survey. Six centers reported no cryopreservation activity and were therefore excluded from **Figure 1**, which summarizes activity only from the 13 centers that confirmed performing cryopreserved leukapheresis. Among active centers, five performed cryopreservation exclusively for Kymriah®, while eight supported both commercial and clinical trial CAR-T programs. From 2023 to 2025, cryopreservation volumes decreased by 25**%** for commercial CAR-T manufacturing and by 64**%** for clinical-trial CAR-T manufacturing (**Figure 1**).



Conclusions: Cryopreserved leukapheresis represents a core competency of Spanish cell-processing laboratories and a critical component of CAR-T manufacturing logistics. The observed decline in activity may reflect the higher complete responses reported with alternative anti-CD19 CAR-T constructs compared with Kymriah® in aggressive B-cell non-Hodgkin lymphoma. The decline in clinical-trial cryopreservation activity may be partly explained by the completion of recruitment in Novartis lymphoma programs in 2024, together with a shift in ongoing Novartis CAR-T trials toward other indications (e.g., autoimmune diseases) that typically enroll smaller cohorts. This trend highlights evolving clinical practice, changes in CAR-T program dynamics, and the importance of continued national monitoring to appropriately adapt capacity and resource allocation.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

P036

PERICATHETER AND SYSTEMIC THROMBOSIS DURING CAR-T LYMPHOCYTAPHERESIS: INCIDENCE AND CLINICAL CORRELATES

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Background: Pericatheter thrombosis (PCT) is a recognised complication of large-bore venous catheters used for cell collection. An incidence of local thrombotic occlusion of approximately 1.8% has been described in literature for Mahurkar catheters used in peripheral blood stem cell collection. Despite these devices being widely used in chimeric

antigen receptor t (CAR-T) cell manufacturing, the incidence and determinants of PCT in this setting are still unclear. This study provides a real-world evaluation of PCT in patients undergoing lymphocytapheresis for CAR-T therapy. The aim is to characterise thrombotic events and explore potentially relevant clinical or procedural factors.

Methods: A retrospective, single-centre analysis was conducted on 158 adults evaluated for CAR-T therapy between September 2019 and October 2025. Of these patients, 62 who underwent lymphocytapheresis using a Mahurkar catheter were included in the analysis. The underlying diseases were large B-cell lymphoma (79.0%), mantle cell lymphoma (9.7%) and B-cell acute lymphoblastic leukaemia (11.3%). Clinical, laboratory, and procedural variables were collected at the time of catheter placement. Two predefined analytical strategies were employed: (1) comparison of patients with pericatheter thrombosis (PCT) versus all other patients (with or without thrombosis at distant sites); and (2) comparison of patients with any thrombotic event (PCT or distant thrombosis) versus those with no thrombosis. Continuous variables (age, platelet count, haemoglobin, white blood cell count, fibrinogen and D-dimer) were analysed using a Student's t-test, while categorical variables (sex, disease status, lactate dehydrogenase -LDH- level above or below the laboratory limit, Khorana score, anticoagulation, catheter site and procedural difficulty) were analysed using a chi-squared test or Fisher's exact test, as appropriate.

Results: PCT occurred in 5 out of 62 patients (8%). An additional 8 patients (13%) developed thrombosis at non-catheter sites, for a total of 13 thrombotic events (21%). No continuous variable was associated with PCT, although platelet count showed a borderline trend ($p = 0.061$). Procedural difficulty was more frequent in PCT cases (66% vs. 18%), though this was not statistically significant after Yates's correction. Sex, LDH, Khorana score, anticoagulation, disease status, catheter site and other laboratory parameters showed no association with PCT. In the overall thrombosis analysis, no clinical or laboratory variable reached statistical significance, with platelet count again demonstrating a borderline trend ($p = 0.098$).

Conclusions: The main finding of this study was that PCT during lymphocytapheresis for CAR-T manufacturing was more frequent than had been reported in historical series of Mahurkar catheters used for peripheral blood stem cell collection. Within the analysed population, no baseline clinical or laboratory variable was found to be associated with an increased risk of thrombosis. This suggests that CAR-T candidates undergoing lymphocytapheresis have a relatively homogeneous thrombotic risk profile. These observations highlight the need for comparative analyses with patients undergoing haematopoietic stem cell apheresis to determine whether the higher incidence observed reflects factors related to the procedure, the disease, or the population.

Disclosure: Nothing to declare.

P038

T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA RELAPSE AFTER CAR-T THERAPY

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Background: Tisagenlecleucel (formerly CTL019), an anti-CD19 chimericantigen receptor (CAR) T-cell therapy, is an establishedtreatment for pediatric patients with relapsed or refractory B-cell acute lymphoblastic leukemia (B-ALL). Although most studies demonstrate high remission rates following CAR-T cell infusion, long-term outcomes, including relapse patterns, are still being evaluated. Likewise, the role of hematopoietic stemcell transplantation (HSCT) after CAR-T therapy remains under investigation, with some studies suggesting improved survival when both strategies are combined.
Recently, an increasing number of secondary T-cell malignancies have been reported following CAR-T cell infusion, with an estimated incidence ranging from 0.03% to 0.1%.

Methods: We report the case of a patient with refractory ALL treated with CAR-T cell therapy. After disease relapse following the first CAR-T infusion, a second CAR-T was administered as a bridge to HSCT. Unfortunately, the patient subsequently developed T-cell acute lymphoblastic leukemia (T-ALL) after CAR-T therapy.

Results: A 16-year-old patient was diagnosed with B-ALL, with a normal karyotype, no central nervous system involvement, and no detectable molecular abnormalities. The disease was refractory to conventional chemotherapy. Prior to CAR-T therapy, the patient received multiple chemotherapy regimens, including RE-ALL (with a measurable residual disease [MRD] of 38.36% at the end of induction phase 2), cytarabine and etoposide, hyper-CVAD, and blinatumomab (post-treatment bone marrow MRD of 59.7% blasts). The final salvage regimen consisted of topotecan, which achieved the best disease control, with a pre-CAR-T MRD of 3.8%. The patient underwent lymphodepletion with fludarabine (120 mg/m²) and cyclophosphamide (1000 mg/m²), followed by the first CAR-T cell infusion. Post-infusion bone marrow evaluations were initially negative; however, three months after the infusion, the patient relapsed. The topotecan regimen was repeated, and a second CAR-T cell infusion was administered. On day +14 after the second CAR-T, blasts were detected by peripheral blood immunophenotyping. A new treatment regimen with vincristine and PEG-asparaginase was initiated, followed by three doses of inotuzumab. After inotuzumab, the patient achieved bone marrow remission and proceeded to HSCT. A haploidentical HSCT from his sister was performed on February 28, 2025, using a Cy-TBI conditioning regimen. Initial post-transplant bone marrow evaluation was negative; however, on day +100, the patient experienced another relapse, with MRD of 40.6% blasts of T-cell lineage.
Currently, six months after relapse, the patient remains on low-dose methotrexate and mercaptopurine, with no blastos on peripheral blood and stable clinical status.

Conclusions: Delays between CAR-T cell therapy indication and infusion may increase relapse risk, particularly in low- and middle-income countries. These data support the

integration of systematic relapse surveillance into post-CAR-T follow-up protocols. Ongoing vigilance by flow cytometry laboratories is crucial for the early identification of lineage switch, including the emergence of T-lineage blasts.

Disclosure: Nothing to declare

P039

IMMUNE RECONSTITUTION AND INFECTIOUS COMPLICATIONS IN PATIENTS UNDERGOING CAR-T CELL THERAPY: A REAL-WORLD SINGLE-CENTER EXPERIENCE

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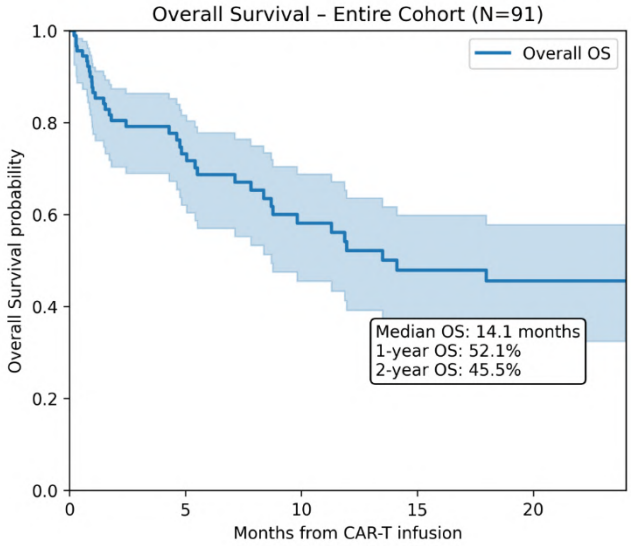
Background: Real-world data on overall survival (OS), non-relapse mortality (NRM), infections, and immune reconstitution after chimeric antigen receptor T-cell (CAR-T) therapy for lymphoma, multiple myeloma (MM), and acute lymphoblastic leukemia (ALL) remain limited, with most evidence from clinical trials. We present a single-center Italian experience with commercial CAR-T products in adults treated from 2020 to 2025, focusing on outcomes, early mortality, infections, and post-infusion immune deficits.

Methods: This retrospective observational , single center, study included 91 adults patients (median age 61 years; 73% male) affected by different hematologic malignancies: diffuse large B-cell lymphoma (DLBCL, 65%), mantle cell lymphoma (MCL, 11%), MM (14%), primary mediastinal B-cell lymphoma (PMBCL, 4%), follicular lymphoma (FL, 2%), and ALL (3%). The first patient with MM was treated only in November 11, 2024. The median follow-up time was 56.1 days in MM patients, 147 days in lymphoma patients, and 155 days in leukemia patients. Most patients (86%) had ECOG 1 performance status; 32% had prior autologous stem cell transplant (auto-SCT). Bridging therapy (62%) yielded complete response (4%), partial response (19%), stable disease (18%), or progression (45%). We assessed OS, NRM (1-Kaplan-Meier), cytokine release syndrome (CRS)/ Immune effector cell–associated neurotoxicity syndrome (ICANS), cytopenias, infections, IV Immunoglobulin (IG) use, readmissions, relapses (38%), and immune reconstitution ($CD4^+$ T cells >200/μL; $CD19^+$ B cells).

Results: Over follow-up, 37% of patients died, for: progression (19%), CRS (4%), viral infections (3%). CRS occurred in 37% (grade 1: 55%; grade 2: 28%; max grade 5: 4%); ICANS was rare (74% none; grade 5: 1%). Cytopenias persisted in 19% at day +30, declining to 3% at day +365. IVIG post CAR-T was needed in 25 %; 25% of patients required readmission. Median OS was 14.1 months (1-year: 52%; 2-year: ~40%) (figure 1); median disease-free survival, 6.1 months. NRM was 11% at day +100 (stable at 1 year), all early events occured in lymphoma (8/75) and ALL (1/3); none in MM (but the first MM patient was infused on November 2024) . Infections affected 27% (25/91 patients; 30 episodes), clustering early (24/30 within 3 months). Documented etiologies (9 cases, all

lymphoma): bacterial (4), viral (3), CMV (2). Immune recovery was delayed: $CD4^+$ >200/µL was documented in only 15% of lymphoma patients (median 180 days), none in MM/ALL; $CD19^+$ B-cell recovery was rare in the first year after infusion. Poor $CD4^+$ reconstitution trended with NRM in lymphoma (not significant); prior auto-SCT and bridging may contribute.



Conclusions: In this real-world cohort, CAR-T yielded median OS of 14.1 months with low early NRM (11%), mainly in lymphoma/ALL. Infections peaked in the first 3 months amid hypogammaglobulinemia and delayed reconstitution, defining a high-risk window. These data advocate structured early surveillance, serial immune monitoring (e.g., $CD4^+$ counts), and tailored support (IVIG, prophylaxis), especially for lymphoma/ALL. Prior therapies warrant further risk stratification.

Disclosure: Nothing to declare.

P040

OUTCOMES OF CD19 CAR T-CELL THERAPY IN DOWN SYNDROME–ASSOCIATED B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A THREE-PATIENT CASE SERIES FROM A CENTER IN THE MIDDLE EAST

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Background: Children and adolescents with Down syndrome–associated acute lymphoblastic leukemia (DS-ALL) have unique therapeutic challenges, including heightened chemotherapy toxicity, increased treatment-related morbidity, and higher relapse risk. Data on the safety and efficacy of CD19 CAR T-cell therapy in this population remain limited. From King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia, we report a three-patient DS-ALL case series treated with tisagenlecleucel (tisa-cel), focusing on toxicity profile, MRD kinetics, and early outcomes.

Methods: Case descriptions:
Case 1: A 15-year-old male with Down syndrome (DS) was diagnosed with B-cell precursor ALL in 2019 and treated with AALL0932, later escalated to AALL1131 for persistent MRD. He attained MRD negativity during interim maintenance and completed therapy in February 2022. He relapsed 27 months later with 50% marrow blasts and received ALL-1331 salvage therapy (anthracycline-free), achieving <1% blasts but residual MRD (0.2%). Following T-cell apheresis and vincristine/dexamethasone/6-MP bridging, pre–CAR T marrow showed morphologic remission with MRD 0.28%. He received tisa-cel on 14 October 2025 after Flu/Cy conditioning, with no CRS or ICANS. Day +30 marrow showed MRD negativity (0.01%) and persistent B-cell aplasia. He remains clinically stable.
Case 2: A 15-year-old male with DS and congenital heart disease achieved MRD-negative remission on AALL0232 but relapsed in June 2025 with 48% blasts. Two doses of inotuzumab ozogamicin induced morphologic remission with MRD 0.75%. His chemotherapy course was complicated by acute necrotizing pancreatitis, a transient LV thrombus requiring anticoagulation, and pacemaker dependence. Despite vincristine bridging, pre–CAR T marrow remained MRD positive (1.2%). He received tisa-cel on 21 October 2025 without CRS or ICANS. Day +26 lymphocyte analysis confirmed B-cell aplasia. Post CAR T bone marrow showed hypocellularity with trilineage regeneration and immunophenotypic findings negative for definite MRD.
Case 3: An 18-year-old male with DS was diagnosed with B-ALL in October 2021 and received an MTX-free AYA protocol due to intolerance risk, achieving CR by day 27 and MRD negativity (0.1%) post-consolidation. Blinatumomab was unavailable, and he proceeded to delayed intensification with reduced-dose doxorubicin. Pre–CAR T evaluation in May 2022 showed MRD negativity and no CNS disease. He received tisa-cel on 22 May 2022, developing grade 2 CRS requiring tocilizumab and one neutropenic fever episode. He remained in remission with persistent B-cell aplasia through 2023 but developed progressive renal dysfunction and hydroureteronephrosis. Lost to follow-up after December 2023, he was later reported deceased in September 2025, with no evidence of relapse during documented care.

Results: Across the three DS-ALL patients, CAR T-cell infusion was feasible with no ICANS and limited CRS (only one grade 2 event). All patients achieved MRD-negative remission after tisa-cel with sustained B-cell aplasia during follow-up. Toxicities were primarily non–CAR T related and related to comorbidities.

Conclusions: Tisagenlecleucel demonstrated favorable tolerability and effective disease control in DS-ALL patients, with low neurotoxicity and consistent MRD clearance. This series highlights CAR T-cell therapy as a viable option for DS-ALL, a population historically vulnerable to chemotherapy-related toxicity. Larger studies are needed to define long-term outcomes.

Disclosure: Authors declare no conflict of interest.

P041

AN UNSUPERVISED APPROACH TO PREDICTING EARLY POST-TRANSPLANT FEVER IN ADULTS WITH ACUTE MYELOID LEUKEMIA UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION USING ROUTINE LABORATORY AND CLINICAL PARAMETERS

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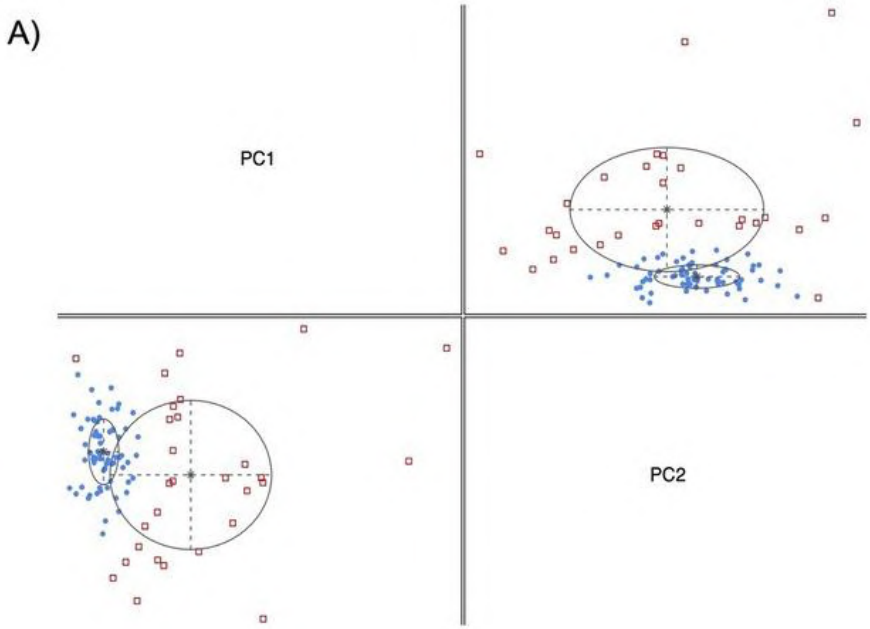
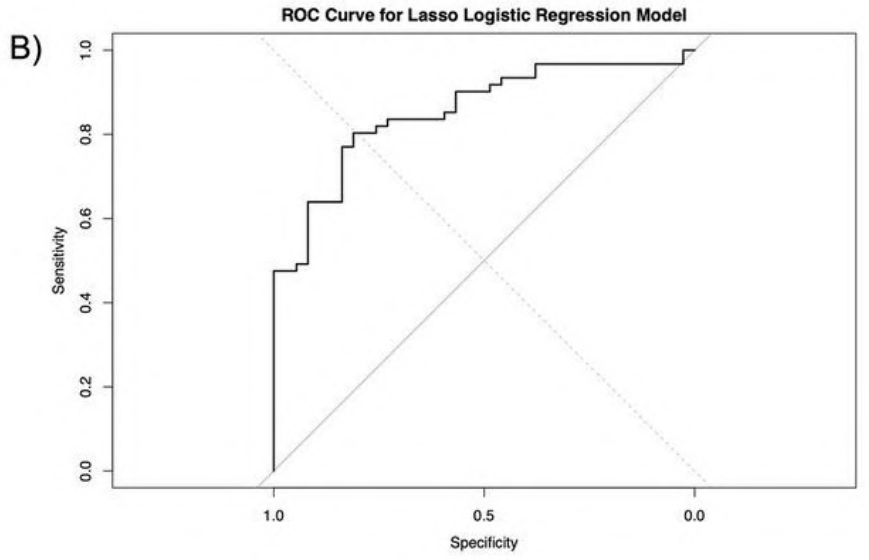
Background: Infections are among the leading causes of morbidity, ICU admission, and death after allogeneic stem cell transplantation (alloSCT) for acute myeloid leukemia (AML). Fever is a key sign of infection, but it also reflects non-infectious inflammation, while microbiological confirmation is often delayed. We hypothesized that an unsupervised, data-driven analysis of routine laboratory and clinical parameters could identify patients who will develop fever and help distinguish infectious from non-infectious causes of fever.

Methods: This study enrolled all adults with AML undergoing alloSCT treated in the years 2017-2024 in a single center (n=90). The primary outcome of interest was fever status in the post-transplant course: no fever (i); at least one episode of fever without microbiologically confirmed infection (ii), and fever with documented infection (iii). The observation window was day 0 to +30 after transplantation. For each patient, we extracted age and 37 routine clinical variables (vital signs, complete blood count, inflammatory markers, renal and liver function tests, glucose, and electrolytes) measured 2 days before fever onset (DAY-2) or the corresponding reference day in afebrile patients.
In the exploratory, unsupervised stage, we applied principal component analysis (PCA) for dimensionality reduction and to identify variables contributing most to overall variance. Model-based clustering (mclust) was applied in PCA space to find distinct clusters of patients. Subsequently, we checked the association of cluster allocation with the primary outcome. In the model-development stage, to obtain a clinically applicable prediction tool, we fitted a LASSO-penalized logistic regression model on non-transformed DAY-2 data. Model performance was assessed by receiver operating characteristic (ROC) analysis.

Results: Among the enrolled patients, the median age was 54 years, and 47% were male. Most patients received matched unrelated donor transplants (54%), followed by matched related donor (26%), mismatched unrelated donor (10%), and haploidentical (10%). Twenty-three percent of patients developed fever with documented infection, whereas 36% had microbiologically negative fevers. Remaining patients (41%) remained afebrile. Among these groups, we found no difference in transplant type distribution. Median time from alloSCT to fever onset was 9 days.
In the unsupervised phase, we found two separate clusters (Figure 1.A), one consisting of both afebrile and febrile patients, the second comprising exclusively fever-positive individuals

($p<0.05$). PCA-based clustering failed to discriminate patients based on fever origin. In the second phase, the final LASSO model retained five DAY-2 predictors: heart rate, C-reactive protein, neutrophil, monocyte, and platelet counts. The resulting logistic model showed good discrimination for subsequent fever, with an area under the ROC curve (AUC) of 0.85 (Figure 1.B). At the chosen decision threshold, sensitivity was 0.80, specificity 0.81, positive predictive value 0.88, and negative predictive value 0.71.





Conclusions: In this alloSCT AML cohort, multivariate analysis of routine laboratory and clinical data obtained two days before fever onset allowed accurate discrimination between patients with and without impending fever. However, discrimination between the cause at

DAY -2 was impossible. The presented approach could support closer surveillance, earlier blood culture ordering, and optimization of empirical antibiotics while awaiting microbiology results. However, these findings need validation in a larger, independent cohort before clinical application.

Disclosure: Disclosures:
Funding statement
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P043

CLINICAL OUTCOMES FOLLOWING TREATMENT WITH CD19 CAR T-CELL THERAPY IN PATIENTS WITH DOWN SYNDROME-ASSOCIATED ALL: A SINGLE-INSTITUTION EXPERIENCE

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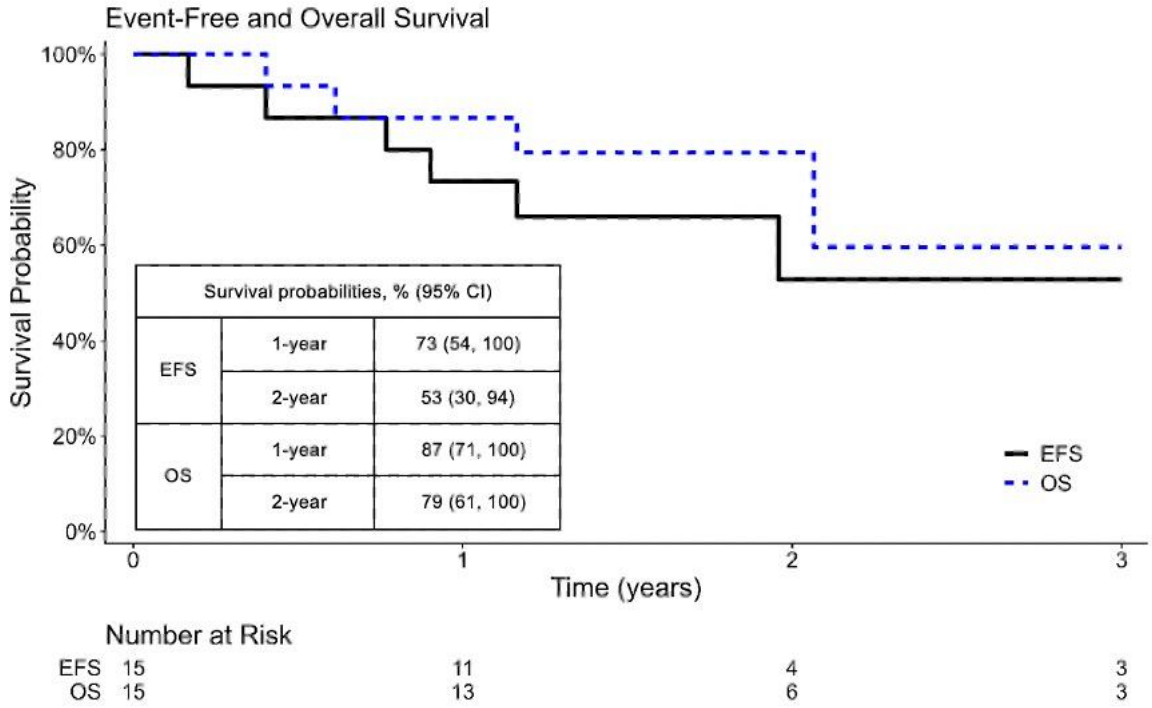
Background: Patients with relapsed or refractory Down syndrome-associated ALL (DS-ALL) have historically poor outcomes, including following hematopoietic stem cell transplant (HSCT). Early reports suggest promising results for DS-ALL patients treated with CD19 chimeric antigen receptor T-cell (CART) therapy, but published data remain limited.

Methods: This single-institution retrospective cohort study evaluated survival outcomes and treatment-related toxicities among pediatric and young adult patients (<26 years) with DS-ALL treated with CD19 CART therapy between 2017 and 2024 at a tertiary academic center. Demographic, disease, treatment, toxicity, and survival data were extracted from the electronic medical record. Survival was estimated using the Kaplan–Meier method, and response and toxicity outcomes were summarized descriptively.

Results:

Figure 1 Kaplan–Meier Estimates of Event-Free and Overall Survival



Fifteen patients receiving 22 CD19 CART infusions were included (median age 14 years; 53% female; 73% Hispanic/Latino; 80% publicly insured). Most patients had high-risk DS-ALL (73%, n = 11) and received CART therapy for first relapse (60%, n = 9). Disease burden at infusion was low, with 73% (n = 11) having M1 marrow status and 93% (n = 14) without CNS involvement. Overall rates of severe toxicity were also low. Cytokine release syndrome (CRS) occurred in 67% of patients (n = 10), with only one case of severe (grade 4) CRS. Immune effector cell–associated neurotoxicity syndrome (ICANS) occurred in 27% (n = 4), with one severe (grade 3) case. Both severe CRS and ICANS resolved with standard steroid and anti-cytokine therapies. Hematologic toxicity was common: 73% (n = 11) developed grade 3–4 cytopenias, with full hematologic recovery at a median of 20 days (range 6–151 days) post-infusion. Two patients experienced rare ocular toxicities, including retinal detachment, which resolved with treatment. All patients were minimal residual disease (MRD)–negative and without CNS disease at first post-CART assessment (21–40 days). Median duration of B-cell aplasia was 402 days (13 months). Seven patients (47%) experienced B-cell recovery, over half within 6 months (n = 4). Four patients (27%) relapsed following CART therapy (three CD19-positive; one unknown). Four patients (27%) underwent subsequent allogeneic HSCT due to early B-cell aplasia loss (n = 3) or relapse (n = 1); two died from transplant-related complications. Among four total deaths, two were due to disease relapse and two due to post-transplant complications. Median follow-up was 21

months (range 5–90). One-year overall survival (OS) and event-free survival (EFS) were 87% and 73%, respectively; two-year OS was 79% and EFS 53% (Figure 1).

Conclusions: CD19 CART therapy was efficacious and generally well tolerated in this DS-ALL cohort, with survival outcomes comparable to or exceeding those previously reported and substantially better than historical outcomes with chemotherapy alone in the relapsed setting. Rates of severe CRS and ICANS were lower than prior reports, likely reflecting low disease burden prior to infusion. Rare ocular toxicities were observed, highlighting potential population-specific toxicity considerations in DS-ALL. Allogeneic HSCT remained highly toxic and accounted for half of all deaths, underscoring persistent transplant-related risks in this population.

Clinical Trial Registry: N/A

Disclosure: Emily Hsieh reports consulting for Novartis. All other authors have nothing to declare.

P045

DEVELOPING PEDIATRIC ALLOGENIC STEM-CELL TRANSPLANTATION IN LOW-MIDDLE- INCOME COUNTRY: REPORT FROM MOROCCO

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Background: The implementation of allogeneic hematopoietic stem cell transplantation (allo-HSCT) in low and middle income countries is a challenge due to the problems of premises, human resources and the difficulty of access to drugs for transplant. We report the experience of the Pediatric Hematology and Oncology Center (CHOP) of Rabat (Morocco) since the initiation of the transplant program in 2020.

Methods: A retrospective analysis of all children who underwent allo-HSCT from June 2020 to October 2025 was done. Clinical characteristics, transplant procedures, and outcomes were analyzed.

Results: This descriptive study included 41 pediatric allo-HSCTs. The median age at transplantation was 5 years (9 months–17 years), with a male-to-female ratio of 1.4. Consanguinity was present in 45% of patients, including 75% first-degree consanguinity. The indications were
aplastic anemia (24 cases, including 11 Fanconi anemia), primary immunodeficiencies (7 cases), acute leukemias (7 cases), and thalassemia (3 cases).
Most donors were HLA-matched related donors (35 cases), while 6 transplants were haplo-identical. The source of stem cells was bone marrow (BM) in 39 cases and peripheral blood

(PB) in 2 cases. A total of 28 patients underwent myeloablative transplants and 13 had reduced intensity conditioning (Fanconi). Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine plus methotrexate (22 cases), cyclosporine plus mycophenolate mofetil (13 cases), cyclosporine, MMF and post-transplant cyclophosphamide in haplo-identical transplants (6 cases). Median time to neutrophil and platelet engraftment was J19 ± 6 and J22 ± 5, respectively. Primary graft failure was observed in 2 cases and secondary graft rejection in 4 cases. At last follow-up, 33 of 41 patients were alive (80%). Day-100 mortality (TRM) was 4/41 (9,5%). Causes of death were graft versus host disease (GVHD)-1, Veno Occlusive Disease (VOD)-1, and septis-2. Four children died post-day-100 due to relapse (2), two patients had rejection (aplastic anemia-1, Fanconi-1). Acute cutaneous GVHD occurred in 5 patients, chronic cutaneous GVHD in 4, and digestive GVHD in one patient.

Conclusions: Pediatric allo-HSCT at the CHOP of Rabat achieves encouraging outcomes with acceptable toxicity, despite limited resources. The progressive implementation of haplo-identical transplantation significantly expands access to curative therapy and represents a major advance for pediatric transplantation in Morocco.

Disclosure: Nothing to declare.

P046

RARE EWSR1 REARRANGEMENT IN AML

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Background: EWSR1 rearrangements are known as hallmark drivers in sarcomas but remain exceedingly rare in acute myeloid leukemia (AML). We report the first documented case of pediatric AML harboring two novel concurrent fusions, EWSR1::HOXA10 and CALD1::MEF2C. Notably, the patient achieved favorable long-term survival following allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Methods: A 5-year-old male presented with thrombocytopenia and fever and was diagnosed with AML-M7 based on MICM criteria. Bone marrow showed >90% cellularity with 52.5% blasts; flow cytometry revealed CD41/CD61/CD11b positivity. Cytogenetics showed a normal karyotype and negative FISH results. Targeted DNA-NGS identified mutations in *APC*, *NFE2L3*, and *EFL1*. Crucially, RNA-based NGS uncovered two in-frame fusion transcripts: an EWSR1 exon 7-to-HOXA10 exon 2 fusion, and a CALD1 exon 8-to-MEF2C exon 4 fusion, both validated by RT-PCR and Sanger sequencing.

Results: Considering the newly identified fusion genes, the patient underwent allo-HSCT from a matched related donor following induction chemotherapy. The transplantation procedure was uneventful, with no significant acute graft-versus-host disease (aGVHD). At last follow-up (9 months post-HSCT), the patient remains in complete morphological and molecular remission, with no evidence of minimal residual disease, demonstrating an excellent response.

Conclusions: This is the inaugural report of concurrent EWSR1::HOXA10 and CALD1::MEF2C fusions in AML. This case demonstrates the critical importance of molecular diagnostics in identifying rare fusion genes and confirms the efficacy of allogeneic hematopoietic stem cell transplantation (allo-HSCT), ultimately resulting in favorable clinical outcomes for the patient. These novel fusion genes may indicate potential therapeutic targets and warrant further investigation.

Disclosure: Nothing to declare.

P047

BETTER SURVIVAL FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN ELDERLY (>65 YEARS OLD) AML PATIENTS - RESULTS OF AN INTERNATIONAL, TWO-CENTER ANALYSES

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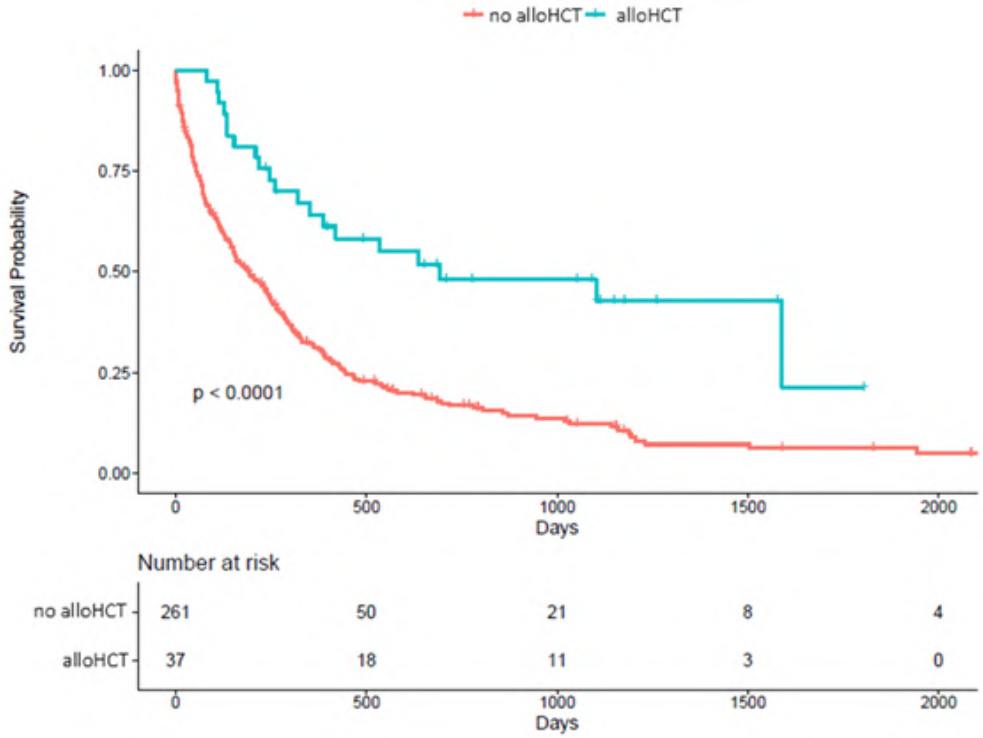
Background: Treatment of acute myeloid leukemia (AML) of elderly patients (>65 years) remains a challenge. Survival in this group is poor and most of the patients are ineligible for intensive treatment at the time of diagnosis. Data on elderly patients qualifying for allogeneic hematopoietic cell transplantation (alloHCT) as well as on the survival of this group of patients remains scarce. Herein, we present experience of Polish and German clinical centers in alloHCT of elderly patients diagnosed with AML.

Methods: In this double-center retrospective study we included 303 adult (>65 years old) patients diagnosed with AML, treated between 2018 and 2024 in the Department of Hematology and Transplantology of Medical University of Gdańsk, University Clinical Center, Poland and in the Department of Hematology, University Medical Centre, University of Rostock, Rostock, Germany. Inclusion criteria included age and AML as underlying disease. The performance status, data on demographics, ELN 2022 risk classification, treatment type and outcomes were evaluated. For the current analyses patients who underwent alloHCT were analyzed and the statistical analysis was performed. In survival analysis, Schoenfeld test was used to assess the proportionality of hazards. Variables which significantly affected survival in univariate Cox proportional hazards models were then considered in multivariate Cox HR analysis.

Results: In the analyzed group 37/303 (12%) patients underwent alloHCT procedure. The group included 21 (56.8%) male and 16 (43.2%) female patients. Median age of the group was 68 years (range 65-75)**.** Most of the patients in the analyzed group were below 70 years of age (n=26; 70%).
According to ELN 2022 AML risk classification, 5 patients (14%) were diagnosed with favorable, 14 patients (38%) with intermediate and 18 patients (49%) with adverse risk

AML. Twenty-six patients (70%) proceeded to alloHCT after completing first line treatment and 25 patients (67.6%) proceeded to alloHCT with complete remission. The median time of survival was 16.1 months (range 2.6-59.3). Seventeen out of 37 pts (46%) remain alive at the time of analysis with median time of follow-up of 2.9 years (range 0.6-4.9; alive pts). Undergoing allo-HCT was significantly associated with an increased probability of surviving 2 years after diagnosis (OR 4.99, 95% CI 1.28-19.50, p=0.0207). In both univariate and multivariate models alloHCT procedure was significantly associated with decreased hazard – HR 0.37, 95% CI 0.24-0.59, p<0.0001 and HR 0.55, 95% CI 0.32-0.97, p=0.0373 respectively. As expected, population that underwent alloHCT presented significantly (p <0.0001) better overall survival compared to the patients who did not undergo the procedure (Figure 1.)

Figure 1. Overall survival analysis comparing survival of elderly patients who underwent and did not undergo alloHCT. Survival was possible to assess in case of 298 patients.



Conclusions: Data on alloHCT among elderly patients remains scarce, hence more data is needed to ensure optimal treatment and care for this group of patients. This two-center analysis adds a new perspective to the treatment of elderly patients. The preliminary findings of the study support that alloHCT eligibility must be carefully evaluated in older individuals in order to identify eligible patients that might benefit from this potentially curative procedure.

Disclosure: Nothing to declare.

P048

BEYOND SUPPORTIVE CARE: ALLOGENEIC STEM CELL TRANSPLANTATION IN CHILDREN WITH FUCOSIDOSIS

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Background: Fucosidosis is a rare autosomal recessive lysosomal storage disorder caused by deficiency of α-L-fucosidase, leading to progressive accumulation of fucose-containing substrates in multiple organs. The disease presents with a broad clinical spectrum, including neurodevelopmental delay, recurrent infections, dysostosis multiplex, angiokeratomas, and progressive neurodegeneration, resulting in significant morbidity and early mortality. Currently, treatment is largely supportive, and no definitive disease-modifying medical therapy is available.
Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents a potential therapeutic strategy for selected lysosomal storage disorders by providing sustained donor-derived enzyme through cross-correction. However, due to the extreme rarity of fucosidosis, evidence regarding HSCT outcomes is limited to small case series, particularly in pediatric patients, and long-term neurological outcomes remain insufficiently characterized. Reporting real-world pediatric HSCT experiences is therefore essential to better define the role and feasibility of transplantation in this ultra-rare disease.

Methods: We performed a retrospective single-center analysis of pediatric patients with fucosidosis who underwent allo-HSCT. Diagnosis was established based on clinical findings, reduced α-L-fucosidase enzyme activity, and/or confirmatory molecular genetic testing. Collected data included demographic characteristics, disease phenotype, pre-transplant neurological and systemic involvement, transplant characteristics, engraftment status, graft-versus-host disease (GVHD), and post-transplant clinical outcomes.

Results: Three pediatric patients underwent allo-HSCT at a median age of 73 months (range: 10–110 months). Bone marrow was used as the stem cell source in all cases. Two transplants were from 10/10 and 9/10 matched-unrelated donors , and one was from a fully HLA-matched maternal donor. All patients received busulfan-based conditioning regimens combined with fludarabine, ATG, and thiotepa. One patient required a second allo-HSCT because of declining donor chimerism and increasing enzyme levels suggestive of graft rejection; defibrotide was administered due to pre-existing hepatic involvement.
Full donor chimerism and sustained engraftment were achieved in all patients. No acute or chronic GVHD was observed. One patient presented with advanced neurological involvement at the time of transplantation and demonstrated clinically meaningful post-transplant neurological improvement, including a marked reduction in dystonia and the emergence of social interaction, followed by sustained neurological stabilization. Of the remaining two patients, the youngest, transplanted at 10 months of age, exhibited mild developmental delay with inability to sit independently at baseline. The third patient had pre-transplant motor impairment with inability to ambulate, a history of seizures, and hearing impairment. All patients are alive and disease-free with stable graft function at a median follow-up of 75

months (range: 50–81 months). The summaries of the patients are available in Table 1.

Table 1. The summary of the cases

Case	Gender	Transplantation age (Months)	Donor	Follow-up time (Months)	The last chimerism	The last Enzyme level (nmol/h/mg protein) (76,7 +/- 29,4)	The last clinical findings
FO	M	110	MRD	75	64	67,9	Decrease in dystonia, no seizures, and partial head control
YEO	M	10	• 1. MUD • 2. 9/10 UD	81	100	92	Obeys commands, walks, and speaks 4-5 words
YD	M	74	MRD	50	99	53,4	Walking with support, trying to speak with nonsensical sounds

M: Male, MRD: Matched related donor, MUD: Matched unrelated donor, UD: Unrelated donor

Conclusions: Allo-HSCT is a feasible and safe disease-modifying treatment option for pediatric fucosidosis, providing durable engraftment and long-term disease-free survival. Neurological stabilization or improvement may be achievable even in patients with advanced disease. These findings support early referral and timely transplantation to optimize outcomes in this rare disorder.

Disclosure: None.

P049

PATIENTS WITH MULTIPLE SCLEROSIS ABOVE AGE 60 HAVE NEUROLOGICAL RESPONSES TO AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTS SIMILAR TO YOUNGER INDIVIDUALS: A SINGLE-CENTER EXPERIENCE

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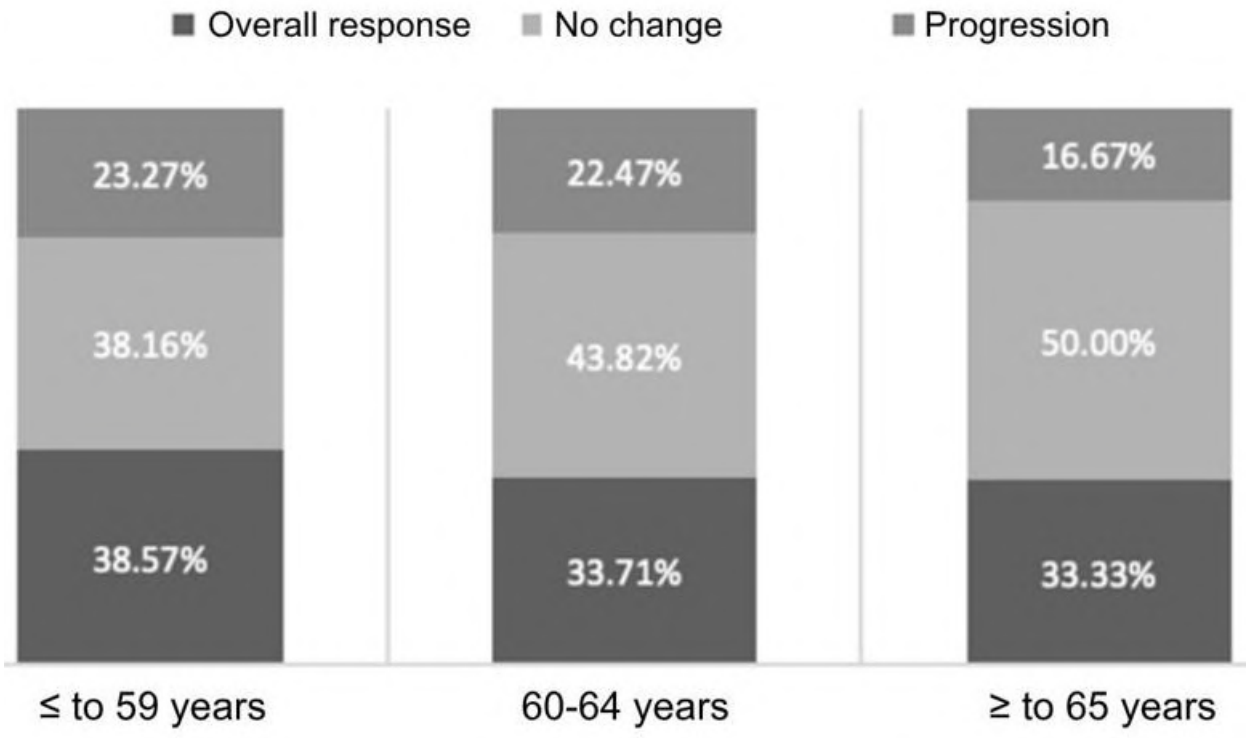
Background: Multiple sclerosis (MS) is an autoimmune disease of the central nervous system characterized by inflammation, demyelination, and progressive neurodegeneration. Autologous hematopoietic stem cell transplantation (aHSCT) has emerged as a therapeutic option that eliminates autoreactive lymphocytes and reconstitutes the immune system. Patients older than 60 years have been reported to fare worse when given aHSCT for other diseases.

Methods: MS patients prospectively treated with aHSCT using the "Mexican Method" were analyzed. This protocol combines high-dose cyclophosphamide (200 mg/kg), rituximab 1 000 mg, filgrastim, and MESNA.

Results:



A total of 1 438 persons were accrued; 120 (8.3%) were ≥ 60 years. The positive response rate (PRR) for the cohort was 75.3% (IQR 72–78%), with 77.4% for RRMS, 72.7% for PPMS, and 74.7% for SPMS. By age, PRR was 75.2% (< 60 years) and 77.0% (≥ 60 years; p = 0.64). Subgroups 60–64 and ≥ 65 showed comparable PRR. Early complications occurred in 2.1% of patients < 60 and 5.8% of those ≥ 60 (p = 0.02).

Conclusions: Employing the "Mexican Method," PRR after aHSCT was 75.3%, with no significant difference between age groups. Although older patients had slightly more early complications, overall outcomes were similar, suggesting that age > 60 should not preclude aHSCT in MS.

Disclosure: Nothing to declare

P050

RESULTS OF AN ITALIAN SURVEY FOR CELLULAR THERAPY PRODUCTS STORAGE AND DISPOSAL: NEED FOR AN UPDATE OF 2014 GUIDELINES

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Background: The current Italian guidelines for disposal of cryopreserved autologous stem cells (SCs) have been published over ten years ago (2014). Due to the rapidly evolving

landscape in hematopoietic stem cell transplantation and cellular therapy, a nationwide questionnaire was administered to the clinical Transplant Programs (TPs), to survey the practice of their Tissue Establishments (TEs) and lay the foundation for updating disposal guidelines. We report the most significant results.

Methods: An online survey, composed of two parts (autologous and allogeneic SCs and lymphocytes) was launched by *Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare (GITMO)* and developed with the contribution of scientific societies in the field and the competent authorities. A total of 56 questions (34 for autologous and 22 for allogeneic setting, respectively) were administered to 87 TPs in January 2025 with the aim of assessing the centers' compliance to the 2014 guidelines throughout the year 2024 and the reasons of non compliance, if any. The survey results provide a basis to develop updated guidelines, taking into account not only the changing clinical landscape, but also the ethical and legal framework and the financial burden and logistics.

Results: A total of 69 out of 87 TPs (79%) replied by May 2025. Although 87% of centers declare to apply the 2014 guidelines for autologous SCs, only 62% of them apply all criteria. The policies of other centers vary due to a lack of specific regulation on this topic or the need of a signed informed consent from the patient Furthermore, 84% of respondents state that that their disposal policy is influenced by the availability of cold storage space. Increased storage demand for both autologous and allogeneic SCs and lymphocytes was documented (17% and 67% of centers, respectively), particularly regarding allogeneic products during the Covid-19 pandemic. However, only 57% of centers have a policy for the disposal of allogeneic products. Fifty-six percent of centers supports an update of 2014 guidelines, including: the application also to allogeneic products, a specific regulation and a standardized informed consent. Finally, over 60% of centers are available for releasing unused cryopreserved allogeneic hematopoietic stem cells for transplantation to other patients.

Conclusions: A nationwide survey on storage and disposal of autologous and allogeneic SCs and lymphocytes, covering the great majority of Transplant Programs in Italy, allowed to appreciate the extent of current application of 2014 guidelines and highlighted heterogeneity of duration of cryopreservation and graft disposal among centers. The questionnaire pointed out the need to update and improve the 2014 guidelines according to the rapidly evolving clinical landscape, ethical, legislation and logistical challenges.

Disclosure: Nothing to declare

P051

SECOND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR RELAPSED ACUTE LEUKEMIA AND MYELODYSPLASTIC SYNDROMES: A SINGLE-CENTER EXPERIENCE

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Background: Relapse after allo-HSCT (allogeneic hematopoietic stem cell transplantation) remains the main barrier to cure in high-risk hematologic malignancies, including Acute Myeloid Leukemia (AML) and Myelodysplastic Syndromes (MDS), and is associated with an extremely poor prognosis. For selected patients, a second allo-HSCT (2nd-alloHSCT) may constitute the only potentially curative option; however, outcomes are highly variable , with high early non-relapse mortality (NRM) which ranges between 30-60% and long-term survival rarely surpassing 20–25% in most published cohorts. We present a single-center retrospective analysis evaluating the real-world outcomes of 2nd-alloHSCT in patients relapsing after a first alloHSCT.

Methods: We retrospectively analyzed data from patients with acute leukemia and MDS who underwent a 2nd-alloHSCT due to progression or relapse at our center between June 2002 and August 2024.

Results: The baseline characteristics of the included patients are summarized in **Table 1**. Despite the expected high-risk profile, the median overall survival (OS) after the second transplant was 6.3 months (95% CI, 2.1–24.4). OS probability at one and five years were 33% (95% CI, 14–55%) and 25% (95% CI, 8–48%), respectively **(Figure 1)**. The cumulative incidence of relapse (CIR) was 39% at one year and 46% at five years. NRM was 28% at both one and five years **(Figure 1)**. Eight patients relapsed after the 2nd HSCT, with an early median time to relapse of 2.9 months (range 0.6–12), 5 out of which had the same donor. As for the 10 patients who received the second allo-HSCT from a different donor, only 3 had a disease relapse. Five patients died due to transplant-related mortality: bilateral pneumonia (n=2), acute GVHD with septic shock (n=1), isolated acute GVHD (n=1) and veno-occlusive disease (n=1).

Table 1: Baseline Characteristics of the 2nd allo-HSCT Cohort (N=18).

Characteristic	Value
Age, median (range), years	45.5 (24 – 62)
Diagnosis, AML / ALL / MDS, n (%)	9 (50%) / 7 (39%) / 2 (11%)
Interval 1st-2nd HSCT, median, months	14.1 (range 3.4 – 64)
ECOG PS at 2nd HSCT (0 / 1 / 2), n=15	9 (60%) / 3 (20%) / 3 (20%)
Second Donor, Same / Different, n (%)	8 (44%) / 10 (56%)
Donor Type, Matched / Mismatched / Haplo	10 (55%) / 5 (28%) / 3 (17%)
Conditioning, MAC / RIC, n (%)	6 (33%) / 12 (67%)

Table 1: Baseline Characteristics of the 2nd allo-HSCT Cohort (N=18).

Stem Cell Source, Peripheral Blood, n	18 (100%)
GVHD Prophylaxis, CNI-based, n (%)	18 (100%)

Abbreviations: HSCT: Hematopoietic Stem Cell Transplantation; **AML:** Acute Myeloid Leukemia; **ALL:** Acute Lymphoblastic Leukemia; **MDS:** Myelodysplastic Syndrome; **ECOG PS:** Eastern Cooperative Oncology Group Performance Status; **MAC:** Myeloablative Conditioning; **RIC:** Reduced Intensity Conditioning; **GVHD:** Graft-versus-Host Disease; **CNI:** Calcineurin Inhibitor.

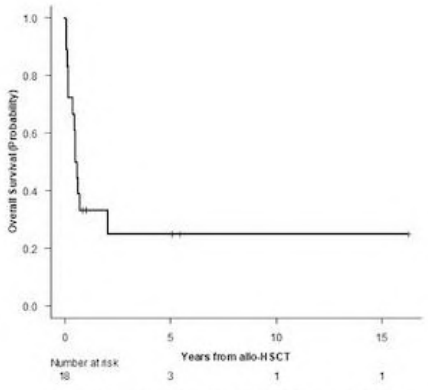

Figure 1. Overall survival after second allogeneic HSCT (N=18)

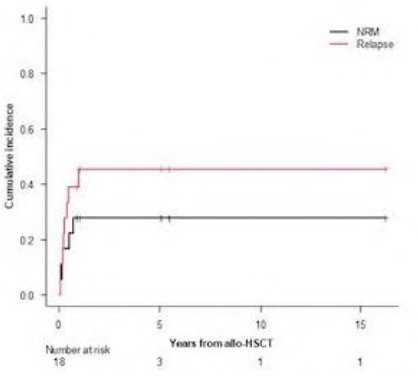

Figure 2. Cumulative incidence of relapse and non-relapse mortality after second allo-HSCT (N=18).

Conclusions: These results highlight the potential of second allo-HSCT as a salvage strategy, despite its poor results. Our data have certain limitations, such as the sample size and the heterogeneity of the procedures, which restrict the ability to identify prognostic factors or draw generalizable conclusions. Despite these constraints , this study underscores the importance of individualized evaluation when considering a second allo-HSCT and supports its use in carefully selected patients.

Disclosure: Nothing to declare

P052

IMPACT OF PRE-TRANSPLANT EVENTS ON THE FEASIBILITY OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remain a potential curative therapy for a variety of malignant and non-malignant diseases. However, various events may hinder or delay its achievement and compromising its benefits. The aim of our study was to assess the impact of pre-transplant events on allo-HSCT feasibility and overall survival (OS).

Methods: Retrospective study conducted over a three-year period (2022–2024) at the National Bone Marrow Transplant Center in Tunisia (CNGMO). It included all patients referred for allo-HSCT and discussed during the bi-monthly transplant committee meetings. Patients' outcome was analyzed according to whether the transplant was ultimately performed as well as the factors responsible for delays or failure to proceed to transplantation. Since 2023, only patients with high-risk hematological malignancies have been eligible for haploidentical HSCT, in accordance with a standardized eligibility checklist established by the CNGMO transplant committee.

Results: Over the three-year study period, 278 patients were referred for allo-HSCT: 97 in 2022, 82 in 2023, and 99 in 2024, corresponding to an average of 93 referrals per year. Acute leukemia (AL) represented the predominant indication (68.5%), including acute myeloid leukemia (AML; n = 93, 33.5%) and acute lymphoblastic leukemia (ALL; n = 97, 35%). Overall, 120 patients (43%) proceeded to allo-HSCT, with a median age of 27 years (range 5–55). Pediatric patients accounted for 28% of the cohort, and the sex ratio was 0.9. Among 18 patients considered for haploidentical HSCT, only 3 underwent transplantation. Transplantation was carried out as initially scheduled in 89% of cases. A delay occurred in 13 patients (11%), mainly due to an infectious complications (n = 5), the need for pre-transplant disease reassessment (n = 4), or a logistical constraints (drug or radiotherapy unavailability, limited bed capacity, n = 4). The median duration of postponement was 30 days (range, 10–50 days). The median time from first presentation to actual allo-HSCT was 3 months (range, 1–12 months).
Among the 96 patients transplanted with malignant hematologic disease, 69 (72%) were in CR1, 24 (25%) in CR2, and 3 (3%) had refractory disease. Total body irradiation (TBI) was performed in 18.5% of patients with ALL. Post-transplant relapse occurred in 24 patients (20%), with a median time of 6 months (range, 1–34 months).
Allo-HSCT was not performed in 158 patients (57%): 48 in 2022, 53 in 2023, and 57 in 2024. The reasons for non-achievement of allo-HSCT are summarized in table 1.
The median overall survival (OS) was 89 months for transplanted patients, versus 36 months for non-transplanted patients ($P < 0.001$). At last follow-up, 76% of transplanted patients were alive, versus 41% of non-transplanted patients.

Table 1 : Reasons for non-achievement of the allo-HSCT

Reasons	N=158
Disease relapse	57 (36%)
Death prior to transplantation	10 (6%)
Signifiant patient comorbidities	13 (8%)
Refusal by either the donor or the recipient	3 (2%)
Age < 5 years or low body weight (referred to a pediatric transplant center)	5 (3%)
Reassessment resulting in withdrawal of the allo-HSCT indication	10 (6%)
logistic constraints	4 (3%)
Unavailability of essential Drugs (cyclosporine, chemotherapy…) or TBI	5 (3%)
Significant donor comorbidities	9 (7%)
For patients referred for haploidentical HSCT • Presence of donor-specific anti-HLA antibodies (DSA) • Rejected indication following committee review • Logistical constraints	15 (9%) 4 4 7
Excessive delay since the last therapy (no dose/intensity effect)	7 (4%)
Lack of feedback information after initial referral	20 (13%)

Conclusions: Pre-transplant events may hinder the completion of allo-HSCT and consequently have a negative impact on overall survival. Early recognition and proactive management of these factors are essential to improve transplant feasibility and patient outcomes.

Disclosure: Nothing to declare.

P053

FAVOURABLE SURVIVAL IN ALLOGENIC STEM CELL TRANSPLANT RECIPIENTS ADMITTED TO INTENSIVE CARE; 6-YEAR RETROSPECTIVE REVIEW FROM A UNIVERSITY HOSPITAL TRANSPLANT CENTRE IN THE UK

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Background: Recipients of allogenic haematopoietic cell transplant (allo-HCT) are one of the most vulnerable groups of haematology patients during critical illness attributed to both severe immunocompromised state and treatment related toxicities. Historically allo-HCT patients have poor outcomes after Intensive care unit (ICU) admissions.
The aim was to evaluate the outcome of allo- HCT recipients admitted to ICU during the peri-transplant period in our centre. Primary outcome measured was 90-day mortality (defined as 90 days mortality from admission to ICU). Other outcomes measured included in-ICU, in hospital (defined as mortality within 90 days from any cause after admission and ICU step down) and 1-year mortality rates.

Methods: Between 1st January 2019 and 31st December 2024, patients who had allo-HCT requiring ICU admission during the peri-transplant period (period between the start of conditioning therapy up to day 100 post cell infusion) were included. Retrospective data were collected from electronic patients' record.

Results: During this period, 17 patients met the inclusion criteria with 23 ICU admissions between them. Three patients required multiple admissions. 294 patients received allo-HCT at our centre with incidence of ICU admission in the peri-transplant period at 5.7% (17/294). The median age was 49 years (range 17-67), 7/17 were female patients (41.1%) and 11/17 patients (64.7%) had high (score≥ 3) Haematopoietic Stem Cell Transplantation-Specific Comorbidity Index (HCT-CI) score. The most common indication for transplant was acute leukaemia 15/17 (88.2%) and 8/17 (47%) patients underwent myeloablative conditioning. The 90-day mortality of this cohort was 29.4% (5/17) which marginally increased to 35.2% (6/17) at one year. The in-ICU and in-hospital mortality rates were 23.5% (4/17) and 35.2% (6/17) respectively. The median length of ICU stay was 8 days (range 2-89). The median time to ICU admission from stem cell infusion was 15 days (range1-90 days). Comparing the in-ICU and 1-year mortality rates in our centre to national published data by Intensive Care National Audit and Research Centre (ICNARC) published in 2022 for non-haematological ICU admissions; 23.5% vs19-26.3% and 35.2% vs 26-28% respectively.
On reviewing baseline characteristics of the 90-day survival cohort to 90-day mortality cohort, no clear trend was noted except younger patients and more females in the latter,

though numbers are small for significance analysis. The median time to ICU admission from stem cell infusion was later in the 90-day mortality cohort at 22.5 days (range 14-75) compared to 15 days (range 1-90) which could be explained by less easily reversible cause of admission such as disease relapse. As expected, those in the 90-day mortality group all needed more than one organ support and the mortality rate was almost double in patients who required invasive mechanical ventilation.

Baseline demographic	**Overall N=17**	**90-day survival N=12**	**90-day mortality N=5**
Median age (range)	49 (17-67)	50.5 (17-67)	31 (19-66)
Age> 65	2 (11.7%)	1 (8.3%)	1 (20%)
Female	7 (41%)	4 (33.3%)	3 (60%)
HCT-CI score Low risk= 0 Intermediate risk= 1-2 High-risk= ≥ 3	 2 (11.7%) 4 (23.5%) 11 (64.7%)	 1 (8.3%) 3 (25%) 8 (66.6%)	 1 (20%) 1 (20%) 3 (60%)
Transplant indication ALL AML CML CMML	 8 (47.05%) 7 (41.1%) 1 (5.5%) 1 (5.5%)	 5 (41.6%) 5 (41.6%) 1 (8.33%) 1 (8.33%)	 3 (60%) 2 (40%) 0 0
Transplant conditioning Myeloablative RIC	 8 (47%) 9 (53%)	 5 (41.6%) 7 (58.3%)	 3 (60%) 2 (40%)
ICU characteristics	Overall episodes N=23	90-day survival N=18	90-day mortality N=5
Median time to ICU admission from stem cell infusion in days (range)	15 (1-90)	15 (1-90)	22.5 (14-75)
Reason for admission 1. Infection/sepsis 2. Mucositis / airway compromise 3. Posterior reversible	 12 (52.1%) 3 (13.0%) 2 (8.6%)	 11(61.1%) 2 (11.1%) 2 (11.1%)	 1(20%) 1(20%) 0

Baseline demographic	Overall N=17	90-day survival N=12	90-day mortality N=5
encephalopathy syndrome (PRESS) 4. Disease relapse 5. Graft-versus-Host Disease 6. Others (endothelial dysfunction, non-infective pulmonary pneumonitis, pulseless electrical activity)	2 (8.6%) 1 (4.34%) 3 (13.0%)	0 0 3 (16.6%)	2 (40%) 1 (20%) 0
Organ support Single Multi-organ support	12 (52.1%) 11 (47.8%)	12 (66.6%) 6 (33.3%)	0 5 (100%)
Invasive mechanical ventilation	6 (26.08%)	4 (22.2%)	2 (40%)

Conclusions: The overall incidence of ICU admission in our centre was low, compared to rates reported in literature (9-20%).This study highlighted overall comparable outcomes of this high-risk cohort from admission to critical care with non-haematological admissions. Additionally, we did not identify any risk factors that could predict survival; thus, we advocate for consideration of allo-HCT recipients for critical care admission regardless of their initial functional status.

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Adrian Maraj- travel grant - Sanofi
Hwai Jing Hiew: Speaker fees Roche Pharmaceutical, Travel grant Jazz Pharmaceutical, Sanofi

P054

G-CSF ADMINISTRATION AND CLINICAL OUTCOMES IN PATIENTS WITH RELAPSED/REFRACTORY B-CELL LYMPHOMAS TREATED WITH CAR-T CELLS: A MONOCENTRIC EXPERIENCE

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Background: Chimeric Antigen Receptor (CAR)-T cells are widely used to treat relapsed/refractory lymphoproliferative disorders, due to their high efficacy. However, hematological toxicity, such as severe neutropenia, frequently occurs. Granulocyte colony-stimulating factor (G-CSF) can be used to manage CAR-T related neutropenia, though concerns remain regarding its impact on toxicity, infection rates and duration of hospitalization. This study evaluates a single-center cohort of patients receiving G-CSF for neutropenia occurring early after infusion (≤30 days).

Methods: We retrospectively analyzed 45 patients treated with CAR-T [Axi-cel (n=29; 64%) or Tisa-cel (n=16; 36%)], between March 2022 and August 2025 for B-cell lymphoproliferative disorders.
G-CSF was administered when neutrophil levels were < 500/μL.

Results: Demographic characteristics are reported in the Table. The median age was 60 years (range 29-75). At the time of apheresis, most patients (80%) exhibited progressive disease. Seventy-one percent of patients (n=32) had received three or more prior lines of therapy. A bridging therapy before CAR-T infusion was required in 78% of cases. Thirty-five (78%) patients experienced severe neutropenia and needed G-CSF support, starting at a median of 4 days post-infusion (range 0-11) with a median duration of 4 days (range 1-124). Following CAR-T administration, cytokine release syndrome (CRS) was observed in 82% of patients, with a median onset of 3 (range 0-13) days and a median duration of 4 (range 1-26) days; only 2% were grade 3-4. Notably, CRS was observed in 89% (n=31) and 60% (n=6) cases of G-CSF and non-G-CSF-treated group, respectively.
Neurological toxicity occurred in 13% of cases, with 7% grade 3-4. Notably, the incidence of neurological toxicity affected only the G-CSF group [6 (17%) vs 0].
Median duration of hospitalization was similar in patients receiving or not G-CSF, being 19 (range 9-67) days in both cases.
Overall infections were documented in 11% of patients, occurring in 4 (sepsis n=1, urinary tract infection n=2, Sars-CoV-19 n=1) cases within the G-CSF group and 1 (sepsis n=1) case in the no-G-CSF.
We observed 6 (13%) deaths, with 5 (11%) attributed to disease progression. With a median follow-up of 17 months (95% CI, 11–20), the median progression-free survival (PFS) was 39 months (95% CI, 26–NR). The rate of PFS at 12 and 18 months was 76% and 72%, respectively. Median overall survival (OS) was not reached with estimated OS rates of 85% at12 and 18 months.

Characteristics (%)	Overall cohort N=45
Median age, years (range) Male	60 (29-75) 23 (51)
Diagnosis DLBCL second line/ ≥ 3 FL PMBCL	 35 (78) 13 (29)/22 (49) 9 (20) 1 (2)
Median number of prior lines of therapy (range) Previus ASCT, n (%)	2 (1-5) 4 (9)
Disease status at time of apheresis CR PR SD PD	 2 (4) 5 (12) 2 (4) 36 (80)
Bridging Therapy R-Pola R-Pola-Benda R-Lenalidomide Zanubrutinib Radiotherapy Other	35 (78) 5 (11) 16 (36) 4 (9) 1 (2) 2 (6) 7 (16)
Disease status at CAR-T infusion CR PR PD SD	1 (2) 21 (47) 4 (9) 19 (42)
Disease status at CART infusion in G-CSF vs no G-CSF group CR PR PD SD	-/1 (2) 16 (36)/5 (12) 3 (7)/1 (2) 16 (36)/3 (7)
CAR-T product Axi-cel Tisa-cel	29 (64) 16 (36)

Characteristics (%)	Overall cohort N=45
CRS grade 3-4 Median time to CRS, days (range) Median duration of CRS, days (range) Use of tocilizumab for CRS Use of steroids for CRS	37 (82) 1 (2) 3 (0-13) 4 (1-26) 18 (40) 7 (16)
ICANS grade 3-4 Median time to ICANS, days (range) Median duration of ICANS, days (range) Corticosteroids for ICANS	6 (13) 3 (7) 4 (3-6) 4 (2-9) 5 (11)
PNN< 500/µL Median time to PNN<µL, days (range) Use of G-CSF Median time to G-CSF, days (range) Median duration of G-CSF use, days (range)	35 (78) 4 (0-11) 35 (78) 4 (0-11) 4 (1-124)

Conclusions: Most patients undergoing CAR-T infusion experience neutropenia that can be managed with the use of G-CSF. Despite in our cohort CRS and neurological toxicity were more frequently registered in the G-CSF group, low numbers prevented us to make comparisons between groups. The potential effects of G-CSF in influencing CAR-T toxicities thus deserves further investigation, with several factors, including those inherent to disease and patient characteristics, which may have influenced post-infusion outcomes.

Disclosure: None.

P055

ROLE OF GILTERITINIB IN PREVENTING RELAPSE IN FLT3-MUTATED ACUTE MYELOID LEUKEMIA FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT: A REAL-WORLD COHORT STUDY

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Background: FLT3 mutations are common in acute myeloid leukemia (AML) and are associated with high relapse rates, even after allogeneic hematopoietic cell transplantation (allo-HCT). Ongoing studies evaluate the efficacy of FLT3 inhibitors as maintenance therapy for relapse prevention following allo-HCT, seeking to establish the relationship with

measurable residual disease (MRD) in the peri-transplant period. Gilteritinib, a highly selective, next-generation FLT3 inhibitor, is functional against both internal tandem mutation (ITD) and tyrosine kinase domain (TKD) mutant forms. We assessed the response and safety of gilteritinib following allo-HCT in patients diagnosed with AML based on the peri-transplant status of MRD.

Methods: This is an observational, retrospective, single-centre study reviewing the medical records from December 2023 to November 2025 of patients diagnosed with AML undergoing post-transplant and gilteritinib use after allo-HCT. Data were collected on demographic characteristics, pre- and post-transplant reassessment by flow cytometry of measurable residual disease performed at months 1, 3, 6, 9, 12, 18, and 24, also monitoring NPM1 status in peripheral blood (PB) during this time, FLT3 mutation and association with NPM1 mutation at diagnosis, timing of drug initiation, dosage and adverse effects.

Results: A total of 8 patients (88% women), diagnosed with either FLT3-ITD (6/8) or FLT3-TKD (2/8) mutations, received gilteritinib (Table 1). They underwent transplantation in cytological remission with just 2 patients having positive MDR prior to allo-HCT, most of them receiving myeloablative conditioning regimens and the donors being haploidentical in most cases.

Patient # Sex	Mutations	ELN Risk	Age at transplant	Pre-HCT status	Conditioning	Donor	Initial dose	Time of initiation (month post-HCT)	Reason
Patient 1 Female	NPM1 FLT-TKD TP53	Adverse	26	Negative MRD	MAC	MUD	80mg *	3	Maintenance
Patient 2 Male	NPM1 FLT3-ITD	Intermediate	63	Negative MRD	RIC	MSD	80mg	3	Positive MRD post-HCT Mixed chimerism
Patient 3 Female	NPM1 FLT3-ITD	Intermediate	67	Positive MRD	RIC	Haploidentical	80mg	3	Positive MRD pre-HCT

Patient 4 Female	t(6;9)/DEK::NUP214 FLT3-ITD	Adverse	22	Aplasia	MAC	MUD	120mg*	1.5	Maintenance
Patient 5 Female	NPM1 FLT3-ITD	Intermediate	38	Negative MRD	MAC	Haploidentical	120mg*	6	Maintenance
Patient 6 Female	NPM1 FLT3-TKD	Intermediate	55	Negative MRD	MAC	Haploidentical	40mg	3	Maintenance
Patient 7 Female	NPM1 FLT3-ITD	Intermediate	32	Negative MRD	MAC	Haploidentical	80mg	3	Maintenance
Patient 8 Female	NPM1 FLT3-ITD	Intermediate	57	Positive MRD	MAC	Haploidentical	120mg*	6	Positive MRD pre-HCT

Table 1. Demographic and transplant characteristics. Underlined patients had positive MRD pre-HCT. RIC: reduced intensity conditioning. MAC: myeloablative conditioning. MUD: matched-unrelated donor. MSD: matched-sibling donor. * Marks patients requiring dose adjustment.

We present the evolution of each patient over time (Figure 1), from transplantation to the last follow-up (November 2025).

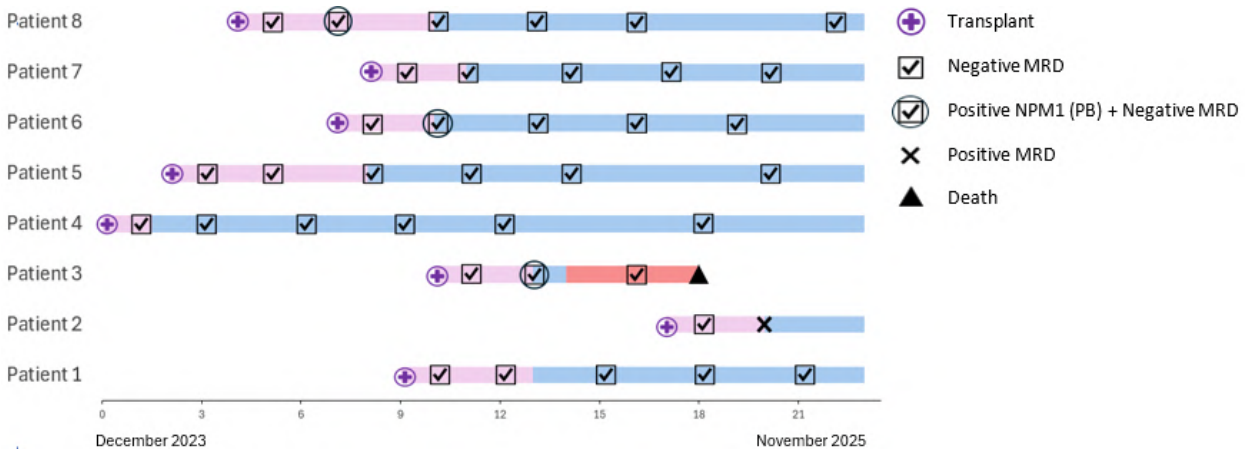

Figure 1. Representing follow-up (months) post-HCT until gilteritinib is initiated (pink segment) and evolution after (blue segment). It also shows drug discontinuation (red segment).

The median time to initiate gilteritinib was 90 days (IQR:45). Regarding its initial dose, 50% of the patients required adjustment due to adverse effects (3/4 suffered from moderate cytopenias, upholding acceptable counts after reducing 120mg to 80mg). The other patient experienced both papilledema and cytopenias, requiring a reduction in dosage from 80mg to 40mg. Other two had their dose reduced to 40mg due to hepatotoxicity with one subsequent discontinuation. This patient died from an undetermined infectious cause after a long hospital stay, with the possibility of an undocumented extramedullary relapse as well. Patient starting at 80mg did not need adjustment and other one with positive MRD at 3 months changed dose from 80mg to 120mg due to mixed chimerism.

Conclusions: Our study shows encouraging results in patients diagnosed with moderate to adverse risk FLT3-mutated AML with both positive and negative pre-transplant MRD treated with gilteritinib after allo-HCT with acceptable toxicity in most cases. The role of gilteritinib after allo-HCT warrants further investigation, as earlier initiation may prevent hematological relapse even in high-risk disease. Larger studies are needed to continue evaluating safety and efficacy of gilteritinib in this setting.

Disclosure: Nothing to declare.

P056

AN EVOLVING LANDSCAPE – HOW CHANGING CONDITIONING REGIMES CAN IMPROVE MYELOFIBROSIS TRANSPLANT OUTCOMES

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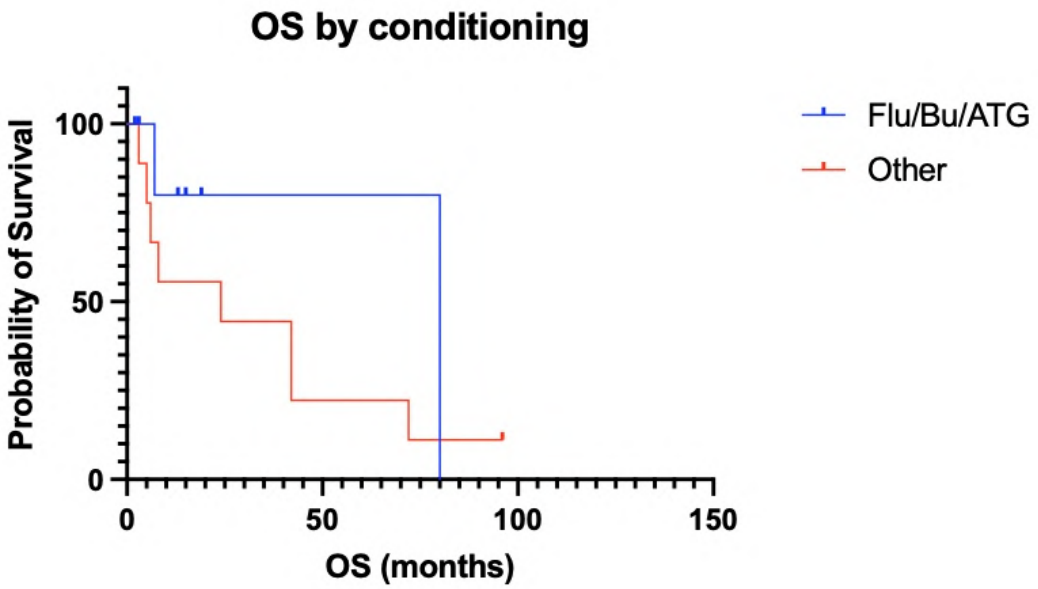
Background: Allogeneic stem cell transplantation (allo-SCT) in myelofibrosis carries significant risks, and outcomes remain suboptimal, reported 5-year survival rates range from 40% to 60%. Despite this, it remains the only potentially curative option. Conditioning regimens vary widely across centres, and with increasing referrals to Barts Health NHS Trust, we aimed to review our outcomes to ensure the highest standard of care.

Methods: We reviewed our transplant data from 2010 to 2025, focusing on outcomes over time, particularly in relation to the introduction of new conditioning regimens. Patient demographics, diagnosis and transplant dates, conditioning regimen, treatment history, cytogenetics, molecular results, and donor type were reviewed. The primary outcome measured was overall survival (OS), secondary was event free survival (EFS).

Results: 16 patients underwent allo-SCT during this period. Seven received stem cells from matched sibling donors, eight from volunteer unrelated donors, and one from a haploidentical donor. 11 patients had primary myelofibrosis, four had secondary myelofibrosis and one had myelofibrosis transformed to AML. The average age at transplant was 55 years, with a male predominance.
Seven patients received Fludarabine/Busulphan/Antithymocyte globulin (Flu/Bu/ATG) conditioning (Fludarabine 30mg/m^2 for 5 days, Busulphan 3.2mg/kg for 2 days and rabbit ATG 2.5mg/kg for 2 days), seven received Fludarabine/Cyclophosphamide (Flu/Cy) (Fludarabine 25mg/m^2 for 5 days and Cyclophosphamide 1g/m^2 for 2 days), and two received Fludarabine/Melphalan (Flu/Mel) (Fludarabine 25mg/m^2 for 5 days and Melphalan 100mg/m^2 on one day). The haploidentical transplant received Fludarabine 30mg/m^2 for 5 days, Cyclophosphamide 14.5mg/kg for 2 days and TBI 200cGy with post-transplant Cyclophosphamide. From 2022, all transplants utilised Flu/Bu/ATG, with only one patient receiving this prior to 2022. In the Flu/Bu/ATG group two have died (29%) and five are alive (71%), compared to eight deaths (89%) and one alive (11%) in the other group.
Five patients had one prior treatment line, five had two, and six had more than two. Therapies included Ruxolitnib, Momelotinib, splenic irradiation and Hydroxycarbamide amongst others.
Cytogenetics were abnormal in four patients (two in each regimen group), normal in nine, and unknown in three. Molecular screening revealed JAK2 positivity in 10 patients, CALR in two, MPL in one and the remainder having a normal screen. Several patients had additional molecular abnormalities.
The median OS and EFS were 42 and 24 months, respectively. Stratifying by conditioning, patients receiving Flu/Bu/ATG had a median OS and EFS of 80 months, compared to 24 months (OS) and 6 months (EFS) for those treated with Flu/Cy or Flu/Mel.
Eight patients developed acute Graft versus host disease (GvHD) (four in each group), four progressed to chronic GvHD (two from each group). Acute GvHD was the cause of death for three patients (one from the Flu/Bu/ATG group and 2 from the other group). Other causes of death included pneumonia, AML and an acute illness. Four causes of death are unknown.

Graft failure occurred in four patients (25%).



Conclusions: Although limited by a small sample size, these findings indicate that the Flu/Bu/ATG conditioning regimen may be associated with improved outcomes. This supports its adoption as the preferred approach, in line with BSH guidelines.

Disclosure: Nothing to declare

P057

VARIATIONS IN BLOOD TRANSFUSION PRACTICES AMONG SOUTH AFRICAN HAEMATOLOGY PROVIDERS: A SURVEY OF HAEMATO-ONCOLOGY AND HAEMATOPOIETIC STEM CELL TRANSPLANT PRESCRIBERS

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Background: Haemato-oncology and haematopoietic stem cell transplant (HSCT) patients are highly transfusion-dependent. Variability in red blood cell (RBC) and platelet transfusion practices, as well as in requests for blood product modifications, may impact patient safety, resource use and costs.

Methods: We conducted a national cross-sectional survey using a 23-item REDCap® questionnaire distributed (July 2022 – June 2023) to clinicians who regularly prescribe RBCs and platelets for patients with haematological malignancies, HSCT and chronic haematological disorders. Eligible respondents included clinical haematologists, medical and paediatric oncologists, trainees, medical officers, internal medicine registrars and haematopathologists. Descriptive statistics and group comparisons were performed using χ^2 or Fisher's exact tests.

Results: Of 155 invitations, 79 responses were received (51%); 58 eligible, complete responses were analysed. Most clinicians across all groups reported using a restrictive RBC transfusion threshold of 6.0–6.9 g/dL. Clinical haematologists more often cited reduced cardiopulmonary reserve as a reason to transfuse additional RBC units, whereas "other" clinicians more frequently reported medico-legal concerns. Prophylactic platelet transfusion thresholds were broadly similar, but the "other" group was significantly more likely to transfuse more than one platelet unit per episode. Marked variation was observed in platelet thresholds for invasive procedures, with clinical haematologists tending to select guideline-concordant thresholds. Indications for irradiation of blood products also differed, with clinical haematologists more frequently requesting irradiation in accordance with current recommendations.

Conclusions: This national survey demonstrates substantial variation in transfusion thresholds and blood product modification practices among SA haematology providers. Targeted education, guideline implementation and audit-and-feedback strategies are needed to harmonise practice, enhance patient safety and support cost-effective use of blood products.

Disclosure: No conflict of interest and no funding was required for this project

P058

VIRUS-SPECIFIC T CELL THERAPY FOR POST-TRANSPLANT VIRAL INFECTIONS: ONE YEAR OF CLINICAL-GRADE MANUFACTURING EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is associated with a prolonged period of immunosuppression, during which patients are at enhanced risk for viral infections, most commonly CMV, EBV, adeno- and BK- virus. A subset of patients does not respond adequately to conventional antiviral therapies, leaving limited treatment options. Virus-specific T cells (VSTs), manufactured under GMP conditions, offer a potential therapeutic alternative for these refractory infections.

Methods: Allogeneic donors—either the original HSCT donor or a haploidentical relative—were screened for circulating virus-specific T cells using a bispecific anti-CD45/IFN-γ antibody. A frequency of ≥0.05% virus-specific T cells was required to initiate manufacturing. Leukapheresis was performed to obtain suitable starting material. VSTs were produced using the closed, fully automated CliniMACS Prodigy system. Cells were stimulated with virus-specific peptide pools, and cells producing IFN-γ in response were identified by a bispecific detection antibody. A secondary magnetic bead–conjugated anti–IFN-γ antibody enabled enrichment of virus-specific T cells via magnetic separation.

Results: Four manufacturing processes were completed during the first year of GMP authorization for hospital exemption: one targeting CMV, one targeting BK virus, and two targeting both BK virus and adenovirus. Product quality and specificity was confirmed using flow cytometry. Donor starting material contained 0.04–0.13% virus-specific T cells, which were enriched to 5.8–68% in the final products. Final yields ranged from 90,000 to 1.1 million virus-specific T cells, with the highest output being for the CMV-specific product and the lowest for BK virus–specific products. Enrichment efficiency ranged from 100- to 1000-fold, consistently providing sufficient cell numbers for clinical infusion. All administrations went without incidents and no unexpected adverse events were detected. The clinical symptoms and/or viral load of the patients decreased post infusion.

Conclusions: The manufacturing process is robust, reproducible, and reliably yields adequate quantities of high-purity virus-specific T cells. All treated patients demonstrated reductions in symptoms and/or viral load following VST infusion, supporting the feasibility of this therapeutic approach.

Disclosure: nothing to declare

P059

COMBINATION ANTIVIRAL TREATMENT IS EFFECTIVE IN TREATING PARAINFLUENZA 3INFECTION IN THE IMMEDIATE POST-TRANSPLANT SETTING, INCLUDING IN PATIENTS WITH IN-VIVO T-CELL DEPLETION

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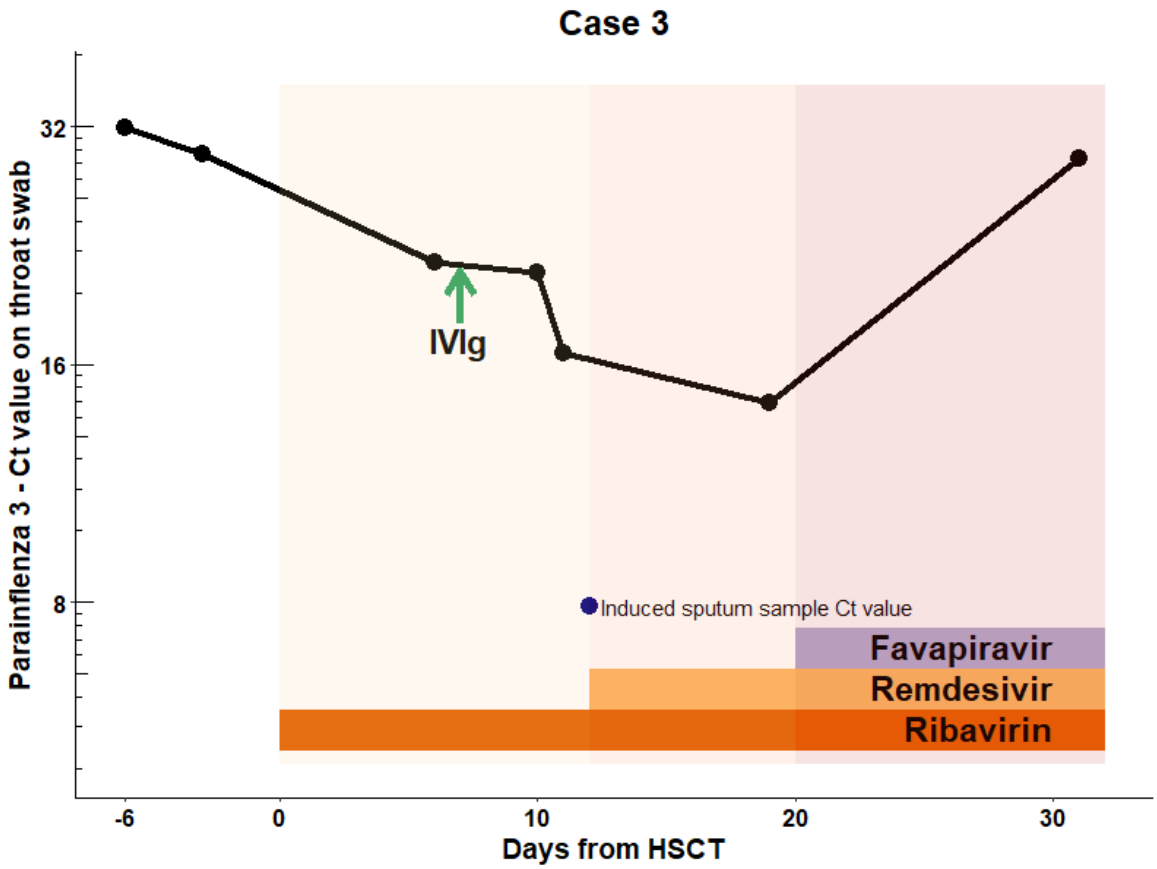
Background: Infection of the respiratory tract with RNA-virus pathogens, including Parainfluenza, in the peri-transplant period is associated with high transplant-related mortality in paediatric allogeneic haematopoietic stem cell transplant (HSCT) (26.5% vs 7% (Ottaviano et al., 2020)). Despite high mortality in vulnerable patient groups, there are no licensed antivirals for human Parainfluenza infections.

Methods: We describe below a series of three cases in which combination antiviral treatment was used to treat Parainfluenza 3 infection in the peri-transplant period.

Results: **Case 1:** A 9-month-old male received a Fludarabine(160mg/m^2)/Treosulfan(36g/m^2)/Thiotepa(10mg/kg) (FTT)-Alemtuzumab (1g/kg) conditioned 12/12 HLA-Matched Unrelated Donor Bone Marrow HSCT for high-risk Infant Acute Lymphoblastic Leukaemia. At Day+5 post-stem cell infusion he developed fevers and recrudescence of Parainfluenza infection was found on throat swab. He developed a progressive oxygen requirement and respiratory distress due to parainfluenza lower respiratory tract infection (LRTI), with low Ct/high viral load PCR positivity on BAL and Chest CT changes. His condition deteriorated quickly such that by D+16 he required intubation and ventilation. Despite treatment with IVIg (intravenous immunoglobulin) at D+21, Nitazoxanide (D+24), Favipiravir (D+25), Ribavirin (D+26), and full supportive care, he died of respiratory failure at D+28.
Case 2: A 1-year-old female received an FTT-conditioned T-replete Unrelated Donor Umbilical Cord Blood HSCT for relapsed Acute Myeloid Leukaemia. At D+6 she developed fevers and was found to have recrudescence of Parainfluenza infection on throat swab. Her respiratory symptoms worsened on D+14 with tachypnoea, widespread crepitations/wheeze on auscultation, and perihilar changes on chest X-ray suggestive of LRTI. She was treated with IVIg (D+14), Ribavirin(D+14), and Remdesivir(D+15), with rapid complete resolution of symptoms, and rapid rise (i.e. decrease in viral load) in Parainfluenza Ct values on throat swabs.
Case 3: A 15-year-old female with severe aplastic anaemia and fungal pneumonia was admitted for a Fludarabine(150mg/m^2)/Cyclophosphamide(120mg/kg)-Alemtuzumab (0.3mg/kg) conditioned 12/12 HLA-Matched Sibling Bone Marrow HSCT. At D-6 she developed a transient oxygen requirement and was found to be Parainfluenza positive on throat swab, with significantly lower Ct value (high viral load) PCR positivity on a later induced sputum sample suggestive of LRTI. She was treated with Ribavirin (D+0) and IVIg (D+7) initially but deteriorated on D+12 and required non-invasive ventilation for progressive hypoxia. She was treated with addition of Remdesivir (D+12) and had resolution of symptoms over 96 hours. Favipiravir was added at D+20 to help viral clearance (graph below).



In these cases, Parainfluenza treatment was well tolerated. There were liver function test derangements in Case 1 (Bilirubin 46µmol/L, ALT 3x upper limit of normal (ULN), AST 5xULN) requiring dose interruption of Nitazoxanide/Favipiravir, but this was in the context of significant deterioration in clinical condition. No other toxicities were seen.

Conclusions: Combination therapy with Ribavirin, Remdesivir, Favipiravir, and/or Nitazoxonide, together with IVIg, can be effective in treating Parainfluenza LRTI in the immediate post-transplant period, including in children with *in-vivo* T-cell depletion. Our cases suggest that early combination treatment, prior to the need for invasive ventilation, may be most effective.
Controlled platform trials are necessary to further investigate the clinical efficacy of combination antivirals in this highly vulnerable population.

Disclosure: Nothing to declare

P060

GENETIC INSTABILITY IN BLOOM: A RARE CASE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Bloom syndrome (BS) is a rare autosomal recessive disorder caused by pathogenic variants in the *BLM* gene (15q26). It is characterized by genomic instability and a significantly increased predisposition to cancer, including hematological malignancies. We report an adult patient newly diagnosed with acute myeloid leukemia (AML), referred for allogeneic hematopoietic stem cell transplantation (HSCT), who was subsequently found to harbor pathogenic *BLM* variants consistent with BS.

Methods: Peripheral blood (PB) cytogenetics was performed using standard G-banding. Next-generation sequencing (NGS) was conducted on an Illumina MiSeq platform using a panel of 193 genes associated with neoplastic diseases. Chimerism analysis in bone marrow (BM) and $CD3^+$ subsets was performed via amplification of nine short tandem repeat (STR) loci, followed by fragment analysis on a SeqStudio Genetic Analyzer (Thermo Fisher Scientific).

Results: A 37-year-old male was diagnosed with AML following BM aspiration and biopsy. PB cytogenetics demonstrated a highly complex karyotype: 43,XY,−5,−7,del(10)(q23),−13,add(18)(q21) and NGS revealed a TP53 mutation, c.818G>A p.(Arg273His). Upon referral to our BMT Unit for HSCT, clinical examination revealed short stature, microcephaly, and a narrow bird-like facies, raising suspicion for an underlying hereditary genomic disorder. NGS identified compound heterozygous *BLM* mutations—**c.772_773del p.(Leu258Glufs*7)** and **c.2015A>G p.(Gln672Arg)**—confirmed by Sanger sequencing. Family studies showed each parent carried one of the variants. With no matched related donor available, a fully matched (10/10) unrelated donor was selected. The patient received reduced-intensity conditioning consisted of Busilvex 45 mg × 8 doses, Thiotepa 5 mg/kg, and Fludarabine 125 mg/m², followed by infusion of 4.78×10^6 $CD34^+$ cells/kg. Neutrophil engraftment was achieved on Day 13.
Post-transplant chimerism on days 29, 62, 76, and 126 showed a progressive decrease in recipient-derived cells. However, on day 163, BM evaluation revealed morphological relapse. Chimerism demonstrated **46.57% recipient cells in BM** and **8.97% in the $CD3^+$ fraction**. STR analysis revealed **loss of one allele at loci D7S1517 and D11S554** in both BM and $CD3^+$ subsets (Figure). These abnormalities were absent in pre-transplant, pre-relapse, and germline samples, indicating an acquired somatic event. The apparent duplication of the remaining allele supported the presence of **copy-neutral loss of heterozygosity (cnLOH)**.

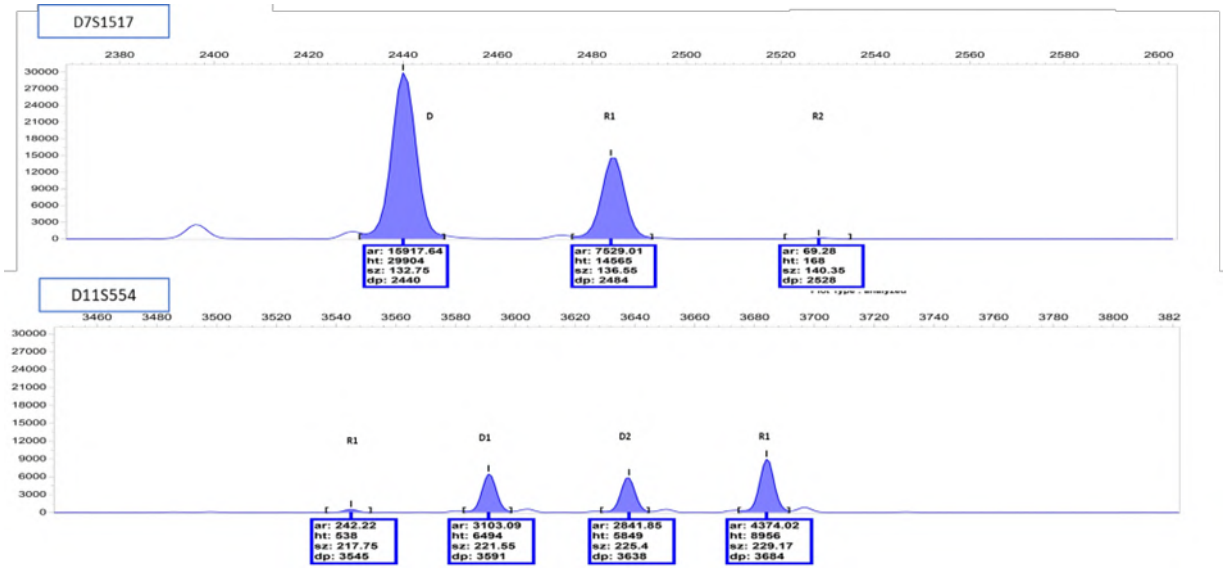

Figure: Post Transplant BM chimerism showing copy-neutral loss of heterozygosity

Post Transplantation Day	29	62	76	126	163
BM	2,75	2.9	-	-	46.57
CD3+	5,19	-	0.91	0,4	8.97

Table: Chimerism analysis post transplantation

Conclusions: This case illustrates AML development and post-HSCT relapse in an adult with previously unrecognized Bloom syndrome. The allelic pattern, at loci **7q31.32** (D7S1517) and 11p11–p12 (D11S554), in which the remaining allele appears duplicated, is consistent with cnLOH, rather than a simple deletion. Its absence in pre-transplant and germline samples represents a somatic event arising in the relapsed leukemic clone, independent of the monosomy 7 observed at diagnosis. Its presence in both BM and $CD3^+$ compartments suggests involvement of early hematopoietic progenitors. The 7q31 region is recurrently altered in myeloid malignancies and may harbor relevant tumor suppressor genes, while the significance of the 11p11–p12 alteration remains uncertain. BS-associated genomic instability likely contributed to these somatic rearrangements, emphasizing the value of high-resolution genomic profiling at relapse for prognosis and therapy guidance, particularly in patients with underlying chromosomal instability syndromes.

Disclosure: Nothing to declare

P061

CLINICAL UTILIZATION OF CORD BLOOD UNITS IN THE FAMICORD GROUP

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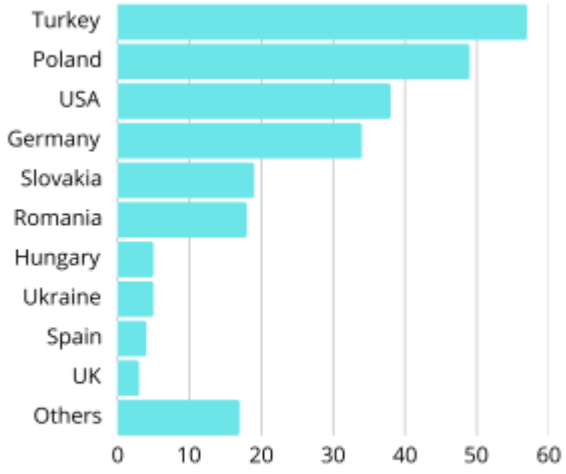
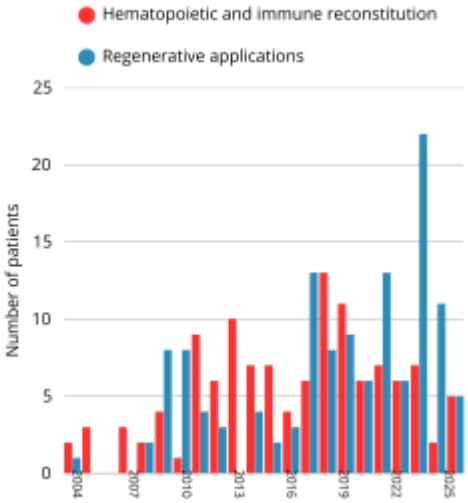
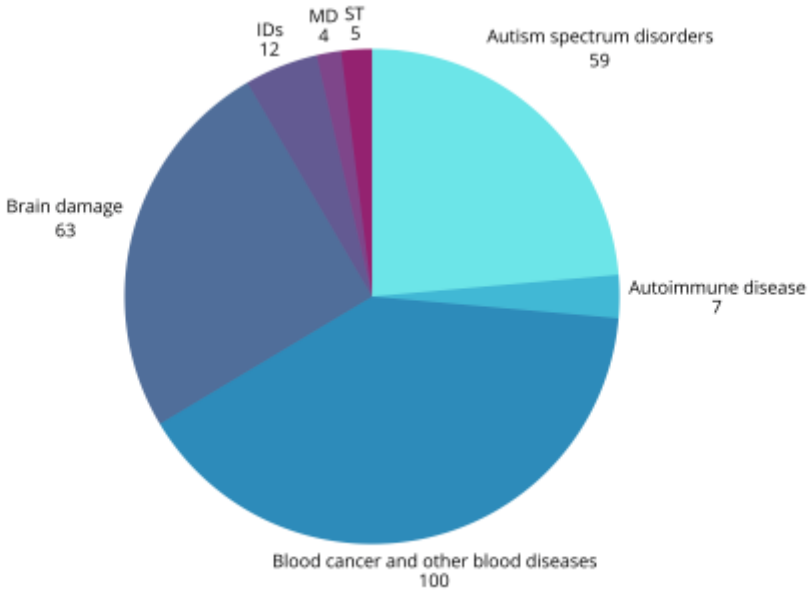
Background: Cord blood (CB) banking aims to enable clinical use of stored units. Three CB banking models exist: public, family, and hybrid. Although most CB transplantations use publicly banked units, CB stored in accredited family banks is also clinically applicable for autologous and related allogeneic use. The FamiCord Group is the largest cord blood bank in Europe, primarily focused on family banking while also offering hybrid and public models. This study reports CB unit releases from FamiCord-affiliated banks between 2004 and 2025.

Methods: Data were extracted from the FamiCord Group release database and analyzed using descriptive statistics.

Results: A total of 250 CB units were released: 120 (48.0%) autologous, 112 (44.8%) related allogeneic, and 17 (6.8%) unrelated allogeneic; relatedness was unspecified in one case. The most frequent indication was bone marrow reconstitution (BMR; n=100, 40%), followed by brain injuries (n=63, 25.2%), autism spectrum disorder (n=59, 23.6%), immunodeficiencies (n=12, 4.8%), solid tumors (n=5, 2.0%), and metabolic disorders (n=4, 1.6%). Eleven units (4.4%) were used in an autologous setting for standard hematological indications. CB units were released to clinics in 23 countries, most commonly Turkey, Poland, the USA, and Germany. Over time, CB releases increased for both hematological and regenerative applications, with greater growth in regenerative medicine.







Conclusions: Family cord blood banks represent a relevant source of CB units for transplantation and investigational regenerative therapies.

Clinical Trial Registry: Not applicable.

Disclosure: All of the authors are employed by the Polish Stem Cell Bank (FamiCord Group), Warsaw, Poland.

P063

EFFICACY AND SAFETY OF SHORT-COURSE BLINATUMOMAB FOR PEDIATRIC B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA WITH MOLECULAR RECURRENCE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Pediatric B-cell Acute Lymphoblastic Leukemia (B-ALL) patients who experienced hematopoietic stem cell transplantation (HSCT), including molecular recurrence, have a poor prognosis with conventional approaches. Molecular recurrence, defined as patients who had genetic markers and immunophenotypic characteristics before treatment, and after treatment, the results of FCM, fusion gene, and other tests turned from negative to positive and remained positive after re-examination, is a critical predictor of subsequent overt relapse and poor survival. Blinatumomab, a CD19/CD3 bispecific T cell engager, has demonstrated high remission rates and favorable tolerability as adjunctive therapy for relapsed pediatric B-ALL during chemotherapy. However, short-course Blinatumomab for post-HSCT molecular recurrence is scarce. This study aimed to evaluate its efficacy and safety.

Methods: Retrospective analysis of 4 pediatric B-ALL patients with post-HSCT molecular recurrence who received short-course Blinatumomab (dose escalated from 5 μg/m²/day to 15 μg/m²/day via continuous IV infusion, completed in approximately 14 days). Efficacy was assessed by FCM/fusion gene re-examination after Blinatumomab; adverse events (AEs) were graded by CTCAE v5.0.

Results: The types of transplantation in 4 pediatric patients were, respectively, 2 cases of haploid transplantation and 2 cases of fully matched transplantation from unrelated donors. Median time from HSCT to molecular relapse was 102.5 days (range: 65.5 - 299.0). Recurrence markers include the fusion genes KMT2A::AFF1, KMT2A::MLLT1, chr3::LMBR1L, and the mutated gene IL7R. After one course of treatment, 3 cases (75%) achieved complete molecular remission, and 1 case remained positive for the fusion gene (1 case). Median follow-up was 20 months, with a 100% overall survival (OS) rate and a 100% progression-free survival (PFS) rate. AEs included grade 1 cytokine release syndrome (CRS) (2 cases), elevated transaminases (1 case), and elevated brain natriuretic peptide (BNP) (1 case), all of which were effectively controlled by supportive treatment. No grade of graft-versus-host disease (GVHD) was observed in any of 4 pediatric patients during and after the treatment of blinatumomab.

Conclusions: Short-course blinatumomab therapy exhibits favorable efficacy and safety in the treatment of post-transplant molecular relapse of B-cell acute lymphoblastic leukemia (B-ALL). It prevents disease progression and reduces the rate of secondary hematopoietic stem cell transplantation, while the long-term efficacy and safety still require verification by large-scale clinical studies.

Disclosure: Nothing to declare.

P065

OUTCOME OF ALLOGENEIC STEM CELL TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROMES: EXPERIENCE FROM A TERTIARY CENTER IN SAUDI ARABIA

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Background: Acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) are characterized with significant mortality rates and poor clinical outcomes. Allogenic stem cell transplantation (AlloSCT) offers potential cure for AML and MDS . However, it carries significant risks of morbidity and mortality. Disease relapse, Graft Versus Host Disease (GVHD) and transplant related mortality (TRM) are potential risks to affect AlloSCT outcomes. This study aimed to report AlloSCT outcomes in AML and MDS at King Fahad specialist Hospital – Dammam (KFSH-D).

Methods: We retrospectively chart reviewed patients with myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), myeloid sarcoma, and chronic myeloid leukemia (CML) with myeloid blast crisis who underwent AlloSCT at KFSHD between 2011 and 2023. We set Endpoints included graft-versus-host disease (GVHD), disease relapse, three-year survival, and overall survival (OS) rates.

Results: The study included 61 patients with a mean age at diagnosis of 37.95 ± 12.1 years. The majority were male (55.74%), and all were of Saudi nationality. AML was present in 91.80% of patients. Cytogenetic analysis revealed abnormalities in 50.83% of patients. Molecular testing showed NPM1 positivity in 9.84% and FLT3-ITD positivity in 34.42% of patients. The mean time to platelet and neutrophil engraftment were 13.88 ± 4.57 and 18.35 ± 4.78 days, respectively. Seventeen patients (27.87%) developed acute GVHD, and 37 patients (60.66%) developed chronic GVHD. Nineteen patients (31.15%) experienced relapse. The 100-day and two-year overall survival rate were 88.52% and 59.02% respectfully. Those who died relapsed more than the survivors (51.61% vs 10.0%, p-value < 0.01).

Conclusions: AlloSCT is a potentially curative therapeutic options for AML and MDS, yet it is associated with significant mortality rates. Our study revealed overall survival comparable to what has been reported in the literature but with significant rates of acute and chronic GVHD. Hence, improving GVHD prophylaxis protocols may reduce such risks.
We demonstrate the outcomes of AlloSCT at KFSH-D, highlighting the importance of careful patient selection and monitoring to improve survival rates and minimize complications.

Disclosure: No conflict of interest.

P067

OUTCOMES OF THIRD ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AMONG HEMATOLOGICAL MALIGNANCY PATIENTS RELAPSE POST SECOND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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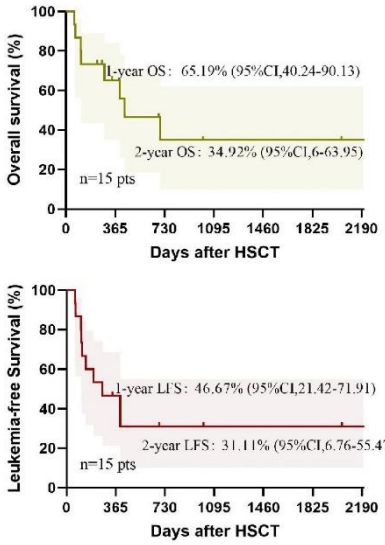
Background: Relapsed hematological malignancy after allogeneic hematopoietic stem cell transplantation (allo-HSCT1) is associated with poor prognosis. A subset of patients can achieve durable remission through a second allo-HSCT (allo-HSCT2). However, a substantial number (30%) of patients experience relapse after allo-HSCT2, and there are limited therapeutic options for these patients. In select patients, a third allo-HSCT (allo-HSCT3) can be administered. Given the substantial risks involved in undergoing allo-HSCT3 , such procedures are infrequently attempted . Consequently, the benefits of allo-HSCT3 remains uncertain.

Methods: We performed a retrospective analysis of patient outcomes for individuals with hematological malignancies who underwent allo-HSCT3 due to either hematological/extramedullary relapse or persistent disease, as indicated by flow cytometry minimal residual disease positivity (FCM-MRD+) or the presence of a fusion gene, following a allo-HSCT2. This study was conducted at Beijing Lu Daopei Hospital and Hebei Yanda Lu Daopei Hospital, covering the period from 2015 to 2024. Patients who had previously undergone autologous hematopoietic stem cell transplantation prior to allo-HSCT3 or who received allo-HSCT following primary graft failure were excluded from the analysis.

Results: Following rigorous screening, 15 patients (6 males, 9 females) were included, with a median age of 15 years (range 1–42) at allo-HSCT1. Diagnoses were AML (n=9), B-ALL (n=3), T-ALL (n=1), MPAL (n=1), and MDS (n=1). All underwent allo-HSCT1 in CR from a haploidentical (HID, n=10), matched sibling (MSD, n=2), matched unrelated (MUD, n=2), or umbilical cord blood (UCB, n=1) donor, following BU/CY-based conditioning. Median time to relapse after allo-HSCT1 was 397 days (range 49–2201).After salvage therapy, 13 patients received allo-HSCT2 in CR, with donor changed in 11 cases. Conditioning was TBI-based (n=11) or BU-based (n=4). Median relapse time after allo-HSCT2 was 265 days (range 60–1913).Before the allo-HSCT3, patients received various salvage regimens. At allo-HSCT3, 9 were in CR and 6 were not. Donor was changed in 11 patients. Conditioning was myeloablative (MAC, n=7) or reduced-intensity (RIC, n=8). Median infused cell doses were 11.37×10^8/kg MNC (range 4.62–16.66) and 7×10^6/kg $CD34^+$ cells (range 2.8–7.37). All engrafted: median neutrophil recovery 15 days (9–21), platelet recovery 20.5 days (12–77). Complications included acute/chronic GVHD (n=11), CMV reactivation (n=10), and EBV reactivation (n=2).With a median follow-up of 340 days (range 63–2261) until July 7, 2025, 7 patients (46.7%) were alive and 8 (53.3%) had died-mainly from relapse (n=3) or infection (n=3), with 2 early deaths from infection within 100 days. Median LFS was 268 days, with 1- and 2-year rates of 46.7% and 31.1%, respectively. Median OS was 436 days,

with 1- and 2-year OS of 65.2% and 34.9%. Two patients remained disease-free >5 years.



Conclusions: Relapse of hematological malignancies after allo-HSCT remains a major therapeutic challenge. In this retrospective analysis,allo-HSCT3 enabled long-term LFS in a considerable proportion of patients, despite its inherent difficulties. While selection bias cannot be ruled out, the favorable outcomes may be partly due to the younger age of our cohort. These findings suggest that allo-HSCT3 can be a potentially curative option for selected patient populations.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

P068

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH LI-FRAUMENI SYNDROME AND HEMATOLOGIC MALIGNANCIES: A SINGLE-CENTER EXPERIENCE

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Background: Li-Fraumeni syndrome is a major hereditary cancer predisposition syndrome. Hematologic malignancies account for about 4% of cases, mainly represented by acute lymphoblastic leukemia (ALL) with hypoploid karyotypes and secondary myelodysplastic syndromes (MDS). The lack of clear guidelines for both diagnosis and treatment, as well as

the genetic basis of the disease, creates significant challenges in selecting the optimal therapy and conditioning regimens prior to HSCT.

Methods: Four cases of Li-Fraumeni syndrome treated at a single center are presented. The patients underwent transplantation in 2024 and 2025.
Patient C, 17 years old; B-ALL, treated since 2022. Treated per a combined chemo-immunotherapy protocol. MRD detected at end of therapy; auto-CAR T given before HSCT, achieving a 3-month remission. Pre-HSCT MRI showed a right iliac bone lesion. Conditioning — see Table 1.
Patient K, 14; B-ALL since 2023. Intermediate risk. Oct 2024: very early isolated marrow relapse. ALL-REZ 2016: after FLAM blasts 45%; inotuzumab—blasts 15%; then blinatumomab: MRD 0.778%, blasts 6%. Pre-HSCT blasts up to 15%. Conditioning—see Table 1.
Patient P, 17. History: embryonal rhabdomyosarcoma of the left gluteal region, pT1N0M0 (May 2009); periosteal sarcoma of the left femur (Aug 2020). Diagnosis: MDS with excess blasts; treated since 2024. From Oct 2024: venetoclax plus low-dose decitabine. After repeat cycles, marrow blasts and MRD increased; decision for HSCT with split conditioning (Table 1).
Patient K2, 14: B-ALL (CNS-0) diagnosed 01/2023. Treated per ALL IC-BFM 2002 then LBL-2018 (high risk). MRD-negative remission on 17 Apr 2023; completed Protocols M and II; maintenance from Sep 2023.
On 14 Jun 2024: very early isolated marrow relapse. ALL-Rez 2016: FLAM block → remission; from 22 Jul 2024 blinatumomab; end of block: blasts <5%, MRD 0%. Conditioning—see Table 1.

Table 1 summarizes the patients' characteristics and main treatment phase.

	Diagnosis	Genetic	Status of disease before HSCT	Conditiotion	HSCT (D, BM|PBS	Preventive therapie GVHD
Patient C. 17 y	B-ALL	NGS - missence mut. c.841 G>A.	Extramedullary lesion in the iliac bone	TBI 12gr + boost 18gr + Flu 150 mg/m^2 Vp 60 mg/kg.	MUD, BM CD34 4.290 (10^6/кг)	Cy +3, +4 d after SCT, ve mg/kg day 0, +14, +28, after SCT, Aba 10 mg/kg +14, +28, +60, +90 d. a SCT Bari 4 mg/d p.o. fron before SCT
Patient K.14 y	B-ALL	Senger - missence mut. in 5 ex. c.395A>T.	AD	Flu 150 mg/m^2 Treo 42 g/m^2 Thio 10 mg/kg.	Haplo (f) PBS+ CAR-T (CD19/22) CD34 9.5 (10^6/kg)	Aba10 mg/kg d -1, +7, + +28; Toci 8 mg/kg -1 d
Patient., P. 17 y	MDS	NGS - missence mut. c.725 G>A in 7 ex.	AD	#1 phase Flu 150 mg/m^2 Ara 10000 mg/m^2 #2 phase	Haplo (f) PBS CD34 8.5 (10^6/kg)	Ruxo 10 mg/m^2 d -3 , Cy 80 mg/kg, +3+4 d Aba 10 mg/kg +5, +14, +

				Thio 300 g/m^2 Treo 42 mg/m^2		+60, +90 Vedo 300 mg/d +14, +28, +60 d after SC
Patient K2, 12y	B-NHL/B-ALL	NGS - missence mut. c.569C>T in 6 ex.	AD	TBI 12gr Flu 150 mg/m^2 Vp 60 mg/kg.	Haplo (f) PBS CD34 8.5 (10^6/kg)	Ruxo 10 mg/m^2 d -3 , Cy 80 mg/kg, +3+4 d Aba 10 mg/kg +5, +14, - +60, +90 Vedo 300 mg/d +14, +28, +60 d after SC

Results: All patients received myeloablative conditioning. Engraftment was achieved in all cases; donor chimerism and remission were confirmed on day +30. The HSCT procedures were completed without serious complications. Three of four patients relapsed. Two underwent a second HSCT.

Conclusions: Our observation indicates good tolerability of myeloablative conditioning.Overall, patients with Li-Fraumeni syndrome are at high risk for malignant tumors but rarely develop hematologic malignancies. Consequently, there are no cohort studies, and isolated case reports do not allow for reliable conclusions about prognosis and the risks associated with myeloablative conditioning regimens.

Disclosure: Nothing to declare.

P069

LATE-ONSET DONOR-DERIVED PDGFR-B–REARRANGED EOSINOPHILIC NEOPLASM FOLLOWING HAPLOIDENTICAL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A SECONDARY ACUTE MYELOID LEUKEMIA

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Background: Donor-derived hematologic neoplasms are rare complications of allogeneic hematopoietic stem cell transplantation (allo-HSCT) and may present diagnostic challenges, particularly when manifesting as late-onset eosinophilia. Distinguishing clonal donor-derived disease from reactive eosinophilia or disease relapse is essential, as donor-derived neoplasms have distinct biological behavior and therapeutic implications. We report a case of late-onset donor-derived platelet-derived growth factor receptor beta (PDGFR-β)–rearranged eosinophilic neoplasm following haploidentical allo-HSCT for secondary acute myeloid leukemia (AML).

Methods: Clinical, laboratory, cytogenetic, and molecular data were retrospectively reviewed. Serial complete blood counts, bone marrow examinations, next-generation sequencing (NGS), and short tandem repeat (STR) chimerism analyses were evaluated. Fluorescence in situ hybridization (FISH) for hypereosinophilic syndrome–associated

rearrangements was performed following the development of persistent eosinophilia in the late post-transplant period.

Results: A 60-year-old female with high-risk myelodysplastic syndrome that transformed to AML achieved complete remission after induction chemotherapy with idarubicin, cytarabine, and venetoclax, followed by consolidation therapy. Pre-transplant NGS identified FLT3, IDH2, and KMT2A (MLL) mutations, with no PDGFR-β rearrangement detected, excluding pre-existing PDGFR-β–driven disease in the recipient. She subsequently underwent haploidentical allo-HSCT using her son as donor. The donor had normal baseline blood counts and no eosinophilia prior to stem cell collection.
Post-transplant bone marrow examinations demonstrated sustained morphologic and flow cytometric remission, and repeat NGS showed no pathogenic mutations. At Day +243 post-HSCT, the patient developed persistent eosinophilia, initially attributed to graft-versus-host disease or drug-related causes. Given its persistence, further molecular evaluation was pursued. FISH analysis revealed a PDGFR-β rearrangement, establishing a diagnosis of a clonal eosinophilic neoplasm. STR chimerism analysis performed after the onset of eosinophilia demonstrated 100% donor engraftment, confirming donor origin of hematopoiesis.
The late timing of presentation, absence of PDGFR-β rearrangement prior to transplant, normal donor hematologic parameters, and complete donor chimerism supported classification as a **l**ate-onset donor-derived myeloid/lymphoid neoplasm with eosinophilia, consistent with post-engraftment expansion of a previously occult donor clone.

Conclusions: This case represents a rare example of late-onset donor-derived PDGFR-β–rearranged eosinophilic neoplasm following haploidentical allo-HSCT. Clinically silent donor clones may exist despite normal donor blood counts and can expand after engraftment under altered immune and hematopoietic conditions. Persistent eosinophilia occurring beyond six months post-transplant warrants molecular evaluation for clonal disorders, even in the presence of complete donor chimerism and sustained remission, to ensure accurate diagnosis and enable timely targeted therapy.

Disclosure: Nothing to declare.

P070

A SINGLE CENTRE EXPERIENCE OF ALLOGENEIC STEM CELL TRANSPLANTATION IN PATIENTS WITH DDX41-MUTATED MDS AND AML

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Background: Germline pathogenic variants in *DDX41* represent the most common genetic predisposition to myeloid malignancies, accounting for approximately 3% of cases. Despite this however, the prognostic implications of DDX41 mutations remains unclear and data on outcomes following allogeneic stem cell transplantation (alloSCT) remain limited.

Methods: This retrospective single-centre study reviewed outcomes of patients with DDX41 mutated MDS or AML undergoing allo(SCT) at our institution between 2019-2024. Outcomes included: overall survival (OS), relapse-free survival (RFS), GVHD-free relapse-free survival (GRFS), relapse incidence, GVHD incidence/severity, chimerism, donor lymphocyte infusion (DLI) requirement, infection, and mortality incidence/cause.
Survival was estimated using Kaplan–Meier method. Cumulative incidences were calculated using competing-risks methods.

Results: 8 patients with a presumed or confirmed germline pathogenic *DDX41* mutation were identified. 7 carried a second likely somatic mutation. 7 had AML (all ELN-2022 adverse risk). 1 had MDS (IPSS-R 3.5).
7 patients were male and the median age at transplant was 65.5 years (IQR 62.5-68.25). 7 patients received Fludarabine/Melphalan/Alemtuzumab (FMC) conditioning and 1 received Thiotepa/Busulfan/Fludarabine/ATG (miniTBF). In all cases a fully matched volunteer unrelated donor was used. (Further characteristics Table 1)
Median follow-up was 1040.5 days. Median OS was 307.5 days. Median RFS was 306 days. Median GRFS was 116.5 days. (Figure 1)
At follow up (24/11/2025), 5 (62.5%) of patients had died. Transplant-related (day 100) mortality was 12.5% (1/8) (Failure to engraft). Relapse-related mortality was 12.5% (1/8). Non-relapse mortality was 37.5% (3/8), due to infection. Cumulative incidence of death was 13% (95% CI 0.48%–44%) at day 180 and 63% (95% CI 18–88%) at one year.
1 patient experienced relapsed disease, at day 148 post-transplant. This patient survived 53 days post-relapse.
Acute GVHD occurred in 3 (37.5%) patients with no Grade III/IV disease. Chronic GVHD occurred in 3 (37.5%) patients (two severe, one moderate), with cumulative incidence of 13% (95%CI: 0.43%–45%) at day 180 and 38% (95%CIL: 6.1%–71%) at one year.
All patients reached complete whole-blood donor chimerism (≥95%) by day 30. 3 (37.5%) achieved complete T-cell chimerism. At day 100, whole-blood chimerism remained complete in 6/7 assessable patients, and complete T-cell chimerism in 2/7. Two patients required DLI both for mixed chimerism and both experienced post-DLI acute GVHD (stage 1 and stage 2 skin).
All patients experienced clinically significant infections post-transplant. Infection directly caused 3 deaths and contributed to two others. Median time to first infection was 134 days (IQR 54.25–359.5). The cumulative incidence of any infection was 63% (95%CI: 18–88%) at day 180 and 75% (95%CI: 23–94%) at one year.

HSCT-CI Score	Number of Patients
0	3
1	0

2	2
3	2
4	0
5	1
ECOG PS	
0	7
1	1
Immunosuppresion Post Transplant	
Tacrolimus	7
Ciclosporin + Mycophenolate Mofetil	1

Table 1 - Further patient characteristics

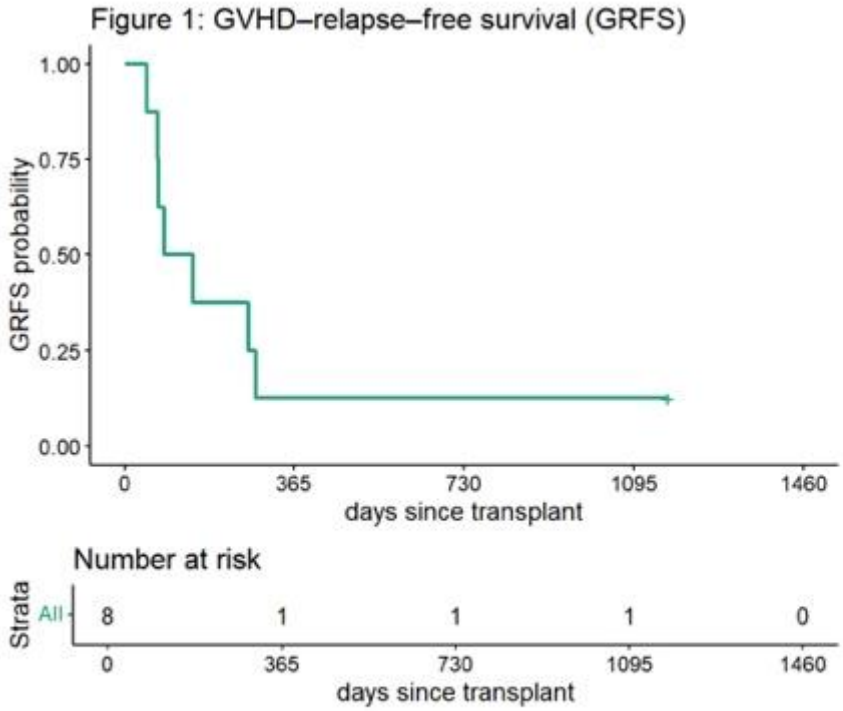

Figure 1: GVHD-relapse-free survival (GRFS) after alloSCT estimated using the Kaplan-Meier method.

Conclusions: AlloSCT for patients with germline DDX41 mutations is feasible but associated with substantial non-relapse mortality and high rates of both GVHD and infection. Further studies are required to optimise management strategies and supportive care for this genetically distinct patient population.

Disclosure: Nothing to declare

P072

SUCCESSFUL IMPLEMENTATION OF CAR-T CELL THERAPY AT THE ONCOLOGY INSTITUTE IN WARSAW

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Background: CAR-T therapy has become the standard treatment for patients with refractory diffuse large B-cell lymphoma (DLBCL) and refractory mantle cell lymphoma (MCL). We present here our initial experience with CAR-T therapy implementation over the past year at our center – tolerability and safety.

Methods: We collected data from 14 consecutive patients (5 with MCL and 9 with DLBCL) who underwent the CAR-T procedure between August 2024 and November 2025 at our center. Cyclophosphamide and fludarabine were administered on days 5-3, followed by the CAR-T cell drug infusion Yescarta (DLBCL) or Tecartus (MCL), depending on the diagnosis.

Results: Median age was 59 years, with a range of 31-71 years. The number of lines of therapy for MCL patients ranged from 3 to 5. All MCL patients were treated with the R-CHOP/RDHAP regimen with autotransplantation consolidation, followed by ibrutinib (n=3) or acalabrutinib (n=2) in subsequent lines. In the case of DLBCL, all patients received the RCHOP/Pola-RCHP regimen as first-line therapy. Two patients received CAR-T therapy as second-line therapy, and the remaining (n=6) as third-line or subsequent lines. The median time from leukapheresis to CAR-T cell administration was 35 days (range: 28-103). Ten patients received bridging therapy before CAR-T therapy, Pola-BR or R-GEMOX chemotherapy for DLBCL, and R-bendamustine for MCL. Cytokine release syndrome (CRS) occurred in 10 patients (71%) after CAR-T cell administration, with grade above 3 in only one patient (7%). The duration of CRS ranged from 2 to 10 days with a median of 2 days. Three patients required tocilizumab. Immuno-Effector Cell-Associated Neurotoxicity Syndrome (ICANS) occurred in 8 patients (57%), in 2 patients above grade 3 (14%), lasting from 1 to 10 days with a median of 2 days. Two patients received four doses of Anakinra. Haematological toxicity occurred in all patients: grade 3/4 neutropenia occurred from day 0 to 7 and lasted from 1 to 12 days with a median of 7 days. One patient developed anaemia requiring RBC transfusion, four patients had grade 3 thrombocytopenia, and one had grade 4 thrombocytopenia. Two patients experienced vomiting and general weakness. None of the patients developed confirmed infections. One patient died due to progressive grade 4 CRS. Following the CAR-T procedure, lymphoma progression occurred in four patients, two of them died due to progressive disease. Ten patients are alive, 8 in complete remission (4 with MCL and 4 with DLBCL) and 2 patients with DLBCL are treated with bispecific antibodies.

Conclusions: CAR-T therapy appears to be a safe and tolerable procedure despite the occurrence of profound neutropenia and the development of CRS and ICAN syndromes. Severe CRS and ICANS occurred in less than 15% of patients.

Disclosure: No disclosures.

P073

LASER DOPPLER-BASED MICROCIRCULATORY MONITORING AS AN EARLY PREDICTOR OF POOR VENOUS FLOW DURING LEUKAPHERESIS

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Background: Reliable venous access and stable blood flow are essential for the efficient collection of hematopoietic progenitor cells or lymphocytes for cellular therapy. Poor venous blood flow during leukapheresis remains a common procedural challenge that can compromise collection efficiency, prolong procedure time, and exacerbate patient burden. Moreover, robust predictive markers enabling early intervention are lacking.

Methods: We retrospectively analyzed 146 leukapheresis procedures (79 in patients with hematologic malignancies and 67 in healthy donors) at two institutions. Continuous peripheral microcirculatory blood flow was monitored using laser Doppler flowmetry during leukapheresis. The incidence, timing, and risk factors for poor venous flow were assessed, and hemodynamic parameters at onset were examined to determine whether microcirculatory changes precede clinically apparent flow deterioration.

Results: Poor venous blood flow during apheresis occurred in 23 of 79 individuals (29.1%) in the hematologic malignancy group and 18 of 67 individuals (26.9%) in the healthy donor group, with median onset times of 23 minutes (range, 0–165 minutes) and 21.5 minutes (range, 0–65 minutes), respectively. In patients, poor venous flow was independently predicted by multiple myeloma, lower baseline microcirculatory flow, and higher pulse amplitude. In healthy donors, older age was a notable predictor. A decline in peripheral blood flow preceded the onset of poor venous flow, while systemic blood pressure and pulse rate remained stable, indicating that microcirculatory changes may serve as an early and sensitive physiologic marker of impending flow deterioration.

Conclusions: Real-time peripheral blood flow monitoring using laser Doppler flowmetry may provide a sensitive early-warning signal for impending poor venous flow during leukapheresis. Incorporating baseline microcirculatory parameters into preprocedural risk assessment may help identify high-risk patients—particularly those with hematologic malignancies—and also support proactive strategies to optimize leukapheresis management. This physiological monitoring approach has the potential to improve the safety and efficiency of stem cell and cellular therapy product collection in clinical transplantation settings.

Disclosure: Nothing to declare.

P074

THE ILLUSION OF DEFEAT: PSEUDO-PROGRESSION FOLLOWING DUAL CD19/CD22 CAR-T THERAPY IN REFRACTORY DLBCL

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Background: CAR-T cell therapy has revolutionized the management of relapsed or refractory B-cell lymphomas. While immune-mediated toxicities such as cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS) are well recognized, pseudoprogression remains a rare and underreported phenomenon. This transient immune-driven flare can mimic disease progression, creating diagnostic uncertainty and management dilemmas.

Methods: A 69-year-old male with relapsed/refractory diffuse large B-cell lymphoma (DLBCL) with secondary CNS involvement which had initially been treated with multiple lines of chemotherapy, including RCHOP, R-HyperCVAD with eventual disease relapse involving the CNS and leptomeninges, The patient achieved partial remission after Zanubritinib R-ICE therapy. Patients admitted for CAR-T therapy (targeting CD19 and CD22). After lymphodepletion with fludarabine and cyclophosphamide, CAR-T cells were infused at a dose of 5.77×10^6/kg.

Results: The immediate post-infusion course was uneventful, with Grade1 cytokine release syndrome (CRS) and no neurotoxicity. On follow-up at three months, PET-CT demonstrated new hypermetabolic lesions in the liver and bone, raising concern for disease relapse. However, the patient remained asymptomatic. Bone marrow biopsy revealed absence of B cells and no clonal lymphoma. GeneXpert for tuberculosis was negative. Surpisingly Fibroblast Activation Protein Inhibitor (FAPI) scan done showed no activity.
Patient had no clinical symptoms, no B cell in bone marrow and persistent CAR-T presence, the findings were interpreted as immune-mediated pseudo-progression, likely due to CAR-T–induced inflammatory changes rather than true relapse. Over subsequent PET scan, the lesions regressed spontaneously without any intervention, confirming pseudo-progression. Next generation sequencing from peripheral blood of patient and daughter reveals DDX41 mutation suspecting possible predisposition of lymhphoma. A FAPI

Conclusions: This case underscores the importance of distinguishing true relapse from pseudo-progression following CAR-T therapy. Recognizing this phenomenon can prevent unnecessary and salvage treatments. Emerging imaging modalities such as FAPI PET may assist in differentiating inflammatory responses from residual disease, but their role remains investigational and requires further validation in larger studies. FAPI imaging may act as a complementary tool to FDG PET CT when metabolic flare creates diagnostic uncertainty.

Clinical Trial Registry: No

Disclosure: Nothing to declare

P075

IMPACT OF REFRACTORY PRE-TRANSPLANT CYTOMEGALOVIRUS INFECTIONS ON SURVIVAL IN CHILDREN UNDERGOING STEM CELL TRANSPLANT FOR PRIMARY IMMUNODEFICIENCY DISORDERS

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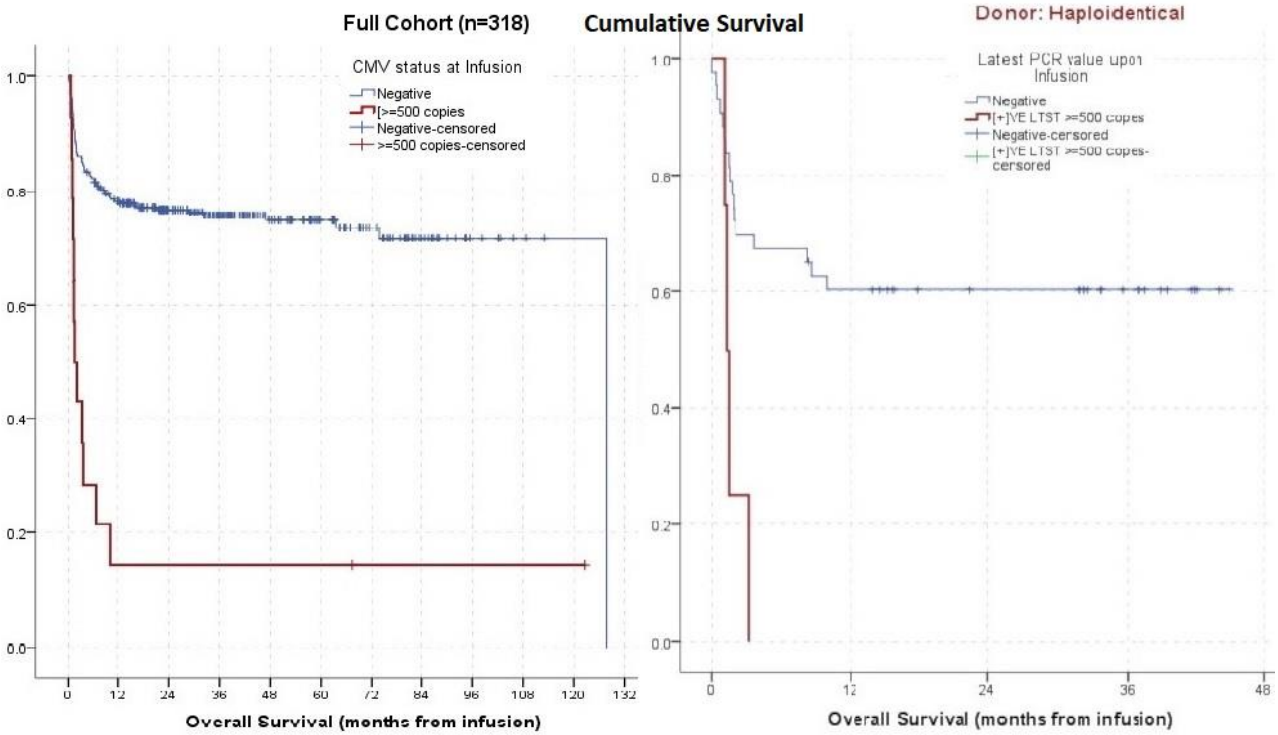
Background: Harbouring a cytomegalovirus (CMV) infection in pre- transplant period has been associated with a negative effect on transplant outcome due to increased risk of graft failure and infections. However, knowledge about its impact on overall survival (OS) in pediatric population with primary immunodeficiency disorders (PIDs) in Saudi Arabia is still limited.

Methods: We retrospectively analyzed all transplant naïve pediatric patients (age at transplant ≤14 years), transplanted for PIDs, from January 2013 to June 2023. Presence of > 500 copies by PCR before infusion of stem cells was considered as positive CMV infection. Patients were included if they had a positive infection, refractory to antiviral treatment, whereas patients who were positive but responded to therapy and had < 500 copies were excluded. Kaplan-Meier curves were drawn for survival analyses by using SPSS Version 20.0 software.

Results:



318 transplants were considered analyzable. Median age at transplant was 0.9 years (0.5 months to 14 years). 56.3% were males. Severe combined immune deficiency (SCID) and combined immune deficiency (CID) were present in 145 (45.6%) patients, with other disease categories also contributing to the cohort (Table 1). Stem cell sources were bone marrow (80.8%), peripheral blood stem cell (9.1%) and cord blood (10.1%) respectively. 70.8% had myeloablative, 2.2% reduced and 27% had no conditioning. 65.1% had full matched, 14.8% haploidentical, 10.1% cord blood, 7.5% matched-unrelated and 2.5% mismatched donors. At infusion, fourteen (4.4%) patients were CMV seropositive.
At a median follow-up of 38.2 months and a mortality rate of 27.7%, the cumulative probability of 5-year overall survival (OS) was 72.1%, with an OS of 74.8% was observed among seronegative recipients, compared to 14.3% in seropositive recipients, which was statistically significant (P<0.001). Further, subgroup analysis showed a better cumulative probability of 5-year overall survival in seronegative patients in conditioned and non-conditioned cohorts and the same was true for fully matched and haploidentical recipients (P<0.001) with no seropositive haploidentical recipient survived (Figure1).
In the subgroup of recipients transplanted from cord blood, no statistically significant difference was seen in cord blood CMV positive and negative recipients.

Conclusions: Our results showed that a refractory pre transplant CMV infection impacts the survival of patients, especially for the recipients of haploidentical bone marrow transplants. Adaptive immune with Cytotoxic T-Lymphocytes (CTL) may be used to treat such patients to improve outcomes.

Disclosure: Nothing to declare.

P076

INCIDENCE AND CHARACTERISTICS OF EXTREMELY RARE COMPLICATIONS OF POST ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A BICENTRIC SAUDI ARABIAN EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an established therapeutic modality in Saudi Arabia, with extensive programs at major tertiary care centres. As the total number of HSCT has steadily increased in recent years, many complications have become more frequent despite improvement in supportive care. While common complications are well-documented, data on extremely rare complications with reported incidences below 1% are relatively low, particularly within the Middle Eastern population. This study details the occurrence of several such rare events at two major tertiary care canters in Riyadh.

Methods: We conducted a retrospective analysis of allo-HSCT recipients transplanted at KFSH&RC and PSMMC in Riyadh from January 2018 to October 2025. We specifically identified cases of pre-defined extremely rare complications as below, mostly these rare complication is ignored and possibly underdiagnose. Patient data regarding baseline characteristics, transplant specifics, time to complication onset, clinical management, and outcomes were abstracted and reviewed.

Results: Out of a total of approximately more than 200 allo-HSCTs performed at both centres during this period we identified a series of rare complications:

- **Post-transplant erythrocytosis:** 5 cases
- **Donor cell leukemia (DCL):** 2 cases
- **Scrotal swelling (non-infectious etiology):** 2 cases
- **Autoimmune disease (new onset):** 2 cases
- **Thoracic air leak syndrome (TALS):** 1 case
- **Arrhythmia/cardiac toxicity (severe):** 1 case
- **Hemophagocytic lymphohistiocytosis (HLH):** 1 case
- **CNS-post transplant lymphoproliferative disorder (**PTLD): 1 case
- **Pulmonary veno-occlusive disease (PVOD): 1 case**

Complication	Number of Cases	Primary Diagnosis	Early <90 /Late >90	Management & Outcome

Post-transplant erythrocytosis	7	4 SAA, 1 AML, 2 DLBCL	Late	Conventional Rx, all resolved; no driver mutation
Donor Cell Leukemia (DCL)	2	AML	Late	Treated with allo-HSCT from different donor
Scrotal swelling (non-infectious)	2	Sickle cell disease	Early	Supportive care, resolved
Autoimmune disease (new onset)	2	ALL	Late	Referred to Rheumatology/Immunology
Thoracic Air Leak Syndrome (TALS)	1	MDS	Late	Standard care, high mortality
Arrhythmia/cardiac toxicity (severe)	1	AML	Early	Patient passed away
HLH	1	AML	Late	Patient passed away
CNS-PTLD	1	Non-Hodgkin's Lymphoma	Early	Resolved with treatment
PVOD	1	AML	Early	Resolved with treatment

The incidences of DCL (~0.1% globally) and TALS are exceptionally low, aligning with international literature reporting them primarily in case studies. The DCL cases presented as late complications, while the TALS case occurred in the context of severe pulmonary cGVHD.

Conclusions: Our single-region, bi-centric experience highlights the spectrum of ultra-rare complications following allo-HSCT. The occurrence of a cluster of these infrequent events, particularly DCL and TALS which carry high morbidity and mortality, emphasizes the need for long-term, specialized follow-up care for transplant survivors. Continuous data sharing through national and international registries (such as the EBMT) is crucial for better understanding, risk stratification, and developing evidence-based guidelines for managing these rare, devastating post-transplant sequelae in the Saudi Arabian context. Introduction of less toxic conditioning regimen allowed the expansion of HSCT to more fragile elderly recipients.

Disclosure: I don't have any disclosure or any conflict of interest.

P077

CHALLENGES IN PERFORMING HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RESOURCE-LIMITED COUNTRIES EXPERIENCE OF THE BONE MARROW TRANSPLANTATION CENTER IN TUNISIA

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Background: In Tunisia, haplo-Hematopoietic Stem Cell Transplantation (haplo-HSCT) has been progressively implemented since 2021 to overcome HLA-matched sibling donors (MSD) unavailability.
A standardized eligibility checklist was established by the transplant committee of our center for patients with hematological malignancies since 2023. The objective of this study was to describe our experience with haplo-HSCT and to highlight the challenges associated with its implementation in resource-limited countries.

Methods: We conducted a retrospective, descriptive study over a 3-year period (2023–2025), including all patients with hematological malignancies referred for haplo-HSCT at the National Bone Marrow Transplantation Center in Tunisia, the unique center in the country.
All patients were hospitalized in rooms with laminar flow, with a capacity of only eight cabins.
Given local constraints, haplo-HSCT was indicated for children aged over 10 years and for adults aged under 40 years with high-risk AML, ALL, MDS, Hodgkin and non-Hodgkin lymphoma.
Conditioning regimens were mainly based on thiotepa, busulfan and fludarabine (TBF). GVHD prophylaxis consisted of cyclosporine, mycophenolate mofetil, and post-transplant cyclophosphamide. Stem cell sources included either bone marrow or peripheral blood stem cells.

Results: Thirty-One patients were referred for haplo-HSCT, of whom only 9 ultimately underwent haplo-HSCT. Among the 22 patients who did not receive transplantation, 8 had highly positive DSA (excluded due to the unavailability of desensitization protocols.), 4 had their transplant indication rejected after committee review, 2 patients relapsed before transplantation, 5 could not be transplanted due to logistical constraints, and 3 patients are currently scheduled for future haplo-HSCT. Among transplanted patients, the underlying disease included 2 cases of ALL, 3 of AML,1 MDS-EB2, and 3 Hodgkin lymphoma.
The median age was 18 years (range 10-40). Before transplant, five patients were in first complete remission, and three patients were in second complete remission.
The conditioning regimen was thiotepa/busulfan-based in five patients, TBI-based in two patients and other regimens in 2 patients. Median duration of hospitalization was 40 days (range 32-150).
Acute GVHD occurred in 8 patients, mainly with gastrointestinal involvement.One patient developed refractory grade IV acute GVHD and received three lines of therapy: corticosteroids, ruxolitinib, and infliximab.

Three patients developed chronic GVH, all with cutaneous involvement. One refractory case responded to ibrutinib.
Six patients experienced CMV reactivation, all of whom had previously developed acute GVHD.
Six Patients developed hemorrhagic cystitis due to BK virus.
The non-relapse mortality (NRM) rate was 33% with a median of 3 months (range, 3–5 months), due to severe infectious complications (n=2) and refractory acute GVHD (n=1). No patients experienced disease relapse.After a median follow-up of 4 months (range 3-60 months), all surviving transplanted patients were in complete remission. Among non-transplanted patients, the median follow-up was 14 months, and five patients died due to disease relapse.

Conclusions: Our experience demonstrated a high-risk of acute GVHD and viral infections, as well as early NRM, probably due to the intensive pre-transplant therapy and advanced disease status. Expanding haplo-HSCT to a larger patient population remains challenging in resource-limited settings.

Disclosure: Nothing to declare

P079

USE OF ORAL AZACITIDINE AS BRIDGING THERAPY TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ALLO-HSCT): A SINGLE TRANSPLANT PROGRAM EXPERIENCE

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Background: Allo-HSCT remains the only curative option for patients with intermediate or high-risk AML. However, clinical issues related to the patient or the donor often delay the transplant procedure, increasing the relapse risk. Since the quality of CR and the timing of allo-HSCT are critical for transplant outcomes, identifying a standardized bridging therapy during delays in the allo-HSCT pathway is essential. We report the experience of a single adult Transplant Program in evaluating the efficacy and safety of oral azacitidine as bridging therapy, between last consolidation and allo-HSCT, for AML in CR.

Methods: From July 2024 to October 2025, 11 patients with intermediate/high-risk AML, according to ELN 2022, received oral azacitidine as bridging therapy during allo-HSCT delays. Inclusion criteria for oral azacitidine bridging therapy were: diagnosis of AML in hematological CR (including FLT3 mutations), off therapy for more than 2 months after

second consolidation, temporary donor unavailability or patient-related clinical issues. The median age was 48 years (range 29–67), with 6 males and 5 females. Oral azacitidine was administered at a dose of 300 mg/day for 14 consecutive days per cycle.
Nine allo-HSCTs were performed using matched related, matched and mismatched unrelated donors in 1, 5, and 3 cases, respectively. All patients received PBSC as the stem cell source, while intermediate and low-intensity conditioning regimens were administered in 5 and 4 cases, respectively.

Results: In our experience, the unrelated donor's unavailability or ineligibility represent the major cause of allo-HSCT delay, corresponding to 15% for year and 64% in the present series (table 1). In this cohort, 7 (64%), 2 (18%), and 2 (18%) patients received 1, 2 or more than 2 cycles of oral azacitidine**,** 6/11 (54%) patients received oral azacitidine in MRD-positive CR and 5/11 (45%) were FLT3 mutated. During bridging therapy, one patient lost transplant eligibility due to an increased frailty and continued oral azacitidine until relapse, while another patient is still awaiting donor availability. Ruling out one patient who loss eligibility to transplant, 10 of 11 (91%) were evaluable for efficacy: 9 of 10 (90%) underwent allo-HSCT in hematological CR, of whom 4 of 9 (44%) were MRD-negative. Overall, all patients MRD negative before bridge therapy, mainteined MRD negativity until allo-HSCT. The median time between oral azacitidine starting and allo-HSCT was 2.9 months (95% CI: 2.36–3.43). Moreover, no grade ≥2 adverse events related to oral azacitidine (CTCAE criteria) occurred in the 11 patients. With a median follow-up of 15.13 months (IC

13.03-17.22) months, DFS and OS after allo-HSCT were 77.8% and 90.9%, respectively.

Table 1: Cause of Bridging Therapy

Patient Id/UPN	Cause of bridging therapy Donor/Patient	Days between last CHT and allo-HSCT*	N of oral Azacitidine cycles
1/229.1	Temporary Unavailability/IFI	111	1
2/237.1	Multiple donors' unavailbility /-	92	1
3/NA	- /E. coli spondylodiscitis, IFI	*567	7
4/242.1	Temporary Unavailability/-	109	1
5/249.1	Temporary Unavailability/-	106	1
6/250.1	Temporary Unavailability/-	330	1
7/263,1	-/IFI	138	2
8/267,1	First unrelated donor ineligibility/-	181	2
9/274,1	-/Fungal skin infection	135	1
10/in progress	No donors identification/-	*158	4
11/278.1	-/IFI	118	1

Legend: Id= Identification; UPN= Unique patient number; Invasive Fungal Infection; NA= Not Applicable; * days to last follow up

Conclusions: Oral azacitidine as bridging therapy to allo-HSCT in patients with intermediate/high-risk AML is feasible and seems effective in maintaining hematological and molecular CR, including FLT3 mutated cases. Futhermore, in our cohort, no patients did not undergo allo-HSCT due to azacitidine related adverse events. Although our experience is limited to a small series, these data are encouraging for the use of oral azacitidine as bridging therapy in case of allo-HSCT delay.

Disclosure: Nothing to declare.

P080

MITIGATING RISK FACTORS FOR PROLONGED HOSPITALIZATION IN PEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER QUALITY IMPROVEMENT STUDY IN SAUDI ARABIA

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Background: Few studies evaluated the risk factors for prolonged hospitalization in pediatric hematopoietic stem cell transplantation (HSCT) recipients, who typically require six weeks of hospitalization. We aimed to reduce the average length of stay (LOS) in pediatric HSCT recipients by 5% from baseline, by identifying factors associated with LOS using the IACT Method.

Methods: One hundred and fifty pediatric patients were included in our study, with an age of 0.5–14 years, potential factors influencing the LOS were identified using a patient flow sheet, Pareto chart and questionnaire-based voting in the preimplementation period. In the implementation phase, interventions including increasing team awareness of early discharge readiness, based on a new discharge criteria, and ensuring medication/nutrition requirements with the aid of home health care were implemented.

Results: Prolonged hospital stay was defined as >21 and >35 days for autologous and allogeneic HSCT respectively, prolonged hospitalization was observed in 35 (39%) patients in the preimplementation group and 13 (22%) patients in the postimplementation group. The need for intravenous medication/nutrition (P 0.001), cytomegalovirus infection (P 0.001), hemorrhagic cystitis (P 0.003), graft-versus-host disease (P 0.007), neutrophil/platelet engraftment at >30 days (P 0.001), and pediatric intensive care unit admission (P 0.001) were significantly associated with prolonged hospitalization. In the postimplementation period, the need for intravenous medication/nutrition remained a significant risk factor for prolonged hospitalization (P 0.001).

Conclusions: Reducing the average LOS from 36 to 25 days was associated with an estimated total cost reduction of 4 356 000 SR (1 159 831 USD) for the study period September 2022 to December 2023. Our findings highlight that implementing tools to mitigate risk factors for prolonged hospitalization in pediatric HSCT recipients is essential for optimizing patient care, improve bed occupancy and healthcare resource utilization.

Clinical Trial Registry: Not applicable.

Disclosure: Author declares no conflict of interest.

P082

ALLOGENEIC TRANSPLANT JOURNEY THROUGH THREE MALIGNANCIES: A 75-YEAR-OLD PATIENT DEFYING THE ODDS

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Background:

Recent advancements in hematopoietic stem cell transplantation (HSCT) have significantly increased long-term survival among transplant recipients.[1] However, a major late complication following allogeneic HSCT is the development of secondary malignancies.[2] Post-transplant lymphoproliferative disorders (PTLDs) associated with Epstein–Barr virus (EBV) reactivation are frequently donor-derived and typically emerge at a median of 2–4 months post-transplant.[3]

Methods: We present a case of a patient who developed acute myeloid leukemia (AML) on a background of myelofibrosis, achieved remission after chemotherapy, and was diagnosed with minimally invasive pulmonary adenocarcinoma during pre-transplant workup. After undergoing a successful HSCT, she subsequently developed EBV-positive diffuse large B-cell lymphoma (DLBCL) in the setting of post-transplant immunodeficiency, and currently remains in remission with appropriate therapy.

Results:

A 75-year-old woman was diagnosed with AML after lymphomonocytosis was detected. Bone marrow biopsy revealed 20% CD34-positive precursors and t(8;21) in 84% of cells. She was treated with azacitidine (7 days) and venetoclax (400 mg daily). After four cycles, blasts were cleared, although reticulin fibrosis (grade 3) with focal collagen deposition indicated myelofibrosis. During HSCT preparation from a matched male sibling donor, chest imaging identified a ground-glass nodule suggestive of adenocarcinoma. Right upper lobe wedge resection confirmed minimally invasive ROS1-positive adenocarcinoma (0.8 cm, 0.5 cm invasive) with negative margins. Multidisciplinary review recommended surveillance at three-month intervals. A total dose of 6.5×10^6 cells per kilogram was infused following Flu/Treo/ATG conditioning. Target cyclosporine levels could not be maintained; therefore, tacrolimus was initiated for GVHD prophylaxis. Bone marrow was normocellular, and complete donor chimerism was achieved by month one. CMV reactivation accompanied by diarrhea occurred on day 47 and was treated with ganciclovir. Due to persistent diarrhea, colonoscopy was performed at the end of month two, initially under suspicion of gastrointestinal GVHD. Unexpectedly, biopsy demonstrated EBV-positive DLBCL without histological evidence of GVHD. Immunosuppression was tapered. PET/CT demonstrated multiple FDG-avid lymph nodes and hypermetabolic nodules in both lungs. Biopsy was deferred due to cytopenia, and the patient received one cycle of rituximab followed by two cycles of R-mini-CHOP. Previously hypermetabolic lymph nodes demonstrated complete metabolic response (Deauville 1–2). Due to the development of profound neutropenia following chemotherapy, it was decided to continue the remaining treatment with rituximab monotherapy. The oncology department recommended follow-up at three-month intervals for the pulmonary malignancy. At the sixth month post-transplant, the patient remains in remission for all malignancies.

Conclusions: Donor cell–derived leukemia/lymphoma (DCL) represents an exceptionally rare complication of allogeneic HSCT. Azacitidine exerts antitumor activity by inhibiting DNMT1, thereby restoring tumor-suppressor gene expression. Real-world observations regarding azacitidine–venetoclax treatment have not shown an increased incidence of solid tumors; accordingly, the pulmonary adenocarcinoma in this case was interpreted as a synchronous malignancy rather than treatment-related. The successful outcomes, sustained remission, and ongoing survival of this elderly patient with three distinct primary malignancies underscore the clinical and academic relevance of this case.

Disclosure: Nothing to declare

P083

HARNESSING GRAFT-VERSUS-LEUKEMIA ALLOREACTIVITY TO TREAT MULTI-REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA AFTER ALLOGENEIC HSCT

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Background: Relapsed or refractory (R/R) acute lymphoblastic leukemia (ALL) after hematopoietic stem cell transplantation (HSCT) remains a major unmet need in pediatric transplant medicine. Children who relapse early after HSCT, develop extramedullary disease, or progress after exposure to both CD19- and CD22-directed CAR-T cell therapies have profoundly poor outcomes. Strategies that intentionally amplify graft-versus-leukemia (GvL) alloreactivity—such as donor lymphocyte infusion (DLI), cytokine priming, or other immunomodulatory approaches—are conceptually appealing but underexplored in heavily pretreated pediatric patients. We report a unique case of a child with pre-B cell ALL who experienced six total relapses, including relapses after two HSCTs and two CAR-T products, who ultimately achieved durable remission through deliberate augmentation of GvL using haploidentical DLI combined with interferon-alpha (IFN-α).

Methods: A retrospective review of the patient's disease course from diagnosis in December 2017 through late 2025 was performed. Data collected included disease characteristics, MRD kinetics, relapse chronology, prior cytotoxic and immune-based therapies, and transplant-related complications. Major interventions evaluated included CD19 and CD22 CAR-T cell therapies, a matched unrelated donor HSCT, and a maternal haploidentical HSCT. Particular attention was given to the rationale, timing, and outcomes of combining inotuzumab ozogamicin with haplo-DLI and IFN-α. Longitudinal assessment focused on the depth and durability of remission, immune-mediated toxicities, and the evolution of acute and chronic GvHD.

Results: The patient experienced six relapses, reflecting an exceptionally aggressive and treatment-refractory disease course. Early events included an extramedullary relapse shortly after induction and a CNS relapse with destructive intracranial chloromas following the first HSCT on 6/15/2018. Marrow relapse after CD19 CAR-T and another relapse after CD22 CAR-

T prompted a second HSCT—a maternal haploidentical transplant—on 4/21/2020. Despite this, an early fifth relapse was detected at day +100. Inotuzumab ozogamicin administered prior to haplo-DLI, followed by IFN-α, triggered a brisk alloreactive response resulting in severe steroid-refractory acute GvHD (SRaGvHD) involving the skin, GI tract, and liver. This immune activation was associated with a potent GvL effect, leading to a deep antileukemic response and achievement of clonoSEQ-negative complete remission (CR) by October 2020. The patient subsequently stabilized and was successfully weaned off all immunosuppression by 2022. A sixth molecular relapse occurred in 2023. Repeat haplo-DLI again led to recurrent SRaGvHD and induced deep molecular remission, demonstrating persistent GvL sensitivity. The patient subsequently developed severe chronic SR-GvHD requiring prolonged therapy with MSCs, ruxolitinib, belumosudil, and axatilimab. Despite chronic GvHD with joint contractures, decreased range of motion, and ongoing treatment with belumosudil and axatilimab, he has remained a full-time university student throughout his therapy, demonstrating remarkable functional resilience. As of late 2025, he remains in sustained NGS-negative remission

Conclusions: This case demonstrates that intentionally harnessed GvL—via haploidentical DLI augmented with IFN-α—can produce deep, durable remission in profoundly multi-refractory pediatric ALL. Although associated with significant acute and chronic GvHD, coordinated multidisciplinary management enabled control of both leukemia and immune dysregulation. These findings support further evaluation of cytokine-enhanced DLI strategies as a salvage modality for high-risk pediatric patients who relapse despite HSCT and advanced cellular therapies.

Disclosure: I have no conflict of interest

P084

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN THE TREATMENT OF SEVERE APLASTIC ANEMIA IN ADULTS: EXPERIENCE OF THE REPUBLIC OF BELARUS

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Background: Transplantation options for severe aplastic anemia (SAA) in adult patients include "upfront" or "delayed" allogeneic hematopoietic stem cell transplantation (alloHCT) after failed immunosuppressive therapy. AlloHSCT from matched sibling donor (MSD) remains the best option for patients at the age of 40 years or younger without significant comorbidities.

Methods: The study included 48 patients with SAA who underwent alloHSCT from 1995 to 2024 in our clinic. Median age of the participants was 25.5 (21.0-30.0) years, 23 of them

were male (48%). Paroxysmal nocturnal hemoglobinuria (PNH) clone was detected with flow cytometry in 6 patients at median level of 1.7 (0.3-5.7)%, 1 patient had PNH clone at 70.4%. Donor-specific antibodies were revealed in 2 patients. The patients were divided into subgroups according the treatment regimen (Table 1). ABO incompatibility was detected in group B in 6 donor-recipient pairs, in group C – in 2 pairs.

Table 1. Patients with SAA treated with alloHSCT from 1996 to 2024 depending on conditioning regimen

Characteristics	Group A (n=27)	Group B (n=16)	Group C (n=5)
Time of alloHSCT	Feb 1995 – Jan 2016	Aug 2016 – May 2024	Feb 2022 – Oct 2024
Median age, y.o.	23.0 (20.0-29.5)	27.5 (20.5-30.8)	26.0 (23.0-27.0)
Male, n	16	5	2
Median time to alloHSCT, months	3.0 (2.0-6.3)	6.6 (3.1-9.8)	7.0 (6.3-52.0)
Donor type: MSD, n Matched unrelated donor (MUD), n Mismatched unrelated donor (MMUD), n	27	8 8	3 2
Conditioning regimen, total dose	Cyclophosphamide (Cy), 200 mg/kg, anti-thymocyte globulin (ATG)*	Cyclophosphamide, 100 mg/kg, Fludarabine (Flu), 100 mg/m^2, ATG*	Cyclophosphamide, 120 mg/kg, Fludarabine, 150 mg/m^2, ATG*
Graft-versus-host disease (GvHD) prophylaxis	Cyclosporin A (CsA), methylprednisolone	CsA, methylprednisolone	MUD - CsA, methylprednisolone, MMUD - CsA, methylprednisolone, micophenolate mofetil

*- dosage depends on the manufacturer (brand) of ATG

Results: By Jan 1st 2025, 39 patients (81.3%) remained alive: 1 patient experienced autologous reconstitution after alloHSCT with complete hematopoiesis. The causes of death in group A were infectious complications (n=2), acute GvHD (n=1), graft rejection (n=1), chronic GvHD (n=1), in group B - infectious complications (n=3). Transplant-related

mortality (TRM) rate was 7.4% in group A and 6.2% in group B. Overall survival rate and 5-year survival in group A was 81.5% and 85.5% and did not differ significantly from group B: 80.8% and 80.8% (p=0,741). In group C 1 patient died because of Covid-19, TRM rate – 0%. PNH clone disappeared in 4 patients after alloHSCT, in 2 patients PNH clone still presents (<1%).

Conclusions: In the absence of MSD alloHSCT from an unrelated donor (matched or mismatched) is an effective and feasible option for patients with SAA. Flu/Cy/ATG and Cy/ATG conditioning regimens were associated with comparable survival rates.

Disclosure: Nothing to declare.

P085

FACTORS ASSOCIATED WITH OVERALL SURVIVAL AND DISEASE-FREE SURVIVAL IN ADULTS WITH ACUTE MYELOID LEUKEMIA AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AT A CENTER IN COLOMBIA

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the main curative treatment option for adults with intermediate and adverse risk acute myeloid leukemia (AML). Real-world outcome data after allo-HSCT from low- and middle-income countries remain limited. The aim of this study was to explore factors associated with overall survival (OS) and disease-free survival (DFS) in a cohort of adults with AML in Colombia.

Methods: We conducted a retrospective study of adults with AML who underwent allo-HSCT between 2013 and 2024 at a single center in Colombia. Overall survival (OS) was defined as the time from transplantation to death from any cause or censoring at last follow-up, and disease-free survival (DFS) as the time from transplantation to relapse. OS and DFS were estimated at 100 days, 1 year, and 5 years using the Kaplan–Meier method. Associations between clinical variables and OS and DFS were evaluated using univariate Cox proportional hazards models.

Results: A total of 47 adults with AML undergoing allo-HSCT were included. Fifty-one percent were male, with a median age of 45 years (range, 18–65). At transplantation, 53.1% had adverse-risk disease, 89.4% were in first complete remission, 17% had an ECOG performance status of 1, and 25.5% had a high comorbidity burden (HCT-CI score ≥3). HLA-identical donors were used in 65.9% of cases, myeloablative conditioning in 51.1%, and peripheral blood as the stem cell source in 97.8%. Acute and chronic graft-versus-host

disease occurred in 61.7% and 57.4% of patients, respectively.
The median follow-up was 44.6 months. One patient died within the first one hundred days; by 1 year, eleven patients (23.4%) had died, and by 5 years, seventeen patients (36.1%) had died. Estimated OS was 97.8% (95%CI 85.8-99.7) at 100 days, 78.7% (95%CI 64.0-87.9) at 1 year, and 58.0% (95%CI 40.3-72.1) at 5 years. The leading cause of death was transplant-related mortality (52.9%), with half of these deaths due to infectious causes. Among the remaining deaths, 17.6% were attributable to disease relapse.
Relapses occurred in 5 patients (10.6%), including 2 events within the first year and 1 event within the first one hundred days. Estimated DSF was 97.8% at one hundred days, 95.6% (95%CI 83.5-98.8) at 1 year, and 87.8% (95%CI 73.1-94.7) at 5 years. In univariate Cox analysis, an ECOG performance status of 1 at the time of transplantation was associated with worse OS at both 1 year (HR 8.19, p = 0.001) and 5 years (HR 4.34, p = 0.007); additionally, relapse was associated with increased mortality (HR 4.79, p = 0.004). No characteristic showed a statistically significant association with DFS.

Characteristics		Overall Survival				Desease-Free Survival			
		1 year % (95%CI)	5 year % (95%CI)	HR (95%CI)	P-value	1 year % (95%CI)	5 year % (95%CI)	HR (95%CI)	P-value
MRC Cytogenetic risk	Intermediate	86 (63.4 - 95.3)	57.5 (31.3 - 76.7)	1.12 (0.43 - 2.92)	0.80	100	89.4 (64 - 97.2)	1.48 (0.24 - 8.87)	0.66
	Adverse	72 (50 - 85.5)	58.1 (33.2 - 76.6)			91.6 (70.4 - 97.8)	86.5 (63.5 - 95.5)		
CR prior to HSCT	CR 1	80.9 (65.5 - 90)	61.5 (42.8 - 75.7)	Ref		97.5 (83.5 - 99.6)	91.7 (76.5 - 97.2)	Ref	
	CR 2	75 (12.8 - 96)	0	2.59 (0.56 - 11.9)	0.22	100	66.6 (5.4 - 94.5)	4.75 (0.49 - 45.94)	0.17
	Refractory	0	0	-	1	0	0	-	1
ECOG	0	87.2 (71.9 - 94.4)	63 (43.1 - 77.6)	4.34	0.007	97.3 (82.7 - 99.6)	88.7 (72.7 - 95.6)	2.1	0.51

	1	37.5 (8.7 - 67.4)	37.5 (8.7 - 67.4)	(1.49 - 12.59)		87.5 (38.7 - 98.1)	87.5 (38.7 - 98.14)	(0.23 - 19.22)	
Sorror HCT-CI score	0	81.2 (52.5 - 93.5)	64.3 (32.4 - 84.1)	Ref		100	84.6 (51.2 - 95.9)	Ref	
	1-2	78.9 (53.2 - 91.5)	55.8 (27.7 - 76.7)	1.18 (0.37 - 3.73)	0.77	-	89.4 (64 - 97.2)	0.84 (0.11 - 5.97)	0.86
	≥3	75 (40.8 - 91.2)	54.7 (22.2 - 78.5)	1.57 (0.45 - 5.44)	0.71	-	88.8 (43.3 - 98.36)	0.73 (0.06 - 8.14)	0.80
HSCT type	Matched sibling	83.9 (65.5 - 92.9)	57.3 (35.1 - 74.4)	1.24 (0.456 - 3.37)	0.66	93.4 (76.2 - 98.3)	86.2 (67.3 - 94.6)	0.56 (0.06 - 5.09)	0.61
	Haploidentical	68.7 (40.5 - 85.6)	60.2 (31.2 - 80.1)			100	90.9 (50.8 - 98.6)		
Conditioning regimen intensity	Myeloablative conditioning (MAC)	91.7 (70.6 - 97.8)	70.3 (44.7 - 85.7)	2.73 (0.99 - 7.51)	0.05	100	90.9 (68.3 - 97.6)	1.99 (0.33 - 12.03)	0.44
	Reduced-intensity conditioning (RIC)	65.2 (42.3 - 80.8)	43.8 (18.7 - 66.5)			90.8 (68.1 - 97.6)	84.8 (59.3 - 94.9)		
Acute GVHD	Yes	72.4 (52.3 - 85.1)	60.5 (39.7 - 76)	1.4 (0.51 - 3.8)	0.50	100	95.2 (70.7 - 99.3)	0.17 (0.01 - 1.52)	0.11
	No	88.9 (62.4 - 97.1)	57.8 (28.1 - 78.9)			88.8 (62.4 - 97.1)	77.7 (51.1 - 91)		

Chronic GVHD	Yes	-	62.6 (39.7 - 78.9)	0.66 (0.25 - 1.72)	0.39	-	96.1 (75.6 - 99.4)	0.16 (0.01 - 1.47)	0.10
	No	-	50.9 (21.5 - 74.4)			-	76 (47.7 - 90.3)		

Conclusions: In this cohort, OS after allo-HSCT was comparable to that reported by large registries from high-income countries, with impaired functional status at the time of allo-HSCT and post-transplant relapses identified as the main determinants of mortality. Relapses rates were low and the small number of patients with ECOG 1 may have led to an overestimation of HR; however, the association remained statistically significant. These findings support the feasibility of achieving competitive outcomes in resource-limited settings resource-limited settings.

Disclosure: The authors declare no conflicts of interest.

P086

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HODGKIN LYMPHOMA: A 16-YEAR SINGLE-CENTER EXPERIENCE FROM EHU 1ST NOVEMBER OF ORAN, ALGERIA

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Background: Autologous hematopoietic stem cell transplantation (ASCT) remains a cornerstone therapeutic intensification strategy in the treatment of relapsed or refractory Hodgkin lymphoma (R/R HL).
The objective of this study was to evaluate the efficacy and safety of ASCT in patients with HL treated at the Hematology Department of EHU 1er Novembre, Oran, Algeria.

Methods: This was a single-center retrospective study conducted over a 16-year period, including patients with HL. ASCT was administered as first-line consolidation therapy in 53 patients with advanced-stage disease (stage III–IV) and in 102 patients with relapsed or refractory R/R HL.
$CD34^+$ hematopoietic stem cells were mobilized using granulocyte colony-stimulating factor (G-CSF) alone (filgrastim or lenograstim) at a dose of 15 µg/kg/day for 5 days, or in combination with plerixafor in cases of mobilization failure. Stem cells were collected by cytapheresis. Graft was stored at +4 °C for 6 days. Cryopreservation of graft with liquid nitrogen freezing at −196 °C was introduced to our center in 2022. Conditioning regimens: CBV (2009–2010), BEAM (2010–2016), Benda-EAM (2015–2016), and EAM (2016–July 2025). The EAM regimen included a total dose of etoposide 800 mg/m², cytarabine 8 g/m², and melphalan 140 mg/m². All patients received Granulocyte colony-stimulating factor (G-

CSF) from day + 5 until neutrophil recovery (absolute neutrophil count > 0.5 G/L. Data of assessment was 31 November 2025.

Results: A total of 155 patients with HL were included between June 2009 and 31 July 2025. The median age was 26 years (range, 14–55 years), with a male-to-female ratio of 0.93 (75 males and 80 females).
Conditioning regimens included CBV in 15 patients (9.6%), BEAM in 45 patients (29%), Benda-EAM in 5 patients (3.2%), and EAM in 90 patients (58%). The median time to neutrophil engraftment was 14 days (range, 8–39 days), and platelet recovery (> 20 G/L) was 13 days (range, 3–42 days). The median number of red blood cell concentrates transfused was 3 (range, 1–5), and the median number of platelet concentrates transfused was 3 (range, 1–9).
At day 100 post-transplant, the TRM was 4.51% (7 patients). With a median follow-up of 5 years, the relapse rate was 16.7% (26 patients) and the OS was 83%. The median PFS and OS were 53 months and 65 months, respectively.

Conclusions: ASCT is a safe and effective treatment for patients with Hodgkin lymphoma. Using predominantly fresh grafts, the procedure showed low treatment-related mortality, rapid hematologic recovery, high remission rates, and durable long-term outcomes.

Disclosure: The authors declare no conflict of interest related to this study.

P087

EXPERIENCE OF MISMATCHED UNRELATED DONOR TRANSPLANTS WITH PTCY BASED GVHD PROPHYLAXIS IN BENIGN HEMATOLOGICAL DISORDERS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) from mismatched unrelated donors (MMUD) is an option for patients with benign hematological disorders (e.g., aplastic anemia, hemoglobinopathies, inherited bone marrow failure syndromes and inborn errors of immunity) who lack matched sibling donors. Post-transplant cyclophosphamide (PTCy) is increasingly used to prevent graft-versus-host disease (GVHD) in mismatched donor settings, but data specifically in benign hematologic disorders are limited.

Methods: We present a retrospective analysis of 3 consecutive patients with benign hematological disorders who received MMUD allo-HSCT with PTCy-based GVHD prophylaxis at our transplant centre. Primary endpoints: neutrophil and platelet engraftment, cumulative incidence of grade II-IV acute GVHD, moderate–severe chronic GVHD, TRM, and OS at 1 year. Secondary endpoints: graft failure, infections, organ toxicities, and hematologic response.

Results: We performed a total of 3 MMUD in 2 patients with Dyskeratosis congenita (DKC) and one Wiskott Aldrich Syndrome (WAS) aged 49 years, 19 years and 18 months respectively. All 3 patients had HLA A mismatch.The child with WAS had 8/10 match with both the mismatches at HLA A locus and the two cases of DKC had single HLA A mismatch. The details of the 3 cases have been mentioned in table 1. All the 3 patients are alive and well with the median follow up duration of 30 months. None of the 3 cases developed any GVHD and immunosuppression could be tapered by Day 150 in all three.

Conclusions: PTCy-based GVHD prophylaxis appears to be a feasible strategy for MMUD allo-HSCT in benign hematological disorders, with acceptable rates of severe GVHD and transplant-related mortality in our cohort. Larger multi-center studies or prospective trials are needed to confirm these findings.

Disclosure: Authors have no conflicts of interest and no disclosures

P088

RISK FACTORS FOR RECURRENT CYTOMEGALOVIRUS INFECTION IN HEMATOPOIETIC STEM CELL AND SOLID ORGAN TRANSPLANT RECIPIENTS: A SCOPING REVIEW

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Background: Recurrent cytomegalovirus (CMV) infection, characterized by the reappearance of detectable CMV DNA following initial viral clearance, is a frequent complication in transplant recipients. It not only increases the risk of end-organ disease and graft rejection but may also contribute to delayed immune reconstitution, heightened susceptibility to other opportunistic infections, and elevated mortality. Early identification of high-risk patients is essential for reducing complications and improving long-term outcomes. This study aimed to identify risk factors associated with recurrent CMV infection in hematopoietic stem cell transplantation (HSCT) and solid organ transplantation (SOT) recipients.

Methods: Following the PRISMA-ScR framework for scoping reviews, a systematic search for literature on risk factors for refractory CMV infection after transplantation was conducted in eight databases including PubMed, EMBASE, the Cochrane Library, Web of Science, CNKI, Wanfang, VIP and CBM (2010-2023). Two reviewers independently extracted data and assessed the risk of bias using the QUIPS tool.

Results: A total of 10 studies were included (HSCT: 5 studies including 331 patients; SOT: 5 studies including 217 patients). A total of 21 risk factors (9 HSCT-specific risk factors and 12 SOT-specific risk factors) for recurrent CMV were identified. The HSCT-specific risk factors for recurrent CMV included 5 host-related [graft-versus-host disease; recipient with higher age; diagnosis with acute myeloid leukemia/myelodysplastic syndrome; diagnosis with

hematological malignancies; progressing to a refractory state after CMV infection]; 3 transplantation-related factors [CMV serological status of donor$^{(-)}$ and recipient$^{(+)}$ / donor$^{(+)}$ and recipient$^{(+)}$ (vs recipient$^{(-)}$); donor type (cord blood vs. non-cord blood, mismatched family vs matched sibling donor, haploidentical blood and marrow transplant vs matched sibling donor, mismatched donor vs matched donor); post-transplantation high-dose steroids use (>=1 mg/kg)]; and 1 viral-related factors [CMV-specific CD8^{+} TcM at day 30 >=0.032 μL (vs. <0.032)]. Moreover, the SOT-specific risk factors for recurrent CMV included 5 host-related factors [chronic kidney disease (CKD); NFKB1 ins/ins genotype (vs ins/del-del/del); pneumonia; organ rejection within 3 months post-transplantation; decreased in absolute lymphocyte count]; 4 transplantation-related factors [CMV serological status of donor$^{(+)}$ and recipient$^{(-)}$ (vs others); delayed graft function; lung transplant (vs. non-lung); using of antilymphocyte therapy]; and 3 virus-related factors [baseline CMV miRNA detection-UL22A-5p; CMV clearance half-life > 3 days (vs < 3 days); higher peak viral load].

Transplant type	Factor category	Factors	Number of recurrent reference
Haematology transplant (n = 5)	Host-related factors	acute or chronic GVHD, any grade (yes vs. no)	1
		aGVHD (grade II-IV vs. grade 0-I)	2
		aGVHD (yes vs. no)	1
		Antilymphocyte therapy (yes vs. no)	1
		Diagnosis-AML/MDS (yes vs. no)	1
		Hematological malignancies (yes vs. no)	1
		Recipient age	1
		Response to treatment (refractory vs. not refractory)	1
	Transplantation-related factors	CMV serostatus (D-/R+ vs. R-)	1
		CMV serostatus (D+/R+ vs. R-)	1
		Donor type (cord blood vs. non-cord blood)	1
		Donor type (HBMT vs. MSD)	1
		Donor type (mismatched family vs. MSD)	1
		Donor type (mismatched vs. matched)	2
		Treatment with high-dose steroids after day 100 (≥1 mg/kg) (with vs. without)	1
	Viral-related factors	CMV-specific CD8+ TcM at day 30 (μL) (<0.032 vs. ≥0.032)	1
Organ transplant (n = 5)	Host-related factors	CKD (yes vs. no)	1
		NFKB1 genotype (ins/ins vs. ins/del-del/del)	1
		Pneumonia (yes vs. no)	1
		Rejection within 3 mo prior (yes vs. no)	1
		Decrease in ALC	1
	Transplantation-related factors	CMV serostatus (D+/R- vs. others)	1
		Delayed graft (days)	1
		Transplant type (lung vs. non-lung)	1
	Viral-related factors	Baseline CMV miRNA detection-UL22A-5p (yes vs. no)	1
		Viral load half-life, days (>3 vs. <3)	1
		Higher peak viral load	1

Figure 1. Hot map of risk factors for recurrent CMV infection.
Notes: The numbers in the hot map indicate the number of articles corresponding to the factors.
Abbreviations: aGVHD, acute graft-versus-host disease; ALC: absolute lymphocyte count; AML: acute myeloid leukemia; CMV: cytomegalovirus; CKD: chronic kidney disease; HBMT: haploidentical blood and marrow transplant; MDS: myelodysplastic syndrome; MSD: matched sibling donor.

Conclusions: This review identified the spectrum of host-, transplantation-, and virus-related risk factors for recurrent CMV in HSCT and SOT recipients, respectively. Early identification of these high-risk populations allows for optimized antiviral strategies, such as the selection of appropriate therapy and the extension of treatment duration, which may reduce the risk of recurrence, associated complications, ultimately improving long-term patient outcomes.

Disclosure: Jingyi Wu and Tingting Wang are employees of Takeda (China) International Trading Co., Ltd. The authors declare that there were no commercial or financial relationships that could be interpreted as potential conflicts of interest in the conduct of this study.

P089

HAPLO-CORD HCT: SAVE THE SIBLING!

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Background: Transfusion dependent thalassemia is a disorder for which allogeneic hematopoietic stem-cell transplantation (HSCT) remains the principal curative therapy. Lack of matched donors limits its broader application. Haploidentical transplant has its own risks of GVHD, and treatment related mortality. The Haplo-Cord transplant is unique method of transplantation which combines haploidentical peripheral-blood stem cells from one donor with cord-blood stem cells from other which may offer rapid engraftment, lower GVHD, and improved immune recovery. We report the successful use of HaploCord HSCT in a 7-year-old male with E Beta thalassemia treated under the *Save the Sibling (STS)* program.

Methods: Patient was older child with transfusion dependency, severe iron load and no sibling. Concept of combined HaploCord transplant was planned with mother as haplo donor and cord from sibling. Under Save The Sibling program which is collaboration between the fertility centre Renew Healthcare, the cord blood bank "Cord life", and the specialty hospital HCG Cancer Centre bone marrow transplantation was planned. A disease-free, HLA-matched sibling is conceived through IVF with preimplantation genetic diagnosis (PGD) in the STS program. Cord Blood Stem Cells collection, transportation, processing, testing, cryopreservation done by Cord life Sciences ,India. Patients received pre-transplant immunosuppression protocol for 6 weeks. Pharmacologic immunosuppression (PTIS) with fludarabine (30mg/m2), dexamethasone (25mg/m2), and azathioprine (1mg/kg), were given. Hydroxyurea (20mg/kg) was given to reduce host erythropoiesis. Hyper transfusion, dual iron chelators Deferoxamine, Deferiprone were used to reduce severe iron overload. Myeloablative conditioning with Fludarabine (25/mg2), Thiotepa (8mg/kg), GVHD prophylaxis with ATG (4.5mg/kg), PTCY, Tacrolimus (later switched to sirolimus) MMF and ruxolitinib were used. Defibrotide prophylaxis was initiated due to a high pre-transplant VOD risk score. Haplo graft cell dose was 11.66 × 10^6 cells/kg infused on Day+0 while Cord graft dose was 1.136 × 10^6 cells/kg ($CD34^+$ 50.2/µL) infused on Day+1.

Results: Patient had Grade 2 CRS responded to tocilizumab. Grad 2 mucositis managed with supportive care. Myeloid engraftment occurred on day +15 and platelet engraftment on day +21. The patient had moderate transaminitis with suspected GVHD responded to steroids. At discharge the patient was afebrile, transfusion-independent, and clinically stable. At Day 30 chimerism was 100% donor 1(mother). At Day 45 T cell chimerism is showing 95% Donor 1 (mother), 5% Donor 2 (cord) suggesting gradual rise in cord component.

Conclusions: Haplo-Cord HSCT provides a viable curative option for transfusion-dependent thalassemia when a matched donor is unavailable. This case demonstrates successful engraftment, manageable toxicity, and complete hematologic recovery with tailored prophylaxis and multidisciplinary care. By merging two graft sources, Haplo-Cord transplantation under *Save the Sibling(STS)* program embodies science and safety to deliver a lasting cure.

Clinical Trial Registry: No clinical trial registration applicable

Disclosure:

Nothing to declare

P090

A CASE OF RESOLVED SEVERE HEMATOLOGICAL TOXICITY AFTER ANTI-BCMA CAR-T THERAPY FOR MULTIPLE MYELOMA

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Background: CAR-T therapy leads to a rapid and durable response in most patients with hematological malignancies, but could be associated with unique toxicities such as cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity (ICANS), and hemophagocytic lymphohistiocytosis (HLH). However, the most common severe adverse events are hematological toxicities associated with immune effector cells (ICAHT), including transfusion dependence and decreased quality of patients life.

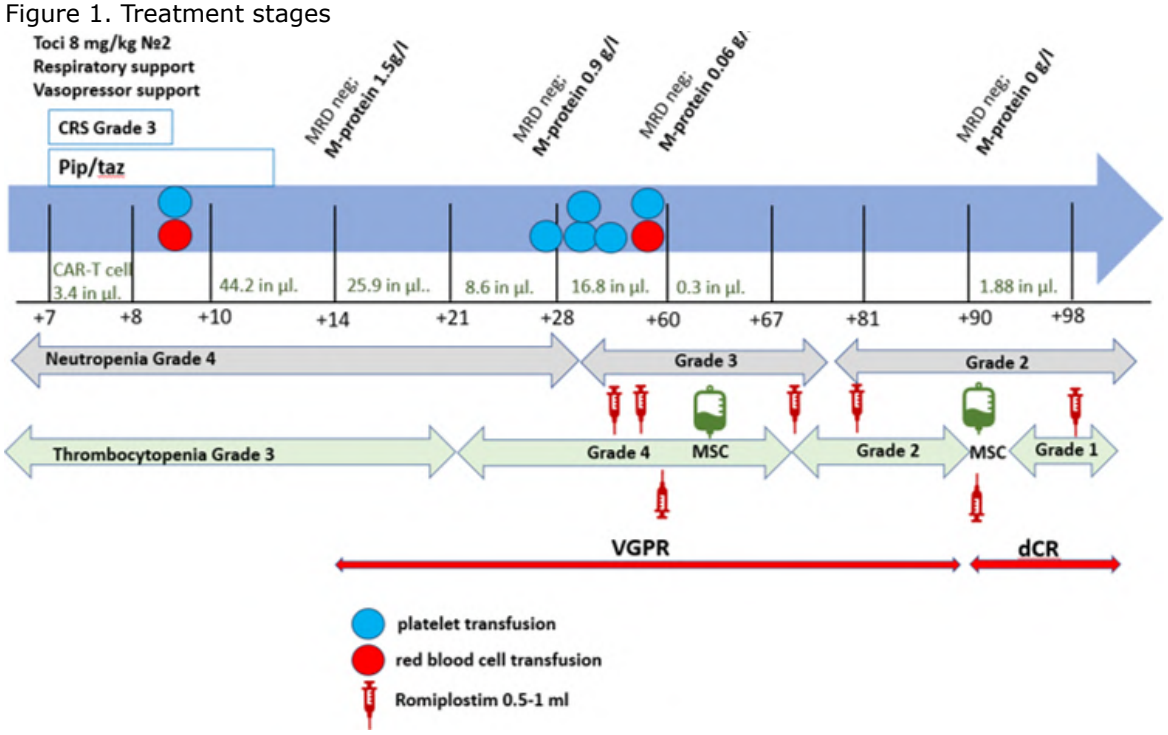
Methods: A 65-year-old woman with relapse/refractory multiple myeloma underwent anti-BCMA CAR-T cell therapy with a locally produced cell product. The study protocol was approved by the local ethics committee (No. 9 from 10/04/2024). Lymphodepleting therapy consisted of fludarabine 30 mg x m^2 and cyclophosphamide 300 mg x m^2 for three consecutive days.The CAR-T cell dose was 1.27 cells x 10^6/kg of patient body weight, the ratio of CD4+ to CD8+ cells was 1.15. Response to treatment was assessed according to the IMWG criteria, severity of adverse events according to CTCAEv5.

Table 1. Clinical characteristics of the patient.

Characteristics	Meaning
DS stage	IIA
ISS stage	II
Lines of therapy	10
Auto HSCT	non-mobilizer
Refractory	double
ECOG	2
CAR-HEMATOTOX score	3
M-protein	13.2 g/l
MRD in bone marrow	negative

Results: By day 14 after infusion, the patient had achieved a MRD negative very good partial response, by day 90 deep, complete response. Grade 3 CRS was detected on day 7, which required 2-fold administration of Tocilizumab at a dose of 8 mg/kg, vasopressor support, and respiratory support. There was no evidence of ICANS or HLH.
From day 3, severe neutropenia (Grade 4) was detected, from day 7 - grade 2 thrombocytopenia with progression to grade 4 from day 21 with the need for transfusion support. Three episodes of infection were verified within 90 days after the start of therapy, including CMV infection, acute respiratory infection, and purulent conjunctivitis with no need for hospitalization. From day 40 after CAR-T administration, Romiplostim therapy was prescribed at dose of 0.5-1 ml weekly; from day 60, mesenchymal stromal stem cells were administered at a dose of 1 million cells per kg monthly with administration of PEG-CSF when the neutrophil level is less than 0.5×10^9.
Currently (day + 140) hematological toxicity has completely resolved, patient in deep complete response and ECOG status - 1 continues outpatient observation with prophylactic administration of human immunoglobulin at a dose of 0.2-0.4 g/kg per month antibacterial and antiviral prophylactic therapy.

Figure 1. Treatment stages



Conclusions: Despite achieving deep durable responses in multiple myeloma, CAR-T therapy may be associated with severe and prolonged hematological toxicity requiring complex and long-term therapy.

Disclosure: Nothing to declare"

P091

JUVENILE MYELOMONOCYTIC LEUKEMIA WITH THERAPY-RELATED AML: A COMPLEX CASE OF MULTIPLE HAPLOIDENTICAL TRANSPLANTS AND CHRONIC GVHD

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Background: Juvenile myelomonocytic leukemia (JMML) is a rare, aggressive hematopoietic disorder of early childhood. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative therapy in refractory cases. However, relapse, graft rejection, and treatment-related complications—including secondary malignancy—continue to present major challenges.

Methods: A 5-year-old boy was diagnosed with juvenile myelomonocytic leukemia (JMML) in 2017, according to the WHO 2016 criteria. He was referred abroad for hematopoietic stem cell transplantation (HSCT). The first transplant was performed on 03/08/2017, using his mother as the donor, with a conditioning regimen consisting of Treosulfan, Melphalan, Cyclophosphamide, and antithymocyte globulin (ATG). Peripheral blood stem cells, processed with α/β T-cell and CD19 depletion, were infused. However, graft rejection occurred on day +18, mediated by persistent anti-HLA-DRB1*04:04 antibodies. A second haploidentical HSCT was subsequently performed on 13/09/2017, using his father as the donor. Pre-transplant interventions included plasmapheresis and bortezomib to reduce donor-specific antibodies. Conditioning consisted of Fludarabine, Cyclophosphamide, Thiotepa, total body irradiation (TBI), and ATG, followed by infusion of an α/β T-cell and CD19-depleted peripheral blood stem cell graft. Engraftment was successful with achievement of full donor chimerism. The post-transplant course was further complicated by acute gut GVHD, treated with methylprednisolone, and renal impairment requiring supportive care. Bone marrow assessment on day +74 confirmed complete remission, and patient was transferred to our center.

Twenty-two months post-transplant, the child developed therapy-related acute myeloid leukemia (t-AML) with newly developed monosomy 7, while maintaining 100% donor chimerism. He received salvage chemotherapy with two cycles of FLA-IDA and subsequently achieved remission. This was followed by a third allogeneic HSCT from his uncle using a T-cell–replete graft on 07/01/2020. Conditioning included fludarabine, busulfan, and cyclophosphamide. GVHD prophylaxis consisted of post-transplant cyclophosphamide, tacrolimus, and mycophenolate. Engraftment was achieved by day +12. This was complicated by steroid-refractory acute GVHD of the skin and eyes, managed with Etanercept, narrow-band UV phototherapy, imatinib, and ruxolitinib, with partial response.

Results: The child remains in morphological and cytogenetic remission. Immunosuppression has been discontinued since August 2022, although chronic skin and ocular graft-versus-host disease (GvHD) sequelae persist. Despite these complications, his overall functional status remains good, with ongoing school attendance and continued follow-up support for learning difficulties.

Conclusions: This case illustrates the clinical complexity associated with JMML, particularly when compounded by graft failure, donor-specific antibodies, and the later emergence of therapy-related AML. The development of t-AML with monosomy 7, two years after HSCT, represents a rare but well-recognized complication. The decision to proceed with a third allogeneic transplant was complex and carried a high risk of mortality and morbidity.
A T-cell–replete graft was selected to optimize the graft-versus-leukemia effect, an especially important strategy in the presence of high-risk cytogenetic features such as monosomy 7. Although the patient subsequently developed severe steroid-refractory GVHD, multimodal immunomodulation—including ruxolitinib, etanercept, imatinib, and narrow-band UV phototherapy—achieved adequate control without major infectious complications. Narrow-band UV phototherapy contributed to partial improvement of cutaneous GVHD and enabled steroid tapering, supporting its recognized role as a safe and effective adjuvant treatment modality.

Disclosure: I have no disclosure

P092

THE ROLE OF APHERESIS PLATELETS IN SUPPORTIVE THERAPY FOR PATIENTS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION - CASE REPORT

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Background: Hematopoietic stem cell transplantation (HSCT) is a key therapeutic approach for patients with malignant hematologic diseases such as acute and chronic leukemias, myelodysplastic syndrome, and relapsed lymphomas, as well as for non-malignant disorders including aplastic anemia, hemoglobinopathies, congenital marrow failure, and primary immunodeficiencies.
The procedure restores normal hematopoiesis after high-dose chemotherapy and/or radiation.
A major post-transplant complication is **severe thrombocytopenia**, which requires transfusion support to prevent bleeding. Among platelet products, **apheresis platelets** (collected from a single donor via cell separator) are preferred over pooled platelet concentrates due to their higher platelet yield, lower risk of infectious transmission, and reduced alloimmunization potential. Donor screening (HBsAg, anti-HCV, anti-HIV 1+2, syphilis, CMV) and microbiological testing ensure product safety.

Methods: Two patients undergoing autologous hematopoietic stem cell transplantation (auto-HSCT) were monitored for hematologic recovery and transfusion support. The first patient received high-dose melphalan conditioning, followed by stem cell reinfusion on February 17, 2025; the second, diagnosed with multiple myeloma, underwent auto-HSCT on April 11, 2025. Post-transplant cytopenia and aplasia were managed with granulocyte-colony stimulating factor (G-CSF) and apheresis platelet transfusions. Daily platelet, leukocyte, and neutrophil counts were recorded to assess recovery kinetics and transfusion efficacy. Patients were discharged after hematologic stabilization and continued outpatient follow-up with scheduled laboratory evaluations.

Results: In both patients, the expected post-conditioning **cytopenic phase** occurred.
Case I: Platelet counts progressively decreased from 132×10^9/L (18.02) to a nadir of 12×10^9/L (28.02). Multiple apheresis platelet transfusions between 25.02 and 05.03 stabilized the counts, which subsequently rose to 42×10^9/L by 25.03.
Case II: Platelet decline began on 17.04 (50×10^9/L) with nadir values around $19–22\times10^9$/L (19–21.04). Three consecutive apheresis transfusions were administered during this period, resulting in gradual hematologic improvement. Platelet counts increased to 109×10^9/L by 28.04 and normalized (>150×10^9/L) by mid-May.
No transfusion reactions or clinical evidence of refractoriness were observed. Both patients demonstrated satisfactory recovery of leukocyte and neutrophil counts with G-CSF support.

Conclusions: Post-transplantation recovery of hematological parameters was accompanied by pronounced thrombocytopenia, which was effectively managed through the use of apheresis platelet transfusions. Their high efficacy, safety profile, and good tolerance make apheresis platelets the standard of supportive therapy for immunosuppressed patients following hematopoietic stem cell transplantation. Continuous monitoring of the therapeutic response showed no evidence of platelet refractoriness. In both presented cases, apheresis platelets successfully controlled thrombocytopenia and contributed to stable hematologic recovery, further confirming their essential role in post-transplant supportive care.

Disclosure: Nothing to declare

P093

ALLOGENEIC STEM CELL TRANSPLANT WITH PERIPHERAL BLOOD SOURCE AS FRONTLINE THERAPY: A SINGLE CENTRE EXPERIENCE

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Background: Allogeneic haematopoietic stem cell transplantation [allo-HCT] represents a potentially curative therapeutic strategy for patients diagnosed with acquired aplastic anaemia [AAA], being considered the first-line treatment of choice in individuals under 40 years of age with a suitable donor. Traditionally, the use of progenitor cells obtained from the bone marrow of an HLA-identical sibling donor has been prioritised in order to minimise the risk of graft-versus-host disease [GvHD] and graft rejection [GR]. However, the introduction of post-transplant cyclophosphamide [PTCy] has enabled the development of alternative platforms, which have shown apparently favourable initial outcomes in small retrospective studies and reports.

Methods: In this report, we describe our centre's clinical experience in the frontline treatment of four patients undergoing a first allo-HCT for AAA between 2022 and 2025, applying transplant platforms based on the use of peripheral blood haematopoietic stem cells, a conditioning regimen including in vivo T-depletion with equine antithymocyte globulin [ATG], and PTCy.

Results: Patient and transplant characteristics are displayed in **Table 1.**

Table 1. Patient and transplant characteristics

	Recipient 1	Recipient 2	Recipient 3	Recipient 4
Age at allo-HCT time (years)	27.4	19.0	40.8	35.8
Gender	Female	Male	Female	Male

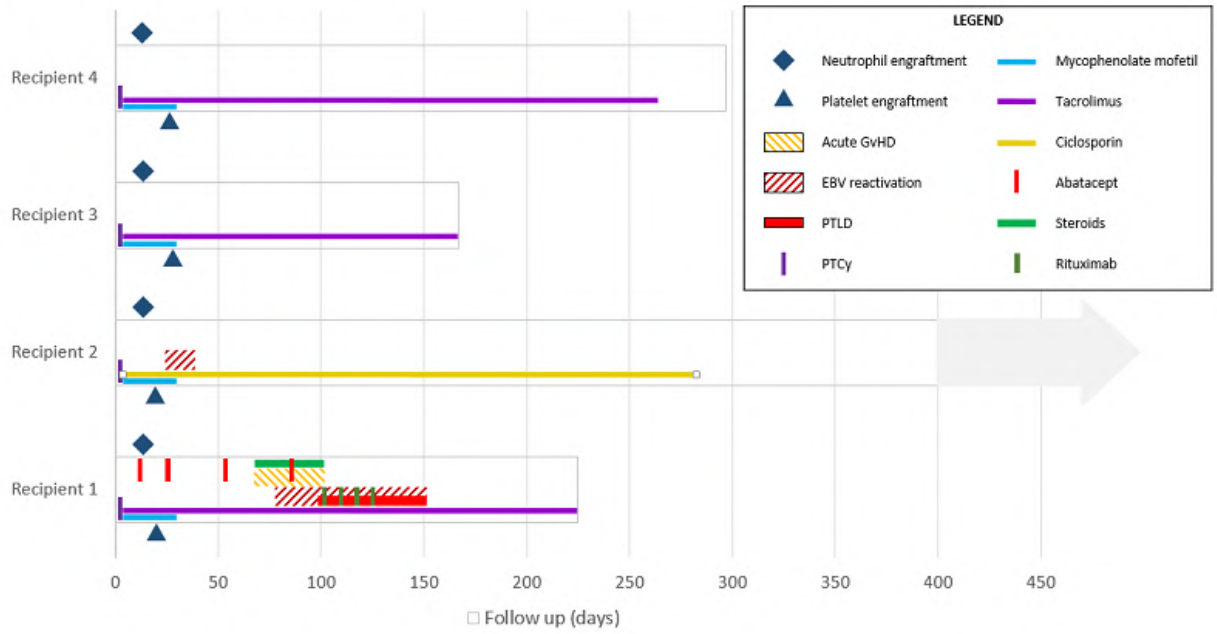
Time from diagnosis to allo-HCT (months)	3.5	2.3	1.3	1.8
Stem cell source	Peripheral blood	Peripheral blood	Peripheral blood	Peripheral blood
Donor type	HLA-mismatched unrelated	HLA-identical sibling	HLA-matched unrelated	HLA-identical sibling
ABO status (donor / recipient)	0 / A	B / B	0 / A	A / A
IgG CMV status (donor / recipient)	Negative / Negative	Negative / Negative	Positive / Positive	Positive / Positive
Conditioning intensity	Reduced intensity	Myeloablative	Reduced intensity	Reduced intensity
Conditioning scheme	Fludarabine Cyclophosphamide Equine ATG	Fludarabine Cyclophosphamide Equine ATG	Fludarabine Cyclophosphamide Equine ATG	Fludarabine Cyclophosphamide Equine ATG
GvHD prophylaxis	PTCy Tacrolimus MMF Abatacept	PTCy Ciclosporin MMF	PTCy Tacrolimus MMF	PTCy Tacrolimus MMF
Anti-infective prophylaxis	Acyclovir Posaconazole Trimethoprim-sulfamethoxazole	Acyclovir Fluconazole Trimethoprim-sulfamethoxazole	Acyclovir Isavuconazole Trimethoprim-sulfamethoxazole Letermovir	Acyclovir Isavuconazole Trimethoprim-sulfamethoxazole Letermovir
Time to neutrophil and platelet engraftment (days / days)	17 / 20	15 / 19	17 / 31	15 / 27
VOD	No	No	No	No
Acute GvHD	Yes (day +69, skin grade 3)	No	No	No
PTLD	Yes (day +98)	No	No	No
Graft failure	No	No	No	No

Follow up (months)	7.4	37.5	5.5	9.8

Allo-HCT: allogeneic haematopoietic stem cell transplantation; ATG: antithymocyte globulin; GvHD: graft-versus-host disease; PTCy: post-transplant cyclophosphamide; MMF: mycophenolate mofetil; CMV: cytomegalovirus; VOD: veno-occlusive disease; PTLD: postrasplant limphoproliferative disease.

Median age at allo-HCT was 31.6 years (interquartile range (IQR), 21.1-39.6), with no gender predominance. Median time from diagnosis to allo-HCT was 2.1 months (IQR, 1.4-3.2). The stem cell source was peripheral blood. The majority (75%) underwent HLA-identical allo-HCT, while two cases (50%) received transplants from unrelated donors, including one (25%) from a mismatched unrelated donor. The greater number (75%) were administered reduced-intensity conditioning [RIC] using fludarabine combined with cyclophosphamide and equine ATG. All patients received GvHD prophylaxis consisting of PTCy, a calcineurin inhibitor and mycophenolate mofetil [MMF]. One patient additionally underwent abatacept owing to an HLA-mismatched unrelated donor.
Median follow-up was 8.6 months (IQR, 6.0-30.6). Median time of neutrophil and platelet engraftment was 16.0 days (IQR, 15.0-17.0) and 23.5 days (IQR, 19.3-30.0), respectively. One patient who underwent RIC allo-HCT from an HLA-mismatched unrelated donor developed grade 3 acute cutaneous GvHD on day +69 (overall grade 2 acute GvHD), showing favourable evolution under systemic corticosteroid therapy until complete resolution within 5 weeks. This patient also developed an Epstein–Barr virus (EBV) reactivation, associated with post-transplant lymphoproliferative disease (PTLD), which was diagnosed on day +98. She was treated with a reduction in immunosuppression and a course of rituximab, with a favourable response (**Image 1**).

Image 1. Patient management and evolution after allogeneic haematopoietic stem cell transplantation



No cases of veno-occlusive disease [VOD] or graft failure were recorded. No further clinically relevant viral reactivations nor significant bacterial or fungal infections were documented. All patients were alive at the end of follow-up.

Conclusions: The results of our centre's clinical experience are consistent with the evidence to date in this field. The use of PTCy may facilitate the adoption of alternative transplant platforms and peripheral blood progenitors when performing allo-HCT in patients with AAA, while maintaining a low incidence of VOD, severe GvHD and graft failure. Careful immunosuppression management appears essential to balance the reduction in GvHD/GR incidence with the risks of infections and viral reactivations, including EBV reactivation and the development of PTLD. Further, larger-scale, prospective studies with extended follow-up are required to provide more robust scientific evidence in this area.

Disclosure: Nothing to declare.

P094

FLAG-VENETOCLAX-ENASIDENIB SALVAGE FOR 7+3 FAILURE

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Background: Acute Myeloid Leukaemia with Myelodysplasia-Related Changes (AML-MRC) represents a high-risk subtype characterized by chemo-refractoriness and poor overall survival. Standard induction regimens, such as "7+3" combined with B-cell lymphoma 2

(BCL-2) inhibitors like venetoclax, have improved outcomes but do not guarantee remission in all patients. In cases of primary induction failure, the patient is often left clinically fragile, making standard myeloablative conditioning (MAC) for hematopoietic stem cell transplantation (HSCT) prohibitively toxic. This study highlights the utility of Next-Generation Sequencing (NGS) in identifying actionable mutations for salvage therapy and the strategic advantage of Reduced-Intensity/Non-Myeloablative (NMA) conditioning to bridge high-risk patients to curative transplant.

Methods: We report the case of a 49-year-old female presenting with anaemia. Bone marrow biopsy (BMB) and NGS confirmed a diagnosis of AML-MRC with high-risk mutations, including RUNX1, SRSF2, ASXL1, and IDH2. The patient underwent standard induction with the "7+3" regimen (Cytarabine/Idarubicin) plus venetoclax. Following treatment failure, a salvage protocol was designed based on NGS findings. The patient subsequently underwent an HLA-matched sibling allogeneic HSCT utilizing an NMA conditioning regimen.

Results: Despite initial intensive induction with "7+3" and venetoclax, the patient experienced primary treatment failure, with a post-induction BMB showing persistent disease (53.8% blasts) and pancytopenia. NGS identified IDH2 mutation (0.55% VAF). Consequently, a salvage regimen comprising FLAG (Fludarabine, Cytarabine, G-CSF), venetoclax, and the IDH2-inhibitor enasidenib (100 mg daily) was initiated. This targeted approach successfully cleared the marrow, resulting in a no detectable blasts by flow cytometry. Given the patient's extensive prior cytotoxic exposure and induction failure, an NMA conditioning regimen was utilized to minimize transplant-related mortality while relying on the graft-versus-leukaemia (GVL) effect. Thirty-two days post-allogeneic stem cell transplant, she achieved 100% donor chimerism on short tandem repeat (STR) analysis and remains clinically well.

Conclusions: This case demonstrates that NGS is indispensable in the management of refractory AML-MRC, specifically for identifying targets like IDH2 when standard venetoclax-based induction fails. The addition of enasidenib to FLAG-based salvage provided a crucial bridge to transplant. Furthermore, for patients who have failed intensive induction, NMA conditioning offers a viable, reduced-toxicity platform for allogeneic HSCT, allowing for successful engraftment and survival in a resource-limited setting.

Disclosure: Nothing to declare.

P095

CLINICAL IMPACT OF HLA-C*04:09 RECLASSIFICATION FROM NULL TO LOW-EXPRESSION ALLELE: A CASE AFTER APPARENTLY 10/10 MATCHED ALLOGENEIC HSCT

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Background: HLA-C*04:09N has historically been classified as a null allele, implying lack of cell-surface expression and absence of involvement in T-cell alloreactivity. However, recent functional analyses have demonstrated low but detectable expression levels, alongside evidence of peptide-dependent T-cell activation. These findings led to its reclassification as C*04:09L in December 2024. This update carries potential implications for donor selection in allogeneic hematopoietic stem cell transplantation (allo-HSCT), where clinical significance of nule alleles has been questioned. We report a case illustrating the potential clinical consequences of this reclassification, involving a patient with C*04:09N (currently classified as C*04:09L) who received a transplant from a donor initially considered 10/10 matched and subsequently developed severe GVHD, relapse and death.

Methods: A retrospective review of the patient's clinical history and transplant course was performed, including HLA typing, donor selection criteria, and post-transplant outcomes. In parallel, a focused review of the literature was conducted to evaluate current evidence on the expression and clinical relevance of HLA-C*04:09 and its recent reclassification from a null to a low-expression allele.

Results: A 66-year-old man with primary myelofibrosis harboring a JAK2 V617F mutation was referred for allo-HSCT. An unrelated female donor aged 56 years was selected. Both donor and patient were CMV seronegative, with minor ABO incompatibility and a permissive HLA-DPB1 mismatch. HLA typing classified the donor as C*02:02,-, and the patient as C02:02*,* *C*04:09N, with the case considered fully matched based on the null designation of C*04:09N. Conditioning consisted of reduced-intensity fludarabine and busulfan, followed by infusion of peripheral blood $CD34^+$ cells. GVHD prophylaxis included tacrolimus, sirolimus, and mycophenolate mofetil.
The early post-transplant course was notable only for expected oral mucositis. Neutrophil engraftment occurred on day +23 and platelet engraftment on day +29. At day +100, the patient achieved complete hematologic and molecular remission with full donor chimerism in bone marrow. On day +151, he developed grade 3 overlap acute/chronic GVHD, involving skin, mucosa, and joints, which responded partially to high-dose corticosteroids and adjustment of tacrolimus/sirolimus. Subsequently, he developed polyserositis attributed to an atypical form of chronic GVHD, requiring restarting systemic corticosteroids. His clinical course was further complicated by a vertebral fracture and two episodes of nosocomial pneumonia. On day +293, bone marrow evaluation revealed 3% blasts and 3% recipient chimerism, raising concern for disease relapse. By day +302, he experienced recurrent inflammatory serositis, and progression to secondary acute myeloid leukemia was confirmed on day +310. Given progressive clinical deterioration, recurrent infection, and leukemic transformation, therapeutic limitations were applied, and the patient died on day +316 post-transplant.

Conclusions: This case illustrates the clinical relevance of the reclassified low-expression allele C*04:09L, which may represent a functionally significant HLA mismatch rather than a null allele. Donor selection algorithms that rely on outdated allele expression data may inadvertently classify such transplants as fully matched, potentially increasing the risk of alloreactivity, GVHD, and adverse outcomes. Continued integration of updated immunogenetic knowledge into routine donor selection is essential to prevent misclassification and optimize allo-HSCT safety.

Disclosure: No

P096

SUCCESSFUL MANAGEMENT OF POST-TRANSPLANT AML RELAPSE WITH SALVAGE CHEMOTHERAPY AND DONOR LYMPHOCYTE INFUSION

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Background: Acute myeloid leukemia (AML) is the most common reason for allogeneic hematopoietic stem cell transplantation (HSCT) in adults. Allogeneic HCT is primarily used to treat intermediate- and high-risk AML due to its potential for long-term survival. Relapse after allogeneic HCT is the leading cause of treatment failure post-transplantation and occurs in about 30% of patients. Here, we present a patient who relapsed following transplantation and experienced an improvement in chimerism loss after salvage chemotherapy.

Methods: Here, we present a patient who relapsed following transplantation and experienced an improvement in chimerism loss after salvage chemotherapy and donor lymphocyte infusion (DLI).

Results: A 64-year-old male patient presented with fatigue and joint pain three years ago. He had no known chronic diseases, and the physical examination was unremarkable. Complete blood count revealed pancytopenia. Bone marrow sampling and flow cytometry results showed diffuse blastic infiltration, consistent with AML. The patient's cytogenetic analysis was compatible with a complex karyotype; therefore, he was classified as high risk. Complete remission was achieved after induction chemotherapy with 3+7 (idarubicin, cytarabine (ara-C)). Following consolidation with high-dose ara-C, the patient underwent sibling-matched allogeneic HCT with a myeloablative conditioning regimen (busulfan/fludarabine/ATG). Methotrexate, ATG, and cyclosporine were administered as graft-versus-host disease (GvHD) prophylaxis. No GvHD was observed during follow-up. In the 20th month post-transplantation, complete blood count showed leukocytes 132.7 $x10^3$/µl (3.9-10.9), neutrophils 5.49 $x10^3$/µl (1.8-6.9), monocytes 53.11 $x10^3$/µl (0.3-0.9), platelets 22 $x10^3$/µl (166-308), and hemoglobin 9.2 g/dl (13.5-16.9). Blastic infiltration was observed in the bone marrow, and chimerism was detected at 5%. No new mutations were identified in genetic tests. HAM (high-dose ara-C, mitoxantrone) chemotherapy was administered due to relapse of AML after transplantation. Remission was achieved following this salvage

chemotherapy, with chimerism at 97%. Subsequently, DLI was given to prolong the response and harness the graft-versus-leukemia (GvL) effect.

Conclusions: The prognosis for patients with relapsed AML after allogeneic SCT is poor, with a two-year overall survival rate below 20%. There is no established standard treatment for relapse post-transplantation. To reduce tumor burden, intensive chemotherapy is recommended for fit patients, while low-intensity chemotherapy or hypomethylating agents are suggested for unfit patients. If a mutation is identified through genetic testing, targeted therapies or venetoclax can be combined. Cellular therapies, particularly those that modulate the immune microenvironment and offer GvL effects, such as CAR-T or NK cell therapies, may improve survival when used in personalized combinations with chemotherapy and targeted agents (like FLT3, IDH, TP53). The relapse rate after allogeneic HCT remains high, and treatment options are limited. The absence of randomized controlled trials indicates that further research is necessary in this area.
This case illustrates the successful application of HAM chemotherapy and DLI in a patient with relapsed AML and loss of chimerism after hematopoietic stem cell transplantation. The recovery of nearly complete donor chimerism and ongoing remission underscores the potential of this approach in high-risk AML. Further research is needed to refine salvage treatments and immunotherapeutic methods in this context.

Disclosure: No conflict of interest.

Gene Therapy – Basic and Translational

Paed4-04

PHASE 1 GENE THERAPY FOR PATIENTS WITH IPEX SYNDROME: PRELIMINARY IN VIVO DATA OF THE TREATMENT WITH ENGINEERED TREG-LIKE CELL CD4^{LVFOXP3}

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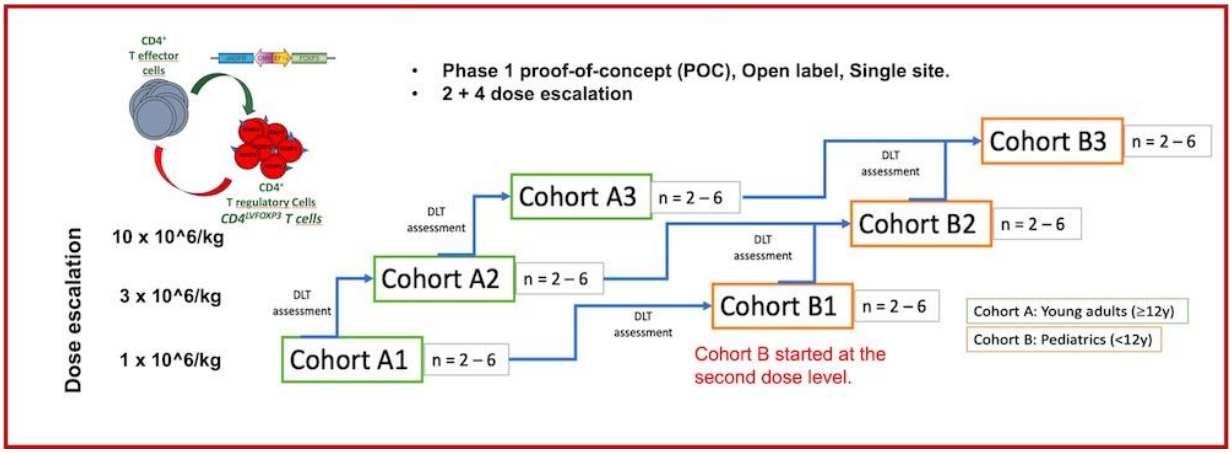
Background: We have developed a First-In-Human (FIH) Phase 1 clinical trial with a novel regulatory T (Treg) cell therapy product to treat IPEX syndrome (NCT05241444), a life-threatening monogenic autoimmune disorder classically associated with enteropathy, early-onset diabetes, and severe atopic dermatitis. The Orphan Drug product consists of engineered CD4^{LVFOXP3} Treg-like cells, obtained from autologous CD4+ T cells lentiviral vector (LV)-transduced with EF1a-FOXP3, fully resembling naturally occurring Treg, and expressing the membrane marker tNGFR (CD271).

Methods: The design is a 2+4 dose escalation in two different age cohorts, ≥12 years and <12 years of age (Figure 1).

Figure 1. Study Design



Results: Eight patients have been treated with a high-purity product (Table 1). Primary endpoints of feasibility and safety have been successfully achieved with the lowest ($1x10^6$/kg; n=2), intermediate ($3x10^6$/kg; n=2), and highest ($10x10^6$/kg; n=2) doses in the older patients and in two of the younger patients at the intermediate dose. There have been no significant or related adverse events. In nearly all patients, we observed a noticeable clinical response, including significant improvement in growth, gastrointestinal symptoms and disease biomarkers after treatment. $CD4^{LVFOXP3}$ are detectable in the blood after infusion with a clear dose-response relationship and persistence. $CD4^{LVFOXP3}$ Treg-like cells demonstrate phenotypic and functional stability at the single cell level by CITEseq on the product preinfusion and ex vivo. $CD4^{LVFOXP3}$ maintains the Thelper subsets' heterogeneity of the parental cells and expresses the transgene *FOXP3-lv* and Treg markers, including *CCR4, CTLA4* and *IL2RA* and low IL7R. After infusion, the patient's peripheral blood samples have exhibited lower expression of the inflammatory cytokines *IL17A, IL17F, IL22, IL15, IFNg*, constrained TCR clone expansion and cycling status, and contain a high proportion of cells that have stem cell memory features, most likely derived from naïve CD4+ T cells.

Table 1. Characteristics of the patients with IPEX treated with Engineered $CD4^{LVFOXP3}$ Treg-like cells

Subject ID	382-002-A1-01	382-003-A1-02	382-004-A2-01	382-005-A2-02	382-006-B2-01	382-007-B2-02	382-008-A3-01	382-009-A3-02
Status (as of 12/12/2025)	Completed Month+36 post-$CD4^{LVFOXP3}$ infusion on 07/31/2025	Completed Month+24 post-$CD4^{LVFOXP3}$ infusion on 01/28/2025	Completed Month+24 post-$CD4^{LVFOXP3}$ infusion on	Completed M+12 post-$CD4^{LVFOXP3}$ infusion on	Completed M+12 post-$CD4^{LVFOXP3}$ infusion on	Completed M+12 post-$CD4^{LVFOXP3}$ infusion on	Completed Month +9 post-$CD4^{LVFOXP3}$ infusion on	Completed Month +6 post-$CD4^{LVFOXP3}$ infusion on

			09/22/2025	03/18/2025	07/03/2025	08/19/2025	10/28/2025	11/11/2025
Assigned Age Cohort, Dose	A, 1 x 10^6 cells/kg	A, 1 x 10^6 cells/kg	A, 3 x 10^6 cells/kg	A, 3 x 10^6 cells/kg	B, 3 x 10^6 cells/kg	B, 3 x 10^6 cells/kg	A, 10 x 10^6 cells/kg	A, 10 x 10^6 cells/kg
Age at Infusion	27 years	15 years	17 years	18 years	11 years	9 years	25 years	13 years
$CD4^{LVFOXP3}$ DP cell number infused	67 x 10^6 cells	51.8 x 10^6 cells	1.63 x 10^8 cells	2.13 x 10^8 cells	1.31 x 10^8 cells	1.14 x 10^8 cells	6.27 x 10^8 cells	4.99 x 10^8 cells
Ethnicity, Race	Not Hispanic/Latino, White	Not Hispanic/Latino, White	Not Hispanic/Latino, White	Hispanic/Latino, White	Not Hispanic/Latino, Black/African American	Hispanic/Latino, White	Hispanic/Latino, White	Not Hispanic/Latino, White
Medical History								
FOXP3 Mutation	c.1040 G>A, p.Arg347His	c.994 A>G, p.Lys332Glu	c.1190G>A, p.Arg397Gln	c.1150G>A, p.Ala384Thr	c.1040G>A, p.Arg347His	c.1222G>A, p.Val408Met	c.1163A>G, p. Asn 388 Ser	c.210+1G>A, Exon 2
Underwent prior HSCT? If yes, date of first HSCT	no	no	no	no	no	no	no	no

Symptoms and/or signs of IPEX prior to infusion	Enteropathy, type 1 diabetes, pancreatic insufficiency, hypogammaglobulinemia Autoantibodies: Anti-GAD65 Anti-Thyroglobulin	Type 1 diabetes, low free T4; muscle weakness and incoordination; hypogammaglobulinemia, mildly elevated IgE and eosinophils Autoantibodies: Anti-GAD65 Anti-Thyroglobulin Anti-TPO	Severe enteropathy, eczema, psoriasis, recurrent sinusitis Autoantibodies: Anti-Zinc Transporter 8	Enteropathy, colitis, asthma, rhinitis, arthritis, eczema, alopecia areata, vitiligo, autoimmune hemolytic anemia	Enteropathy, eczema, asthma, allergic rhinitis, bronchiectasis Autoantibodies: Anti-Thyroglobulin Anti-GAD65	Type 1 diabetes, myasthenia gravis Autoantibodies: Anti-muscle specific kinase	Enteropathy, dermatitis Autoantibodies: Anti-GAD65	Type 1 diabetes, arthritis Autoantibodies: Anti-Zinc Transporter 8 Anti-GAD65
Primary Endpoints								
Feasibility	YES	YES	YES	YES	YES	YES	YES	YES
Safety	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)	YES (no DLTs)

Conclusions: These findings show that $CD4^{LVFOXP3}$products are safe, preserve their Treg-like signatures, and persist after in vivo transfer, with evidence of clinical benefit. Successful completion of this trial will address a significant unmet medical need while also providing proof of safety and feasibility of this novel therapy. These data could expand the application of autologous $CD4^{LVFOXP3}$ to additional autoimmune disorders.

Clinical Trial Registry: https://www.clinicaltrials.gov/study/NCT05241444

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PHARMACODYNAMIC INSIGHTS INTO ADAPTER CAR TECHNOLOGIES

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Background: Adapter CAR platforms critically depend on the pharmacokinetics and pharmacodynamic stability of their adapter molecules (AMs), specifically the integrity of the CAR-targeted epitope on these molecules. We investigated the pharmacokinetics of AMs in the full-size antibody format and the pharmacodynamic impact of the stability of the CAR-targeted epitope on the performance of two distinct adapter CAR technologies: one based on chemical conjugation with NHS-biotin and one based on a peptide tag. Our preclinical assessment provides insights into the rational selection of CAR-targeted epitopes and highlights the need for optimized dosing regimens to maintain stable antigen expression.

Methods: Adapter molecules (IgG1 antibodies) were produced through transient expression, purified, and conjugated to lysine residues using NHS chemistry with LC-LC-NHS-biotin. Separately, peptide tags were integrated into the amino acid sequence of the identical CD33-gemtuzumab-based AM. The pharmacodynamic stability and enzymatic cleavage kinetics of the CAR-targeted epitope of the linker-label-epitope (LLE-biotin) or peptide tag were evaluated both *in vitro* and *in vivo* by indirect flow cytometry in human and NSG mouse sera at various doses and time points. Both adapter CAR systems were based on third-generation CAR architectures. The adapter CARs were tested *in vitro* for cytotoxicity against AML and *in vivo* for leukemia control using longitudinal bioluminescence imaging in a cell line-derived U937 model and benchmarked against a conventional CD33-targeted CAR T.

Results: The adapter CAR technologies and the conventional CD33-CARs demonstrated excellent *in vitro* leukemia control. However, *in vivo* performance was critically dependent on the pharmacodynamic stability of the CAR-targeted epitope conjugated to or integrated into the AM. The enzymatic cleavage was identified as the key mechanism for inactivating the AM, with rapid deconjugation kinetics *in vitro* (ca. 2/3 of the AM deconjugated after 24 hours), and even more extensive deconjugation *in vivo*, reaching around 99% deconjugation four hours after subcutaneous injection and 99.9% three days post administration. Consequently, only a minimal portion of AML-bound AM remained functional, compared to AML-bound AMs that were deconjugated. In contrast, the integrated peptide tag proved to be

stable and resistant to enzymatic cleavage. In the U937 cell line-derived xenograft model, adapter CARs with pharmacodynamically unstable AMs failed to control leukemia *in vivo* and exhibited the same leukemic burden as adapter CARs without AMs or untransduced T cells. Advanced adapter CAR technologies with favorable pharmacodynamics, or conventional CAR T cells can facilitate *in vivo* leukemia control.

Conclusions: Our data demonstrate that the pharmacodynamic stability of the CAR-targeted epitope is essential for adapter CAR-mediated function. In addition to the loss of function when CAR-targeted epitope-devoid AMs are present, the competitive inhibition of functional AMs by the abundance of functionally inert AMs significantly disrupts overall performance of the conceptual framework. *In vivo* leukemia control strictly depends on the pharmacodynamic stability of the AM. Therefore, selecting the appropriate CAR-targeted epitope in adapter CAR technologies must acknowledge its *in vivo* pharmacodynamic stability.

Disclosure: Patrick Schlegel: named inventor and co-inventor on patents concerning adapter CAR technologies; no financial relationship. All other authors: nothing to declare.

A274

A SINGLE-STEP STRATEGY FOR SIMULTANEOUS T-CELL ACTIVATION AND B-CELL ELIMINATION IN CAR-T PRODUCTION USING BISPECIFIC ANTIBODIES

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Background: Chimeric antigen receptor T-cell (CAR-T) therapy shows promise for B-cell malignancies treatment. T-cell activation and expansion are crucial CAR-T production steps. The cost-effective method of T-cells stimulation directly from peripheral blood mononuclear cells (PBMCs) based on OKT3 is widely used. The most significant limitation of this approach is the presence of CD19-expressing leukemic cells susceptible to further transduction, leading to epitope masking [Ruella M. et al. 2018]. The aim of the current study is to test monoclonal bispecific anti-CD3/CD20 antibodies on PBMCs cell source acting as T-cell stimulator and B-cell depleting agent simultaneously.

Methods: PBMCs obtained from four healthy donors were cultured at 1×10^6 cells/mL and activated for 6 days in the presence of 150 IU/mL interleukin-2 (IL-2) and bispecific anti-CD3/CD20 monoclonal antibodies at concentrations of 0.5, 1, 5, and 10 pmol/mL. OKT3 (100 ng/mL) was used in control samples. In parallel, immunomagnetic selection of T cells and B cells was performed, followed by separate activation of selected T cells using the same activation conditions. Cumulative population doubling level (CPDL) was calculated to assess T-cell proliferation. CD3+ and CD19+ cell proportions, T-cell differentiation subsets (effector,

effector memory, central memory, naïve), and expression of activation and metabolic markers CD71 (transferrin receptor) and LDLR (low-density lipoprotein receptor) were analyzed by flow cytometry.

Results: All groups showed T-cells expansion at the end time point. CPDL values were significantly higher in samples treated with anti-CD3/CD20 antibodies at concentrations from 0.5 to 10 pmol/mL compared with controls ($p<0.05$). Complete elimination of B cells was achieved by day 3 in all anti-CD3/CD20-treated samples, whereas only partial reduction was observed in OKT3 controls (3.28±1.2%). B-cell depletion was dependent on the initial CD3:CD19 ratio and was not achieved when the ratio was below 4:1. T-cell immunophenotyping demonstrated a ≥2-fold reduction of effector cells and ≥1.5-fold decrease of effector memory cells, accompanied by an ≥8-fold increase of central memory T cells, with no significant changes in naïve T cells. Expression of CD71 remained stable across all conditions (mean 77±4%) and did not differ from controls, while LDLR expression was preserved, indicating adequate metabolic activation of T cells irrespective of the activation method.

Conclusions: Bispecific anti-CD3/CD20 antibodies provide efficient T-cell activation comparable to OKT3 while simultaneously eliminating CD20+ B cells and promoting a favorable central memory–enriched T-cell phenotype. Bispecific antibodies can also be used as an additional agent to standard activation in cases of poor T-cell selection in patients with a large number of blast cells in the blood. This approach represents a promising alternative CAR-T manufacturing strategy combining activation, depletion, and phenotypic optimization in a single step.

Disclosure: Nothing to declare.

A275

SYSTEMATIC TARGET ANTIGEN VALIDATION AND ANTIBODY VALIDATION FOR CELLULAR IMMUNOTHERAPY

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Background: The rapid expansion of cellular immunotherapies has created strong incentives to discover new target antigens and develop related therapeutic strategies. Insufficient target validation can lead to ineffective treatments and setbacks in clinical translation. Robust validation should integrate orthogonal datasets, genetic perturbation, and matched functional assessment under standardized conditions, including multimodal antibody- and CAR-based testing. Here, we present a systematic validation framework and apply it to the ATP-gated ion channel P2RX7 (P2X7), which regulates cell proliferation, survival, and inflammatory signaling. A conformational "non-functional" P2X7 variant (nfP2X7) has been proposed as a pan-cancer and cancer-restricted antigen on the basis of a putatively unique epitope exposed only on tumor cells.

Methods: We established a multi-step validation pipeline for novel immunotherapy targets. First, we systematically mined public bulk RNA-seq datasets to evaluate tumor coverage and normal-tissue expression of candidate genes. Next, we quantified the surface expression of CD19, CD276, and P2X7 via indirect flow cytometry in well-characterized cell lines. For P2X7, we employed antibodies targeting both the functional P2X7 and the proposed non-functional conformational variant of P2X7 (nfP2X7). We compared these data with publicly available RNA-seq datasets and our qPCR measurements. Additionally, we generated genetic gain- and loss-of-function models using stable lentiviral overexpression and CRISPR/Cas9-mediated P2X7 knockout to demonstrate target-antigen–dependent antibody binding, receptor function, and target-cell recognition by the antibodies and the corresponding CAR-expressing T cells. Finally, we stimulated P2X7 with its natural ligand, ATP, to confirm that receptor function was preserved in the relevant model systems.

Results: Database mining showed that P2X7 is heterogeneously expressed across cancers, with high expression in melanoma, moderate expression in AML, and absent expression in prostate cancer, breast cancer, ovarian cancer, and soft tissue sarcomas. Immunoprofiling using flow cytometry correlated closely with P2X7 transcript levels and aligned with P2X7 knockout and overexpression in an antigen-dependent manner. The P2X7-, CD19-, and CD276-CAR T cells exerted antigen-specific cytotoxicity, consistent with their respective antibody counterparts. Conversely, antibodies designed to recognize the nfP2X7 epitope did not correlate with P2X7 mRNA levels or with P2X7 knockout or overexpression. nfP2X7-CAR T failed to induce antigen-dependent cytotoxicity and could not distinguish P2X7-positive from P2X7-negative targets, while P2X7-CARs retained expected specificity. We found no evidence to support P2X7 as a universal cancer target antigen, and cancer-specific nfP2X7 entity. Instead, the data indicate the recognition of non-specific or context-dependent epitopes unrelated to P2X7.

Conclusions: This systematic validation framework demonstrates that target antigen validation and antibody validation are essential steps in developing immunotherapeutics, especially for new, unvalidated target antigens. The proposed nfP2X7 antigen does not fulfill the criteria for a clinically appropriate, tumor-specific target, and P2X7 itself is not a pan-cancer target antigen. More broadly, our work highlights the importance of multimodal antigen and antibody validation, combining public datasets, orthogonal expression assays, genetic perturbation, and matched antibody-CAR reagents before advancing novel targets into translational immunotherapy efforts. We suggest this structured approach as a model to improve the standards for future target nomination.

Disclosure: **Patrick Schlegel:** named inventor on patents concerning P2X7-targeted therapeutics; no financial relationship. **All other authors:** nothing to declare.

A276

A COMPARATIVE PHENOTYPIC AND FUNCTIONAL STUDY OF WT-1 AND TERT SPECIFIC TCR-ENGINEERED T CELLS WITH MODULAR RECEPTOR DESIGNS

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Background: Chimeric antigen receptor T cells (CAR-T) have substantially improved outcomes in MM by targeting surface antigens such as BCMA and SLAMF7; however, their efficacy may be limited by antigen loss (like in MM) and restricted target availability (like in AML). T-cell receptor–engineered T cells (TCR-T) enable recognition of intracellular tumor antigens in an HLA-restricted manner and represent a complementary therapeutic strategy. Modular TCR designs incorporating PD-1-CD28 switch receptors and leucine zipper (LZ) domains have been proposed to enhance signaling and receptor stability, yet their functional impact remains incompletely defined.

Methods: $CD3^+$ T cells were transduced with a panel of TCR constructs recognizing the tumor-associated antigens WT1 or TERT. For each target, original and affinity-modified variants were generated, with or without incorporation of a PD-1-CD28 switch receptor and/or an LZ domain. A PD-1–only vector, MOCK (empty vector), and non-transduced (NV) T cells served as controls. CAR-T cells targeting BCMA or SLAMF7, established surface markers of MM, were produced in parallel for contextual comparison.
Phenotypic profiling was conducted by multiparameter flow cytometry assessing CD4/CD8 composition, memory differentiation (CCR7/CD45RO), and immune checkpoint expression (PD-1, TIM-3, LAG-3, TIGIT, BTLA, CD39). Functional activity was evaluated in co-cultures

with U266-Luc⁺ cells, a multiple myeloma cell line expressing WT1, TERT, BCMA and SLAMF7 using luciferase-based killing assays (24–72 h) and LDH release, with antigen-negative control conditions.

Results: Across TCR-T, CAR-T, MOCK, and NV products, phenotypic profiling revealed broadly comparable CD4/CD8 distributions, CCR7/CD45RO memory subsets, and immune checkpoint expression profiles; no statistically significant differences persisted after FDR correction. These findings indicate that, within this dataset, global phenotypic features were largely conserved across platforms. The limited and unequal number of CAR-T and control samples restricts the statistical power of phenotypic comparisons, which should therefore be interpreted as contextual rather than definitive.
WT1- and TERT-directed TCR-T constructs mediated robust, antigen-dependent cytotoxicity against U266-Luc⁺ cells, reflected by consistent reductions in luciferase signal and corresponding LDH release, with minimal activity toward control targets. Original TCR variants reproducibly outperformed affinity-modified counterparts, indicating reduced functional potency of mutated receptors. Incorporation of a PD-1-CD28 switch receptor was associated with increased tumor cell killing under conditions expected to engage inhibitory signaling, without evidence of increased off-target cytotoxicity in the applied in vitro assays. Addition of an LZ domain further augmented or accelerated effector responses in a subset of constructs.

Conclusions: TCR-engineered T cells targeting WT1 and TERT exhibit potent, antigen-specific cytotoxicity against MM cells in vitro, which can be fine-tuned through modular design elements such as PD-1-CD28 switch receptors and leucine zipper stabilization. While TCR-T and CAR-T products generated using the same expansion platform display broadly comparable phenotypic profiles, functional differences among TCR-T constructs are primarily driven by receptor architecture rather than baseline T-cell phenotype. Importantly, WT1 and TERT are tumor-associated antigens expressed across multiple malignancies, including acute myeloid leukemia, supporting the potential use of TCR-T therapies targeting these antigens either in additional disease settings or as subsequent lines of treatment in multiple myeloma.
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Disclosure: Nothing to declare.

A277

IMPROVING LENTIVIRAL TRANSDUCTION EFFICIENCY OF CD34+ HEMATOPOIETIC STEM CELLS USING POLOXAMERS OR LENTIBLAST PREMIUM®: OPTIMIZATION TOWARD A GENE THERAPY PROCEDURE FOR SICKLE CELL DISEASE

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Background: Gene therapy is emerging as a curative strategy for sickle cell disease (SCD), relying on efficient lentiviral transduction of autologous CD34⁺ hematopoietic stem and progenitor cells (HSPCs). Optimizing transduction conditions while complying with academic GMP constraints is essential for the development of future clinical-grade protocols. We compared several transduction enhancers, including the poloxamers P338, P188, and P407 provided as reconstitutable powders, in combination with prostaglandin E2 (PGE2), as well as the ready-to-use reagent LentiBlast Premium®. We also assessed the specific impact of PGE2 on vector copy number (VCN).

Methods: CD34⁺ cells from healthy donors (HD) were thawed, pre-activated and transduced with a technical-grade bifunctional lentiviral vector designed to silence βS-globin expression while introducing an anti-sickling β-globin. Four sequential experiments were performed. Quality controls included viability assessment, immunophenotypic purity of CD34⁺, colony-forming unit (CFU) assays of progenitors and quantification of VCN in liquid cultures (LC) and progenitor colony counting on day 14. A VCN ≥ 2 in LC was defined as the minimal acceptable target.

Results: Firstly, the poloxamers P338, P188, and P407 were evaluated in CD34+ cells from HD1 as transduction enhancers. VCN in LC reached 4.86 with P407, 3.31 with P338, and 1.54 with P188. VCN in progenitors mirrored these results, identifying P338 and P407 as the most effective enhancers among the poloxamers tested. For all tests, no VCN was detected under mock conditions.
Secondly, we sought to validate these findings and evaluate the impact of increased cell density on transduction efficiency using the best-performing enhancer, P407. Raising the CD34⁺ cell density from 3×10^6 to 4×10^6 cells/mL further improved P407-mediated transduction, yielding VCN of 20.07 and 6.03 in HD2 and HD3, compared with 10.01 and 4.33 at 3×10^6 cells/mL. In the same experiment, we confirmed the superior performance of P338 and P407 over P188 and the no-enhancer control. VCN measured in progenitor colonies reproduced this hierarchy.
Thirdly, the LentiBlast Premium® was compared with P338 and P407 at different dilutions (1/1000, 1/100, 1/50) in HD3. LentiBlast Premium® demonstrated a dose-dependent increase in VCN, ranging from 4.82 to 6.48 in LC, but P338 and P407 achieved the highest VCN (7.17 and 10) in LC. These results indicate that although LentiBlast Premium® provides concentration-dependent VCN enhancement, its efficiency was lower than P338 and P407. However, these two poloxamers are not fully compatible with GMP use.
Finally, the effect of combining LentiBlast Premium® with PGE2 was evaluated in HD4. PGE2 added to a 1/100 dilution of LentiBlast Premium® lead to a marked increase in VCN (+110%), while the effect on P338, used as positive control, efficiency was more moderate (+60%). VCN in progenitors showed similar increases. Overall, this combination produced the highest and most consistent VCN values.

Conclusions: While P338 and P407 enhanced lentiviral transduction, the combination of LentiBlast Premium® and PGE2 delivered the highest VCN, together with full GMP compatibility. These results support the incorporation of LentiBlast Premium® plus PGE2 into

future GMP-compliant, academic-scale manufacturing protocols for SCD gene therapy. These experiments should also be tested on cells from SCD patients.

Disclosure: Nothing to declare.

Gene Therapy - Clinical

GS2-9

SAFETY AND EFFICACY OF LENTIVIRAL HEMATOPOIETIC STEM AND PROGENITOR CELL GENE THERAPY WITH ETUVETIDIGENE AUTOTEMCEL FOR THE TREATMENT OF WISKOTT-ALDRICH SYNDROME

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Background: Wiskott-Aldrich Syndrome (WAS) is a life-threatening platelet disorder and inborn error of immunity caused by WAS gene mutations. Allogeneic hematopoietic stem cell transplantation (HSCT) can be curative but is still hampered by limited donor availability and potential complications. Etuvetidigene autotemcel (etu-cel) is a gene therapy (GT) product composed of autologous CD34+ hematopoietic stem and progenitor cells (HSPCs) transduced *ex vivo* with a self-inactivating lentiviral vector encoding human WAS cDNA under endogenous promoter control. Recently, etu-cel received EMA CHMP positive opinion and FDA approval for the treatment of WAS patients ≥6 months for whom HSCT is appropriate and lacking a suitable HLA-matched related donor. We report the results of an integrated safety and efficacy analysis in 27 WAS patients treated with etu-cel.

Methods: Source of autologous HSPCs for drug product (DP) manufacturing consisted in mobilized peripheral blood (n=21), bone marrow (n=5) or both (n=1). Etu-cel was infused after rituximab and reduced-intensity conditioning. Patients received fresh [phase I/II trial, NCT01515462, n=8; expanded access program (EAP), n=9] or cryopreserved (phase III trial, NCT03837483, n=10) formulation. Safety endpoints comprehended adverse events (AEs), immune response to transgene, replication-competent lentivirus (RCL) and abnormal clonal proliferation (ACP). Primary efficacy endpoints were overall survival (OS), rate of severe infections from 6 to 18 months post-GT and rate of moderate and severe bleedings in the first 12 months post-GT. Secondary efficacy endpoints included gene-corrected cell engraftment, WASP expression, T-cell function, platelet count, autoimmunity and eczema over time.

Results: Age at treatment ranged between 1.0 and 35.1 years. OS was 96.3%; one EAP subject died 4.5 months post-GT due to deterioration of a pre-existing neurological condition. Median follow-up was 5.72 years (range: 2.31-13.26).
Etu-cel was well tolerated with absence of DP-related AEs, engraftment failure, evidence of ACP, RCL or immunogenicity. None of the treated patients required any secondary procedures after GT.
The rate of severe infections was reduced by 92.5% in the 6-18 months post-GT compared to the rate 12 months before GT. Similarly, moderate and severe bleedings were decreased by 60% in the first 12 months post-GT compared to the year prior to treatment. The majority of patients did not report moderate to severe bleeding after four years post-GT. Stable robust multilineage engraftment of gene-corrected HSPCs led to restoration of WASP expression in lymphocytes and platelets, which resulted in improved immune-cell function and platelet count. Immunoglobulin replacement could be stopped in all patients after GT and cessation of sustained antimicrobial treatment was achieved in 92.6% patients. All patients reached freedom from sustained platelet transfusions after GT and at last follow up, 92.6% reached platelet count $>50\times10^9$/L. After GT, immune dysregulation improved in most patients and eczema resolved in all. Hospitalization rate declined and quality of life ameliorated in all patients. Outcome was similar across different ages, disease characteristics, WAS mutations, and DP formulations.

Conclusions: Results from this integrated safety and efficacy analysis show sustained long-term significant clinical benefit of one single infusion of etu-cel for the treatment of WAS, demonstrating its favorable benefit-risk profile with up to 13 years follow-up.

Clinical Trial Registry: Phase I/II Study TIGET-WAS ClinicalTrials.gov ID: NCT01515462
Phase III Study OTL-103-4 ClinicalTrials.gov ID: NCT03837483

Disclosure: Francesca Ferrua: Consultancy Fondazione Telethon ETS.
Elena Tomasetto, Federica Miotto, Stefano Zancan, Celeste Scotti: Employee Fondazione Telethon ETS.
Koen van Rossem: Consultancy Fondazione Telethon ETS; Karos Healthcare Consulting: current employment; current equity holder in private company.
Sean Russell: Consultancy Fondazione Telethon ETS; PrimeRA Pharma Partners: current employment; current equity holder in private company.
Alessandro Aiuti: Research funding Fondazione Telethon ETS.
All other authors have nothing to declare.

OS21-03

ATIDARSAGENE AUTOTEMCEL IN METACHROMATIC LEUKODYSTROPHY: SAFETY CONSIDERATIONS FROM REAL-WORLD PRACTICE

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Background: Metachromatic leukodystrophy (MLD) is a rare, fatal lysosomal disease caused by biallelic *ARSA* gene mutations. Atidarsagene autotemcel (arsa-cel) is an autologous lentiviral haematopoietic stem cell (HSC) gene therapy that has demostrated durable clinical benefit and a favourable risk–benefit profile in 39 patients treated in the clinical development programme (CDP), with extended follow-up. Arsa-cel is currently approved as standard of care for presymptomatic late-infantile (PSLI) and early-juvenile (PSEJ), or early-symptomatic EJ MLD (ESEJ). We report real-world safety and efficacy in an expanded cohort treated outside the CDP.

Methods: We present a single-centre, real-world series of patients treated with arsa-cel between 2020 and 2025 under individual compassionate-use programmes or in the post-authorization commercial setting. Clinical and laboratory data, as well as adverse events (AEs) and serious AEs (SAEs), were collected.

Results: Thirteen patients were deemed clinically eligible for treatment; one could not be treated because gene-therapy product failed release testing; Twelve patients received arsa-cel: 8 PSLI, 2 PSEJ and 2 ESEJ. Mobilised peripheral blood (G-CSF + plerixafor) was used as the $CD34^+$ source in all cases, with a median collection of 37.6×10^6 $CD34^+$ cells/kg (range 19.2–62.9). All patients underwent myeloablative single-agent busulfan conditioning. Median age at treatment was 11.3 months (range 8.3–128.3). Neutrophil and platelet recovery occurred in all patients, and all remain alive after a median follow-up of 40.3 months (range 5.8–64.2).
Four severe adverse events (SAE) occurred following treatment that were assessed as potentially related to gene therapy or conditioning. One severe hepatic veno-occlusive disease and one severe immune-mediated thrombocytopenia occurred within 3 months post treatment and are solved. One PSLI patient experienced lack of gene-corrected cell engraftment (LoE) in the first month post-treatment. The patient, could not receive a rescue treatment because of rapid disease progression and he is now showing typical MLD neurological manifestations; exploratory T-cell assays suggested a possible immune-

mediated process underlying this event. One asymptomatic B-cell precursor acute lymphoblastic leukaemia was diagnosed 3 years post-therapy. The patient, 4 years of age at the time of the event, is receiving standard therapy and remains under follow-up. Causality assessment, including longitudinal integration-site analyses, is ongoing. No replication-competent lentivirus was detected. Low-titer anti-ARSA antibodies were observed in 9/12 patients early post-therapy, resolving spontaneously in 7/9.
At 1 year post-treatment, 8 evaluable patients showed a median VCN in peripheral blood mononuclear cells of 2.08 copies/cell (range 2.01–4.9), with 52.9–90.5% transduced bone marrow progenitors. As of today, except for the patient with LoE, ARSA activity has risen to supranormal levels in peripheral blood mononuclear cells and to normal levels in cerebrospinal fluid, and most patients continue to show age-appropriate acquisition of motor and cognitive skills.

Conclusions: The robust engraftment, sustained ARSA reconstitution and early outcomes seen in most patients in this real-world cohort of 12 patients with MLD treated with arsa-cel are consistent with those seen in the clinical development programme; however, this cohort highlights the critical importance of systematic, long-term post-therapy monitoring for the continued evaluation of the risk–benefit profile in the real world setting.

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OS21-08

EXAGAMGLOGENE AUTOTEMCEL FOR SICKLE CELL DISEASE AND TRANSFUSION DEPENDENT BETA THALASSEMIA: REAL WORLD DATA, SINGLE CENTER EXPERIENCE

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Background: Exagamglogene autotemcel (exa-cel) is an autologous gene therapy for patients aged 12 years and older with sickle cell disease (SCD) or transfusion-dependent thalassemia (TDT). Successful implementation of this therapy requires comprehensive

preparation, appropriate patient selection, efficient stem cell collection and manufacturing, and post-infusion care. Here, we present our center's experience with exa-cel therapy.

Methods: We describe the outcomes for nine patients who underwent autologous gene-edited hematopoietic stem cell transplantation (HSCT) using exa-cel for SCD or TDT. Data were collected retrospectively including demographics, indications for therapy, infused cell doses, engraftment timing, adverse events. The primary objectives included number of transfusions post infusion in TDT, number of painful crises post infusion in SCD. The secondary objective was the number of hospitalizations post engraftment.

Results: Nine patients received exa-cel therapy—three with TDT and six with SCD—with a median follow-up of 75 days (7–512 days). None had HLA-matched donors for allogeneic HSCT. The median age was 16 years (range: 13–32). All patients had acceptable organ function. Refer to the table for characteristics.
SCD Indications and Comorbidities:

- All six SCD patients had recurrent severe vaso-occlusive crises despite hydroxyurea.
- Acute chest syndrome occurred in 4/6 patients.
- Three had prior ICU admissions.
- Chronic pain and increased opioid use were reported in 2/6.
- Avascular necrosis was present in 4/6; one had osteomyelitis, and one had priapism.
- No patients had a history of stroke, CNS vasculopathy, or recurrent splenic sequestration.
- Median baseline HbF was 13% (range: 1.9–26.5%).

Iron Overload and Transfusion History:

- Iron overload (T2* MRI) was present in 2/6 SCD patients and all three TDT patients.
- Median liver iron concentration was 13 mg/g (range: 10–15), with no evidence of fibrosis.
- One TDT patient had alloimmunization.
- All patients with TDT had received >12 transfusions/year.

Stem Cell Collection, Preparation and Conditioning:

- All patients with TDT required one cycle of stem cell collection
- Stem cell collection was challenging in the first six SCD patients prior to implementing a modified G-CSF protocol; 2/6 received G-CSF with plerixafor.
- Multiple collection attempts were required over 3-12 months.
- Ovarian tissue preservation was done in two prepubertal girls.
- All adult male patients had sperm banking and adult female patients had oocyte cryopreservation.
- Median cumulative busulfan AUC was 80 mg·h/L (range: 70–85)

Outcomes:

- All patients achieved successful engraftment.
- Five patients required G-CSF post-infusion (median: 2 doses, range: 1–9).

- One TDT patient developed platelet refractoriness and delayed platelets engraftment (50 days), requiring HLA-matched transfusions and thrombopoietin receptor agonists.
- All three TDT patients became transfusion-independent, with hemoglobin levels >13–14 g/dL and HbF >95%. Phlebotomy was initiated around six months post-therapy.
- None of the SCD patients experienced pain crises or required hospitalization after initial discharge.
- Post-engraftment HbF% levels in SCD patients reached 50–60%, with sustained hemoglobin improvement.

Patient and Transplant Characteristics (n = 9)	Value median or N (range)	Adverse Events	Value (median or N (range or %)
Median age (years)	16 (13–32)	Mucositis	8 (88%) 2 required TPN
Comorbidity index scores	0: 6 1: 1 2: 2	Veno-occlusive disease	1 (moderate in TDT)
Gender (M/F)	5/4	Fever Neutropenia	4
Positive RBC antibody screen	1	Bacteremia	1
Median cumulative Busulfan AUC (mg·h/L)	80 (70–85)	ICU admission	0
Median infused CD34+ cell dose (×10⁶/kg)	6.9 (4–15)	CMV reactivation	0
Number of product vials	3 (2–5)	Survival	9
Neutrophil engraftment (days)	27 (21–32)	Median follow-up duration for TDT (days)	425 (356–512)
Platelet engraftment (days)	33 (26–50)	Median follow-up duration for SCD (days)	49 (7-94)

Conclusions: Exa-cel gene therapy for hemoglobinopathies is encouraging. With appropriate patient selection, preparation, and post-infusion care, outcomes have been favorable. However, initial CD34+ stem cell collection in SCD patients posed challenges, necessitating protocol optimization. Long-term follow-up is essential to evaluate the durability and safety.

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Paed4-02

EARLY ACCESS EXPERIENCE OF LENTIVIRAL HEMATOPOIETIC STEM AND PROGENITOR CELL GENE THERAPY (ETUVETIDIGENE-AUTOTEMCEL) IN PATIENTS AFFECTED BY WISKOTT-ALDRICH SYNDROME

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Background: Etuvetidigene-autotemcel (Etu-cel), the first gene therapy (GT) to be approved by European Medicines Agency and Food and Drug Administration for the treatment of Wiskott-Aldrich Syndrome (WAS), has been developed in our Centre in the last 15 years. At present, after the completion of the clinical development program (trials NTC01515462 and NTC03837483), Etu-cel has been administered to 8 patients through an early access scheme in Italy.

Methods: Etu-cel is an autologous lentiviral hematopoietic stem and progenitor cell (HSPC) GT indicated for WAS patients aged 6 months and older who have a mutation in the WAS gene and no suitable Human Leukocyte Antigen (HLA) matched related stem cell donor. All the 8 patients treated in the early-access setting presented with severe thrombocytopenia (median platelet count pre-GT 22.75 x10^9/L, range 9-31). Five patients had significant autoimmunity/autoinflammation signs prior to treatment (inflammatory bowel disease, post-Covid-19 Multisystem Inflammatory Syndrome in Children, vasculitis). One patient, notably, was treated after the complete rejection of 3 unsuccessful and complicated allogeneic hematopoietic stem cell transplants, having been rescued with infusion of unmanipulated autologous back-up and without evidence of residual donor cells. All patients received the cryopreserved formulation of Etu-cel product, obtained from mobilized peripheral blood HSPC, after a reduced intensity conditioning based on rituximab, fludarabine and busulfan. Median age at treatment was 2.25 years (0.9-18.4). Vector Copy Number (VCN) on drug product and cell dose were in line with those of the clinical development program.

Results: Current follow-up ranges between 3 and 24 months (median 9 months). All patients are alive and in good clinical condition and did not present any product-related adverse events or reactions. Neutrophil engraftment was achieved at a median of 27 days (range 24-48 days) after infusion of drug product. Multilineage engraftment of gene-corrected cells was demonstrated in all patients and WASP expression increased both on platelets and lymphocytes.
In patients with a minimum follow-up (FU) of 6 months, median platelet count after treatment stably increased above 100 $x10^9$/L. In details, it was 129 $x10^9$/L at FU +6 months (n = 5) and 123.5 $x10^9$/L at +1 year (n = 4). All patients are currently transfusion independent and no bleeding events were recorded. Two patients received a thrombopoietin receptor agonist in the initial post-engraftment phase (PLT count censored).
Infection rate decreased and no moderate or severe infective events were registered after 6 months post-GT. Antimicrobial prophylaxis were stopped in 3 patients and immunoglobulin replacement in 4 patients at FU +1 year, approximately.
Eczema improved and resulted absent from the FU +1 year. No signs of new or previous autoimmunity were detected post-GT.

Conclusions: All patients are alive and experienced clinical benefit, with progressive resolution of WAS manifestations. In this early access scenario, Etu-cel has confirmed the effectiveness and safety already shown in the context of the clinical development program.

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Paed4-05

EXTENSIVE METABOLIC CORRECTION AND FAVOURABLE NEUROLOGICAL OUTCOMES MAINTAINED 5 YEARS AFTER TREATMENT WITH AUTOLOGOUS HAEMATOPOIETIC STEM CELL GENE THERAPY (OTL-203) IN MUCOPOLYSACCHARIDOSIS TYPE-I HURLER

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Background: Mucopolysaccharidosis type I Hurler syndrome (MPS-IH) is a lysosomal storage disorder characterized by deficiency of the enzyme alpha-L-iduronidase (IDUA). The resulting accumulation of glycosaminoglycans (GAGs) causes a wide range of systemic abnormalities, progressive neurological disease and early death. As part of a phase 1/2 trial

(NCT03488394, EU CT 2024-514870-29-00), eight patients with MPS-IH were treated with OTL-203, an investigational autologous haematopoietic stem cell-based gene therapy (median age at treatment: 2.0 years [range: 1.2–2.8]). OTL-203 was associated with extensive metabolic correction and multisystemic improvements up to 4 years post-treatment. Here, we report biochemical and neurological outcomes in all patients 5 years after OTL-203 treatment (median [range]: 5 years [4.9–5.1]).

Methods: Vector copy number was quantified using digital droplet polymerase chain reaction. IDUA activity in the blood and cerebrospinal fluid (CSF) was measured using specific IDUA substrates. Tandem mass spectrometry was used to measure GAGs in the urine and CSF. Motor skills were assessed using the Peabody Developmental Motor Scales, while cognitive function was evaluated by the Bayley Scales of Infant and Toddler Development and the Wechsler Preschool and Primary Scale of Intelligence. Age of achievement for motor and cognitive milestones was compared to the ranges of healthy children defined by the World Health Organization. Brain and spinal abnormalities were measured using magnetic resonance imaging (MRI) and a specific neuroradiological scoring system developed for patients with MPS-IH who have been treated with allogeneic haematopoietic stem cell transplant (allo-HSCT). The parent-reported Pediatric Quality of Life (PedsQL) and the parent-reported PedsQL Family Impact Module were used to assess patient and caregiver quality of life.

Results: All patients are alive to date and continue to show sustained engraftment of gene-corrected cells. At their last evaluation, all patients had supraphysiological blood IDUA activity, resulting in substantial urinary GAG substrate reductions to normal**/**near normal levels. In the CSF, IDUA activity was detected 3 months after OTL-203 treatment and persisted over time, and was accompanied by extensive GAG reductions (to undetectable dermatan sulphate levels in all patients). Compared with baseline, most patients (7/8) had stabilization or improvement in total motor function scores to within low average/average ranges of healthy peers by their last evaluation. Over the follow-up period, most patients (6/8) acquired cognitive skills as expected for their age. By their last evaluation, all patients had experienced improvement or stabilization of brain MRI abnormalities (including perivascular space dilation, white matter abnormalities and subarachnoid space enlargement). Most patients (6/8) also experienced improvements in spinal MRI *abnormalities* (including dorsolumbar kyphosis and foramen magnum stenosis and ***ventriculomegaly***) between baseline and their last follow-up. For most patients, PedsQL scores for physical health (6/8), psychosocial health (6/8) and family impact (5/8) did not worsen markedly over time.

Conclusions: These results indicate sustained engraftment of gene-corrected cells, biochemical correction in the CSF and a favourable neurological response up to 5 years after OTL-203 treatment. Clinical outcomes were supported by the neuroradiological findings. An ongoing phase 3 trial (NCT06149403, EU CT 2022-500306-17-00) is prospectively comparing the clinical outcomes of OTL-203 with allo-HSCT, the current standard of care.

Clinical Trial Registry: NCT03488394 (https://clinicaltrials.gov/study/NCT03488394); EU CT 2024-514870-29-00 (https://clinicaltrials.eu/trial/study-on-gene-therapy-with-autologous-stem-cells-and-drug-combination-for-children-with-mucopolysaccharidosis-type-i-hurler-variant/)

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- Francesca Tucci, Giulia Consiglieri, Matilde Cossutta, Francesca Ciotti, Marina Sarzana, Cristina Puricelli, Emma Restelli, Maurizio Barbera, Cristina Baldoli and Bernhard Gentner have nothing to declare
- Francesca Fumagalli received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd.
- Rossella Parini received fees for consulting from Sanofi Genzyme and Orchard Therapeutics Ltd
- Alessandro Aiuti: Orchard Therapeutics funds gene therapy clinical trials carried out at San Raffaele Hospital for lysosomal genetic diseases (MLD and MPS-IH), of which A Aiuti is principal investigator or investigator. Telethon Foundation funds gene therapy studies at San Raffaele Hospital for genetic diseases of the immune system (ADA-SCID, Wiskott-Aldrich Syndrome), of which A Aiuti is principal investigator or investigator.
- Maria Ester Bernardo received fees for consulting and research activities from Orchard Therapeutics Ltd.
- Vasileios Nikolaou, Jean Brooks, Muska Yarzi, Su Syonmez and Laura Campbell are employees of Orchard Therapeutics Ltd
- Marianna Lalla is a former employee of Orchard Therapeutics Ltd, and is currently employed by Dianthus Therapeutics Inc.

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LONG-TERM CLINICAL OUTCOMES OF ATIDARSAGENE AUTOTEMCEL, AUTOLOGOUS HEMATOPOIETIC STEM CELL GENE THERAPY (HSC-GT) FOR EARLY-ONSET METACHROMATIC LEUKODYSTROPHY, WITH UP TO 13 YEARS OF FOLLOW-UP

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Background: Metachromatic leukodystrophy (MLD) is a rare, autosomal recessive lysosomal disorder caused by arylsulfatase A (ARSA) deficiency, leading to progressive motor and cognitive decline. Atidarsagene autotemcel (arsa-cel) is an *ex vivo* autologous hematopoietic stem-cell gene therapy approved for pre-symptomatic late infantile (PSLI), pre-symptomatic early juvenile (PSEJ) and early-symptomatic early juvenile (ESEJ) MLD subtypes, collectively termed early-onset MLD.

Methods: We present long-term results from 39 patients with early-onset MLD treated with arsa-cel, excluding four patients outside the approved indication for the efficacy analysis. Outcomes in arsa-cel-treated patients were compared with a subtype-matched natural history (NHx) cohort of 49 patients.

Results: Data were collected April 2010–March 2024; median follow-up was 7.1 years (range 3.1–13.2) for PSLI (n=19), 4.0 years (range 1.1–11.0) for PSEJ (n=11), and 10.0 years (range 9.2–10.9) for ESEJ (n=5). All arsa-cel-treated patients achieved durable engraftment of gene-corrected cells and restoration of ARSA activity in peripheral blood and cerebrospinal fluid.
Arsa-cel-treated patients exhibited clinically meaningful preservation of motor function compared with the NHx cohort, demonstrating a significantly reduced risk of severe motor impairment (GMFC level ≥5) or death (PSLI: p<0.001; PSEJ: p=0.003; ESEJ: p<0.001) and motor impairment (GMFC level ≥3) or death (p<0.001 across subtypes). The estimated proportion of treated patients with PSLI MLD surviving without severe motor impairment or death up to age 6 was 100% (95% CI: 100.0, 100.0), whereas NHx LI patients experienced rapid loss of motor function and none were estimated to remain event-free up to age 6. For treated patients with PSEJ and ESEJ MLD, 90.9% (95% CI: 50.8, 98.7) and 80.0% (95% CI: 20.4, 96.9) were estimated to remain event-free up to age 13 and 14, respectively, while none were estimated to remain event-free in the NHx EJ cohort.
Overall survival improved in treated PSLI MLD patients compared with the NHx LI cohort (p<0.001). For PSEJ and ESEJ MLD, overall survival was similar to the NHx EJ cohort (PSEJ: p=0.967; ESEJ: p=0.177), likely due to the extended follow-up required to capture mortality in EJ MLD.
Arsa-cel treatment was associated with clinically meaningful preservation of cognitive abilities. At last follow-up, most treated patients with PSLI and PSEJ MLD (13/19 and 9/11, respectively) were alive with normal cognition (IQ scores ≥85) and with no AEs indicative of cognitive decline. For treated patients with ESEJ MLD, 2/5 maintained normal cognition, 2/5 had mild impairment (IQ scores ≥70), and 1/5 had severe impairment (IQ score ≤55). By contrast, severe cognitive impairment was seen in the NHx EJ cohort at similar ages.
At analysis, there had been no serious adverse events assessed as related to arsa-cel and no evidence of insertional oncogenesis or abnormal clonal expansion. Three patients died due to unrelated causes (two from disease progression and one from cerebral stroke). Transient, low anti-ARSA antibody titres occurred in six patients without clinical impact.

Conclusions: With up to 13 years of follow-up, arsa-cel continues to show a favourable benefit–risk profile, exhibiting a durable effect in slowing progression and preventing severe motor and cognitive impairment in most treated patients.

Clinical Trial Registry: NCT01560182 (201222)
https://clinicaltrials.gov/study/NCT01560182; NCT03392987 (205756)

https://clinicaltrials.gov/study/NCT03392987; NCT04283227 (OTL-200-07) https://clinicaltrials.gov/study/NCT04283227; Hospital exemption: Protocol 205029; Compassionate Use Program: Protocol 206258; Single Patient Compassionate Use Program: 207394.

Disclosure:

- Alberto Zambon, Francesca Ciotti, Maddalena Fraschini, Sara Mazza, Marina Sarzana, Francesco Morena and Marcella Facchini have nothing to declare.
- Vera Gallo: Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd.
- Salvatore Recupero: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd.
- Maura Ruzhnikov, Philippa Nutkins, Jean Brooks and Laura Campbell are employees of Orchard Therapeutics Ltd.
- Andrew Shenker and Phil Weatherill received fees for consulting from Orchard Therapeutics Ltd.
- Sabata Martino: Grant/Contract Description: Service contract to Sabata Martino for ARSA activity on CSF in clinical trial number #205756, contract #201222, #OTL-200-07, #205029, #206258 and #207394.
- Alessandro Aiuti: Orchard Therapeutics is funding gene therapy clinical trials carried out at San Raffaele Hospital for lysosomal genetic diseases (MLD and MPS-IH), of which A Aiuti is a principal investigator or investigator. Telethon Foundation is funding gene therapy studies at San Raffaele Hospital for genetic diseases of the immune system (ADA-SCID, Wiskott-Aldrich Syndrome), of which A Aiuti is a principal investigator or investigator
- Valeria Calbi and Francesca Fumagalli: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd.

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REFRAMING PAIN AND VOES AFTER TRANSFORMATIVE THERAPIES FOR SICKLE CELL DISEASE: INSIGHTS FROM GENE THERAPY WITH LOVOTIBEGLOGENE AUTOTEMCEL

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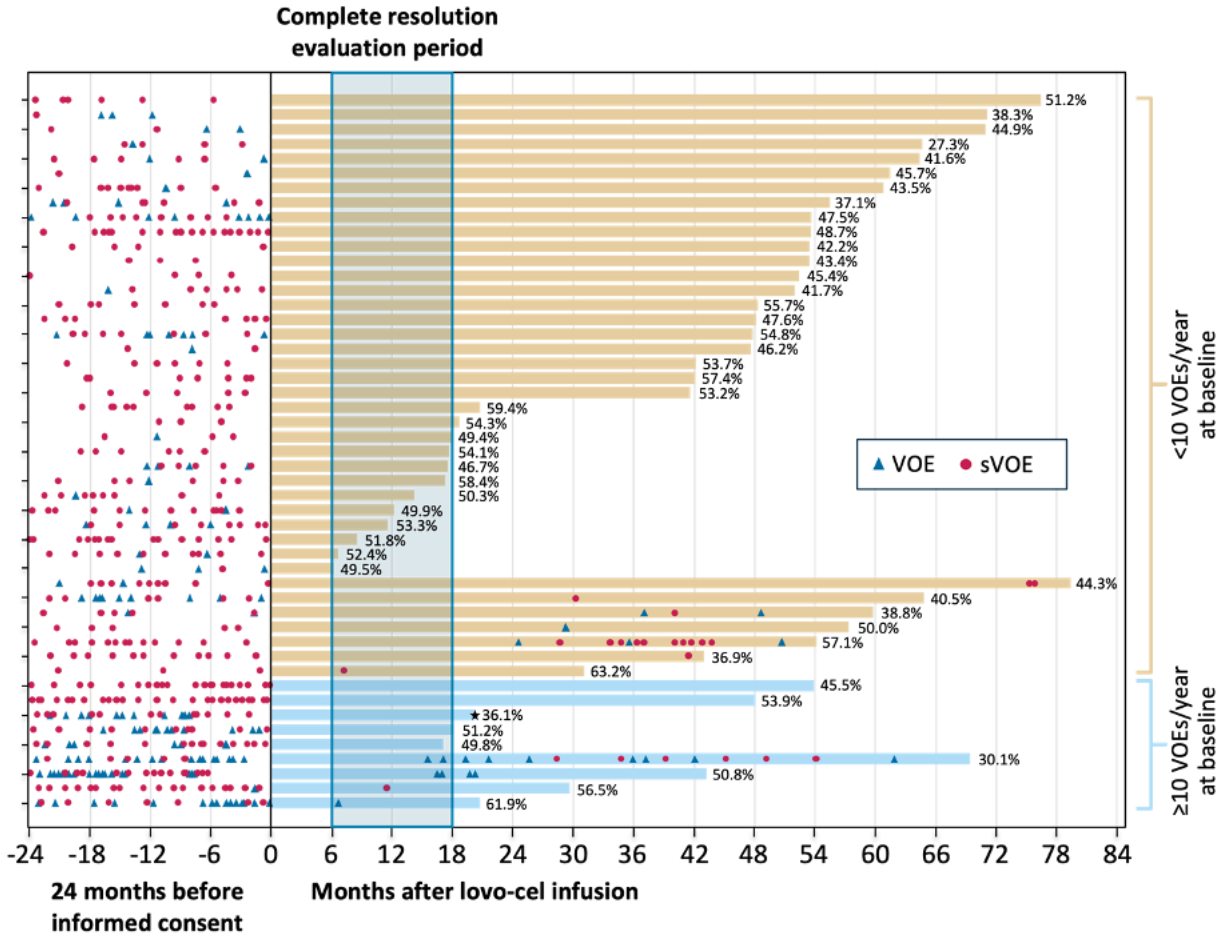
Background: Acute pain crises are the most common and often debilitating complication of sickle cell disease (SCD). Vaso-occlusion has historically been considered the primary cause, although the pathobiology of SCD pain is complex. Transformative therapies such as allogeneic hematopoietic stem cell transplant (allo-HSCT) and lovotibeglogene autotemcel (lovo-cel) gene therapy mitigate hemolysis and reduce vaso-occlusion, yet a subset of patients continue to report pain crises. We characterized pain patterns, risk factors, and outcomes after lovo-cel and compared them to allo-HSCT to better define the etiology of post-treatment pain.

Methods: Participants in HGB-206/210 (Kanter et al., 2022;2023) with ≥4 vaso-occlusive events (VOEs) at baseline and ≥18 months follow-up as of July 2024 (n = 38) were included; updated analyses will be presented. Comparable severe VOE data were obtained from lovo-cel participants (n = 32) and allo-HSCT recipients (n = 163; Leonard et al., 2023) using aligned definitions and follow up. In lovo-cel trials, VOEs were assessed by investigators using a standardized pain evaluation aid and characterized by frequency, hospitalization, and biomarkers; events also underwent independent adjudication. Treatment durability was assessed by transgene expression, hemolysis markers and red cell indices. Patient-reported outcomes (PROMIS-57) were evaluated using mixed-effects models, and predictors of post-treatment VOEs were examined with logistic regression.

Results: Severe VOEs were uncommon following both lovo-cel and allo-HSCT, occurring in 13% (4/32) of lovo-cel recipients and 27% (30/112) of engrafted allo-HSCT recipients without GVHD. Across all VOE event types, 27/38 (71%) lovo-cel participants experienced no post-treatment VOEs, contributing a total of 112 VOE-free patient-years (Figure 1). Opioid use declined from 76% (32/42) at baseline to 36% (15/42) >18 months post-infusion.
To characterize post-treatment acute pain events, a structured classification tool was developed. Forty-five events from 13 participants across 7 sites (May 2022–July 2025) were analyzed. Principal Investigators classified only 11% (5/45) as attributed solely to vaso-occlusion; 38% reflected non-VOE etiologies, and 51% had mixed attribution; however, investigators were only confident of these attributions in 36% of cases, underscoring diagnostic uncertainty. When laboratory assessments were available, biomarker patterns of inflammation and hemolysis did not align with established VOE signatures (Ballas et al., 2012), suggesting distinct causes of acute pain.
Baseline annualized VOE rate was the strongest predictor of post-treatment VOEs (odds ratio [OR], 1.21; 95% CI, 1.0-1.5; p=0.06). Age, sex, chronic pain history, and prior opioid use were not associated with risk, consistent with allo-HSCT findings. Participants with post-treatment VOEs had higher PROMIS pain scores at baseline (mean 6.2 vs 4.7; p=0.03) and after lovo-cel (3.8 vs 2.6; p=0.06). Despite this, substantial reductions in annualized VOE rates and hospitalizations were observed. HbAT87Q expression and red cell indices remained

stable.

Figure 1. VOE (blue) and severe VOE (pink) events prior to consent and after lovo-cel infusion.



Conclusions: Most individuals treated with lovo-cel or allo-HSCT became VOE-free; however, a minority continued to experience acute pain not consistent with traditional VOE. People with acute pain post-treatment need recognition, validation, and counseling; with a focus on long-term management. Improved classification frameworks are needed to optimize long-term approaches to pain management.

Clinical Trial Registry: NCT02140554 (HGB-206), NCT04293185 (HGB-210), NCT04628585 (LTF-307)

Disclosure: **Julie Kanter:** Bausch: Consultancy; Beam: Consultancy, Research Funding; Genetix Biotherapeutics: Consultancy, Membership on Board of Directors or Advisory Committees, Research Funding; CDC: Research Funding; Chiesi: Consultancy, Membership on Board of Directors or Advisory Committees; EcoR1: Consultancy; Emerging Therapy Solutions: Honoraria; Fulcrum: Consultancy; GLG Pharma: Honoraria; GlycoMimetics:

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Anju Chawla: Genetix Biotherapeutics: Current Employee
Heidi Elliot: Genetix Biotherapeutics: Former employee; Consultancy (current)
Ashish O. Gupta: Vertex Pharmaceuticals: Consultancy; Jazz Pharmaceuticals: Speaker bureau and investigator-initiated trial; Beam: Research Funding; Genetix Biotherapeutics: Research Funding; Orchard Therapeutics: Research funding; Emerging Therapies Solutions: Honoraria
Melissa Kinney: Genetix Biotherapeutics: Current Employee
Alexis Leonard: Nothing to disclose
Robert S. Nickel: Janssen: research funding
Lin Pan: Genetix Biotherapeutics: Current Employee
Suhag Parikh: Genetix Biotherapeutics: Research Funding
Stacey Rifkin-Zenenberg: Vertex Pharma: Advisory board; Genetix Biotherapeutics: consultancy
Alexis A. Thompson: Beam: Consultancy, Research Funding; Genetix Biotherapeutics: Consultancy, Research Funding; CRISPR/Vertex: Consultancy, Research Funding; Editas: Consultancy, Research Funding; NovoNordisk, Novartis: Research Funding; Pfizer: Consultancy
Mark C. Walters: Ensoma, Inc.: Consultancy, Current holder of stock options in a privately-held company; Vertex Pharmaceuticals: Membership on an entity's Board of Directors or advisory committees; BioLabs, Inc.: Consultancy; AllCells, Inc.: Consultancy.
Matthew Hsieh: Nothing to disclose
John F. Tisdale: Nothing to disclose

A280

FIRST-IN-WORLD EXPERIENCE OF IMMUNOMODULATION TO PROMOTE RECIPIENT TOLERANCE TO GENE MODIFIED AUTOLOGOUS STEM CELL TRANSPLANT FOR MPS II

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Background: Neuronopathic mucopolysaccharidosis type II (nMPSII, Hunter Syndrome) is a lysosomal storage disorder that leads to intracellular accumulation of glycosaminoglycans, which manifests clinically as progressive multiorgan failure, neurodegeneration and death. Haematopoietic stem cell gene therapy (HSCGT) has been used in several inherited metabolic conditions to engraft gene-modified cells that can produce high quantities of previously deficient protein. However, immune responses to these proteins have been reported and early graft loss of modified cells in pre-clinical and clinical reports. We describe our first-in-world experience of HSCGT in nMPSII and including using additional immunomodulation in the peri-transplant period to reduce the risk of graft rejection in an ongoing clinical trial using a novel ex-vivo lentiviral platform (NCT05665166).

Methods: Three patients to date have undergone CD34+ cell collection via leukapheresis using G-CSF and plerixafor. CD34+ haematopoietic stem cells (HSCs) were then transduced ex-vivo using a lentiviral vector containing the human *IDS* gene tagged with ApoEII driven by a human CD11b myeloid-specific promoter. For two patients treated following protocol amendment, gene-modified HSCs were transplanted after busulfan-based conditioning with the addition of three doses of alemtuzumab at 0.1mg/kg on day -7 to -5 during conditioning and ongoing sirolimus from day -1 with a target therapeutic range of 5 – 10 micromol/L. Engraftment kinetics, biochemical parameters and adverse events were assessed at set time points.

Results: For the first patient, CD34+ leukapheresis was uneventful and the modified cell product met release criteria with a vector copy number of 3.63 copies per cell, cell viability of 73.89% and CD34+ purity of 98.87%. 10.78 $x10^6$ TNC/kg were infused following conditioning as above.
Neutrophil engraftment was achieved on day +19, reticulocyte engraftment was achieved on day +29, and platelet engraftment was achieved on day +30. Minimal supportive transfusion was required during admission. The patient did experience transient cytomegaloviraemia, detectable via PCR from day +6, following which they received foscarnet and ganciclovir and successfully cleared viraemia by day +24. Additional screening for invasive virology remained negative and no other significant adverse events were recorded.
Supraphysiological IDS activity >10x ULN was detectable post-transplant from engraftment onwards in both peripheral blood and bone marrow leucocyte samples. Additionally, plasma IDS activity was detectable at day +30, consistent with clearance of anti-IDS antibody. CNS IDS activity was also measurable from day +30 post-transplant.
A second patient has undergone successful leukapheresis and at time of writing has received the cell product following this modified conditioning protocol without concern. Engraftment kinetics and post-transplant disease monitoring assessments are awaited.

Conclusions: The first patient shows early and sustained biochemical correction of nMPSII, and the second patient has undergone the conditioning regimen without concern, confirming the tolerability of our immunomodulation protocol alongside HSCGT. Further follow-up is required to correlate biochemical correction with developmental and cognitive outcomes. Treatment of a further two patients on this trial using this methodology is planned and if

successful this approach may have wider applicability in inducing recipient immune tolerance to HSGCT products in a range of conditions.

Clinical Trial Registry: NCT05665166

Disclosure: Nothing to declare.

A281

GALLBLADDER ABNORMALITIES IN METACHROMATIC LEUKODYSTROPHY: PRELIMINARY ANALYSIS IN PATIENTS TREATED WITH HEMATOPOIETIC STEM CELL GENE THERAPY AND UNTREATED PATIENTS

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Background: Metachromatic leukodystrophy (MLD) is a fatal lysosomal neurodegenerative disorder caused by arylsulfatase-A deficiency. Atidarsagene autotemcel (arsa-cel), an autologous transplantation of $CD34^+$ cells transduced ex vivo with a lentiviral vector encoding the ARSA gene, represents the only approved treatment for pre-symptomatic late-infantile and early-juvenile MLD, or early-symptomatic early-juvenile MLD forms. MLD is also characterized by extra-neurological features, with gallbladder involvement being the most prominent. Despite the rarity of gallbladder abnormalities in pediatric populations, sulfatide accumulation in the gallbladder wall in MLD is associated with an increased risk of malignant transformation. This study analyzes gallbladder involvement in MLD, both in the natural history of the disease and in patients treated with arsa-cel, evaluating its role as an early diagnostic tool and the potential therapeutic effects on gallbladder abnormalities.

Methods: We retrospectively evaluated 104 patients with MLD (44 late-infantile, 40 early-juvenile, 16 late-juvenile, 4 adult), including 48 untreated and 56 treated with arsa-cel. The gene therapy cohort included 26 pre-symptomatic late-infantile, 24 early-juvenile (15 pre-symptomatic and 9 early-symptomatic), and 6 late-juvenile patients (4 pre-symptomatic and 2 early-symptomatic). Clinical data on the age of onset of neurological symptoms and history of cholecystectomy were collected for all patients, as well as ultrasound findings at baseline and throughout follow-up, specifically assessing wall thickening, gallbladder contraction, biliary sludge, and polyp characterization. In patients who underwent cholecystectomy, histopathological reports were analysed when available.

Results: Gallbladder abnormalities were observed at first available ultrasound in 88.6% (39/44) of late-infantile, 75.0% (30/40) of early-juvenile, 68.8% (11/16) of late-juvenile, and 75.0% (3/4) of adult patients. The earliest and most common alteration was wall

thickening: 68.2% (30/44) of late-infantile with Median Age at First Evaluation (MAFE) 13 months, 55.0% (22/40) of early-juvenile, MAFE 61 months, 50.0% (8/16) of late-juvenile, MAFE 189 months. Wall thickening was detected in the pre-symptomatic phase in 84.6% (22/26) of late-infantile, 73.3% (11/15) of early-juvenile, and 25.0% (1/4) of late-juvenile patients.
Longitudinal analysis showed progression of abnormalities over time in untreated patients, particularly in late-infantile and early-juvenile forms. Among arsa-cel recipients, longitudinal analysis of patients with at least one gallballder ultrasounds after treatment (n=50, median follow-up post arsa-cel 5 years) revealed resolution of baseline wall thickening in 61.5% (24/39) and polyposis in 50% (3/6) of patients. Histopathological analysis of removed gallbladders revealed cases of metaplasia, dysplasia, and even carcinoma in situ. These findings were sometimes undetectable by ultrasound, confirming the risk of malignant progression and supporting early cholecystectomy in the presence of suspicious features.

Conclusions: Our analysis confirms early and frequent gallbladder involvement across all MLD forms. Gallbladder wall thickening emerged as the earliest alteration and may represent the first precursor to more complex abnormalities such as polyps. The detection of ultrasound abnormalities as well as cases of cholecystectomy in patients before neurological symptom onset—including those with late-onset forms— suggests that visceral involvement may serve as an early diagnostic disease indicator. The possibility that treatment with arsa-cel prevents the occurrence of new lesions and partially regresses pre-exiting alterations will need to be assessed as long-term follow-up and real world data accumulate.

Disclosure:

- Salvatore Recupero: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd
- Francesca Fumagalli: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd
- Valeria Calbi: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd
- Alessandro Aiuti: Orchard Therapeutics is funding gene therapy clinical trials carried out at San Raffaele Hospital for lysosomal genetic diseases (MLD and MPSI), of which he is principal investigator or investigator. Telethon Foundation is funding gene therapy studies at San Raffaele Hospital for genetic diseases of the immune system (ADA-SCID, Wiskott-Aldrich Syndrome), of which he isprincipal investigator or investigator

A282

BRIDGING READINESS AND REALITY: U.S. PEDIATRIC HEMATOLOGISTS' PERSPECTIVES ON GENE THERAPY FOR SICKLE CELL DISEASE IN THE POST-APPROVAL ERA

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Background: United States Food and Drug Administration approval of two autologous gene therapy (GT) products exagamglogene autotemcel (Casgevy, CRISPR-based) and lovotibeglogene autotemcel (Lyfgenia, lentiviral-based) marks a watershed moment in curative options for sickle cell disease (SCD). However, the successful and equitable implementation of GT in pediatric care requires more than regulatory approval; it demands provider readiness, clear referral frameworks, and systemic alignment. We conducted a national survey to assess how pediatric hematologists are preparing to integrate GT into clinical practice.

Methods: A 35-item REDCap survey was disseminated to approximately 500 board-certified/eligible pediatric hematology/oncology providers across the US (July–September 2025) via the ASPHO and STAR networks. Eligible respondents provided care to pediatric patients with SCD. Survey assessed (1) referral intent across clinical scenarios, (2) structural and clinical factors influencing decisions, and (3) self-reported counseling confidence. Respondents were classified by practice focus (SCD-focused, general hematology/oncology, HSCT-focused). Comparative statistics used chi-square or Fisher's exact tests with a two-sided $p<0.05$ considered significant.

Results:

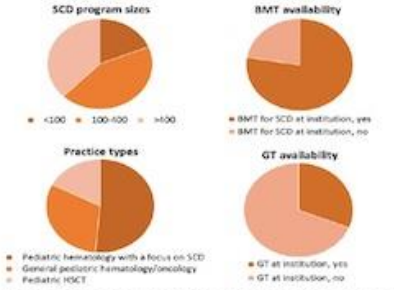

Figure 1a. Broad representation of program sizes, practice types, and institutional Allo-BMT and GT availability based on survey responses

Figure 1b. Most pediatric hematologists/oncologists do not offer product guidance when referring patients with SCD for GT

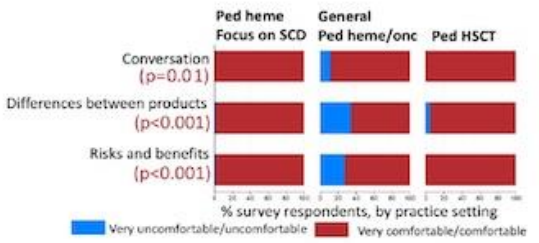

Figure 1c. General pediatric hematologists/oncologist are least comfortable discussing GT options with their patients

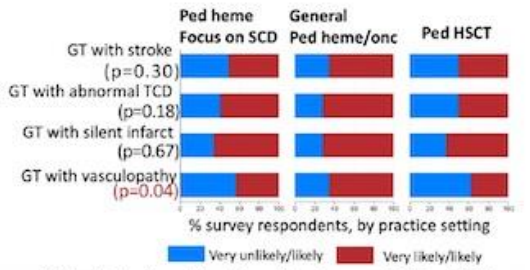

Figure 1d. Pediatric hematologists with a focus on SCD or HSCT are less likely to consider GT in individuals with pre-existing CNS complications

A total of 138 providers responded (27.6% response rate), with broad representation across program sizes, geographic regions, and clinical roles. Most respondents (86%) indicated they were likely or very likely to refer appropriate patients for GT. However, intent to refer varied by clinical scenario and specialty. General hematologists were significantly more likely than SCD-focused or HSCT providers to consider GT for patients with silent cerebral infarcts (63% vs 39%, p=0.01) or cerebral vasculopathy (59% vs 37%, p=0.04), despite reporting lower overall familiarity with GT products and protocols.

Institutional readiness was variable: 77.5% reported access to allogeneic BMT services, while 68.8% indicated GT onboarding capacity. Still, only 18% of providers routinely discussed specific GT products during referral. Among those who did, Casgevy was overwhelmingly favored (94%), though many acknowledged insufficient comparative data to justify a preference. Counseling confidence was uneven: 70% of SCD-focused hematologists felt comfortable discussing GT, compared to just 32% of general hematologists (p<0.001). Confidence was lowest regarding long-term risks (busulfan toxicity, clonal hematopoiesis, secondary malignancies) and mechanistic differences between Casgevy and Lyfgenia.

Insurance approval emerged as the most cited determinant of whether a patient would be referred (72%), ahead of disease severity, caregiver readiness, or institutional infrastructure. Open-text responses highlighted a lack of clear eligibility criteria, uneven payer policies, and limited availability of patient-friendly educational tools as key barriers.

Conclusions: U.S. pediatric hematologists are enthusiastic about GT for SCD, but implementation is constrained by inconsistent referral practices, limited product-specific

knowledge, and payer-driven access barriers. As GT expands globally, these findings offer both contrast and guidance for European systems. While Europe's nationalized health models may mitigate some structural hurdles, the variability in provider knowledge, absence of unified SDM protocols, and need for long-term safety data are universal concerns. Proactive investment in pan-European clinical education, registries, and harmonized counseling tools will be essential to translate gene therapy's promise into equitable, patient-centered care. The U.S. experience underscores that regulatory approval is only the beginning, implementation requires coordinated clinical, educational, and policy efforts to deliver on gene therapy's curative potential for all.

Disclosure: Ngwube, Alexander : Vertex Therapeutics (paid consultant one-time, ended November 2025) and Beam Therapeutics (paid consultant one-time, ended December 2025). All other authors have nothing to declare.

A283

A CASE OF LACK OF ENGRAFTMENT OF GENE-CORRECTED CELLS AFTER LENTIVIRAL HEMATOPOIETIC STEM CELL GENE THERAPY FOR METACHROMATIC LEUKODYSTROPHY: AN INTEGRATED CLINICAL AND IMMUNOLOGICAL INVESTIGATION

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Background: Atidarsagene autotemcel (arsa-cel) is an autologous lentiviral haematopoietic stem cell (HSC) gene therapy indicated for the treatment of early-onset metachromatic leukodystrophy (MLD). We report the first case of complete lack of engraftment of gene-corrected cells after arsa-cel administration and describe a preliminary integrated clinical and immunological investigation into causality of the event.

Methods: A male infant with presymptomatic late-infantile MLD (homozygous *ARSA*c.465+1G>A, null mutation) received arsa-cel at 15 months of age. Mobilization, $CD34^+$ cell yield, drug-product characteristics and busulfan exposure were comparable to that in other patients successfully treated with arsa-cel. Longitudinal laboratory assessments included vector copy number (VCN) and ARSA activity in peripheral blood (PB), bone marrow (BM) and cerebrospinal fluid (CSF), and anti-ARSA antibodies (AAA) determination complete HIV serology. Immune assessments comprised ARSA-specific T-cell assays,

immunophenotyping, immune activation markers, autoantibodies/autoimmunity investigations.

Results: Haematologic recovery was within the anticipated range of arsa-cel successfully treated patients. However, VCN remained below the limit of quantification in all PB and BM samples up to day +180, and ARSA activity was undetectable in PB/BM with minimal CSF activity, indicating lack of engraftment of gene-corrected cells with haematological recovery driven by untransduced autologous HSCs. No deviations in manufacturing, cell dose or conditioning were identified. No anti-HIV antibodies were detected. AAA were negative at baseline, became detectable at day ~30, peaked at day ~60 and declined by day ~180. The patient showed a strong recombinant ARSA-specific $CD4^+$ T cell response from day +30, persisting at day +60 and at 6 months; $CD8^+$ T cell analysis showed no ARSA-specific activation and IFNg release. Other patients with AAA positivity in the clinical development program and post marketing experience, including two with the same *ARSA* genotype, did not show decreases in ARSA activity or VCN. The immune milieu in this highlighted patient displayed a pro-inflammatory profile with eosinophilia, elevated IgE and broad anti-HLA class alloantibodies, in the context of prolonged *Candida parapsilosis* candidemia during aplasia. By the time the lack of engraftment became evident, the patient started to develop typical overt signs of MLD neurological disease and could not undergo further treatment.

Conclusions: This case represents the first failure of engraftment of gene-corrected cells after arsa-cel administration secondary to immune response. A null ARSA genotype (absence of baseline tolerance), in the presence of active infection along with a pro-inflammatory context, sustained ARSA-specific $CD4^+$ T cell responses and humoral activation support a potential multifactorial, T-cell-driven rejection of transduced cells. Individual genetic predisposition, potentially including specific HLA backgrounds, may modulate the risk of immune rejection and warrants comparative analyses with other treated patients. Early monitoring of engraftment of gene-corrected cells may help identify patients in whom immunomodulatory strategies could be considered

Disclosure: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd

A284

STEM CELL MOBILISATION FOR GENE THERAPY IN ADOLESCENT PATIENTS WITH SICKLE CELL DISEASE: EXPERIENCE FROM THE FIRST THREE PATIENTS IN THE UK

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Background: Gene therapy for sickle cell disease (SCD) offers curative potential without the risks of allogeneic transplantation. However, autologous stem-cell mobilisation in SCD is difficult due to endothelial activation, hyperviscosity, vaso-occlusive risk and a pro-thrombotic state. Plerixafor-only mobilisation often yields suboptimal CD34^+ cell numbers and may increase viscosity leading to circuit clotting. Some centres have reported improved yields when combining granulocyte colony-stimulating factor (G-CSF) with plerixafor, but published data remain limited. We describe the first UK experience using this combined approach in three adolescents undergoing mobilisation for autologous gene therapy.

Methods: Three teenagers (ages 14, 15 and 16) with severe SCD were referred for exagamglogene autotemcel (Casgevy®). Each underwent two initial mobilisation cycles: **Cycle 1** with plerixafor alone, and **Cycle 2** with plerixafor + G-CSF (dosed for 3–4 days until WBC >50 × 10^9/L). Both cycles produced insufficient CD34^+ yields for manufacture.
A modified **Cycle 3** protocol was therefore implemented, consisting of:
• G-CSF 5 mcg/kg twice daily for four days prior to apheresis
• Plerixafor 0.24 mg/kg pre-collection
• Increased G-CSF threshold to WBC 75 × 10^9/L
Supportive measures included red cell exchange (RCE) 1–3 days before apheresis, targeting HbS <15%, addition of Aspirin 75 mg to routine LMWH thromboprophylaxis and IV hydration.

Results: Across all patients, CD34^+ yields improved substantially with the modified protocol.

CD34^+ cell yield (×10^6/kg) following three collection cycles

Patient	Cycle 1	Cycle 2	Cycle 3
1	9.0	13.5	26.66
2	9.84	6.79	20.50
3	3.3	7.0	20.0

Mobilisation was well tolerated in all three patients. Patient 1 and Patient 2 experienced circuit clotting during Cycle 1, and Patient 3 had two G-CSF doses omitted in Cycle 2 because of the mild pain, successfully managed with oral morphine.
Peak WBC counts during Cycle 3 were 89.9 × 10^9/L, 103.2 × 10^9/L and 70.9 × 10^9/L for Patients 1, 2 and 3 respectively. Despite recognised concerns that G-CSF may precipitate VOC in SCD, no VOC episodes occurred, and all patients tolerated mobilisation exceptionally well. Other than transient leukocytosis (all patients) and manageable pain (one patient), no significant adverse events were observed. All adolescents returned promptly to school and normal activities, supporting both feasibility and acceptability of this regimen.

Conclusions: The combination of G-CSF and plerixafor with an elevated WBC threshold, preceded by RCE and supported by targeted thromboprophylaxis with LMWH and Aspirin, proved safe, well tolerated, and markedly more effective than plerixafor alone in adolescents

undergoing mobilisation for SCD gene therapy. This modified protocol achieved consistently adequate CD34^+ yields after prior mobilisation failures.
We propose this approach as a potential first-line mobilisation strategy for SCD patients preparing for autologous gene therapy, with the aim of minimising repeated collections, central line procedures and associated anaesthetic exposure. Further multicentre evaluation is warranted to confirm safety and generalisability across broader patient cohorts.

Disclosure: Nothing to declare

A285

THE USE OF GCSF FOR STEM CELLS MOBILIZATION IN PATIENTS WITH SICKLE CELL DISEASE TREATED WITH GENE THERAPY

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Background: Hematopoietic stem cell transplantation (HSCT) remains the only curative option for sickle cell disease (SCD), yet it's constrained by donor scarcity and transplant-related complications. Gene-editing technologies like CRISPR/Cas9—targeting the BCL11A erythroid enhancer—have shown potential in increasing fetal hemoglobin (HbF) expression. This approach demands robust mobilization of autologous $CD34^+$ hematopoietic stem and progenitor cells (HSPCs), ideally $\geq 20\times10^6$/kg, a threshold challenging to achieve in SCD patients.
Standard granulocyte-colony stimulating factor (G-CSF)-based mobilization is generally avoided due to the associated risk of inducing VOCs and acute chest syndrome (ACS), particularly in the presence of high HbS levels. In this study we report the use of GCSF + plerixafor for mobilization of stem cells from patients with SCD.

Methods: The objective is to assess the safety, feasibility, and effectiveness of combining GCSF with plerixafor in stem cell mobilization for Exa-cel gene therapy in SCD patients.
Retrospective analysis of 13 SCD patients undergoing autologous $CD34^+$ cell collection.
Mobilization Protocols:
Group A (n=2): Plerixafor alone.
Group B (n=4): Initial plerixafor, then added G-CSF.
Group C (n=7): G-CSF + plerixafor from outset.
Hydroxyurea held for 8 weeks; exchange transfusions targeting HbS <30% (Group A/B) or <20% (Group C).
Inpatient management included hydration and aspirin prophylaxis.

Results: A total of 13 patients with sickle cell disease (SCD) were enrolled for gene therapy and underwent stem cell mobilization. The median age was 16 years (range: 12–32), with 6 males and 7 females.
The median number of mobilization cycles was 1 (range: 1–6). Seven patients collected with one cycle, one with 2 cycles, 2 with 4 cycles, 1 with 5 cycles and 2 with 6 cycles. In Group A, both patients failed to collect an adequate number of cells after 2 cycles for the first patient and 6 cycles for the second patient. In Group B, the median number of mobilization cycles was 4 (range: 2–6), while in Group C, all 7 patients successfully collected sufficient cells after only one cycle.
The overall median total CD34+ cell count collected was 71 × 10^6/kg, with 27 × 10^6/kg in Group A, 80 × 10^6/kg in Group B, and 74.6× 10^6/kg in Group C. The median manufactured dose was 6.75 × 10^6/kg overall, with 1.5 × 10^6/kg in Group A, 6.35 × 10^6/kg in Group B, and 14.4 × 10^6/kg in Group C.
There was no VOCs, prolonged pain symptoms, or ACS secondary to G-CSF administration. There were no ICU admissions and no reported mortality. Median duration of hospitalization was 6 days for all admissions and 6 days in patients mobilized with G+plerixafor.

Outcome	Group A	Group B	Group C	Overall
Median $CD34^+$ collected ($\times 10^6$/kg)	27	80	74.6	71
Median manufactured dose ($\times 10^6$/kg)	1.5	6.35	14.4	6.75
Median mobilization cycles	2.5	4	1	1
VOC / ACS / ICU admissions	0	0	0	0
Median hospital stay (days)	6	6	6	6

Conclusions: The combination of G-CSF with plerixafor resulted in improved collection of the target cell dose for gene therapy compared to plerixafor alone. No safety concerns were observed with G-CSF use in SCD patients managed under a specific protocol. Further evaluation in a larger cohort, including detailed analysis of the cellular characteristics of collected cells, is planned.

Disclosure: Non to disclose.

P098

EXPLORING THE REIMBURSEMENT OF CAR-T CELL THERAPY FOR MULTIPLE MYELOMA AND B-CELL LYMPHOMA PATIENTS UNDER TURKIYE'S SOCIAL SECURITY SYSTEM (SGK)

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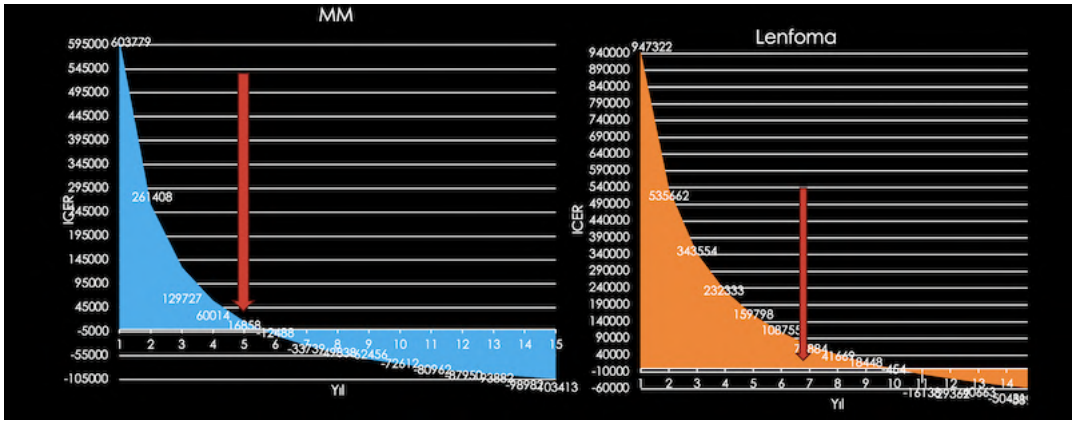
Background: CART therapies are indicated in MM and BCLs. Some countries reimburse CART therapies; most, especially low- and middle-income countries (LMICs), lack access due to high manufacturing costs. Cost-effectiveness analysis guides resource allocation by governments and insurers. Quality-Adjusted Life Year (QALY) measures health quality from 0 to 1, with 1 indicating perfect health; World Health Organization (WHO) considers it very cost-effective if it equals per capita gross domestic product (GDP). Incremental Cost-Effectiveness Ratio (ICER) compares costs and benefits of new technologies; if the ICER is less than three times GDP, it's cost-effective and reimbursable. This study assesses the likelihood of reimbursement by the Social Güvenlik Kurumu (SGK) for CAR-T in Turkiye. It compares the cost-effectiveness of autologous stem cell transplantation (ASCT), CAR-T, and Bi-specific T-cell Engagers (BITEs) over 15 years.

Methods: Fifteen patients, including those with Multiple Myeloma (n=10) and B-cell lymphoma (n=5), were evaluated retrospectively. All had undergone autologous stem cell transplantation (ASCT). The costs of mobilization, stem cell apheresis, and autologous stem cell transplantation at the unit were calculated in TL and converted to USD based on the exchange rates at the time. Costs of CART cell therapy and bispecific antibody treatments (BITEs) were estimated from the literature. In line with World Health Organization (WHO) recommendations, the cost-effectiveness threshold was set at three times the nominal GDP per capita in Turkey (15,147.84 USD). QALYs: The responsible physician determined separate QALYs for MM and BHL for the first three months and the following period, based on the Karnofsky performance scale. QALY values from the literature were used for CART and BITE treatment costs. Monthly costs for followed-up patients were calculated by dividing median treatment costs by the median follow-up periods (83 months or 22 months). Cost and QALY calculations and graphing were performed using Microsoft 365 Excel.

Results: The figure shows the ICER per year for Multiple Myeloma (MM) and B-cell Lymphoma (BCL). The red arrows show the time point of the cost-effective cut-off in 15 years.



The median costs and QALYs of each ASCT, CART, and BITE for MM and BCL are given in Table 1. Considering the median cost, CART therapy is not cost-effective for MM patients in the first years after transplantation (>$45,442), but it becomes cost-effective after the 4th year (including the 5th year), and this effectiveness continues for the next 10 years. In B-cell lymphomas, CART becomes cost-effective after the 7th year post-transplant (including the 8th year), and this effectiveness persists for up to 15 years. BITE treatments were not found to be cost-effective during the 15-year follow-up period. Therapies such as CAR-T become cost-effective compared to BITE after the 2nd month in multiple myeloma and after the 10th month in lymphoma.

		MM (n=10)	Lymphoma (n=5)
		n (%)	n (%)
Female sex		2 (20,0)	5 (100,0)
Age median (min–max)		63 (48-75)	54 (29-73)
Follow-up duration, median (min–max)		83 months (11-110)	22 months (10-72)
QALY coefficient (1)	post-transplant, first 3 months	0,5	0,5
	after 3 months post-transplant	0,7	0,8
QALY CAR-T (2)	post-transplant, first 3 months	0,9	0,9
	after 3 months post-transplant	0,9	0,9
QALY BITE (3)	post-transplant, first 3 months	0,9	0,9
	after 3 months post-transplant	0,9	0,9

Treatment cost (4)	median (USD)	230.401,13	33.869,69
CAR-T cost (USD) (5)	mean (USD)	184.255,75	184.255,75
BiTE cost (6-8)	mean (USD, monthly	64.500 USD	12.721 USD

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Conclusions: The limited number of patients and the retrospective design of our study are our main limitations. Uncertainties in the QALY and ICER calculations for CART and BITE treatments in the literature, along with the fact that these studies cover only a two-year time frame, make it challenging to interpret their long-term effects and treatment costs.

Disclosure: Nothing to declare.

TRANSPLANT-SPECIFIC TOPICS

Stem cell source, mobilization, collection and engineering

OS03-07

UM171-EXPANDED CORD BLOOD AS A SAFE AND POTENT GRAFT SOURCE FOR HIGH-RISK LEUKEMIAS AND MYELODYSPLASTIC SYNDROMES WITH DURABLE LONG-TERM SURVIVAL

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Background: Patients with high (H) and very high (VH)–risk acute leukemia (AL) or myelodysplastic syndrome (MDS) have high relapse rates and poor overall survival (OS) after conventional allogeneic transplantation (alloT). Cord blood (CB) transplantation (T) offers a lower relapse risk in high risk diseases but is limited by low cell dose, delayed engraftment, and high non-relapse mortality (NRM). UM171 is a small molecule that expands hematopoietic stem cells ex vivo and may overcome these limitations.

Methods: We analyzed outcomes of 60 adults with high (H) or very high (VH)–risk AL or MDS who received a single UM171-expanded CB graft in two prospective phase II trials: ECT-002 (Canada) and ECT-004 (United States and the Netherlands). H-risk AL/MDS was defined as disease with an expected 2-year progression-free survival (PFS) <40% after conventional alloT. VH-risk disease was defined as a second allo transplant, AL with active disease, acute myeloid leukemia (AML) with TP53 mutation and complex karyotype, AML with EVI1 mutation, or MDS with multi-hit TP53 mutation. To maximize graft-versus-leukemia activity, we purposely aimed for 5/8 HLA-matched CB units, accepting lower allele-level matching even when better-matched units were available. The primary endpoints were safety and non-relapse mortality (NRM); secondary endpoints included PFS, OS, relapse incidence, engraftment, and graft-versus-host disease (GVHD).

Results: Sixty patients (median age 43 years; range 19–66) were transplanted; 87% had AL (63% myeloid, 37% lymphoid) and 13% had MDS. Thirty percent had failed a prior allogeneic transplant and 57% met VH-risk criteria. As designed, 75% received a 5/8 HLA-

matched graft, and 43% received a CB unit with a pre-expansion cell dose below the minimal threshold required for unmanipulated CBT. Neutrophil engraftment occurred in 92% of patients at a median of 17 days. One primary graft failure occurred in the presence of high-titer donor-specific anti-HLA antibodies. All patients completed planned follow-up (3 years in the Canadian study and 2 years in the U.S. study).
At 24 months, OS was 63.7% and PFS was 57.0%. The cumulative incidences of relapse and NRM were 22.5% and 20.5%, respectively. Age was the strongest predictor of NRM: patients <43 years experienced 0% NRM, with 24-month OS and PFS of 82.8% and 79.3%,respectively. Older patients (≥43 years) had comparable relapse rates but significantly higher NRM. Grade III-IV acute GVHD occurred in 20%, while moderate to severe chronic GVHD was infrequent at 7% at 2 years.

Conclusions: UM171-expanded CBT provides rapid and durable engraftment and achieves promising long-term survival in adults with high and very high–risk AL/MDS, even when using intentionally selected 5/8 HLA-matched and low–cell-dose grafts. Particularly notable were the outcomes observed in patients with VH–risk features such as AL not in remission, TP53-mutated AML/MDS, or 2nd allo transplant. These VH-risk groups are historically associated with extremely poor post-transplant survival. These findings highlight UM171-expanded CB as a safe and potent graft source in H and VH-risk AL/MDS. However, a prospective randomized trial is needed to confirm these results and define the role of UM171-expanded CB relative to other graft sources.

Clinical Trial Registry: NCT03913026, NCT04103879

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Ahmad: ExCellThera: research funding.
Tomellini: ExCellThera: current employment.
Roy: research funding, royalties if sales of UM171.
Caudrelier: ExCellThera: current employment.
Thauvette: ExCellThera: current employment.
Sauvageau: ExCellThera: current employment, current equity holder, membership on Board of Directors, patents & royalties, research funding.
Milano: ExCellThera : research funding.

OS10-03

HEALTHY POOR MOBILIZERS RELATED AND UNRELATED ADULT AND PEDIATRIC DONORS: NATIONWIDE SPANISH EXPERIENCE WITH AND WITHOUT PLERIXAFOR

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Background: Plerixafor (Plex), a reversible CXCR4 antagonist, has currently no formal indication in healthy allogeneic donors (HD), although its efficacy and safety profile have been proved in autologous donors. An off-label use of Plex is widely increasing as pre-emptive or therapy, according with peripheral CD34+ after at least 4 days of GCSF or CD34+ level in apheresis, respectively. Failure mobilization can lead to subsequent apheresis procedures or urgent bone marrow harvest. As there is a need for clarifying its potential indication in HD with problems in mobilization, we addressed a nationwide retrospective study from Spanish Bone Marrow Donor Registry (REDMO) within Spanish Group for Haematopoietic Transplantation and Cellular Therapy.

Methods: We included healthy related (RD) and unrelated donors (UD) classified as poor (peripheral $CD34^+$ 11–20/μL on day +4/+5 of G-CSF and/or $CD34^+$/kg $<4\times10^6$ in 1st apheresis) or very poor (peripheral $CD34^+$ ≤10/μL on day +4 or +5 and/or those yielding $<2\times10^6$ $CD34^+$/kg in 1st apheresis) mobilizers between January 2013 and June 2025, regardless the use of Plex. We compared general and mobilization characteristics between Plex and non-Plex group. Plex was used as "off label" pre-emptive or therapy strategy according with each center policy. We used SPSS for statistical descriptive analysis. The study was approved by local Ethical Committee (HCB/2024/0690).

Results: Seventeen Spanish centers reported a total of 343 adult and pediatric (n:19) healthy donors classified as poor (69.4%) or very poor mobilizers (30.6%) according with definitions reported above. Mean follow up was 2.8 years (0.1-12.5). General and mobilization characteristics are reported in table 1. All donors received a median G-CSF dose of 10 μg/kg/day administered twice daily for at least 4 days, with no statistically differences in the use of original or biosimilar formulation of GCSF between groups. The most frequent donor comorbidities were HTA and smoking. Overall, 92 donors (27%) received Plex (89 RD, 3 UD), and 14 out of them were pediatric. The use of pre-emptive Plex (n:40) was successful in all but one that required a second dose, whereas 52 donors received it as therapy after 1st apheresis (one donor needed 2 Plex doses). Non- Plex group (202 RD, 49 UD) required mostly two apheresis (95.6%). Remarkably Donors receiving Plex achieved a significantly higher median total $CD34^+$ collected (6.6 vs 4.9×10^6/kg $p<0.001$) with respect no Plex group. If a second apheresis was needed, collected CD34+ was significantly higher in Plex group. Consequently, fewer apheresis and lower total volume was processed in Plex group. No final failure mobilization was reported in the whole group. Adverse events were uncommon, and particularly in Plex Group (8%) described as mild (gastrointestinal,

headache and asthenia), with no adverse events reported in pediatrics.

Table 1 general Characteristics

Variables n(%)	**Total n:343**	**Plex (92)**	**No plex (251)**	**p**
Donor Sex Male/Female	117(34)/216 (63)	36 (39)/56(61)	81 (32)/170(68)	0.2
Pediatric donors n (%)	19 (5.5)	14 (15.2)	5 (2)	0.05
Median Donor age (range)	48 (0–78)	51(0-78)	47(1-77)	0.6
Median weight kg (range) Donor Recipient Donor-Receptor weight difference	 66.5 (9.8–125) 77 (17–144) 9.9 (0-83)	 66.5(9.8-125) 75 (17-144) 9 (0-50)	 66.5(12-125) 78 (25-139) 10 (0-83)	 0.1 0.06 0.5
Receptor vs Donor weight > 20%	142(41.3)	39 (42.3)	103(41)	0.6
Donor type Related/Unrelated	290(85)/53 (15)	89 (97)/3 (3)	202(80)/49(20)	0.001
Donor comorbidities	132 (38.4)	41(44.5)	91(36.2)	0.05
Median GCSF dose (µg/kg/day)	11.45 (6.7–26)	10.6(8-26)	11(6-22)	0.5
GCSF type Original Biosimilar	 232(68) 41(32)	 78 (85) 14 (15)	 156 (85) 27(15)	 0.9
Apheresis number 1 2 3	 38 (11) 290 (84) 16 (5)	 38 (40) 49 (54.4) 5 (5.6)	 - 240(95.6) 11(4.4)	0.02
Total Median CD34+ ×10^6/ kg collected First Apheresis Second Apheresis	5 (1.2–54) 2.6 (0.3-20) 1.9(0.5-9.4)	6.6 (2.2-54) 2.4 (0.3-20) 4.2 (0.5-9.4)	4.9 (1.2-13) 2.8 (0.6-7.5) 1.8 (0.4-9.4)	0.001 0.7 0.001
Median Total volume (ls) processed (range)	25(2.7-58)	23(2.7-42)	25 (6-58)	0.02

Mobilizer type				
Poor	237 (69)	40(44.3)	197 (78.4)	0.02
Very poor	106 (31)	52(55.7)	54 (21.6)	

Conclusions: Plex can be used safely in both adult and pediatric healthy donors with a significant better efficacy in mobilization. A pre-emptive strategy with Plex can avoid extra apheresis procedures in poor mobilisers, of special interest for unrelated voluntary donors. Next step will be to design a homogenous protocol including Plex in allogeneic donors.

Clinical Trial Registry: No

Disclosure: No conflict of interest to be declared

OS10-05

EXPANDING ACCESS TO HAPLOIDENTICAL TRANSPLANTATION: CLINICAL FEASIBILITY OF A CENTRALIZED NATIONWIDE DISTRIBUTION MODEL FOR FRESH TCRA/B-DEPLETED GRAFTS IN FRANCE

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Background: TCRαβ/CD19 depletion is an *ex vivo* graft-engineering strategy for haploidentical hematopoietic stem cell transplantation (haplo-HSCT) that removes TCRαβ$^+$ T cells and CD19$^+$ B cells while preserving key innate/adaptive effectors (NK cells and γδ-T cells) supporting engraftment, infection control and graft-versus-leukemia activity. Although extended from pediatric non-malignant to malignant indications, its technical complexity, cost and regulatory burden limit implementation to a few specialized centers. We established a national single-center model for real-time distribution of fresh TCRαβ/CD19-depleted grafts, bringing cells to patients rather than patients to cells. In this abstract, we aimed to evaluate this innovative national centralized fresh-manufacturing strategy, achieving a vein-to-vein time <36 hours.

Methods: We developed an end-to-end logistics and quality framework covering on-site and off-site apheresis, graft collection, fresh-product transport to Necker or external centers (n=10), in-process and final quality controls, graft transformation (TCRαβ/CD19 depletion), and shipment (car, train, plane) to the transplant center. We retrospectively assessed the feasibility of this pathway in patients receiving a TCRαβ/CD19-depleted haplo-HSCT manufactured at Necker since 2014 (n=55). Diagnoses were grouped into major categories: bone marrow failure/DNA-repair syndromes (33%), inborn errors of immunity (62%), hematological malignancies (5%).

Results: The national single-center model was logistically feasible and delivered standardized products. Twenty productions (36%) were performed for external centers, and all grafts met the targeted logistics constraints, achieving a vein-to-vein time <36 h and being infused within the within the product shelf-life (<6 h post-release). Final cellular composition was comparable whether apheresis was performed on-site at Necker or off-site in referring centers. Despite variability in apheresis product composition, 53 (96%) of the products met predefined quality specifications. Two transplants required a second apheresis and CD34+ selection due to low CD34+ mobilization. The median CD34+ cell recovery was >88%, with a median TCRα/β depletion of −3.9 log. Importantly, clinical outcomes were not impacted by the logistics pathway, as time to neutrophil recovery and platelet reconstitution were similar whether grafts were infused at Necker or shipped and infused at the referring transplant center.

Conclusions: This national fresh-product strategy bridges point-of-care and centralized cryopreserved manufacturing. It demonstrates that a centralized academic platform for TCRαβ/CD19 depletion can reliably support nationwide activity, delivering comparable graft quality and post-transplant hematologic recovery regardless of collection or infusion site, enabled by robust logistics (rail/air) and short turnaround times. Activity increased approximately ten-fold between 2014 and 2024, underscoring the growing demand for this platform. Establishing a second authorized center is therefore a logical next step: a structured tech-transfer program with Institut Paoli-Calmettes (IPC, Marseille) was initiated, transferring Necker's experience in manufacturing, stability, transport and regulatory interactions through joint meetings and document reviews.

Disclosure: Nothing to declare

OS15-06

CILTACABTAGENE AUTOLEUCEL OUT-OF-SPECIFICATION MANUFACTURING OUTCOMES IMPROVE WITH EARLIER LINES OF THERAPY

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Background: Ciltacabtagene autoleucel (cilta-cel) is a B cell maturation antigen–directed chimeric antigen receptor-T cell therapy approved for adults with lenalidomide-refractory multiple myeloma as early as first relapse. Cilta-cel is manufactured using autologous T cells, resulting in variability in the initial starting material and subsequent manufactured product, which may not meet health authority specifications (out-of-specification [OOS]). Quality attributes of T cells obtained from patients are the predominant contributors to OOS manufacturing outcomes. Moreover, manufacturing of in-specification drug products is associated with the enrichment of naive and central memory T cell subpopulations, which are more abundant in material collected from patients with relatively fewer prior lines of therapy (pLOTs). This study examined cilta-cel manufacturing outcomes across multiple pLOTs.

Methods: Commercial cilta-cel manufacturing data were analyzed to identify determinants of manufacturing outcomes, define biomarkers predictive of manufacturing success and assess results following OOS-driven remanufacturing or recollection.

Results: Rates of first-time manufacturing success significantly improved using T cells from patients with fewer pLOTs (≥1 versus ≥4 pLOT: 93% versus 89%; N=~3000). CD3+ cell recovery at manufacturing initiation was less favorable in patients with ≥4 versus fewer pLOTs. The initial cellular CD4:CD8 ratio improved by 54% with fewer pLOTs (average CD4:CD8 ratio, 1 versus ≥4 pLOT: 1.0 versus 0.65); these data also suggest that CD4:CD8 ratio >0.5 may contribute to better in-specification, first-time manufacturing outcomes. Recovery of viable cells before lentiviral vector transduction and cumulative population doubling level of cells improved (≤7%) with relatively fewer pLOTs (P<0.05 for both). Markers of metabolic activity were significantly improved with fewer pLOTs (10% average improvement for material from patients with 1 versus more pLOTs).
Across OOS outcomes from all pLOTs (n=317), 63% were released through an expanded access program without remanufacturing. Of the remaining 37%, 8.6% were cancelled. An additional 28.6% (n=90) underwent remanufacturing, 60% (n=54) resulted in OOS or cancellation and 40% (n=36) resulted in within-specification outcomes. Material from patients with ≥4 pLOTs undergoing remanufacturing resulted in the same or additional OOS results or cancellations as the first manufacturing outcome (67% of attempts [n=36]). Remanufacturing new apheresis material was requested in 14% of initial OOS cases due to insufficient remaining material or concerns about effects of prior therapies, suggesting long-lasting impact of prior treatments and/or disease characteristics. Remanufacturing attempts using new apheresis material (n=45) resulted in similar or worse outcomes in 31% of cases and cancellation in 20% of cases. Cancellation and OOS outcome rates for remanufacturing with ≥4 pLOTs were 39.5% and 35.5%, respectively (n=29). The manufacturing success rate improved to 99% when using cells from patients with ≥1 pLOT (6.5% received OOS product) versus 97% for ≥4 pLOTs (9.2% received OOS product).

Conclusions: First and overall manufacturing success rates were higher using cells collected from patients with ≥1 versus ≥4 pLOTs. T cell attributes associated with manufacturing

outcomes were improved in starting material collected from patients with ≥1 versus ≥4 pLOTs. Remanufacture of product often results in additional OOS outcomes, which may further delay treatment. © *American Society of Hematology (2025). Reused with permission*.

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Robert Bowden/Juan Carlos Araque/Gourav Choudhary/Lisa Kallenbach/Victoria Alegria/Jill Vanak/Daniel Ciccone/Monica Onorata/Hannelore Van Eeckhoutte/Vicki Plaks - Employment/Stocks: Johnson & Johnson
Octávio Costa Filho/Matthew Perciavalle/James Salmon/Jay Kang/Michael Mondon - Employment/Stocks: Legend Biotech

A286

HEMATOPOIETIC STEM CELL DONATION IN FAMILY DONORS UNDER 18 YEARS OF AGE. EXPERIENCE OF THE ITALIAN SECOND OPINION COMMITTEE SIMTI / SIDEM FOR DONOR PROTECTION

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Background: In allogeneic transplantation, a compatible donor is initially selected from within the family. If the most suitable HLA-matched family donor is <18 years of age, to protect the donor and avoid the administration of growth factors, in Italy a bone marrow donation is permitted as a standard donation, but peripheral blood stem cell donation is not, according to the SIMTI GIMTO Recommendations (Blood Transfusion 2013). In very specific cases, the SIMTI/SIDEM Committee to donor protection, designated by the relevant scientific societies, may be consulted as a "Second Opinion" to assist the Donor Center (DC) and the Transplant Program (TP) in assessing donor suitability, with the aim of protecting the donor's well-being and safety.
We have evaluated all requests for "second opinions" to the SIMTI/SIDEM Committee, analyzing the impact of the number of donation requests from donors under 18 years of age.

Methods: The possibility of evaluating a donor <18 years of age for the donation of peripheral HSC is provided for by Italian law (State-Regions Agreement 231/2022), but is assessed by the SIMTI/SIDEM Commission only in the absence of comorbidities, associated with one of the following criteria: absence of other compatible related or unrelated donors, urgent transplantation for the recipient, or the need for a second donation from the same donor who has already donated Bone Marrow. The TP sends a request to the SIMTI/SIDEM Commission through the IBMDR (Italian Bone Marrow Donor Registry), with centralized and shared management of Second Opinion requests, both for related and unrelated donations.

Results: From 2009 to 2025, 364 requests were received by the SIMTI/SIDEM Commission, of which 21 were for minor donors (6%), received after 2013. Of these, 16/21 (76% of requests) were sent to assess suitability for peripheral HSC donation, in 13 donors as a first donation, in 3 donors as a second donation (after a previous donation of Bone Marrow), due to graft failure.
Donors were distributed according to the following age groups: <14 years: 1 donor (6.3%); 14-15 years: 8 donors (37.5%), 16-18 years: 9 donors (56.2%).
All requests met the aforementioned appropriateness requirements.
The SIMTI-SIDEM Commission responded with an "affirmative opinion" to all these requests, with the following recommendations: the donor must express his or her "willingness" to donate; consent must be given by both parents; CVC placement is not permitted (it is considered a contraindication to peripheral HSC donation in a minor); follow-up must be conducted for at least 10 years after donation, according to the Recommendations.
All donations proceeded normally, and no adverse events or serious reactions were recorded; no significant problems were reported during follow-up.

Conclusions: Peripheral HSC donation is not considered standard for donors <18 years of age. However, under very select conditions and with Second Opinion approval, it is possible to safely evaluate the donation of growth factor-mobilized peripheral HSC, particularly in the 16-18 age group, ensuring accurate pre-donation hematological and immunological evaluation and follow-up for at least the next 10 years.

Clinical Trial Registry: None

Disclosure: Nothing to declare

A287

LONG-TERM CRYOPRESERVATION CHANGES THE IMMUNE EFFECTOR CELL COMPOSITION OF PERIPHERAL BLOOD STEM CELL GRAFTS

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Background: In an international collaboration between DKMS (Germany) and NMDP (USA), we are comprehensively characterizing the immune effector cell composition of 2,000 donor Peripheral Blood Stem Cell (PBSC) products. Our goal is to correlate the cellular composition of PBSC grafts with patient outcome of allogeneic hematopoietic cell transplantation (alloHCT). As part of this project, we investigated the effect of cryopreservation on the cellular composition of PBSC products. Cryopreservation is thought to influence cellular composition of the graft, but comprehensive data are lacking. Here, we present an analysis on how cryopreservation followed by short-, medium- and long-term storage affected the graft composition.

Methods: A 34-color flow cytometry panel was used to determine the graft immunophenotype in terms of specialized immune effector cells. We analyzed 20 fresh grafts and compared them to their frozen and thawed counterparts after storage in liquid nitrogen for 2 weeks, as well as 2, 6 and 24 months, respectively. Cryopreservation of product samples followed routine clinical procedures using a 10% DMSO containing cryo-medium and a controlled rate freezing. After thawing at 37°C, cells were washed, stained, fixed and analyzed immediately by high dimensional full spectrum flow cytometry. Our panel is designed to capture the major immune cell subsets, hematopoietic stem cells (HSCs) and an extensive set of phenotyping markers focused on the activation and differentiation status of T-cell and dendritic cell (DC) subsets.

Results: We observed significant changes in cell composition after cryopreservation: (i) As known, granulocytes showed a pronounced decline. (ii) Analyzing nine main cell populations (excluding granulocytes) we observed a marked reduction of mDCs following freezing and short-term storage (1.9% of all live cells fresh vs 1.4% two weeks storage, $p<0.001$). Specifically within the mDCs compartment, the CD16+ mDCs was significantly reduced (1.6% vs 0.8%, $p<0.001$) in frozen and thawed samples. After two years of storage, grafts showed ongoing significant decrease of mDCs (1.4% vs 1.0%, $p<0.001$) and especially of CD16+ mDCs (0.8% vs 0.6%, $p<0.04$).

Conclusions: In this longitudinal analysis, we observed a significant decrease of mDCs frequencies within two years of storing in the vapour phase of liquid nitrogen. This population may have a role in the development of chronic GVHD after alloHCT. The results provide further insight into the influence of cryopreservation on PBSC graft composition and warrant further efforts to explore mechanisms behind differential outcomes observed using fresh vs cryopreserved PBSCs.

Disclosure: Nothing to declare.

A288

MYELOID EXPANSION VELOCITY: A NOVEL KINETIC BIOMARKER FOR PREDICTING HEMATOPOIETIC STEM CELL MOBILIZATION FAILURE IN ACUTE LEUKEMIA

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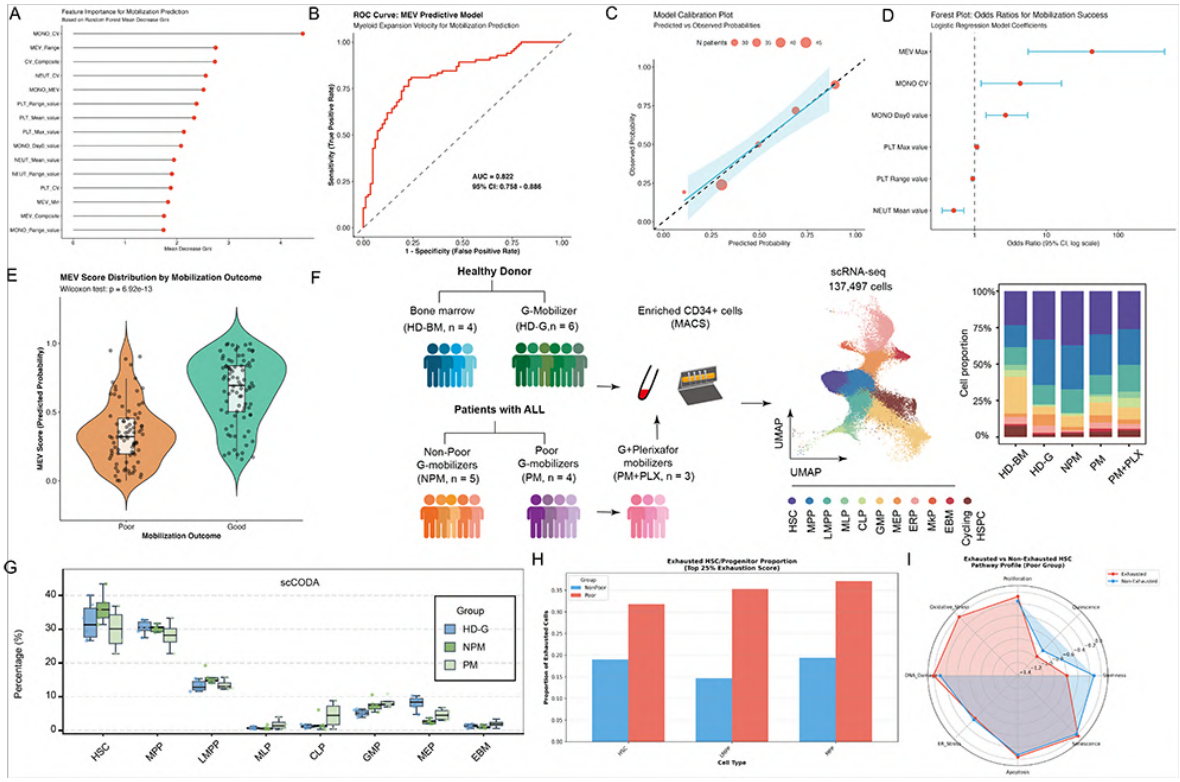
Background: Failure to collect adequate hematopoietic stem cells (HSCs) remains a critical bottleneck for autologous transplantation in acute leukemia. Current prediction methods rely on static "snapshots" of peripheral blood counts, which frequently fail to capture the dynamic nature of hematopoietic recovery. We hypothesized that the trajectory of myeloid recovery during G-CSF priming—specifically the Myeloid Expansion Velocity (MEV)—serves as a superior surrogate for underlying stem cell fitness compared to isolated measurements.

Methods: We analyzed 167 B-ALL patients with complete daily blood count monitoring during mobilization. MEV was defined as the slope of myeloid marker recovery, with additional features capturing trajectory variability and acceleration. A multivariable predictive model was constructed and internally validated. To decode the cellular drivers of these kinetic patterns, we performed single-cell RNA sequencing (scRNA-seq) on 137,497 $CD34^+$-enriched cells from 22 subjects, comparing healthy donors to patients stratified by mobilization outcome.

Results: MEV emerged as a robust predictor, fundamentally outperforming static measurements. The MEV-based kinetic model achieved an AUC of 0.822 (sensitivity 79.8%, specificity 77.1%). Three key kinetic insights highlighted the unique value of MEV. (i) Velocity drives success: Maximum MEV was the strongest individual predictor (OR = 43.2, $p < 0.001$), indicating that the speed of expansion is more critical than absolute counts. (ii) Stability matters: Monocyte variability emerged as a top-ranked feature, suggesting that erratic recovery signals poor outcomes. (iii) The "High-Count" Paradox: High but erratic neutrophil trajectories were inversely associated with success, a phenomenon invisible to static testing but captured by MEV. Mechanistically, scRNA-seq provided the biological rationale for these kinetic failures. Poor mobilizers exhibited genuine HSC depletion (scCODA log-ratio −0.415). Crucially, the residual HSC pool displayed an "Exhausted-like" phenotype, characterized by hyper-proliferation, high oxidative stress, and DNA damage. This exhaustion led to premature myeloid skewing, explaining the clinical observation of transient, ineffective neutrophil surges (high kinetic volatility) that fail to yield harvestable stem cells.



Conclusions: MEV represents a paradigm shift from static to kinetic monitoring. By quantifying the velocity and stability of recovery, MEV identifies at-risk patients earlier and more accurately than conventional methods. The biological basis of low MEV—oxidatively stressed and exhausted HSCs—offers mechanistic clarity, suggesting that interventions targeting oxidative stress could restore stem cell fitness.

Clinical Trial Registry: NCT04645199; https://clinicaltrials.gov/study/NCT04645199

Disclosure: Nothing to declare.

A290

TRANSFORMING TIMELY ACCESS TO STEM CELL COLLECTIONS: EARLY IMPACT OF ANTHONY NOLAN'S FIRST DEDICATED CELL COLLECTION CENTRE

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Background: Stem cell transplantation is a vital curative therapy for blood cancers and blood disorders, but persistent apheresis capacity constraints in the UK have limited timely

access to donor cells. In 2023/24, only 15% of requests for stem cell collections were fulfilled on the clinician's or researcher's "first-choice date," risking delays to life-saving transplants. The UK Stem Cell Strategic Forum has highlighted the urgent need to expand domestic collection capacity and future-proof infrastructure for emerging cell and gene therapies. In response, Anthony Nolan launched England's first dedicated Cell Collection Centre (CCC) at Nottingham University Hospitals NHS Trust, hosted within the NIHR Nottingham Clinical Research Facility at Queen's Medical Centre, with the aim of increasing donation capacity, reducing delays, and supporting research.

Methods: We performed a descriptive analysis of operational performance before and after the CCC launch. The primary metric was the proportion of donor collections completed on the requested "first-choice date," a key driver of successful transplant outcomes and of customer service for both clinicians and researchers. Historical data from 2022/23 and 2023/24 served as baseline comparators. Early post-launch data from July to November 2025 were reviewed, including procedural and patient/donor characteristics, to ensure that apheresis capacity was maximised. Qualitative feedback from donors and operational learnings was also collected. Published reports on UK apheresis capacity were referenced to contextualise the national challenge.

Results: Prior to CCC implementation, the lack of apheresis capacity across the UK meant that only 17% (2022/23) and 15% (2023/24) of requests facilitated by Anthony Nolan were fulfilled on the first-choice date. Following the CCC launch, preliminary data to the end of November 2025 show an increase to 53% for collections facilitated at the CCC, reflecting a substantial improvement in scheduling flexibility and capacity. In its first five months, the CCC facilitated 78 collections from 70 donors, including 46 donors for transplant patients (8 required two-day collections,) and 24 donors for medical research and treatments. The CCC adds up to 1,300 new donation slots annually, directly addressing UK infrastructure gaps. Early feedback suggests an excellent donor experience and streamlined logistics. The CCC also supports collections for research, enabling the development of novel cell-based therapies; quantitative data on research collections will be reported in future analyses. Strategic Forum modelling suggests that expanding domestic donor provision to 45% of UK supply could save the NHS £1.1 million per year and reduce reliance on overseas donors. Operational innovation includes predictive modelling to optimise one-day versus two-day collections, freeing capacity for additional donors.

Conclusions: Establishing a dedicated cell collection centre significantly improves the ability to meet optimal collection dates, a key factor in reducing transplant delays and supporting innovation. These early results underscore the value of targeted infrastructure investment and collaborative models in future-proofing cell supply for both clinical and research needs. Further evaluation will explore the longer-term impact on transplant outcomes, donor satisfaction, and scalability across the UK.

Disclosure: Nothing to declare.

A291

TYPE OF INDUCTION CHEMOTHERAPY INFLUENCES STEM CELL MOBILIZATION CAPACITY IN MULTIPLE MYELOMA PATIENTS – COMPARISON OF VCD VS DARA-VTD IN A LARGE MULTICENTER COHORT

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Background: Treatment of multiple myeloma (MM) has evolved rapidly over the last decades and consequently the choice of induction therapy for patients eligible for autologous stem cell transplantation (ASCT). Incorporating an anti-CD38 monoclonal antibody and immunomodulatory drugs into the induction regimen has resulted in deeper response before ASCT and better overall outcomes as reported recently. However, clinical observation and early reports hints on influences of the induction regimen on subsequent peripheral blood stem cell (PBSC) mobilization.

Methods: This retrospective multicenter cohort analysis collected data from MM patients who underwent ASCT between 2009 and 2025. Patients had to receive first line induction treatment of MM containing of either bortezomib, cyclophosphamide and dexamethasone (VCD) or daratumumab, bortezomib, thalidomide and dexamethasone (D-VTD). The stem cell mobilization regimen consisted of cyclophosphamide followed by G-CSF administration. Evaluated parameters included amongst others: patient characteristics such as age, sex, cytogenetic risk profile, additional use of plerixafor, day of first apheresis, pB $CD34^+$ cells/µL on first day of apheresis, total number of aphereses, cumulative yield of $CD34^+$ cells.

Results: Of 299 patients included, 140 were treated with VCD (median 61 [29-72] yrs) and 159 with D-VTD (median 63 [35-73] yrs) as induction therapy. In the VCD cohort, 20% of patients (n=23) and 22% (n=32) of the D-VTD were to be categorized as high risk cytogenetic profile. All patients could eventually successfully mobilize PBSC. However, additional use of plerixafor became necessary in 4% (VCD, n=5) in contrast to 23% (D-VTD, n=37; $p<0.001$) due to insufficient PBSC mobilization. First day of apheresis did not differ between the cohorts. In terms of pB $CD34^+$ cells/µL on first day of apheresis, VCD patients had significant higher counts compared to the D-VTD patients (104.9/µl vs. 44.0/µl, $p<0.001$) as well as lower total numbers of aphereses, respectively (mean 1.22±0.20 vs. 1.55±0.51, $p<0.001$). Furthermore cumulative yield of $CD34^+$ cells in the VCD group was significantly higher compared to the D-VTD patients ($10.65x10^6$/kg vs. $6.09x10^6$/kg, $p<0.001$).

Conclusions: Our real-world data shows significant differences in PBSC mobilization outcomes between VCD and D-VTD induction therapies in transplant-eligible MM patients. Whether this effect can be attributed to novel drug classes included or antibody

pharmacokinetics is currently unclear. Optimal settings for PBSC mobilization in these have to be determined in the future.

Disclosure: Nothing to declare.

A292

LESS INFLAMMATION, SAME SURVIVAL: PLERIXAFOR MOBILIZATION REDUCES ENGRAFTMENT CRS IN PAEDIATRIC HSCT COMPARED TO GCSF ALONE

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Background: Effective peripheral blood stem cell mobilization is critical for successful paediatric allogeneic haematopoietic stem cell transplantation (HSCT). While granulocyte colony-stimulating factor (G-CSF) remains the standard mobilization approach, a subset of donors exhibit inadequate $CD34^+$ release and may require plerixafor rescue. Although plerixafor use is well characterized in adults, paediatric data, particularly linking mobilization biology to graft composition and transplant outcomes, remain limited. Understanding whether plerixafor influences graft quality, immune reconstitution, toxicity profiles or survival is essential for optimizing donor selection, mobilization strategy, and post-transplant management.

Methods: We conducted a retrospective comparative study of 87 paediatric HSCT recipients transplanted over the past 1 years at our Hospital. Donors were mobilized either using G-CSF alone (n=45) or G-CSF plus plerixafor (n=42). Donor variables included age, sex, mobilization regimen, $CD34^+$ and $CD3^+$ yields, and stem cell collection volume. Recipient outcomes evaluated included engraftment kinetics, CRS, engraftment syndrome, acute GVHD, mortality, relapse, TATMA, secondary graft dysfunction requiring romiplostim, SOS, day +15/+30 chimerism, viral reactivation, and immune reconstitution across CD4 subsets, NK and B cells at days +30, +60 and +90. Statistical testing used t-test/Mann-Whitney for continuous variables and Fisher's exact testing for categorical outcomes, with $p<0.05$ considered significant.

Results: Recipient demographics were balanced between groups, whereas plerixafor donors were younger (24.0 vs 33.6 years). Stem cell volume collected (167.9 vs 178.4 mL; p=0.41) and infused (97.4 vs 90.6 mL; p=0.56) were comparable. CD34 yields were significantly higher in G-CSF-only donors both at collection (p=0.048) and infusion (p=0.03), whereas CD3 yields did not differ significantly. The CD34:CD3 ratio was significantly higher in G-CSF donors, indicating stem-cell–dominant grafts, whereas plerixafor grafts were more T-cell enriched.
Infusion CRS severity was similar (p=0.96), but engraftment CRS was significantly higher in the G-CSF group (p=0.047). Although Anakinra use was numerically higher in the G-CSF cohort (13 vs 6 total doses), differences were not significant. Relapse (p=0.71), mortality

(p=0.20), TATMA (p=0.24), romiplostim requirement (p=0.51) and SOS (trend p=0.07) did not differ significantly between cohorts. Immune reconstitution profiles of effector CD4, memory CD4, total CD4, NK and B-cells were equivalent at all assessed time points (all p>0.05). Neutrophil engraftment was faster in the plerixafor group by ~1 day, but non-significant (p≈0.07). Chimerism at days +15 and +30 demonstrated robust donor engraftment (>98%) in both groups without significant differences.

Conclusions:

- The CD34:CD3 ratio differed significantly between mobilization strategies. G-CSF–only mobilization yielded grafts richer in CD34⁺ stem cells, whereas plerixafor-mobilized grafts were more T-cell enriched. These differences in graft biology did not translate into inferior clinical outcomes in the plerixafor group.
- Engraftment CRS was significantly lower in the plerixafor cohort and anakinra requirement for cytokine control was numerically reduced, indicating a lower inflammatory burden despite graft compositional differences.
- Immune recovery, survival, and complication profiles remained equivalent between mobilization strategies.
- Overall, plerixafor is a safe and effective adjunct for suboptimal mobilizers, permitting adequate graft collection while mitigating engraftment inflammatory toxicity.

Disclosure: No Disclosures

A293

THE SIBCORD SURVEY: ASSESSING CURRENT PRACTICES IN SIBLING CORD BLOOD USE FOR PEDIATRIC HCT ACROSS EBMT CENTERS

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Background: Cord blood transplantation (CBT) is an established alternative source of hematopoietic stem cells for pediatric patients with both malignant and non-malignant disorders. While outcomes after unrelated CBT (UCBT) are well characterized, comparatively less evidence is available for related CBT, particularly sibling cord blood transplantation (SCBT). Existing reports indicate favorable outcomes of HLA-identical SCBT in bone marrow failure syndromes and hemoglobinopathies. However, systematic evaluation across broader pediatric populations remains limited. Furthermore, the role and utilization of SCBT in malignant diseases, as well as its evolution over the past two decades, remain insufficiently documented.

Methods: The SIBCORD survey was distributed to European Society for Blood and Marrow Transplantation (EBMT) Centers via an emailed link. The survey aimed to capture current patterns of sibling cord blood (SCB) utilization, primary clinical indications, and cord blood banking (CBB) practices across countries, with particular attention to heterogeneity in accessibility and resource allocation.

Results: A total of 71 Centers (71/172, 41.3%) responded. Of these, 43 (60.6%) reported active use of CBT as an alternative hematopoietic stem cell source, most frequently for non-malignant diseases (24/43, 55.8%). Notable geographic variation was observed among countries with the highest response rates: continued CBT use was reported by 6/12 Italian Centers, 7/8 in the United Kingdom, 5/7 in France, and 5/6 Centers in Spain. Among CBT Centers, 22 (51.2%) indicated that the CBTs performed involved sibling donors.
Regarding CBB options offered to families at the time of delivery, donation to a public bank was the most common option (18/65, 27.7%), followed by directed donation through a public bank (11/65, 16.9%). Most Centers (32/43, 74.4%) reported never using CBT units originating from hybrid or private/family banks; however, when such units were used, the process was described as straightforward by the majority (13/24, 54.2%). The primary reason for avoiding CB from private banks was lack of trust or concerns about product quality (18/29, 62.1%), followed by ethical concerns (11/29, 37.9%).
Practices related to donor assessment and unit qualification also varied. Nine Centers reported conducting postnatal assessments for genetic abnormalities; however, a substantial proportion (6/34, 17.6%) indicated that this information was unknown at their institution. The date of collection and total volume were considered essential by 20 (46.5%) and 17 (40.5%) Centers, respectively. Total nucleated cell count (36/43, 83.7%) and $CD34^+$ cell

count (34/43, 79.1%) were most often deemed absolutely necessary, as were high-resolution 6-allele HLA typing (28/41, 68.3%) and blood group determination (22/42, 52.4%).

Conclusions: By integrating these preliminary survey findings with existing evidence, our analysis highlights substantial heterogeneity in CBT utilization and banking practices across EBMT Centers and underscores the continued relevance and potential future role of SCBT. The observed country-specific differences suggest opportunities for harmonizing guidelines and optimizing access to this alternative stem cell source. Further investigation, together with recently published literature, is needed to better define the optimal clinical use of SCBT and its role within contemporary HSCT and gene-therapy frameworks.

Disclosure: Nothing to declare.

A294

WORLD MARROW DONOR ASSOCIATION WORLDWIDE SURVEY ON PLERIXAFOR USE IN HEALTHY RELATED AND UNRELATED DONORS

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Background: Several prospective studies have investigated the use of plerixafor in healthy stem cell donors, either alone or in combination with granulocyte colony stimulating factor (G-CSF). Despite local guidelines and practices being developed, there is no formal World Marrow Donor Association (WMDA) guidance on its use. Plerixafor use in healthy donors remains an off-licence indication in many countries; therefore, a worldwide consensus will support registries in its use and ensure that practice remains universal and safe for donors. The group began drafting the consensus with a survey of institutions worldwide, the results of which are presented here.

Methods: The survey was disseminated via the WMDA monthly newsletter "Stem cell matters" and via email. The electronic survey in English was open for responses between August 11, 2025, and October 9, 2025. The primary aims were to understand current practices and experience with the use of plerixafor in healthy related and unrelated donors as

well as to understand the safety measures in place, barriers to use, scheduling and billing. Not all questions were compulsory.

Results: 51 responses were received from 17 countries worldwide. This included responses from donor registries (21.6%), collection centres (CC) (17.6%), transplant centres (TC) (11.8%), 1 individual, and institutions that were registries and CCs (3.9%), CCs and TCs (41.2%) and 1 donor and patient registry.
Two institutions had used plerixafor in a total of > 100 healthy donors, 4 reported using it 10-99 times and 6 reported using plerixafor 1-9 times.
Twirty-one (60.8%) institutions do not currently endorse plerixafor in healthy donors but would consider it and 13 (25.5%) are already using it. Seven (13.7%) reported that they would not consider it. Twenty-six (51%) institutions did not have experience with plerixafor in healthy donors, 2 (3.9%) had used in unrelated only, 12 (23.5%) in related only and 7 (13.7%) in related and unrelated healthy donors.
A table of responses is shown in appendix 1.

Question	**Response**	**Number of institutions**
Which country is your institution from?	Germany, Portugal, Czech Republic, Poland, Greece, Norway, Spain, UK, Belgium, Denmark, France, Netherlands, Algeria, South Africa, Canada, Israel, US	N/a
Is plerixafor approved by pharmaceutical legislation and available for use in healthy unrelated donors in your country?	Yes, available but not approved Yes, available and approved Not available	25 2 14
Is GCSF approved by pharmaceutical legislation and available for use in healthy unrelated donors in your country?	Yes, available but not approved Yes, available and approved	3 47

Does your registry/institution have any experience using plerixafor mobilization alone (without G-CSF) in healthy donors?	No, and we would not consider No, but we would consider Yes	22 19 1	
Which indications are you currently or considering using plerixafor for?		Currently	Considering
	Emergency use following a poor day one collection after G-CSF mobilization	19 2	31 13
	Pre-emptive use for unrelated donors with an unfavourable donor-patient weight discrepancy	9 5	20 9
	Pre-emptive use with a low pre-apheresis peripheral blood CD34+ count	0 3	0 14
	Pre-emptive use to collect high cell doses for patients	3	11
	Pre-emptive use to collect high cell doses for research	2 0	20 5
	Pre-emptive use for a subsequent donation from donors who have mobilized poorly on a previous donation	0 0	6 7
	Pre-emptive use for donors who have not tolerated the full course of G-CSF	1	0
	Pre-emptive use for donors with G-CSF allergy		
	Pre-emptive use for plerixafor induced immunological profile of the stem cell graft		

	Pre-emptive use of plerixafor according to donor preference Pre-emptive use for stem cell donors to research for clients who specifically request mobilization using plerixafor Access / flow issues		
Does your registry ever use more than one dose of plerixafor?	Yes No, but we would consider No, and we would not consider	5 1 7	
Does your registry/institution always check a WBC/CD34+ count prior to administration?	Yes No	8 1	
What time do you administer plerixafor?	<6 hours 6-12 hours 12-18 hours >18 hours	4 6 2 0	
Does your institution administer prophylactic anti-diarrhoeal and anti-emetics?	Yes No	2 9	
Does your registry/institution monitor WBC and/or CD34+ counts after plerixafor?	Yes No	11 2	
How often does your registry/institution find supportive medications (e.g.,	Rarely (1/100) Sometimes (< 1/10) Often (>1/10) Never	4 1 1 3	

antidiarrheals, antiemetics, analgesics) are required?		
Does your registry/institution monitor the donor after 1st plerixafor administration?	Yes </= 1 hour Yes, overnight No	7 3 3
How long do donors report symptoms usually last for after the last dose of plerixafor?	< 24 hours 24-72 hours Unsure	5 3 5
Has your institution experienced any other concerning side effects from plerixafor apart from the gastrointestinal side effects?	No Yes	12 1 - allergy, 1 – SOB
Has your registry/institution recorded any side effects >/= CTCAE Grade 3?	No Yes	13 0
Who incurs the cost of the plerixafor?	Transplant centre Other Collection centre Donor registry	3 1 7 1

Respondents specified cut offs for the administration of plerixafor and mentioned CD34+ cut offs between 5-20/µL or significant weight discrepancy between the donor / recipient. It may also be considered if the target is not reached (2x10*6 CD34+/kg recipient body weight) after the first day of apheresis or if they estimate a poor mobilization on a second apheresis that will compromise the recipient's product.
Respondents highlighted barriers to the use of plerixafor in healthy donors including that it is unlicensed so there is some apprehension and that it is hard to access in some CCs. They

also mention the cost (prior to generic availability) and the requirement in some institutions for a hospital admission to receive it early in the morning before apheresis or the delay to apheresis after administration.

Conclusions: There is clear interest in the use of plerixafor in healthy related and unrelated donors worldwide with varying practices with scheduling, dosing and indications for its administration. A WMDA recommendation collating the published evidence and the results of this survey will be published to guide institutions and most importantly ensure the safety of healthy donors worldwide.

Disclosure: Nothing to declare.

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CENTER- AND DEVICE-RELATED VARIABILITY IN TCRAB/CD19 DEPLETION OF HEMATOPOIETIC PROGENITOR CELL APHERESIS PRODUCTS

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Background: TCRαβ/CD19 depletion in haploidentical hematopoietic stem cell transplantation aims to reduce graft-versus-host disease (GVHD) while preserving engraftment success by retaining CD34⁺ cells, TCRγδ T cells, and NK cells.

Methods: We performed a retrospective, comparative, analytical study evaluating quantitative cell processing outcomes in TCRαβ/CD19 depletion procedures performed at two medical centers, *Hospital Clínico Universitario Virgen de La Arrixaca* (HCUVA) and *Hospital Infantil Universitario el Niño Jesús* (HIUNJ). The objective was to determine whether differences existed in the efficacy of the depletion process between centers and between two depletion platforms, CliniMACS Plus and CliniMACS Prodigy. All calculations were performed by comparing the starting apheresis product with the final graft after TCRαβ/CD19 depletion. Results are reported as median (range).

Results: A total of 247 TCRαβ/CD19 depletion procedures were performed across the two centers.
Center comparison: The first analysis assessed the impact of the cell processing system: bag centrifugation at HIUNJ vs. the Sepax system at HCUVA. Bag centrifugation was used in 68.84% of the procedures and achieved TCRαβ and CD19⁺ cell depletion log reductions of 5.98 (3.16–6.68) and 5.27 (2.14–6.09), respectively. Recovery rates of CD34⁺, TCRγδ, and NK cells were 81.1% (38.6–100), 76.8% (23.5–100), and 75.4% (27.6–100), respectively.

In contrast, procedures using the Sepax system (31.16%) resulted in TCRαβ and CD19⁺ depletion log reductions of 4.83 (2.09–6.24) and 3.42 (1.61–5.64), respectively, with recovery rates of 74.9% (27.6–100) for CD34⁺ cells, 60.8% (17.5–100) for TCRγδ T cells, and 63.4% (20.7–96.7) for NK cells. All variables differed significantly between the two approaches.
Device comparison: The second analysis compared the CliniMACS Plus and CliniMACS Prodigy systems. Among the 225 (91.1%) procedures performed with CliniMACS Plus, TCRαβ and CD19⁺ log depletion levels were 5.81 (2.09–6.68) and 4.87 (1.6–6.09), respectively, with recovery rates of 79.2% (27.6–100) for CD34⁺ cells, 71.3% (17.5–100) for TCRγδ cells, and 71.4% (20.7–100) for NK cells. For the 22 (8.9%) procedures performed using CliniMACS Prodigy, TCRαβ and CD19⁺ log depletion levels reached 6.06 (4.16–6.48) and 5.23 (3.19–5.81), respectively, while cell recovery rates were 71.2% (37.4–100) for CD34⁺ cells, 47.3% (19.4–95) for TCRγδ cells, and 50.5% (24.4–70.2) for NK cells. Significant differences were observed only in recovery rates, not in depletion efficiency.

Conclusions: In this retrospective comparative analysis of 247 procedures, cell processing performed at HIUNJ using bag centrifugation demonstrated superior TCRαβ/CD19 depletion efficiency and better recovery of key cell populations compared with procedures performed at HCUVA using the Sepax system. Additionally, no significant differences were found in TCRαβ or CD19⁺ depletion between the CliniMACS Plus and Prodigy devices. However, CliniMACS Plus was associated with improved cell recovery.

Disclosure: The authors report no conflicts of interest and no external funding was received for this study.

A296

SAFE EMERGENCY TRANSFER OF CORD BLOOD UNITS AFTER CRYOGENIC TANK MALFUNCTION: A RARE OPERATIONAL EVENT

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Background: Loss of vacuum in BioArchive cryogenic tanks is an exceptional but high-risk event that accelerates liquid nitrogen (LN) evaporation, reduces LN levels, and may expose stored cord blood units (CBUs) to transient warming if no corrective action is taken. At the Concordia public cord blood bank (Banc de Sang i Teixits), a malfunctioning BioArchive tank containing 2,880 CBUs—including 14 directed units—showed progressive LN consumption suggestive of a structural fissure leading to vacuum loss. Repair was not feasible with the units in place, and manual removal of more than 2,000 CBUs was not possible. An emergency rescue transfer was therefore planned in collaboration with the tank provider (Consensus). To date, only two rescue transfers have been reported worldwide over more than 30 years.

Methods: A backup BioArchive-compatible tank was prefilled to 50% capacity with LN. In an outdoor elevated parking area, a crane was used to lift the BioArchive structure, laterally remove the malfunctioning tank, and position the backup tank beneath the robotic indexing system (Figure 1). According to the Consensus technician—who performs this manoeuvre annually during training without real CBUs—the transfer could be completed in under one minute. A temperature probe was placed in the vapor phase of the failing tank to monitor temperature stability throughout the procedure.
To evaluate the potential impact of vapor-phase exposure and rapid mechanical transfer, six CBUs stored in the highest tank levels (worst-case scenario) and with available pre-event segment analysis data were selected for post-thaw assessment. Cell recovery, viability and colony-forming unit (CFU) assays were performed.

HELI

Results: The rescue transfer was successfully completed in 40 seconds. Continuous temperature monitoring confirmed stable vapor-phase conditions throughout the procedure. The characteristics of the six selected CBUs are shown in Table 1. CBUs had been stored for more than 20 years. Post-thaw analyses demonstrated high cell recovery, preserved cell viability and functionality (clonogenic capacity, eClone), in all CBUs evaluated, meeting established criteria for release for transplantation (Table 1).

Variables	Cord Blood Units (N=6)	
Storage time, years	25,9 (22,8-26,6)	
TNC (E8), pre-freezing	9,2 (6,4-41,4)	
CD34 (E6), pre-freezing	2,7 (1,3-21,1)	
7-AAD, CD45, pre-freezing, %	94,9 (94,8-98,0)	
7-AAD, CD34, pre-freezing, %	98,8 (96,6-99,6)	
	Segment thawed prior event	Bag (80%) thawed after emergency transfer
TNC recovery after thawing, %	88,3 (84,3-105,7)	94,5 (87,9-110,9)
Total CD34 recovery after thawing, %	N.A	64,7 (47,6-80,6)
7-AAD, CD45, after-freezing, %	N.A	44,9 (13,9-61,8)
7-AAD, CD34, after-freezing, %	N.A	78,9 (54,8-85,0)
eClone, %	25,1 (18,4-35,2)	16,0 (12,0-38,0)

Quantitative variables are shown as median (range); N.A, not available

Conclusions: Emergency rescue transfer of a BioArchive cryogenic tank experiencing vacuum failure is feasible, rapid, and safe when performed by trained personnel under controlled conditions. In this rare operational event—the third reported worldwide—no detrimental impact on CBU viability or functionality was observed. This report provides

practical, real-world evidence to guide cord blood banks in the management of critical cryogenic tank failures.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

A297

FROM ACCESS TO YIELD: PROCEDURAL INSIGHTS INTO PAEDIATRIC STEM CELL APHERESIS

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Background: Autologous peripheral blood stem cell transplantation can be essential in treating some paediatric solid tumours. Collecting adequate CD34+ cells is challenging in young children due to low body weight, limited blood volume, and vascular access constraints. Optimising mobilisation, apheresis settings, and catheter choice is essential for safe and effective collection, but data on procedural aspects in pediatric patients are limited. This study reviews the experience of a single centre in order to assess practical outcomes and safety.

Methods: We retrospectively analysed autologous peripheral blood stem cell collections performed in paediatric patients (<18 years) at a single centre between 2023 and 2025. Apheresis procedures were performed using a Spectra Optia® (Terumo) machine with an ACD and heparin combination solution as the anticoagulant. CD34+ collection efficiency (CE) was evaluated using pre- and post-collection CD34+ counts (CE1) and pre-collection count alone (CE2). Results are reported as median [minimum–maximum].

Results: The analysis included 21 procedures performed on 18 patients. All of the patients had a solid tumour diagnosis, and 83% of them were under five years old. Patient demographics and procedure- and product-related characteristics are presented in Table 1. Blood priming was required in 18 apheresis procedures (85.7%). The collection preference was initially set at 50 but was subsequently reduced in 57% of procedures to optimise stem cell collection, while it remained unchanged in most of the remaining cases (28%). Prophylactic calcium was administered in all apheresis procedures except those performed in two adolescent patients (90%); no hypocalcaemia-related adverse events were reported. Two patients experienced hypotension during and after apheresis; in both patients, it was resolved with fluid infusion. In the first patient, apheresis was resumed once hypotension

resolved.
Eight-French (Fr) non-tunneled central venous catheters (CVCs) were used in most of the patients (72%). Ultrasound-guided peripheral venous access were inserted in the only two adolescent patients in our cohort. Tunneled CVCs were introduced at our centre for apheresis last year (N=3), but two experienced flow issues. A patient's 6.5-Fr CVC collapsed on the day of apheresis and had to be replaced; apheresis was successfully performed the next day using a 7-Fr CVC.
Platelet loss after apheresis was observed in all procedures (-38.6% [-18% - -71.1%]), while haematocrit did not significantly change.
All patients met stem cell collection target for subsequent transplantation, although three patients required two apheresis sessions. CE1 was significantly higher than CE2 (p=0.01), as it considers a generalised drop in CD34+ cells during the apheresis process. CE1 was lower in very low-weight patients (under 20 kg) (p=0.03).

	Parameter	Values
Subject Characteristics (N=18)	Age (years)	2.5 [0.42–16]
	Sex - Female / Male n (%)	10 (56%) / 8 (44%)
	Weight (Kg)	13.4 [7.5-61.5]
	Total blood volume (TBV) (mL)	1020 [683–4116]
	Diagnosis (Neuroblastoma / Ewing sarcoma / Medulloblastoma / Other solid tumours [a])	8 / 3 / 2 / 5
	Subjects undergoing stem cell collection (Once / Twice)	15 / 3
	Stem cell mobilization[b] (G-CSF alone / G-CSF +	13 / 4 / 1

	Plerixafor / G-CSF + chemotherapy)	
	Venous access (Non-tunneled CVC / Tunneled CVC / Ultrasound-guided peripheral venous access)	13 / 3 / 2
Process Parameters (N=21)	Time of the process (min)	241 [168–379]
	TBV processed	4.0 [2.5–5.6]
	AC in the patient (mL)	186 [114–557]
	Collection volume (mL)	117 [76–436]
	Collection volume as percentage of TBV (%)	11.1 [6.2–16.2]
	Maximum flow rate (mL/min)	21 [12–50]
CD34+ Determination and Collection Efficiency (CE) (N=21)	CD34+ cells collected (x10^6/kg of patient)	6.47 [0.56-24.8]
	CE1 (%)	50.4 [17.7–85.8]
	CE2 (%)	36.5 [10.7–65.2]

[a] Other tumours included Wilms tumour, chordoma, retinoblastoma, rhabdoid tumour and embryonal brain tumour

[b] Dose of G-CSF was 10 µg/kg/12 hours; dose of plerixafor was 240 µg/kg.

Conclusions: This retrospective analysis shows that paediatric stem cell apheresis is safe and effective, despite technical challenges. Minor complications, such as hypotension and catheter flow issues, occurred but were successfully managed. CE was lower in patients under 20 kg, likely due to the longer time required to stablish the interface. Overall, the procedure is feasible in children, highlighting the importance of careful vascular access management and specific attention to low-weight patients.

Disclosure: Nothing to declare.

A298

UNIVERSAL GENERIC PLERIXAFOR FOR STEM CELL MOBILIZATION IN MULTIPLE MYELOMA: CLINICAL OUTCOMES COMPARISON WITH RISK-ADAPTED STRATEGY AND INTERNATIONAL BENCHMARKS

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Background: Plerixafor combined with granulocyte colony-stimulating factor (G-CSF) enhances stem cell mobilization in multiple myeloma (MM) patients undergoing autologous stem cell transplantation (ASCT). International studies report optimal harvest rates of 84-94% with upfront plerixafor strategies, while risk-adapted approaches achieve 29-85% depending on patient selection. We evaluated clinical outcomes of universal generic plerixafor administration, comparing results with a published Indian risk-adapted cohort and international benchmarks.

Methods: We analyzed 53 consecutive MM patients receiving universal generic plerixafor (24mg fixed-dose) with G-CSF (10 µg/kg/day for 5 days) at a tertiary care center in Kerala, India (2022-2024). All patients received single subcutaneous plerixafor 12 hours before day-5 apheresis without prior CD34 testing. Primary outcomes were compared with: (1) All India Institute of Medical Sciences (AIIMS), New Delhi data (n=105) using risk-adapted plerixafor for patients with day-4 CD34+ <20 cells/µL (44.8% received plerixafor); and (2) published international studies including MSKCC (USA), Italian multicenter, and recent meta-analyses.

Results: Universal generic plerixafor achieved significantly superior outcomes compared to risk-adapted strategy: mean CD34+ yield was 2.6-fold higher (9.56±6.31 vs 3.63±1.75 $\times 10^6$/kg, $p<0.001$), optimal harvest rate ($\geq 4\times 10^6$/kg) was markedly improved (86.8% vs 29.5%, $p<0.001$), and single-session apheresis completion was substantially higher (96.2% vs 56.2%, $p<0.001$). These results align with international upfront plerixafor outcomes: MSKCC reported 94% optimal harvest ($\geq 5\times 10^6$/kg), Italian multicenter achieved 84.6%, and Emory reported 92.8%. Minimal harvest ($\geq 2\times 10^6$/kg) was comparable across strategies

(98.1% vs 96.2%, p=0.865), consistent with international rates of 94-100%. Engraftment kinetics showed favorable trends (neutrophil: 9.77±0.97 vs 10.30±2.19 days; platelet: 11.23±1.93 vs 12.25±3.37 days) and IV antibiotic duration was significantly reduced (4.28±3.14 vs 7.7±4.29 days, p=0.001). Universal plerixafor negated the adverse effect of prior lenalidomide exposure (exposed: 9.61±6.99 vs unexposed: 9.50±5.70 $\times 10^6$/kg, p=0.948). Cost-effectiveness analysis comparing the two Indian cohorts demonstrated an incremental cost-effectiveness ratio of $9.15 per 1% increase in optimal harvest rate.

Table-1:International Mobilization Comparison

tudy / nstitution	Country	N	Strategy	Study Period	Minimal Harvest ≥2×10⁶/kg	Optimal Harvest ≥4–5×10⁶/kg	Mean Apheresis Sessions	Plerixafor Use		Mean CD34+ Yield ×10⁶/kg	Comparato Yield
IMS Kerala Current)	India	53	Universal Plerixafor (24 mg fixed)	2022–2024	98.1%	86.8%	1.04	100%		9.56 ± 6.31	-
IIMS New elhi	India	105	Risk-Adapted (PB CD34 <20/µL)	2017–2019	96.2%	29.5%	1.49	44.8%		3.63 ± 1.75	3.19 (G-CSF alone)
SKCC (Afifi t al.)	USA	112	Upfront P+G-CSF	2008–2012	NR	94%*	NR	100%		NR	-
ount Sinai Holton et .)	USA	50	Upfront Plerixafor + G-CSF	2008–2011	100%	NR	1.9	100%		16.1	8.4 (G-CSF alone)
zech egistry	Czech Rep.	93	Plerixafor On-demand	2010–2013	94.9%	NR	NR	On-demand		NR	NR
aly ulticenter Milone)	Italy	111	On-demand + Chemo	2014–2016	97.2%	84.6%	1.3	~30%		NR	NR
razil Passos et .)	Brazil	285	Preemptive vs Rescue	2018–2023	89%	NR	NR	Preemptive		NR	NR
hio State Andritsos)	USA	156	Pre-emptive vs Standard	2016–2018	NR	NR	NR	-		NR	NR
mory (Li et .)	USA	138	Upfront P+G-CSF	2010–2014	NR	92.8%*	NR	100%		NR	NR

Footnotes*94% and 92.8% = Optimal harvest defined as ≥5×10⁶ CD34+ cells/kg.NR = Not Reported; POD = Plerixafor On-demand; MD = Mean Difference.

Conclusions: Universal generic plerixafor achieves clinical outcomes comparable to high-resource international centers and significantly superior to risk-adapted strategies. The approach delivers 2.6-fold higher CD34+ yields, nearly 3-fold improvement in optimal harvest rates, and marked reduction in apheresis requirements while effectively overcoming adverse prognostic factors. These findings support universal plerixafor as a clinically superior and cost-effective mobilization strategy for MM patients in diverse healthcare settings.

Disclosure: Nothing to declare

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IMPACT OF VENOUS ACCESS IN THE APHERESIS PERFORMANCE

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Background: Apheresis performance in cell collections is strongly influenced by venous access type and the expertise to maintain stable vascular strategies across multi-day procedures. Understanding how these factors interact in real-world practice is essential for optimising efficiency and safety, particularly in high-volume centres with a wide age range of patients.

Methods: All apheresis procedures performed at the Cell Therapy Department of IPO Porto between 01/July/2024-31/October/2025 were retrospectively analysed. Collections were categorised as extracorporeal photopheresis (ECP), haematopoietic progenitor cell (HPC) collection or lymphocyte/mononuclear cells (MNC) apheresis procedures. This study evaluated venous access patterns, collection speed, calibre usage, multi-day access stability and repuncture events in a large single-centre cohort supported by a specialised apheresis team.
Venous access was classified as central venous catheter (CVC), peripheral venous access (PV), combined CVC+PV or peripherally inserted central catheter (PICC). Collection speed was defined as processed blood volume per minute. Peripheral catheter calibres ranged from 20-16G, while central catheters ranged from 7-11Fr. Multi-day collections were identified using the institutional patient identifier, grouping all attempts on the same date as a single collection day and evaluating access changes and repuncture events.

Results: Of the 1,069 procedures analysed, ECP accounted for 782 procedures, HPC for 224 and lymphocyte/MNC collections for 63; 978 were performed in adults and 91 in paediatric patients.
Paediatric procedures relied almost exclusively on CVCs, with low and tightly controlled flow rates (M=11.2mL/min; range 4.9–17.1). In this group, CVC calibre selection was highly standardised (mean calibre 10Fr; range 8-11Fr), reflecting a preference for central access adapted to patient size.

In adults, PV produced substantially higher flow rates than CVC in ECP (24.1 vs 16.1mL/min); HPC achieved the highest efficiencies overall, with CVC collections reaching a mean of 68.3mL/min (40.5–82.4) and PV a mean of 57.9mL/min (20.1–76.5); Lymphocyte/MNC collections showed consistently high flows with both CVC (54.4mL/min) and PV (51.1mL/min). Peripheral catheter calibre displayed a clear gradient: 20G (M=22.9mL/min; n=875), 18G (M=43.0; n=319), 17G (M=57.9; n=86) and 16G (M=56.6; n=183). PICC lines produced markedly lower flows. Among 280 patients, 56 (20%) required more than one collection day. In 45 multi-day courses beginning with PV, the peripheral approach was maintained in most cases, with identical calibres used across all PV days in 28 patients (62%). Alterations in access or calibre typically followed reduced flow or tolerance during the initial day.
Repuncture occurred in 149 collection-days, predominantly in ECP (n=94), followed by HPC (n=44) and lymphocyte/MNC procedures (n=11); however, it had limited impact on the ability to maintain peripheral access in adults and did not significantly compromise flow safety thresholds.

Conclusions: This study demonstrates that apheresis success is strongly dependent on the expertise of a dedicated team. In ECP procedures, protocolled vascular strategies were consistently maintained. In cell collections, target yields were achieved with a low proportion of multi-day procedures, minimal repuncture rates and no major adverse events. The ability to select appropriate venous access, optimise catheter calibre and preserve stable access across consecutive days directly translates into safe, efficient and reproducible apheresis outcomes.

Disclosure: Nothing to declare.

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OUTCOMES AND PREDICTORS OF HEMATOPOIETIC STEM CELL MOBILIZATION STRATEGIES IN AUTOLOGOUS TRANSPLANTATION: A REAL-WORLD ANALYSIS

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Background: G-CSF is the most commonly used agent for hematopoietic stem cell mobilization, yet up to 30% of patients fail to achieve adequate CD34+ yields. Alternative strategies combining G-CSF with chemotherapy, including cytarabine-based regimens, have shown promising results, but real-world comparative data remain limited.

Methods: We conducted a retrospective single institution analysis including 91 patients undergoing auto-HSCT. Mobilization strategies (G-CSF + cytarabine low-dose vs G-CSF alone) were compared using the CD34+ cell dose normalized by weight (×10⁶/kg), with successful mobilization defined as ≥2.0 ×10⁶ CD34+/kg. Toxicities and patient characteristics were analyzed.

Results:

The most frequent diagnoses were multiple myeloma (n = 55, 58.5%), mantle cell lymphoma (n = 12, 12.8%) and acute myeloid leukemia (n = 3, 3.2%). Of the 91 patients who underwent a mobilization regimen, 68 (74.73%) received G-CSF alone and 23 (25.27%) received cytarabine plus G-CSF. Overall, 41 patients (45.05%) were female, the median age was 58 years (IQR, 17).

The mean peripheral blood CD34⁺ cell count (PBCD34) prior to apheresis was 45.74 ± 50.1 /uL. No significant differences in PBCD34 were observed between the G-CSF–only group and the chemotherapy plus G-CSF group (Mann–Whitney U test, p = 0.51).

Following mobilization, the median CD34⁺ cell yield in the group of G-CSF alone was 4.47 × 10⁶ cells/kg (IQR, 3.7 × 10⁶) compared to 7.06 × 10⁶ cells/kg (IQR, 1.08 × 10⁶) in patients that received cytarabine plus G-CSF. CD34+ count differed significantly between mobilization strategies (Mann–Whitney U test, z = −2.30, p = 0.021). Patients mobilized with chemotherapy plus G-CSF showed higher total cell counts compared with those receiving G-CSF alone measured after 5 days.

Of the 91 patients, 7 (7.7%) failed to achieve the target CD34⁺ cell dose of ≥2.0 × 10⁶ CD34⁺ cells/kg. Among these, 4 patients (4.4%) underwent a second mobilization regime with repeated doses of C-GSF, achieving a successful collection, while 3 patients (3.3%) were deemed ineligible for autologous HSCT.

Mobilization-related toxicities differed according to mobilization strategy. Bone pain was common in both groups, occurring in 43.3% of patients receiving G-CSF alone and 30.4% of those receiving cytarabine plus G-CSF. Mucositis was infrequent and did not significantly differ between groups (3.0% vs 8.7%). In contrast, hematologic toxicities were significantly more frequent with cytarabine plus G-CSF, including neutropenia (43.5% vs 4.5%, p < 0.001) and thrombocytopenia (30.4% vs 6.0%, p = 0.001). Both differences were statistically significant (p = 0.0001)(p = 0.001).

Rescue mobilization with plerixafor was required in 27 patients (29.7%). Among patients mobilized with G-CSF alone, (n=23, 33.8%) required rescue mobilization, compared with (n=4, 17.4%) in the cytarabine plus G-CSF group. No statistically significant association was observed between mobilization strategy and the need for rescue mobilization with plerixafor (Pearson $\chi^2 = 4.76$, p = 0.093; Fisher's exact test p = 0.116).

Table 1. Mobilization outcomes and toxicity according to mobilization strategy

Variable	G-CSF alone	G-CSF + chemotherapy

Table 1. Mobilization outcomes and toxicity according to mobilization strategy

Number of patients, n (%)	68 (74.73%)	23 (25.27%)
Total CD34+ collected (×10⁶/kg), median (IQR)	4.47 × 10⁶ cells/kg (IQR, 3.7 × 10⁶)	7.06 × 10⁶ cells/kg (IQR, 1.08 × 10⁶)
Requirement of rescue mobilization	23 (33.8%)	4 (17.4%)
Adverse events during mobilization, n (%)		
Bone pain	29 (43.3%)	7 (30.4%)
Mucositis	2 (2.99%)	2 (8.70%)
Neutropenia	3 (4.48%)	10 (43.5%)
Thrombocytopenia	4 (5.97%)	7 (30.43%)

Conclusions: Mobilization with intermediate-dose cytarabine plus G-CSF resulted in significantly higher CD34⁺ cell yields compared with G-CSF alone. Nevertheless, this regimen was associated with a higher incidence of hematologic toxicities, specifically neutropenia and thrombocytopenia. No significant differences were observed in the requirement for rescue mobilization.

Disclosure: Beatriz Wills: Consultancy with Johnson, Pfizer, Astrazeneca and Roche, grants with BMS, speaker for Abvie
Rest of authors: nothing to declare.

A302

POOR MOBILIZATION IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: CLINICAL CHARACTERIZATION, RESCUE STRATEGIES, AND THE LIMITED UTILITY OF CONVENTIONAL PREDICTORS

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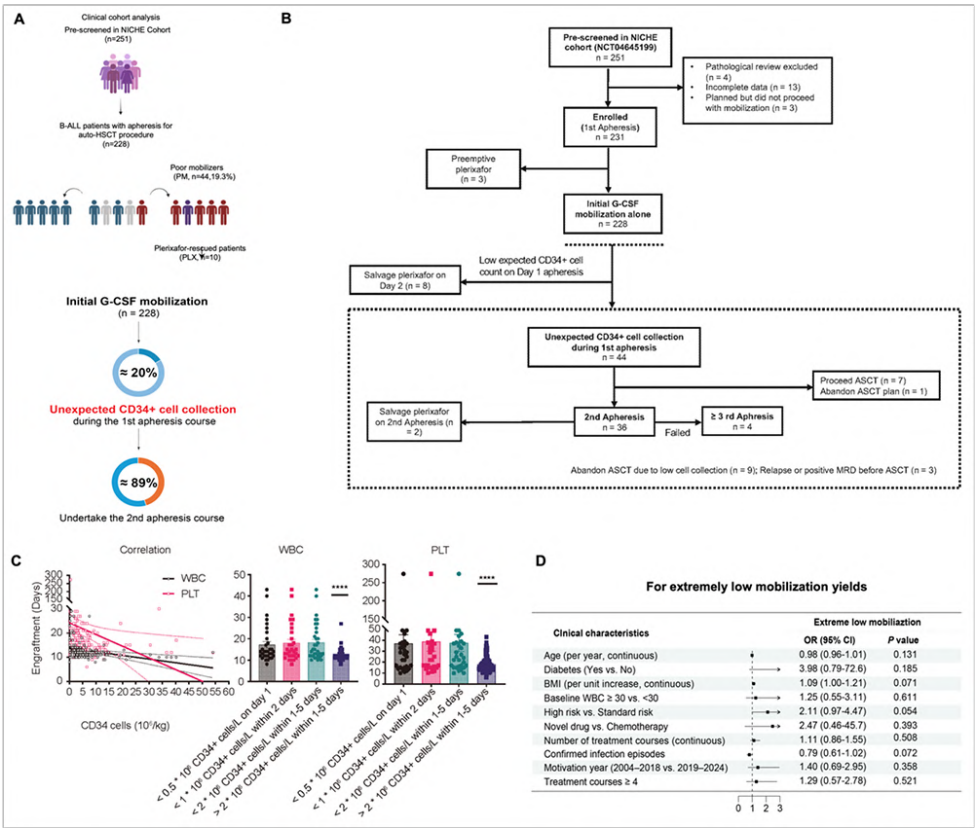
Background: While mobilization failure is well-documented in multiple myeloma and lymphoma, affecting 23–40% of patients, data regarding poor mobilization (PM) in acute lymphoblastic leukemia (ALL) remains scarce. As autologous stem cell transplantation (ASCT) relies on adequate graft collection, defining the epidemiology of PM and evaluating the efficacy of rescue strategies in ALL is critical for clinical decision-making.

Methods: We analyzed mobilization outcomes in 231 patients with B-ALL from the NICHE cohort undergoing their first G-CSF mobilization (10 μg/kg/day for ≤5 days) between 2004 and 2024. Three patients receiving preemptive plerixafor were excluded from the primary

analysis. We applied a hierarchical definition for poor mobilization: PM-I (<2×10⁶ CD34⁺ cells/kg within 5 days), PM-II (<1×10⁶ CD34⁺ cells/kg within 2 days), and Extreme Poor Mobilization (EPM; mean <0.5×10⁶ CD34⁺ cells/kg/day on day 1). Univariate logistic regression evaluated potential predictors of EPM, including age, sex, diabetes, prior chemotherapy exposure, and disease status. We further tracked rescue strategies and subsequent ASCT attrition rates.

Results: Among 228 patients managed with G-CSF alone, PM rates were unexpectedly high: 19.3% (44/228) met PM-I criteria, 17.5% (40/228) met PM-II, and 18.9% (43/228) were classified as EPM. These figures highlight a distinct mobilization challenge in ALL compared to other hematologic malignancies.
Of the 44 patients in the PM-I group, 36 (88.6%) attempted a second collection course using alternative strategies, primarily steady-state collection (52.8%) and bone marrow harvest supplementation (27.8%). Plerixafor was utilized in only 2.1% of cases. Ultimately, 9.1% of PM-I patients required ≥3 courses. Notably, ASCT attrition due solely to collection failure occurred in 3.9% (9/231) of the total cohort, exceeding attrition due to relapse or MRD positivity (1.3%).
Crucially, univariate analysis indicated that standard clinical variables—including age (P=0.38), diabetes (P=0.38), and number of prior chemotherapy cycles (P=0.52)—failed to predict EPM.



Conclusions: Poor mobilization is a frequent and significant barrier in B-ALL, often requiring complex rescue strategies such as bone marrow supplementation. The failure of conventional clinical factors to predict EPM suggests that mobilization outcomes in ALL may be driven by intrinsic marrow microenvironment dysfunction rather than broad systemic parameters.

Clinical Trial Registry: NCT04645199; https://clinicaltrials.gov/study/NCT04645199

Disclosure: Nothing to declare.

A303

MANUAL RED CELL DEPLETION IN PAEDIATRIC BONE MARROW TRANSPLANTATION: APPLICATIONS IN ALLOGENEIC AND AUTOLOGOUS SETTINGS

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Background: While mobilized hematopoietic stem cell (HSC) transplantation has largely supplanted bone marrow (BM) as the primary source of healthy progenitor cells, BM remains the preferred choice for unrelated donor transplantation in children and adolescents undergoing transplantation(1,2), due to a lower risk of graft-versus-host disease compared to peripheral blood stem cells, especially in children.
Red blood cell depletion (RBCD) is a critical step in AB0-incompatible transplantation, particularly in paediatric patients, where weight discrepancies can be an issue. Moreover, RBCD is essential in case of cryopreservation of autologous BM.
There are a few applicable methods for RBC and plasma depletion in BM as hydroxyethyl starch (HES/HAES) with centrifugation; Ficoll/ hypaque (F/H) gradient centrifugation, blood cell automatic processor (previous COBE system or newer Spectra Optia) (3). CD34+ recovery, product quality, and small collection volumes must be carefully balanced, especially in paediatric setting.
References

1. Keesler DA, et al. 2018.
2. Passweg JR, et al. 2025.
3. Sawa M, et al. 2023.

Methods: We herein describe our experience with manual RBCD procedures in a paediatric Cell Processing Laboratory. Manual RBCD was carried out by density gradient centrifugation followed by controlled RBC/plasma removal. The method was previously validated according to a failure mode and effect analysis (FMEA) risk assessment.
The BM was transferred to a CPDA-1 (Citrate, Phosphate, Dextrose, and Adenine) quadruplex bag for whole blood collection with a preassembled Composampler system. The volume of RBCs to be removed was calculated based on the haematocrit, but allowing 10-20 ml of

residual RBCs to be safe. After centrifugation (2000 rpm for 15 minutes without brake), the bag was kept upright and the RBC were drained by gravity from the bottom tube. When necessary, some volume of plasma was removed by the upper tube. After manipulation, the process was evaluated in terms of feasibility, cell recovery, product quality, and suitability for paediatric patients. Cell viability and CD34+ recovery were determined by flow cytometry (DxFleX, Beckman Coulter) according to ISHAGE method. TNC recovery and RBC depletion were evaluated by automated haematology analysis (Xn-1000, Dasit).

Results: We analysed 52 BM allogeneic (related and unrelated) grafts, manipulated and infused in 40 patients, and 9 BM autologous grafts cryopreserved as a backup and not infused, collected from 2020 to 2025. After manual RBCD, the mean TNC recovery was 92.96% (SD 8.80), the mean CD34+ recovery was 93.65 %(SD 8.94) and the mean of RBC depletion was 75.08% (SD 8.32).

Conclusions: Although RBCD values are higher with automatic methods, up to 85% (3), compared to our data of 75.08%, the manual procedure allows for obtaining better results in terms of TNC and CD34+ recovery.
While the automated system offered advantages in terms of standardisation and reduced operator dependency, manual RBCD demonstrated greater flexibility and reliability when processing small-volume products. In several cases, manual RBCD provided superior control over product handling and recovery, particularly for collections below the optimal volume range of the automated system.
The manual RBCD technique remains a valuable and adaptable option when dealing with small or suboptimal volumes, often encountered with paediatric patients.

Disclosure: No disclosure

A304

IMPACT OF PRIOR DARATUMUMAB USE ON CD34+ CELL MOBILIZATION IN MULTIPLE MYELOMA PATIENTS ELIGIBLE FOR AUTOLOGOUS TRANSPLANTATION: SINGLE-CENTER EXPERIENCE

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Background: The use of Daratumumab in first-line therapy for multiple myeloma (MM) patients eligible for autologous transplantation has substantially improved the depth of response. However, some studies suggest lower mobilization efficacy or a greater need for rescue strategies (such as plerixafor) after its use. Our objective is to analyze the impact of prior Daratumumab treatment on CD34+ cell mobilization and collection performance, as well as the need for plerixafor.

Methods: We conducted a retrospective analysis of 100 MM patients undergoing 119 mobilization episodes between December 2013 and November 2025. The mean age was 57.63 ± 7.21 years, with 50% (N=50) men. We evaluated the impact of prior Daratumumab

exposure on CD34+ mobilization performance, number of apheresis sessions, and success rate (>2×10⁶ CD34+/kg). Daratumumab began to be used in our patients in 2022. Statistical tests used included Chi-square, Fisher's exact test, and Mann-Whitney U test.

Results: Of the 119 mobilization episodes analyzed, 22.7% (n=27) corresponded to patients who had received Daratumumab during induction (mean 3 ± 1.4 prior cycles), while 77.3% (n=92) had been treated with another chemotherapy regimen. There were no differences in sex or age distribution between groups (p=1; p=0.19). The clinical characteristics of each group can be seen in Table 1.
The distribution of mobilization regimens differed significantly between cohorts (p=0.001), mainly due to greater use of etoposide + G-CSF after its introduction in May 2022, a date close to the approval of Daratumumab in the first-line setting.
There were no differences in the number of mobilizations attempts between the two subgroups (p=0.079). However, patients exposed to Daratumumab required fewer apheresis sessions (p=0.034). Pre-apheresis CD34+/µL counts were similar between groups (p=0.44). Nevertheless, CD34+×10⁶/kg collected after the first apheresis was significantly lower in the Daratumumab group (p=0.007), with a lower success rate (p=0.004). In the subgroup mobilized with etoposide + G-CSF - where the distribution between patients exposed to Daratumumab and those not exposed was balanced (N = 11 vs 10) - no differences in success rate were observed (p=0.58). Plerixafor use was 44.4% in the Daratumumab group, with no significant difference vs controls (p=0.1).

DARATUMUMAB	YES	NO	p
Number of mobilizations	N = 27	N = 92	
Number of patients	N = 20	N = 82	
SEX - Male - Female	 N = 10 N = 10	 N = 41 N = 41	1
Mean Age	59.06 ± 5.31	56.52 ± 7.83	0.19
Mobilization Regimens - G-CSF - Cyclophosphamide 1.5 g/m² + G-CSF - Polychemotherapy + GCSF - Etoposide 375 mg/m² + G-CSF	 N = 13 N = 2 N = 1 N = 11	 N = 51 N = 30 N = 1 N = 10	< 0.001
Number of Mobilizations - 1 - 2	 N = 15 N = 4	 N = 74 N = 6	0.079

DARATUMUMAB	YES	NO	p
- 3 - 4	N = 0 N = 1	N = 2 N = 0	
Mean Pre-apheresis CD34/uL	59.02±64.54	54.8±38.06	0.44
Number of apheresis procedures - Not performed - 1 - 2 - 3	N = 5 N = 21 N = 1 N = 0	N = 10 N = 56 N = 24 N = 2	0.034
Mean CD34×10⁶/kg collected after the first apheresis	3.55±3.02	4.99±2.8	0.007
Number of CD34+ > 2×10⁶/kg - Yes - No	N = 16 N = 11	N = 78 N = 14	0.004
Plerixafor - Yes - No	N = 12 N = 15	N = 25 N = 67	0.102
Venous Access - Apheresis not performed - Central - Peripheral	N = 5 N = 1 N = 21	N = 10 N = 27 N = 55	0.009

Conclusions: According to our study, prior treatment with Daratumumab has not affected mobilization performance or increased the need for plerixafor, but it has been associated with a significant reduction in the success rate of CD34+ collection. Those exposed to Daratumumab required fewer apheresis sessions, probably due to the time difference between the two subgroups and the availability of a wider range of therapeutic options other than transplantation in recent years, which reduces the need to repeat apheresis to ensure success. Larger studies with the same median follow-up are needed due to sample size imbalance and temporal differences between groups.

Disclosure: Nothing to declare.

A306

ALLOGENEIC BONE MARROW HARVEST IN ADULT AND PEDIATRIC DONORS: A SINGLE-CENTRE EXPERIENCE

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Background: Bone marrow is the preferred graft source for non-neoplastic diseases because a graft-versus-tumor effect is not required and the goal is to minimize the risk of graft-versus-host disease (GVHD). Although this procedure has been standardized, differences in product quality still persist, influenced by technical aspects, collected volume and donor characteristics. We present the experience of a pediatric centre, focusing on safety and differences in product quality between pediatric and adult donors.

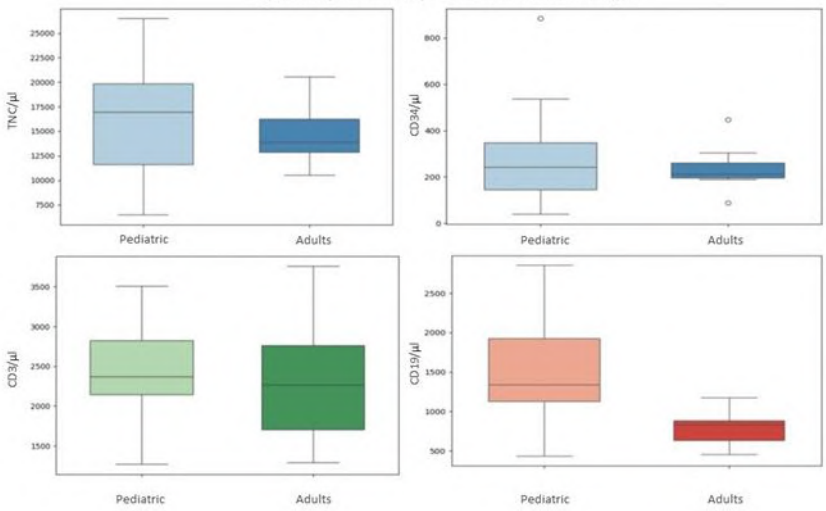
Methods: We retrospectively reviewed all allogeneic bone marrow harvests performed in our centre between 2009 and 2025. Demographic and clinical variables from donors and patients were collected, along with the different cellular subtypes of the product. A descriptive analysis of the data was performed, expressing quantitative variables as median and interquartile range and qualitative variables as frequencies and percentages. Comparison of variables by age was done using the Mann–Whitney U test, with $p < 0.05$ considered statistically significant. Data analysis was conducted in Python.

Results: Twenty-five collection procedures were done in that period but 22 were finally included in the analysis (3 were excluded because some data was missing). The median donor age was 16.5 years (10.75-25.75) with a median weight of 59 kg (37.5-78.5); 54.5% were male and 45.5% female. Fourteen donors (64%) were <18 years old. All donors were related (63.6% identical); 27.3% had minor ABO incompatibility, with none having major incompatibility. The most frequent indication for the procedure was acquired aplastic anemia (SAA) (54.5%). Most donors did not experience relevant adverse events (AEs), but 22.7% had AEs during the procedure and 10% after it, most of them being mild AEs. Only one donor required auto-transfusion after the procedure.
The median collected volume was 686.5 ml (533.25-965.75), with a median of 14.7 ml per donor´s kg (10.4-19.2). The median values for the different cell subtypes were total nucleated cells (TNC) 15,035/µl (12,039-19,568), 213.25 CD34+/µl (179.5-332.5), 2,370 CD3+/µl (1,940-2,827) and 1,152 CD19+/µl (669-1,486). Table 1 shows all demographic and technical variables.
Comparing the quality of the final product between the pediatric (<18-year-old) and adult populations, there were significant differences in the number of CD19+ cells in favour of the pediatric population (1337/µl vs 832/µl, $p=0.03$), whereas no differences were observed for CD3+, CD34+ and TNC. Figure 1.
All patients engrafted except for two: both of them had SAA and required an additional CD34+ boost.

Table 1. Demographic and technical characteristics (n=22)	
Age, median (range) **Pediatric donors (<18-y-o),** n (%)	16.5 (10.75-25.75) 14 (64%)
Weight, median (range)	59 (37.5-78.5)
Male gender, n (%)	12 (54%)
Diagnosis, n (%) • SAA • Immunodeficiencies • Others	 12 (54.8%) 3 (13.6%) 7 (31.6%)
Allogeneic HSCT type, n (%) • Matched related • Haploidentical	 14 (63.6%) 8 (36.4%)
ABO-incompatibility, n (%) • Minor	 6 (27.3%)
Adverse events during procedure, n (%) • Any • Hypotension • Minor bleeding • Anemia	 17 (77.3%) 3 (13.7%) 1 (4.5%) 1 (4.5%)
Adverse events after procedure, n (%) • Any • Back pain • Anemia	 20 (91%) 1 (4.5%) 1 (4.5%)
Positive harvest culture	1 (4.5%)
Harvest volume (ml), median (range)	686.5 (533.25-965.75)
Cell subtypes/µl, median (range) • TNC • CD34+ • CD3+	15,035 (12,039-19,568) 213.25 (179.5-332.5) 2,370 (1,940-2,827) 1,152 (669-1,486)

• CD19+			
Comparison between pediatrics and adults/µl, median	**<18 y**	**>18 y**	**P-value**
• TNC	16,960	13,882	0.616
• CD34+	242.15	213.25	0.868
• CD3+	2,370	2,266	0.860
• CD19+	1,337	832	0.030

Figure 1. Comparison between pediatric and adult harvest cell subtypes



Conclusions: This study describes the safety and characteristics of bone marrow harvests in a donor cohort at a pediatric centre. The procedure was safe in both pediatric and adult donors. Results show that there is a higher number of CD19+ cells/µl in the harvest product of the pediatric population compared with adults, with no differences observed in the other cell types analysed. However, studies with larger, multicentre cohorts are needed to determine the clinical significance of these findings.

Disclosure: Nothing to declare

A307

THE ROLE OF GRAFT CD3 AND TNC DOSES IN TRANSPLANT OUTCOMES: DOES IT STILL MATTER IN THE PTCY ERA?

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Background: Graft cellular composition, particularly infused $CD3^+$ T-cell and TNC doses, has been implicated in transplant outcomes such as GVHD, relapse, and survival. Prior studies—largely from the pre-PTCy era—suggested a higher risk of GVHD with increasing $CD3^+$ cell doses, but their relevance in contemporary PTCy-based GVHD prophylaxis remains uncertain. We therefore evaluated the impact of infused $CD3^+$ and TNC doses on post-transplant outcomes in patients receiving PTCy-based GVHD prophylaxis.

Methods: Between May 2023 and October 2025, 116 allo-HSCT were performed at our center. Among these, 56 patients received PTCy-based GVHD prophylaxis with MUD, MMUD, or haploidentical grafts; after excluding three patients who died within the first 30 days, 53 patients were included in the analysis. Patients were stratified into low and high groups according to the median infused $CD3^+$ and TNC doses. Study endpoints included acute and chronic GVHD, CMV and BK virus reactivation, engraftment times, relapse rates, and overall survival.

Results: A total of 53 patients receiving PTCy-based GVHD prophylaxis were included, with a median age of 44 years (38–59). Transplant characteristics are summarized in Table 1. The median infused $CD34^+$, $CD3^+$, and TNC doses were 6×10^6/kg (5.4–6.5), 19×10^7/kg (13–26), and 11.7×10^8/kg (8.5–17.6), respectively. When stratified by the median CD3 dose, the incidence of CMV reactivation was similar between CD3-low and CD3-high groups (64% vs 67.9%), as were acute GVHD (48% vs 46.4%), chronic GVHD (24% vs 17.9%), and cumulative incidence of relapse (8% vs 17.9%). Platelet engraftment occurred earlier in the CD3-high group (median 13 vs 15 days; p=0.02) (Table 2).

TNC-based stratification likewise showed no significant differences in CMV reactivation (73.1% vs 59.3%), BK viruria (42.3% vs 33.3%), acute GVHD (38.5% vs 55.6%), chronic GVHD (19.2% vs 22.2%), or relapse (11.5% vs 14.8%) (Table 3). Figure 1 shows overall survival rates according to CD3 and TNC groups. Median OS was not reached in any subgroup, and no survival difference was observed between groups. Mean OS was 585 vs 552 days for CD3-low vs CD3-high (p=0.761) and 594 vs 542 days for TNC-low vs TNC-high (p=0.560).

Conclusions: In this study, infused $CD3^+$ and TNC doses were not associated with the incidence of acute or chronic GVHD, relapse, or overall survival. At our center, graft cell doses are maintained within a narrow target range. While pre-PTCy studies reported an increased GVHD risk with higher $CD3^+$ cell doses, and limited PTCy-era data suggest that extreme low or high $CD3^+$ or TNC doses may influence GVHD or relapse outcomes, our results suggest that, when extreme $CD3^+$ or TNC levels are avoided, PTCy-based GVHD prophylaxis may provide protection against GVHD largely independent of infused $CD3^+$ or TNC dose.

Disclosure: Nothing to declare.

A308

COMPARATIVE EVALUATION OF ADAMII IMAGE CYTOMETRY WITH TWO FLOW CYTOMETRY PLATFORMS FOR $CD34^+$ HEMATOPOIETIC STEM CELL ENUMERATION

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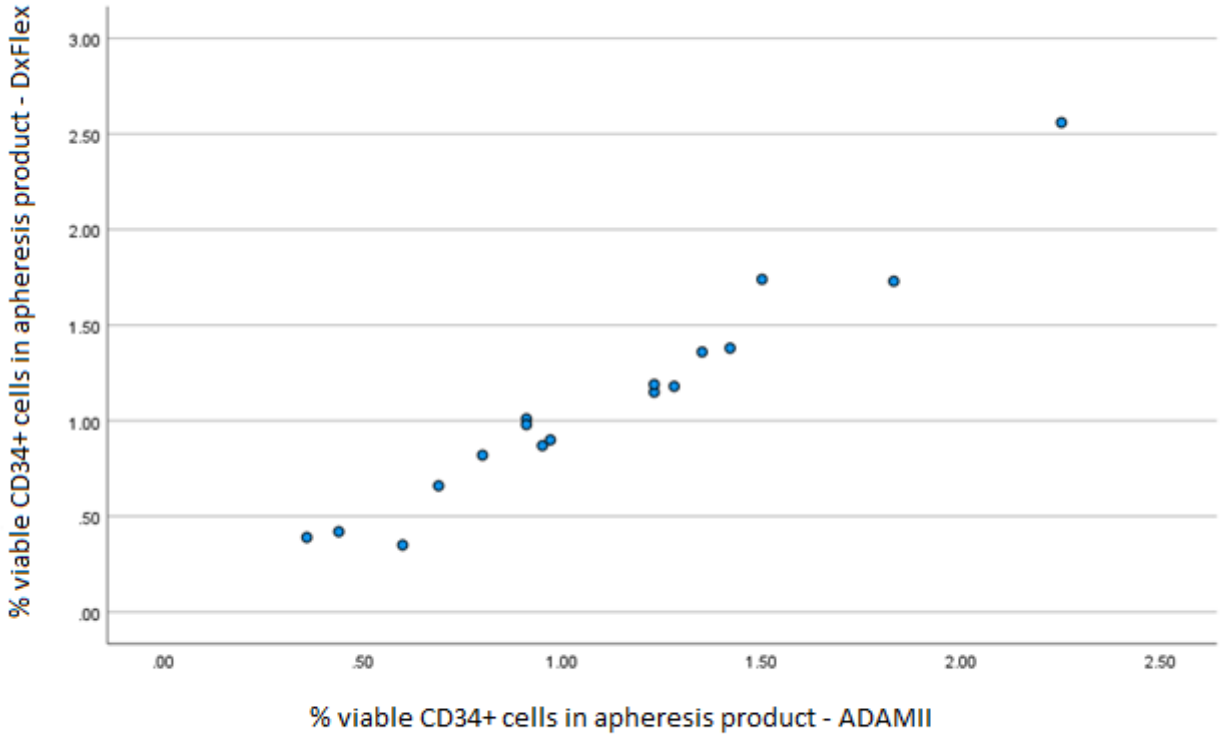
Background: Precise measurement of $CD34^+$ cells is essential for ensuring an adequate hematopoietic stem cell (HSC) dose for transplantation. The measurement should be performed quickly to predict the appropriate volume of apheresis product. The minimal number of CD34+ cells needed for Hematopoietic Stem Cell Transplantation (HSCT) to be successful is $2x10^6$ cells/kg of recipient body weight for autologous, and $4x10^6$ cells/kg for allogenic HSCT.

Methods: We quantified $CD34^+$ cells using the ADAMII image cytometer (NanoEntek, South Korea) in 14/11 peripheral blood samples and 22/17 apheresis products obtained from HSCT donors for comparison with Navios EX/DxFlex, Beckman Coulter Flow Cytometry platforms, USA. The viable $CD34^+$ cell counts enumerated on ADAMII were compared with the corresponding values from DxFlex flow cytometry, and total CD34+ counts were compared with corresponding values from BC Navios EX. The comparison between each of the two methods was done using Spearman or Pearson correlation analysis. The data were statistically processed in the IBM SPSS v27.0 program. The Shapiro Wilk test was used to determine the normality of the data distribution. Pearson's correlation analysis, Spearman's correlation analysis and the Mann Whitney U test were used to determine the statistical significance at the $p<0.05$ level.

Results: ADAMII demonstrated excellent correlation with both flow cytometry methods. Spearman's correlation analysis was performed ($p<0.05$), demonstrating a statistically significant, moderately strong, positive correlation between the percentage of total CD34+ cells measured by ADAMII and the percentage of total CD34+ cells in peripheral blood ($\rho=0.676$, $p=0.008$), and a statistically significant, strong, positive correlation between the percentage of total CD34+ cells in the apheresis product when compared with Navios EX ($\rho=0.973$, $p=0.000$). Spearman's correlation analysis was performed ($p<0.01$) showing statistically significant, strong, positive correlation between the percentage of viable CD34+ cells measured by ADAMII and the percentage of viable CD34+ cells in peripheral blood ($\rho=0.91$, $p=0.000$), and a statistically significant, strong, positive Pearson's correlation between the percentage of viable CD34 in the apheresis product when compared with BC DxFlex ($\rho=0.978$, $p=0.000$). The average number of CD34+ was $4,41x10^6$ cells/kg BW±0.46 per collection ($n=46$). Patients with multiple myeloma have significantly higher values of CD34+ cells in peripheral blood after mobilization, compared with patients suffering from lymphoma (Mann Whitney $U=6.00$, $p=0.047$). Female patients showed a significantly higher number of CD34+ cells in apheresis product per kg of body weight when compared to male

patients (Mann Whitney U=251.00, p=0.002).



Conclusions: The ADAMII image cytometry platform can be reliably employed for point-of-care quantification of CD34⁺ cells, enabling accurate prediction of the CD34⁺ cell number in samples of peripheral blood and apheresis products, prior to and throughout peripheral stem cell collection.

Disclosure: Nothing to declare.

A309

DONOR SELECTION FOR HLA HAPLOTYPE-HOMOZYGOUS PATIENTS UNDERGOING CORD BLOOD TRANSPLANTATION

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Background: HLA haplotype homozygosity occurs in more than 1% of the Japanese population. For these patients undergoing cord blood transplantation (CBT), the optimal donor selection strategy remains unclear. Specifically, clinical outcomes have not been clearly compared among HLA-matched cord blood units (CBU), HLA-mismatched CBU without mismatch in the graft-versus-host (GVH) direction, and HLA-mismatched CBU with mismatch in the GVH direction.

Methods: We conducted a retrospective analysis using registry data from the Japanese Society for Transplantation and Cellular Therapy. The study included patients aged 16 years or older with HLA haplotype homozygosity who underwent their first CBT. We compared transplant outcomes among three donor groups: HLA-matched CBU (homo-to-homo), HLA-mismatched CBU without GVH-direction mismatch (hetero-to-homo GVH=0), and HLA-mismatched CBU with GVH-direction mismatch (hetero-to-homo GVH>0).

Results: The study cohort comprised 40 patients in the homo-to-homo group, 58 in the hetero-to-homo GVH=0 group, and 33 in the hetero-to-homo GVH>0 group. The 5-year overall survival rates were 25.6%, 38.7%, and 20.1%, respectively, with no statistically significant differences observed. However, multivariate analysis revealed that the hetero-to-homo GVH>0 group was associated with a significantly higher risk of non-relapse mortality (NRM) compared to the homo-to-homo group (adjusted hazard ratio [aHR] 2.27, p=0.034). Conversely, the risk of relapse was significantly lower in the hetero-to-homo GVH>0 group (aHR 0.46, p=0.031). No significant differences were observed in the incidence of acute GVHD, chronic GVHD, or neutrophil and platelet engraftment.

Conclusions: These findings suggest that donor selection for HLA haplotype-homozygous patients in CBT may be considered based on the patient's risk of relapse. In high-risk cases, selecting a donor with a mismatch in the GVH direction might offer a protective effect against relapse. However, the potential increase in NRM warrants careful consideration.

Disclosure: Nothing to declare

A310

COMPARATIVE CHARACTERISTICS OF CD3 DEPLETION AND ALPHA/BETA T CELL DEPLETION AS A GRAFT MANUFACTURING PLATFORM

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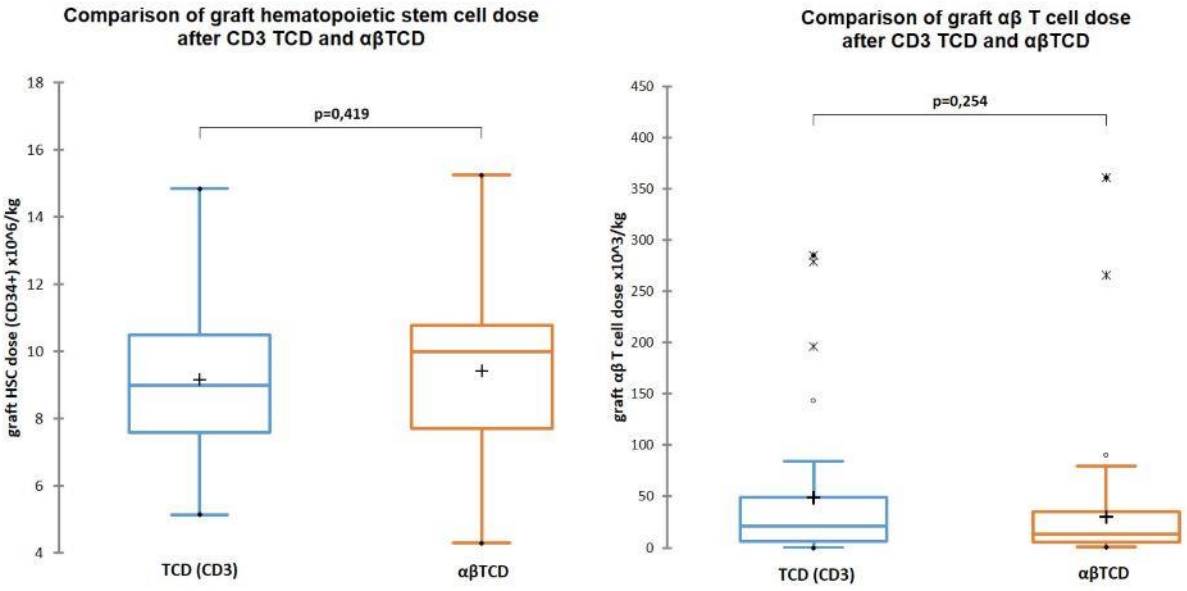
Background: T cell depletion method was developed to reduce the risks of severe graft-versus-host disease and other complications after the hematopoietic stem cell transplantation (HSCT). αβ T cell depletion (αβTCD) was implemented as a platform approach across different indications and donor types at the Dmitry Rogachev National Medical Research Center. Historically, CD3 T cell depletion (CD3TCD) was associated with somewhat inferior results in terms of depth of target population removal. Since 2024, we have used CD3TCD procedure based on reagent from CytoSinct™ to prepare grafts. The aim of this study was to investigate applicability and technical feasibility of CD3TCD in comparison to αβTCD.

Methods: The study cohort includes 33 patients transplanted from 06.2024 to 09.2025 with the help of CD3TCD method (CD3TCD group). CD3TCD group included patients with both malignant (27 patients, 82%) and non-malignant indications (6 patients, 18%). The median age at HSCT was 9.8 years (0.7-17.8). Donors were either haplo-identical related (28 HSCTs) or fully-compatible unrelated (4 HSCTs), one patient received HSCT from fully-compatible related donor. The grafts were processed using magnetic monoclonal antibodies CytoSinct™ CD3 Nanobeads (human) and CytoSinct™ 1000 Depletion Tubing Set (GenScript, China). CD3TCD was performed on a CliniMACS® Plus device (Miltenyi Biotec, Germany) using the standard Depletion 3.1 program. The starting material was prepared by the peripheral blood leukocyte apheresis. CD3TCD quality control was carried out by standardized flow cytometry. We compared the results with the retrospective data of 68 grafts processed by αβTCD with Miltenyi Biotec reagents and tubing set on CliniMACS® Plus device from 2015 to 2020 (αβTCD group). The number of graft cells per kg were compared by Mann–Whitney U-test.

Results: CD3TCD method demonstrated high reproducibility; all grafts were processed successfully without technical failures. The graft cells had high viability – 98% (93%-99%), the yield viable hematopoietic stem cells (HSC) was 89% (58%-100%), the median CD3 cells depletion logarithm was 3.5 (2.3-5.1). The median cell dose per kilogram was $9*10^6$ ($5*10^6$-$15*10^6$) for HSC and $21*10^3$ (0-$286*10^3$) for αβ T cells. The graft composition is shown in Table1. The residual T cell population was dominated by γδ+ T cells, while αβ+ T cells content was lower ($p<0.0001$). The comparison of the CD3TCD group graft composition with αβTCD group showed no significant difference in cell dose of HSC and αβ T cells per kilogram (the median cell dose per kilogram was $10*10^6$ ($4.3*10^6$-$15*10^6$) for HSC and $13*10^3$ ($1*10^3$-$361*10^3$) for αβ T cells in αβTCD group), p-value was 0.419 and 0.254, respectively, Picture1. No episodes of acute toxicity were identified at transplant transfusion.

The engraftment characteristics were consistent with the expected time for the ex-vivo depletion method.

	GRAFT COMPOSITION /kg				
Statistic	NC x 10^8	HSC x10^6	T cells x10^6	αβ T x10^3	
Minimum	1.7	5.2	0.003	0.000	
Maximum	17.9	14.8	7.2	285.5	
1st Quartile	5.8	7.6	0.05	6.2	
Median	7.6	8.9	0.13	21.0	
3rd Quartile	10.5	10.5	0.42	49.0	



Conclusions: CD3TCD with CytoSinct™ detection reagent and CytoSinct™ tubing set by GenScript on the CliniMACS® Plus device by Miltenyi Biotec is implementable and ensures the production of a graft product with target CD3 content. αβ T cell and HSC graft dose after CD3TCD are comparable with αβTCD.

Disclosure: Nothing to declare

A311

ANALYSIS OF CLINICAL AND PROCEDURAL FACTORS ASSOCIATED WITH SUCCESSFUL COLLECTION OF CD34+ HEMATOPOIETIC PROGENITOR CELLS

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Background: Despite therapeutic advances in multiple myeloma (MM), high-dose chemotherapy followed by autologous hematopoietic stem cell transplantation remains the first-line treatment for eligible patients. Mobilization of CD34+ cells may be performed with G-CSF alone or combined with chemotherapy, without conclusive differences between regimens according to the literature. Our objective was to analyze the potential influence of mobilization regimens, complementary use of plerixafor, and type of vascular access on collection success.

Methods: A retrospective analytical study included 119 mobilization attempts in 100 MM patients between 2013 and 2025 in a single center. Mobilization failure was defined as a pre-apheresis peripheral blood CD34+ count below 10 CD34+/µL. Apheresis was performed using the Amicus Femwall separator, with success defined as collection of >2×10⁶ CD34+/kg post-apheresis. We evaluated the influence of mobilization regimen, plerixafor use, and vascular access type. Statistical analyses included Kruskal-Wallis for nonparametric data, Wilcoxon for paired comparisons, and Fisher's exact or Chi-squared tests for categorical variables.

Results: The mean age was 57.63 ± 7.21 years, with 50% (N=50) men. Mobilization regimens were: G-CSF in 53.8% (N=64), cyclophosphamide 1.5 g/m² + G-CSF in 26.9% (N=32), poly-CT + G-CSF in 1.7% (N=2), and etoposide 375 mg/m² + G-CSF in 17.6% (N=21). First mobilizations accounted for 83.2% (N=99). Mean pre-apheresis CD34+/µL was 55.7 ± 45.14, with no significant differences between regimens (p=0.053).
Apheresis was not performed in 12.6% (N=15) of cases due to CD34+ <10/µL. Among the remaining 104 episodes, 21% (N=25) required two apheresis procedures and 1.7% (N=2) three. Mean CD34+ collected in the first apheresis was 4.69 ± 2.89 ×10⁶/kg, with a maximum of 15.43 ×10⁶/kg. Overall success rate was 79% (N=94). No association was found between mobilization regimen and number of apheresis sessions (p=0.757) or final success (p=0.075).
Significant differences were found regarding plerixafor use (p=0.047), with less use in the etoposide + G-CSF group. Although plerixafor use was not associated with final success (p=0.55), paired analysis showed a significant increase in pre-apheresis CD34+/µL following administration (p<0.001), with a mean increment of 31.78 ± 25.94 CD34+/µL. Regarding vascular access, 73% (N=76) used peripheral access and 26.9% (N=28) central access. No significant differences were found in success based on venous access (p=0.059).

	TOTAL MOBILIZATIONS	G-CSF	CYCLOPHOSPHAMIDE + G-CSF	POLYCHEMOTHERAPY + G-CSF	ETOPOSIDE + G-CSF	p
Nº of mobilization episodes	100% (N = 119)	53.8% (N = 64)	26.9% (N = 32)	1.7% (N = 2)	17.6% (N = 21)	
Mean pre-apheresis CD34+ count (CD34+/ µL)	55.7 (DS 45.14)	50.54 (DS 36)	53.37 (DS 41)	11.5 (DS 12)	79.53 (DS 65)	0.053
Nº of apheresis: - Not performed - 1 - 2 - 3	12.6% (N = 15) 64.7% (N = 77) 21% (N = 25) 1.7% (N = 2)	10.9% (N = 7) 62.5% (N = 40) 23.4% (N = 15) 3.1% (N = 2)	15.6% (N = 5) 62.5% (N = 20) 21.9% (N = 7) 0% (N = 0)	50% (N = 1) 50% (N = 1) 0% (N = 0) 0% (N = 0)	9.5% (N = 2) 76.2% (N = 16) 14.3% (N = 3) 0% (N = 0)	0.75
Mean CD34+ Yield from 1st apheresis (CD34+ x10^6 /Kg)	4.69 (DS 2.89)	4.45 (DS 2.81)	5.15 (DS 2.24)	0.6	4.96 (DS 3.8)	0.15
Apheresis Success - Yes - No	79% (N = 94) 21% (N = 25)	76.6% (N = 49) 23.4% (N = 15)	84.4% (N = 27) 15.6% (N = 5)	0% (N = 0) 100% (N =2)	85.7% (N = 18) 14.3% (N = 3)	0.075

	TOTAL MOBILIZATIONS	G-CSF	CYCLOPHOSPHAMIDE + G-CSF	POLYCHEMOTHERAPY + G-CSF	ETOPOSIDE + G-CSF	p
Plerixafor Use - Yes - No	31.1% (N = 37) 68.9% (N = 82)	39.1% (N = 25) 60.9% (N = 39)	31.3% (N = 10) 68.8% (N = 22)	0% (N =0) 100% (N =2)	9.5% (N = 2) 90.5% (N = 19)	0.047
Venous access - Not performed - Central - Peripheral	(N = 15) 26.9% (N = 28) 73% (N = 76)	(N = 7) 28% (N = 16) 72% (N = 41)	(N = 5) 33.3% (N =9) 66.6% (N = 18)	(N = 1) 0% (N = 0) 100% (N =1)	(N = 2) 15.7% (N = 3) 84.3% (N = 16)	0.53

Conclusions: Mobilization in MM showed a high success rate regardless of regimen, supporting decisions based on logistics and tolerability. Plerixafor demonstrated utility as a rescue strategy by significantly increasing CD34+ counts, though without direct impact on apheresis success. Finally, although approaching statistical significance, we did not demonstrate any differences according to the type of venous access. Overall, results highlight the importance of an individualized approach to optimize collection in autologous transplant programs.

Disclosure: Nothing to declare

A312

DIRECTED SIBLING CORD BLOOD BANKING : FOURTEEN YEAR EXPERIENCE IN NHS BLOOD AND TRANSPLANT (NHSBT)

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Background: Matched related donors remain the preferred source of stem cells (SCs) for transplantation. However, paediatric donors cannot donate until they are above a certain

weight or age allowing safe bone marrow (BM) collection. Delaying transplants is not feasible for haematological malignancies and may worsen outcomes for non-malignant conditions. Directed cord blood (DCB) collection provides an alternative source of SCs from siblings. NHSBT has offered DCB collection, processing and storage since 1997. We describe the experience of the programme from 2010 - 2023.

Methods: 531 DCB collections were received in NHSBT processing facilities.

Results: Main disease indications were: acute leukaemia (155), haemoglobinopathy (129), primary immune deficiencies (114), bone marrow failure syndromes (59). 75 DCB units (DCBUs) were discarded because of low volume (<50mls) or cell count (TNC <2.5 x 10^7). 38 bacterially-contaminated collections were banked to be considered for concessionary release if needed for transplant.
Of the banked collections (n=456), medians were: volume 74 mls (range 18-243); TNC 61 x 10^7 (range 1-347); CD34 count 14.2 x 10^5 (range 0.1-243); CD34 viability 99.2% (range 66.9-100%).
Twenty-one DCBUs (4.6% of banked DCBUs) were issued for SC transplantation. Recipients from 3 months to 11 years (median 6 yrs) had haemoglobinopathy (11), bone marrow failure (BMF) (5), myeloproliferative disease (2), ALL (2) and inherited disorders of metabolism (1). Median time of DCBs in storage prior to transplant was 25 months (range 56 days - 61 months). All were 10/10 HLA matches. The cell content of DCBUs transplanted is shown in Table 1. In 10/21 (48%) cases (8 haemoglobinopathy, 2 BMF), BM from the DCB sibling donor was infused at the same time as the DCBU.
Outcome data was available in 17 cases, all alive after median follow up of 9 years (range 2 yrs-12 yrs). Neutrophil engraftment occurred at median of 19 days (range 10-32) and platelet engraftment at median of 32 days (range 16-68 days) in 14 cases. A further 3 cases were reported to have engrafted. PB chimerism was reported in 8 cases, all being 100% donor. All haemoglobinopathy patients were transfusion independent. One patient with myeloproliferative disease relapsed at 9 months and had a mismatched unrelated donor transplant and is in remission 5 years on. Two patients with thalassaemia had grade 3 acute GVHD, one progressing to mild chronic GVHD which fully resolved.

Table 1. Characteristics of DCBUs and Recipients Receiving DCBUs Alone or in Combination with Sibling Donor BM

	Source of Stem Cells Infused *	
	DCBU alone (n=6)	**DCBU plus BM (n=10)**
Recipient age	3.5 yrs (2 to 10 yrs)	9 yrs (3 - 11 yrs)
Recipient weight	17.2 kg (15.2 to 44.6 kg)	24.6 kg (13.2 to 45.8 kg)
DCBU TNC dose infused: median (range)	7.8 x 10^7/kg (3.8-21.2)	1.64 x 10^7/kg (0.66-7.2)
DCBU CD34 dose infused: median (range)	1.26 x 10^5/kg (0.98-11.5)	0.48 x 10^5/kg (0.11-1.8)

Neutrophil engraftment: median (range)	18 days (15-32) (n=3)	16 days (10-28) (n=10)
Platelet engraftment: median (range)	42 days (21-50) (n=3)	31 days (16-68) (n=10)
Sibling donor age at BM donation	Not applicable	26 months (16-30 months)
*Data missing in 4 cases; 1 further case – DCBU given with mesenchymal stromal cells.		

Conclusions: DCB donations can provide a useful number of TNC and viable CD34 cells comparable to CBUs available in public banks. Overall usage was low as most were collected for a sibling with acute leukaemia, the majority of whom will not need a transplant. A higher proportion (11/129 = 8.5%) of collections for haemoglobinopathy was used, some supplemented with a BM donation. Additional information to assess the contribution of the DCBU will be sought. Transplants using DCBUs demonstrated favourable outcomes, with no graft failures and minimal GVHD, underscoring the utility of the collection programme.
Thanks to: transplant teams for outcome data; NHSBT laboratory colleagues.

Disclosure: Nothing to declare

A313

COMPARATIVE ANALYSIS OF MOBILIZATION REGIMENS AND THEIR IMPACT ON STEM CELL YIELD AND ENGRAFTMENT KINETICS IN PATIENTS UNDERGOING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: RETROSPECTIVE STUDY

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Background: For successful autologous stem cell transplantation sufficient mobilization of CD34+ is required, still some of the patients responds poorly to GCSF alone. Plerixafor can improve mobilization, but still local data on its efficacy is limited that emphasizes the necessity for real-world outcome studies. Therefore, the aim of the study is to compare the effectiveness of plerixafor based and non plerixafor based mobilization to achieve optimal stem cell yield and engraftment kinetics among various hematological malignancies.

Methods: For the following retrospective cross-sectional study, purposive sampling technique was performed. The study was conducted at Armed forces bone marrow transplant center where, patients who underwent autologous stem cell transplant between 2021-2025 were included. Patients mobilized with plerixafor based protocol or without plerixafor-based protocol were both eligible. Clinical records were reviewed to record observational data, diagnosis, mobilization regimen, stem cell yield, and engraftment outcomes. For stem cells

yield ≥2 × 10^6 $CD34^+$ cells/kg and ≥2–3 × 10^8 MNC/kg was considered successful engraftment. Neutrophil engraftment was defined as an ANC ≥0.5 × 10^9/L for three consecutive days usually achieved during 9 to 12 days whereas platelet engraftment was with counts ≥20 × 10^9/L without transfusion support is considered to achieve during 12 to16. Ethical approval was obtained from the institutional review board, and informed consent was taken from all participants. Statistical analysis was performed using SPSS version 27.

Results: A total of 137 patients were included in the study who underwent autologous stem cell transplantation with mean age 41.3±16 years, among them 66% were males and 34% were females. Multiple myeloma (54%) was the most common diagnosis followed by HL (28.5%), NHL (8.8%) and DLBCL (8.8%). Plerixafor based mobilization was used in 72.3% of the patients in comparison to non Plerixafor based mobilization 27.7%. Mean neutrophil engraftment was achieved at 11.2±1.9 days while platelet engraftment was achieved at 15.5±9.3 days respectively. The Plerixafor group achieved higher CD34+ yields (5.34±3.36 vs. 4.15±1.72; p=0.003) and higher MNC doses (7.41±2.94 vs. 5.26±2.43; p=0.46) **(Table 1)**. However there was a trend towards early Neutrophil engraftment (p=0.09) in plerixafor arm, while platelet engraftment occurred earlier with plerixafor (p=0.001) across diagnostic groups.

Table 1: Comparison of Engraftment Kinetics and Stem Cell Yield Between Patients Mobilized with and without Plerixafor.

Stem cells and engraftment kinetics	Mobilization with no plex	Mobilization with Plex	p-value	95% Confidence Interval of the Difference	
				Lower	Upper
Engraftment Kinetics					
Day-Neutrophil Engraftment	11.24±1.383	11.23±2.075	0.613	-0.720	0.744
Day-Platelet Engraftment	16.84±13.668	14.99±6.856	**0.051***	-1.775	5.473
Stem cells Yield					
MNC Dose given (x10^8/Kg)	5.26±2.435	7.41±2.945	0.465	-3.577	-0.725
CD34 Dose given (x10^6/Kg)	4.157±1.727	5.341±3.362	**0.003***	-2.31700	-0.04964

Engraftment patterns varied by diagnosis, with DLBCL showing the slowest platelet recovery

and MM achieving the highest CD34+ cell dose. Overall survival among the participants was 91% while disease free survival was observed as 81.9% across all disease groups **(Figure 1)**

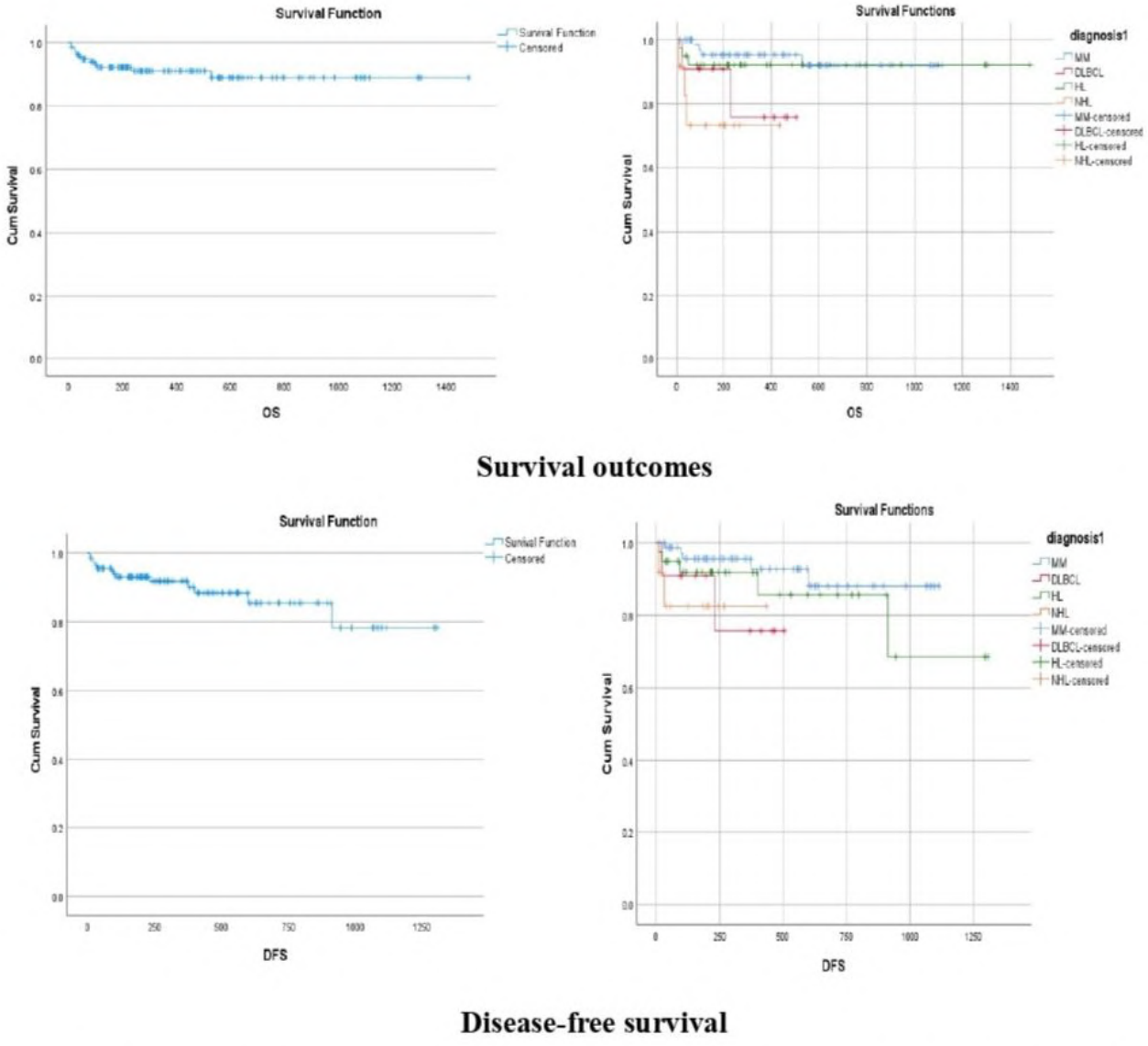

Figure 1. Survival and disease-free survival outcomes among patients with different diagnoses.

Conclusions: Compared to non plerixafor based mobilization, plerixafor based mobilization significantly increased the stem cell production and accelerated the platelet recovery. Overall, both strategies produced high survival rates for all disease groups and equivalent neutrophil engraftment.

Disclosure: Nothing to declare

A314

LEUKAPHERESIS FOR PROGENITOR CELL COLLECTIONS IN LOW WEIGHT CHILDREN: REPORT FROM A SINGLE PEDIATRIC CENTER

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Background: The aim of this study was to assess the performance of the Spectra Optia Apheresis System for collecting peripheral blood progenitor cells (PBPC) in low weight children with respect to collection variables, and CD34+ cells harvest prediction.

Methods: We retrospectively analyzed all procedures performed with that device in our institution, in children with a body weight below or equal to 20 kilograms, collect variables related with the procedure, and adverse events reported. Collection efficiencies were calculated as follows: CE1(%)= CD34+cells collected/((CD34+cells pre-apheresis in PB + CD34+cells post-apheresis)/2)×total blood volumen processed ×100; and CE2(%)= CD34+cells collected/(CD34+cells pre-apheresis in PB×total blood volumen processed) ×100. Apheresis were performed on a Spectra Optia device (Terumo BCT) using either the continuous mononuclear cell collection program (CMNC) or the mononuclear cell collection program (MCN). Central venous catheters were used for all procedures. Adverse events related to the mobilization and the collection were recorded by the nurse in charge during the process.

Results: A total of 105 apheresis from 82 children (62.2% male) were included (diagnosis presented in table 1). The median age was 2 years (interquartilic range (IQR) 1 – 4). The median weight was 14 kg (IQR 11.5 – 16), with the lower weight being 6 kg, and the median total blood volume (TBV) was 1107 mL (IQR 900 – 1284). The median number of TBV processed was 3.2 (IQR 2.8 – 4). The median CD34+ cell count per microliter pre-apheresis was 53 (IQR 26 – 98.5). Median CD34+ cell/kg collected was 4.98×10^6 (IQR 2.69×10^6 – 9.23×10^6). Median CE1 was 49.4% (IQR 39.35 – 60.05), and median CE2 was 39.6% (IQR 31.85 – 47.85).
As previously reported, CD34+ cell/kg collected were related to higher CD34+ cells pre-apheresis ($p<0.0001$), prior chemotherapy and radiotherapy, mobilization schedule (with higher collections using chemotherapy as mobilization agent), and healthy donor or patient status ($p<0.05$).
CE1 and CE2 were related to CD34+ cells pre-apheresis with those procedures with lower counts before the collection having better CEs. CE1, although not statistically related with prior purging of the device, showed clear trend toward significance ($p=0.053$).
Adverse events (AEs) were mostly related to the mobilization with 25.7% of children suffering some; 3% of children had more than 3 AEs related to the mobilization with low

grade fever being the most frequent one (11.9%). During the apheresis, children only presented mild cardiovascular manifestations; these AEs were recorded in 53.9% of children with mild tachycardia in all of them, and in 13.7% presenting with paleness. Median platelet loss was 40.6% (IQR 35.45 – 48.93), and median hematocrit loss was 1% (IQR -1.5 – 4). No procedures had to be canceled or interrupted due to AEs.

Table 1. Diagnosis of the 80 children

Diagnosis	N	**%**
Healthy donor	15	18.3
Neuroblastoma	21	25.6
Central nervous system tumor	20	24.4
Hurler syndrome	8	9,8
Fanconi Anemia	6	7,3
Nefroblastoma	4	4.9
Osteopetrosis	3	3.7
Non Hodgkin Lymphoma	2	2.4
Manosidosis	1	1.2

Conclusions: The Spectra Optia Apheresis System for collecting PBPC is safe for low weight children. Collection efficiencies are related to the peripheral blood CD34+ cell count before the procedure. CD34+ cells/kg can be predicted by several patient characteristics.

Disclosure: Nothing to declare.

A315

NO SIGNIFICANT IMPACT OF GRAFT CD34+/CD3+ RATIO ON TRANSPLANT OUTCOMES AFTER POST-TRANSPLANTATION CYCLOPHOSPHAMIDE-BASED HAPLOIDENTICAL PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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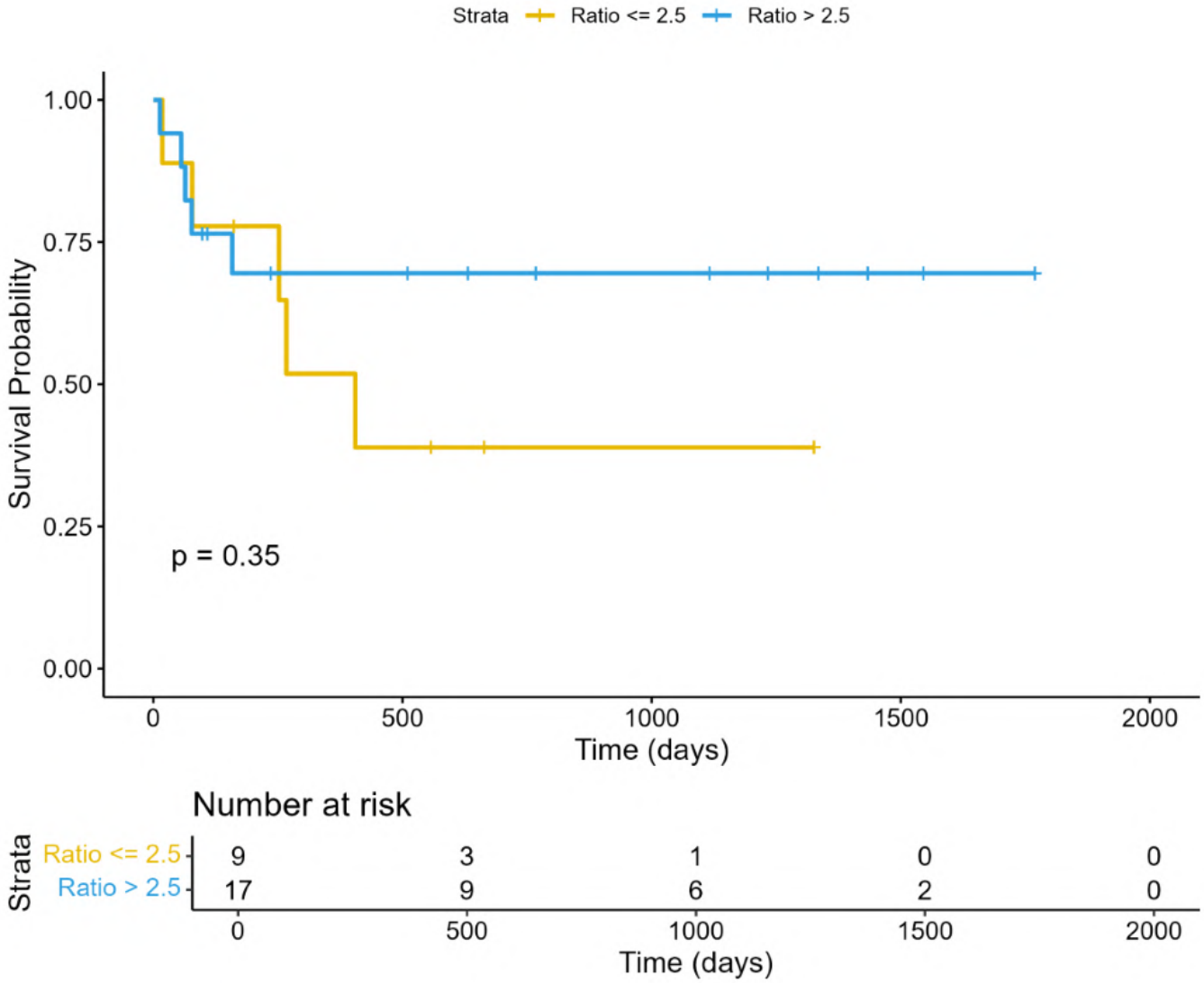
Background: Post-transplantation cyclophosphamide (PTCy)-based haploidentical peripheral blood stem cell transplantation (PBSCT) is widely used for patients lacking HLA-matched donors. The optimal graft composition and cell doses for this alloHSCT platform remains an unanswered question. We sought to investigate the impact of graft composition variables including CD34/CD3 ratio on major clinical transplant outcomes.

Methods: We retrospectively analyzed consecutive adults who underwent related haploidentical PBSCT at our institution between December 2020 and September 2025. Patients received peripheral blood stem cell (PBSCs) grafts and uniform GVHD prophylaxis with post-transplant cyclophosphamide (40-50 mg/kg/day on day +3-4), tacrolimus (n=25) or sirolimus (n=1) and mycophenolate mofetil. Graft composition was quantified by flow cytometry. Cox regression analyses were performed to evaluate the effect of cell doses (CD34 reported as x 10^6/kg and CD3 as x 10^8/kg) and CD34/CD3 ratios on clinical outcomes. For CD34/CD3 ratio a cut-off of > 2.5 versus ≤ 2.5 was used based on prior report by Katagiri et. al. (Blood 2024). Given the paucity of grade III/IV acute GVHD events in this small cohort, a modified GVHD-free, relapse-free survival (GRFS) definition was utilized. A GRFS event was defined as Gr>=2 acute GVHD, chronic GVHD warranting immune suppressive therapy, disease relapse or death from any cause. Time-to-event outcomes were measured from graft infusion (day 0). OS, RFS and GRFS were estimated by the Kaplan–Meier method.

Results: A total of 26 alloHSCT recipients were included. Median age was 61 years (range 19–74), and 20 patients (77%) were male; 17 patients (65%) were Hispanic. Underlying diagnoses included AML (n = 15), ALL (n = 5), MDS (n = 3), CMML (n = 1) and T-cell lymphoma (n = 2); 22 patients (85%) were in complete remission at transplant. Fifteen patients (55%) received reduced-intensity conditioning of which 67% received Fludarabine-Melphalan +TBI 200cGy. Median CD34+ and CD3+ doses were 7.39 ×10^6/kg (range 6.29–9.37) and 1.95 ×10^8/kg (range 1.81–2.96), with median CD34/CD3 ratio 4.10 (range 2.37–4.97). Median follow-up was 11 months. One-year OS and RFS for the entire cohort were 63% (95% CI 46–86) and 80% (95% CI 64–100); modified GRFS at 1 year was 20% (95% CI 9–47). Patients with CD34/CD3 ratio > 2.5 had numerically higher 1-year RFS (84% vs 71%; p= 0.57) and OS (70% vs 52%; p= 0.36) than those with CD34/CD3 ≤ 2.5, but these differences were not statistically significant. The CD34/CD3 ratio did not influence modified GRFS (HR 1.40, 95% CI 0.53-3.71; p=0.5).

Figure I: Overall survival according to graft CD34/CD3 ratio



Conclusions: In this predominantly Hispanic cohort of PTCy-haplo-PBSCT, a higher graft CD34/CD3 ratio was not significantly associated with superior 1-year OS, RFS or modified GRFS. Within the range of graft doses delivered at our institution, higher CD3+ content, reflected in lower CD34/CD3 ratios, did not appear to adversely affect transplant outcomes, supporting the concept that PTCy abrogates the adverse impact of high CD3 graft content. Larger multicenter analyses are required to define optimal graft composition in PTCy haploidentical PBSCT.

Disclosure: Bambace, Nadia: nothing to declare
Perez Perez, Ariel: **Consulting or Advisory Role: Pfizer, Gilead Kite, Abbvie, ADVI**
Feinstein, Lyle: nothing to declare
Linhares, Yuliya: **Consulting or Advisory Role: Pfizer** A**DCT, BMS, GenMab, Genentech,**

Kyowa Kirin, Novartis, Research funding from BeiGene Therapeutics, Miltenyi, ADCT, and Genentech, Personal fees from astra zeneca, Personal fees from Gilead
Nahas, George: **Consulting or Advisory Role: Pfizer, Janssen, BMS, Genzyme**
Ruiz, Marco: nothing to declare
Sun. Ning: nothing to declare
Khan, Munnezzah: nothing to declare
Ravelo Barrero, Rafael: nothing to declare
Al Sagheer, Tiba: nothing to declare
Koehne, Guenther: **Consulting or Advisory Role: Restem LLC, Sellas Life Sciences, Patents, Royalties, Other Intellectual Property: Development of third party EBV-specific T-cells for the treatment of EBV-PTLD**
Alvarez, Harold: nothing to declare

A316

IMPACT OF CD34⁺ CELL DOSE AND GROWTH FACTOR SUPPORT ON EARLY MORBIDITY AND NON-RELAPSE MORTALITY AFTER AUTOLOGOUS STEM CELL TRANSPLANT FOR LYMPHOMA

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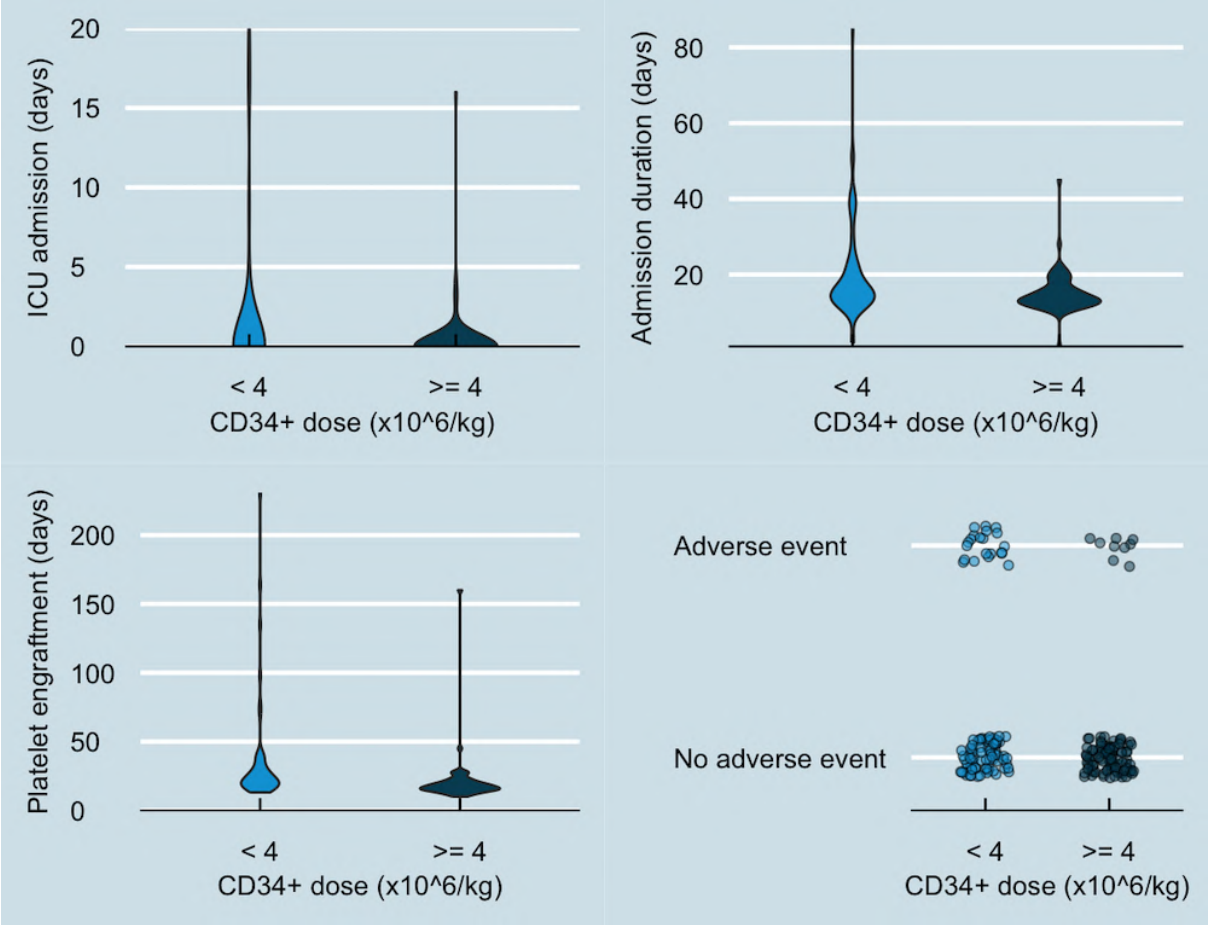
Background: In autologous stem cell transplantation (ASCT), a CD34⁺ progenitor cell dose below 2×10^6/kg is associated with adverse outcomes, including delayed hematopoietic recovery, inferior progression-free survival, and higher non-relapse mortality (NRM). Above 2×10^6/kg, increasing CD34⁺ doses are associated with faster hematopoietic recovery, but the impact on early morbidity and NRM is poorly defined.

Methods: We conducted a retrospective single-center cohort study of adult lymphoma patients undergoing high-dose chemotherapy followed by ASCT between 2020–2024. The primary outcome was 180-day NRM. Secondary outcomes included neutrophil, platelet and lymphocyte engraftment, length of hospital stay, intensive care (ICU) admission, duration of intravenous antibiotics, and a composite of adverse outcomes. Associations were assessed using descriptive statistics and Fisher's exact test.

Results:



Data were collected on 162 patients with diagnoses of Hodgkin lymphoma (26%), primary CNS lymphoma (PCNSL; 15%), low-grade non-Hodgkin lymphoma (19%), and high-grade non-Hodgkin lymphoma (40%). The median CD34+ dose was 4×10^6/kg (range 2 – 27). 33% of patients received plerixafor and/or an additional cycle of cytarabine or cyclophosphamide to mobilise progenitor cells. Overall 180-day NRM was 4.3%. NRM occurred in 2.5% of patients receiving $CD34^+$ doses $\geq4\times10^6$/kg (2/81) compared with 6.2% among those receiving $<4\times10^6$/kg (5/81), which was not statistically significant (Fisher's exact test p=0.443).

Patients receiving a CD34+ dose $\geq4\times10^6$/kg had lower rates of delayed hospital discharge >25 days (3% vs 19%, p=0.002), a trend towards lower rate of ICU admission (6% vs 15%, p=0.06), and no difference in platelet engraftment by day 100 (98% vs 94%, p=0.3). $CD34^+$ dose $\geq4\times10^6$/kg was significantly associated with decreased rate of a composite adverse outcome consisting of any of 180-day NRM, ICU admission, delayed hospital discharge or failure of platelet engraftment by day 100 (9% vs 22%; odds ratio 0.34, 95% CI 0.13–0.83; p=0.01).

Filgrastim was used in 64% of the cohort, while pegfilgrastim was used in 36%. Among patients receiving pegfilgrastim, 90% received additional supplementary filgrastim for a median 5 days (range 0–28). There were no significant differences in haematopoietic

recovery, length of hospital stay, and duration of intravenous antibiotic therapy, between filgrastim and pegfilgrastim.

Conclusions: We did not demonstrate a significant association between CD34+ dose in ASCT and 180-day NRM. CD34+ doses <4×10⁶/kg were associated with a higher rate of ICU admission and a composite adverse outcome. We found similar clinical outcomes with pegfilgrastim compared with filgrastim. CD34+ doses for ASCT in lymphoma should be >4×10⁶/kg where this can be attained without additional risk to the patient. Further health economic analysis is required to determine whether additional apheresis procedures would be cost-effective.

Disclosure: Bernard Maybury: meeting attendance and advisory board: Gilead. Speaker's fees: Roche.

P099

MOTIXAFORTIDE AND G-CSF TO MOBILIZE HEMATOPOIETIC STEM CELLS FOR AUTOLOGOUS TRANSPLANTATION IN HIGH-RISK MULTIPLE MYELOMA: TWO CASES CLINICAL REPORT

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Background: Approximately 5% to 30% of multiple myeloma (MM) patients experience stem cell mobilization failure when undergoing autologous transplantation. Motixafortide, a novel high-affinity CXCR4 antagonist, works by blocking the SDF-1/CXCR4 axis to synergize with G-CSF, particularly reversing the microenvironmental retention effect caused by high-risk factors such as del(17p). Compared to plasmaphorin, motixafortide can be administered once daily for full-day collection. The mobilized products are rich in pre-pDCs (plasma cell-like dendritic cells), which are beneficial for immune reconstruction, while avoiding the common gastrointestinal and cardiac toxicity risks associated with plasmaphorin.

Methods: This study reports two multiple myeloma (MM) patients with high-risk mobilization difficulties, including advanced age, multiple-line therapy, and cytogenetic abnormalities, who received a combination of Motixafortide and Granulocyte colony-stimulating factor (G-CSF) for cell mobilization. Case 1: G-CSF8 μg/kg/day (days 1-4) and Motixafortide 0.83 mg/kg/day (day 4); Case 2: G-CSF10 μg/kg/day (days 1-4) and Motixafortide 2.06 mg/kg/day (day 4). CD34+ stem cell collection was performed using a blood cell separator 10-16 hours after motilferomide administration. All patients underwent daily blood routine tests and venous CD34+ cell counts on days 4-7, with CD34+ cell counts also measured in the collected samples.

Results: Motixafortide significantly enhanced the release efficiency of peripheral blood stem cells, with the peak $CD34^+$ cell counts increasing from 16/μL and 0.49/μL to 56/μL and 90/μL, respectively. Both patients achieved optimal collection targets (total $CD34^+$ cells:

5.66×10⁶/kg and 7.8×10⁶/kg) within 1-2 single draws. The patients demonstrated good tolerance, with only mild injection site reactions and no serious adverse events. Post-transplant hematopoietic reconstitution was rapid, with neutrophil implantation occurring at +9 days and platelet implantation at +10 days.

Conclusions: The combination of Motixafortide and G-CSF provides a new and effective option for the mobilization of high-risk or plethasafu-intolerant MM patients with its excellent mobilization efficiency, convenient administration and good safety.

Disclosure: The authors declare no conflict of interest.

P100

THE COMPARISON OF BONE MARROW PLUS PERIPHERAL BLOOD VERSUS PERIPHERAL BLOOD AS GRAFT SOURCE IN HAPLOIDENTICAL STEM CELL TRANSPLANTATION FOR PATIENTS ≥55 YEARS

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Background: Haploidentical stem cell transplantation (haplo-HSCT) has become increasingly common in elderly patients; however, standardized protocols for selecting the optimal graft source are lacking. It is known that peripheral blood (PB) grafts were associated with faster engraftment while higher risk of graft-versus-host disease (GVHD) compared to bone marrow (BM) grafts. We hypothesize that the combination of BM and PB (BM+PB) grafts might reduce the incidence of GVHD without changing the engraftment speed, but relevant data is very insufficient. Therefore, this study aimed to compare the clinical outcomes of PB-alone grafts versus BM+PB grafts in elderly recipients aged 55 years and older.

Methods: This was a retrospective multicenter study from 6 Chinese centers. Patients were enrolled if they were (1) received first haplo-HSCT; (2) age ≥55 years; and (3) diagnosed with acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL) or myelodysplastic syndromes (MDS). The primary endpoint was 5-year DFS. Secondary endpoints include engraftment, GVHD, TRM, relapse and OS. The OS and DFS were estimated using the Kaplan–Meier method. The cumulative incidences of engraftment, GVHD, TRM, and relapse were estimated using a competing risk model. Prognostic factors were analyzed using Cox regression.

Results: From September 27, 2010 to March 10, 2025, a total of 936 patients were enrolled, including 679 patients received PB-alone grafts and 289 patients received BM+PB grafts. Details of the patients, disease, transplant characteristics and donor characteristics are shown in Table 1.

The median time to neutrophil engraftment was 12 days in both the PB-alone and BM+PB groups (P=0.47), and the median time to platelet engraftment was also identical (14 days in both groups, P=0.43). The cumulative incidences of acute GVHD at 100 days and chronic GVHD at 5 years were comparable between PB-alone group and BM+PB group, 33.8% versus 37.4% (*P*=0.39) and 37.7% versus 42.2% (*P*=0.36), respectively. (Figure 1A, B). The survival outcomes, overall survival (OS) and disease-free survival (DFS) at 5 years, were comparable, 62.1% versus 60.9% (*P*=0.47) and 56.8% versus 57.3% (*P*=0.40). (Figure 1C, D). The cumulative incidences of relapse (CIR) and transplant related mortality (TRM) at 5 years were 17.6% versus 14.9% (*P*=0.39) and 25.8% versus 27.6%(*P*=0.83). (Figure 1E, F). After adjusting for baseline differences in patient age, donor age, and other relevant covariates, multivariate analysis revealed no statistically significant differences between the groups in OS (HR 0.87, 95% CI: 0.66–1.14; *P*=0.30), DFS (HR 0.86, 95% CI: 0.67–1.11; *P*=0.24), TRM (HR 1.01, 95% CI: 0.56–1.83; *P*=0.61), or CIR (HR 0.80, 95% CI: 0.55–1.18; *P*=0.27).

Table 1|Characteristics of patients, donor and transplantation.

Characteristics	All (n=936)	PB (n=679)	BM+PB (n=289)	*P*
Patients' age at HSCT, median (range)	58 (55–75)	59 (55–75)	58 (55–73)	0.01
Donors' age, median (range)	33(15–62)	33 (15–62)	32 (16–62)	<0.01
Donor-recipient gender matching, n (%) Male to Male Female to Male Female to Female Male to Female	 374 (40.0) 193 (20.6) 141 (15.1) 228 (24.4)	 261 (40.3) 130 (20.1) 99 (15.3) 157 (24.3)	 113 (39.1) 63 (21.8) 42 (14.5) 71 (24.6)	0.93
Donor-recipient ABO blood type, n (%) matched mismatch	 507 (54.2) 429 (45.8)	 332 (51.3) 315 (48.7)	 175 (60.6) 114 (39.4)	<0.01
Diagnosis, n (%) AML ELN (low/median/high) ALL MDS	 505 (54.0) 107/242/156 144 (15.4) 287 (30.7)	 355 (54.9) 78/155/122 104 (16.1) 188 (29.1)	 150 (51.9) 29/87/34 40 (13.8) 99 (34.3)	0.26
Status CR NR	 544 (84.8) 105 (16.2)	 381 (83.0) 78 (17.0)	 163 (85.8) 27 (14.2)	0.38

MRD negative positive	 573 (61.2) 363 (38.7)	 481 (64.6) 229 (35.4)	 155 (53.6) 134 (46.4)	<0.01
HCT-CI, n (%) 0 (low risk) 1–2 (intermediate risk) ≥3 (high risk)	 506 (54.1) 321 (34.3) 109 (11.6)	 227 (58.2) 119 (30.5) 44 (11.3)	 145 (53.1) 96 (35.2) 32 (11.7)	0.40
Matched HLA loci at A, B, C, DRB1 and DQB1, n (%) 5/10 others	 642 (68.6) 294 (31.4)	 445 (68.8) 202 (31.2)	 197 (68.2) 92 (31.8)	0.85
Conditioning regimen, n (%) Bu/Cy+ATG Bu/Cy/Flu+ATG others	 327 (34.9) 580 (62.0) 29 (3.1)	 165 (25.5) 468 (72.3) 14 (2.2)	 162 (56.1) 112 (38.8) 15 (5.2)	<0.01
Median CD34+ count, $\times 10^6$/kg (range)	3.98 (0–31.22)	4.00 (0.66–31.22)	3.79 (0–15.60)	0.07
Median MNC count, $\times 10^8$/kg (range)	8.99 (1.94–29.99)	9.11 (1.96–29.99)	8.66 (1.94–22.01)	0.01

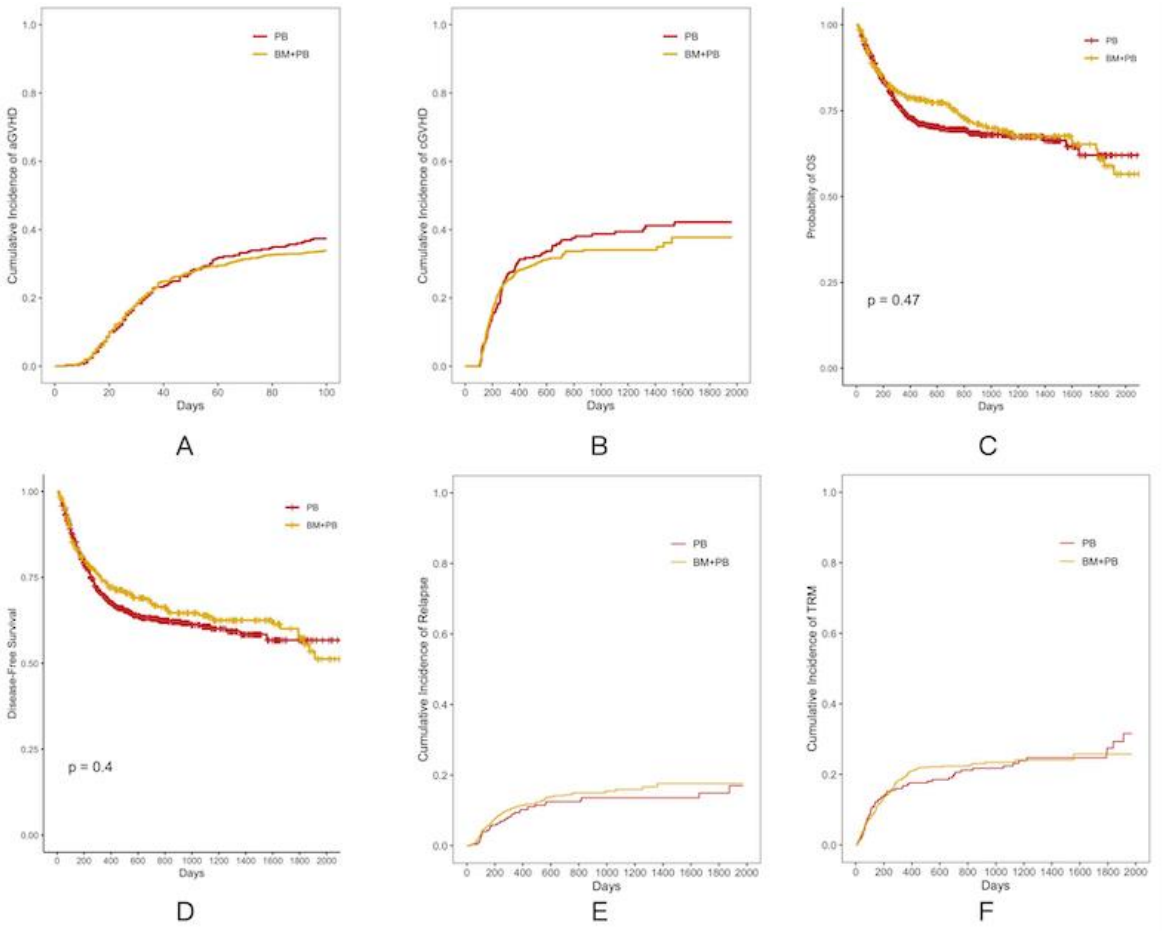

Figure 1. Comparison between PB–alone and BM+PB groups. aGVHD (A), cGVHD (B), OS (C), DFS (D), CIR (E), and TRM (F).

Conclusions: In conclusion, this study suggested the comparable survival outcomes between BM+PB grafts and PB-alone grafts in elderly patients aged 55 years and older undergoing haplo-HSCT.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

P101

QUALITATIVE AND QUANTITATIVE CHARACTERISTICS OF CD34+ HEMATOPOIETIC STEM CELLS AND THEIR ASSOCIATION WITH HEMATOPOIETIC RECOVERY FOLLOWING ASCT

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Background: Qualitative and quantitative characteristics of mobilized CD34+ hematopoietic stem cells reflect the biological diversity of autologous grafts and may influence hematopoietic recovery following autologous stem cell transplantation (ASCT). While CD34+ cell dose remains the standard parameter for graft adequacy, integrating phenotypic and functional features of CD34+ cells may enable a more refined assessment of graft quality.

Methods: We prospectively analyzed 29 patients with lymphoma or plasma cell dyscrasia undergoing ASCT. Mobilized peripheral blood stem cells collected by apheresis were assessed by multicolor flow cytometry for Ki-67, CD38, CD90, and Notch1 expression on CD34+ cells. Colony-forming capacity was evaluated using methylcellulose assays (CFU-GM, BFU-E, CFU-Mix). Clinical endpoints included neutrophil and platelet recovery. Multivariable linear regression analyses were performed (n = 29).

Results: Twenty-nine patients were included (median age 60 years, range 27–73; 52% male), including 14 with non-Hodgkin lymphoma and 15 with plasma cell dyscrasia. Median times to neutrophil and platelet recovery were 10 (8–12) and 12 (9–18) days, respectively, and median graft viability was 85% (70–97%). Total CD34+ yield correlated inversely with time to neutrophil recovery ($\rho = -0.43$, $p = 0.02$) and showed a trend toward faster platelet recovery ($\rho = -0.36$, $p = 0.06$). Higher BFU-E counts correlated with delayed neutrophil recovery ($\rho = 0.42$, $p = 0.03$). CD34+ dose per apheresis correlated positively with total CD34+ yield ($\rho = 0.70$, $p < 0.001$) and inversely with the number of apheresis procedures ($\rho = -0.68$, $p < 0.001$).
In multivariable analysis including graft, functional, and phenotypic parameters, the neutrophil recovery model showed an R^2 of 0.57 (overall $p = 0.0679$), with total collected CD34+ cells independently associated with faster recovery ($p = 0.043$) and BFU-E independently associated with slower recovery ($p = 0.017$). Biomarker expression on CD34+ cells (Ki-67, CD38, CD90, Notch1) was not independently associated with engraftment kinetics; however, Ki-67 correlated inversely with graft viability and number of apheresis procedures, while CD38 showed a trend toward faster platelet recovery. Within the CD34+ compartment, Ki-67 correlated positively with CD38 and infused CD34+ dose, whereas CD38 and CD90 were inversely correlated. No variables independently predicted platelet recovery.

Conclusions: This exploratory analysis confirms total collected CD34+ cell dose as a key determinant of neutrophil recovery following ASCT, while CFU assays and CD34+ biomarker expression highlight additional biological heterogeneity of mobilized grafts. Although CD34+-associated biomarkers were not independently predictive in this cohort, their associations with graft characteristics and progenitor output support further investigation. Larger, adequately powered studies integrating phenotypic, functional, and immune reconstitution endpoints are warranted to further define the clinical relevance of biomarker-based CD34+ profiling and its integration with CFU assays in predicting post-transplant recovery.

Disclosure: Nothing to declare.

P102

INTRA-APHERESIS RECRUITMENT OF CD34⁺ CELLS IN G-CSF VERSUS G-CSF PLUS PLERIXAFOR MOBILIZATION: ASSOCIATION WITH COLLECTION EFFICIENCY AND FINAL HPC(A) YIELD

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Background: Circulating CD34⁺ hematopoietic progenitor cell (HPC) counts before apheresis [HPC(A)] are routinely used to guide the timing of collection, yet they do not fully account for the marked variability seen in collection efficiency (CE) or final yield. The intra-apheresis recruitment (IAR) of CD34⁺ cells, defined as the proportional increase in available progenitors during the procedure relative to baseline, may be an underappreciated biological factor influencing harvest performance. This study aims to characterize the IAR during HPC(A) through the recruitment ratio (RR) of CD34⁺ cells and examines its relationship with mobilization using G-CSF alone versus G-CSF plus plerixafor.

Methods: A retrospective analysis of HPC(A) procedures was performed between January 2023 and November 2025 at Abu Dhabi Stem Cells Center (ADSCC)/Yas Clinic Khalifa City (YCKC) Hospital in Abu Dhabi, United Arab Emirates. Pre- and post-apheresis CD34⁺ cell counts were recorded together with collection-bag CD34⁺ concentrations and a range of donor and procedure variables. Donors were grouped by mobilization regimen (G-CSF or G-CSF plus plerixafor). For each regimen, CE_1, CE_2, crude CE (cruCE), RR, performance ratio (PR), and total CD34⁺ cell yields were compared. All metrics were calculated using standard formulas.

Results: A total of 265 HPC(A) procedures were performed in 214 donors using the Spectra Optia® Apheresis System (Terumo BCT) with software version 11.0. Mobilization with G-CSF alone was used in 112 donors (55 autologous and 57 allogeneic), while 102 autologous donors received G-CSF plus plerixafor. Donors mobilized with G-CSF plus plerixafor were slightly older and had significantly lower total blood volume (TBV) and lower pre-apheresis CD34⁺ counts compared with those mobilized with G-CSF alone. Sex distribution and the use of MNC versus cMNC protocols were similar between groups. Procedure duration did not differ, although donors receiving G-CSF plus plerixafor had a higher TBV-processed ratio. CE metrics (CE_1, CE_2, crude CE, and PR) and RR were comparable, with no statistically significant differences. However, the final CD34⁺ cell yield was significantly lower in the G-CSF plus plerixafor group (p= 0.006). Table 1 summarizes the donor characteristics and apheresis outcomes.

Table 1. Comparison of donor characteristics and HPC(A) collection outcomes in G-CSF and G-CSF plus plerixafor mobilization

Donor characteristics	**G-CSF (n = 136) Median (IQR) †**	**G-CSF + plerixafor (n = 129) Median (IQR) †**	***p*-values [a]**
Age (years); median (range)	38 (2 – 64)	43 (2 – 67)	0.008 **
Sex			
Female; n (% of total)	43 (38.4)	45 (44.1)	0.408 (NS) [b]
Male; n (% of total)	69 (61.6)	57 (55.9)	
TBV (mL)	4,790 (3,992 – 5,382)	4,502 (3,743 – 5,026)	0.030 *
Preapheresis $CD34^+$ cells (/µL)	47 (29 – 76)	42 (25 – 57)	0.039 *
Apheresis outcomes			
Collection protocol			
MNC; n (% of total)	28 (20.6)	24 (18.6)	0.720 (NS) [b]
cMNC; n (% of total)	108 (79.4)	105 (81.4)	
Duration (min)	264 (230 – 294)	271 (232 – 309)	0.203 (NS)
TBV processed (ratio)	3.0 (2.6 – 3.5)	3.2 (3.0 – 3.7)	0.002 **
$CD34^+$ CE_1 (%)	78.2 (65.6 – 91.2)	73.3 (60.6 – 86.7)	0.070 (NS)
$CD34^+$ CE_2 (%)	68.2 (54.4 – 83.7)	64.9 (50.1 – 75.0)	0.061 (NS)
$CD34^+$ cruCE (%)	73.3 (67.1 – 77.6)	73.9 (67.9 – 79.7)	0.357 (NS)
$CD34^+$ RR (ratio)	1.8 (1.1 – 2.5)	1.8 (1.3 – 2.4)	0.841 (NS)
$CD34^+$ PR @35% (%)	223.6 (187.8 – 260.6)	209.5 (173.3 – 247.8)	0.054 (NS)
$CD34^+$ AY (× 10^6 cells/kg)	5.5 (3.7 – 10.6)	4.7 (2.8 – 7.7)	0.006 **

† Median and IQRs (25^{th}–75^{th} percentiles) unless otherwise specified.
[a] *p*-values calculated using the Mann–Whitney *U*-test unless otherwise specified; [b] *p*-values calculated using the Fisher's exact test. Asterisks indicate levels of statistical significance: * $p < 0.05$ and ** $p < 0.01$.
AY: apheresis yield; *CE:* collection efficiency; *cruCE:* crude CE; *IQR:* interquartile range; *NS:* not significant; *PR:* performance ratio; *RR:* recruitment ratio; *TBV:* total blood volume.

Conclusions: Similar RR and CE outcomes were observed between the two mobilization groups, likely reflecting the inclusion of a substantial proportion of allogeneic donors in the G-CSF cohort, while the G-CSF plus plerixafor group consisted exclusively of autologous donors. Because autologous donors often have varying degrees of bone marrow impairment, some impact on $CD34^+$ cell recruitment before and during HPC(A) was evident in our cohort, although this seemed partly overcome by adding plerixafor to the mobilization protocol.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P103

CANNABIS USE AND ITS RELATIONSHIP WITH MOBILIZATION EFFICIENCY TIME AFTER HSCT IN PATIENTS WITH MULTIPLE SCLEROSIS. A SINGLE CENTER EXPERIENCE IN MEXICO

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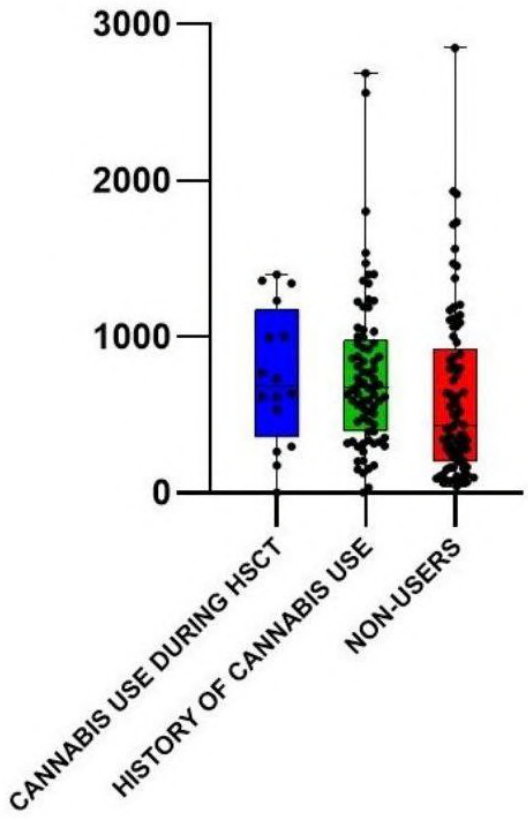
Background: Cannabis use is increasingly common among patients with multiple sclerosis (MS), yet its potential impact on hematopoietic stem cell mobilization and engraftment following autologous transplantation remains largely unexplored. Autologous hematopoietic stem cell transplantation (HSCT) is an effective therapeutic strategy for highly active or treatmentrefractory MS.

Methods: This retrospective single-center study included patients with MS who underwent autologous HSCT between 2018 and 2025. Participants were stratified into three groups according to cannabis exposure: (1) active users during HSCT, (2) patients with a prior history of cannabis use, and (3) non-users. $CD34^+$ cell counts were compared across groups using the Kruskal–Wallis test followed by Dunn's multiple comparison test with Bonferroni correction.

Results: A total of 177 patients were analyzed (16 active users, 76 former users, and 92 non-users). The Kruskal–Wallis test revealed significant overall differences in $CD34^+$ counts among the three groups ($H = 6.53$, $p = 0.038$). Post hoc analysis showed that patients with a history of cannabis use had significantly higher $CD34^+$ mobilization compared with non-users ($p = 0.0478$). No significant differences were found between active users and the other groups, likely due to the smaller sample size of the active-user subgroup ($n = 16$).



Conclusions: A history of cannabis use may be associated with enhanced CD34⁺ progenitor cell mobilization in patients with MS undergoing autologous HSCT, whereas active consumption during transplantation does not appear to confer additional benefit. These findings warrant further investigation in larger, prospective studies to elucidate the underlying biological mechanisms linking cannabis exposure to hematopoietic outcomes.

Disclosure: Nothing to declare

P104

HEMATOLOGIC SHIFTS DURING HPC(A) AND THEIR INFLUENCE ON COLLECTION EFFICIENCY AND CD34⁺ CELL YIELD

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Background: $CD34^+$ hematopoietic progenitor cell apheresis [HPC(A)] induces measurable hematologic changes, including hemoconcentration, redistribution of leukocyte subsets, and platelet loss. These shifts are routinely captured in pre- and post-procedure complete blood counts but remain underutilized as predictors of apheresis performance. This study aims to characterize hematologic changes during HPC(A) and determine their association with collection efficiency (CE) metrics: CE_1, CE_2, crude CE (cruCE), captured cells (CA), and $CD34^+$ apheresis yield (AY).

Methods: A retrospective analysis of HPC(A) procedures was performed between January 2023 and November 2025 at Abu Dhabi Stem Cells Center (ADSCC)/Yas Clinic Khalifa City (YCKC) Hospital in Abu Dhabi, United Arab Emirates. Pre- and post-apheresis $CD34^+$ cell counts were recorded together with collection-bag $CD34^+$ concentrations and a range of donor and procedure variables. CE metrics were calculated using standard formulas. After excluding extreme outliers using the 1.5 × IQR rule, multiple linear regression models were fitted for CE_1, CE_2, cruCE, CA, and AY, including intraprocedural changes in hematocrit, white blood cells, neutrophils, mononuclear cells, and platelets (ΔHCT, ΔWBC, ΔNEU, ΔMNC, and ΔPLT, respectively) as standardized predictors. Δ values were calculated as post- minus pre-apheresis measurements. Standardized regression coefficients (β), 95% confidence intervals, adjusted R^2, and variance inflation factors (VIFs) were also estimated.

Results: A total of 289 HPC(A) procedures were performed in 214 donors using the Spectra Optia® Apheresis System (Terumo BCT) with software version 11.0. The majority of aphereses (n = 264, 91.3%) were performed after mobilization with either G-CSF alone (n = 136) or G-CSF plus plerixafor (n = 128) at standard doses. In the cleaned cohort (n = 225), models explained a modest proportion of outcome variability (adjusted R^2 0.02–0.09). As shown in Table 1, greater platelet decrease was the only consistent independent determinant of CE and AY, being positively associated with CE_1 and CE_2 (β 2.74, 95 % CI 0.38–5.11, p = 0.023; β 3.19, 95 % CI 0.70–5.68, p = 0.012, respectively) and inversely associated with AY (β −0.70, 95 % CI −1.17 to −0.23, p = 0.004). No Δ-variable independently predicted cruCE or CA. Marked collinearity among leukocyte-related predictors (ΔWBC, ΔNEU, ΔMNC; VIF > 700) limited the interpretation of their individual regression coefficients.

Table 1. Multiple linear regression coefficients for CE_1, CE_2, cruCE, CA, and AY of $CD34^+$ cells †

Predictor	CE_1 β (p)	CE_2 β (p)	cruCE β (p)	CA β (p)	AY β (p)
ΔHCT	0.28 (0.804)	-0.71 (0.551)	0.63 (0.181)	3.42 (0.441)	0.17 (0.475)
ΔWBC	-35.70 (0.256)	-37.06 (0.263)	3.51 (0.786)	18.80 (0.878)	-0.08 (0.990)

ΔNEU	35.40 (0.231)	37.77 (0.225)	-3.32 (0.785)	-6.30 (0.956)	-0.07 (0.990)
ΔMNC	3.60 (0.522)	7.60 (0.200)	-2.94 (0.204)	-4.22 (0.847)	-0.46 (0.685)
ΔPLT	2.74 (0.023) *	3.19 (0.012) *	-0.19 (0.700)	4.64 (0.330)	-0.70 (0.004) **

† Predictors were standardized as z-scores, and outcome models were adjusted for ΔHCT, ΔWBC, ΔNEU, ΔMNC, and ΔPLT. Asterisks denote statistical significance: * $p < 0.05$ and ** $p < 0.01$.
AY: apheresis yield; *CA:* captured cells; *CE:* collection efficiency; *cruCE:* crude CE; *HCT:* hematocrit; *MNC:* mononuclear cells; *NEU:* neutrophils; *PLT:* platelets; *WBC:* white blood cells.

Conclusions: ΔPLT emerged as the only robust predictor across all models, showing a positive association with CE_1 and CE_2 and an inverse association with AY. The remaining Δ-variables offered no independent contribution once multicollinearity was accounted for. Intra-apheresis platelet dynamics may therefore serve as a practical biomarker of apheresis system performance. Moreover, these findings may support further investigation into the emerging "G-CSF steal" phenomenon in donors mobilized with filgrastim.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P105

EFFICACY AND SAFETY OF PLERIXAFOR SALVAGE HEMATOPOIETIC STEM CELL MOBILIZATION IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A STUDY OF HETEROGENEOUS RESPONSES

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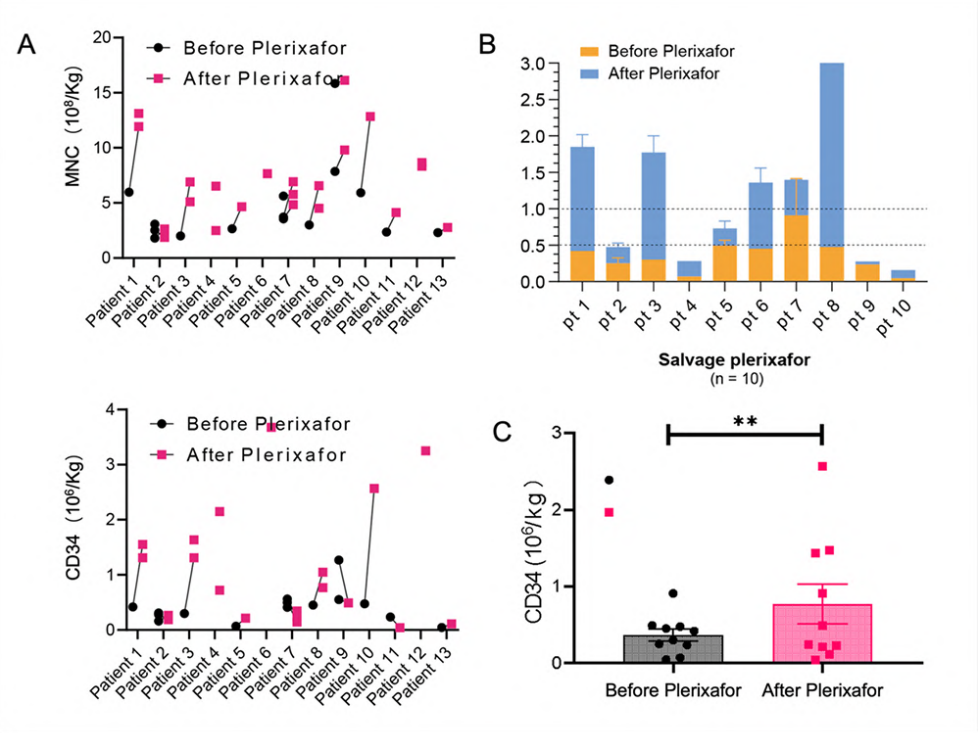
Background: Hematopoietic stem cell mobilization failure remains a challenge for autologous stem cell transplantation (ASCT) in B-cell acute lymphoblastic leukemia (B-ALL). While Plerixafor is a standard rescue agent for mobilization in other malignancies, its efficacy in B-ALL is less defined, and theoretical concerns regarding leukemic cell mobilization persist. This study evaluates the clinical utility of Plerixafor in B-ALL, focusing on response variability and relapse safety.

Methods: We analyzed B-ALL patients from the NICHE cohort (NCT04645199) mobilized between 2004 and 2024. Patients received standard G-CSF-based regimens. Plerixafor was administered as a salvage strategy in patients failing to achieve sufficient $CD34^+$ yields

(n=10) or preemptively in high-risk cases who are predicted to have poor mobilization (n=3). We assessed CD34⁺ collection yields, individual response patterns, and post-transplant relapse rates.

Results: Preemptive use of Plerixafor in 3 high-risk patients resulted in successful collection in all cases. In the salvage setting (n=10), responses to Plerixafor were heterogeneous but statistically beneficial overall. As shown in Figure 1, Plerixafor administration significantly increased the mean CD34⁺ cell yield compared to pre-treatment levels ($P < 0.01$). However, individual outcomes varied: while a subset of patients (responders) achieved substantial yield improvements (e.g., >3-fold increase) enabling successful transplantation, others showed limited incremental benefit, highlighting the biological heterogeneity of mobilization failure in B-ALL. Importantly, despite concerns about tumor contamination, the cell collection following plerixafor administration did not exhibit an increased MRD-positive rate as determined by flow cytometry-based MRD assessment, and Plerixafor usage was not associated with an increased risk of disease recurrence. Long-term follow-up confirmed that patients receiving Plerixafor did not exhibit higher rates of relapse compared to standard mobilization controls.



Conclusions: Plerixafor serves as a viable salvage option for B-ALL patients with mobilization failure. While pharmacological interventions is variable, with distinct subgroups of responders and non-responders, its application leads to a statistically significant overall improvement in stem cell yields. Furthermore, Plerixafor appears safe in this context, offering a potential pathway to ASCT without elevating relapse risk.

Clinical Trial Registry: NCT04645199; https://clinicaltrials.gov/study/NCT04645199

Disclosure: Nothing to declare.

P106

INCREASED RISK OF POOR MOBILIZATION AFTER QUADRUPLE THERAPY IN MULTIPLE MYELOMA

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Background: The use of quadruple induction regimens in first-line therapy has improved outcomes in transplant-eligible patients with multiple myeloma (MM). However, increasing evidence suggests that intensified induction, particularly daratumumab-containing regimens, may adversely affect peripheral blood stem cell (PBSC) mobilization, mainly when granulocyte colony-stimulating factor (G-CSF) alone is used. This study evaluates PBSC mobilization outcomes and apheresis efficiency in MM patients undergoing autologous hematopoietic stem cell transplantation after quadruple versus triple induction therapy.

Methods: The study was performed by the Hematopoetic stem Cell Clinic from Fundeni Clinical Institute in collaboration with the Multiple Myeloma National Registry and included patients mobilized between January 2020 and December 2025. The inclusion criteria were patients with MM in first-line treatment mobilized with G-CSF. The lot was divided into two categories: patients who received triple (proteasome inhibitor, an immunomodulatory agent, or cyclophosphamide, and dexamethasone) or quadruple therapy (daratumumab in addition to triple therapy). Poor mobilizer was defined as a patient mobilizing fewer than 20 CD34+ cells/μL into the peripheral blood after G-CSF, or collecting fewer than 2 × 106 CD34+ cells/kg.Statistical analysis was performed using IBM SPSS Statistics Version 25 (IBM Corp., Armonk, NY, USA). The categorical data were analysed with a chi-squared test. Continuous data were reported as the median and interquartile range (IQR). The differences between groups were analysed with the Mann-Whitney test.

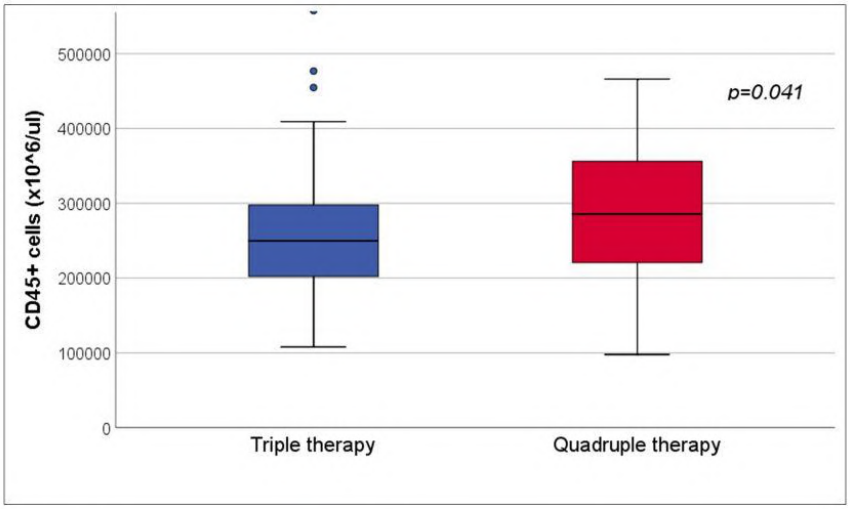
Results: We analyzed 150 patients, including 72 males (48%), with a median age of 57.3 years; 65.7% had cytogenetic high risk. Triple therapy (TT) was administered to 80 patients (53.3%), while 70 patients (46.7%) received quadruple therapy (QT).
In both groups, the CD34+ peak was reached on the fifth day after G-CSF initiation. In the QT group, higher peripheral leukocyte counts were observed (p=0.021), but fewer CD34+ cells in peripheral blood compared to patients treated with TT (p=0.000) (Table 1). Poor mobilizers were more frequent among patients who received QT than those who received TT (36.25% vs. 14.28%, p=0.002).
Regarding the apheresis product, the number of CD45+ cells was lower in the TT group

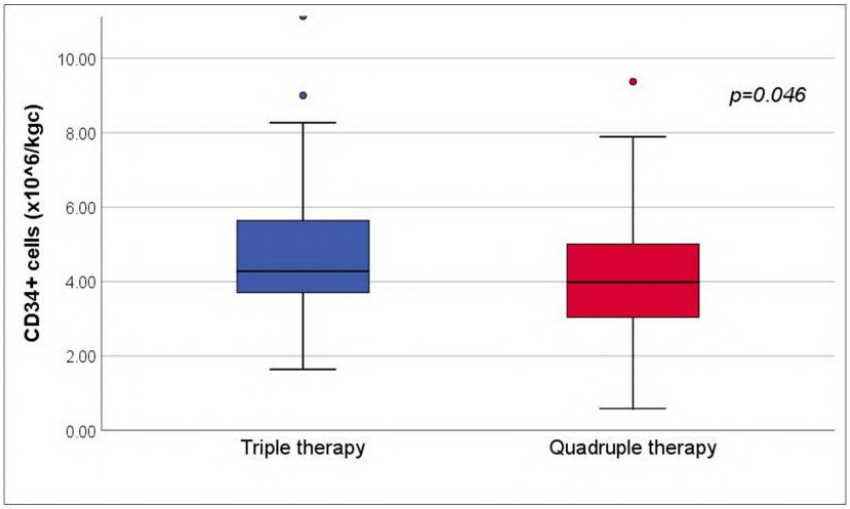
compared with the QT group (p=0.041). However, the number of collected CD34+ cells/kg was significantly lower in patients treated with QT compared with the TT group (median 3.45 vs. 4.28 CD34+ cells/kg, p=0.046) (Figure 1).

Table 1. Mobilization outcomes

	Triple therapy (n=70)	**Quadruple therapy (n=80)**	**p**
Poor mobilizers	10 (14.28%)	29 (36.25%)	0.002
CD34+ peak day - median (IQR)	5 (0)	5 (1)	0.008
Maximum PB CD34+/µl - median (IQR)	36 (27)	27 (22)	0.000
WBC PB (x10^9/L) on apheresis day - median (IQR)	50.87 (17.55)	53.68 (23.19)	0.021

Abbreviations: IQR=interquartile range; PB=peripheral blood; WBC=white blood cell count





Conclusions: In this cohort, quadruple induction therapy was associated with poorer peripheral blood stem cell mobilization compared with triple therapy. Despite similar CD34+ peak timing, patients receiving quadruple therapy showed lower peripheral blood CD34+ counts, a higher rate of poor mobilizers, and fewer CD34+ cells/kg collected by apheresis. These findings are consistent with previously published data suggesting that daratumumab-containing induction regimens may negatively impact PBSC mobilization, particularly when G-CSF alone is used. Further prospective studies are required to define optimal mobilization strategies in this setting better and to determine how to mitigate the adverse effects of quadruple therapy on stem cell collection.

Disclosure: Nothing to declare.

P107

SUCCESS OF HEMATOPOIETIC ENGRAFTMENT AFTER LONG-TERM CRYOPRESERVATION OF PERIPHERAL BLOOD HEMATOPOIETIC STEM CELLS

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Background: Autologous Stem Cell Transplantation (ASCT), using apheresis-collected cells after mobilization, remains a relevant treatment for several hematological malignancies. These cells are immediately cryopreserved for storage until transplant. In some cases, allogeneic cells also require cryopreservation for subsequent infusion (Allo-SCT).
The efficacy of these cells in reconstituting hematopoiesis is well-established, with a target dose of CD34+>2×10^6/kg ensuring a reliable engraftment, including neutrophil recovery and platelet transfusion independence by day +14. Standard cryopreservation (using 5-10% DMSO and controlled-rate freezing) has minimal impact on engraftment when cells are short-term stored.
Transplant is usually performed in a short period of time after cryopreservation. However, due to complications or the need for a second ASCT, infusion may be significantly delayed, requiring the use of long-term stored cryopreserved cells. While successful bone marrow engraftment and cellular viability in long term cryopreserved hematopoietic stem cells (HSC) have been reported, data on the long-term engraftment outcomes of cryopreserved Peripheral Blood HSC (PB-HSC) remain scarce. Therefore, the objective of this work was to evaluate the engraftment results of long-term stored PB-HSC.

Methods: This study included data from 13 consecutive patients who underwent ASCT or allo-SCT between 2013 and 2025 using PB-HSC long-term stored (more than 1 year). Variables analyzed included cryopreservation time (months), infused cell dose (CD34x10^6/kg), pre- and post-thaw viability, transplant and disease characteristics and engraftment (days to absolute neutrophil count (ANC) and platelet recovery).

Results: With a median age of 54 years (range 31-68). The most common underlying disease was multiple myeloma (38.5%). The majority of patients were in complete response (69.2%) and underwent autologous transplantation (92.3%). All patients (100%) were mobilized using only G-CSF. The median collected cell dose was CD34+ 3.77×10^6/kg (range 2.09–32.5), and the median pre-cryopreservation viability was 99%.
The median cryopreservation time for the infused products was 38 months (range 12 – 58 months), with some products stored for nearly five years. The median infused dose was CD34+ 3.50×10^6/kg. While median post-thaw viability was 81%. No primary engraftment failure was reported. Median time to achieve ANC >0.5×10^9/L was 11 days (range 10-16), and the median time to achieve platelet recovery >20×10^9/L was also 11 days (range 9-42).

These times are consistent with results typically reported for fresh or short-term cryopreserved PB-HSC. Table 1 and Figure 1.

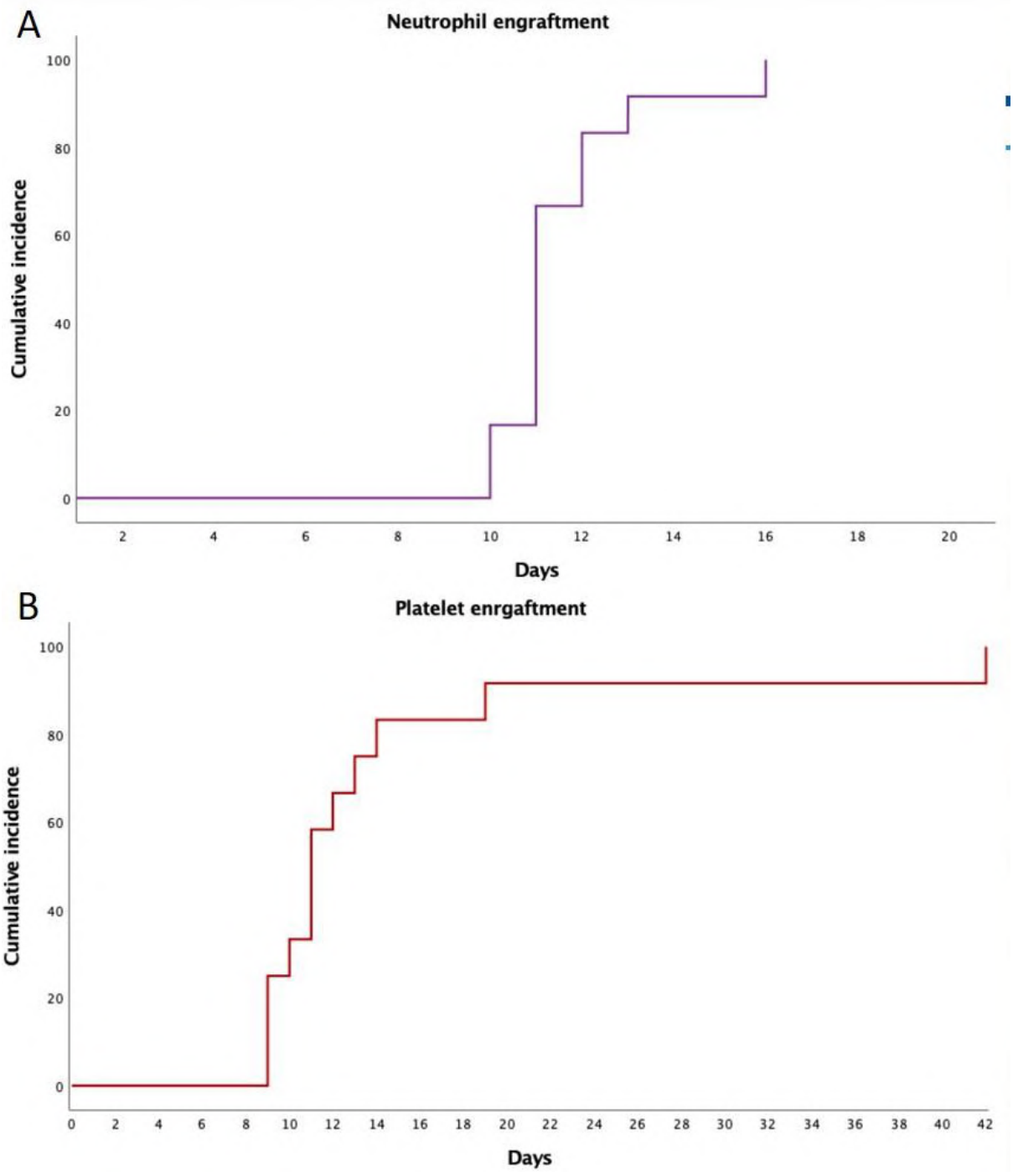
Table 1. Transplant characteristics

Variable	**N=13**
Sex male/female, n (%)	7 (53,8) / 6 (46,2)
Age, median (range)	54 (31-68)
Disease, n (%) Multiple Mieloma Non-Hodgkin Lymphoma Hodgkin Lymphoma Amyloidosis Acute lymphoblastic leukemia	 5 (38,5) 3 (23,1) 3 (23,1) 1 (7,7) 1 (7,7)
Disease status, n (%) Complete response Partial response	 9 (69,2) 4 (30,8)
Autologous/allogeneic transplant, n (%)	12 (92,3) / 1 (7,7)
Single/Double transplant, n (%)	10 (76,9) / 3 (23,1)
G-CSF mobilization, n (%)	13 (100)
Apheresis collection days, median (range)	1 (1-2)
CMN x10^8/kg collected, median (range)	8,27 (2,42-20,90)
CD34+ x10^6/kg collected, median (range)	3,77 (2,09-32,5)
Fresh viability, medium (range)	99 (98,00-100,00)
Cryopreserved time in months, median (range)	38 (12-58)
CMN x10^8/kg infused, median (range)	5,70 (1,28-20,90)
CD34+ x10^6/kg infused, median (range)	3,50 (2,09-16,25)
Post-thaw viability, median (range)	81 (55,00-89,00)
Conditioning, n (%) BEAM BuMel Mel200 Z-BEAM Rt+Cy	 4 (30,8) 3 (23,1) 3 (23,1) 2 (15,4) 1 (7,7)

G-CSF days after infusion, median (range)	5 (0-12)
Graft failure, n (%)	0 (0)
Engraftment Neutrophils >0,5 x10^3/µL, median (range) Platelets > 20 x10^3/µL, median (range) Platelets > 50 x10^3/µL, median (range)	 11 (10-16) 11 (9-42) 20 (11-91)

Figure 1. Engraftment. A) Neutrophil engraftment (ANC >0.5×10^9/L) and B) Platelet

engraftment (Platelets >20×10^9/L)



Conclusions: This study confirms the safety of long-term stored PB-HSC, with no reported cases of graft failure and rapid recovery of neutrophils and platelets similar to the results with those cryopreserved for a short period, indicating that prolonged storage does not

significantly compromise the clinical efficacy of the graft. These findings need to be confirmed in longer series.

Disclosure: Nothing to declare.

P108

MANAGING STEM CELL MOBILISATION FAILURE: LITERATURE REVIEW AND A CASE OF HIGH-DOSE PLERIXAFOR WITH TWICE DAILY G-CSF MOBILISATION STRATEGY FOR AUTOLOGOUS STEM CELL TRANSPLANTATION

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Background: High dose chemotherapy followed by autologous stem cell transplant (ASCT) is a curative therapy for a number of haematologic and non-haematologic malignancies. This requires successful mobilisation and collection of a sufficient dose of peripheral blood stem cells. Standard approaches for mobilisation involve the use of granulocyte colony-stimulating factor (G-CSF) either alone or in combination with chemotherapy. In patients who fail mobilisation, the addition of plerixafor can significantly increase the peripheral blood $CD34^+$ cell count. However, literature guidance on management when plerixafor fails is limited. Furthermore, plerixafor access is often limited by cost or reimbursement criteria. This presents a clinical challenge in patients dependent on adequate mobilisation and collection in order to proceed to curative ASCT.

Methods: A literature review was undertaken to inform management of a 43-year-old man with relapsed germ cell tumour (GCT) who was referred for ASCT. He failed two mobilisation attempts with combined chemotherapy, G-CSF and plerixafor at standard dosing of 240mcg/kg/day. Bone marrow biopsy and cytogenetic studies did not reveal a cause for mobilisation failure. He had previously received pelvic irradiation which was felt to be the mechanism. PubMed and Google Scholar were searched for relevant studies evaluating plerixafor and G-CSF dosing regimens. Key findings are summarised in Table 1. The patient provided informed consent to proceed with additional mobilisation attempts using a novel high dose mobilisation regimen.

Table 1: Plerixafor and G-CSF study summary

Plerixafor			
Study	Study design & participants	Drug regimen	Outcomes
Pantin et al. 2017[1]	Phase 2, open-label, randomised trial;	480 mcg/kg vs 240 mcg/kg; subcutaneous; n = 24.	Higher $CD34^+$ AUC over 24 h with 480 mcg/kg

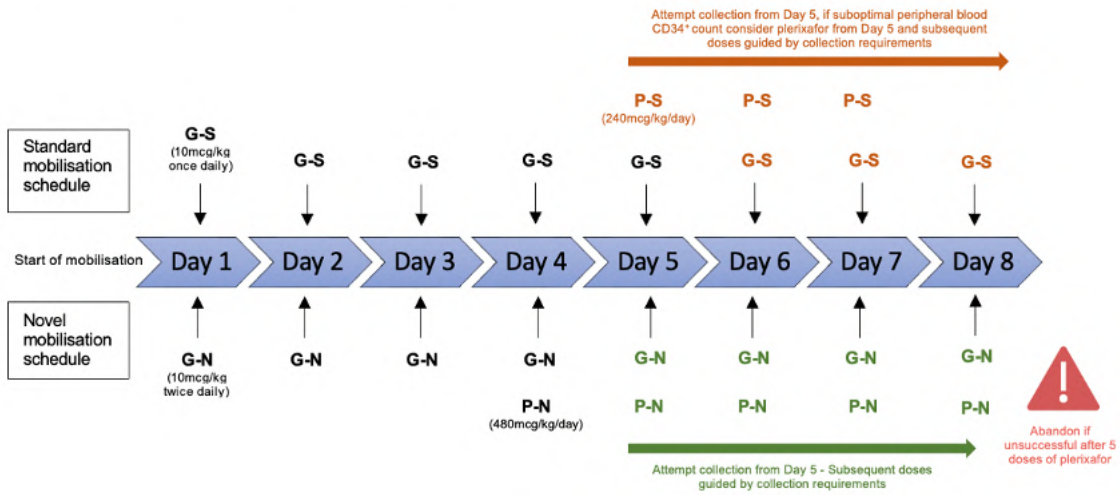
	healthy donors; n = 24		dose. No grade 3 – 4 adverse reactions.
Schroeder et al. 2017[2]	Phase 1/2, open-label trial; healthy donors. Phase 1: n = 21; Phase 2: n = 29	Phase 1: Escalating IV doses 80 – 480 mcg/kg + 240 mcg/kg SC on day 6. Phase 2: 320 mcg/kg IV.	Optimal IV dosing: 320 mcg/kg.
Cashen et al. 2017[3]	Phase 1/2 trial; autologous donors with lymphoma/myeloma. Phase 1: n = 25; Phase 2: n = 36	Phase 1: Plerixafor 160 – 400 mcg/kg IV+ G-CSF. Phase 2: Plerixafor 400 mcg/kg IV + G-CSF.	No efficacy difference between 160 – 400 mcg/kg. Similar adverse reactions rates.
G-CSF			
Study	Study design & participants	Drug regimen	Outcomes
Martinez et al. 1999[4]	Randomised trial; healthy donors; n = 40	10 mcg/kg every 12 h (n = 20) vs 10 mcg/kg every 24 h (n = 20) Apheresis from day 5; PBSC.	Higher $CD34^+$ cells collected in 12 h dosing vs 24 h dosing group ($5.9x10^6$/kg vs $3.1x10^6$/kg) after single apheresis. No discontinuation due to intolerance.
Seggewiss et al. 2003[5]	Retrospective analysis; autologous donors with underlying malignancy; n = 113	300 - 480 mcg/day (n = 55) vs 600 - 900 mcg/day (n = 58); SC.	Higher $CD34^+$ cells/L in 600 – 900 mcg/day vs 300 - 480 mcg/day group ($174x10^6$/L vs $92x10^6$/L).

AUC: Area Under Curve; G-CSF: Granulocyte colony-stimulating factor; IV: intravenous, SC: subcutaneous; PBSC: peripheral blood stem cells.

Results: Mobilisation was successful with the use of high-dose plerixafor (480 mcg/kg/day) and twice daily G-CSF (10 mcg/kg). Adequate $CD34^+$ stem cells were collected for three consecutive transplants over three days of leukapheresis (Spectra Optia), yielding a total volume of 815 mL and stem cell dose of $6.09x10^6$ $CD34^+$ cells/kg. The patient did not experience any adverse reactions related to this dosing regimen. In vitro assessment of viability demonstrated adequate function with an average post-cryopreservation viability of 50% and CFU-GM ranging from 0.23 to 2.25 $x10^4$/kg. The patient proceeded to the first cycle of high-dose therapy, receiving approximately 2.15 $x10^6$ $CD34^+$ cells/kg. Neutrophil and platelet engraftment were achieved by day 23 and 30, respectively, with the delayed engraftment attributed to prior pelvic irradiation. Unfortunately, the patient died from progressive disease. Contemporary literature suggests higher plerixafor doses may be effective in healthy donors and non-GCT patients; however, evidence supporting its use

specifically in GCT are lacking. The optimal dose and duration of plerixafor in difficult mobilisers are also poorly defined[1–3]. Based on data in healthy volunteers and haematology patients, we developed a novel mobilisation schedule incorporating high-dose plerixafor and G-CSF (Figure 1).

Figure 1: Novel versus standard mobilisation schedule.



Conclusions: This case highlights a significant mobilisation challenge in those undergoing ASCT. It provides valuable reassurance that successful mobilisation can be achieved using a novel approach with high-dose plerixafor in combination with twice-daily G-CSF, even in demonstrated poor mobilisers. However, access to this intensified regimen required extraordinary funding approval, which may limit its feasibility and broader implementation in resource-constrained settings.

Disclosure: Nothing to declare

Stem cell donor

OS03-06

OLDER MATCHED SIBLING DONOR VS YOUNG HAPLOIDENTICAL DONOR FOR ALLOGENEIC TRANSPLANTATION WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE IN SECONDARY ACUTE MYELOID LEUKEMIA: A STUDY FROM THE ALWP/EBMT

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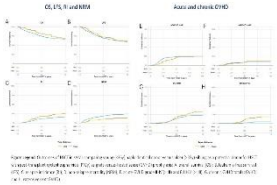
Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative therapeutic option for secondary acute myeloid leukemia (sAML). Whether a young haploidentical donor (yHaplo) is preferred over an older sibling donor (oMSD) for HSCT with post-transplant cyclophosphamide (PTCy) in sAML is unknown.

Methods: The study aimed to assess whether a yHaplo (<35 y)median 27.7y is preferential to oMSD (≥ 35 y) median 57.9y for sAML patients (pts) undergoing HSCT in first complete remission (CR1) with PTCy, between 2012 and 2022. Statistical tests included a multivariable analysis (MVA).

Results: 406 pts were included (yHaplo=306, oMSD=100). Median follow-up was 2.4 y, and the median year of transplant was 2019 (interquartile range [IQR], 2017-2021), with no significant difference between the two donor groups. Median pt age was 58.9 y (IQR, 52.9-63.4), and 61.6% were male, comparable between the groups. The antecedent hematological disease was myelodysplastic/myeloproliferative disorder in both groups, 86.3% vs. 82%(p=0.92). The cytogenetic risk was categorized as intermediate (65.2% vs. 61.4%), adverse (33.6% vs. 37.5%), and favorable (1.2% vs. 1.1%) in the yHaplo and oMSD groups, respectively (p = 0.79) (data missing for 71 pts). Median time from diagnosis to transplant was significantly longer for yHaplo vs. oMSD, being 5.1 vs. 4.1 months, respectively (p<0.001). Bone marrow was the stem cell source in 19% of the yHaplo vs. 5% of the oMSD grafts (p<0.001), following myeloablative conditioning (MAC) in 56.4% vs. 51% (p=0.35). PTCy was most frequently combined with cyclosporine A /mycophenolate mofetil-based immunosuppression as graft-*versus*-host disease (GvHD) prophylaxis. Thiotepa/busulfan (Bu)/Fludarabine (Flu) was the most frequent conditioning in yHaplo pts, while it was Bu/Flu in the oMSD group. Day +30 absolute neutrophil count ($\geq$0.5 x 10^9/L) was inferior in yHaplo compared to oMSD 83.9% vs. 93.8%, hazard ratio (HR) 0.6 (95% CI, 0.43-0.82, p=0.002). Day +60 platelet count (>20,000) was 78.2% vs. 90.4%, respectively. Day +180 incidence of acute (a) GvHD II-IV was 24.5% vs. 25.2 % and of III-IV it was 8.3% vs. 11.6%, respectively. The 2-y total and extensive (ext) chronic (c) GvHD were 26.2% vs. 36.5% and 5.4% vs. 20.2 %, respectively. In MVA analysis, ext cGvHD was significantly lower in the yHaplo compared to the oMSD groups, with an HR 0.38 (95% CI, 0.18-0.78, p=0.008), while aGvHD II-IV and III-IV and total cGvHD did not differ significantly. The 2-y non-relapse mortality (NRM) was higher in HSCTs from yHaplo compared to those from oMSD, being 24.6% vs. 19% (HR 1.86; 95% CI, 1.07-3.2, p=0.028). The main cause of death was sAML, accounting for 40.2% vs. 66.7% of deaths, respectively. The 2-y overall survival (OS:59.6% vs. 49.4%), GvHD-free, relapse-free survival (GRFS: 45% vs. 33.5%), leukemia-free survival (LFS: 53.6% vs. 45.4%), and relapse incidence (RI: 21.8% vs. 35.7%) (Figure) did not differ significantly between the two groups.



Conclusions: HSCT with PTCy for sAML in CR1, from yHaplo vs oMSD, resulted in similar transplantation outcomes, besides a higher incidence of NRM and slower neutrophil engraftment, while a lower incidence of ext cGvHD in the yHaplo compared to the oMSD.

Disclosure: Nothing to disclose

OS10-01

COMPARISON OF UD9/10 WITH DQB1 MISMATCHES VS UD10/10 IN PATIENTS WITH AML TRANSPLANTED IN CR, A STUDY ON BEHALF ON THE ALWP

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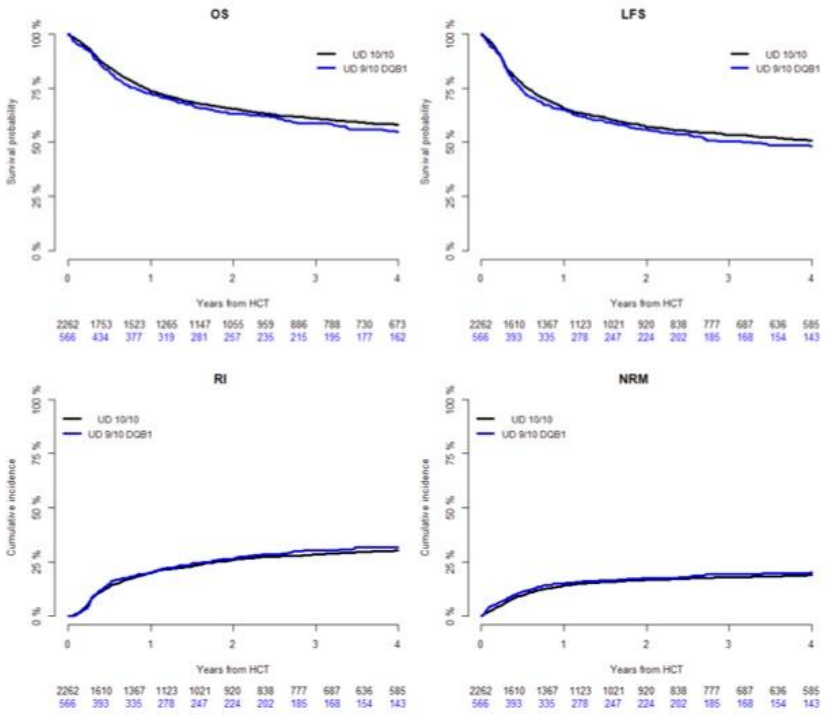
Background: In 8/8 matched unrelated donor (MUD) transplants (HCT), strong linkage disequilibrium between HLA-DRB1 and HLA-DQB1 results in concordance at the DQ locus, yielding a 10/10 match, although isolated DQB1 mismatches still occur. The clinical impact of isolated single HLA-DQB1 mismatching in otherwise fully MUD (UD 9/10) HCT remains uncertain. While disparities in HLA-DQB1 have been reported to be permissive, EBMT guidelines still consider DQB1 during donor selection. With increasing use of reduced-intensity conditioning and evolving GvHD prophylaxis the contemporary significance of DQB1 mismatching warrants re-evaluation.

Methods: We conducted a registry-based study on behalf of the ALWP on adult AML patients in CR undergoing first allogeneic HCT from UD between 2010–2024, with full high-resolution HLA typing at A, B, C, DRB1, and DQB1. HCT from UD 10/10 or UD 9/10 with isolated DQB1 mismatch were included. 16,083 MUD and 627 9/10 were available. A pair-match analysis (1:4) between UD 9/10 with isolated DQB1 mismatch and UD 10/10 was performed based on age at HCT, year of HCT, stem-cell source, disease status, ELN2022 cytogenetics, KPS, patient sex, regimen intensity, use of PTCY and invivo TCD, female-to-male sex matching.

The primary objective was the impact of isolated HLA-DQB1 mismatching on post-transplant outcomes.

Results: Among the 16,710 patients included, the median age at transplant was 57.7 years. Disease status at HCT included 82.5% in CR1. Peripheral blood was the predominant graft source (94.6%). MAC regimen was performed in 42.7%. GvHD prophylaxis included ATG, PTCy and Campath respectively in 68.3%, 9.6% and 7.9% of patients. Median donor age was 28.9 years, 28.8 in UD 10/10 and 31.5 in UD 9/10 DQB1.After matching, 2,828 patients were included (UD10/10 n=2,262; UD9/10 DQB1 n=566). Median donor age remained lower in the UD 10/10 group (28.8 vs 31.5).
With a median follow-up of 4.1 years, HCT outcomes did not differed by HLA matching (figure). In UD 10/10 and in 9/10 DQB1-mismatched recipients, 2y-OS was 65.6% (95%CI 63.4–67.6) and 63.1% (58.7–67.2) (HR 1.09, 0.95–1.27; p=0.23), 2y-LFS was 57.2% (55.0–59.4) and 56.0% (51.5–60.3), (HR 1.06, 0.93–1.22; p=0.38), 2yRI was 26.0% and 26.4% (HR 1.06, 0.89–1.27; p=0.48), and 2y-NRM was 16.7% and 17.6% (HR 1.06, 0.86–1.32; p=0.57), respectively.
The cumulative incidence of grade II-IV aGvHD by day 100 was 26.6% (95%CI 24.7–28.5) and 22.5% (95%CI 19.1–26.1) (HR 0.86, 0.72–1.03; p=0.11), while grades III–IV was 9.5% and 6.9% (HR 0.77, 0.56–1.06; p=0.11). cumulative incidence of 2y cGvHD was 34.4% (32.2–36.6) and 29.4% (25.3–33.7) (HR 0.81, 0.68–0.98; p=0.03), and extensive/severe cGvHD 10.0% and 5.7% (HR 0.55, 0.37–0.81; p=0.002), respectively.



Conclusions: This study demonstrates that isolated HLA-DQB1 mismatching does not affect 2y OS, LFS, RI, or NRM after unrelated donor HCT in AML in CR, confirming its limited clinical relevance when high-resolution matching at A, B, C, and DRB1 is performed. Cumulative

incidence of cGvHD was lower among DQB1-mismatched recipients. This findings may be related to different practice among centers in immunosuppression tapering or experience and deserve further investigations.

Clinical Trial Registry: Not applicable.

Disclosure: No disclosure.

OS10-02

A MACHINE LEARNING APPROACH COMBINING HLA AND NON-HLA FACTORS TO SUPPORT SELECTING THE "BEST" DONOR: ANALYSIS ON 7,609 TRANSPLANTS AND A READY-TO-USE INTERACTIVE TOOL

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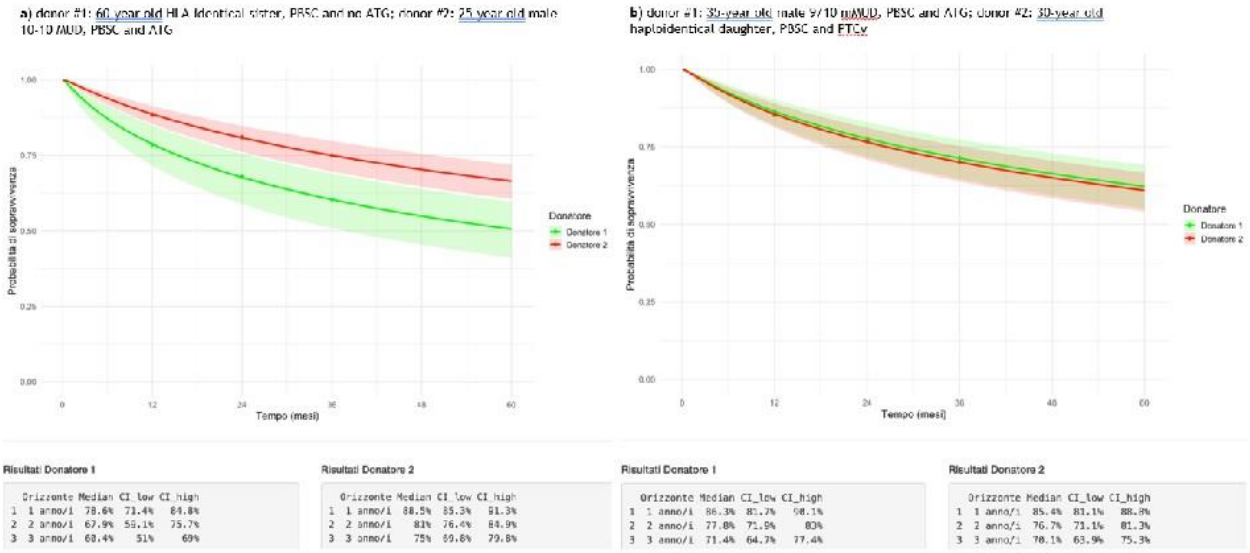
Background: The selection of a donor for allogeneic HSCT is a complex, multi-factorial challenge that requires balancing HLA compatibility with non-HLA factors, including more recent pharmacological advances like PTCy for GvHD prophylaxis. We addressed here the need for interpretable and data-driven decision support by developing a comprehensive framework based on a Bayesian hierarchical Accelerated Failure Time (AFT) model, built on 7,609 HSCTs perfomed in Italy between 2014 and 2024.

Methods: Anonymous data on adult patients were collected on behalf of the Gruppo Italiano per il Trapianto di Midollo Osseo, cellule staminali emopoietiche e terapia cellulare (GITMO). After the selection of those informative from over 24,000 HSCTs, the final dataset maintained comprehensive information on patient demographics, donor characteristics, HLA compatibility, transplantation procedures and post-HSCT outcomes. The final model provides the risk of post-transplant mortality according to the donor type taking into account the main non-HLA factors and importantly, the patients' and disease characteristics. The use of PTCy, anti-thymocyte globulin (ATG) or calcineurin (CNI)-based prophylaxis is also considered.

Results: HLA compatibility between patients and their respective donors was categorised into four donor groups: HLA-identical siblings, haploidentical, 10/10-matched (MUD) and 9/10-mismatched unrelated donors (mMUD). Estimates coefficients are calculated for each of the following variables: patients' and donors' age, disease status, conditioning regimen, performance status at HSCT, stem cell source, donor type; interaction effects between donor type and GvHD prophylaxis were identified. External validation was performed using a held-out test set created through random split (80% training, 20% testing) with stratified sampling to preserve event rate proportion. The robustness and interpretability of the model led us to start to build up an interactive tool to support the donor search, i.e. between an older HLA-identical sibling vs. a younger MUD or a mMUD vs. a haploidentical. The current

version is tailored for two donor options. After having provided baseline input information on patient's status, disease and HSCT, and then information on donor options #1 and #2, the model gives back two survival curves, one associated with each donor for direct comparison between the two options (see Figure 1).

Figure 1. Predicted survival curves for two donor candidates for the same patient type, a 55-year old man with acute leukemia in CR1



Conclusions: In conclusion, our model trained on a large multicenter dataset showed to efficiently combine HLA and non-HLA factors across different donor types and GvHD prophylaxis, for the prediction of post-transplant survival. The output might be used to support the choice of the "best" stem cell donor during the selection process. At the time of writing, a web-based tool is under evaluation for research or clinical purposes.

Clinical Trial Registry: N/A.

Disclosure: There are no conflict of interest to declare.

OS10-04

MATCHED UNRELATED VS. HAPLOIDENTICAL DONOR FOR ALLOGENEIC HSCT IN PATIENTS WITH ACUTE LEUKEMIA WITH IDENTICAL GVHD PROPHYLAXIS – A RANDOMIZED PROSPECTIVE EBMT LABELED TRIAL

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Background: Haplo-identical allogeneic cell transplantation (haploHCT) is increasingly used if no matched related or unrelated donor (MUD) is available. Retrospective studies suggest a stronger GvL effect after haploHCT

Methods: To test the hypothesis that haploHSCT reduces the risk of relapse by 10% we performed an open label, two-arm, multicenter, multinational, randomized phase II trial comparing anti-leukemic activity of HCT for patients with acute leukemia in CR between a MUD and a haploidentical donor using identical GvHD prophylaxis consisting of PTCy, Tacrolimus and MMF. Major inclusion criteria were AML intermediate and adverse risk according ELN and ALL and MDS high risk in CR, age 18-70 years , and availibility of 10/10 HLA MUD and haplo-identical (≥ 5/10 and ≤8/10 HLA) relative donor.
To detect a difference of 10% in relapse incidence at 2 years, 220 patients per arm are needed. A planned interim and futility analysis was performed after 171 patients were included and 158 pts were randomized to MUD (n=78) or HaploHCT (n= 80).

Results: The median age of the pts was 56 years (range 18-70), Disease and patient characteristics were well balanced in both arms. Due to the unavailability of the donor assigned by randomization, 6/69 pts randomized to MUD received a Haplo HSCT and 5/71 pts randomized to HaploHSCT received a MUD; thus, according to Intention to treat (ITT), 78 pts were assigned to MUD while 68 pts received MUD according per protocol (PPP), and in the Haplo HSCT group 80 pts were analyzed acc. ITT and 72 pts according PP, respectively. The cumulative incidence of relapse at 2 years for MUD and Haplo was 33% (95%CI: 20-46) und 28% (95% CI: 17-42) acc. ITT (p=0.9) and 25% (95%CI:13-39) and 29% (95%CI:17-42) acc. PP (p=0.4), respectively. The NRM at 1 year for MUD vs Haplo was 3% (95%CI: 0.5-9) vs 5% (95% CI:2-12) acc. ITT and 5% (95%CI: 1-12) vs 4% (95%CI:1-11) acc. PPP (p=0.9), respectively , resulting in an EFS of 60% vs 64% acc. to ITT- and 65% vs 65% to PPP (p=0.7) and a 2 year OS of 68% vs 77% in the ITT – and 74% vs 75% acc PP (p=0.77), respectively. The GRFS at 2 years acc. to PP was 61% (95% CI: 48-78) for MUD and 60% (95%CI: 47-75) for HaploHCT (p=0.5).
PGF occurred in 3 pts, all after Haplo-HCT, and the median time to neutrophile and platelet engraftment was 18 and 16 days after MUD (p=0.16) and 19 and 23 days after HaploHCT (p= 0.03). The incidence of any acute and cGvHD and SAE did not differ between both arms.

The DSMB recommend stopping recruitment because it is unlikely to show a 10% superiority of HaploHCT to MUD regarding relapse incidence with the planned sample size.

Conclusions: The planned interims analysis of the randomized study comparing 10/10 MUD with haplo-identical HCT using identical PTCy based GvHD prophylaxis showed similar relapse incidence, comparable GvHD incidence, low NRM and favourable outcome in both arms and further recruitment will unlikely show superiority regarding 10% reduction in relapse after HaploHCT.

Clinical Trial Registry: The study was registered under ClinicalTrial.gov: (NCT04232241

Disclosure: The study was supported in part by DKMS
None of the authors has COI in this study

OS10-06

LETERMOVIR ELIMINATES SURVIVAL DIFFERENCES ACROSS RECIPIENT/DONOR CMV SEROLOGY COMBINATIONS IN MATCHED UNRELATED DONOR ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Recipient cytomegalovirus (CMV) seropositivity has historically been associated with increased non-relapse mortality (NRM) following allogeneic stem cell transplantation (allo-SCT). Previous studies have also demonstrated meaningful differences in outcomes across specific recipient/donor CMV serostatus combinations (R+/D+, R+/D-, R-/D+, R-/D-). With the introduction of letermovir prophylaxis into routine clinical practice, it is unclear whether these historically relevant serostatus-related risk differences persist. This study evaluates the impact of letermovir on overall outcomes and, in particular, on the heterogeneity between CMV serology combinations.

Methods: We conducted a retrospective study of 1,353 adult patients undergoing matched unrelated donor (MUD) allo-SCT between 2010 and 2024. Letermovir prophylaxis was implemented in 2022. Patients were divided into a pre-letermovir era (2010-2021; n=1,062) and a post-letermovir era (2022-2024; n=291). The pre-letermovir era was further divided into early (2010-2015) and late (2016-2021) cohorts to account for temporal improvements in supportive care. Outcomes assessed included NRM, relapse, overall survival (OS), progression-free survival (PFS), and acute and chronic GVHD. Subgroup analyses compared all four recipient/donor CMV serostatus combinations.

Results: In the post-letermovir era, 1-year NRM was similar between CMV-seronegative (14%) and CMV-seropositive patients (18%; p=0.41), with multivariate analysis showing no independent effect of CMV serostatus (HR 1.04, p=0.91). In contrast, during the entire pre-letermovir era, CMV-seropositive patients demonstrated significantly higher NRM compared with CMV-seronegative patients (16% vs. 11%; p=0.002; multivariate HR 1.46, p=0.02). This effect was most pronounced in the early pre-letermovir period (17% vs. 12%; p=0.07; HR 1.78, p=0.023), while attenuated in the late pre-letermovir period (15% vs. 11%; p=0.16).
Subgroup analysis revealed substantial heterogeneity among recipient/donor CMV combinations in the pre-letermovir era. One-year OS ranged from 68% in R+/D+ to 76% in R-/D-, and 1-year PFS ranged from 57% in R+/D+ to 69% in R-/D-. NRM varied from 10% in R-/D+ to 20% in R+/D-, while relapse incidence ranged from 16% in R-/D- to 28% in R-/D+. These differences were statistically significant across all combinations. Although some effects lost significance on multivariate analysis, the unadjusted findings confirm that CMV pairing was a meaningful determinant of outcomes before letermovir.
In the post-letermovir era, these differences disappeared entirely. Across all four CMV serostatus combinations, 1-year OS ranged from only 66% to 76% (p=0.52), NRM from 14% to 22% (p=0.67), PFS from 57% to 71% (p=0.28), and relapse incidence from 10% to 22% (p=0.44). Recipients with negative CMV serology receiving grafts from CMV-positive donors (R-/D+) demonstrated outcomes fully comparable to all other combinations. Historically high-risk combinations such as R+/D- also showed no differences after letermovir implementation.

Conclusions: Letermovir prophylaxis was associated with elimination of the historically observed survival differences across all recipient/donor CMV serostatus combinations in MUD allo-SCT. These findings suggest a profound reduction in CMV-related risk heterogeneity and support routine letermovir use in CMV-seropositive recipients, with implications for donor selection and post-transplant risk stratification.

Clinical Trial Registry: NA

Disclosure: No

OS10-07

IMPACT OF DONOR CHARACTERISTICS ON THE OUTCOMES FOLLOWING HAPLO-HSCT IN PATIENTS AGED 55 YEARS AND OLDER

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Background: Haploidentical haematopoietic stem cell transplantation (haplo-HSCT) provides curative potential for older patients with haematological malignancies. Since multiple haploidentical donors may be available for a given patient, identifying factors that influence transplant outcomes, particularly donor-related characteristics, is critical. This study aimed to identify donor factors that are associated with transplant outcomes.

Methods: This retrospective study was conducted at Peking University People's Hospital. Patients were eligible if they: (1) underwent their first haplo-HSCT between January 2019 and June 2024; (2) were aged ≥55 years; and (3) had a diagnosis of acute myeloid leukaemia (AML), myelodysplastic syndromes (MDS), or acute lymphoblastic leukaemia (ALL).

Results: Between January 2019 to June 2024, a total of 460 patients were enrolled. The last follow-up was 9 October 2025. Detailed characteristics are presented in **Table 1**.

Table 1|Characteristics of patients, donor and transplantation.

Characteristics	N = 460
Patients' age at HSCT, median (range)	59 (55,74)
Donors' age, median (range) < 33, n (%) > = 33, n (%)	 184 (40.0) 276 (60.0)
Donor-recipient gender matching, n (%) Female to Male Others	 109 (23.7) 351 (76.3)
Donor-recipient ABO blood type, n (%) matched major dismatch minor dismatch Bidirectional mismatch	 235 (51.1) 100 (21.7) 93 (20.2) 32 (7.0)
Donor-recipient CMV status, n (%) +/+ +/- -/+ -/- missing	 377 (82.0) 7 (1.5) 13 (2.8) 2 (0.4) 61 (13.3)
Diagnosis, n (%) AML ELN (low/median/high) MDS ALL	 232 (50.4) 47/99/86 148 (32.2) 80 (17.4)

DSA, n(%) - +	 395 (85.9) 65 (14.1)
MRD - +	 304 (66.1) 156 (33.9)
Status CR NR	 402 (87.4) 58 (12.6)
HCT-CI, n (%) 0 (low risk) 1–2 (intermediate risk) ≥3 (high risk)	 235 (51.1) 149 (32.4) 76 (16.5)
Matched HLA loci at A, B, C, DRB1 and DQB1, n (%) 5/10 >5/10	 351 (76.3) 109 (23.7)
Conditioning regimen, n (%) Bu/Cy+ATG Bu/Cy/Flu+ATG	 54 (11.7) 406 (88.3)
Stem cell source PB BM+PB	 398 (86.5) 62 (13.5)
Median CD34+ count, $\times 10^6$/kg (range)	3.72 (0.37—31.22)
Median MNC count, $\times 10^8$/kg (range)	8.96 (1.96—22.42)
Follow-up for survivors post-transplant, days, median (range)	746 (38—2343)

"-"=negtive; "+"=positive; AML=Acute Myeloid Leukemia; MDS=Myelodysplastic Syndromes; ALL=Acute Lymphoblastic Leukemia; MRD=Minimal Residual Disease; CR=Complete Remission; NR=Non-Remission; HCT-CI=hematopoietic cell transplant-comorbidity index.

The median follow-up time for survivors was 746 days. At the last follow-up, 340 patients (73.9%) were alive. The cumulative incidence of grade II–IV acute graft-versus-host disease (GVHD) and moderate-to-severe chronic GVHD were 22.9% and 26.0%. The 2-year overall survival (OS) and disease-free survival (DFS) were 72.8% (95% CI: 68.6–77.2) and 66.8% (95% CI: 62.4–71.5), respectively. At the last follow-up, 66 patients (14.3%) had relapsed, the 2-year cumulative incidence of relapse (CIR) and transplant-related mortality (TRM) were 13.1% (95% CI: 10.0–16.5) and 21.2% (95% CI: 17.4–25.2). Univariate regression was performed for all potential predictors, including donor and patient parameters, disease

characteristics and treatment-related variables. Variables with P<0.1 from non-donor categories, together with all donor factors (regardless of significance), were included in the multivariate Cox regression. Multivariate analysis showed that increasing donor age was significantly associated with inferior OS (HR 1.22, 95% CI: 1.10–1.36; P<0.001), poorer DFS (HR 1.20, 95% CI: 1.09–1.32; P<0.001), and higher TRM (HR 1.20, 95% CI: 1.07–1.34; P=0.001). Subgroup comparisons was conducted in different donor age, with the optimal threshold by maximally selected rank statistics. Compared with donors aged ≥33 years, younger donors (<33 years) were associated with better OS (80.8% vs. 67.6%, P=0.002), improved DFS (73.8% vs. 62.6%, P=0.002), and lower TRM (16.6% vs. 24.2%, P=0.03), not CIR. (**Figure 1A-D)**

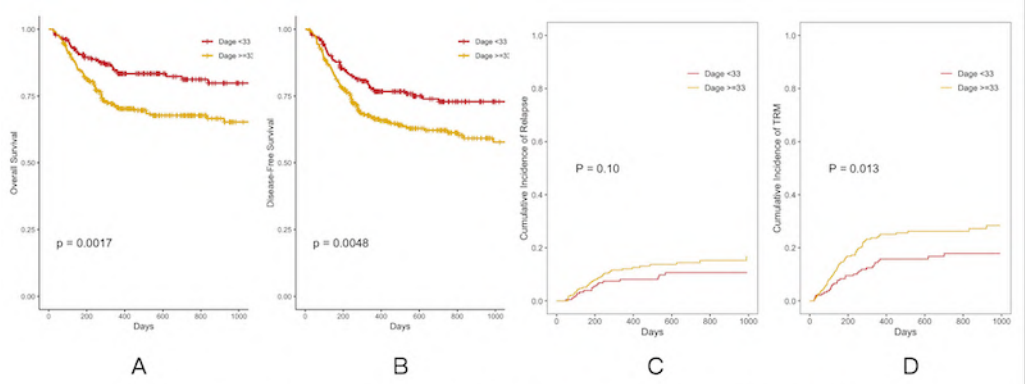

Figure 1. Comparison between Donor age <33 and ≥33 groups. (A) OS, (B) DFS, (C) TRM, (D) CIR.

Dage = Donor Age

Conclusions: This study indicated that donor age significantly influences the outcomes of haplo-HSCT in patients ≥55 years. Younger donors, particularly those aged < 33 years, were associated with better OS and DFS and lower TRM, suggesting that younger donors may be preferred for older patients undergoing haplo-HSCT.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

A317

DIFFERENTIAL IMPACT OF FIRST-FIELD AND SECOND-FIELD HLA MISMATCHES IN 9/10 VERSUS 10/10 MATCHED UNRELATED HSCT, AN ANALYSIS OF GERMAN REGISTRY DATA, DRST

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Background: Allogeneic stem cell transplantation (alloHSCT) from fully HLA-matched (10/10) donors is safest treatment but often limited by donor availability. This study evaluates whether first-field (antigen-level) or second-field (allele-level) mismatches (MMs) at the five major HLA loci (HLA-A, -B, -C, -DR, -DQ) affect transplantation outcomes versus fully matched pairs. All analyzed mismatches were 9/10 HLA matches. Since HLA-DQ mismatches are considered more tolerable and data on DQB1 mismatches are relatively limited, the study focused on this locus.

Methods: This registry-based, retrospective study analyzed adults undergoing first alloHSCT from 2010–2021. We evaluated 3772 fully matched (10/10) and 1071 single HLA-mismatched (9/10) transplants, including 122 DQB1 mismatches. Patients receiving post-transplant cyclophosphamide as graft-versus-host disease prophylaxis (GVHD) were excluded. Endpoints were overall survival (OS), progression-free survival (PFS), graft-versus-host disease-free/relapse-free survival (GRFS), relapse incidence (RI), non-relapse mortality (NRM), grade III–IV acute GVHD (aGVHD), and chronic GVHD (cGVHD). Cox proportional hazard models assessed associations of MM status with OS, PFS, and GRFS; cause-specific Cox regression for competing risks evaluated RI, NRM, aGVHD, and cGVHD.

Results: Univariable analysis demonstrated that HLA-Class I mismatches (HLA-A, -B, -C) were associated with significantly reduced survival compared with 10/10 matches. Especially HLA-A first-field mismatches had consistently negative effects: 5y-OS (32% vs. 46%, $p < 0.001$), 5y-PFS (24% vs. 32%, $p = 0.003$), and 5y-GRFS (14% vs. 21%, $p < 0.001$). Notably, HLA-DQB1 first-field mismatches showed a detrimental impact on outcomes comparable to Class I mismatches, with 5y-OS (27% vs. 46%, $p = 0.011$), 5y-PFS (8.4% vs. 32%, $p < 0.001$), and 5y-GRFS (7.4% vs. 21%, $p = 0.032$). Multivariable analyses confirmed the impaired survivals, specifically for HLA-DQB1, with OS (HR 1.50, $p = 0.022$) and PFS (HR 1.50, $p = 0.009$). HLA-DRB1 mismatches also showed a negative impact, observed only for OS (9/10 second-field HR 1.46, 95% CI 1.05–2.04, $p = 0.025$; 9/10 first-field HR 1.87, 95% CI 1.10–3.17, $p = 0.02$).

HLA-Class I first-field mismatches were consistently linked to higher aGVHD risk, increasing over time compare to 10/10 matches (HLA-A: 6.7% → 23% → 25%; HLA-B: 6.5% → 26% → 26%; HLA-C: 4.4% → 21% → 23% at 28, 100, 365 days; all $p < 0.001$). Cox regression showed significantly increased aGVHD risk for HLA-A (HR 2.27), HLA-B (HR 2.20), and HLA-C (HR 1.91) mismatches (all $p < 0.001$), while Class II mismatches had no significant effect. Except for HLA-A first-field mismatches, we could neither detect an effect on cGvHD for first- nor second-field 9/10 mismatches.
Lastly and interestingly, among the five major HLA loci, only HLA-DQB1 first-field mismatches were found to be significantly associated with increased RI (HR 1.62, 95% CI 1.14–2.31, $p = 0.007$), and not significant for NRM and this effect was not related with DQA1 mismatches.

Conclusions: First-field DQB1 mismatches, similar to HLA Class I mismatches, significantly compromise survival outcomes, whereas second-field mismatches appear to have no impact. These findings underscore the importance of complete HLA matching, including DQB1, in donor selection for alloHSCT. In the absence of a fully matched donor, second-field mismatches may be preferable to first-field mismatches.

Disclosure: Nothing to declare

A318

MODELING SUFFICIENCY AND GROWTH OF THE AUSTRALIAN AND NEW ZEALAND HSC DONOR REGISTRIES TO MEET PATIENT POPULATION REQUIREMENTS IN AN ERA OF MISMATCHED TRANSPLANTATION

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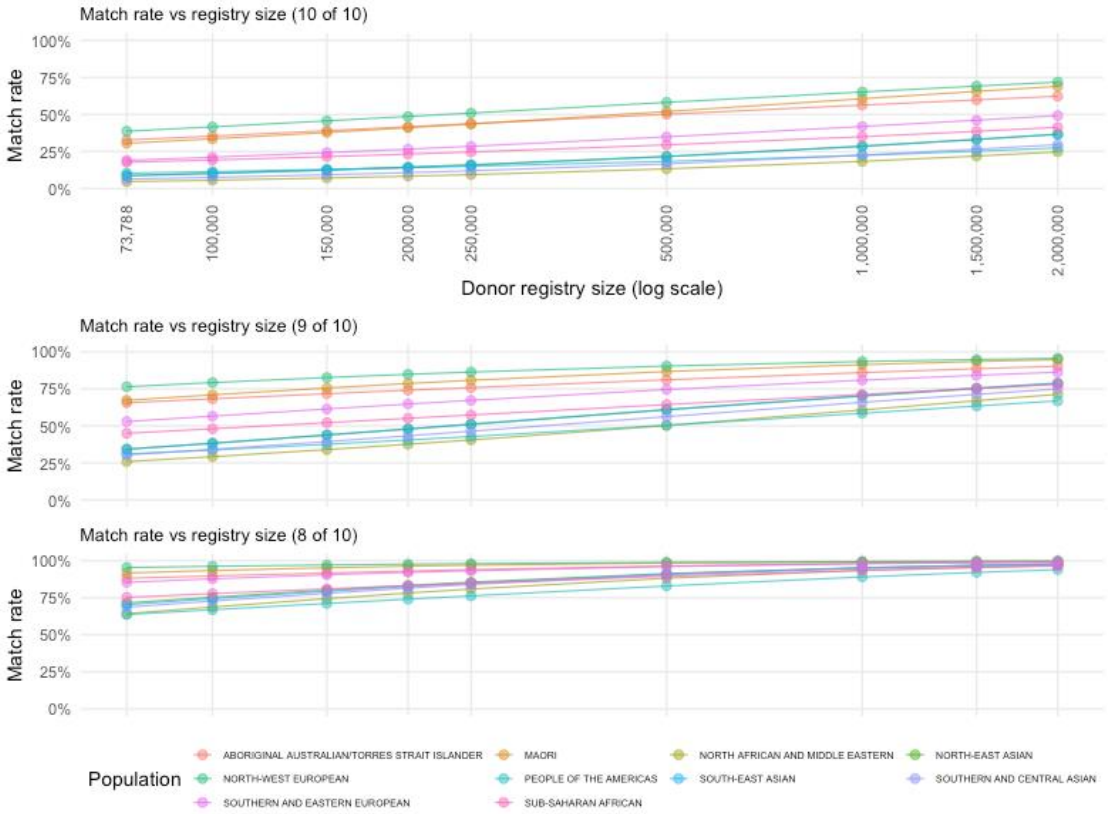
Background: Access to suitably HLA-matched unrelated donors for allogeneic hematopoietic cell transplantation (HCT) in Australia and New Zealand is constrained by registry size and the underrepresentation of some ancestries. We used population-based modeling to quantify current match likelihoods across ancestry groups, evaluate the contribution of international donors, and explore growth strategies that improve equity in donor access for Australasian patients.

Methods: High-resolution HLA-A, -B, -C, -DRB1, -DQB1 (±DPB1) data from 103,106 donors registered since 2015 with Stem Cell Donors Australia and the New Zealand Bone Marrow Donor Registry were analysed to estimate five- and six-locus haplotype frequencies in nine major ancestry groups. Using established NMDP haplotype frequency and population genetics modeling methods, we simulated unrelated donor searches for Australian/New Zealand HSCT

patients from the same period across match stringencies (10of10, 9of10, 8of10 and 8of8, 7of8, 6of8), incorporating donor age. We then modeled registry expansion from the current ≤35-year-old Australasian donor pool (73,788) up to 2,000,000 donors and evaluated the incremental impact of including NMDP (US) donors. We also evaluated the accuracy of self-reported ancestry for the Australian donor cohort since the introduction of online enrolment. Finally, we implemented an optimization framework in which registry growth across ancestries is guided by an equity parameter (λ) that trades off maximizing overall matches versus minimizing ancestry-based variation in match rates.

Results: In the current combined Australian/New Zealand donor pool, 10of10 (or 8of8) match rates exceeded ~40–50% for North-West European patients but were <25% for many Asian and Oceanian (First Nations) groups, with 7of8 and 9of10 match rates ranging from ~36–86% across ancestries. Restricting to donors ≤35years reduced fully matched rates by only ~2–3 percentage points in the best-served groups while preserving overall patterns of disparity. Adding NMDP donors moderately increased match likelihoods for underrepresented ancestries, particularly at the single-mismatch levels (7of8 and 9of10), and significantly raised ≥6/8 or ≥8of10 match probabilities to ~90% for all populations. Registry-growth simulations (**Figure 1**) showed diminishing returns beyond ~500,000 donors for lower stringency thresholds, but continued gains for 9of10 and 10of10 matching, especially for minority groups, even at 2,000,000 donors. For an economically feasible Australian registry growth target, equitable gains in transplant access for all nine ancestry groups is only fully achieved from projected mismatching at 1-2 alleles. In equity-optimized simulations (higher λ), donor recruitment shifted toward Asian, African, and non-European groups, halving the variation in match rates between ancestries, whereas purely throughput-optimized growth preserved current disparities. Balanced strategies (λ ≈ 0.5) achieved high overall match rates with substantially reduced inequity and realistic donor compositions.



Conclusions: For Australia and New Zealand, registry composition and donor availability are stronger determinants of equitable access than registry size alone. Targeted recruitment of younger donors prioritising underrepresented ancestries, combined with access to the global donor pool, improves match likelihoods across populations. Compared with equity gains achieved through registry expansion, the models show the ability to use 1–2 allele–mismatched donors represents the most practical and impactful strategy for reducing disparities in donor access for Australasian HCT patients.

Disclosure: Nothing to declare from all authors.
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A319

DEMOGRAPHICS MATTER: VARIATION IN DONOR AVAILABILITY DURING CONFIRMATORY TYPING

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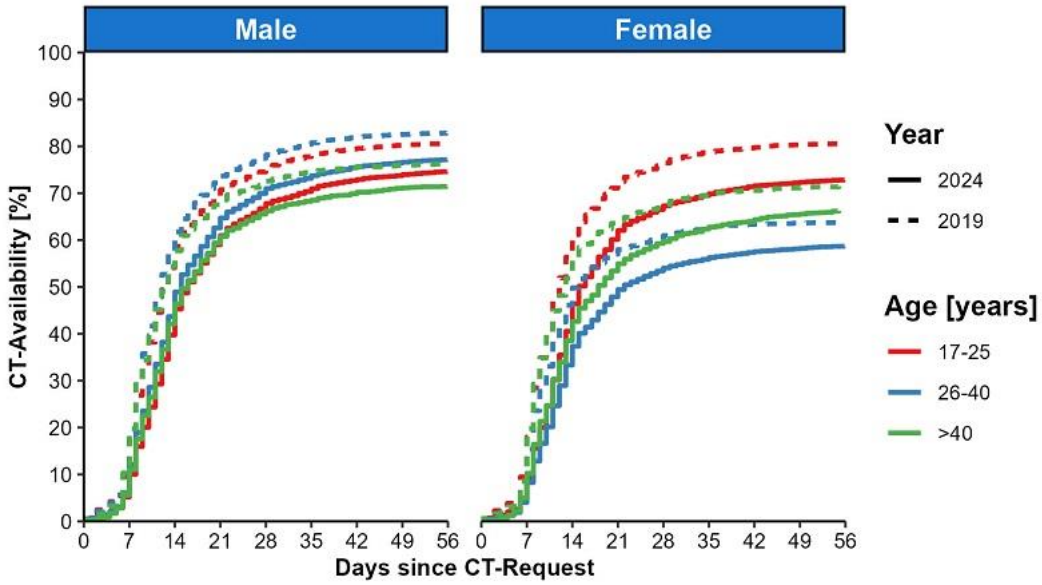
Background: The availability of suitable donors is essential to ensure that patients with severe blood disorders receive hematopoietic stem cell products in time. Donor availability during confirmatory typing (CT), which includes confirmation of HLA compatibility and health assessment, facilitates efficient donor selection.

Methods: We analysed the success rate and time to confirmation of donor availability for CT requests initiated by transplant centers (TCs) to donors registered with DKMS Germany, comparing two time periods. The sex- and age-stratified analysis included all first CT requests in 2019 (n=27,530) and 2024 (n=39,995). CT availability was defined as donors' expressed willingness to donate and medically eligibility, excluding requests that were cancelled by the TC. CT duration was defined as the days between CT request and the results of the health assessment, including review of Health History Questionnaire and infectious diseases markers.
The success rates were analysed using logistic regression, and the CT duration was evaluated using cumulative incidence functions.

Results: Median age of requested donors was 27 years in both, 2019 and 2024 (p=0.5). In 2019, male donors were requested in 63% of searches, compared to 59% in 2024 (p<0.001). CT availability of DKMS donors decreased from 78.2% in 2019 to 72.6% in 2024. This decline was primarily due to donors' unwillingness to donate (4.0% in 2019 vs. 8.7% in 2024). The largest decrease of success rates was observed among female donors aged 17 to 25, with CT availability dropping from 80.9% in 2019 to 74.0% in 2024. The highest CT availability was seen among men aged 26 to 40, with 83.3% in 2019 and 78.3% in 2024. Women in the same age group, by contrast, showed the lowest CT availability, with 64.0% in 2019 and 59.6% in 2024. The main reason is the exclusion of donor searches during pregnancy and up to six months after childbirth. Further, medical ineligibility increases with age, affecting 12.7% of men and 14.5% of women over the age of 40 compared to 2.2% of men and 3.3% of women under 26 years in 2024.
The median CT duration was 11 days in 2019 and 14 days in 2024 (p<0.001). Search time analysis showed that if a donor had not been reported as available by day 14, the likelihood of a positive reply by day 28 ranged between 27% (female donors aged 26-40 years) and 43% (male donors aged 26-40 years).



Conclusions: Differences in donor availability by donor age and sex should be considered during donor search. Strengthening communication between donor registries and TCs could facilitate the timely initiation of additional donor requests at CT level.
The observed decline in donor availability between 2019 and 2024 suggests a need for more personalized and targeted donor communication strategies. Donation behaviour is influenced by a complex combination of individual motivations, socioeconomic factors, and situational circumstances. Further analyses will be required.

Disclosure: Nothing to declare.

A320

PAROUS FEMALE DONOR REDUCES RELAPSE RISK IN HIGH-RISK AML/MDS AFTER HAPLOIDENTICAL PBSCT WITH ATG/PTCY COMBINATION FOR GVHD PROPHYLAXIS

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Background: Haploidentical donors (HIDs) have gained viability with improved graft-versus-host disease (GVHD) prophylaxis. While young male donors are typically preferred, parous female donors have been regarded as suboptimal. However, the combination of low-dose anti-thymocyte globulin (ATG) and post-transplant cyclophosphamide (PTCy) has shown promising efficacy in preventing GVHD following haploidentical peripheral blood stem cell transplantation (haplo-PBSCT).

Methods: From May 2017 to November 2023, we conducted a multicenter retrospective study of 106 patients with acute myeloid leukemia or myelodysplastic syndrome to compare outcomes between parous female donors (n=47) and young male donors under 30 years old (n=59). Adult patients (≥18 years) with myeloid malignancies undergoing haplo-PBSCT with ATG/PTCy combination-based GVHD prophylaxis regimens. The graft source was peripheral blood stem cells (PBSCs) mobilized with granulocyte colony-stimulating factor. All patients received the GVHD prophylaxis regimen combining ATG and PTCy for transplantation. The low-dose ATG/PTCy regimen consisted of ATG (2.5 mg/kg/day on days -2 to -1), PTCy (50.0 mg/kg/day on day +3), cyclosporine A (CsA), and mycophenolate mofetil (MMF) (initiated on day +4).

Results: The parous female donor group exhibited a significantly lower 2-year cumulative incidence of relapse (CIR: 6.50% vs. 24.68%), which was confirmed on multivariate analysis as an independent factor associated with reduced CIR (P=0.033). Non-relapse mortality (NRM) was comparable between the groups (P=0.110). Although differences in overall survival, relapse-free survival, and GVHD-free/relapse-free survival did not reach statistical significance, consistent trends toward improved survival were observed in the parous female donor group, particularly among high/very-high-risk refined disease risk index patients, who exhibited an approximate 20% improvement in survival.

Conclusions: These findings suggest that the parous female donor may provide enhanced relapse protection without increasing NRM in AML/MDS patients receiving ATG/PTCy-based haplo-PBSCT.

Disclosure: The authors declare no conflicts of interest.

A321

OLDER DONOR AGE IS NOT ASSOCIATED WITH INFERIOR SURVIVAL IN CONTEMPORARY HAPLOIDENTICAL TRANSPLANTATION

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Background: Data regarding the association of donor age with haploidentical (haplo) hematopoietic stem cell transplant (HCT) outcomes has been inconsistent, particularly concerning a specific age cutoff. Most published studies on donor age in the haplo setting predated the advancement in cytomegalovirus (CMV) prophylaxis, improved graft-versus-

host disease (GVHD) treatments, maintenance therapy post-HCT.
Objective: Examine the role of donor age in a recent cohort of patients, from 2018-2024.

Methods: We included consecutive adult patients with hematologic malignancies who underwent their first haplo HCT (n=364) at MD Anderson Cancer Center. All patients received post-transplant cyclophosphamide (PTCy)-based GVHD prophylaxis. To determine the optimal donor age cutoff associated with overall survival (OS) and progression-free survival (PFS), we explored a series of donor age dichotomizations as well as categorization by 5-year intervals.

Results: Our analysis, using dichotomization of donor age, did not reveal a clear donor age cut-off to be associated with either OS or PFS. In the absence of a statistically significant age cutoff for OS or PFS, we categorized donor age into three groups (≤30 [n=155], 31-44 [n=139], and ≥45 years [n=70]) for all subsequent analyses based on cohort distribution and clinical relevance. Compared to donor age ≤30 years, the hazards of overall mortality were 0.92 (95% CI 0.62-1.37, *P* = 0.69) for donor age 31-44 years and 1.19 (95% CI 0.78-1.81, *P* = 0.43) for donor age ≥45 years in multivariable analysis (MVA). Similar patterns emerged for PFS. Older donor age was associated with increased hazards of non-relapse mortality (NRM) in MVA: (31-44 years: hazard ratio [95% CI] 1.44 [0.84-2.45], *P*= 0.18) and (≥45 years: 1.52 [0.87-2.66], *P* = 0.14). Consequently, relapse rates were lower in these groups (31-44 years: 0.55 [0.33-0.93], *P* = 0.025) and (≥45 years: 0.70 [0.36-1.36], *P* = 0.29) compared to donors ≤30 years.
Older donors were associated with a significantly increased risk of grade III-IV acute GVHD (31-44 years: 3.77 [1.69-8.39], *P*=0.001; ≥45 years: 3.83 [1.64-8.98], *P*= 0.002) compared to donors ≤30 years. The risk of chronic GVHD was also higher with older donors (31-44 years: 1.44 [0.84-2.45], *P*=0.18; ≥45 years: 1.52 [0.87-2.66], *P* = 0.14) compared to younger donors.
We noted patient and disease-related factors significantly associated with OS in MVA; older patient age (≥ 65 years vs. < 50 years: 1.90 [1.22-2.98], *P*= 0.005) and a high/very high disease risk index (DRI) (1.89 [1.38-2.60], *P*< 0.001). DRI also influenced relapse rates with a 2.5-fold increased risk observed in patients with high/very high DRI (95% CI 1.63-3.90, *P*< 0.001).

Conclusions: Our study suggested that dichotomization of donor age did not reveal it to be a major selection factor. However, it remains to be assessed whether HLA factors play a more dominant role, if improved post-HCT strategies have altered the adverse effect of donor age in this population, or if dichotomization may present a limited methodology of modeling donor age and novel approaches need to be adopted in this contemporary era. Despite the lack of survival differences, older donor age remains a significant predictor of severe acute GVHD risk.

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COI: E.J.S. serves as a consultant for Cimeio Therapeutics AG, New York Blood Center, Celaid Therapeutics Inc, Scientific Advisor for Adaptimmune Limited, Navan Technologie, Axio Research, FibroBiologics, is on the Board of Directors/Management for National Marrow Donor Program, and License agreement for Affimed, Takeda, Rege Nexus, and is a speaker for Dava Oncology. K.R. and The University of Texas MD Anderson Cancer Center have an

institutional financial conflict of interest with Takeda Pharmaceutical and Affimed GmbH. K.R. participates on the Scientific Advisory Board for Avenge Bio, Virogin Biotech, Navan Technologies, Caribou Biosciences, Bit Bio Limited, Replay Holdings, oNKo Innate, The Alliance for Cancer Gene Therapy (ACGT), Innate Pharma, and Shinobi Therapeutics. K.R. is the scientific founder of Syena. R.S.M. served as a consultant reviewer for OrcaBio and received honorarium from Lumanity for providing Expert Opinion.

A323

THE IMPACT OF INDIRECT ALLORECOGNITION IN TRANSPLANT OUTCOMES AFTER UNRELATED DONOR TRANSPLANTATION FOR NONMALIGNANT DISEASES

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Background: Recent studies show that indirect allorecognition, analyzed by the *in silico* PIRCHE (Predicted Indirectly Recognizable HLA Epitopes) model, predicts a higher incidence of acute graft-versus-host disease (GVHD) and worse survival in patients with malignant diseases undergoing hematopoietic stem cell transplantation with unrelated donors (URD-HSCT). However, the impact of PIRCHE on URD-HSCT for non-malignant diseases is currently unknown.

This study aimed to evaluate the effect of indirect allorecognition of HLA-DPB1 mismatches, measured by the PIRCHE-I and -II scores, on the outcomes of URD-HSCT for non-malignant diseases.

Methods: We retrospectively analyzed 181 transplants for non-malignant diseases performed between 2007 and 2024. High-resolution HLA typing was performed by Sanger or next-generation sequencing (NGS). PIRCHE-I and -II scores in the Host-versus-Graft (HvG) and Graft-versus-Host (GvH) pathways were calculated using the pirche.com website. The primary outcomes were overall survival (OS) and graft-free, rejection-free survival (GRFS). The secondary outcomes were neutrophil (NE) and platelet (PE) recovery, graft failure (GF), GVHD II-IV, GVHD III-IV, cGVHD, and extensive cGVHD. Univariate analyses of primary outcomes were estimated using the Kaplan-Meier method and compared between groups using the log-rank test, while secondary outcomes were calculated using cumulative incidence curves considering competing risks and compared using Gray's test. $P < 0.01$ was considered significant. Multivariate analyses were performed using Cox regression, adjusted for competing risks. All statistical analyses were performed using EZR v1.68 software.

Results: The median age of the patients was nine years (range: 0-51). The main indications for URD-HSCT were congenital bone marrow failure (n = 82; 45.3%) and severe aplastic anemia (n = 51; 28.2%). All patients received bone marrow as a source of HSCs, and 96.7% received in vivo T-cell depletion with ATG. Among the 181 donor/recipient pairs, 42 (23.2%) were fully compatible for the HLA-A, -B, -C, -DRB1, -DQB1, and -DPB1 loci, and 139 (76.8%) were HLA-DPB1 mismatch. The presence or absence of PIRCHE-I and -II in the HvG and GvH pathways did not impact the outcomes of hematological recovery, rejection, GVHD, and OS (p>0.01). In the adjusted analyses, the absence and presence of PIRCHE-I and PIRCHE-II, in either the HvG or GvH direction, were significantly associated with poorer GRFS compared with the 12/12 control group (p<0.01; Table 1). However, the groups with HLA-DPB1 mismatches, regardless of the presence or absence of PIRCHE-I and -II, had a lower cumulative incidence of GRFS before 2 years (51.7%; 95% CI: 42.8-59.9%) compared to the fully compatible control group (77.7%; 95% CI: 59.8-88.3%), which was statistically significant in the analysis adjusted for competing risks (HR= 3.66; 95% CI: 1.75–7.69; p<0.001; Figure 1).

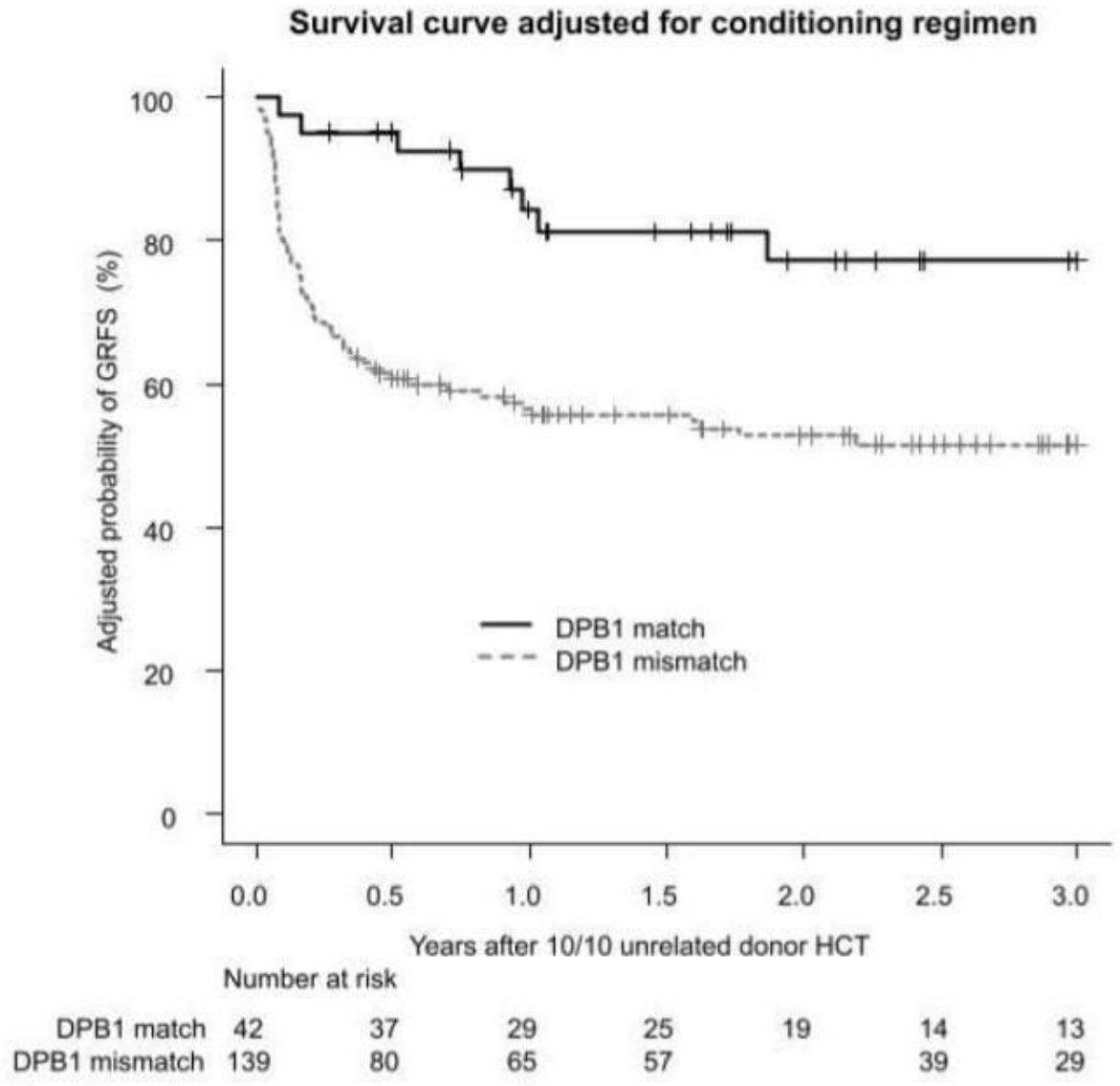
TABLE 1. MULTIVARIABLE ANALYSES FOR GRFS

GRFS[†Ω]	HR (95% CI)	P-value	Overall P-value[€]
Model 1: PIRCHE-I HvG			0.0025
Control 12/12	1 (Reference)	-	
PIRCHE- I HvG Absent	3.39 (1.49-7.70)	0.0036	
PIRCHE-I HvG Present	3.82 (1.78-8.20)	<0.001	
Model 2: PIRCHE-II HvG			0.0027
12/12 Control	1 (Reference)	-	
PIRCHE-II HvG Absent	3.78 (1.65-8.67)	0.0017	
PIRCHE-II HvG Present	3.61 (1.68-7.75)	<0.001	
Model 3: PIRCHE-I GvH			<0.001
Control 12/12	1 (Reference)	-	
PIRCHE- I GvH Absent	4.85 (2.14-10.98)	<0.001	
PIRCHE-I GvH Present	3.25 (1.52-6.96)	0.0025	
Model 4: PIRCHE-II GvH			0.0018
Control 12/12	1 (Reference)	-	
PIRCHE-II GvH Absent	4.55 (1.89-10.93)	<0.001	
PIRCHE-II GvH Present	3.47 (1.64-7.38)	0.0012	

[†]Final models adjusted for conditioning regimen.

[Ω]Cox model considering GRFS for less than 2 years due to violation of the Cox proportional hazards assumption. The Cox model was not performed for GRFS greater than 2 years, as there were no events in the 12/12 control group after 2 years; only censoring occurred.

[€]Overall p value for the Wald test.



Conclusions: Our findings suggest that the PIRCHE model is not a predictor of more permissible DPB1 mismatches. Thus, we conclude that, for non-malignant diseases, a fully compatible donor is always the best strategy to optimize GRFS after URD-HSCT.

Disclosure: Nothing to declare.

A324

EVALUATION OF RECOVERY AND ADVERSE EVENTS IN 1,638 HEALTHY ANTHONY NOLAN DONORS

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Background: Anthony Nolan (AN) is a UK donor registry facilitating donations from healthy related and unrelated donors for allogeneic transplants worldwide. Peripheral blood stem cell (PBSC) donors receive 4-5 days of granulocyte-colony stimulating factor injections, standard 12L processing via apheresis on day 5 and repeat on day 6 if required. Bone marrow (BM) donors collect a maximum 20mls/kg under general anaesthetic. The registry performs short term donor follow-up at day 2-3, day 7, day 30 and long-term donor follow-up annually. Adverse reactions (ARs) are recorded internally and reported to the World Marrow Donor Association (WMDA) via the SPEAR reporting system if required. An AR is any unexpected response in the donor which requires further follow-up, monitoring or reporting to WMDA. These are identified from follow up questionnaire responses or following direct donor contact. The aim of this study was to determine the rate of ARs in donors and assess donor recovery time.

Methods: We retrospectively analysed follow-up questionnaires and ARs from 1,638 healthy donors donating 1st April 2022 - 31st March 2025. Day 2/3 questionnaires were administered via phone call and recorded on the AN CORAL database. Day 7 and 30 questionnaires were administered electronically. Follow-up questionnaires are non-compulsory, and not all questions require responses. Day 2/3 and day 7 questions are a 5-point Likert scale, day 30 a 0-10 scale.

Results: We reviewed responses from 1,486 (90.7% response rate) day 2/3 calls, 1,155 (70.5% response rate) day 7 questionnaires and 659 (40.2% response rate) day 30. Donors had a median age of 27 years. 1,053 (64.3%) males and 585 (34.8%) females.There were 105 (6.4%) BM donors, 238 (14.5%) donor lymphocyte collections (DLC) and 1,294 (79.0%) PBSC.
Self-reported donor recovery data are presented in Table 1 and Figure 1.

Question	**Answer**	**Day 2/3**			**Day 7**		
		BM	DLC	PBSC	BM	DLC	PBSC
In relation to your donation how are you	Much better than usual / Excellent	2 (3.2%)	0 (0.0%)	10 (1.3%)	8 (10.3%)	8 (29.6%)	107 (11.2%)

feeling emotionally?	Better than usual / Very good	8 (12.9%)	9 (8.9%)	122 (16.1%)	15 (19.2%)	7 (26.0%)	204 (21.4%)
	Normal / Good	50 (80.6%)	92 (91.1%)	600 (79.2%)	48 (61.5%)	12 (44.4%)	606 (63.5%)
	Worse than usual / Fair	2 (3.2%)	0 (0.0%)	25 (3.3%)	6 (7.7%)	0 (0%)	35 (3.7%)
	Much worse than usual / Poor	0 (0.0%)	0 (0%)	1 (0.1%)	1 (1.3%)	0 (0%)	2 (0.2%)
	Total	62	101	758	78	27	954
In relation to your donation how are you feeling physically?	Much better than usual /Excellent	0 (0%)	0 (0%)	0 (0%)	2 (2.6%)	6 (22.2%)	62 (6.5%)
	Better than usual /Very Good	1 (1.6%)	0 (0%)	4 (0.5%)	5 (6.4%)	5 (18.5%)	91 (9.5%)
	Normal /Good	28 (44.4%)	120 (90.1%)	543 (70.2%)	38 (58.7%)	13 (48.1%)	726 (75.9%)
	Worse than usual /Fair	33 (52.4%)	12 (9.1%)	212 (27.4%)	32 (41.0%)	2 (7.4%)	72 (7.5%)
	Much worse than usual /Poor	1 (1.6%)	0 (0%)	5 (0.6%)	1 (1.3%)	1 (3.7%)	6 (0.6%)

	Total	63	132	773	78	27	957
Are you able to participate in normal activities?	Yes	25 (25.8%)	192 (92.3%)	859 (72.7%)	56 (71.8%)	25 (92.6%)	946 (97.7%)
	No	72 (74.2%)	16 (7.8%)	322 (27.3%)	22 (28.2%)	2 (7.4%)	22 (2.3%)
Have you recovered from the donation?	Yes	21 (21.6%)	177 (85.0%)	766 (64.9%)	45 (57.7%)	25 (92.6%)	907 (93.5%)
	No	76 (78.4%)	31 (14.9%)	415 (35.1%)	33 (42.3%)	2 (7.4%)	63 (6.5%)
Table 1.							

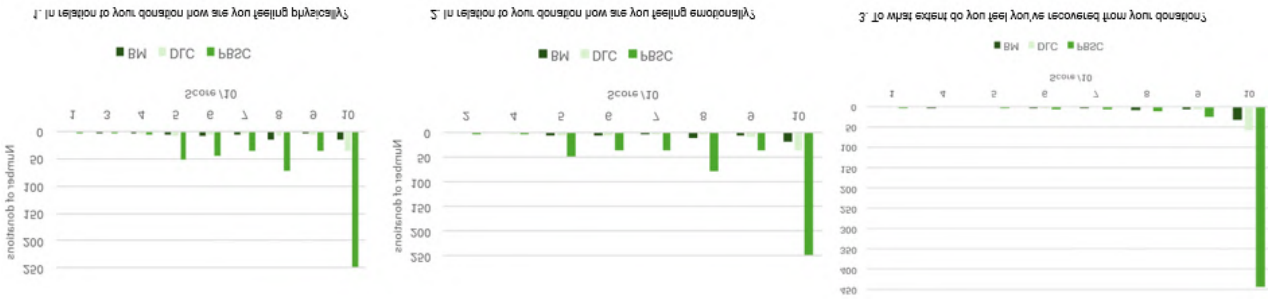

Figure 1. Donor recovery at 30 days

Most PBSC and DLC donors have recovered by 7 days (93.5% / 92.6% respectively) whereas 57.7% BM donors have recovered ($p<0.05$). At 30 days, 97.5% PBSC donors score their recovery >/= 8/10 compared to 91.5% BM donors ($p<0.05$).
96.1% PBSC donors feel emotionally normal or better than normal by day 7 and physically 91.8% are normal or better than normal. Comparatively, 91.0% BM donors feel emotionally normal or better than normal by day 7, only 57.7% physically.
38 ARs were raised relating to potential unexpected or prolonged donor side effects requiring further investigation or management. 12.4% BM donors experience an AR compared to 1.9% of PBSC donations ($p<0.05$). Only one AR was "Common Terminology Criteria for Adverse Events" grade 3 (<1% of BM donations), the remaining ARs were grades 1-2. The median age of donors experiencing an AR is higher (29 years) than in the follow up data (27 years) ($p=< 0.05$). 1.7% of males experience an AR compared to 3.4% females ($p<0.05$).

Conclusions: This data demonstrates excellent recovery for healthy donors to allogeneic transplantation with very low rates of unexpected complications. The recovery from a BM donation is more physically demanding and BM donors are more likely to experience an AR however these remain mild or moderate.

Disclosure: Nothing to declare.

A325

INTEGRATING NGS-BASED GERMLINE MUTATION DETECTION INTO DONOR EVALUATION ENHANCES MYELOID NEOPLASM RISK STRATIFICATION

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Background: Expanding recognition of germline predisposition in myeloid neoplasms has underscored the importance of systematic genetic evaluation into the donor selection process. Recent evidence indicates that germline variants and donor-derived clonal hematopoiesis (CH) can influence transplant outcomes. Our study evaluates an NGS-based strategy for detecting clinically relevant germline mutations in donor–recipient pairs to improve risk stratification in the allo-HCT setting.

Methods: Consecutive sibling donor-recipient pairs in AML patients undergoing allo-HCT in CR1 (17) or >CR1 (13) were retrospectively analyzed. Targeted NGS panel was applied to assess germline-predisposing variants, copy number variations (CNVs) and CH in bone marrow samples. Variants were classified according to American College of Medical Genetics and Genomics (ACMG) criteria. Variant Allele Frequency (VAF) patterns were used to infer germline origin. CH was identified based on VAF ≥2%.

Results: Thirty donor-recipient pairs were analyzed. Donor-derived variants included**:** i) CNVs**:** Six donors carried eight CNVs absent in recipients affecting *CEBPA* (n=2), *HRAS*, *TP53*, *ANKRD26*, *DNMT3A*, *KMT2A*, and *GNB1*. ii) VUS: 10 out of 30 donors (33%) harbored 13 VUS in key myeloid genes, including: *CSF3R(2), ANKRD26(2), GATA2(2), ZRSR2(1), TET2(1), PPM1D(1), CALR(1), KMT2A(1), RAD21(1), PRPF8(1).* iii) CH: Three recipients carried CH-associated mutations in *DNMT3A* and *KMT2A*. Of note, 11 low-VAF *BCORL1* variants (2–5.7%) were interpreted either as CH or as experimental artifacts due to background noise and were excluded from further analysis.
Recipient-side analysis included NGS at diagnosis. Five underwent confirmatory buccal/remission testing for the presence of potential germline variants. One donor–recipient pair shared a *CSF3R* variant. Seventeen recipients carried variants with VAF suggestive of germline origin, including four with possible germline *CEBPA* variants requiring further validation.
The median follow-up post allo-HCT was 17 months (range 5-35) and 1-year actuarial OS was 80%. Advanced disease resulted in a relapse rate of 37%(11/30). No cases of donor-derived leukemia were identified. Relapse was less frequent among patients receiving grafts from donors carrying germline VUS (2/11, 18%) compared with patients with donors not

carrying VUS mutations (8/19, 42%). Two relapses occurred after receiving grafts from donors with CNVs and 2 from donors with CH.
Chronic GVHD developed in 15/30 patients and was enriched among recipients of grafts from donors harboring germline VUS (8/15 vs 2/15 without cGVHD), suggesting increased donor–recipient allo-reactivity. No significant associations were identified between donor CNVs, CH and transplant outcomes at this stage.

Conclusions: NGS-based evaluation of donors reveals a substantial burden of VUS and CNVs in genes implicated in myeloid neoplasms. Less frequent relapse and increased GVHD was documented in patients receiving grafts with VUS donor variants not shared with the recipients, supporting a role of donor–recipient genetic disparity in shaping post-transplant immune responses. Although numbers are small, our observations raise the hypothesis that donor-derived germline variation may influence immune dynamics favoring allo-reactivity. Limited follow-up data prevent a comprehensive assessment of post-transplant complications. Further analyses will focus on expanding the cohort and monitoring long-term outcomes. Our data support the consideration of routine NGS screening of sibling donors in line with emerging international recommendations.

Disclosure: This work was in part supported by an investigator-driven grant from Novartis Hellas.

A326

HAPLOIDENTICAL SCT INDUCES LONG-TERM REMISSION IN PATIENTS WITH BPDCN

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Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare and highly aggressive disorder with dismal survival outcomes of 8-16months. Long-term disease control was only observed after alloSCT. Haplo-donors allows alloSCT in almost every patient and show stronger graft versus tumor(GVT) effect in most haematopoietic disorders. To confirm the benefit, we performed this single center,retrospective study in BPDCN patients who underwent HID-SCT.

Methods: From 2012 to 2025, 50 BPDCN patients received alloSCT in our institute, including 42 HID-SCT, 5 MSD and 3 URD. We analyzed the HID-SCT patients in this study. Diagnosis was confirmed by institute review according to the 2008 World Health Organization classification. All patients received myeloablative conditioning regimen(Bu/Cy-based in 41 and 8Gy TBI-based in 1). GvHD prophylaxis comprised cyclosporine A, MMF and short-term MTX, plus ATG (2.5mg/kg, days -5 to -2).

Results: The median age at SCT was 21(4-67)yrs with male predominantly(69%). Involvement of the skin, bone marrow (BM) and lymph node at diagnosis was observed in 50% of patients, of note there was a higher incidence of extra nodal lesions including sinus

(n=7), bone (n=6), the central nervous system(CNS, n=4), and testis in two boys(see table). 38 patients had chemotherapy(NHL-like in 7,leukemia-like in 31) as 1st line treatment resulting in a high CR rate of 86.8%, the other 4 progressed post surgery with a median interval of 4m. All but one received intrathecal chemotherapy (ITC, median=2) prophylaxis, 4 patients with documented CNS involvement had additional high dose MTX (or variant) before SCT. Thirty-four patients were in CR,4 in PR and 4 not remission at SCT. All patients achieved CR at D30 with full donor engraftment. The median time of neutrophil and platelet recovery were 11(range 10-21) and 13(range 9-33)days. The incidences of acute and chronic graft versus host disease (GvHD) were 44.5% and 55% respectively.
Until Nov 30,2025, the median follow up was 872(60-4947) days post SCT. Three-year overall survival (OS) and progression-free survival (PFS) were both 94.7%. Two patients died of infection and TMA each, resulting the D100 and 1y transplant-related mortality (TRM) of 3% and 6%, respectively. No relapse occurred, and donor stem cell infusion(DSI) proceeded prophylactically on D60 in patients with PD at SCT.
To the best of our knowledge, this is the first report to demonstrate long-term outcomes of HID-SCT for BPDCN with a reasonably large number of patients. The promising results indicated that BPDCN patients can achieve a durable remission with HID-SCT even those with poor disease status beyond CR1, and deserves further evaluation in the setting of prospective trials.

Table Patients characteristics and treatment outcomes

Characteristics	n (range)
Age，Median（range），y	21（4-67）
M:F	29:13
Localization：skin/BM/LN (%)	85.7 / 71.4 /78.6
Skin+BM+LN Skin+BM other：bone/sinus/CNS /testis	21例 （50%） 24例 （57.1%） 6/7/4/2例
BM blast, Median（range）	23（0-95%）
Chemo before SCT， Median（range）	4 (3-13)
ITC Median（range）	2（0-9）
Status @ AlloSCT :CR/PR/PD	34/4/4
Diagnosis to SCT(d) Median(range）	160 (89-495)
HLA Mismatch 1-2 loci/ 3 loci	4 /39
D-R relation sib/parents/children/other	5/23/12/2

Conditioning: Bu/Cy/ATG TBI/CY/ATG BU/FLU/CY/ATG	37 1 4
Graft BM+PBSC/ PBSC	13/29
MNC Median,10^8/kg	8.58 (5.3-17.3)
CD34+Median, 10^6/kg	3.30 (0.74-10.1)
Engraftment, Median (d) ANC BPC	 11 (10-21) 13 (9-33)
F.U	872 (60-4947)

Conclusions: HID-SCT was feasible and with low TRM resulting in excellent survival in BPDCN patients, even in no-remission patients. No one relapsed in this cohort, and this demonstrated the stronger GVT effect and long-term diseased control of HID-SCT in BPDCN patients.

Disclosure: NO

A327

PROBABLE DONOR – RECIPIENT TRANSMISSION OF HEPATITIS E VIRUS WITH A HAEMATOPOIETIC STEM CELL TRANSPLANT. WMDA RECOMMENDATIONS ON HEV ASSESSMENT IN DONORS AND RECIPIENTS

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Background: Haematopoietic Stem Cell (HPC) Donors are tested for numerous infection disease markers (IDM) to prevent infection transmission from donor to recipient, according to local and international standards both on verification typing (VT) and physical examination (PE). Some Donor Registries and Donor Centres additionally perform IDM testing on collection day. Hepatitis E Virus nucleic acid (HEV NAT) testing is not a standard in HPC donors but is included in IDM panels in some countries.
Objectives: To evaluate the number of serious adverse (product) events and reactions

(SPEARs) reported to WMDA (World Marrow Donor Association) on collection day donor positive HEV NAT results. To propose recommendations for donor registries, collection and transplant centres on the assessment of donor related risk of HEV transmission based on data revied by WMDA SPEAR Committee.

Methods: In 2025 WMDA was informed through the SPEAR Reporting Tool of a probable case of donor–recipient HEV transmission via a Peripheral Blood Stem Cell (PBSC) product. Reports submitted to the WMDA between JAN 2019 and DEC 2025 were analysed to identify all similar cases. The SPEAR Committee prepared a communication to share details on the case and considerations for HEV testing of donors.

Results: Among 2661 reports, 16 incidents concerned positive HEV PCR on collection day. In 12 cases the products were infused before the results were available with only one case of probable transmission described below.
The donor was asymptomatic during work up and collection, with normal liver function tests and negative for HEV NAT at PE. Routinely performed collection day IDMs were available 3 days post donation and revealed HEV NAT positivity. The TC was informed immediately and initiated serial recipient testing. Recipient became HEV NAT positive approximately 4 weeks post transplantation, apparently caused by HEV transmission with HPC product. To WMDA knowledge the patient remained asymptomatic.
High HEV seroprevalence is defined as >25–30% of the population anti-HEV IgG positive and is seen in many European countries (France, Germany, the Netherlands, Poland) where it is contracted zoonotically as a result of consumption of uncooked or undercooked meat (mostly pork), and in many Asian countries (mostly contracted with contaminated water). There are numerous cases of transfusion-transmitted HEV, which can be dangerous for immunocompromised patients. This has led to the implementation of HEV screening strategies among blood and HPC donors in some countries.

Conclusions: **WMDA SPEAR Committee communication and recommendations:**

- Transplant centres should be aware of the risk of HEV transmission with cellular products.
- Consider HEV testing at PE and day of collection, when donor is from high prevalence area.
- Transplant centres should be aware of collection day IDMs being performed and what IDMs are tested, if results are pending – usually available post product infusion.
- Collection day IDMs should be acquired promptly and in case of positive findings should be communicated to transplant centres immediately.
- Serial HEV NAT should be taken into consideration in case of unexplainable post-transplant liver complications.
- All cases of collection day HEV NAT positive findings should be reported as SPEAR depending on outcome.

Disclosure: Nothing to declare

A329

CLINICAL PERSPECTIVES ON GERMLINE VARIANTS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: A NATIONWIDE SURVEY IN JAPAN

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Background: Hereditary hematologic disorders have increasingly attracted attention and represent a critical consideration in the management of hematologic malignancies, particularly in the context of hematopoietic stem cell transplantation (HSCT). In Japan, insurance-covered panel sequencing for hematologic diseases was launched in 2025, enabling broader identification of germline variants in clinical practice. However, the integration of genetic findings into transplant decision-making remains challenging, and awareness and consensus among transplant physicians have not been systematically evaluated. This study aimed to assess transplant physicians' perspectives, experiences, and perceived challenges regarding the issue.

Methods: A nationwide, web-based questionnaire survey was conducted targeting transplant physicians at Japan Society for Transplantation and Cellular Therapy–certified transplant centers from March to April 2025. Personal invitations were sent to eligible physicians. The survey included questions on awareness of germline predisposition, understanding of clinical genetics terminology, experience with HSCT for inherited hematologic disorders, institutional genetic support systems, and unresolved issues related to donor coordination and confirmatory genetic testing. Responses were analyzed descriptively.

Results: A total of 257 physicians responded (response rate, 30%), including 183 adult hematologists, 70 pediatricians, and 4 from other or mixed specialties. Overall, 79% of respondents worked at institutions providing genomic medicine services. Awareness of germline involvement in inherited hematologic disorders was high (95%), as was recognition of germline contributions to solid tumors (87%). Understanding declined with increasing complexity of genetic concepts, particularly regarding variant pathogenicity classification, interpretation of variants of uncertain significance, and confirmatory testing strategies. Differences were observed between pediatricians and adult hematologists, with pediatricians reporting higher familiarity with inherited hematologic disorders and greater experience incorporating genetic information into clinical decision-making, including HSCT for inherited hematologic disorders than adult hematologists (63% vs. 31%, $p<0.001$). The latter more frequently reported uncertainty regarding genetic interpretation and donor-related genetic evaluation, likely reflecting differences in disease spectrum and prior training or clinical experience.
Access to genetic counseling did not differ significantly between the institutions with established genomic medicine infrastructure and non-genomic centers (99% vs. 97%; $p=0.48$). In contrast, confidence in genetic terminology was significantly higher among physicians working at genomic centers than among those at non-genomic centers (59% vs.

25%, $p<0.001$). Although approximately 40% of physicians reported experience with HSCT for inherited hematologic disorders, no national consensus or standardized framework existed for donor coordination among related donor candidates. The necessity, timing, and scope of confirmatory genetic testing for related donors, as well as counseling strategies and subsequent genetic support for patients and family members, varied substantially by specialty and institutional background, and respondents reported persistent operational gaps in these areas.

Conclusions: As germline variants become an integral part of routine HSCT practice, this survey showed that increasing awareness has not yet translated into uniform clinical implementation in Japan, reflecting structural and educational gaps. While international societies have begun to establish shared principles for genetic risk assessment and donor screening, there remains a clear need in Japan to develop comprehensive frameworks for integrating genomic testing into HSCT, including evidence- or consensus-based guidelines, standardized clinical pathways, and cross-disciplinary education.

Disclosure: Nothing to disclose.

A330

AGE-DEPENDENT CHANGES IN LYMPHOCYTE COMPOSITION OF PERIPHERAL BLOOD STEM CELL GRAFTS FOR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Younger donor age is a major determinant of allogeneic hematopoietic cell transplantation (allo-HCT) outcomes, consistently associated with lower non-relapse mortality, improved overall survival, and reduced graft-versus-host disease (GVHD). However, the immunological mechanisms underlying this advantage remain insufficiently defined.

The lymphocyte composition of younger donors may influence graft composition and post-transplant immune recovery, but systematic comparisons of these populations in stem cell products remain limited. This study characterizes age-associated differences in lymphocyte subsets in peripheral blood stem cell (PBSC) grafts to identify immunological features that may contribute to the superior outcomes observed with younger donors.

Methods: We conducted a retrospective single-centre analysis of samples collected from consecutive PBSC grafts from healthy related and unrelated donors between 2024 and 2025. All PBSC products were collected after granulocyte colony-stimulating factor (G-CSF) mobilization, and the study samples were cryopreserved immediately after collection. Lymphocyte subsets were quantified using multiparametric flow cytometry. Donor age was

analyzed as a continuous variable and by predefined cut-offs (30, 40, and 50 years). Statistical comparisons were performed using Pearson/Spearman correlations and Mann–Whitney or t-tests, as appropriate.

Results: Thirty-four consecutive PBSC grafts were analyzed. Median donor age was 36 years (range 15–69), 11 (32%) were ≥40 years and 11 (32%) were female.
As described in Table 1, donor age was associated with a clear shift from a naïve-dominant to a more differentiated lymphocyte graft profile. More specifically, increasing donor age correlated with a significant decline in naive CD4+ T cells (r = -0.36, p = 0.037), total CD8+ T cells (r = -0.379, p = 0.027), and naive CD8 T cells (r = -0.526, p = 0.0014). Moreover, double-negative T cells (CD3+CD4-CD8-), also decreased with age (-0.384, p = 0.025). In contrast, no significant age-related differences were observed in NK cells, $CD19^{+}$ B cells, or γδ T-cell populations.

Table 1. Pearson's correlation according to age.

Subpopulation	Correlation	Confidence interval	*p* value
CD3	-0.226	-0.524 - 0.121	0.198
CD4	0.123	-0.224-0.443	0.487
CD4 Central Memory	0.289	-0.0541-0.572	0.097
CD4 Effector	-0.106	-0.429-0.241	0.551
CD4 Effector Memory	0.301	-0.0416-0.58	0.084
CD4 CD25	-0.047	-0.427-0.347	0.819
CD4 DR	0.067	-0.314-0.429	0.736
CD4 naïve	-0.36	-0.622-(-0.0248)	0.037
CD8	-0.379	-0.635-(-0.0464)	0.027
CD8 CM	0.0189	-0.321-0.355	0.916
CD8 effector	0.286	-0.0579-0.569	0.101
CD8 temra	0.1	-0.246-0.424	0.573
CD8 CD25	0.271	-0.13-0.596	0.18
CD8 DR	-0.0648	-0.428-0.316	0.743
CD8 naïve	-0.526	-0.734-(-0.229)	0.0014
CD19	0.13	-0.218-0.449	0.463
CD NK	-0.203	-0.507-0.145	0.249
DN	-0.384	-0.639-(-0.0525)	0.025
DP	-0.179	-0.488-0.169	0.311
LT Tfh.CXCR5	0.252	-0.134-0.571	0.196
LTTh1 CXCR3 CXCR6	0.264	-0.121-0.58	0.174
LTh1.17 CXCR3 CCR6	0.299	-0.0833-0.605	0.122

NK56 NK56.dim	0.111 0.077	-0.236-0.433 -0.268-0.405	0.532 0.664
LTreg CD12low TCRalfabeta TCRgammadelta Treg mem Treg naïve Treg Th1 Treg Th17 Treg Th2 Treg Th17	0.0064 -0.265 0.178 0.268 -0.0055 0.0906 0.171 0.393 0.351	-0.349-0.36 -0.554-0.0801 -0.17-0.487 -0.0958-0.568 -0.402-0.305 -0.292-0.449 -0.215-0.512 0.023-0.668 -0.0259-0.64	0.973 0.13 0.313 0.146 0.766 0.646 0.383 0.0387 0.0674

Complementary age-stratified analyses confirmed these findings: donors ≥30 or ≥40 years showed significantly lower levels of naïve CD4⁺ and naïve CD8⁺ subsets compared with younger donors (Figure 1). Effector CD4⁺ and CD8⁺ T-cell populations, as well as total regulatory T cells, did not show significant differences across age groups. However, aging was associated with expansion of more differentiated lymphocyte populations, including Th2-polarized regulatory T-cells (r = 0.393, p = 0.0387) and higher CD4⁺ central memory T-cell frequencies in donors ≥40 years (19.18% vs. 26.93%, p = 0.0317).

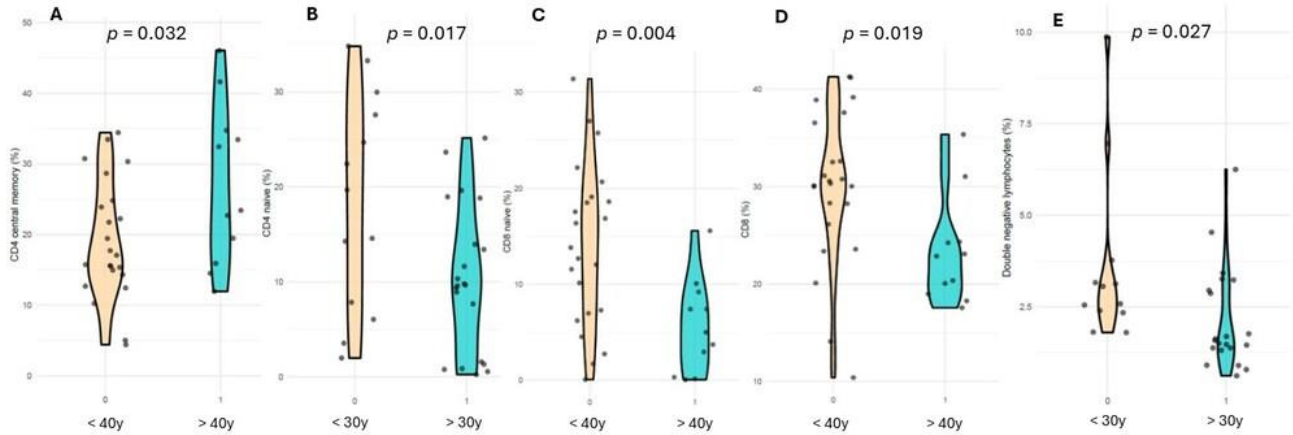

Figure 1. Differences in lymphocyte subsets between donors according to age. A: CD4 central memory; B: CD4 naïve; C CD8 naïve; D: CD8; E: double-negative lymphocytes.

Conclusions: Donor age markedly influenced the immunological composition of PBSC grafts. Younger healthy donors showed a graft profile enriched in naïve CD4⁺ and CD8⁺ T cells and double-negative T cells, consistent with a more plastic and less differentiated immune repertoire that may support robust peripheral expansion during the early post-transplant period and favor more efficient and balanced immune reconstitution. These results offer a biological explanation for the enhanced immune reconstitution, lower immunogenicity, and reduced GVHD risk consistently observed in recipients of younger donors.

Disclosure: Nothing to declare.

A331

CLINICAL VALUE OF ROUTINE BONE MARROW EXAMINATION IN RELATED STEM CELL DONORS

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Background: At some transplant centres, bone marrow aspiration is part of the evaluation of potential related allogeneic haematopoietic stem cell transplant (HSCT) donors. We aimed to determine how often morphological bone marrow examination – performed irrespective of blood counts, peripheral smear findings, or known predisposing germline mutations - influenced donor eligibility and whether abnormal findings led to a haematological diagnosis.

Methods: Retrospective audit of medical records of 208 individuals evaluated as potential related donors for adult patients receiving HSCT at Oslo University Hospital between January 2018 and June 2025.

Results: A total of 902 adult transplants were performed during the audit period; haematological malignancies accounted for 94.8% (n=856). Related donors were used in 15.3% (n=138) of procedures.
Of the 208 potential donors assessed, 207 (99.5%) underwent bone marrow aspiration. The cohort included 140 males (67.3%) and 68 females (32.7%). The familial relationship was as follows: 55% siblings, 12% parents, 26% sons or daughters, 1% half-siblings, and 6% unspecified. The median donor age was 37 (16-69) years.
Six (2.9%) of the evaluated individuals were excluded due to bone marrow abnormalities, of which four (1.9%) had abnormal peripheral counts and/or blood smear, and two (1.0%) had isolated bone marrow findings. Four (1.9%) were excluded due to abnormal peripheral counts and four (1.9%) because of non-hematological conditions.
Of the individuals with abnormal bone marrow smears, two were found to carry variants of uncertain significance (VUS), in PDGFRA (n=1and ATRX (n=1). As of August 2025, none of these have developed hematologic disease. One potential donor was later diagnosed with a hematologic malignancy; this individual had a normal bone marrow smear but abnormal peripheral counts and a sibling with a predisposing germline ERCC6L2 mutation.
Out of 208 individuals 194 (93.3%) were cleared as donors while 14 (6.7%) were not cleared, and to date stem cells have been collected from 164 (79.0%).

Conclusions: Among potential related stem cell donors, isolated morphological bone marrow abnormalities led to donor exclusion in only 1% of cases – and no disease was detected in these. Based on these findings, routine bone marrow assessment has been removed from our related donor evaluation protocol. Ready access to unrelated donors means that related donors are typically evaluated only when there is little concern for family predisposition. Although these findings may not be fully applicable to settings with greater

reliance on family donors, morphological assessment alone appears both insufficient - and likely redundant - as a criterion for donor acceptance.

Disclosure: Nothing to declare.

A332

NOT ALL LOW PLATELET COUNTS ARE SPURIOUS: DUTY OF CARE IN CORD BLOOD BANKING

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Background: FACT NetCord standards require cord blood banks to perform a full blood count (FBC) on collected cord blood units (CBUs) and to investigate abnormalities, with notification of the baby's physician when indicated. Low platelet counts in CB collections can arise from clotting within the placenta or cord, but, if ignored, genuine neonatal thrombocytopenia—including congenital thrombocytopenia or fetal/neonatal alloimmune thrombocytopenia (FNAIT)—could be missed. Following consultation with neonatal haematology and general neonatology experts in our collection hospitals, it was agreed that CB units (CBUs) with platelet counts <100 × 10^9/L should be reported to the baby's neonatal physician.

Methods: The NHS Cord Blood Bank (NHS CBB) established a clinical communication pathway whereby CBB staff notify hospital obstetric or neonatal teams when a platelet count of <100 × 10^9/L is identified in a CBU. Hospital teams decide whether the baby requires follow-up blood testing, and the CBB obtains results of any subsequent FBCs. Further clinical information may be requested to inform donor authorisation and the safety of the donation. This study summarises our findings and compares CBU platelet counts with those obtained directly from babies.

Results: Since July 2016, 15,567 CBUs have been collected. The median platelet count was 270 (mean +/- 2SD: 149-391) (Y. Li, personal communication). A total of 111 CBUs (0.7%) had platelet counts <100 × 10^9/L. Of these babies, 68 (61%) had an FBC performed within 48 hours of birth. Twelve babies (18% of those with follow-up) had confirmed thrombocytopenia. Only two of these twelve had been tested before contact by the CBB -one due to hypoglycaemia and one due to clinical illness of unclear cause. In the remaining ten cases, testing was initiated after CBB notification. One of these babies was anaemic, raising suspicion of congenital viral infection. The other nine were clinically well, but three mothers were found to be thrombocytopenic, with immune thrombocytopenia (ITP) suspected.

Conclusions: While clotting in the placenta or cord often explains low platelet counts in CBUs, identifying true neonatal thrombocytopenia is clinically important. Our findings indicate that 18% of CBUs (12/68) with platelet counts <100 × 10^9/L corresponded to genuine thrombocytopenia in the baby. Although common causes of neonatal thrombocytopenia may be clinically evident, rarer conditions such as FNAIT may not be. Because FNAIT has significant implications for future pregnancies, timely notification of low CBU platelet counts represents an important duty of care. Additionally, maternal immune thrombocytopenic purpura was identified in one-third of cases with confirmed neonatal thrombocytopenia, underscoring the value of this communication pathway for both infant and maternal health.

Disclosure: Nothing to declare.

A333

FEMALE DONORS IMPROVE SURVIVAL OUTCOMES IN HIGH-RISK MALE RECIPIENTS UNDERGOING BONE MARROW TRANSPLANTATION

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Background: In allogeneic hematopoietic stem cell transplantation (allo-HCT), recipients with high-risk diseases often require a strong graft-versus-leukemia (GVL) effect to prevent relapse. However, this benefit is accompanied by increased risks of graft-versus-host disease (GVHD) and non-relapse mortality (NRM). Therefore, the optimal donor and stem cell source for these patients remain unclear.
An HLA-matched related donor is generally considered the preferred option when available. Nevertheless, allo-HCT with female donor and male recipient (F-to-M) is associated with increased risks of chronic GVHD and NRM, even if an HLA-matched related donor is selected. These adverse effects are thought to result from allogeneic immune responses of female donor cells against Y-chromosome antigens in male recipients.
Taken together, recipients with high-risk diseases may potentially benefit from the enhanced allogeneic response in F-to-M allo-HCT through a stronger GVL effect, although this

advantage may come at the cost of a higher risk of chronic GVHD.
Thus, we evaluated whether the effect of sex-mismatched allo-HCT on clinical outcomes differs according to stem cell source among recipients with high-risk disease.

Methods: We analyzed recipients with high-risk diseases who had received their first allo-HCT from an HLA-matched related donor between 2007 and 2024 in Japan, using Japanese registry database. Their diseases included AML (>CR2 or on disease), ALL (>CR2 or on disease), or CML (>CP2 or on disease). Overall survival (OS) was estimated using the Kaplan–Meier method and compared by the log-rank test. Cumulative incidences of relapse and NRM were compared using Gray's test, treating each event as a competing risk. Multivariable analyses used the Cox proportional hazard model for OS and the Fine–Gray model for cumulative incidences. Hazard ratio (HR) of F-to-M allo-HCT was adjusted for recipient age, donor age, disease type, performance status (PS), HCT-CI, conditioning intensity, year of transplantation, and GVHD prophylaxis.

Results: Focusing on male recipients undergoing bone marrow transplantation (BMT), the 2-year OS was significantly higher in the F-to-M group than that in the M-to-M group (54.4% vs. 35.1%, P= 0.025). Multivariable analysis confirmed that F-to-M allo-HCT was associated with improved OS (HR 0.70; 95% CI 0.51–0.96, P= 0.028). Specifically, NRM did not differ significantly between the F-to-M and M-to-M groups (HR 1.03; 95% CI 0.55–1.96, P= 0.92). However, the relapse risk was significantly reduced in F-to-M allo-HCT (HR 0.66; 95% CI 0.47–0.93, P= 0.018), leading to superior survival.
Among male recipients undergoing peripheral blood transplantation (PBSCT), the 2-year OS did not differ between the F-to-M and M-to-M groups (36.2% vs. 35.2%, P= 0.51). Multivariable analyses revealed that F-to-M allo-HCT was not associated with survival outcomes in the PBSCT cohort (HR 1.15; 95% CI 0.95-1.39, P= 0.16). Although the mild reduction in relapse risk might exist (HR 0.86; 95% CI 0.70–1.07, P= 0.18), this benefit was offset by an increased risk of NRM (HR 1.55; 95% CI 1.10–2.19, P= 0.013).

Conclusions: Male recipients with high-risk diseases might benefit from selecting a female donor through increasing GVL effect when BMT was selected as a cell source, but not when PBSCT was selected.

Disclosure: Nothing to declare

A335

TRANSIENT ACUTE MYOCARDIAL INJURY DURING G-CSF MOBILIZATION IN HEALTHY PERIPHERAL STEM CELL DONORS: A CASE SERIES

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Background: Peripheral blood stem cell (PBSC) donation for allogeneic transplantation is widely used thanks to its established efficacy, safety, and lower procedural burden compared to bone marrow donation. The most frequent G-CSF (*Granulocyte-Colony Stimulating Factor*)

– related adverse events are mild musculoskeletal pain and headache, while severe complications are rarely reported. Cardiovascular effects of G-CSF remain controversial, with sporadic reports of vasculitis, myocarditis and myocardial infarction.We report three cases of acute myocardial injury in otherwise healthy donors.

Methods: We retrospectively collected data of 3 healthy donors (2 related and 1 unrelated) who developed acute myocardial injury during PBSC mobilization with biosimilar filgrastim (10 µg/kg/day for 5 consecutive days), observed at our Department between January 2024 and December 2025. Two donors were aged 21 (one male, one female) and had no cardiovascular risk factors, while the third 54 year-old female donor had hypertension and was overweight. In the same period 67 healthy donors were collected in our institution.

Results: All donors presented to the Emergency Room (ER) because of persistent precordial chest pain starting during mobilization and worsening during and after stem cell collection. In two cases hospital admission was required, while the latter case was discharged by the ER and managed as an outpatient. Laboratory testing showed elevated troponin I levels with "raise-and-fall" kinetics (range 21–237 ng/L, normal value < 12 ng/L in females and < 20 ng/L in males) in all donors, with subsequent normalization. In all cases, ECG was normal at admission and discharge. In the 21-year-old male donor, transthoracic echocardiography (TTE) revealed moderate left ventricular (LV) dilatation with preserved ejection fraction (EF); cardiac MRI confirmed the mild LV dilatation with 46% EF in absence of myocardial/pericardial tissue characterization abnormalities. Holter ECG monitoring, coronary angio-CT and anti-myocardial antibodies were negative. He was discharged without specific therapy; at follow-up LV EF normalized. In the 21-year-old female donor TTE showed preserved biventricular function and mild pericardial effusion that was treated with a short ibuprofen therapy. At follow-up she was asymptomatic and pericardial effusion resolved. The 54-year-old female donor had normal TTE and coronary angio-CT; no arrhythmias were detected at continuous monitoring and troponin levels rapidly decreased. She was discharged with indication to perform cardiac MRI, which is planned.

Conclusions: This is among the first reports of transient myocardial injury in healthy PBSC donors after receiving G-CSF, suggesting a possible association. Cardiovascular adverse events should be considered in the differential diagnosis of donors reporting chest pain during HSCs mobilization, leading to prompt cardiological evaluation. Careful clinical monitoring and multidisciplinary management are crucial. Larger datasets are needed to better define the cardiovascular safety profile, long-term cardiac prognosis and possible mechanisms of myocardial injury of G-CSF in healthy donors.

Disclosure: Nothing to declare

A336

EVALUATION OF RELATED HEMATOPOIETIC STEM CELL DONORS IN THE CONTEXT OF FACT-JACIE STANDARDS IMPLEMENTATION

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Background: The appropriate evaluation of donors aims for donor safety, product quality, and recipient safety. Our objective was to describe the results of these evaluations in a setting of FACT-JACIE standards implementation.

Methods: Data from related allogeneic hematopoietic stem cell donors between 2019 and 2025 were retrospectively analyzed. Donors were evaluated in the Bone Marrow Transplant and Cellular Therapy Program at Hospital Privado Universitario de Córdoba, Argentina. Data were collected on laboratory studies, type of donation, and associated complications. Both pediatric and adult donors were included.

Results: Between 2019 and 2025, 252 potential related donors were evaluated (median age 36 years; range 3 to 70 years; males 135, 53.6%).
Among mandatory infectious disease screening tests in Argentina, positivity was as follows: syphilis serology, 7 cases (2.8%); Chagas serology, 6 cases (2.4%); HTLV-I/II, 1 case (0.4%); and hepatitis B core antibody (anti-HBc), 1 case (0.4%). No positive cases were detected for HIV (serology and NAT), HCV (antibodies and NAT), HBV (surface antigen and NAT), or brucellosis. All donors with positive results were considered ineligible.
Other relevant test results were as follows: CMV IgG positivity in 222 cases (88.1%), EBV IgG positivity in 241 cases (95.6%), and toxoplasmosis positivity in 61 cases (24.4%).
Of all hemoglobin electrophoresis performed, only one case (1.5%) was heterozygous for sickle cell disease (SCD) and was excluded. This subject presented mild anemia on the blood count.
In total, 15 donors were considered ineligible (5.9%), of which 12 were later deemed suitable to donate after further evaluation and/or treatment of the cause of ineligibility and donated without evidence of recipient-related complications. The remaining three patients were considered not suitable for the following reasons: SCD (also with Chagas positivity), dysfibrinogenemia (also with syphilis positivity), and HTLV-I/II positivity.
Additionally, five donors who were eligible were not suitable for donation due to the following reasons: breast cancer diagnosed during the evaluation, uncontrolled comorbidities, Wolff-Parkinson-White diagnosed during evaluation, positive pregnancy test, and history of antiphospholipid syndrome with pulmonary thromboembolism.
A total of 244 subjects donated for a relative (96.8%): 205 cases by peripheral blood (apheresis; 84.0%), 37 cases by bone marrow (harvest; 15.2%), and 2 cases by both methods (0.8%). Among apheresis donors (median age 38.5 years; range 3–70; 100 females), 22 required more than one apheresis (10.7%), 30 (14.6%) required catheter placement, and 18 (8.8%) received plerixafor in addition to filgrastim. Catheter placement

was more frequent in female donors (26.0% vs 3.7%; p < 0.001).
Overall, significant adverse events occurred in only three cases (1.2%): thrombosis in one patient and bleeding in another, both related to the apheresis catheter and resolved completely without hospitalization; and one donor who required hospitalization for G-CSF–associated bone pain.

Conclusions: Stem cell donation, whether from peripheral blood or bone marrow, is a safe procedure in the context of implementing FACT-JACIE quality standards. The most frequent positive tests in our setting are syphilis and Chagas disease, which did not contraindicate donations. Conversely, detection of SCD was a rare event in our series and among patients with normal hemoglobin levels.

Disclosure: Nothing to declare.

A337

SERIOUS ADVERSE REACTIONS AND EVENTS IN RELATED HAEMATOPOIETIC CELLS DONORS – WMDA COMMUNICATION AND RECOMMENDATIONS ON RELATED DONORS FOLLOW UP AND REPORTING OF SAE

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Background: WMDA (World Marrow Donor Association) governs a global biovigilance system for serious (product) events and reactions (SPEAR) reporting that allows submission of SPEARs for unrelated and related haematopoietic cells (HPC) donors. We present data on SPEARs concerning related donors submitted to WMDA.

Methods: SPEAR reports submitted between 31.12.2018 and 28.11.2025 were grouped to show number of reports in related (RD) and unrelated donors (UD), difference in number of reporting organizations, report types, HPC collection methods in the reported incidents, median age of RD and UD that were subject to harm.

Results: Overall, 88 RD reports were submitted by 17 organizations. Number of reports per organisation varied from 1 to 56, with most reporting single incidents. By law, some registries are required to conduct UD and RD follow-up (FU) starting 6 months post donation. All the reports were accepted, but 4 did not fulfil the SPEAR definition. There were 78 Harm to Donor (HtD) reports, 5 Risk of Harm (RoH) and 1 Harm to Recipient (HtR) report. One minor RD was lost to FU until six years when reported chronic and persistent pain and a lump

at the collection site which proved clinically relevant.
Table 1 summarises details on reports.
There were 31 Short Term HtD reports (occurred within 6 months post donation). Two solid tumours diagnosed within the first 6 months of donation were probably present at the time of donation (59-year-old male with kidney cancer and 67-year-old male with a prostate cancer). Two donor deaths – none deemed related to the donation procedure. Among the 47 Long Term HtD reports (>6 months post donation), 32 malignancies were reported (5 haematological and 27 non-haematological). Median age of RD was 47 years.
The number of SPEARs reported for UD was 2402 with 1929 HtD, 340 HtR and 133 RoH reports. There were 917 short term HtD reports, with the most frequent report types presented in table 1. Long term HtD (974) were predominantly malignancies and autoimmune diseases reported per WBMT Minimal Data Set, not related to donation. Median age of UD was 30 years.

Table 1. Summary of incidents reported on related versus unrelated donors	**Related Donors**		**Unrelated Donors**	
Number of reports accepted as SPEAR	84		2402	
PBSC	67 (80%)		1962 (82%)	
BM	10 (12%)		355 (15%)	
MNC	7 (8%)		41 (2%)	
Harm to Donor	78		1902	
Short Term Harm	31		917	
The most frequent types of donor harm	Thrombotic/embolic	6	Infections	192
	Infections (COVID-19)	5	Acute systemic toxicity during mobilization or collection	111
	Cardiovascular	4	Autoimmune disease	82
	Bleeding complications	3	Unnecessary Donor Burden	72

Table 1. Summary of incidents reported on related versus unrelated donors	Related Donors		Unrelated Donors	
	Allergic reaction	3	Allergic reaction	68
	Unnecessary Donor Burden	3	Cardiovascular	42
	Autoimmune disease	2	Mechanical damage	41
	Non-haematological malignancy	2	Non- haematological malignancy	26
	Other	3	Thrombotic/embolic	25
Long Term Harm	47		974	
Autoimmune diseases	12		378	
Malignancies	32		560	
Other	3		36	

Conclusions:

- Reporting of RD SPEAR is considerably smaller than in UD, rather caused by underreporting, especially considering that per WBMT data even up to 53% of transplants are performed using related donors.
- The reports originate mostly from one organisation legally obliged to conduct RD FU and from organisations that facilitate coordination of HPC collection from RD.
- Median age of RD, whose harm was reported, is higher than of UD (47 versus 30 years).

WMDA communication and recommendations on related donor follow up:

- It is essential to conduct follow-ups for all donors, including related, and report all SPEARs.
- Clear protocols of FU should reach minor donors through their guardians, with sensitivity to privacy and consent.

- Follow-up should be age-appropriate, with tools and communication tailored to minors and their families.
- Consider extending the standard 10-year follow-up period until the minor donor reaches the age of majority to ensure the independence of the information collected.

Disclosure: Nothing to declare.

A338

EVOLUTION OF UNRELATED DONOR ACTIVITY IN CHILE: RETROSPECTIVE ANALYSIS OF DKMS DONOR SEARCHES FROM 2018 - 2024

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Background: Unrelated donors (URDs) remain essential for stem cell transplantation (SCT) in patients lacking matched sibling donors (MSDs). Despite global growth in donor registries, individuals from ethnically diverse and admixed populations—such as those in South America—remain underrepresented, resulting in reduced match probabilities. DKMS Chile was established in 2018 and has since recruited over 302,000 URDs and facilitated the shipment of 650 stem cell products, including 243 for Chilean patients. The DKMS Registry, active in Chile since 2016, supports nationwide URD searches in collaboration with public and private transplant centers. Beginning in July 2024, all WMDA donors were included in the searches. The main objective is to demonstrate the impact on patients in Chile by analyzing donor activity within the country.

Methods: We performed a retrospective analysis of all DKMS Registry searches for Chilean patients from July 2018– June 2024. High-resolution typing was available for HLA-A, -B, -C, -DQB1, and -DRB1. For each search, the number of 10/10 matched unrelated donors (MUDs) and 9/10 mismatched unrelated donors (MMUDs) was recorded. Searches were categorized by whether they yielded 0, 1, or ≥5 donors. URD SCT activity reported to the WMDA from 2018–2024 was analyzed, comparing use of DKMS Chile versus international donors. Donor utilization trends were also assessed for pediatric SCT in three major Chilean transplant centers (Luis Calvo Mackenna Hospital, Davila Clinica and UC Christus).

Results: During the analyzed period, 586 URD searches were conducted. The proportion of patients without any available MUD or MMUD donors decreased from 21% (July 2018–June 2019) to 17% (July 2023–June 2024). At the same time, searches resulting in at least one available MUD donor increased from 42% to 46%. The number of bone marrow (BM) and peripheral blood stem cell (PBSC) URD products shipped to Chile and reported to the WMDA increased from 5 to 75. In 2024, products shipped by DKMS Chile represented 64% of the

total. Three pediatric transplant centers reported a total of 510 SCT during this period. Utilization of URDs rose from 7% to 56%, while the use of cord blood units (CBUs) declined from 50% to 3% ($p < 0.001$). The proportion of URDs used was evenly distributed between MUD and MMUD.

Conclusions: The establishment of the DKMS Chile donor center and its integration into national transplant programs have contributed to significant improvements in unrelated donor (URD) matching and have supported the expansion of allogeneic stem cell transplantation within the country. The continued growth of a large, locally recruited donor registry—now comprising over 302,000 fully HLA-typed individuals—has led to a steady reduction in the proportion of patients without suitable matches.
While these outcomes are promising, it is crucial to pursue further analysis using larger datasets or more granular methodologies. Nevertheless, considering the persistent underrepresentation of HLA types and the high degree of genetic admixture in South American populations, the Chilean experience provides a scalable model that could inform the development of comparable initiatives throughout the region.

Disclosure: Nothing to declare

A339

EXPANDING DONOR ACCESS IN DEVELOPING COUNTRIES: EXPERIENCE WITH PEDIATRIC HAPLOIDENTICAL STEM CELL TRANSPLANTATION AT A PRIVATE CENTER IN JORDAN

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Background: Hematopoietic stem cell transplantation (HSCT) is an established therapeutic modality for a broad range of malignant and non-malignant conditions. Matched sibling donors (MSD) are not frequently available, and access to large unrelated donor registries remains limited in the Eastern Mediterranean region. Haploidentical HSCT (haplo-HSCT) has emerged as an increasingly important alternative, offering rapid donor identification and wider applicability. The introduction of post-transplant cyclophosphamide (PTCy) has significantly enhanced the safety and feasibility of haplo-HSCT. Despite its expanding global use, published data from our region remains limited.

Methods: A retrospective medical file review of all pediatric patients who received haplo-HSCT at the Bone Marrow and Stem Cell Transplantation Center, Istishari Hospital, Jordan, from June 2016 till, June 2025.

Results: Twenty-seven patients underwent 29 T-replete haplo-HSCT with PTCy. The median age was 7.6 (range, 0.6–21) years and 20 (74%) were males. Thirteen patients had acute leukemia, including 6 with acute lymphoblastic leukemia (ALL) and 7 with acute myeloid leukemia (AML). Fourteen patients had non-malignant disorders, including severe aplastic

anemia (SAA; n = 9), hemoglobinopathies (n = 3), and inborn errors of metabolism (n = 2). A parent served as the donor in 80% of transplants. Peripheral blood stem cells (PBCs) were the graft source in 20 transplants (69%). Donor-recipient ABO incompatibility was documented in 8 (28%) and gender mismatch in 19 (66%) transplants. The median infused CD34+ and CD3+ cell doses were 8.4 $\times 10^6$/kg (range1.4–19) and 21.7 $\times 10^7$/kg (range 3.4–48), respectively. Total body irradiation (TBI) was incorporated in the conditioning regimen in majority of the transplants (n=26, 90%), with single fraction TBI of 300 cGy was used in 16/29 transplants (mostly for non-malignant disorders). Engraftment was documented in 26/27 patients with a median of 15 (11–32) days for neutrophil and 21 (13–75) days for platelets engraftment. One patient with SAA had primary graft failure and subsequently engrafted following a second haplo-HSCT.
Post-transplant complications included CMV reactivation (n=12, 41%), EBV reactivation (n=2, 6%), BK virus cystitis (n=2, 6%), adenovirus colitis (n=1, 3%), HHV-6 reactivation (n=1, 3%), mucor mycosis sinusitis (n=1, 3%), central venous line-associated bloodstream infection (n=4, 13%), idiopathic pneumonitis (n=1, 3%), posterior reversible encephalopathy syndrome (n=3, 10%), and pneumatosis intestinalis (n=1, 3%). Only one patient required ICU admission for sepsis and subsequently recovered.
At a median follow-up of 49 months (range 6–109), 20 patients are alive with overall survival of 75%. Notably, survival among patients with non-malignant disorders was excellent (93%). We lost 7 patients, 4 of them due to leukemia relapse. One patient with infantile ALL is still alive and disease-free following an second haplo-HSCT due to disease relapse.

Conclusions: Haplo-HSCT offers a reasonable and effective option for patients lacking MSD, specially in regions with scanty unrelated donors registries. We documented favorable outcome and excellent survival that compares to international data, particularly for patients with non-malignant hematological diseases, highlighting its feasibility and effectiveness in a resource-limited settings.

Disclosure: Nothing to declare.

A340

IDENTIFYING REASONS FOR LOCAL VS INTERNATIONAL UNRELATED DONOR SELECTION IN HEMATOPOIETIC CELL TRANSPLANT IN CANADA

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Background: Understanding factors impacting unrelated donor selection for allogeneic hematopoietic cell transplantation continues to evolve. An examination of donor usage in for Canadian patients was undertaken to understand what donor factors are prioritized, and why international donors may be chosen in preference to local Canadian donors. Our aim was to inform the optimal recruitment of registrants to the unrelated donor registry at Canadian Blood Services.

Methods: Retrospective cohort study of consecutive unrelated allogeneic donor transplants performed in Canada (excluding Quebec) in 2023.

Results: We identified a total of 500 patients (mean age 51.7 years; 8.2% < 18 years; 62% male) who underwent transplants involving HLA-matched (n=416, 83%) or mismatched unrelated (17%) donors. Indications for transplant were: Leukemias (59.8%), myelodysplasia (17.6%) and other malignant and non-malignant diseases (22.6%). Mean donor age was 28.7 years. Donor/recipient CMV concordance was present in 73% and ABO match or minor mismatch was present in 62%. Selection of Canadian (CDN) donors for CDN patients (n=50, 10% of all transplants) was characterized by a preference for 10/10 HLA-matched, young (≤ 30 years old), male registrants and was positively influenced by availability of donor CMV serostatus and ABO blood group typing at time of initial donor search. In cases where an international donor was used and where an HLA-matched CDN donor option was also present at search, transplant centres prioritized young (≤ 30 years), male, CMV matched donors. ABO matching and HLA-DP-matching appeared as lower priorities in donor selection.

Conclusions: This real world evidence study demonstrated that donor youth (<30), male donor sex, and baseline CMV and ABO serology are important variables associated with domestic donor selection. To best serve the Canadian patient population, HLA matched donors will benefit from CMV and ABO results available as these data will facilitate timely donor selection.

Disclosure: All authors are employees and/or paid consultants with Canadian Blood Services. The authors have no other disclosures.

A341

AN INTERSTING CASE OF DONOR DERIVED LEUKAEMIA POST CORD BLOOD TRANSPLANT

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Background: Donor-derived leukemia and clonal haematopoiesis are rare, often hard-to-recognize complications of allogeneic HSCT with poor prognosis. We report a case of donor-derived JMML with a PTPN11 variant occurring eight months after cord blood transplant for high-risk AML.

Methods: A 13-year-old boy underwent a T-cell–replete 6/8 mismatched cord blood transplant (CBT) with treosulfan-based myeloablative conditioning for high-risk post-transplant relapse of KMT2A-mutated, therapy-related AML in molecular remission. Third-party granulocytes were administered peri-transplant under the GRANS trial to enhance CD8 cytotoxic T-cell expansion and augment the graft-versus-leukaemia effect from the engrafting cord blood. His previous medical history included pre-B acute lymphoblastic

leukaemia (ALL) treated successfully according to UKALL 2019 guidelines, following which he unfortunately developed therapy-related AML with a KMT2A::MLLT3 rearrangement. After achieving molecular remission with debulking chemotherapy, he underwent a matched unrelated donor HSCT with busulfan-based conditioning. He remained in molecular remission with full donor chimerism until a molecular relapse occurred 14 months post-transplant. Following venetoclax-based therapy and renewed remission, he proceeded to a second HSCT as described above.
He engrafted promptly with full donor chimerism. His post-transplant course was complicated by grade 4 biopsy-proven gut graft-versus-host disease requiring multiple therapeutic agents. Secondary to the GVHD process, he developed transplant-associated thrombotic microangiopathy (TA-TMA) and received eculizumab with partial response. Six months post-transplant, he developed progressive leucocytosis characterised by neutrophilia and left-shifted myeloid precursors. Baseline monocytosis gradually increased without circulating blasts. Persistent nucleated red cells were initially thought to reflect consumptive processes in the context of active TMA. Over the following months, his white cell count rose above 100×10^6/L, with chimerism consistently donor in all lineages, unremarkable bone marrow assessments, and persistently negative KMT2A::MLLT3 transcripts. Myeloid NGS identified a PTPN11 missense variant (VAF 46%), establishing a diagnosis of donor-derived JMML. He deteriorated and died shortly thereafter. The DDL event was reported to the cord blood registry for donor follow-up.

Results: Donor-derived leukaemia (DDL) after umbilical cord transplantation is rare but clinically important. Reported prevalence is 80.5 cases per 100,000 transplants, with cumulative incidences of 0.067%, 0.132% and 0.363% at 5, 10 and 25 years after HSCT. Both patient and donor factors appear contributory. Inconsistent genetic screening during donor selection, significant donor germline variants, and acquired donor clonal haematopoiesis within a heavily treated recipient marrow microenvironment all increase risk. MDS and AML are the most frequent DDL subtypes, whereas donor-derived ALL, CML and multiple myeloma are rarely described. This represents the first documented case of donor-derived JMML. Data regarding donor outcomes in DDL are limited and especially difficult to obtain for cord blood donors. Notably, in an EBMT survey, only a modest proportion of donors (8–20%) subsequently developed haematological malignancy on follow-up. These observations highlight the need for systematic long-term monitoring of both recipients and donors to better characterise risks overall.

Conclusions: We document the first donor-derived JMML with a PTPN11 mutation after cord blood transplant. This case underscores diagnostic challenges, the need for awareness of DDL, and the importance of standardised donor genetic screening despite ethical and logistical barriers.

Disclosure: Nothing to declare

P109

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION USING DECEASED DONOR DERIVED CRYOPRESERVED BONE MARROW: A POTENTIAL ALTERNATIVE GRAFT SOURCE FOR PATIENTS WITH UNMET NEED

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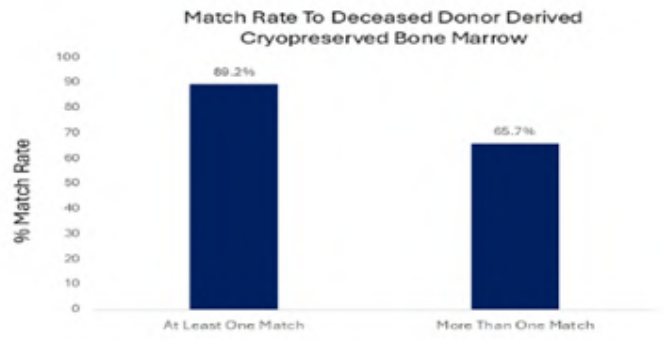
Background: It's been reported that expanding access to allogenic hematopoietic cell transplant (HCT), for patients is feasible as the outcomes of using mismatch unrelated donors (MMUD) along with post-transplant cyclophosphamide are similar to those obtained using a related haploidentical donor. A significant unmet need remains in the timely provision of suitable unrelated donor grafts. An alternative hematopoietic progenitor cell (HPC) graft source obtained from the vertebral bodies (VBs) of deceased organ donors could alleviate many of the obstacles for patients that lack a suitable HLA-matched donor and for high risk patients who require faster HLA-mismatched donor options.
We have developed a GMP compliant process to recover and cryogenically bank HPCs from deceased organ donors (OD). Here we present the results from 988 deceased donors to quantify if unmet needs in patients who require allogeneic transplants can be addressed by an on demand cryopreserved bone marrow product.

Methods: Nineteen clinical sites involved in recruitment of acute leukemia patients who are eligible for allogenic transplant were evaluated to determine the potential for matching to an OD-HPC, Marrow (Cryopreserved) product if a suitable living donor was not available in a timely fashion. Patients who could not find more than three fully HLA matched living donors were evaluated for availability of an OD-HPC product from the bank. The sites participating in PRESERVE I and the HOPE program were evaluated. PRESERVE I is a clinical trial studying safety and efficacy of 4-8/8 HLA-matched HPC, Marrow (Cryopreserved) recovered by organ procurement organizations (OPOs) and shipped to our manufacturing facility for processing. The HOPE program is an expanded access program offered to patients who do not qualify for PRESERVE.

Results: Two hundred and thirty-two patients with hematological malignancies eligible for allogenic HCT treatment were matched to Ossium's cryopreserved HPC, marrow inventory. The match rate was 89.2% (n=207/232). 65.7% of patients matched to more than one cryopreserved product. Donor age ranged from 7 to 55 years old (mean age=36) and average dose available was 5.9M CD34 cells/kg for a 70kg patient.



Conclusions: Since 2024, through our combined efforts, Eleven patients received life-saving bone marrow transplants for whom a suitable living donor was not available. We are partnering with key OPOs to increase the bank size, which will increase access to life saving bone marrow transplants for patients with unmet needs. Timely availability of a HPC, Marrow (Cryopreserved) product obtained from deceased donors can serve as another important option for expanding access to HCT for patients with hematological malignancies and non-hematological conditions. Ongoing clinical studies are evaluating efficacy and safety of this novel, OD-HPC, Marrow (Cryopreserved) product.

Clinical Trial Registry: NCT05589896, NCT07145411

Disclosure: Sagar Munjal is an employee of Ossium Health
Termeh Shamloo is an employee of Ossium Health
Preethi Prasad is an employee of Ossium Health
Brian H. Johnstone is an employee of Ossium Health
Erik J. Woods is an employee of Ossium Health

P110

FIRST REPORT OF SUCCESSFUL, LIFESAVING AND TIMELY GRAFT RESCUE USING AN OFF-THE-SHELF CRYOPRESERVED, CADAVERIC

MARROW IN TRANSPLANT FOLLOWING UNAVAILABILITY OF A LIVING MATCHED UNRELATED DONOR

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Background: Allogeneic hematopoietic cell transplantation (alloHCT) remains a curative therapy for patients with acute myeloid leukemia (AML) and relies on timely donor availability. When a donor becomes unavailable after conditioning, outcomes can be catastrophic, especially following myeloablative regimens. This case report describes the timely and successful use of cryopreserved, off-the-shelf, hematopoietic progenitor cells (HPC) derived from cadaveric bone marrow (BM), after an unexpected living donor unavailability.

Methods: A 34-year-old male with AML in first complete remission (CR1) began myeloablative fludarabine/busulfan conditioning in preparation for a 10/10 HLA-matched unrelated donor peripheral blood stem cell transplant. On Day -3 of conditioning, the donor experienced a severe allergic reaction to filgrastim, rendering the donor ineligible. Conditioning was interrupted after receiving 3 of 4 planned doses of fludarabine 40 mg/m^2/d and busulfan 131 mg/m^2/d To facilitate faster receipt of an allograft, an emergency request for a cryopreserved HPC-BM product from a deceased donor was submitted. Within 24 hours of request, a 6/8 HLA-matched, bidirectional ABO mismatched marrow graft was chosen among six allograft options and within 72 hours, the product was shipped to the treating institution.
The deceased donor was a 41-year-old White female and 6/8 HLA matched to the recipient. The BM was available as an off-the-shelf product, obtained by harvest from vertebral bodies and processed and cryopreserved via proprietary methods. The product contained 5.57 × 10^6 CD34$^+$ cells/kg.
A fourth fludarabine 40 mg/m2 dose was given and the HPC-BM infusion was infused 48 hours after the planned day 0 and was well tolerated. GVHD prophylaxis consisted of tacrolimus, mycophenolate mofetil, and post-transplant cyclophosphamide.

Results: Neutrophil engraftment was achieved on Day +14 (ANC: D+14 = 1.17 K/µL; D+15 = 5.61 K/µL; D+16 = 10.36 K/µL) with robust platelet engraftment reported by Day +16 (D+16 = 108 K/µL; D+17 = 115 K/µL; D+18 = 138 K/µLDay +30, donor chimerism increased to 61% for CD3$^+$ cells and remained 100% donor in the CD33$^+$ lineage. By day 100, CD3 chimerism increased to 87% and CD33 chimerism remained at 100%. Day 30 and 100 marrow biopsy confirms molecular and morphologic remission with donor-derived hematopoiesis.
The patient developed steroid-responsive grade II acute upper GI GVHD (stage 1) on Day

+27, and Grade 1 skin GVHD responsive to topical therapy.

Fig 1: Patient safety journey

Conclusions: Timely access to an off-the-shelf marrow product prevented catastrophic graft failure or debilitating opportunistic infections. Day 0 was delayed by only 48 hours and the product was identified within 24 hours of request. A clinical trial using cryopreserved, off-the-shelf marrow grafts as primary graft option is underway (NCT #05589896).

Clinical Trial Registry: NCT07145411

Disclosure:

1. Sumithira Vasu – Advisory board : Alexion and Omeros
2. Sarah Wall – Nothing to declare
3. Karilyn Larkin – Nothing to declare
4. Sagar Munjal is an employee of Ossium Health
5. Marcos de Lima – Abbvie Consulting: Pfizer, Autolus, Kite Research collaboration: Pfizer, Miltenyi Biotec Board Member: Greenjay Therapeutics
6. Gabriela Sanchez -Petitto, MD Consulting: GamidaCel and BMS.

P111

OUTCOMES AFTER HAPLOIDENTICAL STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE: A RETROSPECTIVE SINGLE-CENTER COHORT STUDY

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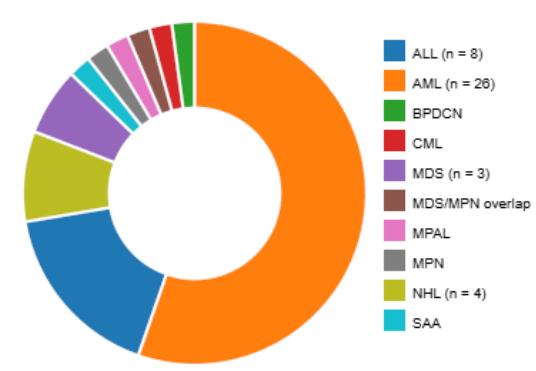
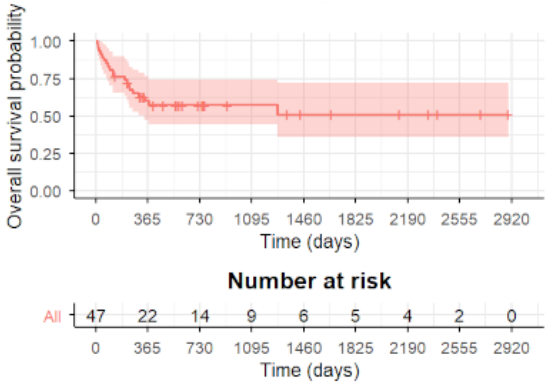
Background: Haploidentical stem cell transplantation (haploSCT) with post-transplant cyclophosphamide (PT-Cy) has broadened donor availability and is increasingly used when a matched unrelated donor (MUD) is unavailable or when urgent transplantation is required. Several studies have shown comparable outcomes between haploSCT and MUD transplantation when PT-Cy-based graft-versus-host disease (GvHD) prophylaxis is used. We report outcomes of all consecutive patients who underwent haploSCT with PT-Cy at a single center in Germany.

Methods: We retrospectively analyzed 47 adult patients undergoing alloSCT from a haploidentical donor at the Charité, Universitätsmedizin Berlin (Germany) between January 2016 and May 2024. Statistical analysis was performed in R version 4.5.2.

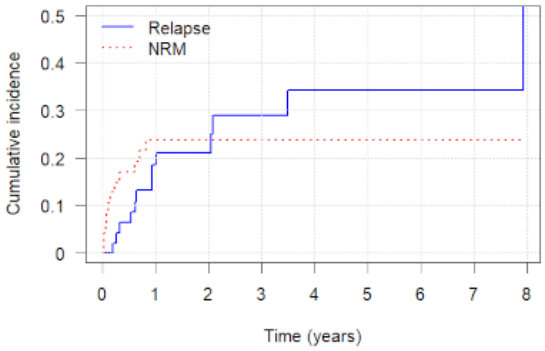
Results:



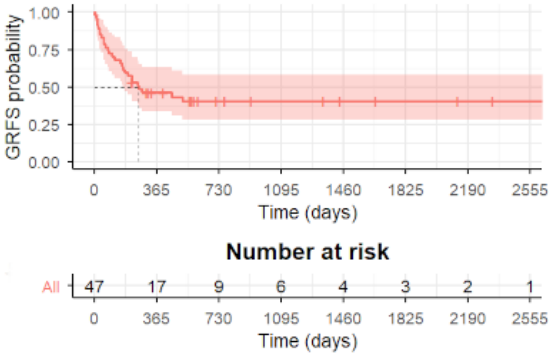
a. Underlying diseases in patients undergoing haploSCT



b. Probablility of Overall Survival



c. Cumulative incidence of relapse and non relapse mortality (NRM)



d. Probability of GvHD-free, relapse-free survival (GRFS)

Median time of follow-up was 25 months (range, 9 days-95 months). The median age at transplant was 41 years (range, 21-67). Donors had a median age of 36 years (range 14-72). AML was the most frequent indication for transplantation (51%), followed by ALL (17%). Patient characteristics are summarized in Table 1, and underlying diseases are displayed in Figure 1a. At the time of transplant, 57% of patients were in complete remission (CR1 or CR2), while 28% presented with relapsed or refractory disease; 19% had previously undergone an alloSCT. High HCT-CI (≥3) was present in 30% of patients, and 23% had a Karnofsky score ≤70%, reflecting a relevant proportion of high-risk candidates. The day 100 cumulative incidence of CMV reactivation was 21%. Acute GvHD (aGvHD) grade II-IV occurred in 27% (95% CI: 13-39%) and grade III-IV in 4% (95% CI: 0-10%) of patients. The 1- and 3-year Cumulative Incidence of Relapse (CIR, Figure 1c) was 19% (95% CI: 7-31%) and 30% (95% CI: 14-46%), respectively. Non-Relapse Mortality (NRM, Figure 1c) at day 100, 6 months, and 1 year was 14% (95% CI: 5-25%), 17% (95% CI: 6-28%), and 23% (95% CI: 11-35%). Overall Survival (OS, Figure 1b) at 1 year and 3 years was 60% (95% CI: 47-77%) and 57% (95% CI: 44-74%), respectively.

Variable	Level	n	%	median	range
HaploSCT Timepoint	2016-2018 2019-2021 2022-2024	13 9 25	28 19 53	-	-
Patient Sex	Male Female	33 14	70 30	-	-
Patient Age (years)	-	-	-	41	21-67
Donor Age (years)	-	-	-	36	14-72
Disease Status before HaploSCT	CR1/CR2 Refractory/relapsed PR n/a	27 13 2 5	57 28 4 11	-	-
CMV Serostatus Match, Donor/Recipient	Negative/Negative Positive/Negative Negative/Positive Positive/Positive n/a	8 4 13 21 1	17 9 28 45 2	-	-
Table 1.	**Patient and Donor Characteristics**				

Conclusions: Outcomes in our cohort were consistent with contemporary reports of PT-Cy-based haploSCT. The relatively low CIR alongside notable early NRM suggests a pronounced graft-versus-leukemia effect, achieved despite a low incidence of severe aGVHD. Importantly, these results were observed in a high-risk patient population with a substantial proportion of relapsed/refractory disease, prior alloSCT, high comorbidity burden (HCT-CI ≥3), and impaired performance status, supporting the feasibility and effectiveness of haploSCT even in this challenging setting. While early NRM remains a key limitation, long-term survival was achievable in patients surviving beyond the early post-transplant period. HaploSCT therefore represents a robust option for patients lacking a suitable MUD or requiring urgent transplantation. Prospective comparative studies are warranted to determine optimal donor choice and refine patient selection for haploSCT.

Disclosure: No conflicts of interest in relation to this abstract.

P112

MANAGEMENT OF GROUP B STREPTOCOCCUS IDENTIFIED DURING STERILITY TESTING OF CORD BLOOD UNITS

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Background: All cord blood units (CBUs) collected by the NHS Cord Blood Bank (CBB) undergo sterility testing. Very infrequently, the NHS CBB identifies contamination of CBUs with Group B Streptococcus (GBS).
GBS infection *(Streptococcus agalactiae)* is the most frequent cause of severe early-onset infection in newborn infants. There is no national screening programme for GBS in the UK but, when GBS is identified in pregnancy, UK guidelines require specific follow-up in subsequent pregnancies, to minimise the risk of neonatal GBS infection. The clinical significance of GBS identified on CBU sterility testing is less clear.

Methods: Subject matter experts and stakeholders (microbiologists, neonatologists, NHS CBB medical and laboratory staff) agreed that it was clinically appropriate to share GBS positive results with donor mothers and healthcare staff, retrospectively and prospectively. A communication process had to be developed, considering that the retrospective follow-up period spanned a decade. The donor's current general practitioner (GP) was identified and contacted by NHS CBB medical staff, to provide rationale for contact and explore the most appropriate approach to the donor mother. Where appropriate, medical staff then contacted the mother directly, explained the result and provided patient information. The GP was then updated on outcome of communication and asked to record the results in the mother's record.

Results: From December 2014 to September 2025, 8751 CBUs underwent sterility testing, 259 were bacterially contaminated and of those, 11/8751 (0.13%) were reported positive for GBS (3 month period in 2016 excluded - data unavailable).
8 GPs were contacted for retrospective follow-up. In one case, the GP strictly advised not to contact the mother due to unrelated reasons. For the remaining seven cases, the GP deemed it appropriate to contact the donor mother and this was done as per process described above.
It was possible to communicate with all 7 mothers. They were satisfied with the information provided. No neonatal complications attributed to GBS were reported for the index or subsequent pregnancies.
For two cases, no retrospective follow-up was undertaken: due to a combination of donor not being registered with a GP, together with length of time since donation (9 years) and current maternal age (49 years) (one case). In another case, donation was over 10 years prior to case identification and current maternal age 52 years.

One case was identified prospectively and the mother contacted directly on day 13 post donation

Conclusions: Retrospective identification of relevant cases and communication between GP practices, donors and the NHS CBB were logistically challenging and required a careful step-by-step process. Experience has highlighted the importance of engaging with the GP to avoid potentially inappropriate contact with the donor. Feedback from GPs and mothers has been very positive, and the process has minimised impact on GP workload.
Although risk and impact are low, the NHS CBB has a duty of care to communicate test results that may have clinical significance. Future prospectively identified cases are expected to be managed and donor mothers notified within 6 weeks post cord blood donation.

Disclosure: Nothing to declare

Relapse and Graft-versus-Leukemia

OS17-02

TP53 VARIANT ALLELE FREQUENCY AS A GENETIC MRD MARKER PREDICTS RELAPSE AND GUIDES SUBTYPE-SPECIFIC THERAPY IN TP53-MUTATED AML/MDS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: TP53 mutations occur in up to 20% of acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS) patients, defining a high-risk disease with poor outcomes. Allogeneic stem cell transplantation (HCT) remains the only potential curative option, but relapse due to measurable residual disease (MRD) remains a major challenge. Despite the established prognostic value of genetic MRD in specific AML subtypes (e.g., those with NPM1

or FLT3-ITD mutations), the predictive significance of pre- and post-transplant genetic MRD across TP53-mutated AML/MDS subtypes remains unclear in patients undergoing HCT.

Methods: This multicenter cohort study enrolled 139 adult patients with TP53-mutated AML, MDS, or MDS/AML who underwent their first HCT between September 2016 and April 2024. TP53 variant allele frequency (VAF), as genetic MRD, is assessed using digital droplet PCR. Multiparametric flow cytometry (MFC) is also employed for MRD evaluation. Key endpoints included overall survival (OS), event-free survival (EFS), and cumulative incidence of relapse (CIR). Patients were stratified by disease subtypes (AML and MDS/AML with blasts ≥10% vs. MDS with blasts <10%) and pre-transplant genetic MRD thresholds. The impact of conditioning regimens, including decitabine-based protocols, was analyzed based on MRD status.

Results: When stratified by pre-HCT genetic MRD into three groups (VAF≤0.01%, 0.01–0.1%, and >0.1%), patients with VAF >0.1% had significantly inferior outcomes compared to the other two groups (2-year OS: 55.4% vs. 76.7%/75.0%, p=0.240;2-year EFS: 40.3% vs. 69.7%/75.0%, p=0.028; 2-year CIR: 52.0% vs. 13.3%/0%, p=0.001). After adjustment for confounding variables, pre-HCT TP53 VAF >0.1% remained an independent predictor of worse outcomes (EFS: aHR 3.3, 95%CI 1.5-7.2; CIR: aHR 8.2, 95%CI 2.6-26.2; OS: aHR 2.5, 95%CI 1.0-6.1). Post-HCT VAF >0.01% also independently predicted inferior OS (aHR 2.7, 95%CI 1.2-6.0), EFS (aHR 2.7, 95%CI 1.4-5.0), and CIR (aHR 4.1, 95%CI 2.1-8.2). Dynamic peri-transplant MRD monitoring showed superior prognostic discrimination. Combining genetic MRD with MFC enhanced risk stratification pre-HCT, with dual-positive patients having the worst survival (EFS: aHR 7.0, 95%CI 2.6-18.9; CIR: aHR 30.3, 95%CI 4.5-205.0; OS: aHR 4.5, 95%CI 1.5-13.6).
Clearance of TP53-mutated clones pre-transplant improved survival in AML and MDS/AML (2-year OS: 77.2% vs. 47.2%, p=0.025; 2-year CIR: 12.8% vs. 62.3%, p<0.001) but had no significant impact in MDS. Regarding conditioning regimens, myeloablative conditioning and reduced-intensity conditioning regimens showed no significant survival differences regardless of MRD status. For patients with pre-HCT VAF >0.1%, decitabine- incorporated conditioning reduced 2-year CIR (23.8% vs. 63.4%, p=0.016) with trends toward better EFS (58.9% vs. 32.5%, p=0.072), while no benefit was observed in those with VAF≤0.1%. Melphalan-based conditioning and donor type (haploidentical vs. matched sibling/unrelated) had no significant impact on outcomes across MRD strata.

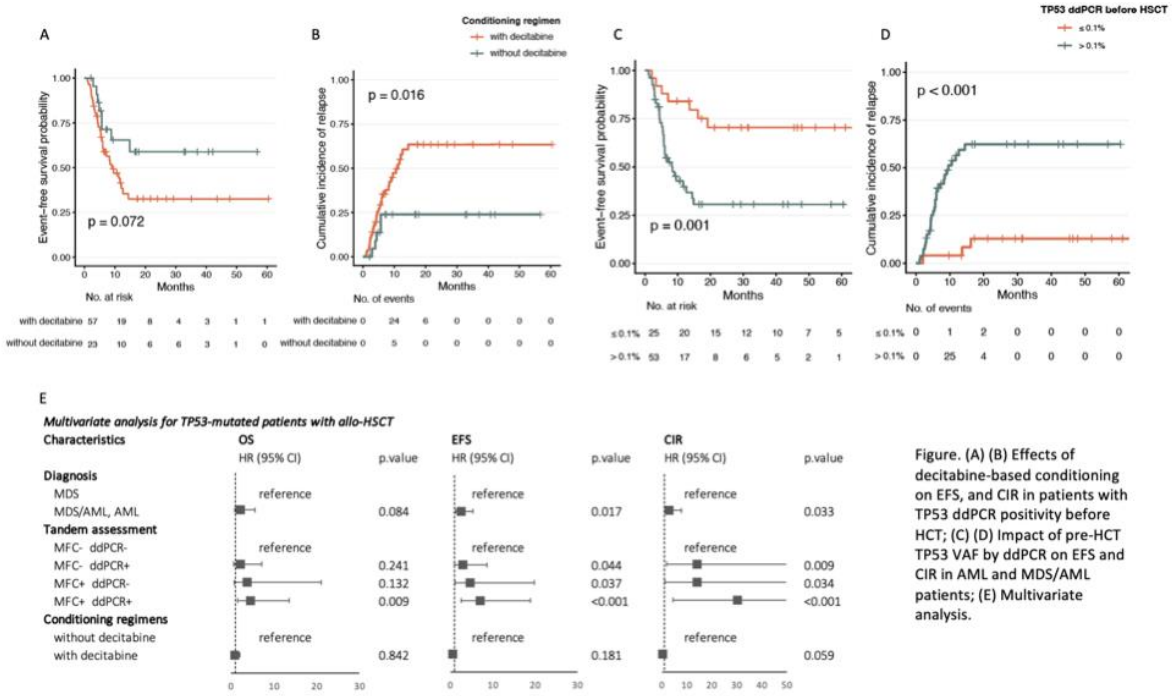

Figure. (A) (B) Effects of decitabine-based conditioning on EFS, and CIR in patients with TP53 ddPCR positivity before HCT; (C) (D) Impact of pre-HCT TP53 VAF by ddPCR on EFS and CIR in AML and MDS/AML patients; (E) Multivariate analysis.

Table. Baseline data of TP53-mutated AML/MDS patients	
Characteristics	**%, median (N = 139)**
Gender Female Male	 42% (58/139) 58% (81/139)
Age at transplantation	52 (Range 15,69)
Diagnosis MDS MDS/AML AML	 27% (38/139) 29% (41/139) 43% (60/139)
Complex/monosomal karyotype	54% (67/123)

Table. Baseline data of TP53-mutated AML/MDS patients	
Characteristics	**%, median (N = 139)**
MFC-MRD	
negative	44% (61/139)
positive	56% (78/139)
TP53-ddPCR before HCT	
≤0.1%	26% (29/110)
>0.1%	74% (81/110)
Conditioning regimen	
MAC	66% (92/139)
RIC	34% (47/139)
with decitabine	26% (36/139)
without decitabine	74% (103/139)
with melphalan	26% (36/139)
without melphalan	74% (103/139)
Donor Type	
MSD	8% (11/139)
HID	84% (117/139)
URD	8% (11/139)
TP53-ddPCR after HCT	
≤0.01%	66% (66/100)
>0.01%	34% (34/100)

Conclusions: Pre-transplant genetic MRD monitoring effectively refines risk stratification in TP53-mutated AML/MDS. Intensive pre-transplant therapy to achieve MRD clearance benefits AML and MDS/AML patients, while early HCT may suffice for MDS regardless of deep MRD clearance. Decitabine- incorporated conditioning reduces relapse risk in patients with high pre-HCT MRD, highlighting the value of MRD-guided regimen selection. Eradicating TP53-mutated clones post-transplant is paramount to improving survival in this high-risk population.

Disclosure: There is nothing to disclose.

OS17-03

ALLOHEME SURVEILLANCE ENABLES EARLY DETECTION OF RELAPSE IN POST-HCT AML AND MDS PATIENTS

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Background: Allogeneic hematopoietic cell transplantation (HCT) is an effective treatment option for acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Still, relapse of the primary disease remains the leading cause of post-HCT mortality. Current peripheral blood-based standard-of-care surveillance methods, such as CD3 and CD33 lineage-specific chimerism by short tandem repeat–PCR (STR-PCR), have poor sensitivity and lack standardization. Measurable residual disease (MRD) testing, either by multi-flow cytometry (MFC) or molecular methods, provides higher specificity but often requires bone marrow sampling. Thus, both STR-PCR and MRD tests are limited in post-HCT relapse monitoring. AlloHeme (CareDx, Brisbane, CA), a next-generation sequencing (NGS)-based test coupled with a proprietary algorithm, has been developed to predict the likelihood of a relapse.

Methods: ACROBAT study (NCT04635384) prospectively enrolled 162 AML and 65 MDS subjects (total 227) in 11 US sites. Testing was performed at 14 post-HCT time points over 2 years. NGS chimerism was tested in unsorted whole blood, and CD3+ and CD33+ fractions with a limit of detection of 0.02%. The AlloHeme Algorithm utilizes multi-analyte longitudinal chimerism data to determine relapse risk. 32 subjects were excluded due to the occurrence of early post-transplant events (non-relapse mortality (NRM), and relapse), non-compliance with testing regimen or consent withdrawal before the algorithm could be applied (<49 days), resulting in an analytical cohort of 195 subjects. Relapse was determined by the treating physicians per CIBMTR criteria. Here, we present interim 18-month results from the study on the performance of the AlloHeme test for relapse prediction, with the intention of a complete study readout at EBMT 2026.

Results: At the data cut-off date, the median follow-up in the AML and MDS group was 23.4 months (IQR, 10-24). Among the cohort of 195 AML and MDS subjects, 37 (19%) experienced relapse, and 26 (13%) had NRM. The cumulative incidence of relapse was significantly higher in patients who were AlloHeme positive compared to AlloHeme Negatives following 3-, and 6-month landmark time points (Figure 1A). Overall, the AlloHeme test demonstrated high sensitivity (91%) and specificity (92%) for relapse prediction, with a positive predictive value (PPV) of 74% and a negative predictive value (NPV) of 98%. The median lead time from a positive test to clinical relapse was 45 days (IQR: 22-108 days),

with 40% identified at least 60 days before clinical relapse (Figure 1B). Compared with modeling NGS-chimerism at the best STR-PCR sensitivity threshold of 1% increased mixed chimerism or the site-reported multi-flow cytometry-measurable residual disease (MFC-MRD), AlloHeme demonstrated superior test performance in predicting relapse (Table 1).

Figure 1: Landmark analysis at 3 and 6 months shows that the subjects positive for AlloHeme are at increased risk for post-HCT relapse (Panel A). Lead time from AlloHeme positive results to relapse in relapsed AML and MDS patients (Panel B).

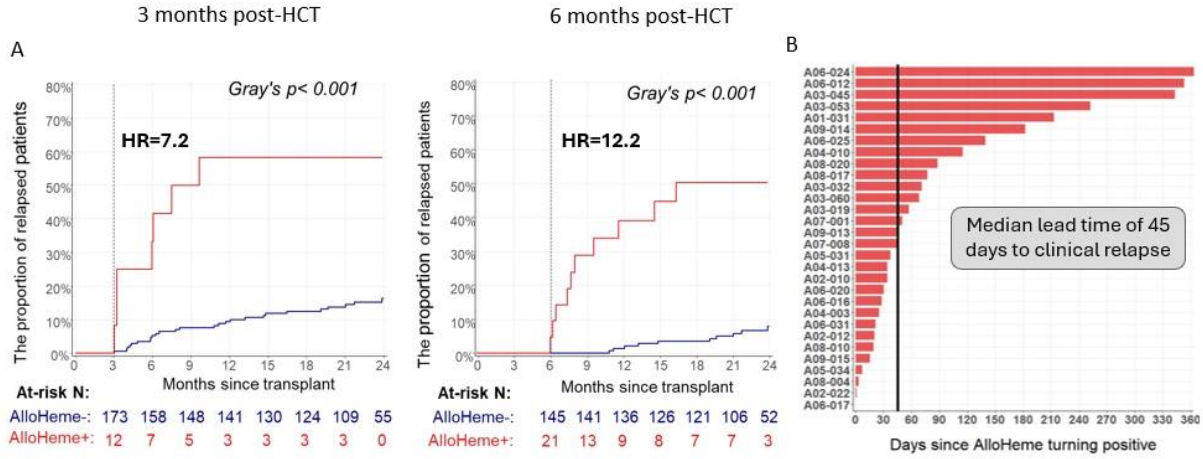

Table 1: AlloHeme test performance compared to other testing modalities

Test	Sensitivity	Specificity	PPV	NPV	AUC	N Relapse	N Total	Lead time to Relapse (Median [IQR] in days) ~	
AlloHeme	0.91	0.92	0.74	0.98	0.88	32	160	45 [22 - 108]	
STR-PCR*	0.50	0.93	0.64	0.88	0.71	32	160	20 [1 - 38]	
BM MFC-MRD**	0.50	0.94	0.72	0.85	0.72	26	104	0 [0 - 11]	
*STR-PCR is an NGS-chimerism modelled at 1% threshold (STR-PCR equivalent).									
**MFC-MRD is based on site-reported bone marrow testing; thus, the analysis set has different N relapse and N total.									

Table 1: AlloHeme test performance compared to other testing modalities

~Lead time to relapse is calculated from the first positive AlloHeme test, the first increasing mixed chimerism of >1% (STR-PCR), or the first positive MFC-MRD test reported at the site.	

Conclusions: ACROBAT interim results demonstrate that AlloHeme monitoring in post-HCT AML and MDS patients can accurately predict relapse with a significant lead time over current relapse-defining criteria, potentially reducing unnecessary bone marrow testing for relapse-free patients while enabling timely interventions by accurately predicting early relapse.

Clinical Trial Registry: ACROBAT (NCT04635384).

Disclosure: ACROBAT (NCT04635384) is a CareDx,inc. sponsored multi-center study.
Monzr M Al-Malki: Ossium Health, Inc, Gilead, Gamida Cell, Jazz Pharma, Incyte, TScan Therapeutics, CareDx, Tr1X,
Corey Cutler: Consulting: CareDx, Sanofi, CSL Behring, Incyte, Syndax; Consulting with Equity: OrcaBio, Cimeio, Oxford Immune Algorithmics
Iskra Pusic: Advisory consulting -CareDx
Ran Reshef: reports consulting or advisory role with Allogene, Gilead Sciences, Incyte, Sanofi, TScan, Orca Bio, Pierre Fabre Pharmaceuticals, CareDx, Sana Biotechnology, Sail Biomedicines and Autolus, expert witness role with Bayer, and research funding from Atara Biotherapeutics, Incyte, Sanofi, Immatics, Abbvie, Takeda, Gilead Sciences, CareDx, TScan, Cabaletta, Synthekine, BMS, J&J, Allogene, Genentech, Vittoria Therapeutics, AstraZeneca, Kinomica, Sonoma Bio, Arcellx and Imugene.
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Arpita Gandhi - Nothing to declare
Jing Shi - CareDx employee
Yangyang Hao - CareDx employee
Nishant Dwivedi - CareDx employee
Ashish Kothari - CareDx employee
Piyanuch Kongtim - Advisory consulting -CareDx
Roland Sobecks - Nothing to declare

OS17-04

PROGNOSTIC VALUE OF PERI-TRANSPLANT MOLECULAR MRD MONITORING BY TARGETED NGS FOR ALLO-HCT RECIPIENTS WITH FLT3-ITD MUTATED ACUTE MYELOID LEUKEMIA: A MULTICENTER STUDY OF TROPHY GROUP

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Background: Relapse remains the primary cause of treatment failure after allogeneic hematopoietic stem cell transplantation (allo-HCT) in patients with FLT3-ITD–mutated acute myeloid leukemia (AML). Dynamic monitoring of measurable residual disease (MRD) offers an early predictor of post-transplant relapse. While PCR–next-generation sequencing (PCR-NGS) is sensitive for FLT3-ITD MRD detection, data in Asian populations are scarce, and its utility to guide conditioning regimens or post-transplant tyrosine kinase inhibitor (TKI) maintenance remains unclear.

Methods: We conducted a multicenter cohort study across three TROPHY group sites in China, enrolling 219 adult FLT3-ITD AML patients in morphologic complete remission undergoing allo-HCT between November 2016 and June 2024. Peri-transplant MRD was systematically assessed using multiparameter flow cytometry (MFC), capillary electrophoresis (CE), and PCR-NGS. The prognostic value of pre- and post-transplant MRD and its utility in guiding conditioning intensity and post-HCT TKI maintenance were evaluated.

Results: Pre-transplant MRD positivity (>0.001%) by PCR-NGS was associated with significantly inferior outcomes compared with MRD-negative patients (2-year RFS: 56.8% vs. 86.5%; CIR: 30.0% vs. 6.9%; OS: 65.9% vs. 88.4%; all $p < 0.001$). Notably, low-level FLT3-ITD (0.001%-0.1%) molecular MRD (M), below the detection threshold of CE, conferred a substantial risk of post-transplant relapses (CE-/M- vs. CE-/M+: 8% vs. 25%, $p < 0.001$). Dynamic peri-transplant assessment incorporating both pre- and post-HCT MRD status provided superior risk stratification compared with static measurements at either time point alone (C-index: 0.76 vs. 0.66 vs. 0.67 for RFS; 0.73 vs. 0.64 vs. 0.67 for OS). Given the dynamic behavior of FLT3-ITD clones, tandem MRD using both PCR-NGS and MFC was assessed. The most favorable outcomes were observed in the MFC-MRD-negative/molecular MRD-positive (F-/M+) group (2-year CIR: 6.4%; RFS: 92.9%; OS: 92.9%), whereas the

poorest outcomes were seen in the double-positive (F+/M+) group (CIR: 45.0%; RFS: 34.3%; OS: 43.1%; all p < 0.001). Among flow MRD-negative patients, molecular MRD further stratified risk (F-/M- vs. F-/M+: CIR 6.4% vs. 23.0%, p=0.024; RFS 88.3% vs. 66.0%, p=0.003; OS 89.8% vs. 73.6%, p=0.024), whereas among molecular-negative patients, flow MRD had no significant prognostic impact. Combined assessment increased negative predictive value (PPV 0.48; NPV 0.89), enhancing relapse exclusion with modest increase in false positives. Among pre-transplant molecular MRD-positive patients, myeloablative conditioning conferred significantly better outcomes than reduced-intensity regimens (2-year RFS: 61.3% vs. 20.0%, p = 0.002; OS: 72.1% vs. 40.0%, p = 0.002). Post-transplant TKI maintenance independently improved survival in pre-transplant molecular MRD-negative patients (OS: aHR 0.3, p = 0.029; RFS: aHR 0.3, p = 0.019), whereas for the molecular MRD-positive cohort, gilteritinib shows a slight trend toward improved RFS compared to sorafenib (no maintenance vs. sorafenib vs. gilteritinib: 38.5% vs. 58.1% vs. 72.7% p=0.065).

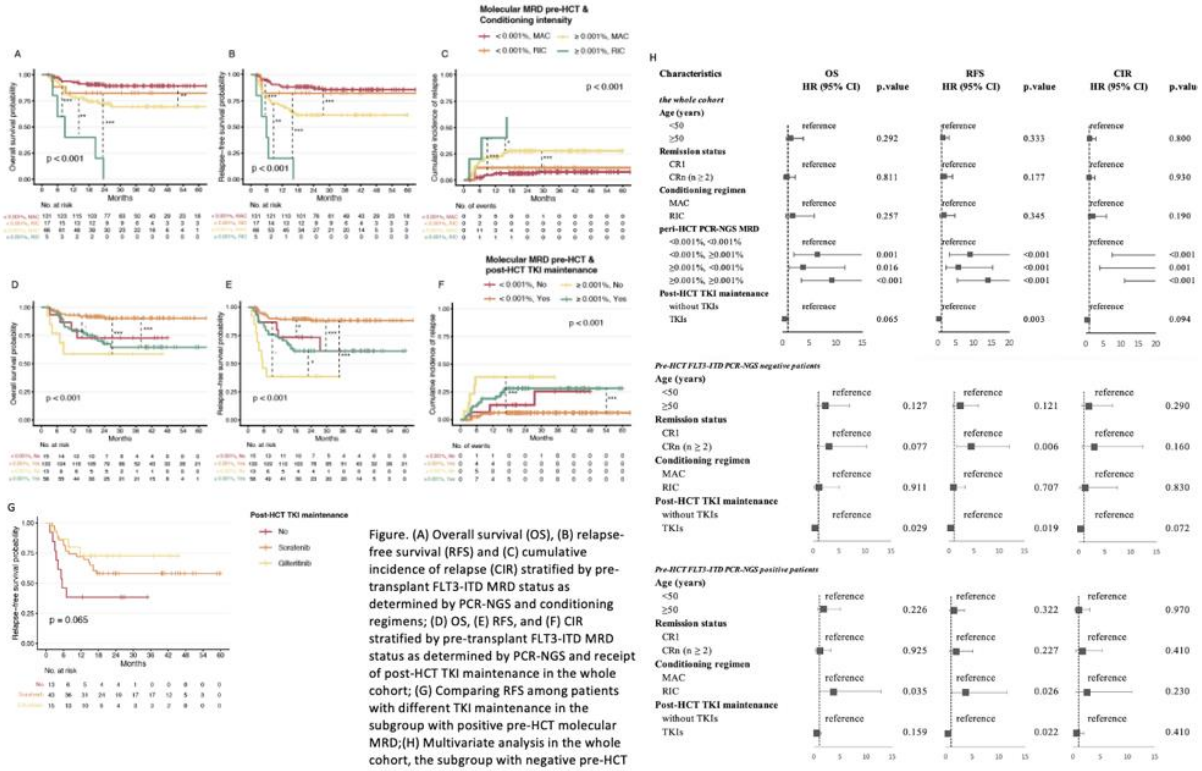

Figure. (A) Overall survival (OS), (B) relapse-free survival (RFS) and (C) cumulative incidence of relapse (CIR) stratified by pre-transplant FLT3-ITD MRD status as determined by PCR-NGS and conditioning regimens; (D) OS, (E) RFS, and (F) CIR stratified by pre-transplant FLT3-ITD MRD status as determined by PCR-NGS and receipt of post-HCT TKI maintenance in the whole cohort; (G) Comparing RFS among patients with different TKI maintenance in the subgroup with positive pre-HCT molecular MRD;(H) Multivariate analysis in the whole cohort, the subgroup with negative pre-HCT molecular MRD, and the subgroup with positive pre-HCT molecular MRD.

Table. Baseline characteristics of FLT3-ITD patients with allo-HCT

Characteristics	all patients (N = 219)	pre-HCT molecular MRD- (N = 148)	pre-HCT molecular MRD+ (N = 71)	p.value
Age (years)	44 (Range 16-67)	44 (Range 16-66)	43 (Range 17-67)	0.700
Gender Female Male	 51% (111/219) 49% (108/219)	 49% (73/148) 51% (75/148)	 54% (38/71) 46% (33/71)	0.800
Remission status CR1 CRn(n≥2)	 87% (191/219) 13% (28/219)	 89% (131/148) 11% (17/148)	 85% (60/71) 15% (11/71)	0.400
MFC-MRD before HCT <0.01% ≥0.01%	 81% (177/219) 19% (42/219)	 86% (128/148) 14% (20/148)	 69% (49/71) 31% (22/71)	0.002
CE-MRD before HCT <0.1% ≥0.1%	 92% (177/192) 8% (15/192)	 100% (123/123) 0% (0/123)	 69% (49/71) 31% (22/72)	<0.001
Conditioning regimen MAC RIC	 90% (197/219) 10% (22/219)	 89% (131/148) 11% (17/148)	 93% (66/71) 7% (5/71)	0.300
Post-HCT TKI maintenance sorafenib gilteritinib without TKIs	 73% (159/219) 14% (31/219) 13% (29/219)	 78% (116/148) 11% (16/148) 11% (16/148)	 61% (43/71) 21% (15/71) 18% (14/71)	0.021

Conclusions: PCR-NGS–based molecular MRD monitoring enables dynamic risk stratification and can inform personalized transplant strategies, including choice of conditioning intensity and post-HCT TKI maintenance, to improve outcomes in patients with *FLT3*-ITD AML.

Disclosure: There is nothing to disclose.

OS17-07

REGULATING VERY EARLY CICLOSPORIN IS CRITICAL IN DETERMINING DISEASE RESPONSE EARLY AFTER CORD BLOOD TRANSPLANT FOR HIGH-RISK PAEDIATRIC AML

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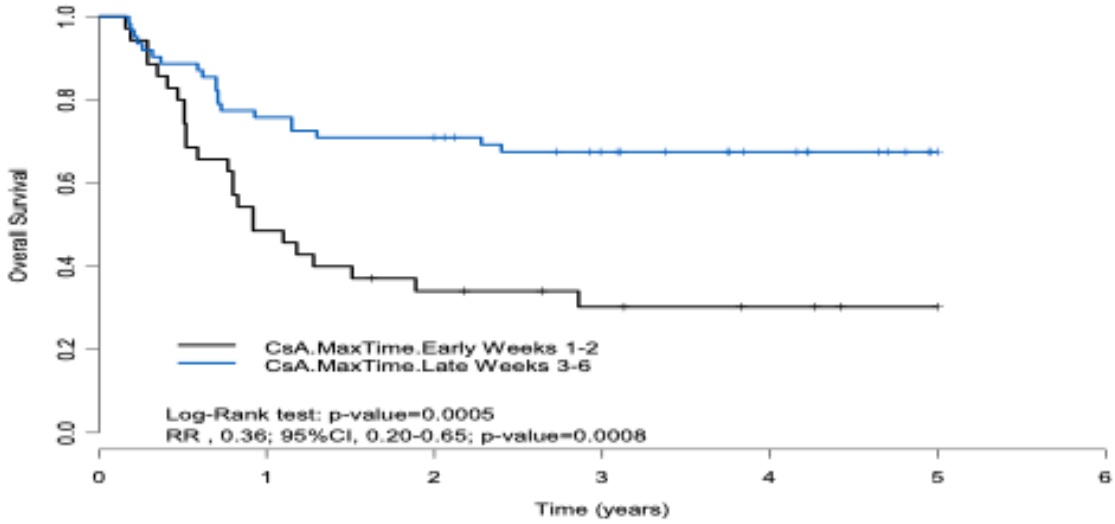
Background:

Ciclosporin is the principal GVHD prophylaxis in allogeneic HSCT, but its use may attenuate the graft-versus-leukaemia (GVL) effect. Although higher ciclosporin exposure has been linked to increased relapse risk, inadequate immunosuppression raises the risk of severe GVHD and associated morbidity and mortality. Target trough levels and treatment duration vary widely between centres due to limited evidence. T-cell–replete cord blood transplantation (TRCBT) offers superior GVHD-free, relapse-free survival (RFS) in AML. We report a multicentre analysis evaluating the association between ciclosporin exposure and relapse in a large, homogeneous paediatric AML cohort undergoing TRCBT. The analysis adjusted for pre-transplant minimal residual disease (MRD) and GVHD, providing guidance for optimal ciclosporin dosing to maximise RFS.

Methods: This retrospective study included all UK paediatric transplant centres and examined patients who received TRCBT for high-risk AML from 2013–2023. Case records provided patient, donor and transplant characteristics; GVHD prophylaxis; ciclosporin trough levels in the first 8 weeks; and outcomes including GVHD, relapse and transplant-related mortality (TRM). The primary endpoint was time to relapse. Associations between relapse and ciclosporin exposure, duration and serum levels at defined post-transplant intervals were assessed using multivariate Cox regression.

Results: The cohort comprised 172 patients, including 82 who were MRD-positive pre-transplant, with a median follow-up of 737 days (range 24–3540). All received ciclosporin and MMF as GVHD prophylaxis; Overall mortality was 40.7%, with nearly three-quarters of deaths occurring in MRD-positive patients. Relapse was the leading cause of death, accounting for 68.7% of deaths in the MRD-positive group and 41.6% in the MRD-negative

group. Median time to relapse was 180 days (range 32–949), with one-third occurring within 6 months. TRM was 13% and represented the main cause of death in MRD-negative patients.



Target ciclosporin trough levels varied substantially across centres (100–350 ng/mL). Patients were grouped by when their peak median levels occurred: early (weeks 1–2) or later (weeks 3–6). Overall survival was significantly better (p=0.0008) in those maintaining higher levels (>150 ng/mL) during the later post-engraftment period (weeks 3–6) and lower levels (<150 ng/mL) earlier. This supports the importance of preserving the early T-cell response to reduce relapse risk, while intensified immunosuppression in weeks 3–6 may reduce GVHD-related mortality without compromising disease control.
On a patient hierarchical clustering heat map, patients with lower ciclosporin levels in the first 2 weeks followed by higher levels thereafter (Cluster 4) showed a trend towards improved overall survival (p=0.05) compared with clusters showing the opposite pattern, underscoring the impact of temporal immunosuppression on outcome.

Conclusions: Lower pre-engraftment ciclosporin levels (<150 ng/mL) were associated with improved OS and RFS, likely reflecting enhanced early cord blood–derived T-cell responses in AML HSCT. Recent work demonstrates that very early T-cell responses during double CBT (DCBT) and granulocyte infusions occur and can control relapse; high ciclosporin exposure during this period suppresses these critical responses. This study shows that a structured, temporally tailored ciclosporin regimen can effectively balance GVHD control with GVL preservation, optimising RFS and OS in high-risk paediatric AML.

Disclosure: nil

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MUTATIONAL LANDSCAPE CHANGES OF AML IN PATIENTS RELAPSING AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Relapse of acute myeloid leukemia (AML) after allogeneic hematopoietic cell transplantation (allo-HCT) remains a major clinical challenge with poor outcomes. Although relapse biology is influenced by AML molecular heterogeneity and the selective pressures of allo-HCT, the specific mutational and clonal dynamics at relapse and their prognostic significance are incompletely defined. Understanding these dynamics is critical for improving post-transplant surveillance and therapeutic strategies.

Methods: This retrospective, multicenter study analyzed 57 adult AML patients who received allo-HCT at centers in Freiburg (Germany), Toronto (Canada), and Patras (Greece) between April 2005 and March 2024 and subsequently experienced hematologic relapse by December 2024. Paired next-generation sequencing (NGS) myeloid panels (38–84 genes) were performed at diagnosis/pre-HCT and at relapse. Mutational trajectories were categorized as constant, linear, branching, or parallel evolution. Primary endpoints included overall survival (OS) and progression-free survival (PFS), assessed by Kaplan-Meier analysis. Multivariable logistic regression was used to identify predictors of early relapse (<6 months post-HCT).

Results: At relapse, 68% of patients showed genetic instability with acquisition or loss of mutations, predominantly affecting FLT3-ITD, NRAS, and KRAS. In contrast, founder mutations such as DNMT3A and TP53 commonly persisted. Clonal evolution patterns varied: 35% of cases displayed a constant profile, 29.8% linear, 22.8% branching, and 12.3% parallel evolution. Survival analysis revealed that these evolution categories were not significantly associated with OS or PFS. However, timing of relapse was highly prognostic. Patients who relapsed within six months after transplant had markedly reduced OS compared to those with later relapse (p=0.049), regardless of clonal evolution pattern. Increased mutation burden at diagnosis was an independent predictor for early relapse (OR 1.84, 95% CI 1.02–3.33, p=0.04), while branching evolution reduced the odds of early relapse. Low rates of acute and chronic GVHD were seen across the cohort, and salvage therapies were broadly utilized after relapse.

Conclusions: AML relapse after allo-HCT was characterized by substantial genetic and clonal instability. However, the specific mutational dynamics or clonal evolution pattern observed at relapse did not independently impact survival outcomes. The timing of relapse—especially early recurrence within six months post-transplant—was found to be the strongest predictor

of poor prognosis. Increased mutational complexity at diagnosis also elevated the risk for early relapse. These findings highlight the value of intensified molecular monitoring in the early post-transplantation phase and the preferable use of persistent mutations for measurable residual disease (MRD) assessment. Larger studies and integration of multi-omics data are needed to elucidate clonal-immune interactions driving relapse and to inform risk-adapted interventions.

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A343

GRANULOCYTE TRANSFUSION DURING CORD-BLOOD TRANSPLANT PRODUCES EARLY, REPRODUCIBLE, EFFECTOR MEMORY CD8+ T-CELL EXPANSION WITH CLINICALLY SIGNIFICANT CLINICAL RESPONSES IN REFRACTORY AML

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Background: Cord blood transplant (CBT) has been showed to have favourable outcomes in high-risk relapsed/refractory leukaemia compared to other cell sources. The use of CBT has declined, mainly as PTCy has enabled easier access to mismatched family and unrelated donors where there is no matched donor.
We have previously reported on our use of pooled granulocyte infusion to augment the graft vs leukaemia effect during CBT, by promoting an early and transient CD8+ T-cell expansion, associated with a cytokine release syndrome and improved outcomes. Here we extend our report on CD8 donor-derived T-cell expansion early after CBT, and its clinical significance.

Methods: In total, 29 patients with high-risk paediatric leukaemia have received pooled granulocyte infusion in combination with T-replete CBT at our centre (registration: NCT05425043). Lymphocyte subset evaluation was performed at regular timepoints during early post-transplant follow-up. Comparison was made to a cohort of 26 AML patients who received CBT without granulocyte infusion at our centre between 2015 to 2023 for markers

of initial cytokine release syndrome (CRS), engraftment kinetics and clinical outcomes including relapse rates and overall survival.

Results: Donor-derived lymphocyte expansion occurred early post-transplant (prior to day +14) in 22/29 patients, reaching a median peak absolute lymphocyte count of 1.6 (IQR 0.89 – 2.86) at day +9 post-transplant (IQR day +8 to +11). When stratified by lymphocyte subset, early CD3+ and CD8+ expansion was significantly higher than CD4+ expansion. CRS was universally provoked by granulocyte infusion in all patients, with grade 1 CRS in 64% and grade 2 CRS in 28%, however no admission to intensive care was required.
Post expansion, CD8+ contraction was noted with sustained detectable CD8+ levels in all. CD8+ count recovery to within normal range was noted by 3 months in 4/15 (27%), 6 months in 5/13 (38%), 9 months in 5/10 (50%) and 12 months in 7/9 (78%). CD8+ recovery to normal range was associated with improved survival. Graft failure occurred in 5/29 patients, all who did not experience lymphocyte expansion. For the 24/29 patients who achieved engraftment, the 1-year overall survival was 74.8% and the 1-year event free survival was 58.3%. OS in those who did not have early lymphocyte expansion was poor.

Conclusions: The administration of granulocytes during CBT induces a CD8+ biased T cell expansion and clinical CRS in most patients. Following early expansion, CD8+ counts contracted but remain detectable until count recovery, with levels within the normal range for by 1 year in most patients surviving to this time point. The presence of CD8+ response is associated with induction of remission, as has been described by Milano et al. in Seattle where granulocyte infusion has been replaced by pooled, expanded CB units with reports of a similar excellent disease response.
The phenotype switch of these cells, from naïve to memory, suggests that this is antigen-specific T-cell response. This CB derived T cell response might therefore be redirected against tumour antigens, for example by vaccination, and form the basis of a new transplant technology to reduce disease relapse.

Clinical Trial Registry: NCT05425043

Disclosure: Nothing to declare.

A345

PROGNOSTIC IMPACT OF PRE-TRANSPLANT MEASURABLE RESIDUAL DISEASE AND GVHD PROPHYLAXIS IN AML PATIENTS UNDERGOING ALLO-HCT

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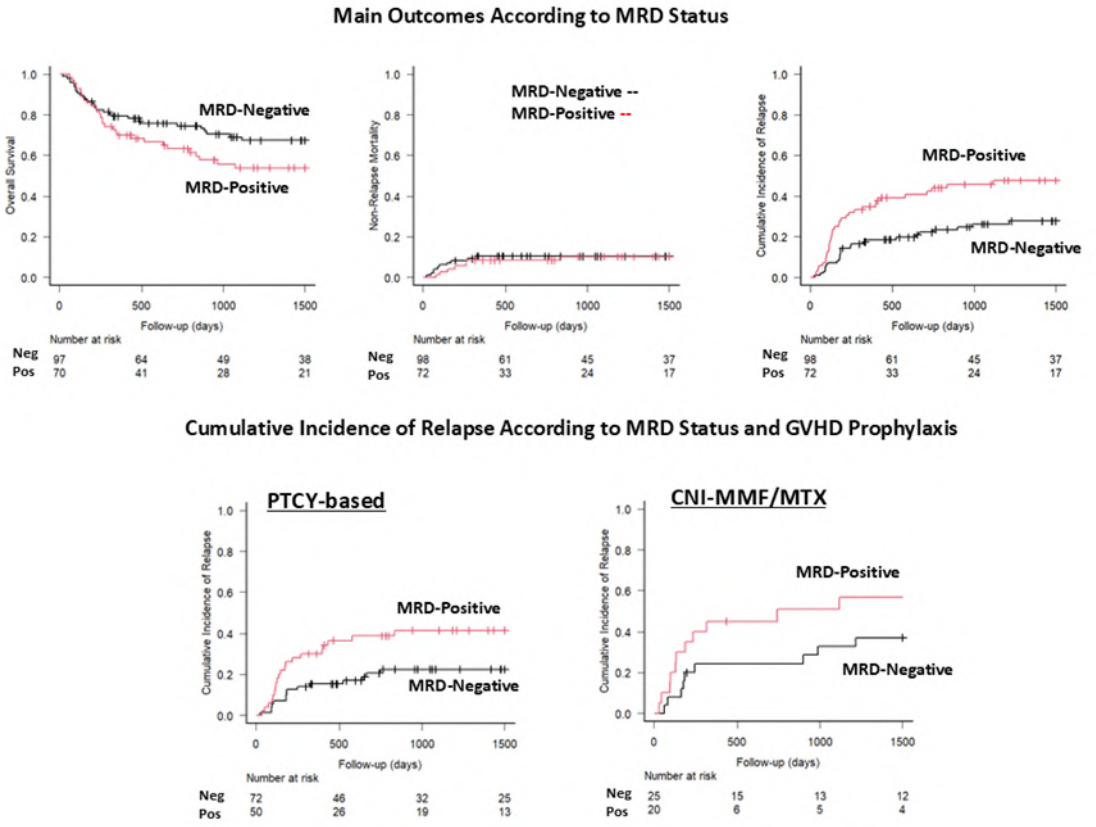
Background: Allogeneic hematopoietic cell transplantation (allo-HCT) remains a curative treatment for patients with acute myeloid leukemia (AML), with substantial expansion of its use secondary to reductions in transplant-related toxicity and advances in supportive care. Measurable residual disease (MRD) before transplantation is considered a key prognostic factor, but lack of standardized assessment limits its consistent application. In parallel, post-transplant cyclophosphamide (PTCy) is being widely used for graft-versus-host disease (GVHD) prevention by substantially reducing chronic GVHD, although concerns persist about potential effects on relapse. This study evaluates the prognostic impact of pre-transplant MRD in AML patients undergoing allo-HCT in complete remission (CR) and explores whether PTCy use impacts on relapse risk.

Methods: The 167 consecutive adults with CR AML with available pre-transplant MRD data who underwent their first allo-HCT between 2014 and 2024 at our center were included. MRD assessment was performed by multiparameter flow cytometry and, when applicable, molecular techniques. MRD positivity was defined as any detectable residual disease. Disease relapse was defined as any morphologic or molecular recurrence of disease after allo-HCT in patients who had previously achieved CR. This definition was adopted due to its direct implications for clinical practice in the allo-HCT setting.

Results: Median age was 53 years, and 70 (41.9%) patients were MRD-positive at transplant. Baseline characteristics were largely balanced except for a higher proportion of HCT-CI >3 among MRD-positive patients. Most patients (n=122, 73.1%) received PTCy-based GVHD prophylaxis, and 89 (53.3%) underwent reduced-intensity conditioning.
Rates of acute and chronic GVHD were similar between MRD groups. Overall, 55 patients (32.9%) experienced relapse (48 morphological and 7 molecular), occurring more frequently among MRD-positive individuals (44.3% vs. 24.7%, p=0.008). As shown in **Figure 1,** , cumulative incidence of relapse (CIR) at 3 years was higher in MRD-positive patients (45.7% vs. 26.1%, p=0.006), while non-relapse mortality remained comparable (10.1% vs. 10.2%, P=0.884). Three-year overall survival (OS) was inferior in MRD-positive compared with MRD-negative recipients (53.8% vs 69.0%, p=0.044).
In multivariate analyses (**Table 1),** MRD positivity independently predicted increased relapse risk (HR 2.27, p=0.005) and inferior OS (HR 1.83, p=0.023). High/very-high Disease Risk Index also conferred adverse outcomes, whereas PTCy remained independently associated with improved OS (HR 0.46, p=0.013). Conditioning intensity, donor type, and HCT-CI did not significantly influence relapse or survival.
Lastly, we further analyzed outcomes according to GVHD prophylaxis showing that the negative effect of MRD positivity on relapse risk persisted regardless of prophylactic strategy. Among patients receiving PTCy, the 3-year CIR was 41.4% in MRD-positive vs. 22.3% in MRD-negative patients. In those not receiving PTCy, rates were 50.8% and 32.7%, respectively **(Figure 1).**

Table 1. Impact of Pre-Transplant MRD Status on Outcomes

Univariate Analysis	**OS HR (95% CI)**	**P value**	**CIR HR (95% CI)**	**P value**
MRD Detection Positive (vs. Negative)	1.65 (1.01-2.71)	0.046	2.01 (1.19-3.40)	0.008
Diagnosis of mod-sev cGVHD Time-Dependent	0.67 (0.25-1.80)	0.433	0.54 (0.17-1.68)	0.290
Multivariate Analysis	**OS HR (95% CI)**	**P value**	**CIR HR (95% CI)**	**P value**
MRD Detection Positive (vs. Negative)	1.83 (1.08-3.10)	0.023	2.27 (1.27-4.03)	0.005
GVHD Prophylaxis PTCy-based (vs. others)	0.46 (0.25-0.85)	0.013	0.59 (0.31-1.17)	0.110
Age Continuous (Range)	1.01 (0.97-1.03)	0.856	0.99 (0.96-1.02)	0.630
HCT-CI > 3 (vs. 0-3)	1.32 (0.75-2.30)	0.330	1.28 (0.72-2.29)	0.390
Disease Rik Index High-Very High (Low-Intermediate)	4.54 (2.56-8.04)	<0.001	3.85 (2.01-7.45)	<0.001
Conditioning Regimen RIC (vs. MAC)	1.62 (0.74-3.55)	0.222	2.01 (0.85-4.71)	0.11
Donor type MMUD/Haplo vs. HLA-matched	1.05 (0.55-2.03)	0.866	0.60 (0.29-1.24)	0.17



Conclusions: Pre-transplant MRD positivity remained a strong and independent predictor of relapse and mortality after allo-HCT in AML. The prognostic relevance of MRD was consistent across GVHD prophylaxis regimens, and PTCy did not increase relapse risk while providing a survival advantage. These findings support systematic MRD assessment before transplantation and reinforce the use of PTCy for GVHD prevention without compromising disease control.

Disclosure: Nothing to declare

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AZACITIDINE MAINTENANCE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN HIGH-RISK AML: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Disease relapse remains the main cause of allogeneic hematopoietic stem cell transplantation (allo-HSCT) failure in high-risk acute myeloid leukemia (AML). Maintenance strategies with hypomethylating agents are under investigation, with heterogeneous results.

Methods: This single-center retrospective matched case-control study enrolled adult patients (≥18 years) with high-risk AML undergoing allo-HSCT between 2018 and 2025. All patients in the AZA cohort received post-transplant azacitidine maintenance (37.5–75 mg/m²/day subcutaneously, days 1–5 every 28 days) for 24–36 cycles, starting between 35- and 120-day after allo-HSCT. High-risk AML was defined as adverse-risk disease according to ELN2017 or ELN2022 criteria; primary refractory disease; ≥5% blasts or ≥1% measurable residual disease by multiparameter flow cytometry (MFC-MRD) and/or droplet digital polymerase chain reaction (PCR-MRD) at the start of conditioning; second or subsequent allo-HSCT; ≥0.1% MFC-MRD and/or PCR-MRD within 120-day after allo-HSCT. Hematologic engraftment, complete remission (CR), ECOG score 0-2, no uncontrolled infection, and no active grade 2-4 acute Graft versus Host Disease (aGvHD) were required. FLT3-ITD mutated AML was excluded. Outcomes of the AZA cohort were compared with those of a matched historical control group that did not receive maintenance therapy (NO AZA cohort). Primary endpoints were overall survival (OS) and relapse-free survival (RFS).

Results: The AZA cohort included 29 patients as reported in Table 1. With a median follow-up of 18 months (95%CI, 12–25), 2-year OS, RFS, cumulative incidence of relapse (CIR) and non-relapse mortality (NRM) were 69% (95%CI, 48–98), 60% (95%CI, 40–88), 40% (95%CI, 16–65), and 0%, respectively. Patients received a median of 12 cycles (2–25) of azacitidine, with discontinuation in 13 patients, mainly due to relapse (28%). Treatment was well tolerated; the most common adverse events were constipation (62%), nausea (55%), neutropenia (grade 3–4, 41%) and thrombocytopenia (grade 3–4, 14%). Infections occurred in 52% of patients (grade 3–4, 21%). The median time to relapse was 13 months (95%CI, 4–22), and predominantly involved (67%) TP53 mutated and/or complex/monosomic karyotype AML. During maintenance, 14% of patients received additional therapy due to MRD relapse/persistency: azacitidine ± donor lymphocyte infusion ± venetoclax. The comparison between the AZA cohort and the NO AZA cohort (n=21), with similar characteristics at baseline except for a higher frequency of MFC-MRD ≥ 1% in the AZA cohort (p=0.026) (Table 1), showed no significant differences in OS (p=0.72) nor RFS (p=0.95). Similarly, CIR (p=0.50), NRM (p=0.16), grade 2-4 (p=0.96) and grade 3-4 (p=0.69) aGVHD, any grade (p=0.97) and moderate-severe (p=0.69) cGvHD, were comparable. In the overall study population (n=50), multivariable Cox regression analysis identified advanced disease (AD) and TP53 mutation associated with worse OS (AD: HR=2.91, p=0.06; TP53mut: HR=6.68, p=0.004) and RFS (AD: HR=3.41, p=0.01; TP53mut: HR=4.61, p=0.01). Subgroup analysis showed no benefit from azacitidine maintenance in any high-risk category (TP53mut, CMK, AD, reduced-intensity conditioning).

Table 1.

	Global population (n=50)	AZA cohort (n=29)	NO AZA cohort (n=21)	p value
Patient characteristics				
Age, median (range)	62 (22-74)	61 (28-74)	63 (22-73)	0.875
HCT-CI, n (%)				
> 3	20 (40)	14 (48)	6 (29)	0.266
≤ 3	30 (60)	15 (52)	15 (71)	
Gender, n (%)				
Male	34 (68)	18 (62)	16 (76)	0.454
Female	16 (32)	11 (38)	5 (24)	
HSCT number, n (%)				
1	49 (98)	29 (100)	20 (95)	0.420
2	1 (2)	0 (0)	1 (5)	
Recipient CMV status, n (%)				
Positive	37 (74)	20 (69)	17 (81)	0.515
Negative	13 (26)	9 (31)	4 (19)	
Donor characteristics				
Donor type, n (%)				
Unrelated donor	45 (90)	26 (90)	19 (91)	1.000
Haploidentical donor	5 (10)	3 (10)	2 (9)	
HLA matching, n (%)				
8/8	36 (72)	21 (73)	15 (71)	1.000
7/8	9 (18)	5 (17)	4 (19)	
Haploidentical	5 (10)	3 (10)	2 (10)	
Age, median (range)	26 (19-56)	28 (19-56)	26 (19-39)	0.207
Transplant characteristics				
Conditioning intensity, n (%)				
Myeloablative	21 (42)	12 (41)	9 (43)	1.000
Reduced intensity	29 (58)	17 (59)	12 (57)	
GvHD prophylaxis, n (%)				
CNI + MMF/MTX + ATLG	45 (90)	26 (90)	19 (91)	0.083
FK + MMF + PT-Cy	5 (10)	3 (10)	2 (9)	
Disease characteristics				
ELN2017 risk, n (%)				
Adverse	39 (78)	24 (83)	15 (71)	0.327
Intermediate	9 (18)	5 (17)	4 (19)	
Favorable	2 (4)	0 (0)	2 (10)	
TP53mut	9 (18)	8 (28)	1 (5)	0.061
Complex and/or monosomic karyotype	15 (30)	8 (28)	7 (33)	0.900
Months from diagnosis to allo-HSCT, median (range)	6 (1-47)	6 (3-15)	6 (1-47)	0.905
AML status pre-HSCT, n (%)				
CR1	28 (56)	15 (52)	13 (62)	0.669
AD	22 (44)	14 (48)	8 (38)	
≥ 0.1% MFC-MRD pre-HSCT, n (%)	21 (42)	18 (62)	3 (14)	0.068
≥ 1% MFC-MRD before allo-HSCT, n (%)	11 (22)	11 (38)	0 (0)	**0.026**
≥ 0.1% MFC-MRD before azacitidine, n (%)	7 (14)	7 (24)	0 (0)	1.000

HCT-CI, Hematopoietic Cell Transplantation Comorbidity Index; HSCT, Hematopoietic Stem Cell Transplantation; CMV, CytomegaloVirus; GvHD, Graft versus Host Disease; ATLG, Anti-T-Lymphocyte Globulin; PT-Cy, Post-transplant Cyclophosphamide; CNI, Calcineurin Inhibitor; MMF, Mycophenolate Mofetil; MTX, Methotrexate; FK, Tacrolimus; ELN, European Leukemia Network; CR, Complete Remission; AD, Advanced Disease; MRD, Minimal Residual Disease; MFC, Multiparameter Flow Cytometry; PCR, Polymerase Chain Reaction.

Conclusions: Post-transplant azacitidine maintenance, while feasible and safe, did not improve OS nor RFS. Prospective randomized studies are needed to define the role of hypomethylating agents and explore alternative strategies to reduce post-transplant relapse.

Disclosure: FB: scientific advisory boards and speaker fees: NEOVII, NOVARTIS, KITE, GILEAD, PFIZER, CELGENE, MSD.

A348

CLINICAL OUTCOMES OF AZACITIDINE–VENETOCLAX IN RELAPSED AML AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE STUDY OF THE ASOVASNA CELLULAR THERAPY GROUP

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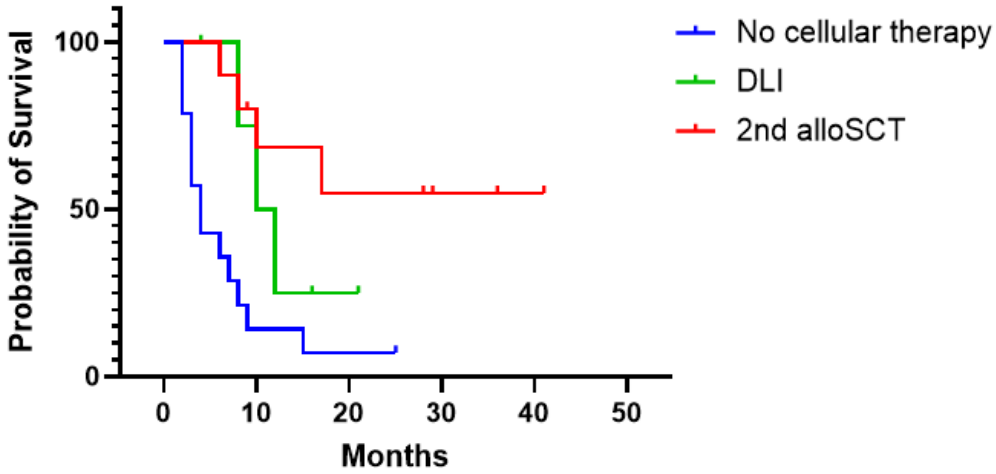
Background: Azacitidine plus venetoclax (Aza/Ven) is a standard frontline therapy for newly diagnosed AML in unfit patients; however, its role in relapsed AML after allogeneic hematopoietic stem cell transplantation (alloHSCT) remains unclear. Outcomes in this setting are poor, and therapeutic options are limited. We evaluated the efficacy and safety of Aza/Ven, alone or combined with cellular therapies, in patients with relapsed AML after alloHSCT.

Methods: We conducted a retrospective multicenter study including patients with first relapse of AML after alloHSCT treated with Aza/Ven ± cellular therapy between October 2021 and December 2025. Overall response rate (ORR; CR/CRi per ELN 2022) and overall survival (OS) were assessed. Safety and factors affecting treatment tolerability were analyzed.

Results: Thirty-three patients received Aza/Ven as first-line therapy for post-transplant relapse. Donor types included matched related (30%), matched unrelated (24%), mismatched unrelated (42%), and haploidentical donors (4%). Patients exhibited a high-risk genetic profile, predominantly with myelodysplasia-related mutations involving SRSF2, ASXL1, RUNX1, IDH1/2, DNMT3A, TET2, STAG2, and BCOR. TP53 mutations and complex or monosomic karyotypes were mainly observed in therapy-related and secondary AML. The median time to relapse was 7 months (range, 1–190), with 48.5% occurring within 6 months post-transplant. Clonal evolution was detected in 51% of cases. The mean bone marrow blast percentage at relapse was 14.3%. One patient presented with extramedullary relapse (sarcoma).Full-dose azacitidine was administered in 94% of patients, while venetoclax dosing was adjusted according to antifungal prophylaxis and cytopenias or patient frailty. The median number of treatment cycles was 3 (range, 1–13). Cellular consolidation included second alloHSCT (30%) or donor lymphocyte infusion (DLI, 36%); 34% did not receive cellular therapy, mainly due to active GVHD or rapid disease progression.
The ORR was 57.6%, and the median OS was 9.4 months. Median OS differed significantly by treatment strategy (p=0.001), reaching 17.3 months after second alloHSCT, 10 months with DLI, and 4 months without cellular therapy. In the adjusted Cox regression model, consolidation with 2nd alloHSCT was associated with a significantly reduced risk of death (HR 0.20; 95% CI, 0.06–0.63; p=0.006), while DLI demonstrated a trend toward benefit (HR 0.37; p=0.059).

Cytopenias and infections were the most common adverse events, frequently requiring treatment modifications, including dose adjustments, delays, or interruptions. Severe infections occasionally led to treatment interruption. GVHD was observed in 2 of 11 patients receiving DLI.



Conclusions: This analysis suggests that Aza/Ven may serve as an effective therapeutic backbone for patients with relapsed AML after alloHSCT, particularly when used as a bridge to cellular consolidation. Consolidation with cellular therapies, especially second alloHSCT, was associated with improved survival outcomes. Prospective studies are warranted to define optimal patient selection and consolidation strategies.
Although Aza/Ven is generally well tolerated, the high incidence of infections and cytopenias frequently requires dose adjustments and close monitoring to optimize treatment adherence and clinical outcomes.

Disclosure: Nothing to declare.

A349

OUTCOMES OF SECOND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION USING POST-TRANSPLANT CYCLOPHOSPHAMIDE AND A DIFFERENT DONOR AFTER RELAPSE FOLLOWING A FIRST ALLOGRAFT: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Relapse after allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the leading cause of treatment failure in patients with hematologic malignancies. A second allo-HSCT represents a potentially curative option for selected patients; however, it is associated with substantial toxicity, non-relapse mortality, and a persistent risk of disease recurrence. Real-world data on long-term outcomes after second allo-HSCT remain limited, particularly in the PT-CY era. We report our single-center experience with second allo-HSCT performed after relapse following a first allograft.

Methods: A unicentric retrospective study was conducted including adult patients who underwent a second allo-HSCT due to hematologic malignancy between 2012 and June 2025 after relapse following a first allograft. Data were collected from institutional databases and medical records. The choice of conditioning intensity for the second allo-HSCT was based on disease status, prior transplant-related toxicity, and comorbidity burden. In all cases, a donor distinct from the one used for the first allo-HSCT was selected. In patients who had previously received a haploidentical transplant, a different haploidentical donor was selected based on the results of HLA loss studies in the relapsed underlying disease. PBSC were used as stem cell source and GVHD prophylaxis consisted on PT-CY administered on days +3 and +4, followed by a calcineurin inhibitor (CNI) and mycophenolate mofetil (MMF) in all cases.

Results:

N	34
Age, median (range)	42 (22–67)
Male sex, n (%)	18 (53%)
Diagnosis/status before HSCT2, n (%)	Acute leukemia (AML/ALL): 22 (65%) CR MRD− 9 | CR MRD+ 6 | Active 7 MDS: 3 (9%) – Active MPN (MF/CML): 6 (17%) CR MRD− 4 | CR MRD+ 2 LPD: 3 (9%) – CR 1 | Active 2
HSCT1 donor type, n (%)	MUD 12 (35%) | Haplo 10 (30%) MRD 7 (21%) | MMUD 3 (9%)
Conditioning HSCT1	MAC 27 (80%) | RIC 7 (20%)
GVHD prophylaxis	PT-CY + CNI + MMF
HCT-CI, median (range)	3 (0–7)
HCT-CI ≥3, n (%)	17 (50%)
DRI, n (%)	Intermediate 9 (26%) | High/Very high 25 (74%)
HSCT2 donor type, n (%)	MUD 12 (35%) | Haplo 12 (35%) MRD 7 (21%) | MMUD 3 (9%)
Conditioning HSCT2, n (%)	Intermediate TCI 24 (70%) | High TCI 10 (30%)
Time 1st–2nd HSCT, months	13.2 (5.6–320.2)
Early complications HSCT2, n (%)	Mucositis ≥G2 47% | Hepatotoxicity ≥G2 41% Cystitis 26% | CMV 35% | VOD 18% Endothelial injury 12% | Sepsis 24%

A total of 34 second allogeneic HSCTs were performed during the study period. Patient baseline characteristics and transplant-related complications are summarized in Table 1. The study population represented a very high-risk cohort: 50% of patients had an HCT-CI ≥3, and the majority were classified as high or very high Disease Risk Index (DRI) at the time of the second transplant. In addition, more than half of the patients underwent transplantation with suboptimal disease control, including active disease or measurable residual disease (MRD) positivity. With a median follow-up of 48.6 months, the estimated 4-year OS was 38% and 36% for 4-year EFS. The[K.1] [LCG2] cumulative incidence of NRM was 23% at 4 years. Relapse remained the main cause of treatment failure, with a cumulative incidence of 41% at 2 years and 46% at 4 years. Overall survival was superior in patients transplanted in remission, particularly those with MRD-negative disease, who achieved a median OS of 27.0 months (IQR 16.9–66.8) compared with 7.0 months (IQR 4.2–26.9) in the remaining patients.

Conclusions: In our experience, second allo-HSCT after relapse using PT-CY as GVHD prophylaxis and a different donor, provided meaningful long-term survival, with nearly 40% of patients alive at 4 years despite a highly adverse-risk profile. NRM was acceptable in this high-risk population, while relapse continued to be the main cause of failure. Optimization of pre-transplant response and post-transplant strategies, including maintenance approaches, may still lead to improved outcomes. These data support second allo-HSCT using PT-CY, as a valid therapeutic option in selected patients relapsing after a prior allograft.

Disclosure: Nothing to declare.

A350

DONOR DERIVED LEUKEMIA, SINGLE CENTRE EXPERIENCE

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Background: Donor-derived leukemia (DDL) is a rare complication following allogeneic hematopoietic stem cell transplantation (HSCT). Although it frequently mimics relapse of the original malignancy, it originates from donor hematopoietic cells that undergo leukemic transformation within the recipient's microenvironment. The incidence of DDL is estimated to be less than 1% of all HSCT cases, and its pathogenesis is very heterogenous and remains still poorly understood.

Methods: We retrospectively analyzed patients diagnosed with donor-derived hematologic malignancy. When feasible, donor origin was confirmed using chimerism analysis, and molecular genetic testing and cytogenetic changes were evaluated alongside demographic data and primary disease characteristics. Structured case reports were compiled.

Results: Over a 15-year period,1,308 allogeneic transplants were performed at our center. Six cases of donor-derived hematologic malignancy were identified (0.46%). In half of these,

transmission from donors with germline mutations was suspected; the remaining donors showed no similar changes. Notably, one patient with primary CBF leukemia (CBFβ/MYH11+) developed CBF DDL (AML1/ETO+), and another with initial chromosome 7 involvement exhibited recurrent chromosome 7 abnormalities with different breakpoints. Two patients with donor-derived polycythemia vera acquired germline JAK2 R1063H mutations, considered to have limited impact on the JAK/STAT pathway. One donor harboring TP53 (VAF 2%), ZRSR2 (0.4%), and two PPM1D mutations (0.04% and 0.4%) remained clinically healthy ten years later, showing modest clonal expansion (TP53 3%, ZRSR2 12%, PPM1D 3% and 9%), while the recipient's DDL exhibited the same mutational profile with markedly increased VAFs (TP53 34%, ZRSR2 2%, PPM1D 0.08% and 1.8%) and AML diagnosis.

Conclusions: Donor-derived leukemia (DDL) represents an extremely rare complication of HSCT, with current knowledge largely based on individual case reports. Despite the heterogeneity of this condition, available evidence supports the hypothesis that the recipient's microenvironment plays a crucial role in leukemogenic processes. This environment may not only damage healthy donor hematopoiesis but also enable clonal expansion of cells carrying germline or somatic mutations that have not manifested as disease in the donor. A deeper understanding of these mechanisms could substantially advance our knowledge of the etiopathogenesis of DDL as well as de novo hematologic malignancies.

Disclosure: I have no conflict of interest.

A351

EFFICACY AND TOXICITY OF DONOR LYMPHOCYTE INFUSION IN A FIXED-DOSE COHORT: CLINICAL OUTCOMES AND PATIENT-REPORTED BURDEN

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Background: Patients with relapse after allogeneic hematopoietic stem cell transplantation (alloSCT) have poor outcomes regardless of the underlying disease. In this setting, donor lymphocyte infusion (DLI) constitutes an established cellular therapy but carries significant risks of inducing graft-versus-host disease (GvHD). No international standardized dosing protocols are established to optimally balance graft-versus-leukemia effects against GvHD. At our institution, we employ the commonly used four-step escalation regimen (1, 5, 10, 50 × 10^6 CD3+/kg) at 4-week intervals. Several episodes of severe GvHD after the fourth DLI dose were observed in our cohort, and in view of the expanding use of combination therapies, this dosing approach may warrant re-evaluation. This retrospective analysis was performed to characterize the outcomes associated with this dosing regimen.

Methods: We analyzed 60 patients receiving DLI post-alloSCT at our tertiary care center (2014-2025). Indications were preemptive (measurable residual disease (MRD)/mixed chimerism) or therapeutic (hematological/extramedullary relapse). Overall survival (OS) and event-free survival (EFS) were estimated using the Kaplan-Meier method. Cumulative incidences of relapse, non-relapse mortality (NRM), and GvHD were calculated using competing risks. Prognostic factors were identified using Cox regression models. Response was defined as morphological remission, MRD negativity, or improved donor chimerism. Additionally, patient-reported outcomes (PROs) were assessed cross-sectionally in a survivorship sub-cohort (≥ 3 months post-last dose) using the NCI PRO-CTCAE.

Results:

Parameter	**Value (n (%))**
Sex (Male / Female)	32 (53%) / 28 (47%)
Diagnosis (AML / MDS+MPN / Other*)	29 (48%) / 14 (23%) / 17 (28%)
HCT-CI Score (0 / ≥1)	35 (58%) / 25 (42%)
Conditioning (MAC / RIC or RTC)	22 (37%) / 38 (63%)
Donor (MUD / MRD / Mismatch)	32 (53%) / 17 (28%) / 11 (18%)
History of aGvHD (prior to DLI)	40 (67%)
Time alloSCT to DLI, months (median)	8.2 [3.0–62.1]
Indication (Preemptive / Therapeutic)	38 (63%) / 21 (35%)**
DLI Strategy (Mono / +Hypomethylating agents / +Other***) **Other: ALL, CLL, MM ***Other: Venetoclax, TKI, IMiDs etc.*	13 (22%) / 29 (48%) / 18 (30%) ***1 Patient not assessed*

Median age was 58 years (range 24-74); acute myeloid leukemia (AML) (48%) and myelodysplastic syndromes/myeloproliferative neoplasms (23%) were the most common underlying diseases. DLIs were administered preemptively in 63% and therapeutically in 35%. Thirty-four patients (57%) received the maximum DLI dose (≥ 4). Response was observed in 34 patients (57%). Median OS and EFS were 17.3 and 5.4 months, respectively. The cumulative incidence of acute GvHD (aGvHD) was 58% (grade III-IV: 18%), while chronic GvHD (cGvHD) occurred in 38% (moderate/severe: 15%). Notably, 51% of aGvHD events occurred in patients receiving ≥ 4 doses, with 33% being grade III-IV. In univariate analysis, early treatment discontinuation (1-2 doses) was significantly associated with inferior EFS (HR 2.68, p=0.017) and OS (HR 2.15, p=0.045). In multivariate analysis, this lower dose level remained significantly associated with inferior EFS (HR 3.09, p=0.005), while cGvHD emerged as the strongest independent predictor for favorable outcomes in both EFS (HR 0.25, p<0.001) and OS (HR 0.42, p=0.022). Unexpected hospitalizations occurred in 63% (n=38; median 9 days), primarily triggered by infections (n=24) and GvHD (n=19).

NRM was 27%; primary causes of death included infections (n=12) and GvHD (n=3). PROs (median 36 months from first DLI; response rate 74%; n=17) identified cutaneous toxicity (Δ mean severity +1.36) and fatigue (Δ +1.00) as dominant stressors, while cognitive function remained stable. Despite high concordance between clinical GvHD status and PROs (rash severity 3.29 in GvHD vs. 0.00 in controls), global treatment satisfaction remained preserved in the GvHD cohort (mean 3.57).

Conclusions: Fixed-dose escalation is an effective treatment option, though the clustering of adverse events at the highest dose level indicates a narrow therapeutic window. Consequently, the optimal use of DLI regarding dynamic, response-adapted dosing strategies requires further investigation to better balance efficacy and safety.

Disclosure: Nothing to declare

A352

EFFECT OF MINIMAL RESIDUAL DISEASE GUIDED POSTTRANSPLANT 6-MERCAPTOPURINE AND METHOTREXATE MAINTENANCE ON PROGNOSIS OF HIGH-RISK PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE-CENTER EXPERIENCE

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Background: The role of preemptive 6-mercaptopurine (6-MP)/methotrexate (MTX) maintenance after allogeneic stem cell transplantation (allo-SCT) in children with high-risk acute lymphoblastic leukemia (ALL) is not well-established. For years, leukemia physicians have used 6-MP and MTX maintenance with excellent results for ALL. However, only two consecutive studies from the Minnesota transplant group revealed no consensus on the efficacy of posttransplant maintenance therapy with 6-MP/MTX in a small mixed-age cohort of high-risk ALL patients. This study aimed to investigate the effect of flow cytometric minimal residual disease (Flow-MRD)-guided posttransplant maintenance with 6-MP/MTX on the prognosis of high-risk pediatric ALL.

Methods: Forty high-risk ALL children were divided into two groups: Group 1 (n=16) received posttransplant 6-MP/MTX maintenance, and Group 2 (n=24) did not. The detection of Flow-MRD positive (≥0.1%) results was assessed monthly for the first 100 days, then every three months for the next 365 days. All patients' transplant data were retrospectively reviewed.

Results: After allo-SCT, six patients (35%) in Group 1 and eleven (65%) in Group 2 had overt relapse. In Group 1, Flow-MRD-directed maintenance was initiated after the detection of positive MRD in 11 patients within the first three months of transplantation and 5 patients six months later. Overt relapse occurred in two (20%) of eleven individuals and in four

(80%) of five patients on maintenance. Reversible grade 1-2 hematological and liver toxicity were detected in twelve (75%) of the 16 subjects in Group 1. In group 2, seven patients died from refractory leukemia within six months of transplantation, while the other four survived. Patients on maintenance had a significantly higher cumulative survival (82%) compared to those without maintenance (38%) ($p<0.05$). Older recipient age (>6 years) [Hazard Ratio (HR): 2.4], TBI-based conditioning [HR: 3.1], acute GVHD complications [HR: 2.6], short relapse time (<1 year after allo-SCT) [HR: 3.2], and lack of maintenance therapy [HR: 4.1] were all risk factors for mortality.

Conclusions: To our knowledge, this is the first pediatric study to assess preemptive, flow-MRD-guided 6-MP/MTX maintenance after allo-SCT in high-risk ALL. This approach to relapse prevention in pediatric ALL may enhance survival with minimal toxicity and low cost; nevertheless, further research is needed for a full assessment of these potential approaches.

Clinical Trial Registry: No

Disclosure: The authors have no conflict of interests

A353

CLINICAL COURSE AND SURVIVAL OF AML PATIENTS WITH CLONAL EVOLUTION AT RELAPSE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Acute myeloid leukemia (AML) exhibits substantial genetic diversity, which plays a key role in determining disease prognosis. Relapse following allogeneic stem cell transplantation (alloSCT) is largely driven by residual leukemic subclones, their evolution under therapeutic selective pressure, and mechanisms of immune evasion. Despite advances in treatment, post-transplant relapse remains a major clinical challenge, particularly in patients harboring high-risk genetic alterations. This study aims to investigate patterns of clonal evolution in individuals with AML who experience relapse after alloSCT, and to correlate these molecular and genetic dynamics with the patients' subsequent clinical course in order to better understand factors that influence treatment response, disease progression, and overall outcomes.

Methods: NGS analysis using a 64-myeloid gene panel (Agilent Technologies) at diagnosis, during disease remission, and at relapse after alloSCT revealed clonal evolution in 24 patients with AML (10 women and 14 men). All patients had undergone alloSCT at our institution within the past 6 years. Age ranged from 29 to 71 years (median 58 years). 14 of the 24 patients (71%) had secondary AML after MDS. Most patients (84%) were transplanted from matched unrelated donors.

Results: At diagnosis, most patients carried distinct genetic alterations—most commonly in TP53, SF3B1, RUNX1, TET2, DNMT3A, ASXL1, and SRSF2. These mutations became undetectable in complete remission after therapy and alloSCT. At relapse, however, original clones re-emerged together with newly developed subclones, leading to a mutational profile that differed substantially from diagnosis. Relapse samples not only retained baseline mutations but frequently acquired additional alterations, particularly in RUNX1, NRAS, KRAS, NF1, and FLT3. Mutations observed exclusively during clonal evolution at relapse included NRAS, KRAS, PHF6, DDX41, STAG2, and WT1, underscoring dynamic clonal progression. Overall survival varied considerably within the cohort, with only a subset of patients achieving long-term remission. A complete loss of mutations or mutations such as DNMT3A, TET2, and ASXL1 were more commonly observed among longer-term survivors, whereas alterations including TP53, NRAS, and KRAS were predominantly associated with early relapse and inferior survival. The impact of donor lymphocyte infusion (DLI), graft-versus-host disease (GVHD) and relapse therapy on clonal evolution and outcome requires further analysis in this heterogenous cohort.

Conclusions: Allogeneic stem cell transplantation (alloSCT) is the treatment of choice for AML patients with poor prognosis, but relapse remains common. Relapsed AML with clonal evolution is associated with adverse outcomes. Original clones persisted, while new subclones with additional mutations emerged, resulting in a mutational profile distinct from diagnosis. A better understanding of these dynamics may aid in preventing relapse and tailoring targeted therapeutic approaches.

Disclosure: Nothing to declare.

A355

MONOCYTE-T CELLS CROSSTALK ORCHESTRATES EARLY GRAFT-VERSUS-LEUKEMIA IMMUNITY IN AML PATIENTS AFTER TRANSPLANTATION

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Background: Acute myeloid leukemia (AML) is the most common acute leukemia in adults, for which haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is a key curative strategy. This study builds on prior research (Huo, et al., Sci Immunol. 2023) to investigate early immune reconstitution post-transplant and its association with graft-versus-leukemia effects in early relapse.

Methods: Firstly, we performed single-cell RNA sequencing on serially collected fresh peripheral blood (PB) and bone marrow (BM) samples from three AML patients and four aplastic anemia (AA) patients at 14, 30, and 60 days after haplo-HSCT. We next generated

single-cell transcriptomics and TCR repertoires using thawed BM samples from six additional AML patients - three maintaining continuous complete remission (CCR) and three experiencing ER within 6 months post-HSCT, at 30 days, 90 days (representing the pre-relapse phase), and at the time of relapse (for the ER group only) post-HSCT. Functional assays were conducted to assess the effect of galectin-9 (Gal-9) expression on monocytes on T cell exhaustion.

Results: AML patients exhibited fundamentally distinct post-HSCT expansion kinetics compared to AA patients, characterized by sequential monocyte (day 30) and T cell (day 60) activation phases. Monocytes from AML patients at 30 days post-transplant showed elevated expression of genes related to tumor immunity and T-cell proliferation, such as TNFSF10 and JAK2, along with their corresponding transcription factors. Concurrently, early post-transplant T cells underwent rapid activation, with significant upregulation of genes associated with antigen presentation and TCR signaling. Furthermore, we found that monocyte-T cell interactions in AML patients at 30 days post-transplant were substantially stronger than in AA patients, with heightened activity in tumor progression-related pathways such as Galectin, ADGRE, and LAIR1.
We further investigated GVL mechanisms through comparative analysis of monocyte and T cell dynamics in AML patients achieving CCR versus those experiencing ER following haplo-HSCT. CCR patients developed a distinct $CD8^+$ T cell subset characterized by high FCER1G expression at 30 days post-HSCT. In contrast, $CD8^+$ T cells in ER patients exhibited more exhausted phenotypes, with impaired signal-incoming capacity, while their monocytes remained hyperactivated and overexpressed Gal-9. Flow cytometry confirmed that monocytes from ER patients at 30 days post-transplant highly expressed Gal-9, while $CD8^+$ T cells exhibited greater exhaustion at both 30 and 90 days. Co-culture experiments demonstrated that ER-derived monocytes exacerbated T-cell exhaustion. Exogenous Gal-9 suppressed the reversal of CD8+ T cell exhaustion in a dose-dependent manner, an effect that was significantly rescued by MG-T-19.
Finally, TCR repertoire analysis revealed distinct TRBV gene usage preference between CCR and ER patients. Affinity prediction indicated that dominant TCR clones in both groups retained some affinity for AML antigenic peptides.

Conclusions: Hematopoietic and immune reconstitution differ between AML and AA post-HSCT. TCR clones from both CCR and ER patients retain leukemia-associated antigen reactivity, but T cells in ER exhibit a significantly enhanced exhaustion signature. This phenomenon is likely driven by monocyte-derived Gal-9 upregulation at 30 days post-HSCT, impairing $CD8^+$ T cell-mediated GVL effects and promoting relapse. Pharmacologic inhibition (MG-T-19) significantly reduces exhaustion, highlighting its therapeutic potential.

Disclosure: Nothing to declare.

A356

APPLICATION OF PLASMA FOURIER-TRANSFORM INFRARED SPECTROSCOPY (FT-IR) FOR MONITORING OF ACUTE MYELOID LEUKEMIA AND EXTRAMEDULLARY RELAPSE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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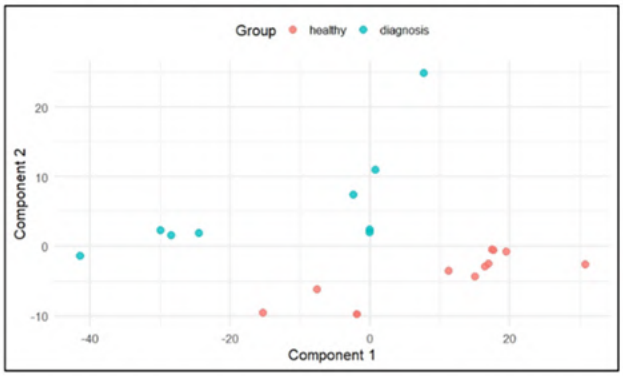
Background: Relapse of Acute Myeloid Leukemia (AML) remain a major cause of treatment failure. Among relapse patterns, extramedullary disease, referred to as myeloid sarcoma, representing a rare yet clinically significant condition characterized by infiltration of the leukemic blasts into tissues outside the bone marrow. Its diagnosis is often challenging and requires a multimodal approach that integrates imaging, histopathology and immunophenotyping to confirm the myeloid origin of infiltrating cells. Prognosis depends on factors such as localization, overall burden, biological characteristic and response to therapy.

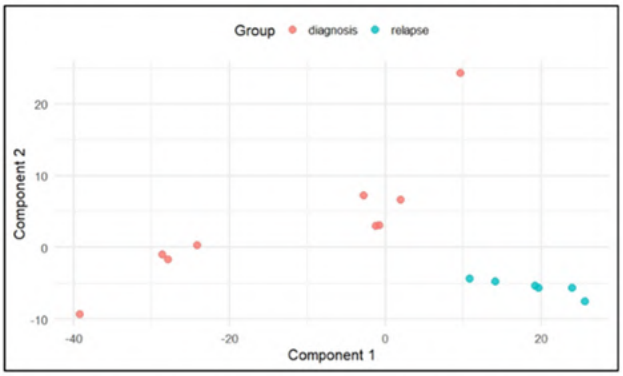
Methods: In this single-Centre study, we applied a liquid biopsy approach based on Fourier-Transform Infrared (FT-IR) spectroscopy to analyze plasma samples from patients with AML collected at diagnosis, pre- and post- allogenic hematopoietic stem cell transplantation (allo-HSCT), at bone marrow (BM) relapse, and at the onset of myeloid sarcoma, as well as from healthy controls. Spectral data were normalized using standard normal variate and evaluate through multivariate and machine-learning analysis with leave-one-patient-out cross-validation.

Results: The global comparison between healthy and pathological subjects demonstrated strong discriminatory performance (AUC=0.866; Accuracy=0.826), with an optimized sensitivity of 100% and specificity of 80%, indicating the presence of a characteristic FT-IR spectral signature associated with the AML and extramedullary disease (Fig. 1A). Comparison between the diagnostic phase and those from BM relapse or sarcoma showed excellent discrimination (Fig 1B-C), as did the comparison between medullary and extramedullary relapse (Fig 1D). These finding suggests that, despite shared features, the metabolic, molecular and structural profile captured by FT-IR differ between the two relapse patterns, reflecting distinct biochemical characteristics linked to their clinical presentations. Post-HSCT spectral analysis revealed a progressive reversion toward a physiological profile, with normalization observed in 94.4% of patients by day +90, consistent with a partial metabolic recovery and re-establishment of immune and hematopoietic homeostasis.

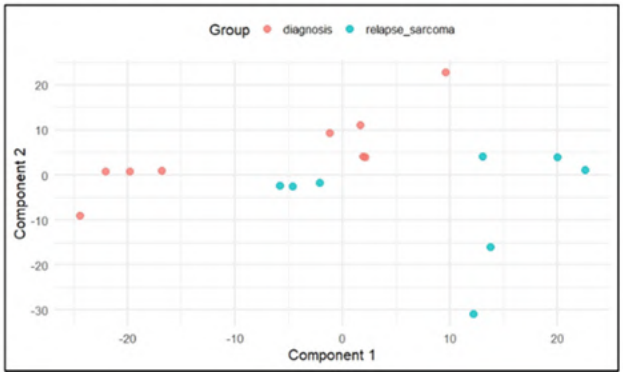
1A – PLS-DA - Healthy vs AML diagnosis



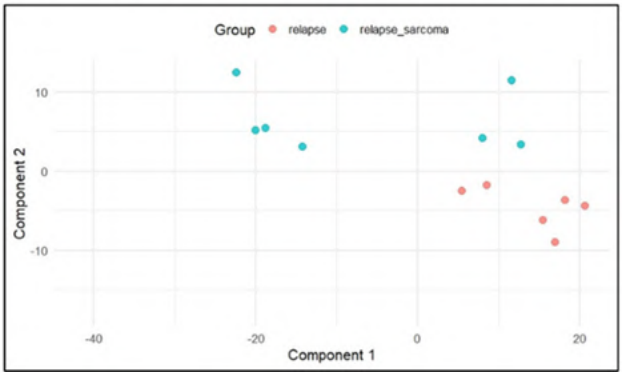
1B – PLS-DA - AML diagnosis vs BM relapse



1C – PLS-DA - AML diagnosis vs Myeloid Sarcoma



1D – PLS-DA – BM relapse vs Myeloid Sarcoma



Conclusions: In conclusion, our findings indicate for the first time that plasma-based FT-IR spectroscopy represents a promising liquid biopsy tool for monitoring AML and its post-HSCT. The method's ability to discriminate the diagnostic phase from relapse, differentiate relapse types, and capture the progressive normalization of the spectral profile in post-transplant samples (up to 94.4% of patients by day +90) suggest that plasma biochemical variation reliably reflect patients' clinical and metabolic status, supporting its potential use in clinical practice. This partially normalization could reflect improvements in amino acid availability, lipid composition, and systemic inflammatory status, key components of immunometabolic recovery. FT-IR thus offers a sensitive and non-invasive approach for detecting biochemical alterations, potentially providing complementary biomarkers for disease monitoring, immune reconstitution assessment and early relapse detection. When compared to other liquid biopsy approach, FT-IR offers unique advantage of rapidity, cost-effectiveness and reagent-free assessment.
Further investigation are needed to validate these FT-IR-derived signatures, such as lipid subclasses, protein secondary structures, and nucleic acid–related bands and to assess their integration into precision monitoring strategies for AML patients.

Disclosure: Nothing to declare.

A357

REFINED DISEASE RISK INDEX OUTWEIGHS PRE-TRASPLANT RESPONSE IN PREDICTING RELAPSE AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION: RESULTS FROM THE NATIONAL CANCER INSTITUTE IN LIMA, PERÚ

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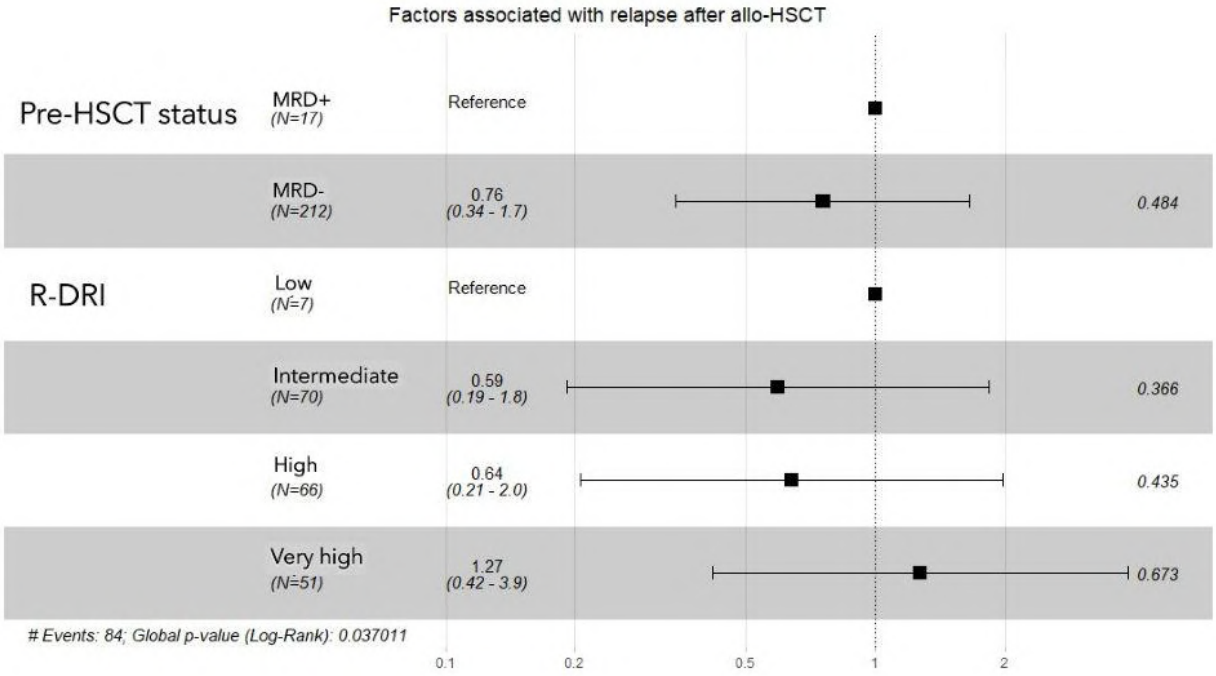
Background: Post-transplant relapse remains a major challenge after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Identifying factors associated with the risk of relapse is critical for patient stratification and post-transplant management. We aimed to evaluate clinical and disease-related predictors of relapse, with particular focus on pre-transplant response and disease risk.

Methods: We retrospectively analysed 235 adult patients undergoing allo-HSCT at a single centre. Data were collected from the unit registry and both physical and electronic medical records. Relapse was defined as disease recurrence after transplantation. Time to relapse and progression-free survival were analysed using Kaplan–Meier estimates. Factors associated with relapse were assessed using Cox proportional hazards models. Variables evaluated included age, sex, underlying diagnosis, measurable residual disease (MRD) status of response before HSCT, and refined Disease Risk Index (R-DRI). Multivariable models were adjusted for R-DRI.

Results: Relapse occurred in 94 patients (40%), with a median time to relapse of 8 months. Most relapses (89%, n=84) occurred within the first year post-transplant. The most relapsed diagnosis was acute lymphoblastic leukaemia (ALL) with 57 (60.6%), acute myeloid leukaemia (AML) with 19 (20.2%), and chronic myeloid leukaemia (CML) with 7 (7.4%) relapsed patients (4 of them were from the blastic phase group). Underlying diagnosis showed a trend toward association with relapse risk, although statistical significance was not reached (p=0.056).
In a univariate analysis, age and sex were not associated with risk of relapse. The R-DRI showed a significant overall association with relapse (p=0.01). Patients with negative MRD before HSCT experienced a lower risk of relapse compared to MRD-positive patients (hazard ratio [HR] 0.57; 95% CI 0.30–1.10; p=0.09). However, this association did not remain significant after adjustment for R-DRI (Figure 1) (HR 0.76; 95% CI 0.34–1.66; p=0.48). Among patients with available GVHD data, those who developed GVHD experienced a significantly lower incidence of relapse compared to those without GVHD (Fisher's exact test, p = 0.0003), consistent with a graft-versus-leukaemia (GvL) effect. Of the 94 patients who relapsed, 84 (89%) did so while receiving immunosuppressive therapy, including 76 during GVHD prophylaxis and 7 during active GVHD treatment, while 10 relapsed during routine observation. Post-transplant relapse was strongly associated with the clinical context at evaluation (Fisher's exact test, $p<2.2\times10^{-16}$). This association reflects the clinical circumstances at the time of relapse and cannot be interpreted as an independent risk factor for relapse.

Among relapsed patients, no significant association was observed between underlying diagnosis and timing of relapse (<6 vs ≥6 months; p=0.12), nor between relapse timing and the presence of graft-versus-host disease (GVHD) (p=0.84). Likewise, time to relapse did not differ significantly across diagnostic groups (p=0.61).



Conclusions: Relapse after allo-HSCT is predominantly driven by disease-related risk rather than pre-transplant response alone. The R-DRI remains a key predictor of relapse, while the lower incidence of relapse observed in patients with GVHD supports a GvL effect. Associations between relapse and immunosuppressive or clinical context variables reflect post-transplant circumstances rather than causal risk factors. These findings highlight the central role of disease biology in relapse risk stratification.

Disclosure: Nothing to declare.

A358

VENETOCLAX AND HYPOMETHYLATING AGENT WITH DONOR LYMPHOCYTE INFUSION FOR RELAPSED ACUTE MYELOID LEUKAEMIA POST ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Relapse remains a significant cause of mortality following haematopoietic stem cell transplantation (HSCT) in patients with myeloid malignancies. Donor lymphocyte infusion (DLI) may be used as salvage therapy but requires disease control for efficacy. Venetoclax/hypomethylating agent (ven/HMA) provides a lower intensity, often outpatient therapy to reduce disease burden. There is limited data on efficacy of this strategy particularly from an intention to treat perspective.

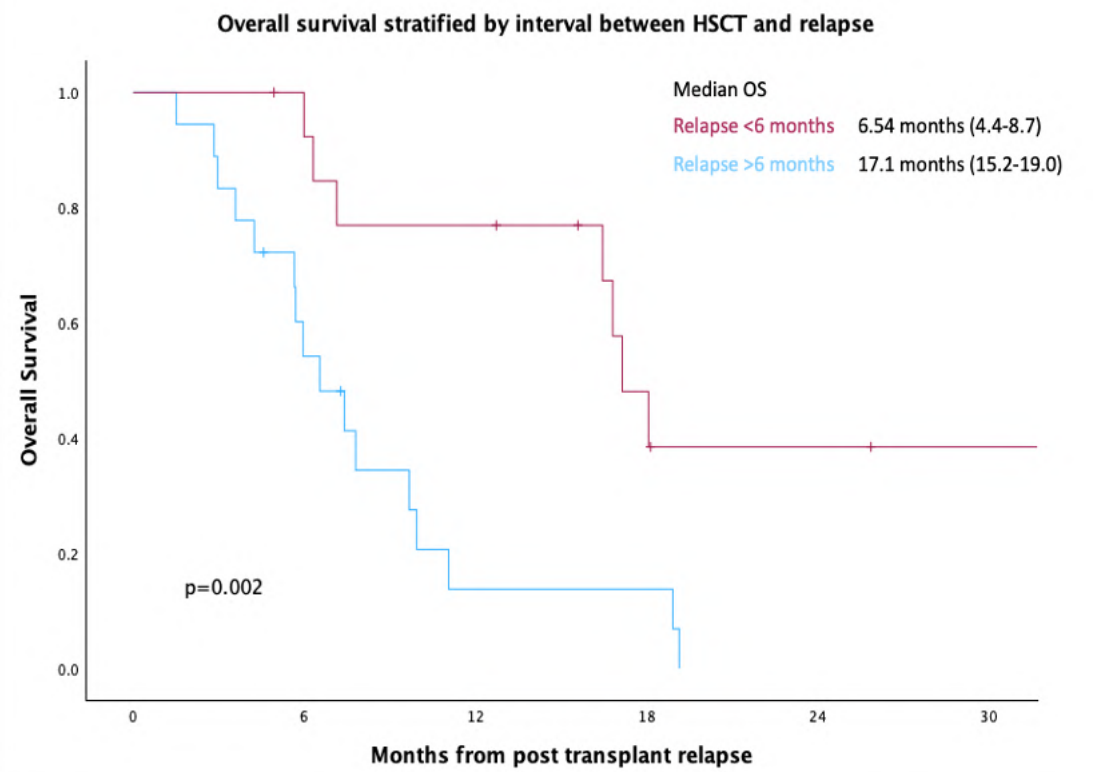
Methods: We performed a retrospective analysis of all patients with relapsed myeloid malignancies following allogeneic stem cell transplant intended for ven/HMA/DLI between 2020-2025 at King's College Hospital. Descriptive statistics were performed for baseline characteristics, Kaplan-Meir estimates for survival outcomes and Cox regression for baseline characteristics associated with overall survival (OS).

Results: Median age was 62.4years (range 24.9-79.9), 20(62.5%) were male, 9(21.1%) received venetoclax prior to HSCT and 5(15.6%) received DLI for mixed chimerism or MRD prior to relapse. Venetoclax was combined with azacytidine n=30 or decitabine n=2 typically for 3 cycles followed by HMA monotherapy based on trust funding. Characteristics at disease relapse are shown in table 1. Median follow up from relapse was 18.1 months.
Thirty-one of 32 patients commenced ven/HMA, for a median of 2 cycles with 10 proceeding to azacytidine monotherapy and one to low dose cytarabine. Twenty-three patients (71.9%) received at least one DLI (1 n=13, 2 n=3, 3 n=7). Reasons for not proceeding to DLI were graft versus host disease (GVHD) (3), persistent disease (3), clinical deterioration or death prior to DLI (2) and second allogeneic transplant (1).
Complete remission (CR/CRi) was achieved in 18 patients (56.3%), 10 MRD negative. Two patients achieved aplasia as best response and nine had persistent disease. Median time to best response was 2 cycles (range 1-6). Estimated median duration of response was 12.3 months (95%CI 1.2-23.3).
GVHD data was available for 26 patients. Two patients experienced aGVHD and one cGHVD from the time of relapse however only one patient developed GVHD after DLI. One year cumulative incidence of any GVHD was 11.7% (95%CI 0-24.5%).
The estimated median OS from relapse was 9.9 months (95%CI 5.3-14.5). Among those who achieved a complete response median OS was 17.1 months (95%CI 9.1-24.6) compared to 5.7 months (95%CI 3.0-8.4) among those who did not (p=0.002). Of the 15 patients with ≥2years follow-up three remain alive, all of whom are in remission.
In univariate analysis only relapse >6 months from HSCT was associated with superior OS (hazard ratio [HR] 0.27 95%CI 0.11-0.68, p=0.005). There was a trend towards improved survival in those with mixed chimerism at relapse (HR0.50, 95%CI 0.21-1.17, p=0.11). None of the other baseline characteristics in table 1 were statistically significant. Only relapse >6 months retained significance in a multivariate analysis (HR 3.35 95%CI 1.24-9.07, p=0.017) Kaplan-Meir estimates shown in figure 1.

Table 1. Characteristics at disease relapse	**n (%)**
<6months from HSCT to relapse	14 (43.8)

Diagnosis at relapse	Acute myeloid leukaemia (AML)	23 (71.9)
	Burden at relapse <1% /1-5% /6-20% />20%	4/ 1/ 8/10
	ELN favourable / intermediate/ adverse	1 / 3/ 18
	Myelodysplastic syndrome with excess blasts	6 (18.8)
	Other^	3 (9.4)
Myeloablative conditioning		8 (25)
T cell depletion	Alemtuzumab	13 (40.6)
	Anti-thymocyte globulin	16 (50)
	Post-transplant cyclophosphamide	2 (6.3)
	T replete	1 (3.1)
Donor type	Matched sibling	5 (15.6)
	Matched unrelated donor	19 (59.4)
	Mismatched (<9/10) unrelated donor	6 (18.8)
	Haploidentical	2 (6.3)
Mixed (<95% CD3) chimerism at relapse, n(%)		18 (58.1)
Biallelic T53 at diagnosis or relapse, n(%)		9 (28.1)
AML-MR mutations at relapse, n(%)		13 (40.6)

^blastic plasmacytoid dendritic cell neoplasm, chronic myelomonocytic leukaemia 1, myelodysplastic/myeloproliferative neoplasm with 13% blasts



Conclusions: Ven/HMA/DLI is a viable treatment option for post-transplant relapse however only a minority of patients initially intended for treatment are likely to attain long term disease control. To the best of our knowledge this is one of the largest cohorts of patients treated with Ven/HMA/DLI.

Disclosure: Nothing to declare

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MOLECULAR AND FUNCTIONAL CHARACTERIZATION OF SOLITARY EXTRAMEDULLARY RELAPSE OF AML AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HCT) can cure acute myeloid leukemia (AML), but relapse remains the main cause of treatment failure. Most relapses are medullary, whereas extramedullary (EM) relapse may arise in conjunction or independently of marrow involvement. Solitary EM relapse after allo-HCT is rare and poorly characterized, with limited tissue-based data available. Improved molecular and functional characterization is needed to optimize diagnostics and therapy.

Methods: We analyzed nine patients with solitary EM relapse after allo-HCT. DNA capture-based next-generation sequencing (NGS) applying a 101-gene myeloid NDC assay was performed on snap-frozen or formalin-fixed, paraffin-embedded EM tissue. In four patients who had received allo-HCT from HLA-mismatched (including haploidentical) donors , genomic loss of the patient-specific HLA was assessed on snap-frozen EM tissue using PCR-based NGS. Leukemic blasts isolated from one EM lesion underwent a 72-hour drug response profiling (DRP) analyzing 46 compounds; cytotoxicity was measured by using the CellTiter-Glo luminescent Cell Viability Assay and apoptosis by imaging real-time live cell caspase-3/7 binding.

Results: The median age at EM relapse was 45 years (range, 25–68 years). EM relapse sites included skin (n= 4), pleura (n= 1), brain (n= 1), breast (n= 1), lymph node (n= 1), and soft tissue (n= 1). Four patients had previously received a second allo-HCT. The median interval from allo-HCT to EM relapse was 440 days (range, 150-1289 days). Two patients received haploidentical grafts; among the remaining transplants, HLA mismatches in the graft-versus host direction involved HLA-B (n= 1) and/or DPB1 (n= 2), in addition to one matched sibling and three fully matched unrelated (12/12 MUD) grafts. No HLA loss was detected in EM samples from the four informative patients transplanted with an HLA-mismatched donor. DNA capture sequencing revealed *RAS* pathway mutations (*CBL, NRAS, KRAS)* in five of nine patients. In total, eight activating signaling mutations (*FLT3, NRAS, KRAS, JAK2*) in seven patients and nine chromatin-modifying/epigenetic mutations (*ASXL1, EZH2, BCOR, BCORL1, KMT2A*-PTD) in five patients were identified. Seven patients harbored structural variants, including *FLT3*- ITD (n = 3), *KMT2A* rearrangements (n = 2), *KMT2A*-PTD (n = 1), *BCR::ABL1* (n = 1), rearrangements involving *ETV6* and *PDGFRB* (n= 1), and an *IKFZ1* deletion (n= 1). No mutations in DNA methylation-related genes were detected.

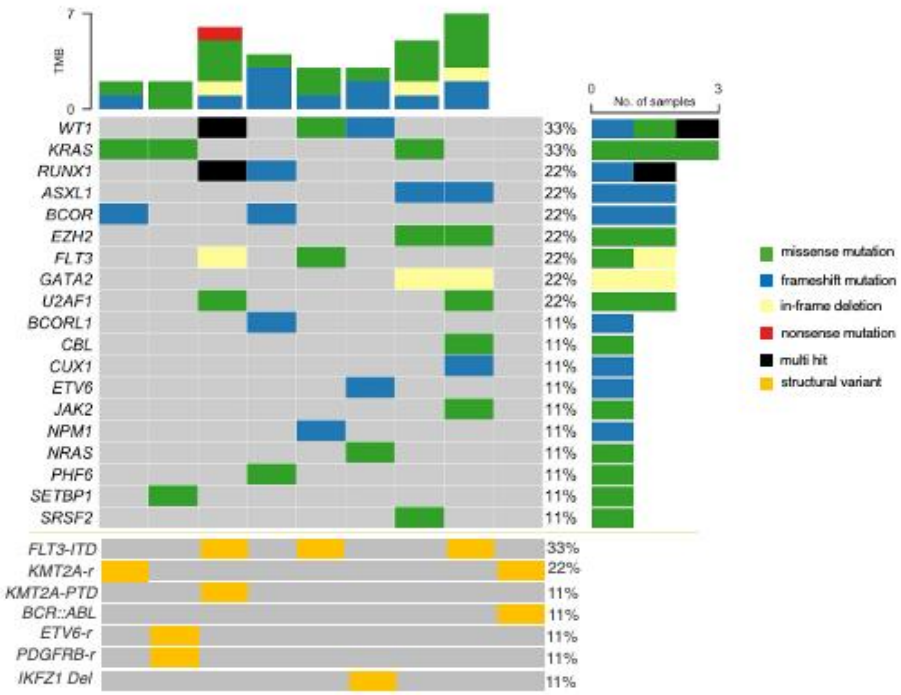

Figure 1. Oncoplot of somatic variants in nine EM AML relapses after allo-HCT.

First drug response profiling based on a single patient sample identified venetoclax as one of the effective agents, with caspase 3/7-dependent apoptosis confirmed for this agent.

Conclusions: In this cohort, solitary EM relapse of AML after allo-HCT appeared to be enriched for *RAS*-pathway and other signaling mutations, as well as chromatin-modifying and epigenetic alterations, whereas no mutations in DNA methylation-related genes were detected. The mechanism of relapse has yet to be fully understood, however, in our small cohort, we could not identify a role for genomic loss of mismatched HLA in informative patients. Ex vivo drug response profiling combined with molecular characterization in EM relapse will help to better define the underlying mechanisms and the most effective, individualized therapy, to optimize patient outcomes.

Disclosure: Nothing to declare.

P114

AZACITIDINE AS POST-TRANSPLANT MAINTENANCE THERAPY IN ACUTE MYELOID LEUKEMIA AND MYELODYSPLASTIC SYNDROMES: EFFECTS, SAFETY AND IMMUNE RECONSTITUTION DYNAMICS

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Background: Disease relapse after allogenic hematopoietic stem cell transplantation (HSCT) is a major adverse prognostic event in patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS). To reduce this risk, post-transplant maintenance strategies have been incorporated into clinical practice. Azacitidine (AZA) is currently the only available maintenance option for high-risk MDS and adverse-risk AML without FLT3 mutations, although published efficacy data remain inconsistent. In this single-center retrospective study, we compared survival outcomes, safety, and immune reconstitution patterns in patients receiving and not receiving post-HSCT AZA.

Methods: We evaluated 83 adult patients undergoing HSCT in our center between September 2019 and November 2024. Patients were grouped as follows:

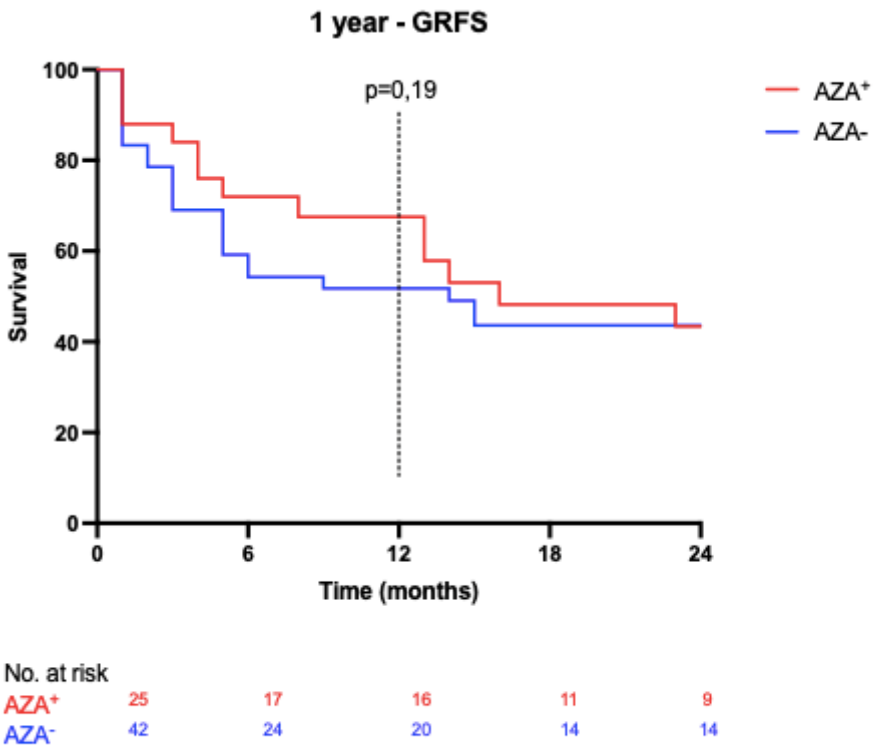
1. AZA^+ (n = 25): patients receiving post-HSCT AZA at 32 mg/m²/day subcutaneously for 5 consecutive days every 28 days, for a planned total of 12 cycles. Most had ELN adverse-risk AML or high/very high-risk R-IPSS MDS.
2. AZA^- (n = 42): patients not receiving AZA post-HSCT, diagnosed with AML or MDS across variable risk categories.

A third, smaller cohort (n = 16) included patients with FLT3-mutated AML receiving FLT3-targeted maintenance therapies (Sorafenib or Gilteritinib) ($FLT3^+$). Patients' baseline characteristics are summarized in Table 1. Immune reconstitution was assessed through lymphocyte-subset analyses at predefined post-transplant time points (days +60, +120, +180, +365, +730).

	Total (N=83)	**AZA^+ (N=25)**	**AZA^- (N=42)**	**$FLT3^+$ (N=16)**
Sex - N° (%)				
Males	43 (52%)	12 (48%)	24 (57%)	7 (44%)
Females	40 (48%)	13 (52%)	18 (43%)	9 (56%)
Median Age at Diagnosis, yrs. (range)	56 (48-63)	55 (49.50-63.50)	60.50 (53-63.25)	48 (36.50-57)
Diagnosis - N° (%)				
MDS	24 (29%)	8 (32%)	16 (38%)	0
AML	59 (71%)	17 (68%)	26 (62%)	16 (100%)
ELN Risk Profile - N° (%)				
Favorable	11 (19%)	1 (6%)	10 (38%)	0
Intermediate	14 (23%)	2 (12%)	5 (19%)	7 (44%)
Adverse	34 (58%)	14 (82%)	11 (43%)	9 (56%)

IPSS-R Risk Score - N° (%)				
Very Low	2 (8%)	1 (12%)	1 (6%)	
Low	2 (8%)	1 (13%)	1 (6%)	
Intermediate	7 (29%)	3 (38%)	4 (25%)	
High	5 (21%)	1 (12%)	4 (25%)	
Very High	8 (34%)	2 (25%)	6 (38%)	
Karyotype - N° (%)				
Normal	35 (42%)	6 (24%)	15 (36%)	14 (88%)
Complex	10 (12%)	1 (4%)	8 (19%)	1 (6%)
Others	35 (42%)	16 (64%)	18 (43%)	1 (6%)
NE	3 (4%)	2 (8%)	1 (2%)	0
TP53 Mutation - N° (%)	13 (16%)	6 (24%)	7 (17%)	0
Additional Criteria - N° (%)				
MDS and AML Therapy-related	11 (13%)	4 (16%)	6 (14%)	1 (6%)
AML Myelodysplasia-related	17 (20%)	7 (28%)	8 (19%)	2 (13%)
sAML following MPN	7 (9)	3 (12%)	4 (9%)	0

Results: AZA maintenance was not associated with increased rates of acute or chronic graft-versus-host disease (aGvHD/cGvHD) compared with AZA^- patients (aGvHD: 20% vs. 36%, p = 0.26; cGvHD: 20% vs 24%, p = 0.77). No increase in infections of any kind (64% vs. 79%, p = 0.25), nor any increase in CMV (32% vs. 40%, p = 0.65) or EBV (36% vs. 43%, p = 0.61) reactivation was observed. Survival outcomes showed non-inferiority of the AZA^+ cohort relative to AZA^- patients, with median overall survival (OS) and progression-free survival (PFS) not reached in both group (p = 0.68; p = 0.73). Median GvHD-free/Relapse-free survival (GRFS) was longer in AZA^+ patients (16 months) than in the AZA^- cohort (14 months), with a trend toward improved GRFS at 1-year post-HSCT (p = 0.19). Regarding immune reconstitution, AZA^+ patients displayed an early trend toward higher NK-cell counts during the first post-transplant months compared with AZA^- individuals (1-year post-HSCT median NK-cell counts: 298/µL vs. 220/µL, p = 0.11). Moreover, at 1-year post-HSCT, AZA^+ patients showed significantly higher median levels of total T cells (1768/µL vs. 1121/µL, p = 0.03), $CD8^+$ T cells (731/µL vs. 387.5/µL, p = 0.04), and NK cells (298/µL vs. 170.5/µL, p = 0.01) compared with the $FLT3^+$ cohort, supporting a favorable immunologic pattern consistent with the known immunomodulatory effect of AZA.



Conclusions: Post-HSCT Azacitidine maintenance is safe and well tolerated. Despite a higher baseline-risk profile, AZA-treated patients achieved OS and PFS comparable to untreated patients and demonstrated early signals of improved GRFS and enhanced immune reconstitution. Overall, these findings support the use of Azacitidine as a post-transplant maintenance strategy in patients with high-risk AML and MDS.

Disclosure: Nothing to declare

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DONOR LYMPHOCYTE INFUSION AFTER ALLOGENEIC TRANSPLANTATION FOR MYELOID MALIGNANCIES: CLINICAL OUTCOMES AND THE ROLE OF CD3⁺ CELL DOSE

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Background: Relapse remains the leading cause of treatment failure after allogeneic hematopoietic cell transplantation (allo-HCT) for myeloid malignancies. Donor lymphocyte infusion (DLI) can induce potent graft-versus-leukemia effects but is limited by graft-versus-host disease (GvHD). Although $CD3^+$ T cells mediate the immunologic activity of DLI, the optimal cumulative $CD3^+$ dose that balances disease control and toxicity remains undefined.

Methods: We retrospectively analyzed 77 patients with myeloid malignancies who received DLI after allo-HCT between 01/2005 and 09/2025. The primary objective was to evaluate the association between cumulative $CD3^+$ dose and clinical outcomes and development of acute (grade 2–4) or chronic (moderate–severe) GvHD. Patients were stratified into three dose groups: $<0.5\times10^7$/kg (Group A, n=20), $0.5–3\times10^7$/kg (Group B, n=29), and $>3\times10^7$/kg (Group C, n=28). Fine–Gray competing-risk regression and nonlinear spline models were used to assess dose–response patterns.

Results: Median age was 56 years (IQR 44–61); 36% were female. Underlying diseases included AML (n=61), CML (n=10), and other myeloid neoplasms (n=6). Median cumulative $CD3^+$ dose was 1.6×10^7/kg (IQR 0.5–5.0), with a median of two DLI (range 1–4). DLI were given prophylactically in 25%, preemptively (MRD positive or mixed chimerism) in 32%, and therapeutically in 43% of patients.
Among therapeutic DLI recipients, median time from HCT to hematologic relapse was 15.5 months, and to molecular relapse 4.5 months. Five patients relapsed >5years post-HCT, and one relapsed 13 years after transplant. At DLI, 66 patients were in complete remission (n=23 MRD positive; n=3 mixed chimerism), while 11 had active extramedullary disease. Progression-free survival differed significantly across indications: prophylactic (13.4 years), preemptive (2.8 years), and therapeutic DLI (2.0 years) (p=0.03).
GvHD ≥ grade 2 acute or ≥ moderate chronic occurred in 22 patients, including severe chronic GvHD in nine and grade ≥3 acute GvHD in four; one patient died from GvHD. Higher $CD3^+$ doses (Groups B/C) were associated with increased risk of ≥moderate chronic GvHD (p=0.003).
In Fine–Gray models, cumulative $CD3^+$ dose showed no association with GvHD incidence (SHR 1.02, 95% CI 0.94–1.11, p=0.65). A borderline association with relapse was observed in the prophylactic or preemptive indication (SHR 1.06, 95% CI 1.00–1.13, p=0.052), although spline models did not confirm a significant nonlinear dose–response relationship.
At last follow-up, 41 patients (53%) were alive including 47% of patients given DLI prophylactically, 64% after preemptive and 48% after therapeutic DLI. Of note, 48% remained in complete hematologic remission after a median follow-up of 6.8 years.

Characteristic	Overall cohort (n = 77)
Age, years, median (IQR)	56 (44–61)
Female sex, n (%)	28 (36%)
Underlying disease, n (%) Acute myeloid leukemia (AML)	 61 (79%)

Characteristic	Overall cohort (n = 77)
Chronic myeloid leukemia (CML) Other myeloid malignancies	10 (13%) 6%)
Donor type, n (%) Related donor Unrelated donor	 30 (39%) 47 (61%)
Median cumulative $CD3^+$ DLI dose, $\times 10^7$/kg, median (IQR)	1.6 (0.5–5.0)
Indication for DLI, n (%) Prophylactic Preemptive Therapeutic	 19 (25%) 25 (32%) 33 (43%)
Disease status at DLI, n (%) Complete remission Active disease (extramedullary)	 66 (86%)* 11 (14%)
Median Follow-up in years	6.8
*MRD pos n=23; Mixed chimerism n=3	

Conclusions: Cumulative $CD3^+$ DLI dose did not show a clear dose–response relationship for relapse, survival, or GvHD. Higher doses were associated with more chronic GvHD but not with improved outcomes. Because patients receiving therapeutic DLI inherently have higher relapse risk and often receive escalated dosing, associations between higher dose and relapse likely reflect indication bias rather than causality.
More than half of patients achieved long-term survival including patients given DLI after relapse of myeloid disease, underscoring that durable responses are attainable with DLI-based strategies

Disclosure:

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RETROSPECTIVE ANALYSIS OF THE INCIDENCE OF RELAPSE AFTER ALLOGENEIC STEM CELL TRANSPLANTATION FOR MYELOID MALIGNANCIES: TREATMENT CHALLENGES FOR PATIENTS IN NORTH MACEDONIA

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Background: Relapsed disease after allogeneic stem cell transplantation (allo SCT) is one of the leading causes of posttransplant death among patients with myeloid malignancies. Posttransplant interventions, in conjunction with optimal conditioning regimens and donor selection, are increasingly supported by evidence for their potential to prolong patient survival by promoting antileukemia or graft-versus-leukemia effects. Aims of the study: Retrospective analysis of the outcomes of patients with relapsed myeloid malignancies after allo SCT. The second aim was to present institutional strategies aimed at reducing post-transplant disease relapse.

Methods: A total of 78 patients with myeloid malignancies treated with allo-SCT during a 5-year period at the University Clinic for Hematology, Skopje, North Macedonia were included in the study. Patients were referred for allogeneic HSCT according to donor availability (matched related, matched unrelated and haploidentical donors. Multivariable Cox Proportional Hazards models were made for time to relapse (TtR) and time to death following relapse (TtD). The analysis of the transplant outcome is based on pretransplant factors, graft versus host disease (GVHD) and post relapse management. Kaplan Meier Estimates were used to predict median survival time with 95% confidence intervals and Cox Proportional Hazard models to estimate hazard rates.

Results: Overall survival (OS) at one-year posttransplant was 81.1% (95% confidence interval [CI], 70% to 100%) in MRD transplants and 69.5% (95% confidence interval [CI], 65% to 100%) in MUD transplants and 55.5% (95% confidence interval [CI], 40% to 100%) in haploidentical donor transplants. TRM during the first year posttransplant was 10%. There is a statistically significantly higher DFS rate in MUD compared to MRD transplants and in haploidentical transplants (p= 0.0476, Log-rank, Mantel-Cox test, Chi square = 6.089. The TtR after transplantation was 6,5 months (range, 3 to 25 months). High risk cytogenetics had a 2.22 increased HR for relapse (p=0.086) [0.89-5.54]. For TtD, patients with GVHD prior to relapse had a marginally significant 57% lower HR for death (p=0.074) [0.17-1.09], while patients who developed GVHD after relapse had a 2.74 greater risk of death (p=0.123) [0.76-9.82]. Patients that received DLI had a 90% reduced risk of death (p<0.001) [0.03-0.26]. The relapse after allogeneic HSCT was treated with chemotherapy in 26.4% of patients, HMAs and venetoclax in 34.4%, targeted therapy in 10.4%, DLI 10%, second allogeneic transplant in 4,5% of relapsed patients.

Conclusions: Patients with myeloid malignancies who experienced relapse after allo SCT had poor prognosis. Development of GVHD prior to relapse trended toward improved survival after relapse. In this cohort, maintenance chemotherapy prior increased time to relapse and DLI improved survival after relapse.

Disclosure: no conflict of interest

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HIGH-DOSE CRYOPRESERVED BONE MARROW FROM DECEASED DONORS MAY REDUCE RELAPSE IN HLA-MISMATCHED ALLOGENEIC TRANSPLANTATION: DAY 180 POST-TRANSPLANT HOPE UPDATE

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Background: Historically, transplant outcomes have been closely tied to the degree of HLA matching, with higher degrees of mismatch correlating with poorer survival. We are evaluating the safety and efficacy of 4–8/8 HLA-matched cryopreserved hematopoietic progenitor cells (HPCs) derived from bone marrow harvested from deceased solid organ donors (ages 7–55 years) under two programs: the HOPE Expanded Access Program and the PRESERVE-I clinical trial (NCT05589896). These cells are processed using minimal manipulation. Initial engraftment success has been reported in the first patient treated with cryopreserved HPC-marrow. Four patients have enrolled in HOPE. This report presents Day 180 data for the first three HOPE-treated patients.

Methods: Three patients had acute myeloid leukemia (AML) in first complete remission (CR1) and lacked suitable matched donors. A fourth patient had a living donor who could not donate due to an allergic reaction to G-CSF. Patient 1 (age 68) and Patient 2 (age 69) received reduced-intensity conditioning (RIC); Patient 3 (age 63) and Patient 4 (age 34) received myeloablative conditioning (MAC). Transplants used 4/8 HLA-matched grafts for Patients 1–3 and 6/8 for Patient 4. CD34+ cell doses were 5.27, 4.45, 4.80, and 5.57 × 10^6 cells/kg, respectively. GVHD prophylaxis included tacrolimus, mycophenolate mofetil, and post-transplant cyclophosphamide (50 mg/kg on Days +3 and +4).

Results: Day 180 update: three of four patients remain Day +180 post-transplant. Neutrophil engraftment occurred on Days +16, +20, and +15; platelet engraftment on Days +21, +34, and +18, respectively, for the first three patients. Full donor chimerism (100%) was confirmed on Days +30 and +60 for the first three patients. No cytokine release syndrome (CRS) events were reported. Acute GVHD was manageable in these three patients: Patient 1 Grade 2 GI with Stage 2 lower GI involvement, onset Day +26; Patient 2 Grade 3 GI with Stage 2 GI and Stage 1 skin involvement, onset Day +54; Patient 3 Grade 2 GI with

Stage 1 skin involvement. All GVHD cases were steroid-responsive and resolved. No significant viral reactivation was reported.
At Day 180, all patients remained relapse-free with sustained cell counts. Survival at Day 180 was 100%. Patient 1 subsequently died on Day 282 from non-relapse causes, determined not to be related to HPC-marrow.

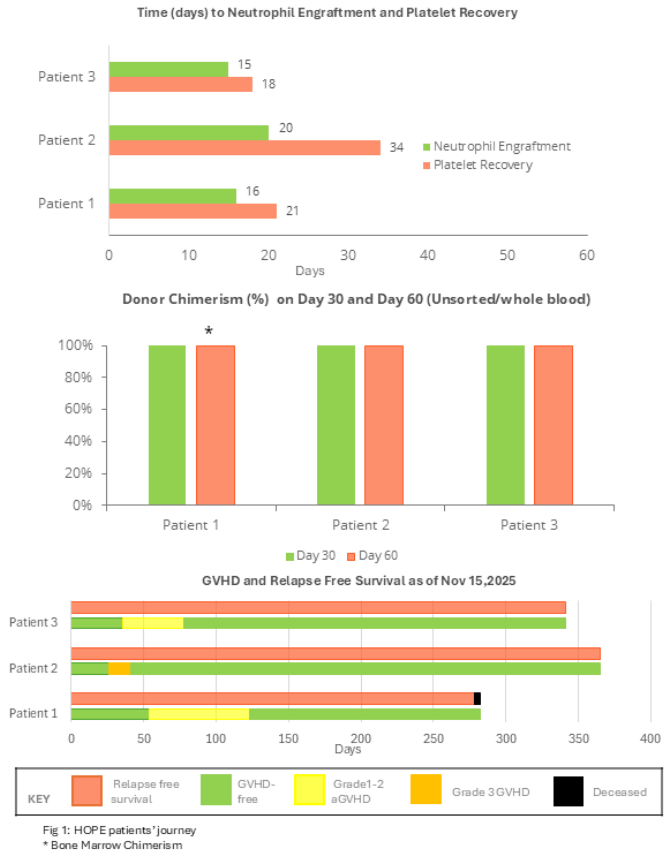

Fig 1: HOPE patients' journey
* Bone Marrow Chimerism

Table 1: Patient demographics and characteristics for first four patients

Patient	Age (years)	Gender (M/F)	Race		Disease	Conditioning Regimen (MAC vs. RIC)	CD34+ Dose (x10^6/kg)
Patient 1	68	Female	African American		AML (CR1)	RIC	5.27
Patient 2	69	Female	African American		AML (CR1)	RIC	4.45
Patient 3	63	Male	African American		AML (CR1)	MAC	4.80

Patient 4	34	Male	White		AML (CR1)	MAC	5.57

Conclusions: These preliminary findings indicate that high-dose, cryopreserved CD34+ cells from deceased donors are feasible and safe for infusion, supporting timely engraftment and disease control in HLA-mismatched allo-HCT. The absence of relapse and chronic GVHD through Day 180, together with manageable acute GVHD, highlights the potential of this novel graft source for patients with unmet medical needs.

Clinical Trial Registry: NCT07145411

Disclosure:

1. Sagar Munjal is an employee of Ossium Health
2. Muneer H. Abidi – Nothing to declare
3. Jeremy Pantin – Nothing to declare
4. Preethi Prasad is an employee of Ossium Health
5. Vicki L. Graves is an employee of Ossium Health
6. W. Scott Goebel is an consultant to Ossium Health

Erik J. Woods is an employee of Ossium Health

P119

COMPARISON OF UMBILICAL CORD BLOOD TRANSPLANTATION OUTCOMES BETWEEN FLT3-MUTATED AND -WILD-TYPE AML IN A MATCHED-PAIR COHORT

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Background: FLT3-mutated acute myeloid leukemia (AML) has long been associated with poor prognosis. The introduction of FLT3 inhibitors has improved outcomes, and according to ELN 2022, FLT3-mutated AML is now classified as intermediate risk. While allogeneic hematopoietic stem cell transplantation (allo-HSCT) is commonly performed, data on umbilical cord blood transplantation (UCBT) in FLT3-mutated AML remain limited. UCBT is thought to provide a stronger graft-versus-leukemia (GVL) effect compared with other graft sources. We aimed to compare UCBT outcomes between FLT3-mutated and wild-type AML and to identify prognostic factors using a matched-pair cohort.

Methods: We retrospectively analyzed relapsed or refractory adult AML patients who underwent their first UCBT at Toranomon Hospital between January 2019 and December 2023. Patients without FLT3 mutation testing, with active infections, or with ECOG performance status >2 at transplantation were excluded. Among 177 eligible patients in the total cohort, 36 had FLT3 mutations. Matched-pair cohorts of FLT3-mutated and FLT3–wild-type AML were created using age, sex, ELN 2022 risk (excluding FLT3 mutation), disease

status, HCT-CI score, conditioning intensity, and year of transplantation as covariates. The caliper width was set at 0.2 times the standard deviation. Survival probabilities were estimated using the Kaplan–Meier method, with group comparisons assessed by log-rank tests. Cox regression and Fine–Gray models were used for multivariate analyses, accounting for competing risks. This report summarizes interim 1-year results.

Results: Each cohort included 31 patients. All patients in the FLT3-mutated cohort had ITD mutations. The median age was 56.4 years in both cohorts. The numbers of patients with de novo AML were 30 and 29, and those with ECOG performance status 0–1 at transplantation were 29 and 27 in FLT3-mutated and FLT3–wild-type cohorts respectively, showing no significant differences. There were also no significant differences in total nucleated cell (TNC) count, $CD34^+$ cell count, or CFU-GM number per kilogram of body weight of the cord blood units used.
The FLT3-mutated cohort showed a trend toward better 1-year progression-free survival (PFS; 70.6% vs. 51.6%, P = 0.14) and overall survival (OS; 70.6% vs. 54.5%, P = 0.39) compared with the wild-type cohort, along with a significantly lower relapse rate (7.0% vs. 27.0%, P = 0.02), while non-relapse mortality (NRM) did not differ significantly (21.0% vs. 34.5%, P = 0.55) in univariate analysis. In multivariate analysis, factors associated with poor OS were older age (>59 years) and higher HCT-CI (≥2); factors associated with poor PFS were older age (>59 years), higher HCT-CI (≥2), FLT3 wild-type status, and reduced-intensity conditioning; male sex was associated with higher NRM. No factors were significantly associated with relapse. In the FLT3-mutated cohort, 19 patients received post-transplant maintenance with gilteritinib, showing 78.6% PFS and OS, 5.3% relapse, and 16.1% NRM.

Conclusions: In this matched-pair cohort analysis of first-time UCBT recipients, FLT3-mutated AML was associated with superior PFS and a lower relapse rate compared with FLT3–wild-type AML. Post-transplant FLT3 inhibitor maintenance therapy showed potential benefit, although results should be interpreted cautiously due to possible selection bias. Larger studies are warranted to validate these findings.

Clinical Trial Registry: jRCT1031230158 (https://jrct.mhlw.go.jp/latest-detail/jRCT1031230158)

Disclosure: Aya, Nishida; Astellas Pharma Inc. (honoraria)
Shinsuke, Takagi; Astellas Pharma Inc. (honoraria, consultation fee)
Naoyuki, Uchida; Astellas Pharma Inc. (honoraria, research funding)

P120

POST-TRANSPLANT RELAPSE AS A MAJOR DETERMINANT OF OVERALL SURVIVAL AFTER ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION: RESULTS FROM A SINGLE CENTER IN AN UPPER-MIDDLE INCOME COUNTRY

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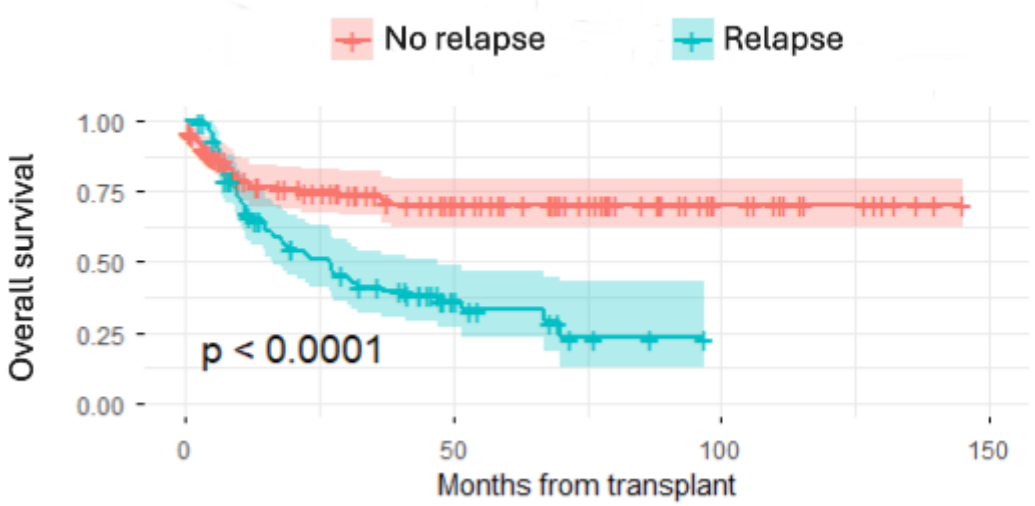
Background: Relapse remains an important cause of treatment failure after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite advances in transplant strategies and rescue treatments, the impact of post-transplant relapse on long-term survival continues to be significant. We aimed to evaluate the overall survival (OS), progression-free survival (PFS), and the impact of relapse on survival outcomes in a real-world cohort of allo-HSCT recipients.

Methods: We conducted a retrospective study including 235 adult patients undergoing allo-HSCT at a single centre. Data were collected from the unit registry and both physical and electronic medical records. Overall survival was defined as the time from HSCT to death from any cause or last follow-up. Progression-free survival was defined as the time from HSCT to relapse or death. Relapse was detected by molecular testing in chronic myeloid leukaemia and by flow cytometry in the rest of the diseases. Survival curves were estimated using the Kaplan–Meier method and compared using the log-rank test. Median follow-up was estimated using the reverse Kaplan–Meier method.

Results: Median age at HSCT was 28 years (range 15–63), and 123 patients (52%) were male. The most frequent diagnoses were acute lymphoblastic leukaemia (ALL, n=115), acute myeloid leukaemia (AML, n=63), mixed phenotype leukaemia (n=17), chronic myeloid leukaemia (n=15, 9 of them in blastic phase), and myelodysplastic syndrome (n=8). Before HSCT, 212 patients (90.2%) were in complete remission, 17 (7.2%) had measurable residual disease (MRD+), and 6 (2.6%) had unknown disease status.
Relapse occurred in 94 patients (40%), with a median time to relapse of 8 months (range 1–43). Most relapses (89%, n=84) occurred within the first year after HSCT, including 48 cases within the first six months. With a median follow-up of 49.8 months (range 0.8–140), OS at 2 and 5 years for the entire cohort was 64.5% and 54.7%, respectively. PFS at 2 and 5 years was 43.2% and 38.8%, respectively.
Patients who relapsed had significantly inferior survival compared with those without relapse (Figure 1). OS at 2 and 5 years was 50.9% and 32.9% in relapsed patients versus 76.6% and 72.8% in non-relapsed patients (log-rank $p<0.001$). Relapse was the strongest determinant of mortality in the cohort, according to the univariate analysis.



Conclusions: Relapse after allo-HSCT remains frequent and is the strongest determinant of long-term survival. These findings emphasise the critical need for optimised relapse prevention strategies and early post-transplant approaches to improve outcomes in high-risk patients.

Disclosure: Nothing to declare.

Graft-versus-host Disease - Basic and Translational

OS04-06

PENTRAXIN 3 AS EARLY BIOMARKER TO PREDICT ACUTE GRAFT-VERSUS-HOST DISEASE AND TRANSPLANT-RELATED MORTALITY

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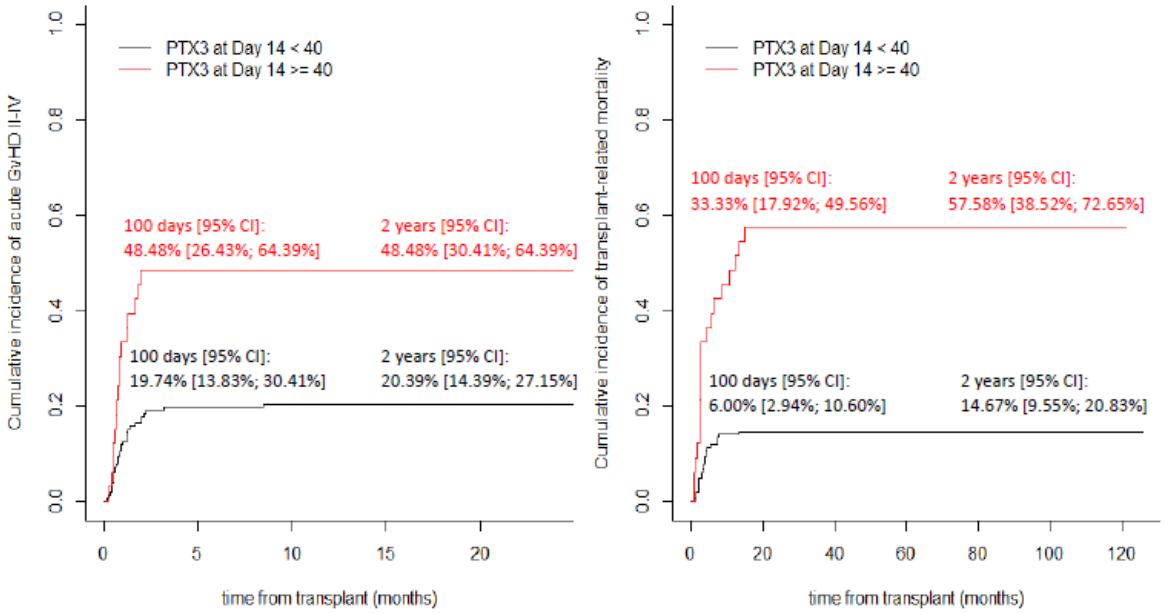
Background: In the context of allogeneic hematopoietic stem cell transplantation (allo-HSCT), different biomarkers have been studied for their potential in prediction of Graft-versus-Host Disease (GvHD) and transplant-related mortality (TRM). Pentraxin3 (PTX3) is an essential component of the humoral arm of innate immunity, involved in controlling infections and modulating inflammation.

Methods: We conducted a prospective multicenter observational study to ascertain the potential of plasma PTX3, measured before conditioning, at day of cell infusion, days +7 and +14 after allo-HSCT, in predicting the main transplant outcomes (OS, TRM, relapse-free survival, incidence of acute GvHD II-IV and moderate-severe chronic GvHD). Moreover, we evaluated PTX3 levels at acute GvHD diagnosis and day+7 follow-up, for their ability to predict aGvHD clinical course.

Results: We enrolled 207 consecutive adult allo-HSCT patients, mainly affected by acute leukemia (67%). Donors were haploidentical (n=62), sibling (n=68), unrelated (n=77). Peripheral blood was the graft source in 55% of cases. Through adjusted univariate regression analysis, evaluating the role of PTX3 levels at longitudinal timepoints in predicting the main transplant outcomes, we identified Day+14 after transplant as a relevant timepoint, in which higher PTX3 concentration predicted more frequent occurrence of acute GvHD II-IV (HR 1.64, 95% CI 1.17-2.3, Holm adj. p-value=0.0168) and higher TRM (HR 2.19, CI 1.62-2.95, p<0.0001). Coherently, Day+7 PTX3 levels showed a trend towards higher acute GvHD II-IV risk (HR 1.45, CI 1.07-1.98, p=0.0540) and higher TRM (HR 1.4, CI 1.05-1.88, p=0.0690). We then performed adjusted univariate regression analysis evaluating PTX3 levels in patients with acute GvHD (any grade) and outcome of GvHD. PTX3 values at GvHD diagnosis and day+7 follow-up could not predict peak acute GvHD severity (II-IV vs I), steroid refractoriness or subsequent development of moderate-severe chronic GvHD, however, we cannot exclude an effect of the limited sample size (samples were not available for all GvHD cases). Focusing on Day+14 post allo-HSCT timepoint, we identified a cut-off of plasma PTX3 rounded as 40 ng/ml, to predict the occurrence of acute GvHD II-IV in the first 100 days after transplant. Patients with PTX3 ≥40 ng/ml at Day+14 had a higher 100-day cumulative incidence of acute GvHD II-IV (48.48% [26.43%; 64.39%] vs 19.74% [13.83%; 30.41%]), higher 100-days TRM (33.33% [17.92%; 49.56%] vs 6.00% [2.94%; 10.60%]) and higher 2-years TRM (57.58% [38.52%; 72.65%] vs 14.67% [9.55%; 20.83%]).



Finally, we estimated multiple Fine-Gray regression models for predicting acute GvHD II-IV and TRM from Day 14 from transplant and the only variable retained in the final model after backward variable selection was PTX3 concentration. From these models, PTX3 concentration ≥40 ng/ml at Day+14 could predict a higher risk of acute GvHD II-IV occurring after Day+14 (HR 2.84, CI 1.44-5.63, p=0.0027) and a higher risk of TRM occurring after Day+14 (HR 5.12, CI 2.8-9.36, p<0.0001).

Conclusions: This prospective multicenter observational study confirms plasma PTX3 levels at Day+14 after allo-HSCT as a valuable biomarker in identifying patients at risk of acute GvHD and TRM, providing a window for additional prophylactic or preemptive strategies.

Disclosure: Funding as part of Ricerca Finalizzata *RF-LOM-2008-1164043*: "Diagnostic and prognostic significance of PTX3 levels in pediatric and adult patients with acute leukemia". No conflict of interest to declare.

OS11-01

TGF-B–ENRICHED ENTERAL NUTRITION MODULATES SYSTEMIC INFLAMMATION IN ACUTE GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE

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Background: Although acute gastrointestinal graft-versus-host disease (GI-aGVHD) is a severe immune-complication after allogeneic hematopoietic stem cell transplantation (allo-HCT) with substantial impact on non-relapse mortality, evidence supporting the use of enteral nutritional supplements remains sparse. Given the shared pathophysiological features between Crohn's disease and GI-aGVHD, we here investigate a TGF-β-enriched drinking supplement (Modulen IBD®) shown to be effective in Crohn's disease.

Methods: In a pilot clinical study assessing feasibility, patients scheduled for allo-HCT (n = 3 to 4) received 250 ml Modulen IBD® daily from the first day of conditioning therapy until withdrawal of consent; serum and stool samples were analyzed.
Mechanistic effects were explored using a well-established major histocompatibility complex-mismatched murine allo-HCT model (BALB/c → C57BL/6). Mice received either Modulen IBD® or vehicle orally from day 0 to 14 after transplantation before examination of stool and tissue samples.
Finally, we initiated a phase II clinical trial enrolling patients at onset of GI-aGVHD. Patients receive 250 ml of Modulen IBD® three times a day in addition to guideline-based steroid treatment. Serum and stool samples are collected at onset of GI-aGVHD, after 1 and 2 weeks and at discontinuation.

Results: In pilot study patients, targeted liquid chromatography-mass spectrometry (LC-MS) of serum samples revealed changes in the fatty acids (FA) signature after treatment with Modulen IBD® including increased levels of anti-inflammatory long-chain FA (LCFA) oleic, eicosatrienoic and linoleic acid as well as elevated kynurenic acid.
In the murine allo-HCT model, histological aGVHD scores were significantly reduced in the colon, small intestine and liver of Modulen IBD®-treated mice. Comparable to the human samples, serum LC-MS showed an increase in oleic and eicosatrienoic acid. Pro-inflammatory LCFA like palmitic, stearic and arachidonic acid decreased as well as amino acids like arginine, ornithine, leucine and aspartate, all the latter being linked to promote aGVHD. In colon tissue and stool butyrate levels were elevated, stool 16s rRNA gene sequencing showed an increased abundance of *Lactococcus* and *Bacillus*. Flowcytometry of colonic immune cells showed increased intracellular levels of TGF-β in $Ly6G^+$ neutrophils, of IL-10 in $CD4^+$ T-cells and increased $Ly6C^+$ monocytes in the colon epithelium, accompanied by reduced $CD3^+$ T-cell infiltration in the colon. Enhanced IL-10 abundance in $CD4^+$ T-cells was also observed in the serum.
Enrollment of patients in the phase II clinical study is still ongoing.

Conclusions: Modulen IBD® seems to induce an anti-inflammatory phenotype in the gut, likely driven by three complementary mechanisms:
1. Cytokine-mediated immunomodulation due to increased levels of anti-inflammatory cytokines such as IL-10 and with changes in colonic T-cell infiltration, hinting for reduced local alloreactivity.
2. Changes in the microbiome, including a shift towards butyrate-producing bacteria important for endogenous epithelial TGF-β production.
3. Alterations in metabolic profiles characterized by reduced pro-inflammatory and increased anti-inflammatory lipids and amino acids. The observed changes in kynurenic acid and butyrate levels suggest enhanced support for intestinal barrier integrity and local immune regulation.

Overall, TGF-β-enriched enteral supplementation seems to be a promising additional therapy in patients with GI-aGVHD. The ongoing phase II clinical study will provide further data.

Clinical Trial Registry: The phase II clinical study is registered as FRKS005255 at Freiburger Register für Klinische Studien. The ethics approval was granted on 10/23/2024 under number 24-1255-S1.

Disclosure: Lena Riegler: Nothing to declare. Sangya Chatterjee: Nothing to declare. Ina Martin: Nothing to declare. Tamina Rueckert: Nothing to declare. Marie Czech: Nothing to declare. Valentin Wenger: V.W. has received a honorarium from AbbVie. The honorarium was outside this work. Francesca Biavasco: Nothing to declare. Claudia Wehr: Nothing to declare. Joerg Buescher: Nothing to declare. Alina Hartmann: Nothing to declare. Annette Schmitt-Graeff: Nothing to declare. Wolfgang Melchinger: Nothing to declare. Natalie Köhler: Nothing to declare. Robert Zeiser: R.Z. has received honoraria from Novartis, Incyte, Sanofi, Neovii and Therakos. All honoraria and support were outside this work. Christine Greil: Nothing to declare.

OS11-02

ASCC1 DEFICIENCY IN DONOR T CELLS AGGRAVATES AGVHD THROUGH TRANSCRIPTIONAL DOWNREGULATION OF IL-10

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Background: Acute graft-versus-host disease (aGVHD) continues to hamper the efficacy of allogeneic hematopoietic cell transplantation (alloHCT). Independent of HLA disparity, our previous study has demonstrated the dominant contribution of non-HLA genetic features to aGVHD across different types of alloHCT. In this study, we identified for the first time a significant correlation between the loss-of-function variations in donor gene Activating Signal Cointegrator 1 Complex Subunit 1 (ASCC1) and an increased risk of aGVHD. However, the intrinsic function of ASCC1 in T-cell biology and the underlying molecular mechanisms remain unexplored.

Methods: ASCC1 was disrupted in human peripheral blood mononuclear cells (PBMCs) using CRISPR-Cas9 technology. T-cell differentiation and cytokine production were assessed following in vitro stimulation. Furthermore, we generated a T-cell-specific *Ascc1*-knockout (KO) C57BL/6 (H-2K^{b}) mouse model using the Cre-LoxP system. T cells from wild type (WT) or *Ascc1*-KO mice were transplanted into lethally irradiated CB6F1 (H-2K$^{b/d}$) recipients. Mechanistic insights were derived from transcriptome sequencing (RNA-seq) of both human and murine T cells, followed by functional rescue experiments using the recombinant target protein.

Results: Both human and murine ASCC1-deficient T cells exhibited significantly enhanced reactivity. This was characterized by skewed differentiation towards Th1 and Tc1 subsets, reduction in regulatory T cells (Tregs), elevated productions of proinflammatory cytokines

(IFN-γ and TNF-α), and increased cytotoxic potential (CD107a). In the alloHCT setting, mice receiving Ascc1-deficient T cells developed exacerbated GVHD, characterized by rapid weight loss, higher GVHD scores (representing worsening ruffled fur, posture, and diarrhea), and extensive tissue damage in the skin, small intestine, and liver. Recovered Ascc1-deficient T cells displayed an enhanced effector memory phenotype, accompanied by a significantly lower expression of exhaustion molecules (PD-1 and TIM-3). This observation suggests the persistent hyper-inflammatory state of Ascc1-deficient T cells recovered in recipient mice. Consequently, the survival of recipients transplanted with *Ascc1*-KO T cells was significantly reduced compared to the WT group. Transcriptomic profiling revealed a conserved mechanism: ASCC1 deficiency consistently downregulated the transcription of an anti-inflammatory cytokine, Interleukin-10 (IL10), in both human and murine T cells. This reduction was also confirmed at the protein level. Crucially, in vitro treatment with recombinant IL-10 effectively reversed the hyper-reactive phenotype of Ascc1-KO T cells, restoring normal differentiation patterns and dampening excessive proinflammatory cytokine production.

Conclusions: Our study implicates ASCC1 as a pivotal negative regulator of T-cell reactivity. The loss of ASCC1 reversed this anti-inflammatory capacity, at least partially through the transcriptional downregulation of IL10, leading to unleashed T-cell responses and severe aGVHD. These findings underscore the significance of the ASCC1-IL-10 axis as a novel non-HLA immunoregulatory pathway and propose new avenues for investigating the immunogenetic mechanism of T-cell alloreactivity. From a clinical perspective, our research suggests that genotyping donor ASCC1 may enhance risk stratification for aGVHD and targeting the IL-10 pathway could provide innovative therapeutic strategies to prevent aGVHD in high-risk patients.
This work was supported by the Major Program of the National Natural Science Foundation of China (No. 82293630) and National Natural Science Foundation of China (No. 82570266).

Disclosure: Nothing to declare

OS11-03

T CELL RESISTANCE TO GLUCOCORTICOIDS IN GRAFT-VERSUS-HOST DISEASE

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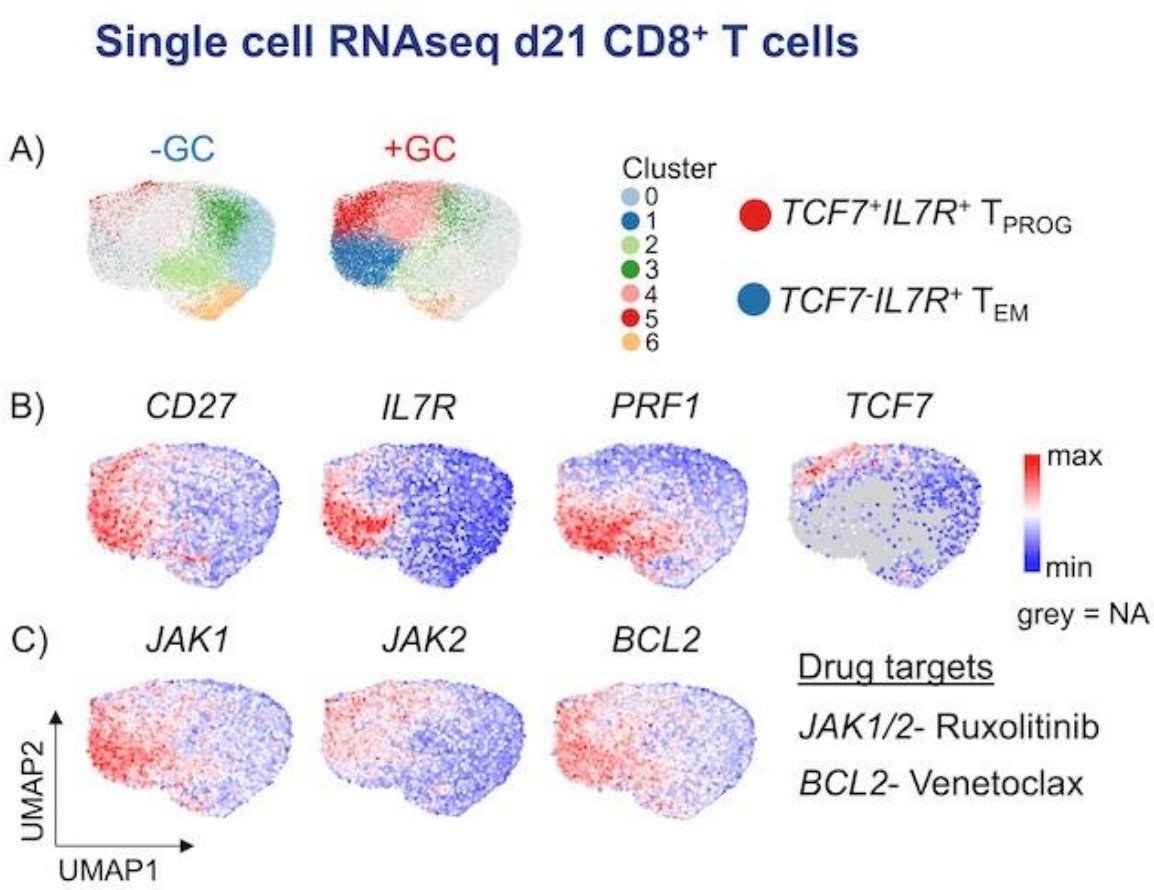
Background: Gut biopsies from patients with glucocorticoid (GC)-refractory graft-versus-host disease (GVHD) are frequently characterised by large clonal expansions of $CD8^+$ T cells[1]. Experimental models of GVHD have suggested that these T cell expansions are

sustained by progenitor-type T cells expressing the transcription factor TCF1, which possess inherent proliferative and self-renewal potential[2,3]. We hypothesised that a similar progenitor-type population can be found in humans and is resistant to GC treatment.

Methods: We drove the expansion and differentiation of human T cells by repeated stimulation with anti-CD3/CD28 beads over three weeks, comparing the addition of clinically relevant concentrations of methylprednisolone versus no GC controls. We determined output population architecture and function using a combination of multiparametric flow cytometry, bulk and single cell transcriptional profiling.

Results: GC-treated $CD8^+$ T cells showed increased proliferation and overall expansion than control cells, concomitant with greater retention of surface markers (e.g., IL-7RA, CD27, CXCR4) and a transcriptional profile (e.g., *KLF2, LTB, BCL2)* associated with a 'less-differentiated', memory-associated state. *In vitro* assays indicated intact cytokine-generating function and killing capacity of the GC-resistant $CD8^+$ T cells versus controls. These GC-driven changes to T cell proliferation and phenotype were largely restricted to $CD8^+$ T cells, occurring independently of $CD4^+$ T cells. scRNAseq revealed that the $CD8^+$ T cell population showed a distinct differentiation trajectory (Fig. A) composed primarily of two *IL7RA*-expressing clusters: a major effector memory-like cluster expressing cytotoxic genes (e.g., *PRF1*) and a smaller cluster composed of progenitor-like cells, expressing *TCF7* (encoding TCF1) and *LEF1* (Fig. B) To test the clinical relevance of these findings *in vivo*, we interrogated patient scRNAseq data derived from n=19 biopsies of acute lower gut GVHD[1], treated with (n=14) or without GC (n=5) at the time of biopsy. We identified strong enrichment for our $TCF7^{hi}$ progenitor-like cluster in patients with severe GVHD treated with GC (median 35.1% versus 9.5% of $CD8^+$ T cells, $p<0.05$).
The ruxolitinib targets JAK1/2 were enriched in our GC-induced $CD8^+$ T cell states (Fig. C). To address how JAK1/2 inhibition would influence the GC-resistant phenotype, we applied RUX at clinically relevant concentrations and showed that its addition blocked proliferation in GC-treated cultures to a greater extent than controls. However, RUX simultaneously further enriched for the TCF-1^{hi}IL-$7RA^{hi}$ progenitor-like population, which displayed elevated expression of the anti-apoptotic molecule, BCL-2. To target the progenitor population, we additionally applied clinically relevant concentrations of venetoclax (VEN). VEN treatment alone did not block proliferation but reduced the frequency of progenitor-like cells arising in the presence of GC. When combined, VEN and RUX blocked proliferation and reduced progenitor frequency in parallel to increased activated caspase-3 expression by CD8 T cells, particularly in the presence of GC.



Conclusions: These data suggest that treatments used for GVHD including GC and RUX may select for progenitor-like CD8+ T cells with the potential to sustain tissue injury and lead to refractory disease. Strategies combining drug targets which can inhibit T cell proliferation whilst preventing the retention of multipotent and proliferative progenitor populations may be required to overcome the limitations of current GVHD treatment approaches.

Disclosure: Nothing to declare

OS11-04

HOW DOES A SINGLE PRETRANSPLANT ORAL HIGH DOSE OF VITAMIN A PREVENT CHRONIC GRAFT VERSUS HOST DISEASE? TRANSCRIPTOMIC INSIGHTS INTO MECHANISM

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Background: Oral high dose vitamin A given once before allogeneic hematopoietic stem cell transplant (HSCT) reduced chronic graft versus host disease (cGVHD) in a randomized double blinded placebo-controlled trial in children (*Blood* 2024) but the mechanism of this effect was unclear. Vitamin A reduces NFκβ -mediated pro-inflammatory gene expression, e.g. TNFa and IL-6 in macrophages. We hypothesized that vitamin A induces a tolerogenic phenotype in host dendritic cells in the gut, which in turn reduces inflammatory phenotype of engrafted donor cells, thereby reducing cGVHD.
Objective: To examine differences in expression of pro-inflammatory and pro-fibrotic pathways in donor cells between recipients of vitamin A and placebo at day+100 post HSCT.

Methods: Peripheral blood mononuclear cells from eight children (four vitamin A, four placebo; Table 1) enrolled in the randomized trial were profiled by single-cell RNA sequencing. Vitamin A and placebo patients were matched 1:1 by age, HLA match, stem cell source, preparative regimen intensity and acute GVHD prophylaxis. All four placebo recipients developed cGVHD at a median of day+290 (range 170-392 days) post HSCT, whereas no vitamin A recipients developed cGVHD with >4 years' follow-up. Cells with >15% mitochondrial genes, doublets, and ambient RNA contamination were removed. Pseudobulk differential expression was performed using placebo as reference. Ingenuity Pathway Analysis (Qiagen) identified enriched canonical pathways and upstream regulators. Pathway and DEG significance was defined as FDR < 0.05.

Vitamin A Patient#	**Age at HSCT (years)**	**HLA Match**	**Stem cell source**	**Conditioning intensity**	**Acute GVHD prophylaxis**	**Chronic GVHD (yes/no)**
1	9.8	10/10	Bone marrow	Myeloablative	CSA/MMF/abatacept	No
2	12.5	10/10	Bone marrow	Myeloablative	CSA/MMF	No
3	20	10/10	Bone marrow	Reduced intensity	CSA/MMF/abatacept	No
4	7.5	10/10	Bone marrow	Myeloablative	CSA/MTX	No
Placebo patient #	**Age at HSCT(years)**	**HLA Match**	**Stem cell source**	**Conditioning intensity**	**Acute GVHD prophylaxis**	**Day post HSCT of chronic GVHD diagnosis**
1	9.6	10/10	Bone marrow	Myeloablative	CSA/MTX	392

2	13	9/10	Bone marrow	Myeloablative	CSA/MMF/abatacept	170
3	19.5	10/10	Bone marrow	Myeloablative	CSA/MMF/abatacept	212
4	8	10/10	Bone marrow	Myeloablative	CSA/MMF/abatacept	368

Table 1. Demographics

Results:

Figure 1A. CD16+Monocytes ingenuity pathway analyses

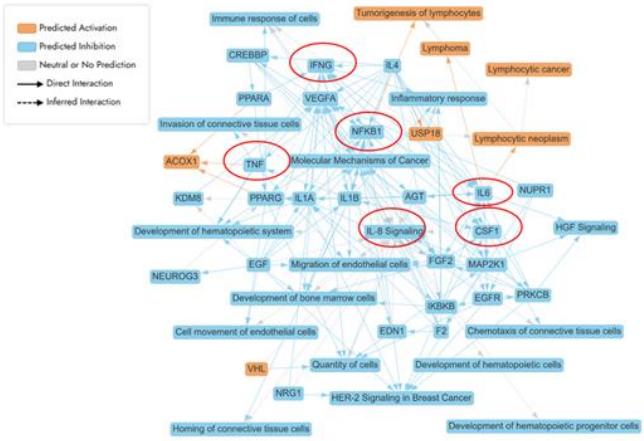


Figure 1B. Dendritic cells ingenuity pathway analyses

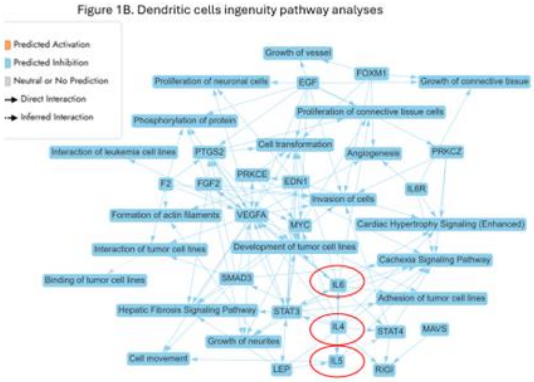


Figure 1C. Naïve B- cells ingenuity pathway analyses

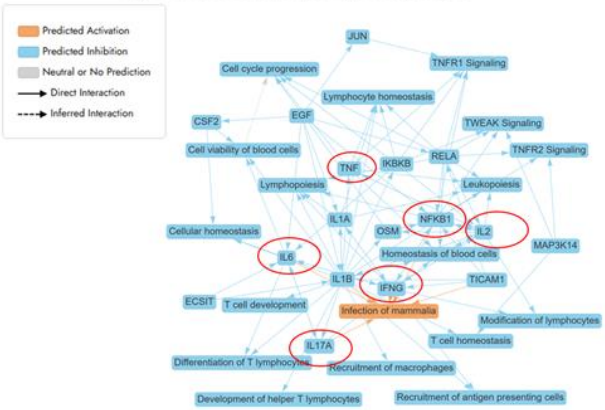


Figure 1D. CD4+T-cells ingenuity pathway analyses

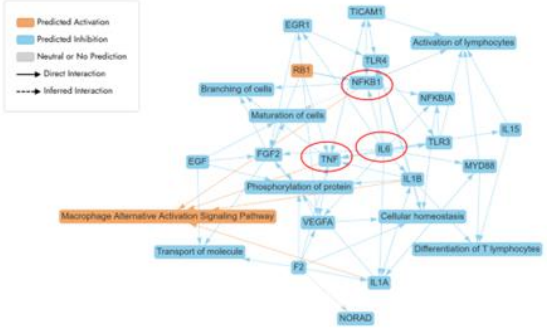
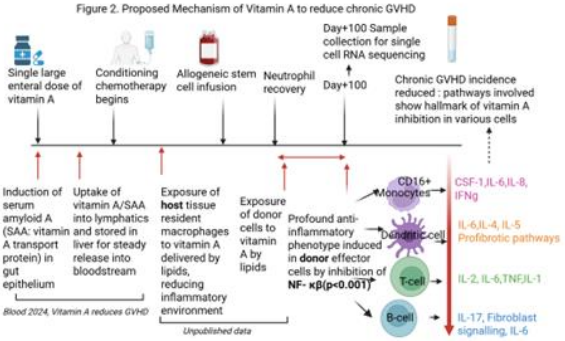


Figure 2. Proposed Mechanism of Vitamin A to reduce chronic GVHD



UMAP demonstrated similar numerical distribution of cells in vitamin A and placebo recipients. However, there were striking differences in functional cellular phenotypes, with suppression of pro-inflammatory pathways mediated by NFκβ in vitamin A recipients. Non-classical (CD16+) monocytes showed reduction in CSF1, IL-6, IL-8, NFκβ, IFN-γ in the vitamin A cohort compared to placebo (Figure 1A all blue shaded pathways, $p<0.001$). Classical (CD14+) monocytes showed significant downregulation of IL17A, TNF, IL-6 in the vitamin A cohort($P<0.001$). Dendritic cells also demonstrated downregulation of proinflammatory signaling genes including IL-6, IL-4, IL-5 and profibrotic pathways (Figure 1B $p < 0.001$). Notable downregulation in naïve B cells showed downregulation in IL-17A, IL-2, IL-6 TNFR1, IL-1β, IFNγ, reduction in fibroblast signaling and inhibition of macrophage

activation pathways (Figure 1C $p < 0.001$), while CD4 T- cells in the vitamin A cohort involved downregulation of IL-6 and TNF (Figure 1D $p < 0.001$). Collectively, profound anti-inflammatory activity and reduction of profibrotic pathways and macrophage activation was observed in the vitamin A cohort compared to placebo (Figure 2).

Conclusions: Vitamin A given as a single large enteral dose before HSCT induces significant downregulation of proinflammatory and profibrotic signaling pathways in donor monocytes, T-cells, B cells and dendritic cells more than three months later, likely contributing to lower incidence of cGVHD.

Clinical Trial Registry: NA

Disclosure: Nothing to declare

OS11-05

MICROBIOTA-DERIVED PROPIONATE INDUCES DELETIONAL TOLERANCE AND DECREASES GRAFT-VERSUS-HOST DISEASE

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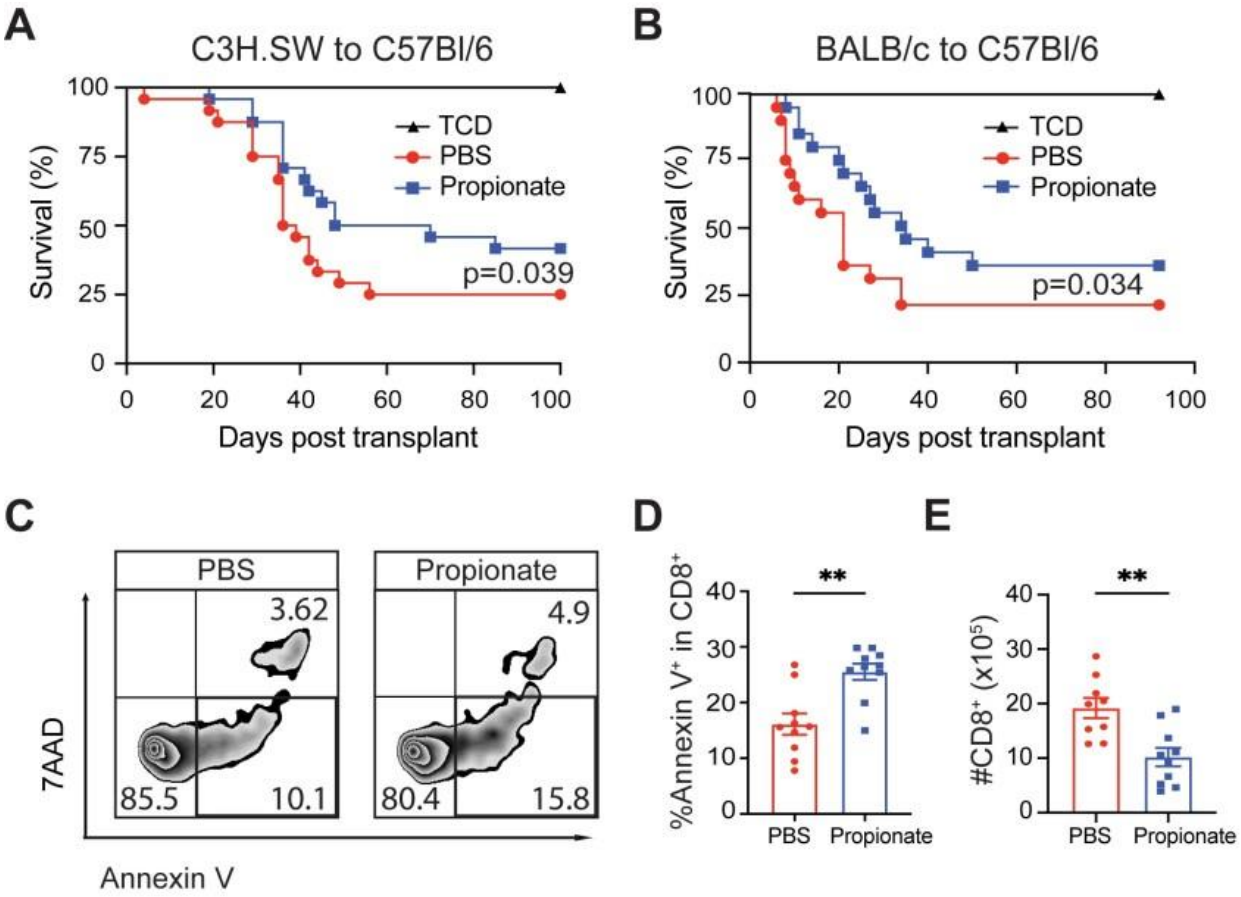
Background: Functionally diverse, anaerobe-rich microbial communities have consistently been associated with improvements in clinical outcomes in patients receiving allogeneic hematopoietic stem cell transplantation (HCT). We have used mouse models of HCT to investigate the capacity of propionate – a microbe-derived short-chain fatty acid – to modify immunopathology.
We previously demonstrated that pre-HCT Flt3-L promoted deletional tolerance via expanding $CD8^+$ DC, which in turn, drive activation-induced cell death of donor $CD8^+$ T cells. Here, we demonstrate that microbe-derived propionate can act upstream of this process, and our results contribute important insight into the mechanism by which propionate regulates alloimmunity.

Methods: We used a $CD8^+$ T cell-dependent model (C3H.SW→ C57Bl/6) and a $CD4^+$ T cell-dependent model (BALB/c→C57Bl/6) of HCT, and administered oral propionate (15mM/kg/dose) from d-4 to d+9, or PBS control. For quantifying leukemia relapse, we used GFP^+ MLL-AF9 primary mouse leukemia. *B. thetaiotaomicron* was administered by oral gavage of log-phase live bacteria at $\sim 10^8$ CFU/dose. We performed 16s rRNA amplicon-based sequencing on fecal pellets to assess the intestinal microbiome. Statistical analyses were performed using GraphPad Prism or R (for competing risk analyses in leukemia experiments).

Results: In steady-state C57Bl/6 mice, exogenous propionate administration increased cecal but not systemic Flt3L concentration (p=0.0013; propionate vs. PBS control in cecal contents; n = 10/grp). In both the C3H.SW→C57Bl/6 and BALB/c→C57Bl/6 models, we observed improved GVHD survival with propionate treatment compared with PBS-treated control mice (n=20-24/group from 3 independent replicate experiments (Fig.A-B). We hypothesized that this was due to the deletion of incoming donor CD8+ T cells, and when we labeled donor T cells with the Cell Trace Violet (CTV) dye to track early proliferation, we found that propionate reduced $CD8^+$ T cell proliferation (%CTV^{low}) (n=10/grp, p=0.035). In parallel, we observed an increase in $CD8^+$ T cell apoptosis using Annexin V staining on d+3 after HCT, and a decrease in the absolute number of donor $CD8^+$ T cells (Fig.C-E). Furthermore, in propionate-treated mice, we observed improved gut integrity at day 3 post-HCT, as measured by FITC-dextran (n=10/group, p=0.0057), and supported by qPCR assays of specific genes associated with gut integrity (p=0.0325 for *HNF4a*; p=0.02 for *ZO-1*). The intestinal microbiome was also reshaped by propionate administration. We observed an enrichment of SCFA-producing taxa, including *Clostridium*, *Prevotella*, and *Robinsoniella*, suggesting a protective feed-forward loop. To establish a 'living' therapy to provide long-term propionate *in vivo*, we administered the propionate-producing bacteria *B. thetaiotaomicron* from d-7 to d+7 in the C3H.SW→ C57Bl/6 model and this phenocopied the administration of propionate alone (n=24/grp, p=0.05). Furthermore, we demonstrated that our tolerance induction strategy did not impair GVL, by performing in vivo relapse experiments in the C3H.SW→ C57Bl/6 model with GFP^+ MLL-AF9 primary mouse leukemia cells (p=0.09 for relapse rate using competing-risk analysis).



Conclusions: Our studies highlight multiple preciously unappreciated pathways by which microbe-derived SFCAs promote tolerance. This highlights that microbe-targeted interventions that enhance propionate availability during the early peri-transplant period may facilitate favorable long-term outcomes with decreases in alloreactivity, improved intestinal tract integrity and maintenance of protective intestinal microbial communities.

Disclosure: Nothing to declare.

OS11-06

TISSUE-RESIDENT MEMORY T CELLS PREDICT STEROID-REFRACTORY COURSE IN ACUTE GASTROINTESTINAL GRAFT-VERSUS-HOST DISEASE

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Peter Neumeister[1], Thomas Kroneis[1], Alexander Deutsch[1], Georg Stary[2,3], Hildegard Greinix[1,2]
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Background: Acute graft-versus-host disease of the lower gastrointestinal tract (GI-GvHD) remains a major cause of non-relapse mortality following allogeneic hematopoietic cell transplantation (allo-HCT). While high-dose corticosteroids are the standard first-line therapy, up to 70% of patients with grade III–IV GI-GvHD develop steroid-refractory disease (SR-GvHD), which is associated with poor survival. Previous studies have suggested a role for tissue-resident lymphocyte populations in GvHD pathogenesis, but data on their prognostic relevance in GI-GvHD are limited. We aimed to determine whether selected intestinal immune cell subsets at the time of GI-GvHD diagnosis are associated with subsequent response to corticosteroid therapy.

Methods: We retrospectively analysed intestinal biopsies from 50 patients who developed acute GI-GvHD following allo-HCT at the Medical University of Graz between 01/2015 and 06/2021. Biopsies were taken at first clinical diagnosis of acute GvHD. Patients were categorized into steroid-sensitive (SS, n=26) and steroid-refractory (SR, n=24) groups based on clinical response. Multicolour immunofluorescence and image analysis were used to quantify different T cell subsets, like Th17 and tissue-resident memory T cells (TRMs), mast cells, and group 3 innate lymphoid cells (ILC3s). Logistic regression analyses adjusted for clinical covariates and Mann-Whitney-U-Test were performed to identify independent predictors of steroid-refractory disease. A control group of 13 patients with normal-appearing intestinal mucosa (from adenoma resections) was included.

Results: SR-GvHD patients showed significantly higher TRM content compared to SS patients (median 34.3% vs. 23.6% of all T cells, p=0.009). Within the TRMs compartment, SR-GvHD was characterized by a shift toward $CD4^+$ TRMs and a decrease in $CD8^+$ TRMs. Increased TRMs proportions were also associated with higher GI-GvHD organ severity (stage 3–4 vs. stage 1–2: 33.4% vs. 22.9%, p=0.005). In adjusted logistic regression, a higher proportion of TRMs independently predicted SR-GvHD (adjusted OR 1.07, 95% CI 1.01–1.16, p=0.044). In contrast, no significant differences in other T cell subsets ($CD4^+$, $CD8^+$, Th17) were observed between response groups. Mast cells were significantly reduced in SR-GvHD (0.68% vs. 1.85%, p=0.002), while ILC3 levels were higher in GvHD patients compared to controls but not associated with steroid response. Sensitivity analyses excluding patients pre-treated with corticosteroids (n=15) confirmed the robustness of these findings.

Conclusions: Intestinal TRMs, particularly $CD4^+$ TRMs, are associated with poor response to steroid therapy in acute GI-GvHD and may serve as tissue-level biomarkers for early risk stratification. These results highlight the importance of the local immune contexture of the gut and support further investigation into TRM-targeted strategies for steroid-refractory GvHD.

Disclosure: Nothing to declare.

OS11-07

IDENTIFICATION OF A PLASMA IMMUNE MARKER PANEL FOR EARLY DETECTION OF ACUTE GRAFT-VERSUS-HOST DISEASE IN CHILDREN

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[1]*University Medical Center Utrecht, Utrecht, Netherlands (the),* [2]*Princess Máxima Center for Pediatric Oncology, Utrecht, Netherlands (the)*

Background: Acute Graft-versus-Host-Disease (aGvHD) is a common complication following allogeneic hematological cell transplantation (HCT), significantly contributing to treatment-related-morbidity and -mortality. To optimize clinical outcome, there is an urgent need for individualized aGvHD treatment approaches. These may include earlier initiation of therapy or tailored dosing regimens that balance the control of symptoms with the minimization of treatment-related toxicity. Therefore, reliable predictive markers are essential to support the personalized adjustment of aGvHD management protocols. With current validation of prognostic markers for severity and survival after aGvHD, clinically validated predictive markers for aGvHD in pediatric HCT recipients are lacking.

Methods: In this study, we performed a multiplex-based search for plasma immune markers associated with aGvHD in children and young adults, using least absolute shrinkage and selection operator (LASSO) logistic regression applied to plasma proteomics data from a two-stage retrospective cohort of pediatric HCT-recipients. The primary objective was to identify predictive plasma immune biomarkers of aGvHD grade II-IV in the pediatric HCT setting. All consecutive patients receiving their first HCT between Jan-2016 and Nov-2023 at the Wilhemina Children's Hospital and Princess Máxima Center, in Utrecht, were included. Biobanked EDTA-plasma samples were collected one week prior to aGvHD diagnosis, or at a matched timepoint for non-aGvHD patients.

Results: A total of 223 children and young adults (mean age 9 Years, range 0-20 Years) were included and randomly divided into a training (n=165) and test cohort (n=58). Overall, 20.1% of patients developed aGvHD grade I and 29.6% grade II-IV. LASSO regression applied to the training cohort data identified plasma immune markers that were subsequently validated and quantified in absolute concentrations in the test cohort. The final selected immune marker panel consisted of CCL17 and galectin-1, combined with either CXCL10 and IL6, or with Reg3a. The calculated area under the curve (AUC) of the receiver operator characteristic (ROC) curve was 0.9 for the panel combining CCL17, galectin-1, CXCL10, and IL6, with 75% sensitivity, 86% specificity, 75% positive predictive value (PPV), and 86% negative predictive value (NPV). The panel combining CCL17, galectin-1, and Reg3a performed even better ($p < 0.001$) with an AUC of 0.95, 92% sensitivity, 86% specificity, 79% PPV, and 95% NPV.

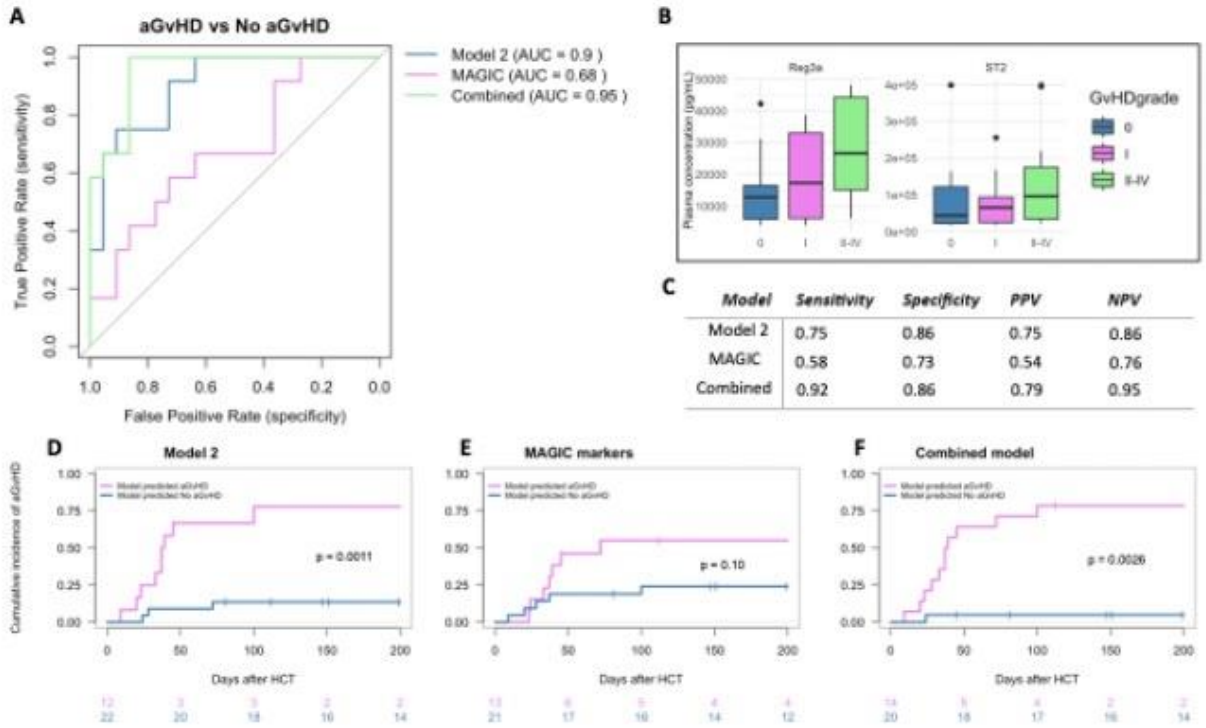

Figure 1: Comparison of plasma immune marker panel and MAGIC marker score to predict aGvHD grade II-IV. A) ROC-curves for multivariable logistic regression models differentiating aGvHD and no aGvHD patients based on absolute marker concentrations in the test cohort. ROC-curves for Model 2, comprising CCL17, galectin-1, CXCL10, and IL6 (AUC = 0.9), calculated MAGIC markers MAP Score based on Reg3a and ST2 (AUC = 0.68), and a combination of markers, existing of CCL17, galectin-1, and Reg3a (AUC = 0.95). ROC-curves are plotted for grade II-IV patients. B) Boxplots showing plasma concentrations of the identified plasma immune markers and the MAGIC markers Reg3a and ST2 for controls, grade I, and grade II-IV patients. C) Table showing sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the multivariable models. D) Cumulative incidence for aGvHD stratified in high and low risk (threshold = 0.4) by Model 2 in the test cohort, plotted for grade II-IV patients. E) Cumulative incidence for aGvHD stratified in high and low risk (threshold = 0.4) by the MAGIC markers in the test cohort, plotted for grade II-IV patients. F) Cumulative incidence for aGvHD stratified in high and low risk (threshold = 0.4) by the combined marker panel (CCL17, galectin-1, and Reg3a) in the test cohort, plotted for grade II-IV patients.

Conclusions: Pending prospective validation, our two-stage retrospective study design identified the first immune marker panel that can potentially predict aGvHD, approximately one week prior to onset of symptoms, in pediatric HCT-recipients. When measured (bi-)weekly after graft infusion, the identified plasma immune marker panel can potentially predict if pediatric HCT-recipients will develop aGvHD grade II-IV within approximately one week after measurement. The potential prediction of aGvHD by the identified immune marker panel enables the development of an individualized approach for preemptive treatment.

Disclosure: Nothing to declare.

OS11-08

RESTRICTION OF SLC7A5-MEDIATED L-LEU UPTAKE IN ALLOGENIC T CELLS EFFICIENTLY PREVENTS ACUTE GRAFT-VERSUS-HOST DISEASE AND MAINTAINS GRAFT-VERSUS-TUMOUR RESPONSE

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Background: The amino acid transporter SLC7A5, which mediates the uptake of L-Leu and other essential amino acids in activated T cells and in malignant cells, has become an important target in controlling inflammation and cancer. However, its role in acute graft-versus-host disease (aGVHD) and graft versus tumour (GVT) has not been explored before.

Methods: We first determined whether SLC7A5 deletion in T cells affects mortality in a fully MHC-mismatched model of aGVHD. For this purpose, B6.SJL mice or C57BL/6 β-actin-eGFP were used as bone marrow (BM) cell donors, while Tmt+SLC7A5^{WT}, Tmt+SLC7A5$^{\Delta CD4}$ or CD45.1+SLC7A5^{WT} mice were used as splenic T cells (STC) donors, and BALB/cJRj were transplant recipients. L-Leu-deprived and isocaloric regular diet were obtained from Research Diets, Inc. After 2–3 weeks on formulated diets, all BALB/c mice were irradiated and injected with allogeneic CD45.1+ TCDBM cells and allogeneic Tmt+ SLC7A5WT STC cells. For the GVT model, KLN205 cells were subcutaneously (sc.) inoculated into the left flank of BALB/cJRj recipient mice, the following day of allogenic transplantation. BALB/c irradiated and transplanted with complete BM from BALB/c donors fed with regular or (-)Leu diet were used as controls. Tumour sizes were measured with an electronic calliper every 2–5 days by a specialised researcher blinded to experimental groups.

Results: In this study, we demonstrate that SLC7A5 genetic deletion affected the activation and proliferation of allogenic T cells, promoted apoptosis and reduced IFNγ and granzyme B secretion by CD4 and CD8 T cells. Genetic deletion of SLC7A5 completely prevented aGVHD-induced lethality in mice but did not control tumour growth. On the other hand, the administration of an L-Leu-free diet efficiently reduced aGVHD mortality in mice by controlling allogenic T cell expansion, inducing apoptosis, and affecting granzyme B secretion. However, CD8 T cells do not fail to activate or secrete IFNγ in the absence of Leu and show an increased proportion of central memory T cells, which contribute to the GVT

response.Genetic deletion of SLC7A5 in T cells severely compromises mTORC1, glycolysis and mitochondrial oxidation. However, removing L-Leu mildly reduces mTORC1 signaling, completely blocks glycolysis but improves mitochondrial function, favoring the generation of central memory responses and expression of stemness marker TCF1. Dietary L-Leu restriction controls the increase of metabolites derived from tricarboxylic acid cycle and ketogenesis induced by aGVHD, with potential proinflammatory effects. Hence, dietary restriction of L-Leu is sufficient to target SLC7A5 in allogenic cells during aGVHD, preserving GVT response.

Conclusions: This study addresses a critical knowledge gap by defining the role of the amino acid transporter SLC7A5 in aGVHD and GVT responses. By integrating genetic and dietary approaches, including a leucine-restricted diet, this work demonstrates how modulation of leucine availability and SLC7A5-dependent transport influences T-cell activation, expansion, and effector function during aGVHD. The study also identified β-hydroxybutyrate as a key metabolic marker for SLC7A5-dependent T cell expansion in aGVHD. Notably, the study provides insight into whether dietary and metabolic interventions can attenuate pathogenic alloreactivity while preserving GVT activity, highlighting a novel, non-pharmacologic strategy to improve outcomes after allogeneic hematopoietic stem cell transplantation.

Disclosure: Nothing to declare.

A360

ATG EXPOSURE AND IMMUNE RECONSTITUTION IN CHILDREN WITH HEMOGLOBINOPATHIES FOLLOWING HSCT: DIFFERENT PATTERNS FOR ATG-GRAFALON AND THYMOGLOBULINE

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Background: Anti-thymocyte globulin (ATG) is central to graft-rejection and GvHD prophylaxis in pediatric allogeneic HSCT. ATG exposure, not nominal dose, determines immunosuppression, viral susceptibility and immune reconstitution (IR). Rabbit ATG preparations differ markedly in antibody spectrum and pharmacokinetics (PK), resulting in non-interchangeable exposure–response profiles.

Methods: Eighty-six pediatric patients (90 HSCTs; 4 re-transplantations; median age 11.13 years) underwent transplantation for hemoglobinopathies (2011–2025) using treosulfan/fludarabine/thiotepa conditioning. Serotherapy consisted of ATLG (Grafalon®) (n=57), ATG-T (Thymoglobuline®) (n=35). ATG levels were measured daily from day −7 to +7 and twice weekly until week 4. AUC_{total}, AUC_{pre} and AUC_{post} HSCT were calculated. Reconstitution of CD4+, CD8+, CD19+ and CD16/56+ cells was assessed to day +180. Endpoints included engraftment, GvHD, viral reactivation, donor chimerism and overall and disease-free survival (OS/DFS).

Results: OS and DFS were excellent (97.67% and 94.17%). Graft rejection and autologous recovery occurred in 2.33% and 3.49%. The incidence of aGvHD II–IV was comparable between ATLG and ATG-T (16.7% vs. 14.3%), and cGvHD II–IV was low (7.41 and 5.71%). ATG-T exposure correlated more strongly with body weight than ATLG exposure (ATG-T r=0.7333, p=0.0311; ATLG r=0.3191, p=0.0448), indicating that weight-based dosing disproportionately affects ATG pharmacokinetics. CD4+ IR at day +100 showed the strongest exposure–response relationship: higher AUC_{post} was consistently associated with delayed CD4+ recovery (r=-0.44, p=0.0052). Stratification by AUC_{post} (<100; 100–200; >200 µg*day/mL) demonstrated a graded exposure–response effect (p=0.0014), highlighting delayed CD4+ reconstitution as a sensitive indicator of ATG overexposure.
Viral reactivations for CMV, HSV, VZV, ADV, HHV-6, BK and JC occurred at similar frequencies across serotherapy preparations. EBV reactivation, however, was substantially more common after ATG-T than ATLG (56.5% vs 20.4%). NK-cell recovery also differed by product: ATG-T was associated with higher early NK counts (day +30: 192/µL vs 143/µL), whereas ATLG showed higher late NK-cell recovery (day +180: 160/µL vs 130/µL). Overall, ATG-T displayed faster clearance and earlier recovery across additional subsets.
Complete donor chimerism (≥99%) occurred in 41/54 ATLG vs 22/35 ATG-T recipients; mixed chimerism was more frequent after ATG-T (24.1% vs 37.1%; OR 1.86; RR 1.54; p=0.18). In the ATLG cohort, 46.3% also received post-transplant cyclophosphamide (ptCy), which was associated with reduced severe cGvHD without evidence of impaired IR. Low-grade cGvHD occurred more often in the ATLG group.

Conclusions: ATG exposure is a key determinant of IR in pediatric hemoglobinopathy HSCT. ATLG and ATG-T display distinct PK/PD profiles, underscoring the need for individualized, product-specific exposure–response assessment. Weight-based dosing results in substantial variability, particularly in older children. Our data provide the opportunity for adapting ATG dosing to the individual risk profile for mixed chimerism vs. GvHD.

Disclosure: Neovii has financially supported research related to this work.

A361

SKIN TAPE STRIPPING ENABLES NON-INVASIVE MONITORING OF INFLAMMATORY CYTOKINES IN ACUTE SKIN GVHD

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[1]*Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark,* [2]*University of Copenhagen, Copenhagen, Denmark,* [3]*Bispebjerg Hospital, University of Copenhagen, Copenhagen, Denmark*

Background: Acute GvHD remains a major contributor to transplant-related morbidity and mortality after allogeneic HSCT. Over the past decade, several blood-based biomarkers have been identified for predicting and monitoring aGvHD severity. However, these markers provide limited insights into early, localized immune processes in the skin, which is the organ

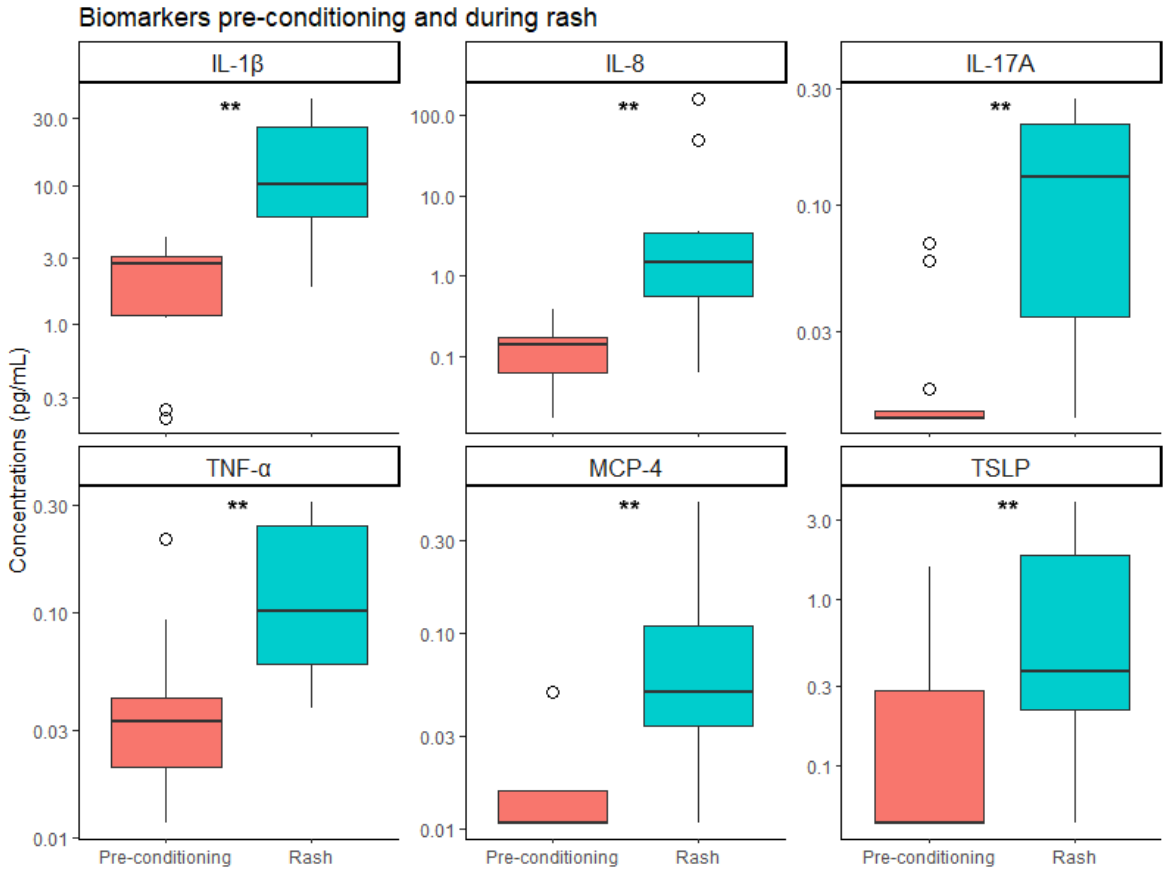
most frequently affected by aGvHD. Thus, there is a need for minimally invasive approaches that enable longitudinal assessment of local immune reactions in the skin following allogenic HSCT.
In this prospective study, we evaluated the feasibility of monitoring biomarkers in skin using skin tape stripping in patients with acute skin GvHD.

Methods: We included 16 patients (five children and 11 adults) undergoing HSCT between 2024-2025 in Denmark. Patient and transplant characteristics are specified in Table 1.
Skin tape stripping using D-squame technology (Clinical & Derm, Dallas, TX) was performed prior to conditioning (n =12) and at the time of diagnosis/suspicion of skin aGvHD (n=16). Thereafter, patients were followed with additional skin tape sampling either at changes in aGvHD staging or skin morphology, or weekly if the skin condition remained stable (n=25). Overall sampling was performed as previously described by Thyssen et. al (JACI, 2023). Following storage at -80°C, skin tape strips were eluted in a phosphate-buffered saline supplemented with Tween20® and analytes were measured using the Meso Scale S-plex and V-plex platforms, for eotaxin-1, IFN-γ, IL-1α, IL-1β, IL-1RA, IL-4, IL-6, IL-7, IL-8, IL-10, IL-12, IL-17A, IL-17C, TNF-α, TNF-β, MCP-1, MCP-4, MIP-1α, MIP-1β, TNF-α, TNF-β, and TSLP.

Table 1: Patient and transplant characteristics	
Sex, no. (%)	
Male	11 (69)
Age at transplantation (years), median (range)	
Recipients	46.5 (8.1-67.6)
Disease at transplantation, no. (%)	
Malignant	15 (94)
Benign	1 (6)
Donor type, no. (%)	
Matched sibling donor	3 (19)
Matched unrelated donor (10/10)	9 (56)
Matched unrelated donor (9/10)	3 (19)
Haploidentical donor	1 (6)
Stem cell source, no. (%)	
Bone marrow	6 (38)
Peripheral blood	10 (62)

Conditioning regimen, no. (%)	
TBI (12 GY) + CY/VP16	6 (38)
Treo + Flu (RIC)	8 (50)
Other conditioning regimens	2 (12)

Results: IL-1α, IL-1RA, IL-1β, IL-4, IL-6, IL-8, IL-10, IL-17A, IL-17C, TNF-α, TNF-β, MCP-1, MCP-4, and TSLP were measurable in skin samples both before and after HSCT, while eotaxin-1, IFN-γ, IL-7, IL-12, MIP-1α, and MIP-1β generally were below the limit of detection.
Affected skin from patients presenting with an erythematous rash exhibited higher concentrations of IL-1β, IL-8, IL-17A, TNF-α, MCP-4, and TSLP compared with healthy skin sampled prior to conditioning (IL-1β: 2.7 vs. 8.4 pg/mL, p=0.005; IL-8: 0.1 vs. 0.8 pg/mL, p=0.02; IL-17A: 0.01 vs. 0.1 pg/mL, p=0.004; TNF-α: 0.03 vs. 0.08 pg/mL, p=0.007; MCP-4: 0.01 vs. 0.05 pg/mL, p=0.01; and TSLP: 0.05 vs. 0.33 pg/mL, p=0.06).
Combined longitudinal measurements of affected skin during rash (including active erythema and beginning brownish resolution), revealed median levels of IL-1β, IL-8, IL-17A, TNF-α, MCP-4, and TSLP to be significantly higher compared with pre-conditioning levels (Figure).



Conclusions: In conclusion, this study demonstrates the feasibility of non-invasive monitoring of skin inflammatory biomarkers in patients with aGvHD. Elevated levels of both pro-inflammatory and immunoregulatory cytokines reflect the presence of a rash post-HSCT. These findings support the potential of skin tape stripping as a clinical tool for *in vivo* monitoring of aGvHD activity.

Disclosure: Nothing to declare.

A363

THERAPEUTIC TARGETING OF CCR7 IMPROVES OUTCOMES IN A PRECLINICAL MODEL OF ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: Graft-versus-host disease (GvHD) is a major cause of morbidity and mortality after allogeneic haematopoietic cell transplantation (allo-HCT) and strategies for its prophylaxis are not free from serious adverse effects. Understanding the pathogenesis of GvHD is a cornerstone for developing novel therapeutic approaches to HCT. GvHD is triggered in the secondary lymphoid organs (SLOs) when donor-derived alloreactive T cells recognize host antigens presented by either patient- or donor-derived dendritic cells (DCs). To do this, both T lymphocytes and mature DCs reach the SLOs through a migratory process largely mediated by the chemokine receptor CCR7, making CCR7 an attractive therapeutic target for this complication.
In a previous preclinical GvHD model following xenotransplantation of human lymphocytes into mice, we showed that an anti-human CCR7 antibody delays or even prevents GvHD, increasing the survival of treated mice (Cuesta-Mateos *et al*., Bone Marrow Transplant. 2020). However, this model excluded any contribution of recipient DCs to the disease, since human lymphocytes do not effectively recognize mouse MHC molecules. We therefore aimed to confirm the pathogenetic and therapeutic role of CCR7 in an allogeneic murine model.

Methods: The approach consisted of a murine MHC-disparate GvHD model in sublethally irradiated C57BL/6 mice receiving either bone marrow alone (BM control group) or bone marrow plus BALB/c splenocytes (GvHD groups). Recipients in the GvHD groups were treated with PBS (PBS group) or 200 µg of anti-CCR7 4B12 (therapeutic anti-CCR7 group) every 3 days for 12 days, starting treatment on day 1 post-transplant, and then on a weekly basis until day 65. Survival and score of disease severity were assessed weekly until day 180.

Results: Survival analysis demonstrated marked differences among the study groups. Mice treated with the anti-CCR7 antibody maintained a survival rate of 75% throughout the entire observation period (180 days). In contrast, the PBS group exhibited a 50% reduction in survival within the first 60 days, stabilizing at approximately 25% from day 100 onwards,

while BM group showed a sharp decline during the first 20 days and maintained a survival rate of 40% from day 30 onwards (Figure 1A). Clinical score assessment, measured according to criteria detailed in *Table 1*, revealed that mice treated solely with the vehicle (PBS group) exhibited severe clinical signs throughout the first two months and remained clinically affected thereafter (Figure 1B). Remarkably, the anti-CCR7-treated group maintained values near zero throughout the follow-up, indicating the absence of clinically relevant signs in mice receiving anti-CCR7 therapy.

CRITERIA	SCORE 0	SCORE 1	SCORE 2
FUR TEXTURE	Normal	Mild-to-moderate ruffling	Severe ruffling/poor grooming
WEIGHT LOSS	≤10%	>10%	
POSTURE	Normal	Hunching noted only at rest	Severe hunching impairs movement
SKIN INTEGRITY	Normal	Scaling of paws	Obvious areas of denuded skins
DIARRHEA	No	Mild-to-moderate diarrhea	Severe diarrhea
FUR LOSS AROUND EYES	No	Light fur loss	Obvious fur loss
EARS INTEGRITY	Normal	Loss of integrity in only one ear	Loss of integrity in both ears
TAIL INJURIES	No	Scaling of tail	Visible injuries

Table 1. Assessment of clinical score of graft-versus-host disease in transplanted animals.

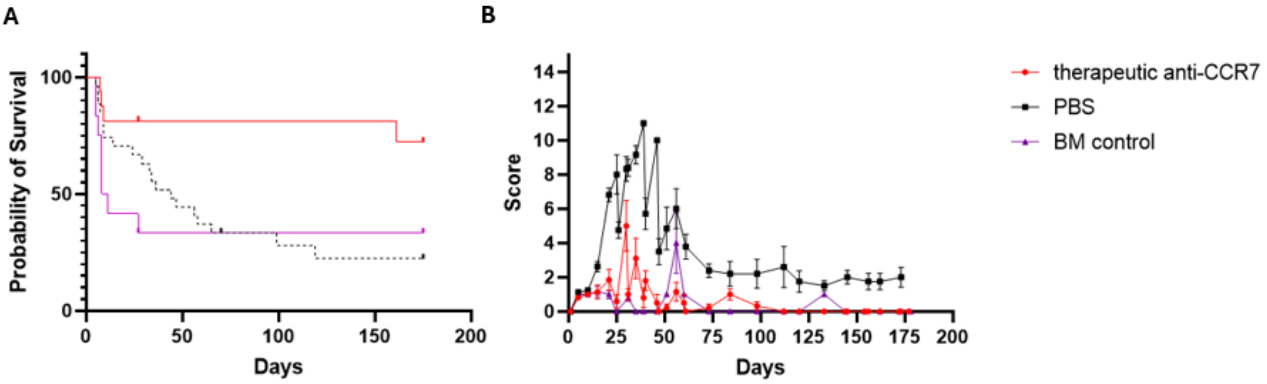

Figure 1. Probability of survival and clinical evaluation of graft-versus-host disease (GvHD) in a transplanted animal model. A. Probability of survival after GvHD model is established. Survival probability was plotted against days post-transplantation. The key statistical differences were therapeutic anti-CCR7 vs. PBS (p=0.0092) and therapeutic anti-CCR7 vs. BM (p=0.0130). Group comparisons were analyzed with log-rank test. The marks on the curve indicate censored subjects. **B.** Assessment of clinical score of GvHD. The severity of the disease was quantified weekly for 180 days using a clinical score detailed in Table 1, and is presented as the mean ± SEM. The key statistical differences were therapeutic anti-CCR7 vs. PBS (p<0.0001) and PBS vs. BM (p<0.0001). Group comparisons were analyzed with one-way ANOVA, followed by Sídák's multiple comparisons test. The number of mice per group was: PBS (black, n=21), BM (purple, n=13) and anti-CCR7 (red, n=17) carried out in three independent experiments.

Conclusions: In a murine model of GvHD, anti-CCR7 treatment markedly improves survival and mitigates clinical severity compared with PBS and BM controls, emphasizing its potential translational value as a promising addition to the therapeutic options for human GvHD. Future studies will investigate the mechanistic roles of donor CCR7⁺ T cells and donor versus recipient DCs in mediating this therapeutic effect.

Disclosure: Nothing to declare

A364

PRE-TRANSPLANT T/NK-LIKE DERIVED EXTRACELLULAR VESICLES ASSOCIATE WITH GVHD AND DISTINCT IMMUNE RECONSTITUTION PATTERNS, INFLUENCED BY GUT MICROBIOME AND CHEMOTHERAPY EXPOSURE IN PEDIATRIC STEM CELL TRANSPLANTATION

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Background: Extracellular vesicles (EVs) released by immune and tissue-derived cells may carry early predictive information on allogeneic stem cell transplant (allo-SCT) complications. Their biological role in shaping post-transplant immune reconstitution and gut microbiota recovery remains unclear, especially in pediatric recipients. We prospectively evaluated the

dynamic profile of circulating EV subsets before and after allo-SCT and investigated their association with clinical outcomes, immune reconstitution, and intestinal microbiota diversity.

Methods: Thirty-one pediatric patients undergoing allo-SCT were enrolled (Table I). Pre-transplant plasma and stool samples were uniformly collected within 7 days from the start of conditioning. EVs were characterized using MACSPlex Immuno-Oncology flow cytometry (37-marker panel) and validated for key immunological markers (CD69, CD56, HLA-DR, CD69/HLA-DR) using ExoView™, enabling single-vesicle phenotyping across tetraspanin-captured EVs (CD9/CD63/CD81). Additional clinical variables included: age, diagnosis, time elapsed since last chemotherapy before SCT, and antibiotic exposure within 60 days before conditioning. Gut microbiota was profiled by 16S rRNA gene sequencing, and immune reconstitution was assessed through serial immunophenotyping at 1, 3, 6 and 12 months.

Results: Higher pre-transplant levels of HLADR$^+$, HLAABC$^+$, CD56$^+$, CD25$^+$, CD69$^+$ and CD69$^+$/HLA-DR$^+$EVs, validated across both MACSPlex and ExoView platforms, were strongly associated with the subsequent development of grade II–IV acute GVHD. Conversely, patients who later experienced disease relapse displayed the opposite pattern, exhibiting significantly lower CD69$^+$HLA-DR$^+$EVs counts (Fig. 1A-B). Even if small number of events prevent reaching significance in cumulative incidence analysis for relapse, this suggests divergent immunological trajectories underlying GVHD versus relapse biology.
The interval between last chemotherapy exposure and transplantation showed opposite associations for EVs and microbiota: shorter intervals were linked to higher CD69$^+$HLA-DR$^+$EVs levels, while longer intervals correlated with higher gut microbial diversity (Fig. 1C). In contrast, antibiotic exposure in the 60 days preceding conditioning showed no significant association with either EVs abundance or microbiota diversity in this cohort.
Higher pre-transplant CD69$^+$/HLA-DR$^+$EVs levels were associated with reduced gut microbial diversity, indicating a potential inflammatory or tissue-stress signature linking intestinal mucosal status and EVs release (Fig. 1D).
Correlation heatmaps at 1, 3, and 6 months revealed time-dependent associations between EVs subsets and immune recovery (Fig. 1E). At 1 month, CD56$^+$ and CD25$^+$EVs inversely correlated with Tregs; at 3 months, multiple EVs subsets showed strong negative associations with dendritic cells and CD4$^+$CD8$^+$ T-cell counts, while CD69$^+$ and CD25$^+$EVs correlated positively with M-MDSC expansion. At 6 months, CD25$^+$, CD69$^+$, and HLA-ABC$^+$EVs negatively correlated with γδ T-cell reconstitution. No significant correlations were observed at 12 months.

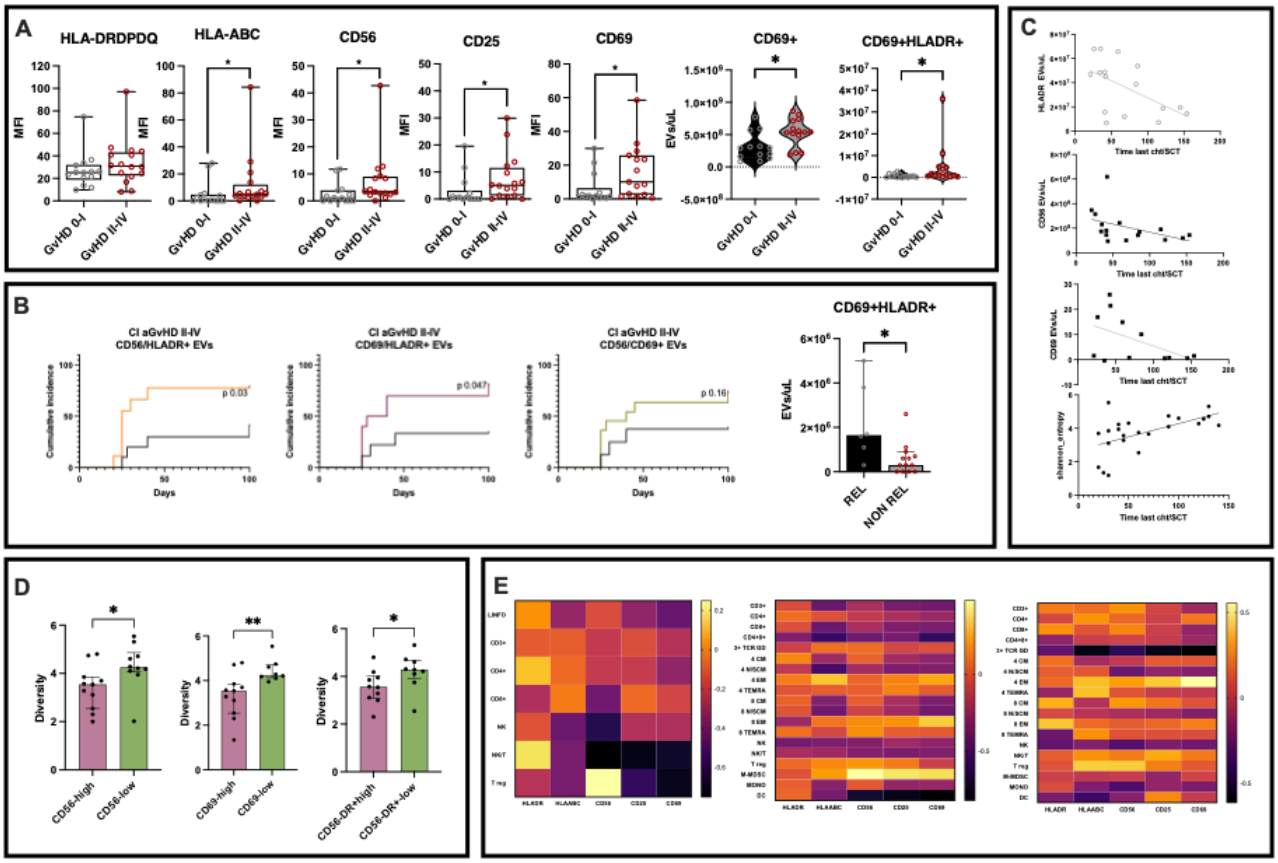

Table I: Baseline demographic, clinical and transplant characteristics

	N (%) of patients
Number of patients	31
Median age at HSCT	8,9 (1-20)
Male sex	24 (77%)
Diagnosis	
ALL	13 (42%)
AML	7 (23%)
LBL	1 (3%)
JMML	4 (13%)
MDS	2 (6%)
SAA	3 (10%)
WAS	1 (3%)
Pre-HSCT infections (from day-60)	
Bacterial	10 (32%)

Table I: Baseline demographic, clinical and transplant characteristics	
Viral	6 (19%)
Fungal	1 (3%)
mMRD at HSCT	
positive	8 (26%)
negative	13 (42%)
NA	10 (32%)
Donors	
MUD	11 (35%)
HAPLO	14 (45%)
SIBLING	6 (19%)
Conditioning regimen	
Busulfan-based	15 (48%)
TBI-based	9 (29%)
Treosulfan-based	7 (22,6%)
GvHD prophylaxis	
ATG-CNI/MTX	9 (29%)
PT-Cy/CN//MMF	17 (55%)
CNI/MTX	5 (16%)
HSC source	
BM	25 (81%)
PBSC	6 (19%)

Conclusions: Circulating EVs profiles obtained just prior to conditioning capture both inflammatory activation and tissue-stress signals relevant to microbiota status, immune reconstitution, and GvHD. In particular, $CD69^{+}$/$HLA\text{-}DR^{+}$ EVs emerge as a multimodal biomarker linking mucosal biology, chemotherapy timing, and clinical outcomes. Integration of EVs profiling with microbiome and immunological monitoring may support early risk stratification and personalized supportive care in pediatric allo-SCT.

Disclosure: Nothing to disclose.

A365

HIGH THROUGHPUT METABOLIC ANALYSES DEMONSTRATE AMINO ACID PATHWAY PERTURBATIONS IN ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: Acute graft-versus-host disease (aGVHD) is a serious inflammatory complication affecting 20–50% of allogeneic haemopoietic stem cell transplant (alloHSCT) recipients, arising when donor immune cells attack host tissues. While the cytokine and immune cell alterations associated with aGVHD are increasingly well characterized, its metabolomic landscape remains less understood. Altered lipid, amino acid, and microbiota-derived metabolite pathways have been linked to aGVHD (1–3). To define its metabolic signature, we analyzed the serum metabolome of alloHSCT recipients to distinguish patients who developed aGVHD from those who did not.

Methods: Serum samples from alloHSCT recipients and day-100 post-transplant controls were analyzed using untargeted metabolomic profiling by high-performance liquid chromatography–mass spectrometry. Sparse Partial Least Squares Discriminant Analysis (sPLS-DA) was used to identify discriminatory metabolites. Metabolites with non-zero loadings on at least one selected component were retained. All sPLS-DA and clustered heatmap analyses were performed in R version 4.3.3 using the 'mixOmics' package. Pathway enrichment analysis was performed with MetaboAnalystR 4.0, referencing the Kyoto Encyclopedia of Genes and Genomes (KEGG) database for Homo sapiens.

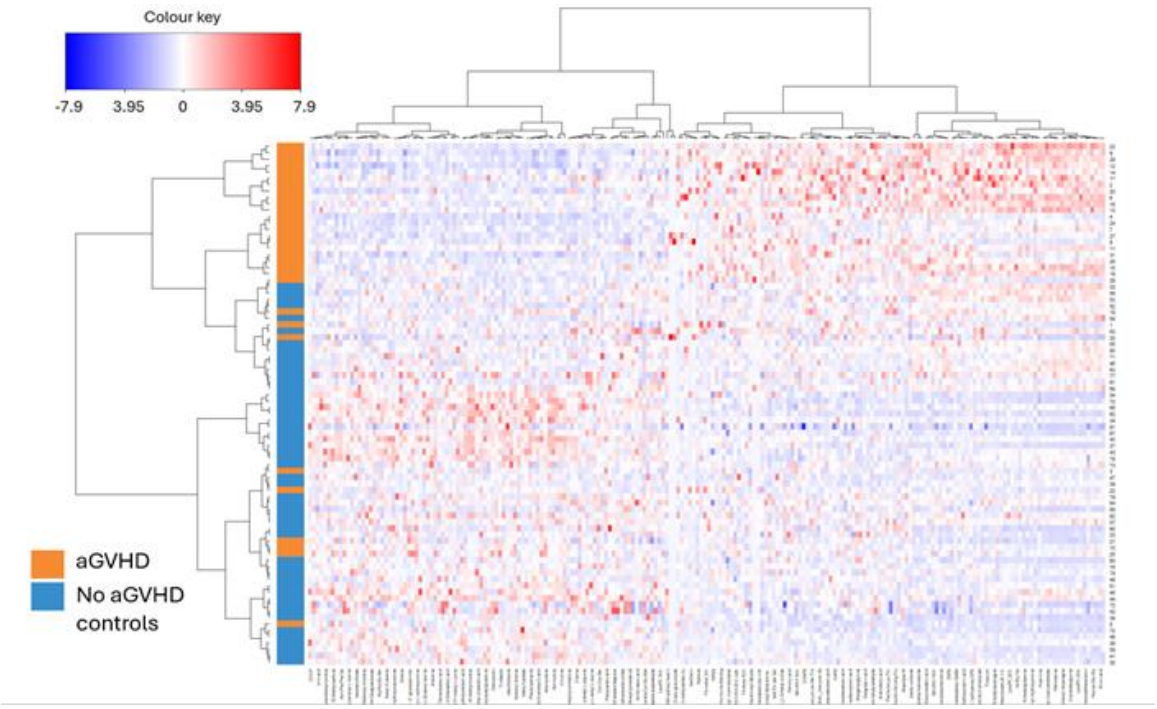
Results: A total of approximately 1,400 metabolites across 59 metabolic pathways were analyzed in 31 patients with acute graft-versus-host disease (aGVHD) and 51 alloHSCT controls. Patient characteristics are summarized in **Table 1**. sPLS-DA identified 210 discriminatory metabolites, which were used to construct a heatmap signature distinguishing patients with aGVHD from controls (**Figure 1**). Notably, 1-pyrroline-5-carboxylic acid (P5C; loading score [LS] = −0.266) was the top discriminatory metabolite which was decreased in aGVHD (fold change = 0.77). Pathway enrichment analysis revealed significant alterations in tryptophan metabolism ($p < 0.001$, FDR = 0.0118), tyrosine metabolism ($p < 0.001$, FDR = 0.0118), arginine biosynthesis ($p = 0.001$, FDR = 0.026), arginine and proline metabolism ($p = 0.002$, FDR = 0.044), and glycine, serine, and threonine metabolism ($p = 0.004$, FDR = 0.044). After correction for multiple comparisons using the Holm–Bonferroni method, the tryptophan and tyrosine pathways remained statistically significant.

Table 1: Basic patient characteristics

	Patients (N)	Percentage (%)
Age, median (interquartile range), year	60 (46 - 67.8)	-
Male sex, number (n), %	58	70.7
Diagnosis, n, % Acute myeloid leukaemia	35	42.7
Acute lymphoblastic leukaemia	12	14.6
Myelodysplastic syndrome	11	13.4

Myeloproliferative neoplasm	12	14.6
Lymphoma	9	11.0
Others	3	3.7
Donor type, n, % Matched sibling	21	25.6
Matched unrelated donor	34	41.5
Haploidentical	27	32.9
Conditioning regimen intensity, n, % Myeloablative	15	18.3
Reduced Intensity/Non myeloablative	67	81.7
Graft-versus-host disease (GVHD) prophylaxis, n, % Post transplant cyclophosphamide	72	87.8
Methotrexate	3	3.7
Alemtuzumab	5	6.1
Others	2	2.4
Anti-thymocyte globulin use, n, %	1	1.2
Acute GVHD Grade 2 to 4	29	35.4

Figure 1: Clustered heat map of 210 discriminatory metabolites comparing the metabolic signature of patients with aGVHD and alloHSCT controls. Samples (y-axis) and metabolites (x-axis) are hierarchically clustered based on their scaled abundance profiles. Heatmap colours denote standardised metabolite intensities (z-scores), with red indicating higher and blue lower relative abundance compared with the mean level of each metabolite.



Conclusions: Our analysis reveals significant perturbations in amino acid pathways at aGVHD onset, many of which are integral to immune and inflammatory responses. Notably, P5C, a key intermediate in proline, ornithine, and glutamate metabolism, emerged as the top discriminatory metabolite and may play a critical role in modulating allogeneic immune responses. Alterations in P5C, tryptophan, and tyrosine metabolism represent potential mechanistic drivers of aGVHD and merit focused investigation in preclinical models to elucidate their functional significance.

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Clinical Trial Registry: NA

Disclosure: Nothing to declare

A369

COMPARATIVE ANALYSIS OF GRAFT-VERSUS-HOST DISEASE INCIDENCE AND PATTERNS AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE VERSUS STANDARD PROPHYLAXIS

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Background: GVHD remains a major cause of morbidity and mortality complication following allogeneic hematopoietic cell transplantation (allo-HCT). Traditional prophylaxis has relied on calcineurin inhibitors (CNI) combined with methotrexate or mycophenolate mofetil (MMF). Over the last decade, post-transplant cyclophosphamide (PTCy)-based prophylaxis has become widely adopted after demonstrating a reduced incidence of acute (aGVHD) and chronic GVHD (cGVHD).
Although the overall protective effect of PTCy on GVHD is well established, comparative data on organ-specific involvement and severity relative to CNI-based prophylaxis remain limited. This study evaluates differences in incidence, clinical presentation, and severity of GVHD in patients receiving PTCy-based versus CNI-based prophylaxis.

Methods: We retrospectively analyzed all adults undergoing their first peripheral blood allo-HCT at our institution between 2014 and 2024. GVHD prophylaxis strategies evolved over time, with progressive adoption of PTCy across donor types. Acute and chronic GVHD were graded according to MAGIC and 2014 NIH criteria, with systematic assessment of organ involvement. Primary endpoints included cumulative incidence (CIF) of aGVHD and cGVHD (with relapse and death as competing risks), as well as severity and organ manifestations.

Results:

TABLE 1. Main Results

	All patients N= 569 (100%)	PTCY-based N=374 (%)	Other prophylaxis N=195 (%)	P-value
ACUTE GVHD, n(%)	275 (48)	160 (43)	115 (59)	<0.001
Acute GVHD **MAGIC 1** **MAGIC 2**	 140 (49) 70 (25)	 91 (56) 39 (24)	 49(40) 31(25)	0.109

MAGIC 3 **MAGIC 4**	42 (15) 23 (8)	19 (12) 11(7)	23(19) 12(10)	
Cumulative Incidence Function **All grades** **Grade II-IV** **Grade III-IV**	45.5 (41.4-49.6) 23.2 (19.8-26.7) 11.2 (8.8-14.0)	39.8 (34.9-44.8) 17.9 (14.2-22.0) 7.8 (5.3-10.8)	56.4 (49.1-63.1) 33.3 (26.8-40.0) 17.9 (12.9-23.7)	<0.001 <0.001 <0.001
Steroid-Refractory	59 (21)	35 (22)	24 (21)	0.76
Second Line of Treatment **Ruxolitinib** **Extracorporeal photopheresis** **Calcineurin inhibitor** **Mesenchymal cells** **Micofenolato** **Etarnecep**	6 (2) 33 (12) 12 (4) 3 (1) 6 (2) 3 (1)	5 (3) 21(13) 2 (1) 3 (2) 4 (3) 0 (0)	1 (1) 12 (10) 10 (9) 0 (0) 2 (2) 3 (3)	0.56
Mortality Rate Day +60	15 (5)	9 (6)	6 (5)	0.15
CHRONIC GVHD	166 (29)	82 (22)	84 (43)	
Chronic GVHD **Mild** **Moderate** **Severe**	63 (38) 67 (40) 36 (22)	50 (61) 21 (26) 11 (13)	13 (15) 46 (55) 25 (30)	<0.001
2-Year Cumulative Incidence of cGVHD **All grades** **Moderate-Severe**	33.1 (29-37.3) 19.8 (16.4-23.5)	24.8 (20.2-29.6) 8.8 (6.0-12.2)	48.6(40.8-56.0) 40.9 (33.4-48.2)	<0.001 <0.001
Requirement of	77 (28)	21 (26)	56 (67)	<0,001

complementary treatment to Corticosteroids (first line)				
Complementary Treatment (first line)	32 (19)	3 (4)	27 (32)	<0,001
Relapse Rate after cGVHD	22 (4)	12 (3)	10 (5)	0.604
Survival Outcomes				
Overall Survival, (95% CI) **1-year** **3-year**	72.6 (68.7-76.1) 61.5 (57.2-65.6)	77.1 (72.4-81.0) 65.1 (59.5-70.0)	64.1 (56.9-70.4) 54.6 (47.4-61.3)	<0.001
Non-Relapse Mortality, (95% CI) **1-year** **3-year**	14.0 (11.3-17.0) 16.6 (13.6-19.9)	12.5 (9.3-16.1) 14.6 (11.1-18.6)	16.9 (12.0-22.5) 20.1 (14.8-26.0)	0.029
Cumulative Incidence of Relapse, (95% CI) **1-year** **3-year**	31.9 (28.0-35.9) 24.2 (20.8-27.8)	21.9 (17.8-26.2) 31.2 (26.3-36.2)	28.7 (22.5-35.2) 33.5 (26.9-40.2)	0.43

Graft-versus-Host Disease (GVHD); acute Graft-versus-Host Disease (aGVHD); chronic Graft-versus-Host Disease (cGVHD).

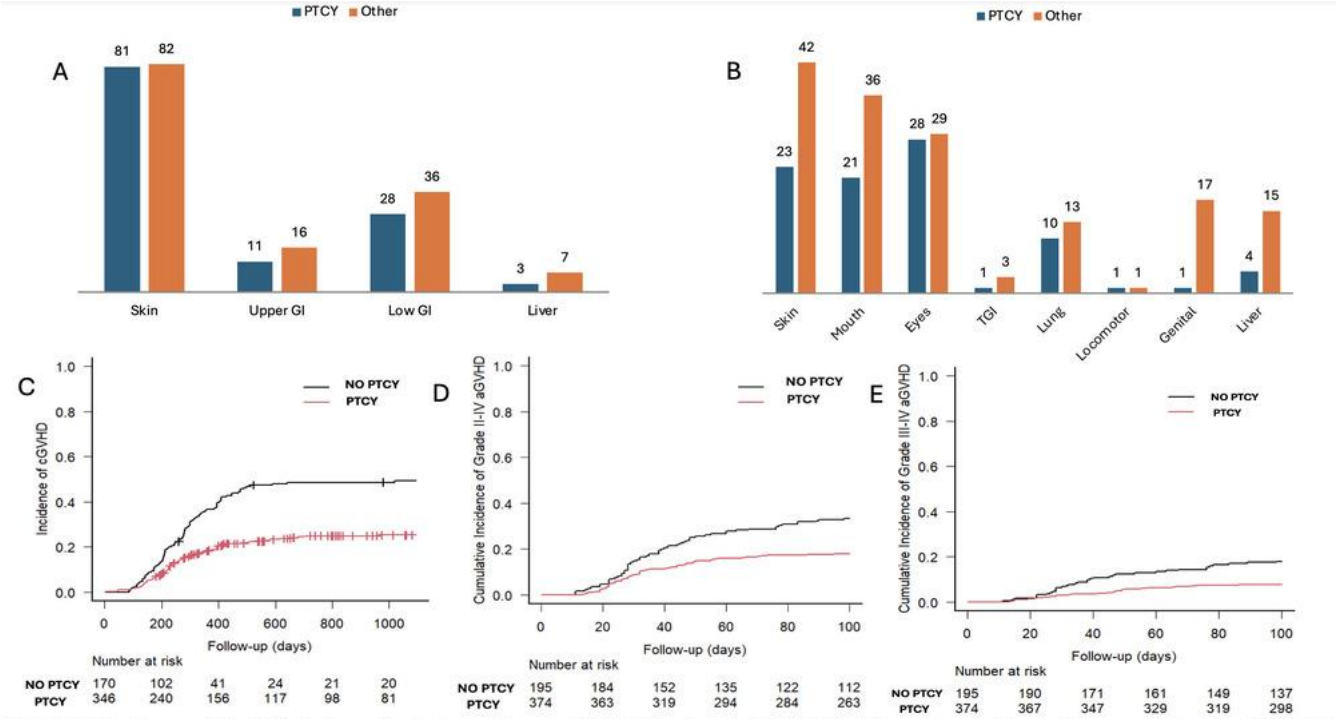

FIGURE 1: Incidence (%) of clinical manifestations of acute GVHD (A), chronic GVHD (B), 2-Year Cumulative Incidence of chronic GVHD (C), Day +100 Cumulative Incidence of Grade II-IV aGVHD (D) and Grade III-IV cGVHD (E)

A total of 569 patients were included; 374 (66%) received PTCy-based and 195 (34%) CNI-based prophylaxis. Baseline characteristics were comparable, although patients aged >64 years (17% vs. 7%, P=0.001) and those receiving alternative donor grafts (73% vs. 47%, P=0.001) were more frequent in the PTCy group.

PTCy was associated with a lower incidence of grades II–IV aGVHD (Day +100 CIF: 17.9% vs. 33.3%, P<0.001) and grades III–IV (7.8% vs 17.9%, p<0.001) (**Table 1).** Patterns of organ involvement were similar between groups, including skin (81% vs 83%), upper gastrointestinal (12% vs 16%), lower gastrointestinal (28% vs 36%) and liver involvement (3% vs 7%) (p>0.1) (**Table 1**). Rates of steroid-refractory aGVHD 22% vs 21%) and day +60 mortality rate were similar between groups (6% vs. 5%, P=0.15).

The incidence of cGVHD was markedly lower the PTCy-group (2-year CIF: 24.8% vs 48.6%, p<0.001), with a profound reduction in moderate-to-severe cGVHD (2-year CIR: 8.8% vs 40.9%, p<0.001) (**Table 1).** PTCy was associated with significantly reduced involvement of skin (23% vs 42%, p<0.001), oral mucosa (23% vs 42%, p0.019), liver (4% vs 15%, p=0.009), and genital tract (1% vs 17%, p=0.001), whereas ocular, gastrointestinal, pulmonary whileand musculoskeletal involvement remained similaracross groups (**Figure 1**). Refractory cGVHD with requirements of 2nd-line treatment were lower with PTCy (26% vs 67%, p<0.001).

Survival analyses demonstrated improved outcomes in the PTCy cohort, with superior overall survival (3-year: 65.1% vs. 54.6%, *P*<0.001), lower non-relapse mortality (3-year: 14.6% vs. 20.1%, *P*=0.029), and incidence of relapse than those receiving CNI-based prophylaxis (3-year: 31.2% vs. 33.5%, *P*=0.43) (**Table 1)**.

Conclusions: PTCy-based GVHD prophylaxis significantly reduced the incidence and severity of acute and chronic GVHD. While the clinical presentation of aGVHD was similar to conventional CNI-based approaches, PTCy was associated with a marked decrease in severe and organ-damaging forms of cGVHD. Importantly, these benefits translated into reduced non-relapse mortality and improved overall survival without compromising disease control.

Disclosure: The authors declare no relevant conflicts of interest, financial or otherwise.

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IMPAIRED CIRCULATING T_{FH} SUBSETS AS EARLY INDICATORS OF CHRONIC GVHD PATHOGENESIS

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Background: Chronic graft-versus-host disease (cGvHD) is a major long-term complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT), driven by dysregulation of both T and B cell immunity. Clinically, it resembles autoimmune and rheumatologic disorders, with many patients developing autoreactive or allo-reactive antibodies contributing to tissue inflammation and fibrosis. Aberrant germinal center (GC) reactions are thought to underlie these pathogenic immune responses. T follicular helper (T_{FH}) cells, defined by CXCR5 and PD-1 expression, are central regulators of GC output, promoting memory B cell and plasmablast differentiation. In cGvHD, T_{FH} cells have been implicated in enhanced immunoglobulin production and autoantibody generation, correlating with clinical manifestations such as sicca symptoms, sclerotic skin changes, and pulmonary involvement. This study aims to identify additional T_{FH}-related signatures linked to the onset and progression of cGvHD.

Methods: In a prospective trial, peripheral blood from 66 transplanted patients was collected on median day +120 (range +91 to +190) after allo-HSCT. All patients received peripheral blood stem cells as source of stem cells, and GvHD prophylaxis consisted of either CNI+MTX (38,6%) or CNI+MMF (61,4%). In 24 patients, additional samples- besides the earlier day +120 time point- were obtained at cGvHD onset (median day +187, range +98 to +410) and then, 4 and 8 weeks later during treatment for cGvHD. $CD4^+$ T cell subsets, particularly cT_{FH} cells, were analyzed by flow cytometry.

Results: At day +120 after allo-HSCT, patients without GvHD, and also remaining cGVHD-free during follow-up, exhibited markedly higher frequencies of circulating PD-1$^+$ CXCR5$^+$ T_{FH} cells than individuals who subsequently developed cGvHD (median 9,63% versus 3,81 %, p=0,002). In those who later-on manifested cGvHD, cT_{FH} frequencies remained comparably low at the onset of clinical symptoms. Phenotypic analysis on day +120 revealed distinct distribution patterns of cT_{FH} subsets in the two groups. Patients who remained free of cGvHD exhibited lower frequencies of $cT_{FH}2$ (CXCR3$^-$CCR6$^-$ of T_{FH}) compared to those who later developped cGvHD (median 10,6 % versus 15,7 %, p=0,008), but higher proportions of $cT_{FH}1/17$ (CXCR3$^+$CCR6$^+$ of cT_{FH}) (18,15 % versus 7,0 %, p=<0,001) than those individuals who are subsequently diagnosed with cGvHD. These differences indicate that alterations in cT_{FH} subset composition are already detectable before the clinical onset of cGvHD and may reflect early dysregulation as well as changes in homing patterns within the adaptive immune compartment. Supporting the relevance of these early alterations, ROC analysis at day +120 demonstrated that cT_{FH} frequencies have a significant prognostic value for subsequent cGvHD development (AUC = 0.77; p = 0.0019).

Conclusions: Our analysis shows that the adaptive immune compartment in cGvHD patients becomes progressively disrupted, with a notable overall reduction in PD-1$^+$ CXCR5$^+$ T_{FH} cells in the peripheral blood accompanied by a selective increase of CXCR3$^-$CCR6$^-$ $cT_{FH}2$ subsets as disease emerges. This shift in T_{FH} composition reflects an early imbalance that can identify patients who later develop cGvHD during the course of this study, supported by solid predictive accuracy. Together, these findings point to cT_{FH} dynamics as an informative early marker of future chronic immune dysregulation.

Disclosure: None

A372

PERTURBATIONS IN THE MICROBIAL DERIVED TRYPTOPHAN METABOLITES UNDERLIE ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: The gastrointestinal flora has been shown to shape immune homeostasis in allogeneic haemopoietic stem cell transplant (alloHSCT) recipients via their interactions with the host metabolome. Tryptophan-derived indole and kynurenine metabolic pathways depend on microbiota-driven enzymatic processes and may modulate aryl hydrocarbon receptor (AhR)-mediated intestinal resilience, thereby influencing the pathogenesis of acute graft-versus-host disease (aGVHD) (1). To characterize these changes, we analysed the serum metabolome of alloHSCT recipients to identify metabolic differences between patients who did and did not develop aGVHD, with a particular focus on tryptophan metabolism.

Methods: Serum samples were collected from alloHSCT recipients at the onset of aGVHD (prior to treatment) and from alloHSCT controls at day 100 post-transplant. Untargeted

metabolomic profiling was performed using high-performance liquid chromatography–mass spectrometry. Pathway enrichment analysis was performed using MetaboAnalystR 4.0, referencing the KEGG (Kyoto Encyclopedia of Genes and Genomes) database for *Homo sapiens*. All additional statistical analyses and data visualisation were performed in R version 4.3.3 using the 'mixOmics', and 'fmsb' packages. Differences in metabolite concentrations were assessed using Welch's *t*-test.

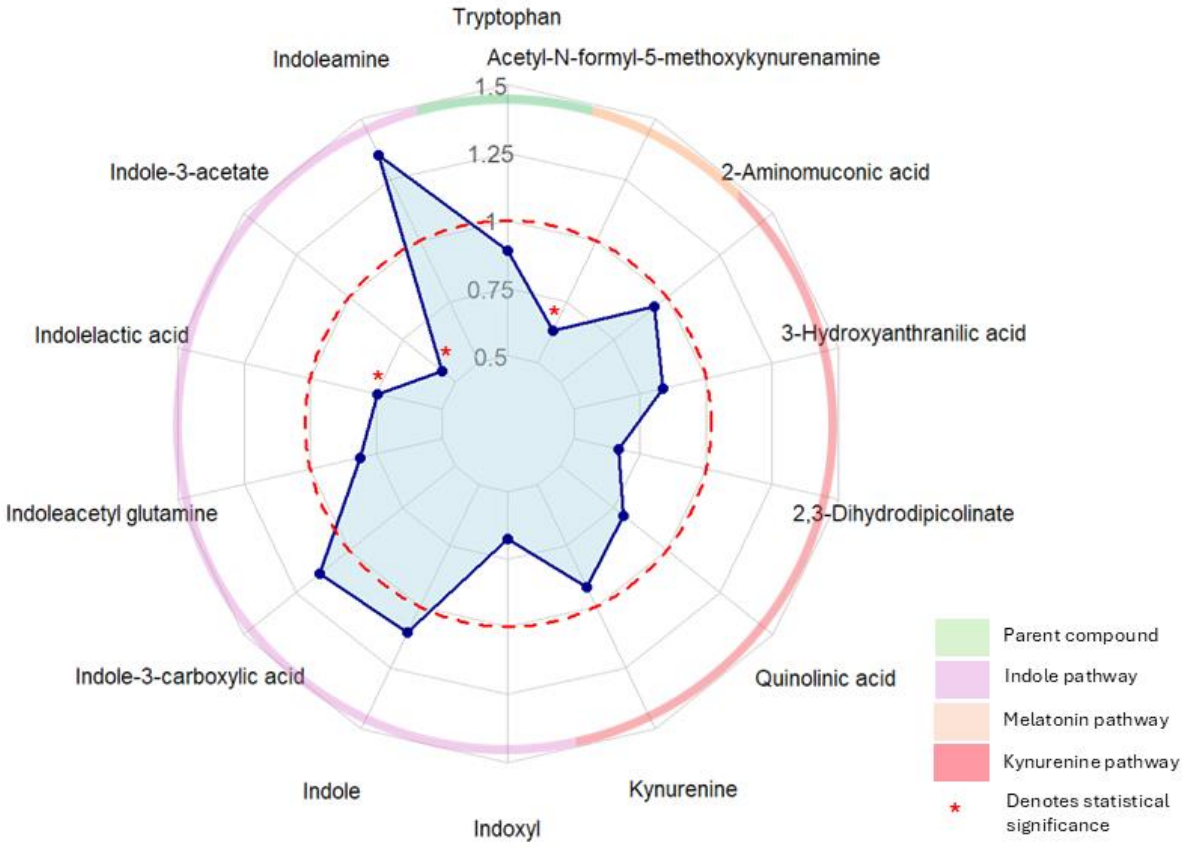
Results: A total of 82 patients (31 with aGVHD of any grade and 51 controls) and approximately 1,400 metabolites across 59 metabolic pathways were analysed. All patients had natural feeding at the time of serum collection and their characteristics are summarised in **Table 1**. Pathway enrichment analysis demonstrated that tryptophan metabolism was the most significantly altered pathway in patients with aGVHD compared with controls ($p < 0.001$; Holm-adjusted $p = 0.013$; false discovery rate (FDR) = 0.011). Several downstream tryptophan metabolites were significantly reduced in patients with aGVHD, including indole-3-acetate (fold change (FC) 0.56, $p = 0.005$), indolelactate (FC 0.74, $p = 0.006$), and acetyl-N-formyl-5-methoxykynurenamine (FC 0.64, $p = 0.04$). **Figure 1** illustrates the fold changes of tryptophan and its downstream metabolites. No significant differences between tryptophan metabolites were observed between patients with gastrointestinal (GI) and those with non-GI organ involvement of aGVHD.

Table 1: Basic patient characteristics

	Patients (N)	Percentage (%)
Age, median (interquartile range), year	60 (46 - 67.8)	-
Male sex, number (n), %	58	70.7
Diagnosis, n, % Acute myeloid leukaemia	35	42.7
Acute lymphoblastic leukaemia	12	14.6
Myelodysplastic syndrome	11	13.4
Myeloproliferative neoplasm	12	14.6
Lymphoma	9	11.0
Others	3	3.7
Donor type, n, % Matched sibling	21	25.6
Matched unrelated donor	34	41.5
Haploidentical	27	32.9

Conditioning regimen intensity, n, % Myeloablative	15	18.3
Reduced Intensity/Non myeloablative	67	81.7
Graft-versus-host disease (GVHD) prophylaxis, n, % Post transplant cyclophosphamide	72	87.8
Methotrexate	3	3.7
Alemtuzumab	5	6.1
Others	2	2.4
Anti-thymocyte globulin use, n, %	1	1.2
Acute GVHD Grade 2 to 4	29	35.4

Figure 1: Comparison of tryptophan metabolites in patients with and without aGVHD



Conclusions: Our analysis reveals an association between the development of aGVHD alterations in the tryptophan metabolic pathway at the host–microbiota interface, particularly within the indole pathway. The absence of differences in tryptophan metabolite levels between patients with and without gastrointestinal organ involvement suggests that these alterations are not driven by changes in bowel function. These findings support further investigation of host-microbial metabolic pathways as potential biomarkers and therapeutic targets for aGVHD prevention and treatment.

Reference:
1. Donoso-Meneses D, Padilla C, Moya-Guzmán MJ, Alegre ML, Pino-Lagos K. Contribution of tryptophan and its metabolites to transplant outcome: a mini-review. Front Immunol. 2024 Oct 15;15:1395421. doi: 10.3389/fimmu.2024.1395421. PMID: 39474416; PMCID: PMC11518742.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare

A374

PRE-TRANSPLANT TREC LEVELS MODULATE POST-TRANSPLANT GUT INTRINSIC DNA-DAMAGE AND IMMUNE RESPONSES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: The signal-joint T cell receptor excision circles (TREC) are an established marker of immunosenescence that inversely correlates with chronological age. Allogeneic hematopoietic stem cell transplant (HSCT) recipients present with premature onset of age-related decline of organ functions. Dysfunction of the lower gastrointestinal (LGI) tract negatively affects HSCT outcome. DNA-damage response (DDR) and cellular senescence (CS) represent cellular mechanisms capable of modulating tissue-intrinsic immune responses.
We hypothesized whether pre-transplant immunosenescence contributed to post-transplant accelerated organ senescence in HSCT recipients and analyzed pre-transplant TREC whole blood levels and DDR and CS markers in nucleated cells of the intestinal stroma of patients with LGI dysfunction after HSCT.

Methods: TREC levels were analyzed using triplex quantitative TaqMan™ PCR amplification of TREC, CD3, and unrearranged VD-J. The TREC value was estimated as the ratio of TREC to 100000 T cells.
Using the multiplex immunofluorescence (Lunaphore Comet™) we analyzed a tissue microarray marked with antibodies targeting immune cells, DDR and CS from 19 colonic

biopsies of patients with LGI symptoms. Promyelocytic leukemia protein (PML) and p53-binding protein 1 (53BP1) nuclear bodies as DNA-damage markers and CS marker p16INK4a were analyzed in all nucleated cells and in CD3 and CD68 cellular subsets infiltrating the intestinal stroma. Nuclear markers were quantified per nuclei count and per nuclear area. Immune cells were quantified per cell count and per stromal area. Mean fluorescence intensity was measured for every marker. PCR detection of viral DNA (CMV, EBV, HHV-6) in gut biopsies was performed.

Results: The cohort consisted of 19 patients with the median age of 53 years (range 18-68) allografted for various hematologic malignancies. All patients developed LGI symptoms in the median time of 64 days (range 12-524) after HSCT.
Patients with pre-transplant TREC levels above the average (469 TREC/10^5 T cells) were significantly younger than those with low TREC levels (44 years [range 18-53] and 57 years [range 40-68], respectively, *p<0.01*). Patients who developed LGI symptoms later than the median time (D+64) had significantly less pre-transplant TREC levels than those with earlier LGI symptoms onset (355 [range 229-904] and 512 [range 344-1014], respectively, *p=0.04*). Pre-transplant TREC levels below the average (pre-transplant TREC<AVG) was confirmed to have impact in the analysis of cumulative incidence of LGI symptoms (hazard ration 0.37, 95% CI: 0.12-1.21, *p=0.02*).
Consequently, we focused on the pre-transplant TREC<AVG subgroup of patients. In these patients, there were positive correlations found between the time of LGI symptoms onset and the expression of PML, 53BP1 and p16INK4a in the donor-derived $CD3^+$ T cells infiltrating the intestinal stroma (R=0.73, *p=0.01*; R=0.64, p=*0.03*; R=0.93, *p<0.001*; respectively). Furthermore, out of pre-transplant TREC<AVG patients, those who reactivated CMV, EBV and HHV-6 in the gut had lower pre-transplant TREC levels (p=0.05) and higher expression of p16INK4a in the intestinal stroma (p=0.06).

Conclusions: Our pilot results suggest that pre-transplant immunosenescence might contribute to premature functional decline and promote senescence on the organ level in HSCT recipients. Verification on larger cohorts is warranted.
Supported by NW25-03-00327, Ministry of Health, Czech Republic and Prchal Foundation for Molecular and Cellular Hematology.

Disclosure: Nothing to declare.

A375

SYNERGISTIC EFFECTS OF AXATILIMAB AND RUXOLITINIB IN AN INFLAMMATORY IN VITRO MODEL OF GVHD

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Background: Chronic graft-versus-host disease (cGVHD) is characterized by sustained dysregulation within both the myeloid and lymphoid compartments, driving persistent cytokine signaling and progressive tissue injury. Colony-stimulating factor 1

(CSF-1)–dependent monocytes and macrophages have emerged as important contributors to this chronic inflammatory milieu, consistent with the observed clinical activity of axatilimab, which targets and blocks the CSF-1 receptor (CSF-1R). At the same time, cytokines active in cGVHD frequently utilize the Janus kinase/signal transducer and activator of transcription (JAK/STAT) pathway to shape lymphocyte activation and differentiation, supporting the therapeutic benefit of the JAK1/JAK2 inhibitor ruxolitinib. The intersection of CSF-1 responsive myeloid pathways with JAK-driven cytokine networks in cGVHD, however, remains incompletely defined. Clarifying these interactions may help guide rational combinations of CSF-1R and JAK inhibitors for treatment of cGVHD.

Methods: To evaluate the effects of combining CSF-1R and JAK inhibition on immune responses, peripheral blood mononuclear cells from healthy donors were stimulated in a two-way mixed leukocyte reaction (MLR). Cultures were treated with axatilimab, ruxolitinib, or both across a range of doses. Monocyte viability was quantified by flow cytometry, and supernatants were analyzed for a panel of cytokines implicated in cGVHD pathogenesis, including monocyte chemoattractant protein 1 (MCP-1), interferon gamma-induced protein 10 (IP-10), and interleukin 10 (IL-10), as well as other inflammatory mediators. The relative and combined contributions of each agent were evaluated by comparing monocyte survival and cytokine output across treatment conditions.

Results: Axatilimab and ruxolitinib exhibited a cooperative effect on monocyte depletion in inflammatory MLR cultures. Mean (SD) monocyte survival was reduced from 85% (8.83%) in untreated controls to 40% (16.1%) when both therapies were combined. Axatilimab or ruxolitinib alone did not significantly affect survival; mean (SD) monocyte survival was 71% (10.9%) with axatilimab and 90% (5.7%) with ruxolitinib. Cytokine profiling revealed selective pathway-specific effects with some cytokines affected by axatilimab or ruxolitinib individually and some synergistically affected by axatilimab and ruxolitinib together.

Conclusions: Our in vitro findings demonstrate that CSF-1R– and JAK-dependent cytokine networks function as interconnected drivers of cell survival and inflammatory activity relevant to cGVHD. Combined CSF-1R and JAK inhibition produced coordinated effects on monocyte viability and cytokine output not observed with either agent alone, suggesting that dual targeting disrupts reinforcing circuits between myeloid and lymphoid pathways. These results support the mechanistic rationale for therapeutic combinations of axatilimab and ruxolitinib to interrupt the immunologic programs sustaining cGVHD more effectively.

Disclosure: Shannon Kahan, Linda Solomon, Paul Wilson, and Chryssa Kanellopoulou are employees and shareholders of Incyte Corporation.

A376

VON WILLEBRAND FACTOR-ENHANCED EASIX FORMULA CORRELATES WITH CGVHD SEVERITY IN THE INFLAMMATORY CGVHD PHENOTYPE AND CYTOKINE CONCENTRATIONS

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Background: Chronic graft versus host disease (cGvHD) is an alloimmune allogeneic hematopoietic stem cell transplantation (allo-HSCT) complication. Endothelial injury and activation are crucial for cGVHD pathophysiology. EASIX score (Endothelial Activation and Stress Index) calculated by the formula lactate dehydrogenase (LDH) (U/L) x Creatinine (mg/dL) divided by platelet count (10^9/L) is an endothelial dysfunction parameter tested in acute graft versus host setting, predicting non-relapse mortality in patients who have undergone reduced-intensity conditioning allo-HSCT, and was also tested in conditions where endothelial injury has a significant pathophysiological role. In the context of cGVHD, von Willebrand factor (VWF) is a marker of endothelial dysfunction, potentially a valuable addition to the existing EASIX formula. In this exploratory analysis, we aim to evaluate EASIX score in cGVHD, assessing correlations with clinical cGVHD manifestations and cytokine concentrations, i.e. the hypothesis is that EASIX score may correlate with cGVHD clinical phenotypes and underlying cGVHD biology.

Methods: Patients with cGVHD (73 samples from 54 patients, Table 1) were enrolled in a protocol at the UHC Zagreb (4/2017 - 12/2019; Croatian Science Foundation project IP-2016-06-8046). Patients were evaluated by a multidisciplinary team, and clinical manifestations were documented in detail. Samples were grouped into 3 cGVHD phenotypes: inflammatory (n=21), sclerotic (n=22), mixed (n=21). Samples taken from patients who underwent alloHSCT, without cGvHD, were control samples (n=9). Patients with active infection or overlap cGvHD were excluded. Selected cytokine levels were analysed by commercial essays (BAFF and CXCL9 – both Quantikine, CCL15 -DuoSet ELISA kit; all by R&D Systems, Minneapolis, MN, USA). Cytokines and clinical phenotypes were determined according to the proposed biological cGvHD model (Cooke et al., The Biology of Chronic Graft-versus-Host Disease, BBMT, 2017). B-cell activating factor (BAFF) is a cytokine vital to B-cell survival and is a promising cGvHD biomarker. C-X-C motif ligand 9 (CXCL9) is an interferon-gamma inducible chemokine stimulating T-cell migration to target tissues, and C-C motif ligand 15 or MIP5 – macrophage inflammatory protein 5 (CCL15) is a monocyte/macrophage chemoattractant. The EASIX score was calculated using the standard formula. Formula was additionally expanded with von Willebrand antigen (VWF:Ag) and activity (VWF:RCo), as follows: LDH (U/L) x Creatinine (mg/dL) x VWF:Ag (or VWF:Rco, %) / platelet count (x10^9 /L), all a part of the standard cGVHD workup.

Results: When the standard EASIX formula was used, statistically significant correlation was observed in CXCL9 (Figure 1) and VWF:Ag, only in the inflammatory phenotype (p=0.03 and p=0.013, Spearman rank correlation). When the VWF-modified (VWF:Ag and VWF:RCo) formula was used, a significant correlation with CXCL9 (p<0.001, Spearman rank correlation) and BAFF (p=0.002) was observed for all cGVHD patients, and more interestingly, EASIX formula with VWF:Ag and VWF:RCo was significantly correlated with BAFF (VWF:Ag p=0.013, VWF:RCo p=0.009), CXCL9 (VWF:Ag p=0.006, VWF:RCo p=0.003) and 2015 NIH severity score (VWF:Ag p=0.030, VWF:RCo p= 0.020) in the inflammatory phenotype.

Table 1 Demographics

		Control (n=9)	Inflammatory (n=21)	Mixed (n=21)	Sclerotic (n=22)	Total (n=73)
Age	Median (IQR)	49 (38-56)	50 (38.5-57)	46 (30.75-52)	40 (27-47)	46 (33.25 56)
	Range	24-63	22-64	17-63	10-65	17-65
Gender	F	4 (44.4%)	14 (66.7%)	11 (50%)	10 (47.6%)	39 (53.4%
	M	5 (55.6%)	7 (33.3%)	11 (50%)	11 (52.4%)	34 (46.6%
Main disease	ALL, AML, and MDS	5 (55.6%)	14 (66.7%)	15 (68.2%)	15 (71.4%)	49 (67.1%
	CML (IMF, myeloproliferative disorders)	1 (11.1%)	5 (23.8%)	5 (22.7%)	5 (23.8%)	16 (21.9%
	Other	3 (33.3%)	2 (9.5%)	2 (9.1%)	1 (4.8%)	8 (11%
Global NIH score	NA	9 (100%)	0 (0%)	0 (0%)	0 (0%)	9 (12.3%
	0	0 (0%)	1 (4.8%)	0 (0%)	0 (0%)	1 (1.4%)
	1	0 (0%)	5 (23.8%)	0 (0%)	2 (9.5%)	7 (9.6%)
	2	0 (0%)	12 (57.1%)	5 (22.7%)	9 (42.9%)	26 (35.6%
	3	0 (0%)	3 (14.3%)	17 (77.3%)	10 (47.6%)	30 (41.1%

Intensity of immunosuppression *"Sandy's scale": None-0, Mild (single agent prednisone<0.5 mg/kg/day)-1, Moderate (Prednisone 0.5 mg/kg/day and/or any single agent/modality)-2, High (2 or more agents/modalities ± prednisone 0.5 mg/kg/day)-3	NA	9 (100%)	0 (0%)	0 (0%)	0 (0%)	9 (12.4%
	0	0 (0%)	12 (57.1%)	12 (54.5%)	9 (42.9%)	33 (45.2%
	1	0 (0%)	1 (4.8%)	2 (9.1%)	2 (9.5%)	5 (6.8%)
	2	0 (0%)	6 (28.6%)	6 (27.3%)	10 (47.6%)	22 (30.1%
	3	0 (0%)	2 (9.5%)	2 (9.1%)	0 (0%)	4 (5.5%)
Lines of systemic therapy	Median (IQR)	NA	0 (0-1)	0 (1-2)	1 (0-3)	1 (0-2)
	Mean ± SD	NA	0.7±1.1	1.4±1.1	1.5±1.5	1.2 ±1.3

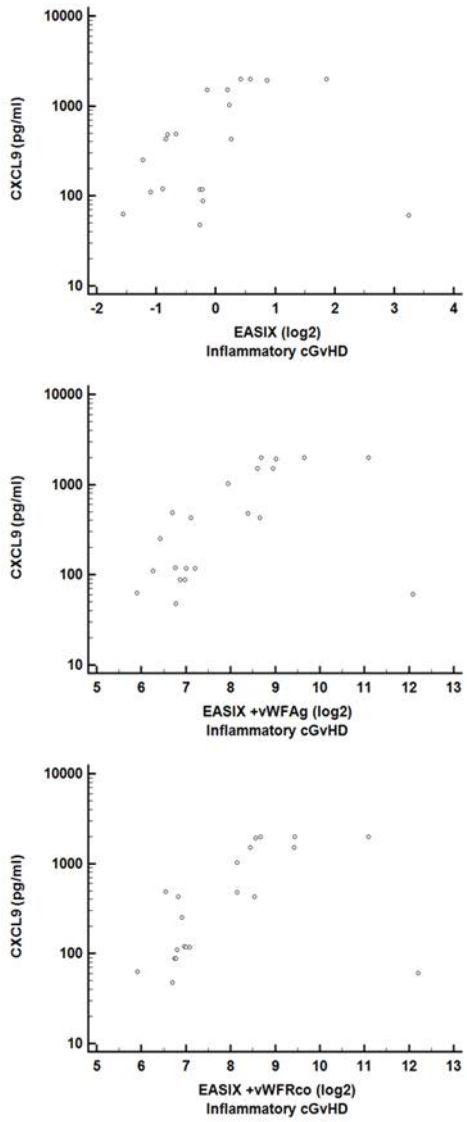

Figure 1

Conclusions: Von Willebrand factor-modified EASIX formula probably reflects the severity of inflammation in this cGVHD cohort, correlating with cytokines implicated in cGVHD pathophysiology, as well as the standardized clinical assessment tool, the 2015 NIH severity score.

Disclosure: Nothing to declare.

A377

THE INTERPLAY BETWEEN CYTOMEGALOVIRUS REACTIVATION, CONDITIONING REGIMENS, AND GRAFT-VERSUS-HOST DISEASE IN ALLOGENEIC HSCT: A 10-YEAR RETROSPECTIVE ANALYSIS FROM RESOURCE-LIMITED SETTING

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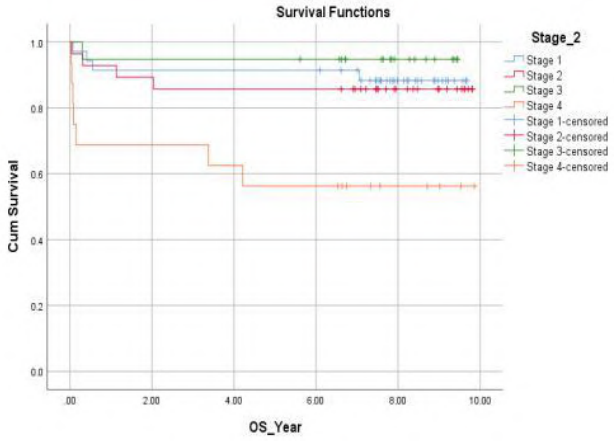
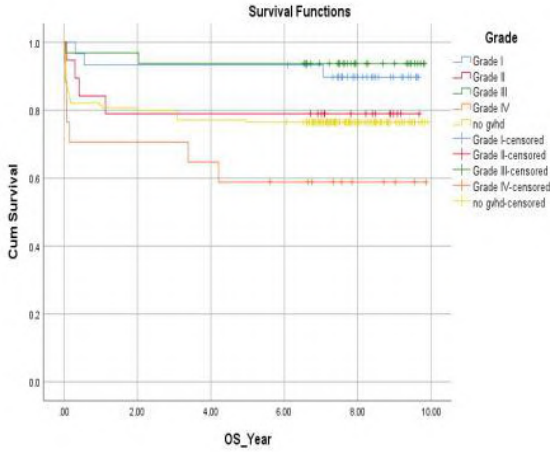
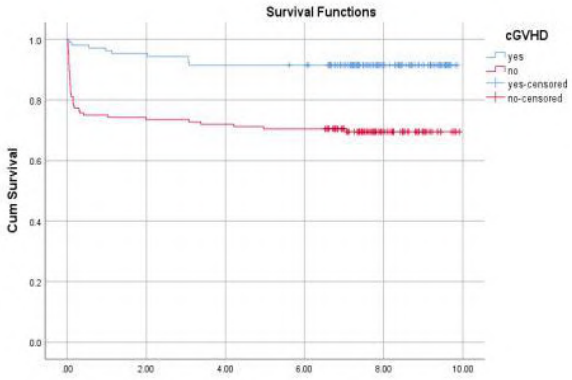
Background: Acute graft-versus-host disease (aGVHD) and chronic graft-versus-host disease (cGVHD) are the most common complications of hematopoietic stem cell transplantation (HSCT). Despite advancements in HLA matching and immunoprophylaxis, it remains a major cause of morbidity and mortality in low- and middle-income countries (LMICs).

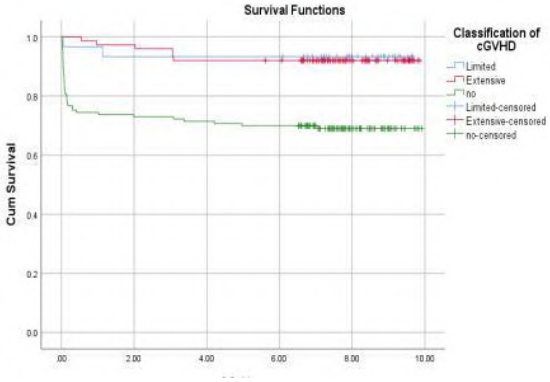
Methods: This 10-year retrospective single-center study included 238 patients with malignant and non-malignant hematological disorders who had received an allogeneic HSCT. The aGVHD was graded as per the Glucksberg-Seattle criteria. Logistic regression was applied to calculate the association of aGVHD and cGVHD with CMV reactivation and conditioning regimen, whereas the Kaplan-Meier and log-rank tests were used to calculate overall survival (OS) and its relationship with aGVHD and cGVHD, CMV reactivation, and conditioning regimen.

Results:









The median age of the cohort was 9 years (IQR: 4.5-20), with a male-to-female ratio of 2.3:1. The most common indication for HSCT was beta thalassemia major (35.7%). The majority of donors were siblings (88.7%), followed by parents (10.1%) and cousins (1.3%). The most common conditioning regimen used was myeloablative conditioning (MAC), which was given to 135 (56.7%) patients, followed by non-MAC in 71 (29.8%) and reduced intensity conditioning (RIC) in 32 (13.4%). aGVHD developed in 71/238 (29.8%), in which 21.8% had gut GVHD, followed by liver GVHD (7.6%) and eye GVHD (1%). Out of 71 cases, 13.4% had Grade III and 7.1% had Grade IV aGVHD. cGVHD developed in 106/238 (44.5%), in which 10.9% had gut GVHD, followed by liver GVHD (8.8%) and eye GVHD (3.4%), lung (17.6%), oral (16%), and skin (39.5%). Meanwhile, limited cGVHD was in 30 (12.6%) and extensive in 75 (31.5%). The overall survival (OS) was 79.4% with a mean survival of 8 years post allo-HSCT (95% CI: 7.5-8.5). There was significant association of stage (P=0.003) and grades (P=0.02) of aGVHD, cGVHD (P=0.0001), and classification of cGVHD (P=0.0001) with OS (Figures 1-4). On the multivariate analysis, RIC was associated with a higher incidence of aGVHD (OR: 4.0, p = 0.03). CMV reactivation occurred in 93/238 (39%) of patients and was significantly associated with a reduced risk of aGVHD (OR: 0.26, p = 0.001).

Conclusions: The association of RIC conditioning with a higher incidence and CMV reactivation with a lower incidence of aGVHD in LMICs highlights the need for optimization of conditioning regimens and institution of early CMV monitoring in LMIC settings to improve GVHD-related mortality and morbidity.

Disclosure: Nothing to declare

A378

SINGLE-AGENT CSF-1R OR JAK INHIBITION REDUCES FIBROSIS IN A MURINE MODEL OF CHRONIC GRAFT-VERSUS-HOST DISEASE

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Background: Chronic graft-versus-host disease (cGVHD) is characterized by persistent immune dysregulation, leading to tissue injury and fibrosis. Colony-stimulating factor 1 (CSF-1)–dependent myeloid pathways and Janus kinase/signal transducer and activator of transcription (JAK/STAT)-driven cytokine networks are both implicated in cGVHD pathogenesis. While CSF-1 receptor (CSF-1R) inhibition (axatilimab) and JAK1/JAK2 inhibition (ruxolitinib) have each shown clinical benefit, the potential for combined targeting of these pathways warrants further exploration.

Methods: A murine model of cGVHD was established in BALB/c (H-2^d) mice by transplantation of bone marrow cells and splenocytes from B10.D2 donors, which results in a minor antigen mismatch. Upon onset of clinical signs of GVHD, mice were treated with either anti–CSF-1R or ruxolitinib. Clinical status was monitored and disease severity was evaluated using standardized scoring criteria. At study endpoint, lung and skin tissues were harvested for assessment of fibrosis, hydroxyproline content, and dermal thickness. Additionally, RNA sequencing (RNA-seq) analysis was performed on skin samples to evaluate transcriptional changes associated with each treatment.

Results: Treatment with either anti–CSF-1R or ruxolitinib reduced clinical GVHD scores, decreased hydroxyproline levels in skin and lung tissues, and improved dermal thickness compared to controls. RNA-seq analysis of skin revealed transcriptional changes in response to each treatment, providing further insight into the molecular mechanisms underlying their therapeutic effects.

Conclusions: Both CSF-1R and JAK pathway inhibition individually attenuated in vivo tissue fibrosis and improved clinical outcomes in a murine cGVHD model. RNA-seq analysis of skin identified transcriptional changes associated with each treatment. These findings, derived from single-agent therapeutic approaches currently used in cGVHD, support the therapeutic potential of targeting CSF-1R and JAK pathways in this setting. Future studies will explore whether combination approaches could offer additional benefit.

Disclosure: Paul Wilson, Shannon Kahan, Melissa Parker, and Chryssa Kanellopoulou are employees and shareholders of Incyte Corporation. Jörg Distler has consultancy relationships with Active Biotech, Anamar, ARXX, AstraZeneca, Bayer Pharma, Boehringer Ingelheim, Callidatas, Calluna, Galapagos, GSK, Janssen, Kyverna, Ono Pharmaceutical, Merck, Novartis, Quell Therapeutics, Tyra, and UCB; has received research funding from Anamar, AstraZeneca, ARXX, BMS, Boehringer Ingelheim, Cantargia, Celgene, CSL Behring, Exo Therapeutics, Galapagos, GSK, Incyte, Inventiva, Kiniksa, Kyverna, Lassen Therapeutics, Mestag, Sanofi-Aventis, SpicaTx, RedX, UCB, and ZenasBio; has received writing support from Boehringer Ingelheim and Endeavor Biosciences; and is CEO of 4D Science and scientific lead of FibroCure.

P121

ADAPTIVE AND MYELOID DYNAMICS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN ACUTE OR CHRONIC GRAFT-VERSUS-HOST DISEASE UNDERGOING EXTRACORPOREAL PHOTOPHERESIS VERSUS NON–GRAFT-VERSUS-HOST DISEASE AND HEALTHY DONORS

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Background: Allogeneic stem cell transplantation (HSCT) is often associated with Graft-versus-Host Disease (GvHD) resulting from dysregulated alloreactivity. Extracorporeal photopheresis (ECP) is an established therapy for immunomodulation in GvHD, but underlying cellular mechanisms remain largely unclear. We compared myeloid and adaptive immune cell compositions from patients with acute GvHD (aGvHD) / chronic GvHD (cGvHD) receiving ECP to healthy individuals and patients without GvHD after HSCT (NoGvHD).

Methods: ECP was administered using the Therakos™ CELLEX™ Photophoresis system. Flow cytometric analysis of blood samples (Healthy N=10, NoGvHD N=19, cGvHD N=18, aGvHD N=6) was performed at baseline (d0) and after 13 weeks (d90), with or without ECP treatment, followed by statistical analyses.

Results: Baseline (d0): cGvHD vs. NoGvHD

- Adaptive: ↑ memory T-cells, ↓ Tregs, ↓ Bregs

- Myeloid: ↑ activated dendritic cells (DCs), ↓ myeloid derived suppressive cells (MDSCs)

NoGvHD (Course d0 → d90)

- Adaptive: T-cells, Tregs, Bregs → stable
- Myeloid: Monocytes, DCs, MDSCs → stable

cGvHD during ECP (Course d0 → d90)

- Adaptive: memory T-cells ↓ (composition similar to NoGvHD), T-cell proliferation ↓, Tregs ↑ (partial recovery), Bregs ↑ (partial recovery)
- Myeloid: activated DCs ↓, inflammatory monocytes ↓, MDSCs ↑ (composition similar to NoGvHD)

Post-treatment (d90): cGvHD vs. NoGvHD

- Adaptive: memory T-cells still ↑, but lower compared to d0,
  Tregs still ↓ despite partial recovery
- Myeloid: activated DCs stay ↑, MDSCs ↓

Conclusions: At baseline compared to NoGvHD, cGvHD before ECP showed pronounced adaptive and myeloid dysregulation. By d90, NoGvHD profiles showed stable levels of cells while ECP induced partial normalization of dysregulated immune compartments in cGvHD (compared to d0). Immune hyperactivation persisted but was attenuated after ECP. Clinical correlations will be presented at the congress.

Disclosure: This work was funded by an external collaborative research (ECR) grant provided by Therakos EMEA Limited.

P122

EXPERIENCE IN HAPLOIDENTICAL TRANSPLANTATION OVER THE LAST 3 YEARS, IN THE TRANSPLANT UNIT OF MEXICO'S NATIONAL REFERENCE MEDICAL CENTER

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Background: Allogeneic hematopoietic cell transplantation(HCT) is a potentially curative procedure for benign and neoplastic hematologic disorders. The probability of finding an HLA-compatible donor is 25%. The use of post-transplant cyclophosphamide(CYpost) on days +3 and +4 has reduced graft failure and the occurrence of graft-versus-host disease(GVHD). At our center, the dose of CYpost for haploidentical HCT has been adjusted to40 mg/kg. In this study, 46 patients who underwent haploidentical HCT in the last 3 years were described.

Objectives: To determine progression-free survival(PFS) and overall survival(OS) in patients who underwent haploidentical HCT in a transplant unit at a tertiary referral medical center in Mexico City from 2022 to 2025. To describe the demographic characteristics and clinical outcomes that patients have presented after haploidentical HCT.

Methods: Retrospective, descriptive, and observational study. Inclusion criteria: all patients who underwent transplantation in the hematopoietic cell transplant unit of one mexican medical center, from January 2022, to April 2025, with a haploidentical transplant.

Results:

Grado global aGvHD MAGIC	PIEL Percentaje 100%	HEPÁTICA Percentaje 100%	GI BAJO Porcentaje 100%	GI UPPER Percentaje 100%
0	15.2%	39%	71.7%	54.3%
1	52.2%	39%	17.4%	41.3%
2	21.7%	16%	6.5%	2.2%
3	2.2%	4%	2.2%	1.1%
4	0%	2.2%	2.2%	1.1%

Acute-Graft-Versus-host-disease-aGvHD-Characteristics

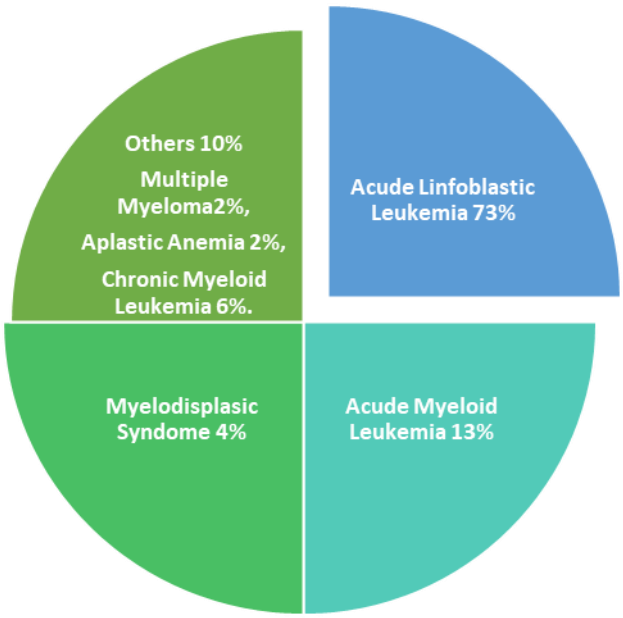

Figure1.Distribution-of-hematological-pathologies-undergoing-haploidentical-transplantation.

Patients who received haploidenticalHCT were 63% male and 37% female. The mean age

was 32 years. The post-transplant diseases are shown in Figure1. Hematopoietic cell donors were 65% male and 35% female, with 46.8% aged 18–35 years, 52.2% older than 35 years, and 1% underage. According to the EBMTscore, 8 patients(17.4%) had 3 points, 36 patients (78.3%) 4 points, and 2 patients(4.3%)5 points. Prior chemotherapy lines were as follows: 27% had one previous line of treatment, 30% had 2 lines, 39% had 3 lines, and 4% had 4 lines. A total of 82.6% of patients went to transplant with negative MRD. ABO blood group compatibility was found in 84.8% of patients, with 13% minor incompatibility and 2.2% major incompatibility. The dose of post-transplant cyclophosphamide in the haploidentical setting(CYpost-haploidentical) was 50 mg/kg in 41.3% of patients, 40mg/kg in 39.1%, and 35mg/kg in 19.6%. The dose was adjusted according to the complications. Cytokine release syndrome: gradeI in 60.9%, gradeII in 32.6%, and grade3–4 in 6.5%, with lower cyclophosphamide doses. The source of hematopoietic cells was: peripheral blood. No patients were transplanted with donors who had positive anti-HLA antibodies. The average waiting time to transplant was: 123 days. The mean engraftment day for neutrophils was +13, reticulocytes +15, and platelets +13. The mean length of stay was 40days. AcuteGVHD occurred in 78.3%, chronicGVHD in 8.7%, overlap syndrome in 4.3%, and 8.7% had no GVHD. Figure2 shows the GVHD characteristics. Mortality was 37%, due to infections: 17.4%(CMV 67% and Clostridioides 28.3%), relapse:15%(associated with the number of treatments), and graft failure:4.3%. Overall survival ranged from 184days to 5,526 days. Progression-free survival at 1,000 days was 85%.

Conclusions: 46 patients were analyzed, where the leading cause of mortality was infections, which confirms that measures should be taken regarding their control in the hematopoietic stem cell transplant unit. 63% of the surviving patients experienced low grades ofGVHD, which does not diminish their quality of life and is considered an acceptable alternative when a 100% compatible allogeneic donor is not available.

Disclosure: Nothing to declare.

Graft-versus-host Disease - Clinical

GS2-8

MAAT013 FOR RUXOLITINIB-REFRACTORY ACUTE GRAFT-VERSUS-HOST DISEASE WITH GASTROINTESTINAL INVOLVEMENT: FINAL RESULTS FROM THE ARES PHASE III TRIAL

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Background: Fecal microbiotherapy has shown promising results in pilot studies involving patients with refractory acute Graft-versus-Host Disease with gastrointestinal involvement (GI-aGvHD). We report the final results from ARES (NCT04769895), a multicenter, open-label, phase 3 study exploring the pooled allogeneic microbiotherapy MaaT013 in subjects with refractory-GI-aGvHD previously treated with systemic steroids and ruxolitinib.

Methods: AlloHCT recipients with GI-aGvHD, identified as corticosteroid-refractory and either refractory or intolerant to ruxolitinib, were eligible. The treatment included rectal administration of 3 MaaT013 doses (D1,D5,D10). Each MaaT013 contained a minimum of 1.35×10^{11} viable bacteria. A supplementary MaaT013 dose was authorized in case of relapse after D28 if CR/VGPR was achieved before D28.
The primary endpoint was GI-overall response rate (GI-ORR) at D28 assessed by an independent review committee. Secondary endpoints included ORR for GI-and all-organ at D28, D56 and Month3 (M3), overall survival (OS), and safety analysis.

Results: Sixty-six adult subjects with grade II-IV GI-aGvHD were enrolled and received at least one MaaT013 dose (median=3; range,1-4). Median age at informed consent was 55.5 years (range,24-76); 53% were male. Most subjects presented with grade III (58%) or IV (33%) aGvHD; 86% were steroid-resistant and 14% (n=9) steroid-dependent, all were resistant to ruxolitinib. 77% of patients had exclusive lower GI (LGI) involvement, 17% had LGI and skin involvement, 3% had LGI and liver involvement and 3% had LGI, skin and liver involvement.
The study met its primary endpoint, with a D28 GI-ORR of 62% (n=41, 95% CI, 0.49-0.74), significantly higher than the pre-established 22% threshold ($p<0.0001$). Most subjects achieved D28 GI-complete response (GI-CR:38%) or GI-VGPR (20%), while 5% achieved GI-partial response (PR). Responses for all-organ ORR were similarly frequent with D28 ORR of 64%, including 36% with CR and 18% with VGPR.
At D56 and M3, GI-ORR was maintained in 47% (95%CI, 0.35- 0.60) and 44% (95% CI, 0.32-0.57) subjects, respectively, with a prevalence of GI-CR (35% and 36%, respectively).
At the end of the study, the median OS was not reached. The OS was 59% at M6 and 54% at M12, exceeding the previously reported 12-month OS of 15% (Abedin, 2021)**.** Importantly, the OS was significantly higher in responders (achieving at least GI-PR at D28, n=41)

compared to non-responders (n=25): 76% versus 28% at M6; 68% versus 28% at M12, respectively (Log-rank p<0.0001)**.** The median OS of responders was not reached while it was 54 days in non-responders (95% CI, 24.0-116.0).
MaaT013 demonstrated an acceptable safety profile despite the vulnerability of subjects with refractory GI-aGvHD. 36 treatment-related adverse events (AEs) were reported in 19 (29%) subjects. Of these, 8 events in 7 subjects (11%) were considered serious. Out of 29 fatal AEs, one was deemed related to MaaT013 by the investigator.

Conclusions: Final ARES results demonstrate that MaaT013 induces frequent and deep responses translating into prolonged survival and acceptable safety profile in subjects with aGvHD who previously failed both systemic steroids and ruxolitinib, a population characterized by poor clinical outcomes with limited therapeutic options. These positive results support MaaT013 as the first microbiome-based therapy for the treatment of refractory aGvHD.

Clinical Trial Registry: NCT04769895

Disclosure: Jaime Sanz, Clemence Mediavilla, Lucia Lopez-Corral, Alexander Schauwvlieghe, Marc Bernard, Michael Loschi, Chama Mokeddem, Francesca Bonifazi, Daniela Heidenreich, Verena Wais, Elisa Sala, Stefan Koeck, Johannes Clausen: Nothing to declare
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Mélanie Tilte, Marion Bruelle, Emilie Plantamura: MaaT Pharma current employees, stock options
Behzad Kharabi Masouleh: Consultancy for MaaT pharma
Ernst Holler: Advisory Board at MaaT Pharma
Mohamad Mohty: Honoraria and/or advisory boards: Adaptive Biotechnologies, Amgen, Astellas, Celgene-BMS, GSK, Gilead, Janssen, Jazz Pharmaceuticals, Medac Pharma, Novartis, Oncopeptides, Pfizer, Sanofi, Takeda, Therakos. Research funding: Janssen, Sanofi

OS12-01

HUMAN MILK OLIGOSACCHARIDE (2'-FUCOSYLLACTOSE) MODIFIES THE GUT MICROBIOME AND REDUCES ACUTE GI GVHD: RESULTS OF A PROSPECTIVE, FIRST IN-PEDIATRICS PHASE II STUDY

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Background: Dysbiosis after allogeneic hematopoietic stem cell transplant (allo-HSCT) predisposes to acute gastrointestinal graft-versus-host disease (GI GVHD). We have

previously shown that human milk administration reduces peri-transplant dysbiosis by virtue of human milk oligosaccharides (HMO) that are known prebiotics (*Breastfeeding Medicine*, 2019). We have additionally conducted a phase I study of the most abundant HMO, 2'-fucosyllactose (2'-FL), and have demonstrated safety and established dosing. We hypothesized that peri-transplant oral 2'-FL administration would reduce dysbiosis and acute GI GVHD in children and young adult HSCT recipients.

Methods: We performed a prospective, single-center phase II study in which patients 0-34 years of age received oral, once daily 2'-FL from start of conditioning therapy until day +30 after HSCT. Patients were considered evaluable based on ≥60% compliance. Twenty-nine age- and prep-matched HSCT recipients with available samples in our institutional biorepository served as controls. Stool samples were evaluated for metabolomics by nuclear magnetic resonance (NMR) and for the microbiome by metagenomic shotgun sequencing before transplant (baseline) and days +7, +14, and +28 after HSCT. Urine 3-indoxyl sulfate (3-IS) was measured at baseline and day +7 as a surrogate of dysbiosis, with lower urine 3-IS levels suggesting greater dysbiosis (Weber et al., *Blood*, 2016). Plasma regulatory islet 3α (reg3α) and suppressor of tumorigenicity (ST2) levels were measured via enzyme-linked immunosorbent assay (ELISA) at baseline and day +7.

Results: Seventy patients, median age 8.8 years (range 0.5-33.5 years), were enrolled, of which 43 were evaluable based on compliance to 2'-FL (**Table 1**). Shannon diversity, a measure of species richness and abundance, was preserved in 2'-FL recipients longitudinally compared to a significant decline from baseline to day +28 in controls (p=0.04) (**Figure 1A**). Generalized linear mixed model (GLMM) analysis accounting for antibiotic exposure demonstrated significantly higher association of *Bifidobacteria* species and *Blautia* species with 2'-FL treatment (adjusted p<0.05), representing a favorable gut microbiome (**Figure 1B**). Urine 3-IS was higher at day +7 in 2'-FL recipients compared to controls (p=0.003), supporting reduced dysbiosis (**Figure 2**). Predominance of known anti-inflammatory fecal metabolites was observed in 2'-FL recipients at day +7, including higher aspartate (p=0.02), isoleucine (p=0.005), phosphocholine (p=0.007), taurine (p=0.04), and tyrosine (p=0.05) compared to controls (**Figure 3**). Median plasma reg3α levels were 5.5 ng/mL (range 0.02-46.8 ng/mL) in 2'-FL recipients and 9.9 ng/mL (range 0.02-99.5 ng/mL) in controls (p=0.05). Median ST2 levels were 18.1 ng/mL (range 7.8-200.0 ng/mL) in 2'-FL recipients and 37.5 ng/mL (range 20.5-200.0 ng/mL) in controls (p=0.038). Incidence of day +100 acute GI GVHD was 2% in 2'-FL recipients compared to 17% in controls (p=0.035). Adenovirus reactivation was 0% in 2'-FL recipients compared to 17% in controls (p=0.009), similar to our human milk study (**Table 1**). No increase in bloodstream infections was observed in 2'-FL recipients compared to controls, further confirming the 2'-FL safety profile.

Table 1. Patient Demographics and HSCT Outcomes in Evaluable 2'-FL Recipients and Controls.

Variable	2'-FL N=43 (%)	Control N=29 (%)	P value

Table 1. Patient Demographics and HSCT Outcomes in Evaluable 2'-FL Recipients and Controls.

Sex			
Male	27 (62.8)	19 (65.6)	>0.99
Female	16 (37.2)	10 (34.4)	>0.99
Age (years)			
0-5	16 (27.2)	13 (44.8)	0.63
5.1-10	12 (27.9)	6 (20.7)	0.59
>10	15 (34.9)	10 (34.5)	>0.99
Underlying Diagnosis			
Malignancy	15 (34.9)	14 (48.3	0.33
Immune Dysregulation	12 (27.9)	6 (20.7)	0.58
Bone Marrow Failure	11 (25.6)	5 (17.2)	0.56
Non-Malignant	5 (11.6)	2 (6.9)	0.69
Hematology	0 (0.0)	2 (6.9)	0.16
Genetic/Metabolic			
Conditioning Regimen			
Myeloablative	29 (67.4)	24 (82.8)	0.18
Reduced Intensity	14 (32.6)	5 (17.2)	0.18
HLA match			
≥2 antigen mismatch	6 (14.0)	5 (17.2)	0.74
9/10	10 (23.3)	6 (20.7)	>0.99
10/10	27 (62.7)	18 (62.1)	>0.99
Donor relation			
Related	16 (37.2)	13 (44.8)	0.63
Unrelated	27 (62.8)	16 (55.2)	0.63
Stem cell source			
PBSC	9 (20.9)	6 (20.7)	>0.99
Cord blood	6 (14.0)	3 (10.3)	0.72
Bone marrow	28 (65.1)	20 (69.0)	0.80
Acute GVHD prophylaxis			
Calcineurin inhibitor-based	19 (44.2)	11 (38.0)	0.63
T-cell depletion	4 (9.3)	5 (17.2)	0.47
Abatacept to standard	19 (44.2)	12 (41.4)	>0.99
	1 (2.3)	1 (3.4)	>0.99

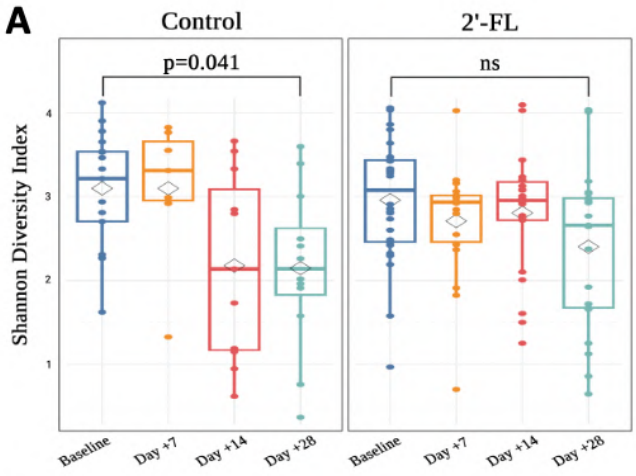
Table 1. Patient Demographics and HSCT Outcomes in Evaluable 2'-FL Recipients and Controls.

prophylaxis Post-transplant cyclophosphamide			
BSI Any BSI MBI-LCBI	5 (11.6) 1 (2.3)	4 (13.8) 2 (6.9)	>0.99 0.56
Viral reactivation Any viral reactivation EBV CMV BK polyomavirus Adenovirus HHV6	30 (69.8) 11 (25.6) 12 (27.9) 14 (32.6) 0 (0.0) 5 (11.6)	19 (65.5) 8 (27.6) 8 (27.6) 13 (44.8) 5 (17.2) 2 (6.9)	0.80 >0.99 >0.99 0.33 **0.009** 0.69
***Acute GVHD by day +100** Skin (grades I-IV) Gastrointestinal tract (grades I-IV) Liver (grades (I-IV)	 4 (9.3) 1 (2.3) 0 (0.0)	 7 (24.1) 5 (17.2) 1 (3.4)	 0.10 **0.035** 0.40

Abbreviations: HLA: human leukocyte antigen, PBSC: peripheral blood stem cell, GVHD: graft-versus-host disease, BSI: bloodstream infection, MBI-LCBI: mucosal barrier injury laboratory confirmed bloodstream infection, EBV: Epstein-Barr virus, CMV: cytomegalovirus, HHV6: human herpesvirus 6

*Acute GVHD grading is based on modified Glucksberg criteria (Glucksberg, *Transplantation*, 1974).

P values obtained with Fisher's Exact test.



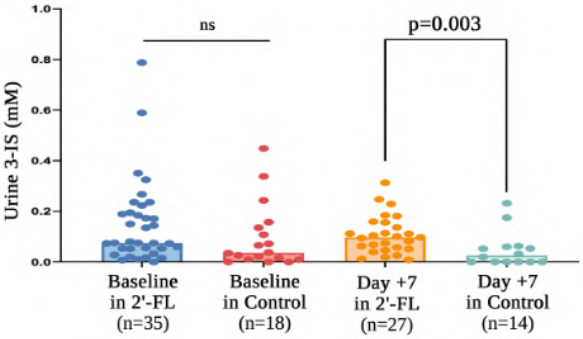


Figure 2. Urine 3-IS via NMR at day +7 in 2'-FL recipients and controls. Urine 3-IS was higher at day +7 in 2'-FL recipients compared to controls (p=0.003), supporting reduced dysbiosis in 2'-FL recipients.

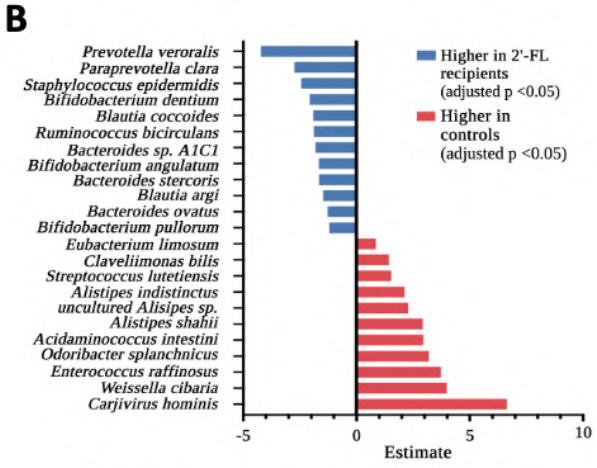


Figure 1. Metagenomic shotgun sequencing in 2'-FL recipients and controls. (A) Shannon diversity, a measure of species richness and abundance, is preserved longitudinally in 2'-FL recipients compared to a significant decline (p=0.041) in controls. **(B)** Generalized linear mixed model analysis from baseline to day +28 showing microbial species significantly associated with 2'-FL treatment (all with adjusted p <0.05). Higher *Bifidobacteria* and *Blautia* species were observed in 2'-FL recipients, representing a favorable microbiome. Time in the model is a fixed effect.

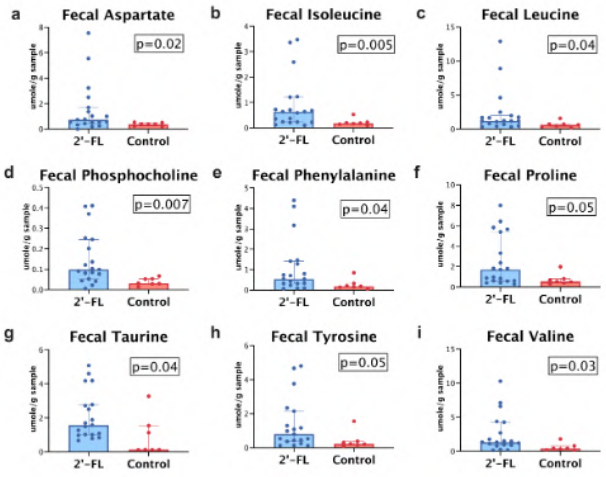


Figure 3. Fecal metabolites via NMR at day +7 in 2'-FL recipients and controls. Predominance of anti-inflammatory fecal metabolites was observed in 2'-FL recipients at day +7, including higher (**a**) aspartate (p=0.02), (**b**) isoleucine (p=0.005), (**d**) phosphocholine (p=0.007), (**g**) taurine (p=0.04), and (**h**) tyrosine (p=0.05) compared to controls.

Conclusions: Oral 2'-FL supplementation is safe and reduces peri-transplant dysbiosis and acute GI GVHD in children and young adult HSCT recipients.

Disclosure: Ashley Tuesink, PharmD serves as a medical science liaison for Sobi, Inc.

OS12-03

ITACITINIB IN COMBINATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE AND TACROLIMUS (ICT) AS GVHD PROPHYLAXIS FOR REDUCED INTENSITY MATCHED DONOR HEMATOPOIETIC CELL TRANSPLANTATION (HCT): FINAL ANALYSIS

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Background: Post-transplant cyclophosphamide (PTCy) is a cornerstone of graft-versus-host disease (GvHD) prophylaxis in reduced intensity allogeneic hematopoietic cell transplant (HCT). Still, infection and GvHD remain significant challenges. Itacitinib, a selective JAK1 inhibitor, may reduce GvHD with less impact on hematopoietic recovery than other JAK inhibitors. We conducted a single-center study (NCT05364762) evaluating the safety of adding itacitinib to PTCy-based prophylaxis with tacrolimus, for 60 or 90 days, in patients undergoing matched related or unrelated peripheral blood stem cell (PBSC) HCT following fludarabine (25 mg/m^2: days -7 to -3) and melphalan (100 mg/m^2: day -2) conditioning.

Methods: GvHD prophylaxis was PTCy (50 mg/kg: days +3 and +4), itacitinib (200 mg daily, days +5–100), and tacrolimus (starting day +6). The primary objective was to assess safety of adding fixed-dose itacitinib to PTCy-based GvHD prophylaxis with 90 (cohort 1) or 60-day (cohort 2) tacrolimus. The primary safety event (PSE) was grade 3-4 acute GvHD (aGvHD) per MAGIC criteria. Observation continued from first PTCy dose until grade 3-4 aGVHD, competing risks (relapse, NRM, DLI or second HCT), or day +100 post-HCT.

Results: Twenty patients were enrolled. Median age was 63 years (range: 56–77), 55% were male, and 80% non-Hispanic. Most patients (80%) received unrelated donor HCT. KPS was 90-100 in 16 (80%) and HCT-CI ≥ 3 in 50% (n=10). Diagnoses included AML in CR1/2 (n=8; 40%), MDS (n=7; 35%), ALL in CR1/2 (n=2; 10%), CMML (n=2; 10%), or MF (n=1; 5%). All patients achieved engraftment with median neutrophil and platelet recovery at 16 days (range: 13-25) and 27 days (range: 17-137). Grade ≥3 adverse events (AEs) at least possibly related to itacitinib included anemia (n=14), febrile neutropenia (n=3), and sepsis (n=3). Grade ≥3 thrombocytopenia occurred in 18 patients, most within 6 weeks post-HCT, a median duration of 16 days (range: 8–102), resolving without significant bleeding. No unexpected safety signals or PSEs were observed with either tacrolimus schedule. Cytokine release syndrome (CRS) occurred in 3 patients (15%; all grade 1–2). During the first 100 days, bacterial infections occurred in 35% (grade 1: 10%, grade 2: 25%), and fungal/bacterial infections in 5% (grade 1) and 20% (grade 1: 5%, grade 2: 15%) of patients, respectively. No grade 3 infections were reported.
At the median follow-up duration of 366 days (range: 358-376) for 18 survivors, 1-year overall survival (OS) and relapse-free survival (RFS) were 90% (95% CI: 66–97) and 85% (95% CI: 60–95), respectively. One-year relapse and NRM were 15% (95% CI: 4–34.0) and 0%, respectively. Day 180 grade 2-4 and 3-4 aGvHD were 10% (n=2) and 0%, respectively.

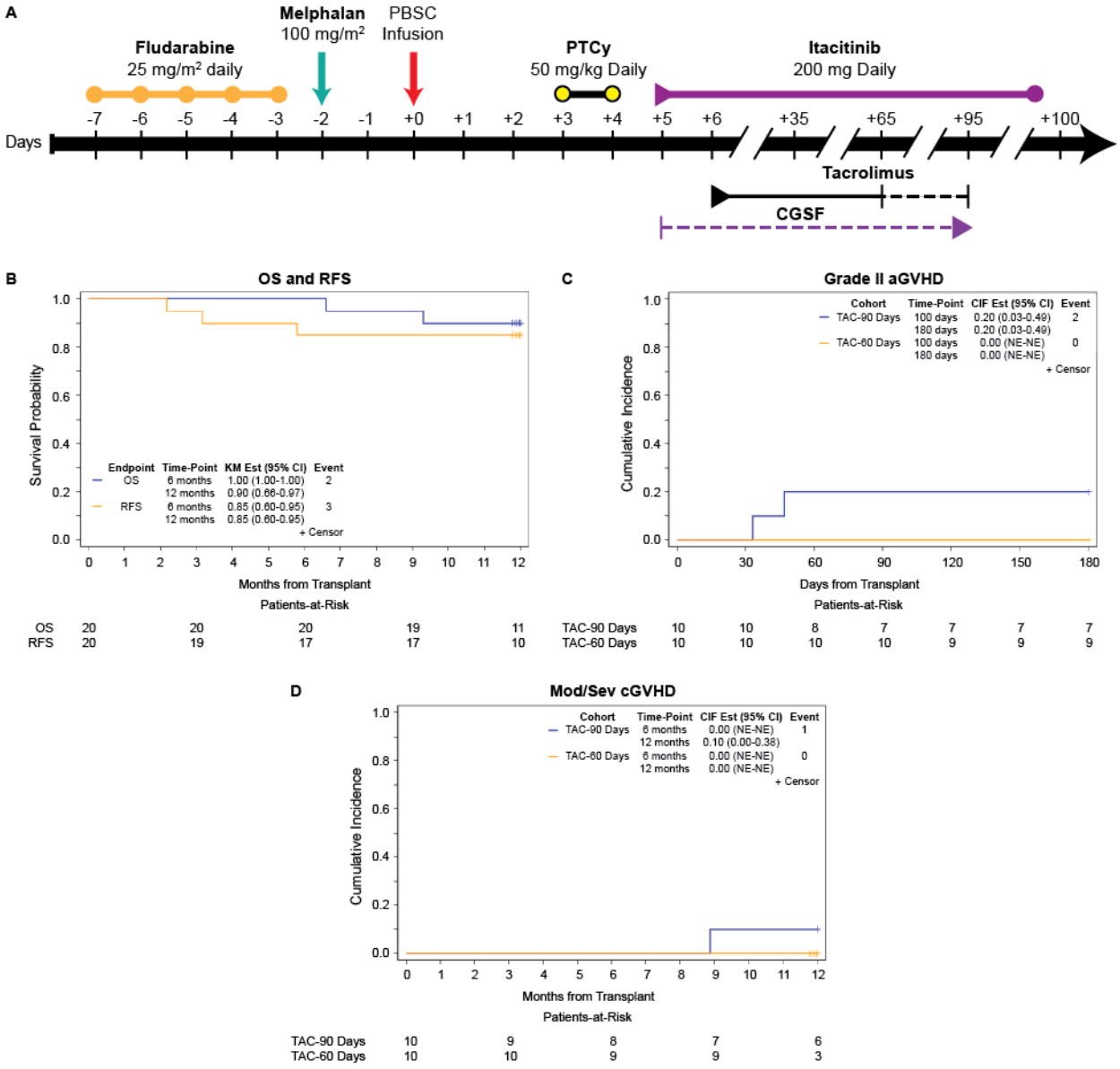
One-year moderate-severe chronic GvHD was 5% (95% CI 0–2.1), and no patient required immunosuppression at 1 year. One-year GVHD-free, relapse-free survival (GRFS) was 75% (95% CI: 50–89).

Patient and Transplant Characteristics

	TAC-90 Days (N=10)	TAC-60 Days (N=10)	Total (N=20)
Age at HCT, years Median (Range)	65 (59-77)	63 (56-68)	63 (56-77)
Gender			
Female	5 (50%)	4 (40%	9 (45%)
Male	5 (50%)	6 (60%)	11 (55%)
Ethnicity			
Hispanic or Latino	0 (0%)	3 (30%)	3 (15%)
Non-Hispanic or Non-Latino	10 (100%)	6 (60%)	16 (80%)
Not Disclosed	0 (0%)	1 (10%)	1 (5%)
Race			
Caucasian	9 (90%)	7 (70%)	17 (85%)
Black	0 (0%)	1 (10%)	1 (5%)
Asian	1 (10%)	1 (10%)	2 (10%)
Not Disclosed	0 (0%)	1 (10%)	1 (5%)
Primary Diagnosis			
ALL	0 (0%)	2 (20%)	2 (10%)
AML	6 (60%)	2 (20%)	8 (40%)
CMML	1 (10%)	1 (10%)	2 (10%)
MDS	2 (20%)	5 (50%)	7 (35%)
MF	1 (10%)	0 (0%)	1 (5%)
CMV Status			
Missing	0 (0%)	1 (10%)	1 (5%)
Negative	5 (50%)	1 (10%)	6 (30%)
Positive	5 (50%)	8 (80%)	13 (65%)
Karnofsky Performance Status			
80	3 (30%)	1 (10%)	4 (20%)
90-100	7 (70%)	9 (90%)	16 (80%)

Patient and Transplant Characteristics

HCT Comorbidity Index			
0	3 (30%)	1 (10%)	4 (20%)
1-2	3 (30%)	3 (30%)	6 (30%)
3+	4 (40%)	6 (60%)	10 (50%)
Donor Type			
MRD	2 (20%)	2 (20%)	4 (20%)
MUD	8 (80%)	8 (80%)	16 (80%)



Conclusions: Adding itacitinib to PTCy and tacrolimus-based GVHD prophylaxis (ICT) was safe and well-tolerated, with low GVHD rates, no NRM, and promising 1-year survival. These results support further study of JAK1 inhibition with the PTCy platform to optimize immune tolerance post-HCT.

Clinical Trial Registry: NCT05364762

Disclosure: Monzr M. Al Malki: Ossium Health, Inc., Gilead, Gamida Cell, Jazz Pharma, Incyte, TScan Therapeutics, CareDx, Tr1X, Inc.

Brian Ball: Bristol Myers Squibb, Syndax, Sanofi, Rigel
Paul Koller: Takeda, Bristol Myers Squibb, Ascentage, Novartis, Bayer, Daiichi Sankyo
Ibrahim Aldoss: Takeda, Syndax, Ascentage, Autolus, AstraZeneca, Jazz Pharma, Novartis, Pfizer, Kite, Servier, Adaptive, AbbVie, Amgen
Andrew Artz: AstraZeneca, Abbvie, Daichii Sankyo
Guido Marcucci: Patents concerning aspects of BN-CD38 technology
Stephen Forman: Allogene
Ryotaro Nakamura: Omeros, Pfizer, Ono Pharmaceutical, Sanofi, Blue Bio, Miyarisan Pharmaceutical
Haris Ali: GSK, Karyopharm, PharmaEssentia, Sobi, Incyte

OS12-04

ENDOTHELIAL DYSFUNCTION AND IMMUNE ACTIVATION INTERACT AND DETERMINE MORTALITY IN ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: Severe acute graft-versus-host disease (aGVHD) is a life-threatening complication after allogeneic stem cell transplantation (alloSCT). We tested the hypothesis that simultaneous immune activation and endothelial dysfunction shape survival outcomes in aGVHD.

Methods: In the training cohort, 1,332 allografted patients provided informed consent; the cumulative incidence of any-grade aGVHD by day +180 was 43.4% (n = 512), grade 3–4 aGVHD 22.6% (n = 260), and steroid-refractory aGVHD 10% (n = 114). Cohort IA comprised 321 patients with serum for biomarker assessment obtained ≤14 days before aGVHD onset. In the training cohort IB, 537 patients had EASIX and CRP measured at onset. To validate our serum biomarker findings, cohort II included 125 independent patients with plasma at onset of aGVHD (CRYOSTEM/SFGM-TC); CRP and EASIX were not available. To validate the EASIX and CRP results, cohort III comprised 220 patients from Berlin and Seattle, with CRP/EASIX data at onset of GVHD; in subsets (n = 57, 61), values were also available on days +14 and +28.
Inflammatory biomarkers (Reg3a, TIM3, IL-18, CXCL9) and endothelial markers (ST2, angiopoietin-2, sCD141, CXCL8) were measured at aGVHD onset. Using random survival forests, we analyzed their association with non-relapse mortality (NRM) and overall survival

(OS) in two independent patient cohorts. In parallel, we evaluated the interdependency of C-reactive protein (CRP) as an inflammatory marker and the Endothelial Activation and Stress Index (EASIX) in a training cohort (n=537) and validated the findings in an independent cohort (n=220).

Results: Survival modeling showed that increasing inflammatory markers influenced outcome only when combined with increasing endothelial markers. This pattern was independently confirmed for IL-18 and CXCL9 when combined with any of the four endothelial markers. CRP and EASIX similarly displayed a synergistic effect on post-aGVHD outcomes. After intensified immunosuppression for severe aGVHD, endothelial markers rose between days 14–56 exclusively in patients who died within one year, but not in survivors. Patients with combined high EASIX and elevated CRP had markedly increased NRM risk in multivariable analyses in the training cohort, and this predictive power was confirmed in the validation cohort at aGVHD onset and days +14–56 after onset, both for continuous values and for pre-established cut offs (CRP>5 mg/dl, EASIX>3.57, both high: HR for NRM at aGVHD onset 7.03 (3.80-13.01, p<0.001). A direct link between endothelial and inflammatory pathology could be demonstrated by immune histology of gut biopsies from 25 severe aGVHD cases, where CRP deposition on endothelial surfaces was most pronounced in patients with high EASIX.

Conclusions: Mortality after aGVHD is driven by inflammation coupled with progressive endothelial injury. CRP binding to endothelial cells in the context of high EASIX provides a molecular explanation for the mutual enhancement of inflammatory and endothelial pathology during aGVHD.

Clinical Trial Registry: na

Disclosure: Nothing to declare

OS12-05

VEDOLIZUMAB FOR TREATING STEROID-REFRACTORY LOWER GASTROINTESTINAL ACUTE GRAFT-VERSUS-HOST DISEASE: A SINGLE-CENTER REAL-WORLD STUDY

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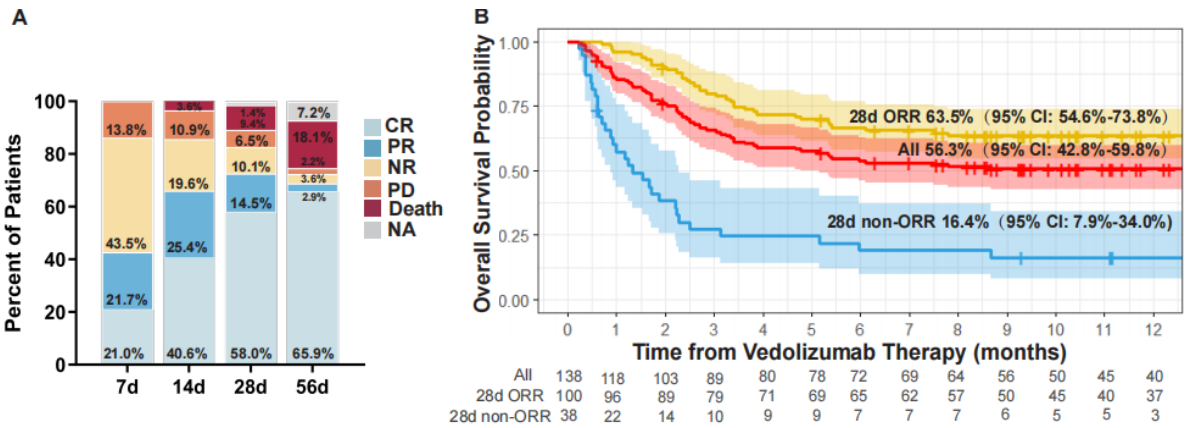
Background: Steroid-refractory lower gastrointestinal acute graft-versus-host disease (SR-LGI-aGVHD) remains a life-threatening complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Vedolizumab (VDZ), a gut-selective anti-integrin α4β7 monoclonal antibody, has shown preliminary efficacy in LGI-aGVHD by selectively inhibiting T-cell trafficking to the intestinal mucosa.

Methods: We retrospectively analyzed patients with SR-LGI-aGVHD treated with VDZ at the Institute of Hematology & Blood Diseases Hospital between January 2022 and December

2024. The primary endpoint was the lower gastrointestinal overall response rate (ORR) at day 28 after VDZ initiation. Secondary endpoints included 1-year overall survival (OS), steroid tapering, immune marker dynamics, treatment safety, and prognostic factors.

Results: A total of 138 patients received a median of two doses of intravenous VDZ (300 mg/dose). The median time from aGVHD onset to VDZ initiation was 7 days (IQR, 4-14). All patients received VDZ in combination with basiliximab, as second-line therapy in 42.8% and as third-line therapy in 57.2%. At treatment initiation, 65.2% had grade III-IV aGVHD, and 56.5% were classified as high-risk by Minnesota criteria.
The ORR at days 7, 14, 28, and 56 was 42.8% (CR 21.0%), 65.9% (CR 40.6%), 72.5% (CR 58.0%), and 68.6% (CR 65.9%), respectively. Median times to ORR and CR were 9 days (IQR, 6–14) and 19 days (IQR, 10.5-32). Sustained CR was achieved in 76.8% of patients (figure A).
Multivariable logistic regression identified older donor age (OR=2.443, 95% CI, 1.021-5.846, P =0.045), higher Minnesota risk grade at onset (OR=3.737, 95% CI, 1.026-13.613, P=0.046), and GVHD progression after VDZ initiation (OR=2.622, 95% CI, 1.017–6.757, P=0.046) as independent risk factors for failure to achieve ORR at day 28. A $CD34^+$ cell dose >3 × 10^6/kg was independently associated with a higher 28-day ORR (OR=0.300, 95% CI, 0.110-0.818, P=0.019).
After a median follow-up of 13.5 months (95% CI, 11.2-15.8), patients achieving ORR at day 28 had significantly higher 1-year OS (63.5% vs. 16.4%, P<0.001) (figure B), relapse-free survival (59.6% vs. 16.4%, P<0.001), and cumulative incidence of moderate-to-severe chronic GVHD (27.4% vs. 8.7%, P=0.049). The cumulative incidence of relapse did not differ significantly between groups (11.2% vs. 5.4%, P=0.315).
By day 28, 70.0% of patients achieved a ≥50% reduction in steroid dose from baseline (median 60 mg/day vs. 20 mg/day, P < 0.001). Compared with baseline (pre-VDZ), post-treatment peripheral blood samples showed decreased IL-5 levels (P=0.023), reduced proportions of NK cells (P=0.026) and Treg cells (P=0.019), and increased proportions of total T cells (P=0.011) and cytotoxic T lymphocytes (P=0.035).
No severe VDZ-related adverse events were observed within five half-lives (~4 months). Infections were the most common complications, including bacterial pneumonia (25.4%), gastrointestinal or urinary tract infections (21.0%), CMV viremia (18.8%) and EBV viremia (15.9%).



Conclusions: VDZ demonstrated substantial efficacy and a favorable safety profile as second- or third-line therapy for SR-LGI-aGVHD. Treatment response correlated more closely with baseline GVHD severity than the timing of intervention. VDZ was associated with a distinct immunological profile, leading to rapid and durable remission, improved survival, and reduced steroid dependence.

Disclosure: Nothing to declare.

OS12-06

RISE OF CIRCULATING ENDOTHELIAL CELLS AT ENGRAFTMENT IS A HALLMARK OF STEROID-REFRACTORY GVHD

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Background: Steroid-refractory acute graft-versus-host disease (SR-aGVHD) remains a major cause of transplant-related morbidity and mortality. Emerging evidence indicates that tissue injury in SR-aGVHD extends beyond classical target organs and reflects a systemic hyperinflammatory state. Rebound inflammation following corticosteroid withdrawal contributes further to bone marrow suppression and endothelial dysfunction, ultimately predisposing patients to severe infections and multiorgan damage. This early inflammatory cascade is predominantly driven by interferon-γ; however, the complexity of alloreactivity and the rapid expansion of immune effector cells result in a narrow therapeutic window for effective intervention. Given the central role of endothelial injury in this GVHD phenotype, we sought to characterize the temporal dynamics of circulating endothelial cells (CECs) in patients who develop SR-aGVHD.

Methods: Between July 2024 and November 2025, 54 adult patients undergoing allogeneic stem cell transplantation were prospectively analyzed. CECs were determined in peripheral blood samples at predefined time points: before conditioning, after conditioning, on day +7, at engraftment, on day +28, and at the onset of GVHD. All patients provided written informed consent. CECs were identified and quantified by flow cytometry. Changes in CECs over time were quantified using fold change (FC), defined as the ratio between CEC values measured at hematopoietic regeneration and day 0. FC values were summarized as medians with interquartile ranges (IQR). Comparisons between patients with SR-aGVHD and those without SR-aGVHD were performed using the Mann–Whitney U test (two-sided).

Results: 54 patients were included in the analysis; 19 (35%) were female, and the median age was 55 years. The median duration of follow-up was 9.7 months (interquartile range, 6.5–13.1 months). Twelve patients developed SR-aGVHD. Baseline characteristics were well balanced between patients with SR-aGVHD and those without, with no significant differences in disease-related variables, donor type, conditioning strategy, or the incidence of engraftment syndrome.
Median baseline CEC levels before conditioning were comparable between patients who later

developed SR-aGVHD (33.5/ml) and those who did not (29/ml). At day 0, median CEC counts were lower in patients with SR-aGVHD (37/ml) compared with patients without SR-aGVHD (68/ml).
At engraftment, patients with SR-aGVHD exhibited higher median CEC levels (167/ml vs. 127/ml) and a markedly greater relative increase from day 0 (4.5-fold vs. 1.8-fold). Following engraftment, patients without SR-aGVHD demonstrated a progressive decline in CECs, whereas patients with SR-aGVHD showed a continued rise. Although absolute CEC values were influenced by previous therapies, conditioning intensity, infectious complications, the dynamic increase at engraftment emerged as a distinctive feature of SR-aGVHD. Median fold change was higher in patients with SR-aGVHD compared with those without SR GVHD (SR: 2.85 [IQR 1.1–9.0], n=12; non-SR: 1.0 [IQR 0.5–2.0], n=42; Mann–Whitney U test, two-sided p≈0.01.

Conclusions: Our findings demonstrate that a pronounced rise in circulating endothelial cells at engraftment represents a robust biological hallmark of SR-aGVHD. This dynamic biomarker may allow preemptive identification of patients at risk for SR-aGVHD. Endothelial injury occurring before and after transplantation likely contributes to an endothelial-driven GVHD phenotype, supporting the need for refined disease classification and therapeutic strategies.

Disclosure: Nothing to declare.

OS12-07

POST-TRANSPLANT CYCLOPHOSPHAMIDE DOSE REDUCTION WITHIN AN ENTIRELY CALCINEURIN AND MTOR INHIBITOR-FREE GVHD PROPHYLAXIS REGIMEN: INTERIM RESULTS OF THE ABC PHASE I-IIB TRIAL

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Background: Optimal graft-versus-host disease (GvHD) prevention following allogeneic hematopoietic stem cell transplantation (AHSCT) should be effective, well tolerated, and of limited duration to allow timely immune reconstitution and, when appropriate, early introduction of maintenance therapy. As such, we evaluated a calcineurin- and mTOR inhibitor-free platform combining post-transplant cyclophosphamide (PTCy), bortezomib and abatacept. We herein report the interim results of the ABC phase I-II clinical trial.

Methods: Patients undergoing peripheral blood AHSCT for hematological malignancy were enrolled into 2 cohorts: matched (related or unrelated) and mismatched (7 out of 8) donor

transplants. Conditioning regimens consisted of fludarabine and busulfan (2 days) or fludarabine, busulfan (3 days) and thiotepa. rATG, 5mg/Kg total dose, split over days -4 to -2, was added in unrelated donor recipients. GvHD prophylaxis included PTCy (50mg/Kg, days +3 and +4), bortezomib (1.3mg/m², days 0 and +3) and abatacept 10mg/Kg. During phase I, abatacept was escalated in standard 3+3 design: 1 dose on day +5, 2 doses on days +5 and +14, and 3 doses on days +5, +14 and +28. No dose limiting toxicity occurred and the three-dose regimen was adopted for phase II. After the first 25 patients, the protocol was amended, decreasing PTCy to 37.5mg/Kg/dose. Survival outcomes were estimated by Kaplan–Meier analysis. Estimated cumulative incidence (ECI) was calculated using Gray's competing risk model.

Results: 58 patients have been enrolled with median follow-up of 13.2 months. Patient characteristics are summarized in Table 1. Median time to ANC and platelet engraftment was significantly shorter with reduced-dose PTCy compared with full-dose (15 vs 17 days, p=0.003 and 22 vs 25.5 days, p=0.04, respectively). Two patients have not achieved platelet engraftment. No primary or secondary graft failure occurred. Four patients, all receiving full-dose PTCy, experienced poor graft function; three requiring CD34+ boost. There were no differences in CD3+, CD4+, CD8+ or CD19+ cell recovery between the two PTCy groups (Figure 1a). Natural killer (NK) cell recovery was comparable at days +30 and +100. However, by day +180, NK cell count was higher for patients with full-dose PTCy (p=0.006). The incidence of *CMV, EBV and adenovirus reactivation requiring intervention were 31%, 17.2% and 3%, respectively.* Day +180 ECI of grade II-IV acute GvHD was 4% (0.26-17.3) and 12.8% (0.0392–0.2715), p=0.49) in full-dose and reduced PTCy groups, respectively. No grade III or IV events occurred. Additionally, the 1-year ECI of moderate and severe GvHD were 12% (2.9–28.1%) and 7.6% (1.3-22%) in full and reduced-dose groups, respectively, p=0.75. The ECI of relapse and treatment related mortality at 1-year were 18.6% (8.9-31.1%) and 4.1% (0.7-12.7%), respectively. At 1-year, estimated overall survival, progression-free survival and GvHD and relapse free survival were 89.3% (77.5-95%), 77.3% (61.5-86.5%) and 69.3% (53.4-80.1%).

Table 1. Patient Characteristics

		All Enrolled n=58	PTCy 50mg/kg n=25	PTCy 37.5mg/kg n=33
Age (years)	Median (range)	59 (24-76)	59 (24-68)	59 (27-76)
Sex	Male, Female	33, 25	9, 16	24, 9
Disease	AML	31	16	15
	MDS	10	5	5

	NHL	8	4	4
	Others	9	0	9
Disease Risk Index	Low	2	0	2
	Intermediate	34	16	18
	High or Very High	22	9	13
Disease Status	CR1	38	18	20
	CR2+	8	3	5
	Active Disease	12	4	8
Donor	MRD	10	9	1
	MUD	32	13	19
	MMUD (7 out of 8)	16	3	13
Conditioning Regimen	Flu, Bu, TT, rATG	19	5	14
	Flu, Bu, rATG	29	11	18
	Flu, Bu, TT	7	6	1
	Flu, Bu	3	3	0

Figure 1. Immune Reconstitution by PTCy Dose and Survival Outcomes

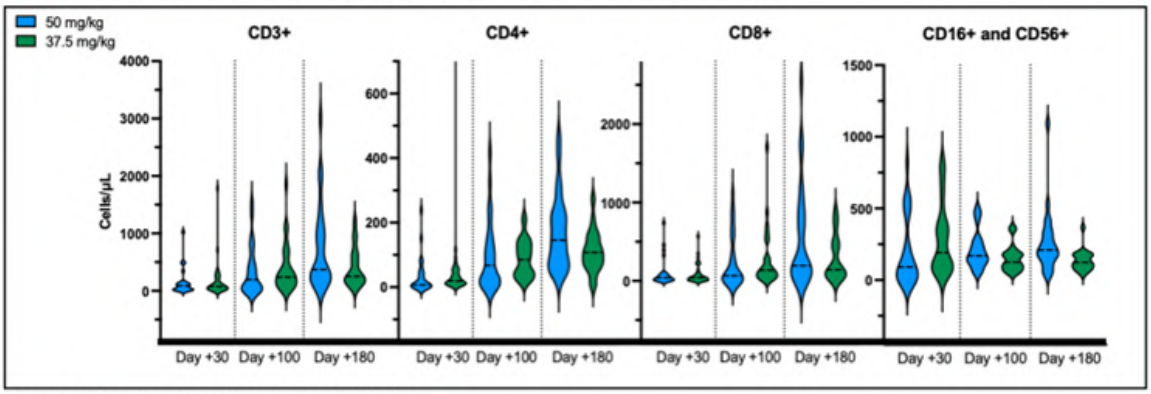

Figure 1a. Immune Reconstitution by PTCy Dose

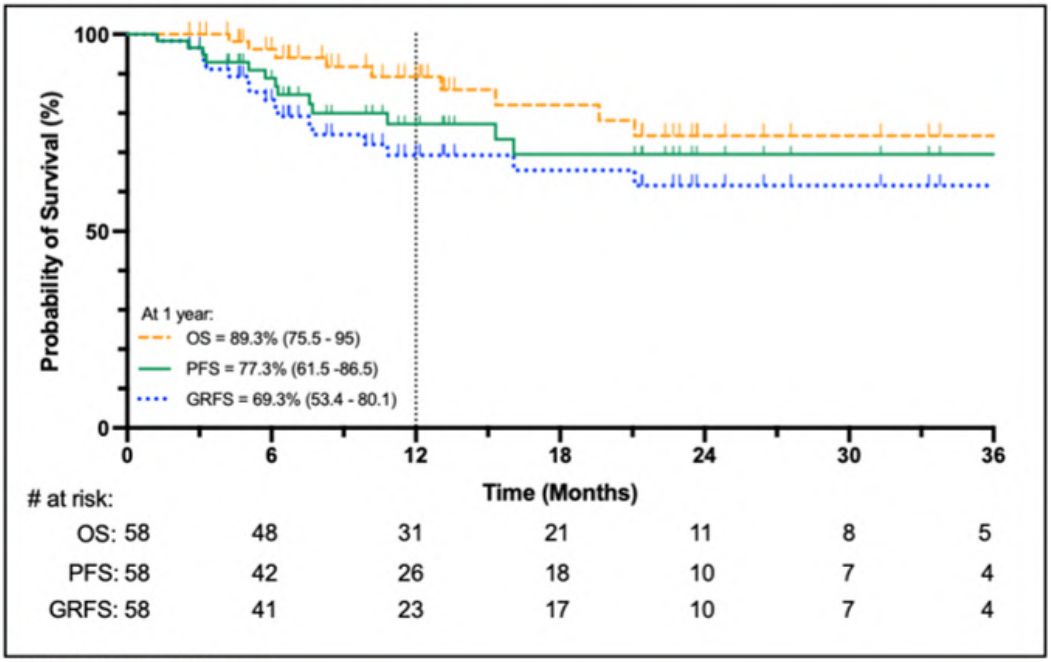

Figure 1b. Survival Outcomes

Conclusions: ABC is an effective, non-toxic and short-duration GvHD prevention that is entirely calcineurin- and mTOR inhibitor–free. Reducing the dose of PTCy resulted in faster engraftment without negatively affecting the incidence of acute or chronic GvHD. This did not translate into enhanced recovery of CD3+, CD4+, CD8+ and CD19+ lymphocyte subsets.

Clinical Trial Registry: NCT06681922

Disclosure: Maher Abdul-Hay: Advisory boards: Incyte, Daiichi, Servier, Amgen, Novartis, Autolus; Consultancy: Abbvie, PureTech. No other disclosures to report.

OS12-08

PREDICTIVE, TARGETABLE, SCALABLE: SIGNALING LYMPHOCYTE ACTIVATION MOLECULE FAMILY 7 (SLAMF7) IS DIFFERENTIALLY EXPRESSED AT SITES OF ACUTE GRAFT-VERSUS-HOST DISEASE AND CONFERS A FAVORABLE CLINICAL OUTCOME

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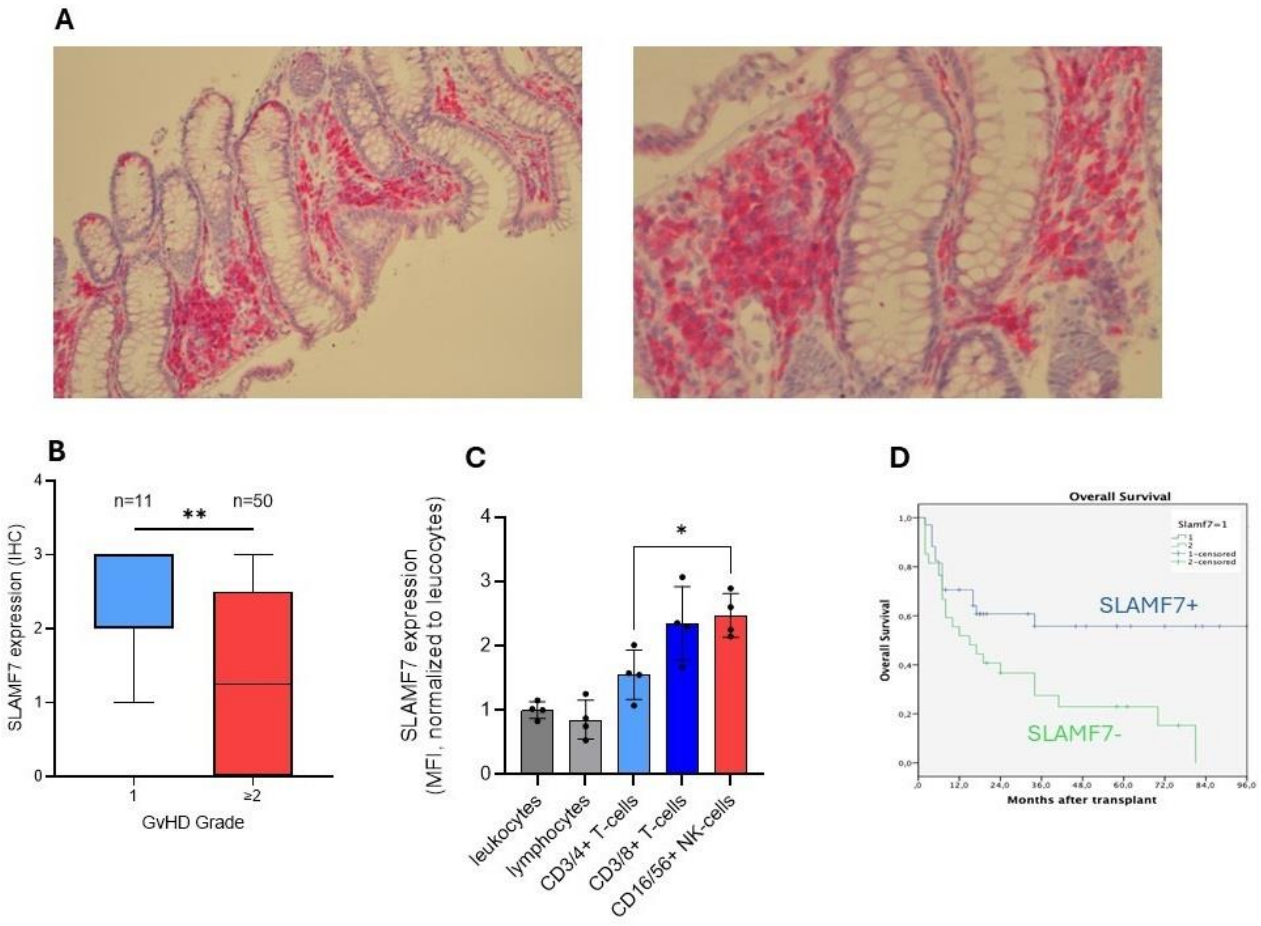
Background: Graft-versus-host disease (GvHD) is a major barrier for therapeutic success after allogeneic hematopoietic stem cell transplantation (allo-HCT). The identification of potentially actionable targets and biomarkers to predict outcomes and provide personalized treatments for GvHD is still an unmet need. SLAMF7 belongs to a group of heterophilic cell surface receptors expressed in a wide range of immune cells, including B-, T-, NK- cells as well as monocytes and macrophages (Zhang, Z., et al., 2025). Here, to our knowledge for the first time, we investigate the role of SLAMF7 in acute GvHD (aGvHD).

Methods: We consecutively analyzed 61 HCT recipients with aGvHD transplanted at our institution between 2014 and 2024. SLAMF7 was stained using immunohistochemistry (IHC) on histological specimens from the most easily accessible aGvHD-involved organ and expression levels were graded by an expert pathologist on a scale from 0 (no expression) to 3 (ubiquitous expression). We further defined a SLAMF7-negative (expression score 0-1) as well as a SLAMF7-positive (expression score 2-3) subgroup and compared these subgroups with respect to histologic aGvHD grade, overall survival and potentially confounding variables. SLAMF7 expression was also measured in the peripheral blood cells using a flow-cytometry based assay. Therefore, peripheral blood mononuclear cells were stained for CD45, CD3, CD4, CD8, CD16, CD56 and SLAMF7 to determine differences in SLAMF7-expression among lymphocyte subsets.

Results: Of 61 patients, 34 patients were classified as having SLAMF7-positive and 27 as having SLAMF7-negative aGvHD using the above described IHC-based grading approach (figure 1A). Median recipient and donor age were well balanced between the two groups. There was a numerically predominance of male patients in both cohorts, but without statistically significant differences. No significant differences were observed with regard to the underlying hematologic disease, conditioning regimens, GvHD-prophylaxis, CMV-serostatus or donor-selection.
Comparing SLAMF7-expression with the respective GvHD grade revealed an inverse correlation, with lower SLAMF7-expression in histologically higher-grade GvHD. SLAMF7-expression in Lerner-grade I GvHD was significantly higher than in Lerner-grade II-IV (figure

1B). Flow-cytometry based analysis of peripheral blood samples from patients with SLAMF7-positive aGvHD revealed cytotoxic T- and NK-cells as main reservoir for SLAMF-7 expression (figure 1C). Caplan-Meyer analysis demonstrates a significant better 5-year overall survival of the SLAMF7 positive cohort (55,7 %± 9,2% compared to 22,9% ± 8,6% in patients with GVHD without SLAMF7 expression (p<0,014). Intriguingly, SLAMF7 negativity conferred a detrimental prognostic impact with a median overall survival of only 18 months and no long-term survivors (figure 1D).



Conclusions: SLAMF7 is expressed on inflammatory cells in a significant subset of patients with aGvHD. High SLAMF7 expression might limit tissue destruction as evidenced by a significant lower histological aGvHD grade in this subgroup. Expression of SLAMF7 might be considered as a new and independent prognostic factor and potential therapeutic target in patients with aGvHD.

Disclosure: Nothing to declare.

OS16-01

BELUMOSUDIL FOR CHRONIC GRAFT-VERSUS-HOST DISEASE IN CHILDREN UNDER 12: A RETROSPECTIVE ANALYSIS OF EFFECTIVENESS AND SAFETY

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Background: Chronic graft-versus-host disease (cGVHD) in children occurs in 30% to 70% of cases after allogeneic hematopoietic stem cell transplantation (allo-HSCT), often involving multiple organs, leading to growth disorders and decreased quality of life. The traditional treatment regimen mainly consists of steroids combined with calcineurin inhibitors (CNIs), but about 50% of patients respond poorly, and long-term side effects are significant. Belumosudil, the first selective ROCK2 inhibitor, was approved by the FDA in 2021 for patients aged ≥12 years, but data for patients under 12 years old are scarce.

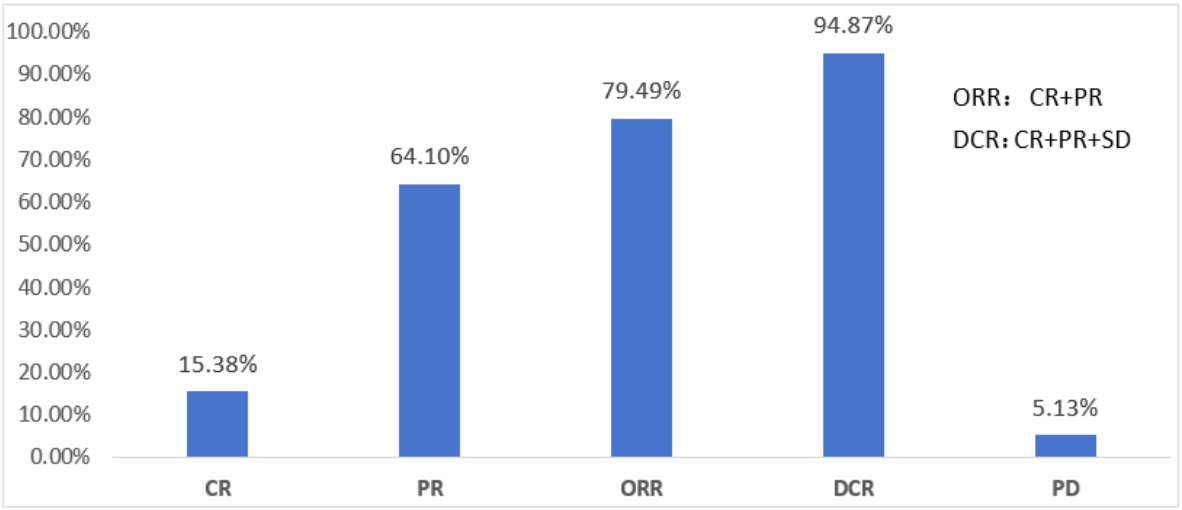
Methods: This study adopted a single-center retrospective observational design, including 39 children aged ≤12 years with cGVHD diagnosed according to the 2014 National Institutes of Health (NIH) consensus criteria and who had failed at least one line of systemic treatment. All children received Belumosudil Mesylate for at least 4 weeks, with the dose adjusted according to body weight (<30kg children received 100mg once daily, ≥30kg children received 200mg once daily). Immunosuppressive agents used in combination were tapered gradually after the onset of effect of Belumosudil.

Results:

Feature	**Data**
Total number of cases	39 cases
Median age	8 years (range: 3–12 years)
Gender ratio	Male: 28 cases (71.8%), Female: 11 cases (28.2%)
Primary disease	Thalassemia: 34 cases (87.2%), Aplastic anemia: 4 cases (10.3%), Pyruvate kinase deficiency: 1 case (2.6%)
Type of transplantation	Haploidentical: 29 cases (74.3%), Unrelated fully matched: 8 cases (20.5%), Sibling fully matched: 2 cases (5.1%)
Median time from transplantation to cGVHD diagnosis	12 months (range: 3–24 months)

Median number of organs involved	2 organs
Proportion of organ involvement	Skin (69.2%), Eye (46.2%), Liver (33.3%), Lung (33.3%), Oral cavity (30.8%), Nail (25.6%), Gastrointestinal tract (15.4%), Joint/fascia (12.8%)
Multorgan involvement (≥2 organs)	28 cases (71.8%)
Previous treatment failure	All patients had previously received at least one immunosuppressive agent (such as steroids, FK506, ruxolitinib, sirolimus, etc.) and failed or had poor response before using Belumosudil

Fig 1 Response Rates



1. Disease Patterns : Skin involvement (69.2%) was the most common, followed by pulmonary (33.3%), ocular (46.2%), and hepatic (33.3%) manifestations. 71.8% of patients had multi-organ involvement (≥2 organs).

2. Therapeutic Efficacy :

12. The overall response rate (ORR) was 79.5% (31/39) at 12 weeks and 84.6% (33/39) at 6 months. Organ-specific responses were heterogeneous:
13. Skin/Nail manifestations showed the highest response (80.0% at 12 weeks, improving to 85.7% by 6 months).
14. Pulmonary symptoms exhibited progressive improvement (from 60.0% to 80.0%).
15. Ocular and hepatic involvement had delayed responses (from 40.0% to 60.0% for ocular; from 33.3% to 50.0% for hepatic).

16. Notably, hepatic and articular responses required over 6 months for partial remission, underscoring the need for extended treatment patience.

3. Critical Modulators of Response : Early initiation of belumosudil (≤3 months post-cGVHD onset) achieved 90.0% efficacy versus 50.0% with delayed treatment (>3 months). The response rate of early intervention for lung symptoms was 100%, while only 20.0% of patients with delayed treatment responded.
4. Treatment Resistance : Four failures occurred in patients with advanced pulmonary disease (2 cases, 1 fatal), multi-organ involvement with late intervention (>12 months), or severe hepatic dysfunction (AST >200 U/L).
5. Mechanistic Implications : The rapid response in skin and lung symptoms may suggest an antifibrotic effect potentially associated with Th17-related pathways, while delayed hepatic remission could reflect slower pathological processes.

Conclusions: Belumosudil is a highly effective and safe therapeutic agent for children under 12 with difficult-to-treat cGVHD. It exhibits strong anti-fibrotic activity, leading to high response rates in the skin, joints, and other fibrotic tissues. Our findings strongly suggest that early intervention is a key determinant of success, especially for visceral cGVHD of the liver and lungs. Belumosudil represents a pivotal advancement and should be considered a preferred second-line option for this vulnerable patient population.

Disclosure: Nothing to declare

OS16-02

EFFICACY AND SAFETY OF AXATILIMAB IN JAPANESE PATIENTS WITH RECURRENT OR REFRACTORY CHRONIC GRAFT-VERSUS-HOST DISEASE AFTER AT LEAST 2 PRIOR LINES OF SYSTEMIC THERAPY

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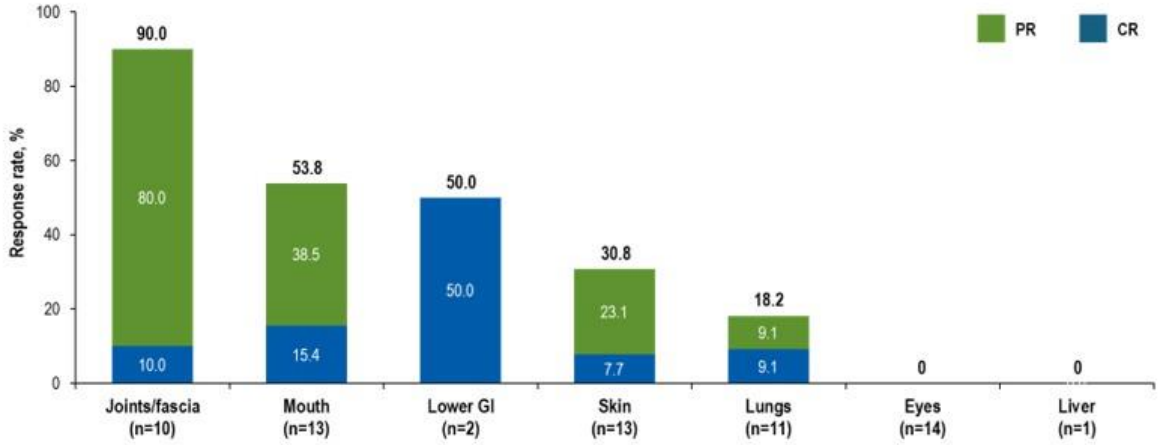
Background: Chronic graft-versus-host disease (cGVHD) is a major cause of morbidity and nonrelapse mortality among patients who undergo allogeneic hematopoietic stem cell

transplantation. Colony-stimulating factor 1 receptor (CSF-1R)–dependent monocytes and macrophages potentiate inflammation and fibrosis, contributing to multiorgan damage. Axatilimab is a high-affinity monoclonal antibody targeting CSF-1R. In the pivotal phase 2 AGAVE-201 study (NCT04710576), axatilimab 0.3 mg/kg every 2 weeks (Q2W) demonstrated clinical benefit and was generally well tolerated in patients with cGVHD. This analysis describes the results of a phase 3 study (NCT06263478) evaluating the efficacy and safety of axatilimab in Japanese patients with recurrent or refractory cGVHD.

Methods: In this phase 3, open-label, multicenter study, Japanese patients aged ≥6 years with recurrent or refractory cGVHD after ≥2 prior lines of therapy received intravenous axatilimab 0.3 mg/kg Q2W for ≤24 months. The primary endpoint was overall response rate (ORR) in the first 6 treatment cycles per the National Institutes of Health 2014 Consensus Criteria. Secondary endpoints included organ-specific responses, percent reduction in average daily dose of corticosteroids, symptom improvement (defined as a ≥7-point reduction in the modified Lee Symptom Scale [mLSS]), and safety and tolerability.

Results: Among the 21 patients enrolled, median (range) age and weight were 53.0 (7–63) years and 50.4 (19.0–75.5) kg, respectively; 61.9% of patients were male. Median (range) time from cGVHD diagnosis to Cycle 1 Day 1 was 33.0 (5.6–128.6) months. Patients received a median of 3 prior lines of therapy (range, 2–6); 19 (90.5%) were refractory to their last cGVHD therapy. Patients had a median (range) of 3.0 (1–5) involved organs at baseline, and 71.4% of patients had severe cGVHD at study entry. ORR (95% CI) in the first 6 cycles was 71.4% (47.8%–88.7%; all partial responses); at the analysis cutoff, no patients with a response had progressive disease, and all patients with a response were still on treatment. Median (range) time to first response was 1.9 (1.0–5.6) months. Among 20 patients with baseline mLSS assessments, 10 (50.0%) reported a ≥7-point improvement in their symptoms on study. Organ-specific responses in the first 6 cycles are reported in the Figure. Among 20 patients receiving corticosteroids at baseline, mean (SD) average daily dose was 21.4 (13.9) mg/d. Among the 18 patients receiving axatilimab and systemic corticosteroids up to Day 168, 11 patients (61.1%) reduced their average daily corticosteroid dose from baseline, and 1 patient (5.0%) tapered off corticosteroids by Day 140. Twenty patients (95.2%) experienced treatment-emergent adverse events (TEAEs); 8 (38.1%) had grade ≥3 TEAEs. Six patients (28.6%) had treatment-related TEAEs; all treatment-related TEAEs were grade 1/2 and not serious. No TEAEs led to dose reduction or treatment discontinuation. TEAEs of any grade occurring in >15% of patients were nasopharyngitis (n=7, 33.3%); influenza (n=5, 23.8%); and diarrhea, headache, peripheral edema, and pruritus (n=4 each, 19.0%).

Figure. Organ-Specific Responses* in the First 6 Cycles per 2014 NIH Consensus Criteria



CR, complete response; GI, gastrointestinal; NIH, National Institutes of Health; ORR, overall response rate; PR, partial response.
Denominators include patients with organ involvement in the first 6 treatment cycles. Differences in percentage totals are due to rounding.
* No patients had esophageal or upper GI involvement.

Conclusions: Axatilimab 0.3 mg/kg Q2W demonstrated clinical benefit and was well tolerated in Japanese patients with recurrent or refractory cGVHD.

Clinical Trial Registry: NCT06263478
Clinicaltrials.gov

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OS16-03

IMPACT OF GRAFT-VERSUS-HOST DISEASE ON THE MAIN OUTCOMES FOLLOWING ALLOGENIC HEMATOPOIETIC STEM CELL TRANSPLANTATION BASED ON EX-VIVO ALPHA BETTA T CELL DEPLETION

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Background: Acute and chronic graft-versus-host disease (GVHD) directly or indirectly accounts for up to 40% of mortality after hematopoietic stem cell transplantation (HSCT) in hematological malignancies. One of the most promising methods for processing hematopoietic cell transplants to reduce the risk of GVHD is the depletion of TCRαβ T-lymphocytes. However, the impact of clinically significant GVHD on the main HSCT outcomes when TCRαβ depletion is used is not fully studied. To this end, we analyzed the impact of GVHD on overall and event-free survival, relapse risk, and transplant-related mortality in HSCT from unrelated and haploidentical donors using TCRαβ depletion as the primary GVHD prevention strategy.

Methods: The analysis included 438 patients (median age 8,7y) with ALL, n=236 and AML, n=202, who received their first allogeneic HSCT from an unrelated or haploidentical donor using TCRαβ depletion as the primary method for GVHD prevention from May 2012 to February 2022. The main characteristics of the group are presented in Table 1.
The median follow-up was 4.5 years (0.5 – 10). Landmark analysis (LA) was used to study the impact of GVHD on HSCT outcomes. The analysis included patients who survived to a specific point in time without significant events (relapse, transplant-associated death). For acute GVHD, the reference point was day +35, and for chronic GVHD, it was day +100. On day +35 - 414 patients were alive and leukemia-free, on day +100 336 patients were alive and leukemia-free.

Table 1 Clinical Characteristics of Patients

Remission status	CR1	181	41%
	>CR1	191	44%
	AD (all AML)	66	15%
Conditioning regimen	TBI	156	36%
	Treo	282	64%

Donor type	MUD	79	18%
	Haplo	359	82%
Serotherapy	ATG (+)	157	36%
	ATG (-)	281	64%

Results: Primary engraftment was achieved in 98% of patients with median time to engraftment of 13 days for neutrophils and 14 days for platelets. The CI of NRM was 8 % (95%CI:5-10), of relapse 34% (95%CI:29-39).EFS and OS were 57% (95% CI, 51 - 61) and 67% (95% CI, 60 - 71) respectively.
The CI of aGvHD grade I-IV was 49% (95% CI, 44 - 53), II-IV was 21% (95% CI, 17- 23), grade 3-4 was 6% (95% CI, 4 - 8) and chronic GvHD – 15% (95% CI: 12-19).
In the LA, the development of aGVHD stage 2-4 and stage 3-4 significantly increase the risk of transplant-related mortality 18% vs 3% and 35% vs 4% , p< 0,0001 with no significant effect on the relapse rate and event-free survival. The presence of grade 2–4 and 3–4 aGVHD were associated with lower overall survival (OS 70% vs 59%, p=0.04 and 69% vs 53%, p=0.03).
Patients with CGVHD had a significantly low relapse rate 7% vs 33% with p=<0.0001 and high rate of NRM 16% (p=0,006). EFS was higher in CGVHD group 82% vs 63% with p=0,003 without effect on OS 83% vs 75%, p=0,145.

Conclusions: HSCT performed using TCRαβ depletion reduces the risks of developing acute and chronic GVHD and transplant-related mortality.
However, despite the relatively low frequency, aGVHD stage 2-4 and stage 3-4 significantly increases transplant-related mortality and reduces overall survival. cGVHD affects the risk of transplant-related mortality, but reduces the risk of relapse, with no significant effect on overall survival.

Disclosure: Nothing to declare

OS16-04

AXATILIMAB IN COMBINATION WITH RUXOLITINIB IN PATIENTS WITH NEWLY DIAGNOSED CHRONIC GRAFT-VERSUS-HOST DISEASE: UPDATED SAFETY ANALYSIS OF A RANDOMIZED, PHASE 2 STUDY

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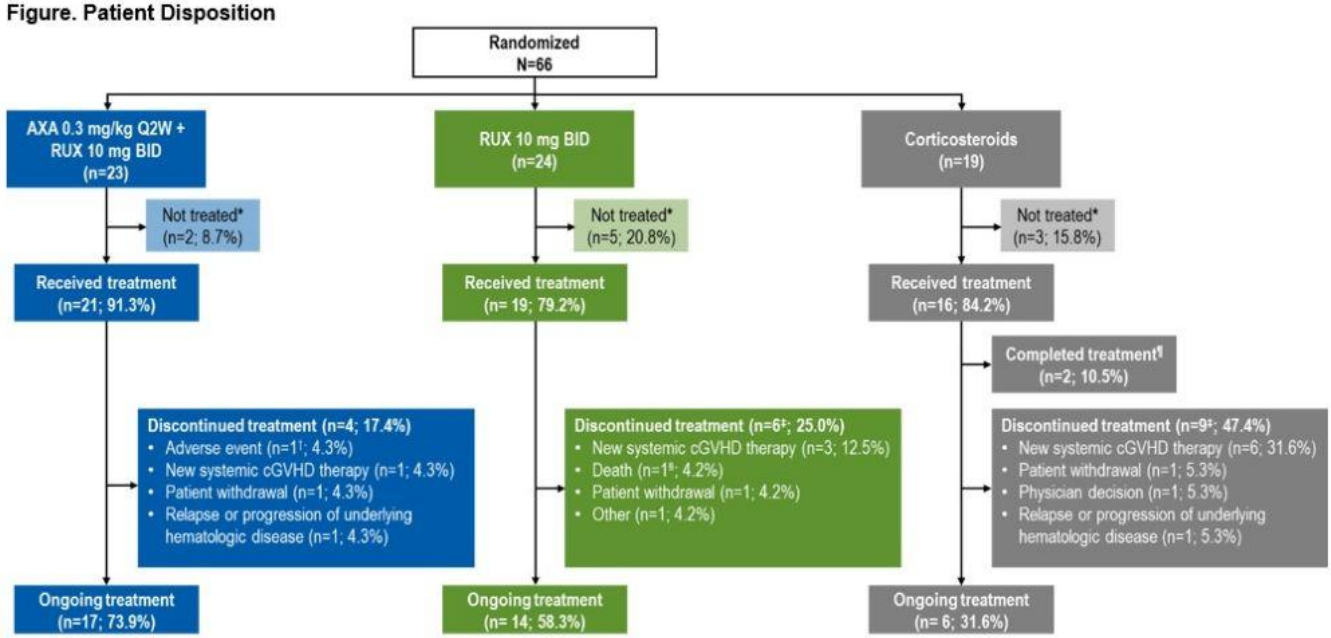
Background: Chronic graft-versus-host disease (cGVHD) is a leading cause of morbidity and nonrelapse mortality following allogeneic hematopoietic stem cell transplantation. Axatilimab (AXA), a monoclonal antibody targeting colony-stimulating factor 1 receptor (CSF-1R), depletes the monocytes and macrophages that mediate fibrosis and end-organ damage in cGVHD. Ruxolitinib (RUX) is a selective inhibitor of Janus kinase (JAK)1/JAK2, which mediate cytokine signaling, T-cell activation, and inflammation in cGVHD. Both AXA and RUX have demonstrated clinically meaningful efficacy and were generally well tolerated as single agents in previously treated cGVHD. Owing to their distinct mechanisms of action, combining AXA and RUX may improve efficacy without overlapping safety concerns. The objective of this analysis is to report on the safety of AXA and RUX combined and of RUX alone among patients with newly diagnosed cGVHD.

Methods: In this ongoing, randomized, open-label, phase 2 study (NCT06388564), eligible patients were aged ≥12 years with new onset, moderate or severe cGVHD with no prior systemic cGVHD treatment. Patients were randomized to AXA 0.3 mg/kg every 2 weeks in combination with RUX 10 mg twice daily (BID; AXA+RUX), RUX 10 mg BID, or corticosteroids for up to 24 months; randomization was stratified by cGVHD severity and use of concomitant systemic immunosuppressants. The primary endpoint is overall response at 6 months in the absence of a new systemic cGVHD therapy. Safety assessments include treatment-emergent adverse events (TEAEs). A prespecified interim safety analysis occurred after ~30 patients received ≥1 cycle of treatment.

Results: As of the data cutoff (October 3, 2025), 66 patients were enrolled (AXA+RUX, n=23; RUX, n=24; corticosteroids, n=19), and 56 patients received treatment (AXA+RUX, n=21; RUX, n=19; corticosteroids, n=16; **Figure**). The median age of enrolled patients was 65.0 years (range, 16–77), and 35 patients (53.0%) were male. The median time from transplant to diagnosis of cGVHD was 7.6 months (range, 1.7–72.3), and 31 patients (47.0%) had severe cGVHD at enrollment per the National Institutes of Health consensus criteria. Commonly involved organs included the mouth (71.2%), eyes (65.2%), and skin (62.1%). Nineteen patients discontinued treatment (AXA+RUX, n=4; RUX, n=6; corticosteroids, n=9); 1 patient in the AXA+RUX group discontinued owing to concurrent TEAEs of fatigue and anxiety. Among all treated patients, 44 experienced TEAEs (AXA+RUX, n=15 [75.0%]; RUX, n=16 [84.2%]; corticosteroids, n=13 [81.3%]), and 11 experienced grade ≥3 TEAEs (AXA+RUX, n=5 [25.0%]; RUX, n=3 [15.8%]; corticosteroids, n=3 [18.8%]). TEAEs of any grade occurring in >2 patients in a group were anemia (n=4, 20.0%) in the AXA+RUX group; anemia, increased aspartate aminotransferase (both n=4, 21.1%), decreased platelet count, diarrhea, fatigue, increased amylase, increased alanine aminotransferase, peripheral edema, pyrexia, and upper respiratory tract infection (each n=3, 15.8%) in the RUX group; and insomnia (n=4, 25.0%) and constipation (n=3, 18.8%) in the corticosteroid group. Anemia was the only grade ≥3 TEAE that occurred in 2 patients (n=1 each in AXA+RUX and RUX).

Figure. Patient Disposition



AXA, axatilimab; BID, twice daily; cGVHD, chronic graft-versus-host disease; Q2W, every 2 weeks; RUX, ruxolitinib.
* The majority of the 10 untreated patients were randomized before the data cutoff date and therefore have no dosing information reported yet.
† Treatment-emergent adverse events leading to treatment discontinuation in 1 patient were concurrent fatigue and anxiety.
‡ For ruxolitinib 10 mg BID and corticosteroids, 1 patient in each group discontinued treatment prior to receiving the first dose.
§ Death due to bronchospastic crisis and considered unrelated to treatment.
¶ Treatment is considered complete if a patient achieves a complete or partial response and completes the study treatment taper.

Conclusions: In the updated safety analysis of this phase 2 trial, the combination of AXA+RUX was well tolerated and had a similar safety profile to RUX alone, with no evidence of additive toxicity.

Clinical Trial Registry: NCT06388564
Clinicaltrials.gov

Disclosure: Robert Zeiser received honoraria from Incyte Corporation, Medac, Neovii, Novartis, Sanofi, and Therakos-Mallinckrodt. Amandeep Salhotra received research funding from Bristol Myers Squibb, Orca Bio, and Rigel Pharmaceuticals; served as a speakers bureau member for Sanofi; and served on an advisory board for Incyte Corporation and Servier. Francesca Bonifazi has served on advisory boards and received honoraria for lectures or educational events from Gilead, Kite, and Novartis. Francesca Kinsella received honoraria from Incyte Corporation, Sanofi, Therakos-Mallinckrodt, and Vertex; served on an advisory board for Incyte Corporation, Sanofi, and Vertex; and received research funding from Gilead. José Luis Piñana received advisory support for preclinical/clinical research from AstraZeneca, Gilead, GSK, Moderna, MSD, Pfizer, and Takeda and received travel support from Gilead/Kite, MSD, and Pierre-Fabré. Simon Bulley received honoraria and/or consulting fees from BDO Services, Hartley Taylor, Janssen, McKinsey and Company, Sanofi, Therakos, and Vertex. Amin M. Alousi received honoraria from Incyte Corporation. Mi Kwon served as an advisor or consultant for AbbVie and Sanofi and as a speakers bureau member for Gilead, Pfizer, and Takeda. Lucía López-Corral served as an advisor or consultant for Novartis and Sanofi. Alexander Schauwvlieghe received consulting fees from Alexion, Basilea, Gilead, MaaT

Pharma, Novartis, and Sanofi; received honoraria from Pierre-Fabré and Pfizer; received travel support from AbbVie, Gilead, and Pfizer; participated on a data safety monitoring or advisory board for Alexion, Basilea, Gilead, MaaT Pharma, Novartis, and Sanofi; and held a leadership or fiduciary role on the Treasurer Belgian Hematology Society. Albert Assad, Maureen R. Bleam, and Peixin Zhang are employees and shareholders of Incyte Corporation. Annie Im served as a consultant for Incyte Corporation and Sanofi and received research funding from Incyte Corporation.

OS16-05

EFFICACY AND SAFETY OF THE ROCK2-INHIBITOR BELUMOSUDIL FOR CHRONIC GVHD: UPDATE FROM A MULTICENTER RETROSPECTIVE ANALYSIS OF A LARGE GERMAN-AUSTRIAN COHORT OF THE BELUMOSUDIL MAP

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Background: Chronic GvHD (cGvHD) is the most significant risk factor for late morbidity and mortality after allogeneic stem cell transplantation (alloSCT). There are no standard treatment options beyond firstline corticosteroids and second-line ruxolitinib. The selective ROCK-2 inhibitor belumosudil, a novel FDA-, but not yet EMA-approved agent, has shown efficacy in phase-2 trials and has recently been made available to German and Austrian patients within a managed-access program (MAP). In this study, we analyzed the clinical benefits of belumosudil within the MAP program in the German Austrian cohort.

Methods: This updated retrospective multicenter study will include 143 patients who received belumosudil in the MAP provided by Sanofi-Aventis. Seventeen German and one Austrian transplant center contributed data to this analysis. Patients could enter the MAP

after at least two and a maximum of five prior lines of treatment (LOT) for chronic GvHD, which had to include ruxolitinib if not intolerant. Organ scoring and response assessment were performed according to the NIH-consensus criteria before start, and at month 1, 3, 6 and 12 thereafter. Events defining failure-free survival (FFS) are relapse, death or start of a new immunosuppressive agent. Adverse events are reported according to the CTCAE criteria (version 5.0). The last-follow-up was on July 31th 2025.

Results: In total, 130 patients (60% male) with a median age of 61 years (range, 20 – 77) were included into the analysis by now. Initial cGvHD presentation was quiescent onset in 57%, progressive onset in 15%, and de novo onset in 28% of patients. The cohort had undergone a median of 3 prior LOT (range, 2 – 13). Ninety-three percent of patients were refractory to the previous treatment line. Patients had a history of ruxolitinib and ibrutinib pre-treatment in 95% and 13%, respectively. At belumosudil initiation, 81% of patients presented with severe cGvHD with a median of 3 NIH-defined organ manifestations (range, 1 – 7). Belumosudil was started at a median of 28 months after alloSCT (range, 2 – 243). The objective response at one and three months was partial remission or better in 48 and 61 patients (37% and 53%), respectively. Responses were observed across all organ systems. Median time to response was 3.1 months. At six months, 47 of 80 patients evaluable showed partial remission or better (59%). Belumosudil treatment was discontinued in 21 patients (19%) and a new immunosuppressive medication was commenced in 15 patients (13%) over the complete observation time. Forty-four percent of patients were treated with steroids at belumosudil start. Steroid dose reduction was achieved in 17 of these patients (34%). FFS was 82,7% and 65,3% at six and 12 months. One-year overall survival was 89,9%. Treatment-emergent adverse reactions CTCAE grade III-IV were mostly infectious complications and occurred in 28 patients (22%).

Conclusions: This retrospective analysis of a large real-world cohort demonstrates efficacy and safety of belumosudil in refractory chronic GvHD patients. Updated results on dynamics of organ response and belumosudil combinations of 143 patients will be presented. Further prospective trials are needed to determine the duration of response and the impact on GvHD-related mortality.

Clinical Trial Registry: n.a.

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OS16-06

A COMPREHENSIVE ANALYSIS OF AXATILIMAB IN PATIENTS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE AND RELATED BRONCHIOLITIS OBLITERANS SYNDROME: INTEGRATED ANALYSIS FROM 2 CLINICAL STUDIES

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Background: Lung manifestations of chronic graft-versus-host-disease (cGVHD), particularly bronchiolitis obliterans syndrome (BOS), are associated with high morbidity/mortality and poor responses to conventional treatment. Axatilimab treatment demonstrated clinical benefit in patients with pulmonary cGVHD in a phase 1/2 study (NCT03604692) and in the pivotal AGAVE-201 study (NCT04710576). The objective of this analysis was to describe clinical outcomes of axatilimab treatment in patients with cGVHD-BOS in 2 clinical studies.

Methods: In the phase 2 dose expansion study, intravenous (IV) axatilimab 1 mg/kg every 2 weeks (Q2W) was assessed. In the pivotal AGAVE-201 study, patients were randomized to IV axatilimab 0.3 mg/kg Q2W, 1 mg/kg Q2W, or 3 mg/kg every 4 weeks (Q4W). Responses were assessed by 2014 National Institutes of Health (NIH) cGVHD consensus criteria, which included forced expiratory volume in 1 second (FEV_1) and lung symptom score. This analysis evaluated lung-specific clinical responses by baseline FEV_1 and lung symptom score, as well as improvement in modified Lee Symptom Scale shortness of breath (SOB) scores among patients with cGVHD-BOS (obstructive lung defect with FEV_1 <75% predicted, FEV_1:vital capacity ratio <0.07, evidence of air trapping, and absence of infection). Logistic regression analysis was performed to investigate factors associated with NIH lung response.

Results: Of 117 patients with cGVHD-BOS at baseline, 84.6% had prior treatment with belumosudil, ibrutinib, and/or ruxolitinib, and the median (range) number of organs involved at baseline was 4 (1–9). The median (range) patient age was 55.0 (7–76) years; 69.2% of patients were male. The NIH lung response rate on study was 38.5%; the median (range) time to first response was 2.6 (1.0–14.8) months. Response rates were 37.1% and 40.5% for patients with baseline FEV_1 >39% and ≤39%, respectively, and were 37.0% and 40.2% for patients with baseline NIH lung scores of 3 and <3, respectively (**Table**). A ≥2-point improvement in SOB at rest or with exercise was observed regardless of NIH response. Based on univariate analysis, there was no significant association between baseline clinical features (eg, lung score, FEV_1, best response to last therapy) and lung response. The most common infections among patients with cGVHD-BOS were pneumonia (n=24; 20.5%), upper respiratory tract infection (n=22; 18.8%), and COVID-19 (n=19; 16.2%), which were grade ≥3 in 17 (14.5%), 2 (1.7%), and 7 (6.0%) patients, respectively.

Table. Efficacy Outcomes by Subgroup*

Outcome	**Axatilimab (n=117)**
NIH lung-specific response by baseline characteristics, n (%) [95% CI]	
Predicted FEV_1 >39% (n=62)†	23 (37.1) [25.2–50.3]
CR, n (%)	11 (17.7)
Predicted FEV_1 ≤39% (n=37)	15 (40.5) [24.8–57.9]
CR, n (%)	1 (2.7)
NIH lung score <3 (n=87)	35 (40.2) [29.9–51.3]
CR, n (%)	17 (19.5)
NIH lung score of 3 (n=27)	10 (37.0) [19.4–57.6]

Table. Efficacy Outcomes by Subgroup*

CR, n (%)	0
≥2-point improvement from baseline in mLSS SOB at rest,‡ n (%)	
NIH responder (n=26)	4 (15.4)
NIH nonresponder (n=37)	7 (18.9)
≥2-point improvement from baseline in mLSS SOB with exercise,‡ n (%)	
NIH responder (n=42)	17 (40.5)
NIH nonresponder (n=66)	15 (22.7)

CR, complete response; FEV_1, forced expiratory volume in 1 second; mLSS, modified Lee Symptom Scale; NIH, National Institutes of Health; PR, partial response; SOB, shortness of breath.
* Best response on study. † Patients with FEV_1 ≥75% at baseline were excluded. ‡ Score range, 0–4; patients with scores of 0 at baseline were excluded.

Conclusions: Axatilimab demonstrated clinical and symptom responses in patients with cGVHD-BOS across a spectrum of lung involvement, including those with FEV_1 ≤39% and NIH lung scores of 3. Symptom responses were observed in some patients who were NIH nonresponders. There were no statistically significant differences in NIH lung response among patients with different baseline characteristics, suggesting that a broad range of patients with BOS may respond to axatilimab.

Clinical Trial Registry: NCT03604692; NCT04710576
Clinicaltrials.gov

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OS16-07

CHRONIC GRAFT-VERSUS-HOST DISEASE: REAL-WORLD OUTCOMES AND EFFICACY OF RUXOLITINIB COMPARED WITH CONVENTIONAL TREATMENTS

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Background: Chronic graft-versus-host disease (cGVHD) remains a major challenge in allogeneic hematopoietic stem cell transplantation (HSCT), affecting 30–50% of recipients and leading to significant morbidity through multi-organ involvement. Approximately 50% of patients develop steroid-refractory disease requiring second-line treatment, but no standard therapy existed until the advent of ruxolitinib, a Janus kinase (JAK) inhibitor. While ruxolitinib demonstrated superior efficacy in the phase 3 REACH3 trial, real-world data comparing its effectiveness with conventional therapies in routine clinical practice settings remain limited.

Methods: We performed a single-centre retrospective analysis of 1,026 adult allogeneic HSCT recipients transplanted between January 2014 and December 2023. Among 374 patients who developed cGVHD requiring systemic treatment, 229 required second-line therapy. Response was assessed using National Institutes of Health criteria. To evaluate the real-world efficacy of ruxolitinib and account for baseline differences between treatment groups, we conducted a propensity score-matched (PSM) analysis comparing ruxolitinib with conventional second-line agents. Covariates matched included donor age, disease-risk index, graft source, conditioning intensity, GVHD prophylaxis, cGVHD severity, and prior glucocorticoid use in first-line therapy.

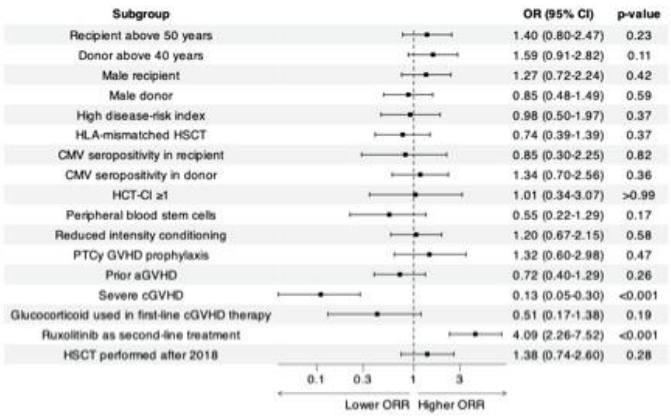
Results: Among 229 cGVHD patients requiring second-line treatment, 125 (55%) received ruxolitinib and 104 (45%) received conventional agents, primarily thalidomide (54%) and sirolimus (14%). For the whole cohort, severe cGVHD was associated with significantly inferior ORR (odds ratio, OR: 0.13; 95% confidence interval, CI: 0.05–0.30; P<0.001), while ruxolitinib treatment was associated with significantly superior ORR (OR: 4.09; 95% CI 2.26–7.52; P<0.001) (Figure 1A).
In the balanced PSM cohort, 66 patients were included in each of the conventional and ruxolitinib group (Table 1). Ruxolitinib, compared with conventional treatment, led to significantly higher ORR (68% versus 39%, P<0.001), superior failure-free survival (hazard ratio, HR: 0.37; 95% CI: 0.22–0.61; P<0.001) (Figure 1C), higher probability of achieving immunosuppression-free remission (HR: 1.81; 95% CI: 1.04–3.16; P=0.036) (Figure 1D), and decreased need of more than three sequential treatment lines (6% versus 20%, P<0.001).
Furthermore, ruxolitinib compared with conventional treatment showed better response in liver (77% versus 47%; P=0.013) and ocular involvement (68% versus 32%; P=0.021). However, however, pulmonary cGVHD remained poorly responsive (ruxolitinib: 22%; conventional: 13%) (Figure 1E). Grade 3 or higher infection rates were comparable and acceptable between ruxolitinib and conventional treatment (24% versus 23%; P=0.84) (Figure 1F). Overall survival was similar in both groups (HR: 0.90; P=0.78).

Table 1. Characteristics of Patients Receiving Second-line Chronic GVHD Treatment.

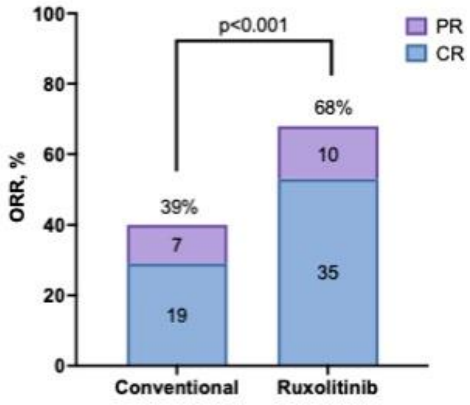
	Unmatched Cohort					
	Conventional (N=104)	**Ruxolitinib (N=125)**	**SMD**	**P-value**		**Conventi (N=66**
Age – no. (%)						
Recipient above 50 years	47 (45)	64 (51)	0.120	0.37		31 (47
Donor above 40 years	45 (43)	73 (58)	0.306	0.02		28 (42
Sex – no. (%)						
Male recipient	60 (58)	70 (56)	0.034	0.80		37 (56
Male donor	55 (53)	64 (51)	0.034	0.80		34 (52
High disease-risk index	15 (15)	36 (29)	0.328	0.02		11 (17
HLA-mismatched HSCT	29 (28)	38 (30)	0.055	0.68		19 (29
CMV seropositivity						
Recipient	96 (92)	110 (88)	0.145	0.28		61 (92
Donor	77 (74)	94 (75)	0.027	0.84		47 (71
HCT-CI ≥1	11 (11)	8 (6)	0.150	0.25		6 (9)
Peripheral blood stem cells	84 (81)	114 (91)	0.304	0.02		59 (89
Reduced intensity conditioning	31 (30)	57 (46)	0.330	0.01		24 (36
PTCy GVHD prophylaxis	8 (8)	33 (26)	0.514	<0.001		7 (11)
Prior grade II-IV aGVHD	42 (40)	39 (31)	0.192	0.15		27 (41
Severe cGVHD	35 (34)	8 (6)	0.724	<0.001		7 (11)
Glucocorticoid used in first-line therapy	100 (96)	103 (82)	0.456	0.001		62 (94

Figure 1.

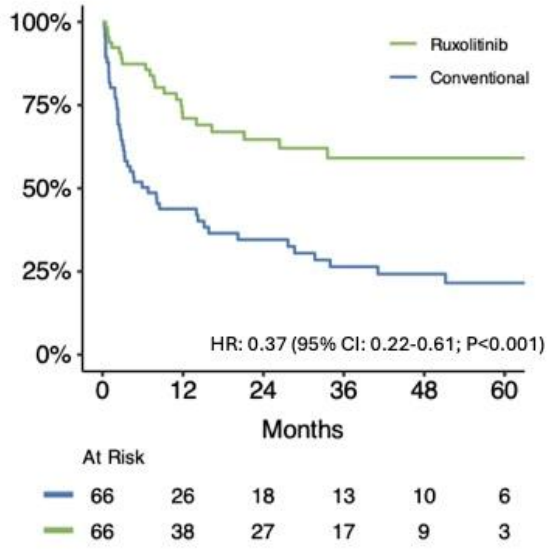
A. Odds Ratios of Overall Response in 2L cGVHD Treatment.



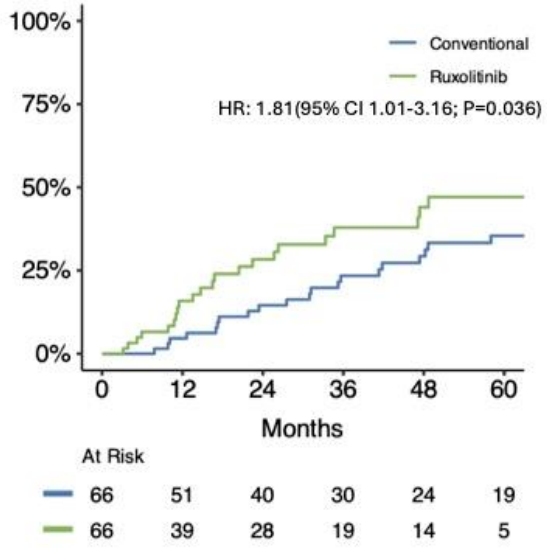
B. Overall Response Rates



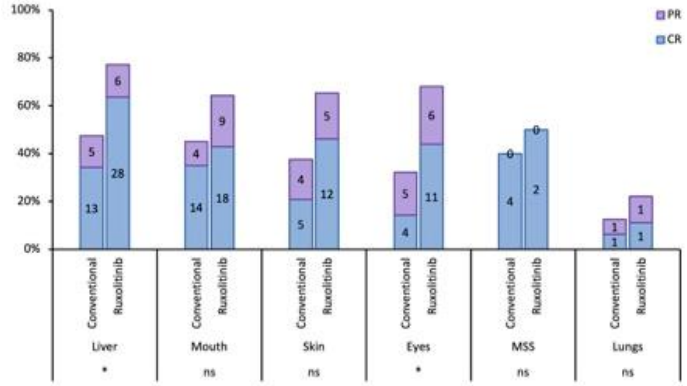
C. Failure-free Survival in PSM Cohorts.



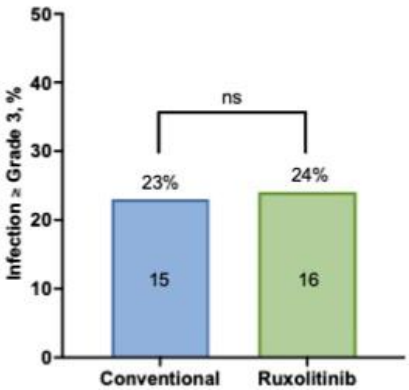
D. Probabilities of IST-free in PSM Cohorts.



E. Organ-specific Responses in PSM Cohorts.



F. Infection Risks in PSM Cohorts.



Conclusions: Our results showed that ruxolitinib was superior to conventional second-line agents for steroid-refractory cGVHD in ORR, failure-free survival, and successful immunosuppression tapering. These findings support ruxolitinib as the preferred second-line treatment for most patients with cGVHD. However, pulmonary GVHD remains an unmet clinical need, representing an important area for future therapeutic development and investigation.

Disclosure: Nothing to declare.

OS16-08

CHGVHD IMMUNE RECONSTITUTION-SCORE: INTEGRATING IMMUNOLOGICAL AND CLINICAL FEATURES TO PREDICT OUTCOMES IN CHRONIC GVHD

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Background: Chronic-GvHD (chGvHD) is a frequent and clinically relevant late complication in long-term survivors of allogeneic HSCT, exerting a substantial impact on patients' quality of life as well as on overall morbidity and mortality. Previously, we demonstrated how a composite score based on post-transplant immune reconstitution (IR) and clinical parameters is effective in predicting chGvHD outcomes.

Methods: chGvHD IR-score was calculated according to previously published alghoritm (Figure 1A) evaluating CD3CD4, NK, IgA, IgM, platelets and Karnofsky performance status. Based on the chGvHD IR-score, patients were stratified into three risk categories: low-risk, intermediate-risk, and high-risk. We analyzed prospectively data from 180 patients who underwent allogenic HSCT at our Institute between 2016 and November 2023 and subsequently developed chGvHD; IR score was available in 166 patients, with a median follow up of 1132 days (range 386-2648). We then evaluated the correlation between the IR-score-defined risk and the probability of being alive, in remission, and free from active GvHD or the need for immunosuppressive therapy five years after the onset of chGvHD, in all the patients (from both the historical cohort – 127 patients - and contemporary cohort – 78 patients) with a potential follow-up period of five years (figure 1B).
Our objective was twofold: first, to validate the chGvHD IR-score in a contemporary cohort of patients; and second, to evaluate its ability to predict free survival from chGvHD and recurrence, 5 years after the onset of chGvHD itself.

Results: Among the 166 patients of the contemporary cohort, 65 patients were classified as low-risk, 73 as intermediate-risk, and 28 as high-risk at the time of chGvHD diagnosis. The 3 years-OS was 92%, 86%, and 60% for low-, intermediate-, and high-risk respectively

(p=0.0006), confirming the validity of chGvHD IR-score (Figure 1C).
Overall 127 patients in the historical cohort and 78 in the contemporary cohort were evaluable for the 5-year response. Eighty-nine patients (43%) were alive, in complete remission and off-immunosuppressive treatment, 76 patients (37%) were dead or relapsed while 40 patients (20%) were still under immunosuppressive treatment due to active chGvHD at 5 year after chGvHD onset. Probability of being alive, in complete remission and off-immunosuppressive treatment was higher among low-risk patients, while, high risk patients showed higher probability of death. This confirms the 5-year prognostic value of chGvHD IR-score (p<0.0001) (Figure 1D).

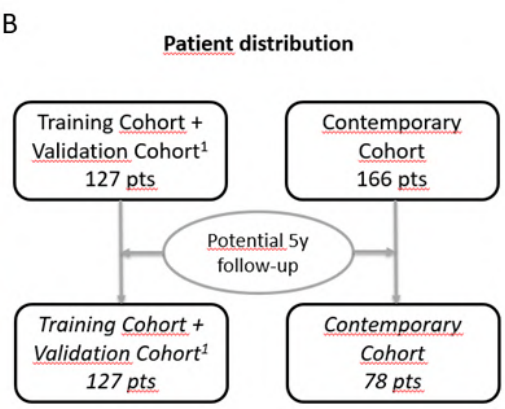
A

chGvHD IR-Score

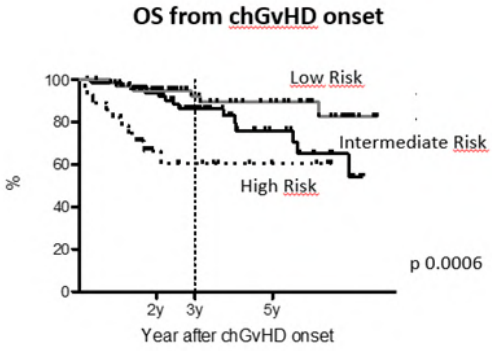
Parameters	Value of reference	B-coefficient
CD3CD4	>233/mcl	3.09
NK	<155/mcl	1.75
IgA	<0.43 g/L	1.47
IgM	<0.45 g/L	2.22
Platelets	<100x10^9/L	2.18
PS Karnofsky	<80%	5.05

Low Risk	Intermediate Risk	High Risk
<3.09	3.09-6.9	>6.9

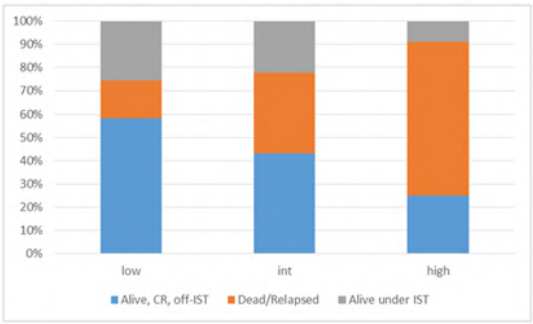
B



C



D



Conclusions: ChGvHD IR-score is a valid predictor tool of both short and long-term outcomes in chGvHD, effectively stratifying overall survival at 3 and regarding immunosuppressive therapy on long-term. Integration of immunological and clinical parameters into this composite score provides a practical and prognostic tool for a personalized, risk-adapted management strategy for cGvHD. Further multicentre confirmation is warranted.

Disclosure: Nothing to declare.

B001

LOW-DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE (PTCY) IN HAEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) FROM AN 10/10 HLA-IDENTICAL DONOR: A NEW PARADIGM? STUDY CONDUCTED ON BEHALF OF GETH-TC

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Background: Graft-versus-host disease (GVHD) prophylaxis in HSCT from 10/10 HLA-identical donors has improved with the use of PTCY, incorporating the same dose used in haploidentical HSCT. However, PTCY can add toxicity to conditioning regimens (cardiotoxicity, delayed engraftment, infection, etc.) and even increase the risk of alkylating agent-induced endothelial injury. For this reason, the GETH-TC (Spanish Group for HSCT and Cell Therapy) conducted a retrospective, multicentre study to evaluate the efficacy and safety of using reduced doses of PTCY (low-PTCY) in 10/10 HLA-identical donor HSCT (related – MRD, and unrelated – MUD).

Methods: Patients diagnosed with acute myeloid leukaemia and myelodysplastic syndrome who underwent their first allo-HSCT with peripheral blood stem cells (PBSC) from 10/10 HLA-identical donors in 2023 and 2024 were recruited. Primary endpoints included overall survival (OS), non-relapse mortality (NRM), and GVHD-free/relapse-free survival (GRFS). Secondary endpoints included cardiotoxicity, endothelial syndrome, and haemorrhagic cystitis.

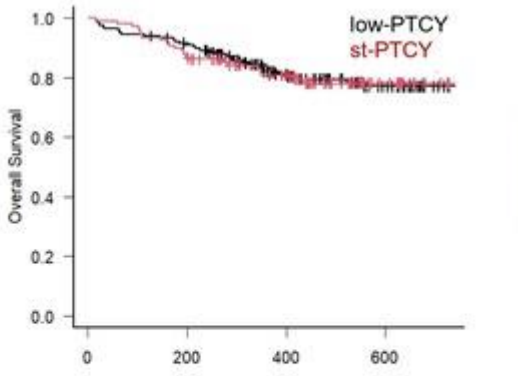
Results: 276 patients met the study criteria, with a mean age of 61 years (range 18–75), of whom 65.6% received PBSC from MUD. Conditioning was reduced in 86.4% of patients. As GVHD prophylaxis, 167 patients received standard doses of 50 mg/kg/day on days +3 and +4 of PTCY (st-PTCY) and 109 received low-PTCY (defined as $\leq$40 mg/kg/day), mostly combined with calcineurin inhibitors ± mycophenolate. A HCT CI $\geq$ 3 was observed in 64.7%

of patients with st-PTCY and in 73.4% with low-PTCY, and 25.4% had active disease at HSCT (21% vs 32%, respectively) – see Table 1.
Engraftment was achieved in 97.8% of cases, with a median of 18 vs 17 days (p 0.007) for neutrophils, and 22 vs 15 days (p<0.001) for platelets in st-PTCY and low-PTCY, respectively. There were no differences in the incidence of endothelial syndrome or cardiotoxicity. 206 patients had some type of infection (74.6%), with a higher percentage observed in the st-PTCY group (47.8% vs 26.8%, p 0.027). Notably, BK virus haemorrhagic cystitis was more frequent with st-PTCY (cumulative incidence function (CIF) at day +100, 16.8% vs 2.8% p < 0.001). No patients with low-PTCY developed severe haemorrhagic cystitis.
No differences were found in CIF for grade II–IV aGVHD (18.6%, 95% CI: 13.1–24.8 vs 23.9%, 95% CI: 16.3–32.2) and III–IV up to day +100 (6.6%, 95% CI: 3.5–11 vs 11.9%, 95% CI 6.7-18.8) and also in moderate-severe cGVHD one year post-HSCT (19.8%, 95% CI: 13.9–26.6 vs 18.6%, 95% CI: 11.7-26.8). Estimated 2-year incidence of OS, relapse-free survival (RFS), NRM, relapse, and GRFS for both groups was 77.1% vs 78.1% (p 0.86), 70.6% vs 63.8% (p 0.51), 11.1% vs 9.4% (p 0.65), 26.8% vs 26.8% (p 0.26), and 48.5% vs 45.7% (p 0.84), respectively.

BASELINE CHARACTERISTICS	**Total N=276**	**ST-PTCY N=167**	**LOW-PTCY N=109**	**P value**
Median Age	61 (18-75)	60 (18-74)	62 (25-75)	0.027
Male **Female**	129 (46.7) 147 (53.3)	80 (47.9) 87 (52.1)	49 (45.0) 60 (55.0)	0.631
Baseline Diagnosis AML MDS	 179 (64.9) 97 (35.1)	 112 (67.1) 55 (32.9)	 65 (59.6) 44 (40.4)	0.142
Disease Risk Index High/Very High	107 (38)	71 (42.5)	36 (32.0)	0.105
HCT-CI>2	188 (68.1)	108 (64.7)	80 (73.4)	0.128
Cardiac Morbidity	19 (6.9)	8 (4.8)	11 (10.1)	0.089
Number of lines Allo-HCT Upfront 1 Line of treatment >1 Lines	 12 (4.3) 178 (64.5) 71+12+3	 7 (4.2) 110 (65.9) 43+6+1	 5 (4.6) 68 (62.4) 28+6+2	
Disease Status at HSCT CR1 CR2	 165 (59.8) 36 (13.0)	 107 (64.1) 23 (13.8)	 58 (53.2) 13 (11.9)	

CR3 or more PR Stable Disease R/R	5 (1.8) 14 (5.1) 41 (14.9) 15 (5.4)	2 (1.2) 3 (1.8) 22 (13.2) 10 (6.0)	3 (2.8) 11 (10.1) 19 (17.4) 5 (4.6)	
Conditioning TBF Flu/Bu TTF Other	 133 (48.2) 64 (23.2) 11 (4.0) 68 (24.6)	 96 47 (28.1) 1 (0.6) 23 (13.8)	 37 (33.9) 17 (15.6) 10 (9.2) 45 (41.3)	
Intensity (Cassic) MAC RIC / NMA	 65 (23.6) 211(86.4)	 44 (26.3) 123 (73.7)	 21 (19.3) 88 (80,7)	 0.175
TCI Low Intermediate High	 112 (40.6) 150 (54.3) 14 (5.1)	 59 (35.4) 101 (60.5) 7 (4.2)	 53 (48.6) 49 (45.0) 7 (6.4)	 0.040
Letermovir	97 (35.14)	37 (22.2)	50 (45.9)	0.001
Donor type MSD MUD	 95 (34.49) 181 (65.6)	 55 (33.0) 112 (67.0)	 40 (36.7) 69 (63.3)	 0.520
MAIN POST-TRASPLANT OUTCOMES	**Total N=276**	**ST-PTCY N=168**	**LOW-PTCY N=108**	**P value**
Median Days to Engraftment (IQR) Neutrofil Platelet	 17 (15-21) 19 (14-27) 154 (111-193)	 18 (15-21) 22 (16-29) 151 (110-180)	 17 (15-18) 15 (12-21) 153 (107-197)	 0.007 <0.001 0.768
SOS **TA-TMA**	9 (3.3) 7 (2.5)	7 (4.2) 5 (3.0)	2 (1.8) 2 (1.8)	0.281 0.549
Infectious Complications **BK Cystitis (any)** Day +100 CIF ECE Day +100 CIF ECE **SLP**	 31 (11.2) 10.9 (7.5-14.9) 5.8 (3.5-9.0) 0	 28 (16.8) 16.7 (11.0-22.2) 9.6 (5.7-14.6) 0	 3 (2.8) 2.8 (0.7-7.2) 0 0	 <0.001 <0.001 <0.001 0

Cardiac Toxicity Any event Day +100 CIF ECE 1-year CIF Any CE	 14 2.5 (1.1-4.9) 4.0 (2.1-6.8)	 8 3.0 (1.1-6.5) 3.6 (1.5-9.7)	 6 (5.5) 1.8 (0.4-5.9) 4.6 (1.7-9.7)	 0.882 0.545 0.692
GVHD Prophylaxis (all 2 days) **Reduced Dose*** 40x2 35x2 30x2 ≤25x2	 59 (54.1%) 2 (1.8%) 29 (26.6%) 19 (17.4%)	* *Main causes of dose reduction:* 1. *Hospital protocol (43.1%)* 2. *Frail patient (15.6%)* 3. *Risk of relapse (14.7%)* 4. *Heart disease (1.8%)*		



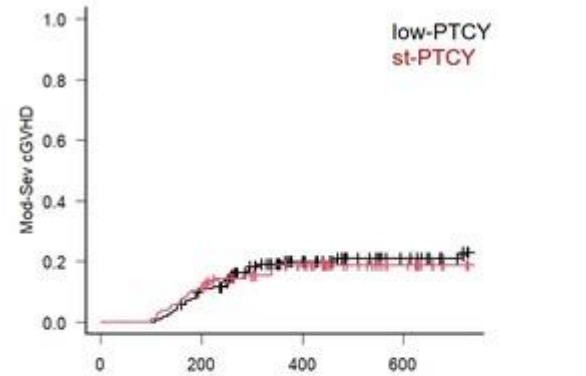
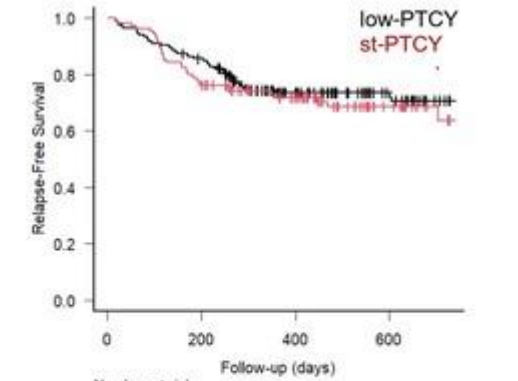


Image 1. A

Overall Survival	Total	St-PTCY	Low-PTCY	P value
1-Year	81.5 (76.2-85.8)	82.1 (75.1-87.3)	80.8 (71.7-87.2)	0.861
2-Year	77.5 (71.5-82.3)	77.1 (69.0-83.3)	78.1 (68.6-85.1)	

Image 1. C

	1-Year Moderate-Severe cGVHD	St-PTCY	Low-PTCY	P value
		19.8 (13.9-26.6)	18.6 (0.117-0.268)	0.701



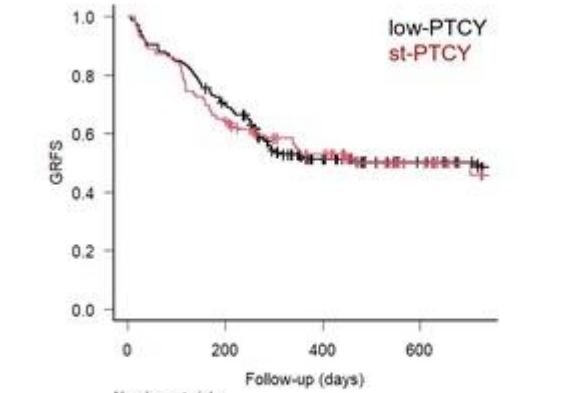


Image 1. B

Relapse-Free Survival	Total	St-PTCY	Low-PTCY	P value
1-Year	72.8 (67.0-77.7)	73.5 (65.9-79.6)	71.9 (62.2-79.5)	0.514
2-Year	68.3 (61.3-74.2)	70.6 (62.2-77.5)	63.8 (49.7-74.99	

Image 1. D

GRFS	Total	St-PTCY	Low-PTCY	P value
1-Year	51.8 (45.6-57.6)	51.3 (43.2-58.7)	52.8 (42.8-61.9)	0.84
2-Year	47.5 (40.6-54.1)	48.5 (39.9-56.5)	45.7 (33.5-57.1)	

Conclusions: In our experience, low-PTCY in MRD and MUD allo-HSCT do not increase the incidence of GVHD, offering survival results not inferior to st-PTCY doses. Low-PTCY appears to shorten time to engraftment and decrease the incidence of infections in general, particularly BK virus haemorrhagic cystitis. These findings should be explored in clinical trials evaluating whether there is an optimal PTCY dose that can improve HSCT outcomes in this context.

Disclosure: Nothing to declare.

B002

DECODING LONG-TERM IMMUNE SIGNATURE THROUGH AUTOANTIBODY EXPRESSION AS PERSISTENT IMMUNE SIGNALS IN POST-TRANSPLANT PAEDIATRIC ALL

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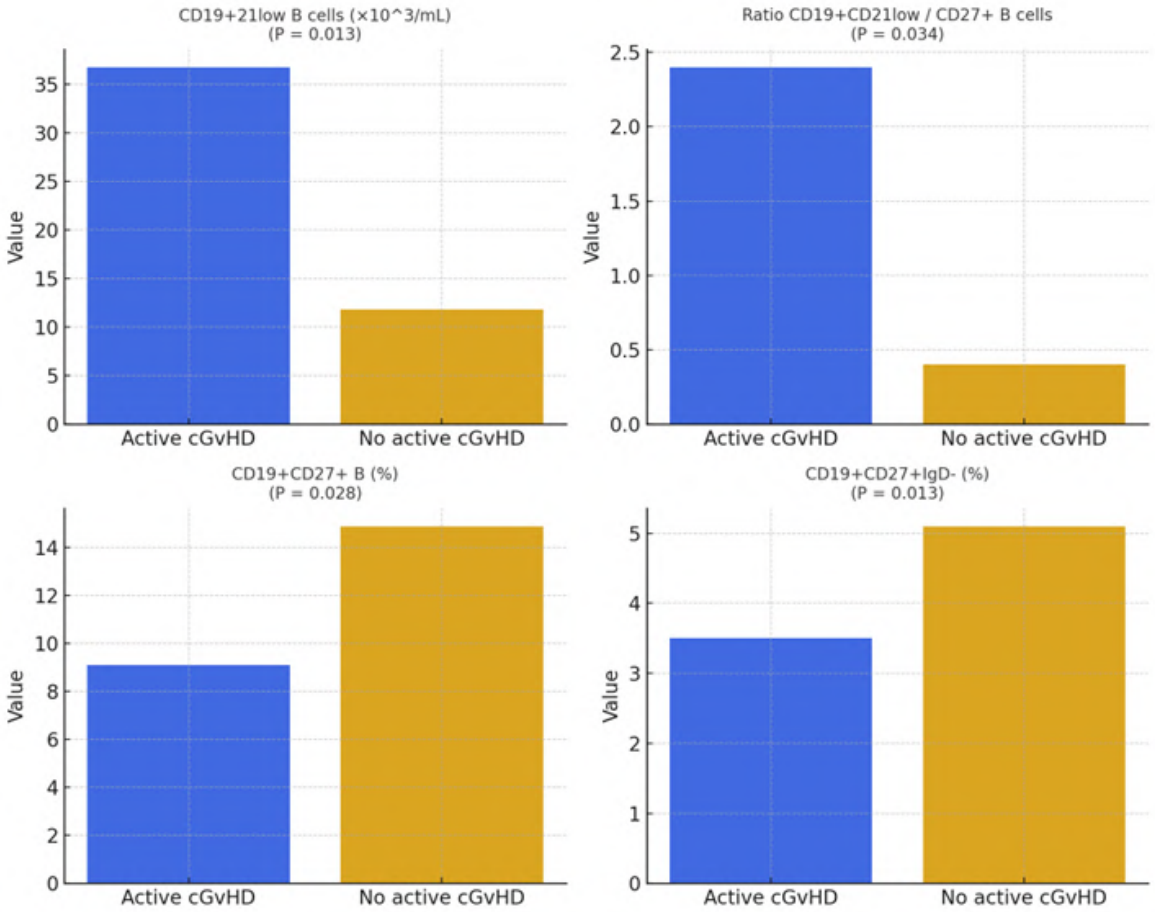
Background: Chronic graft-versus-host disease (cGvHD) following haematopoietic stem cell transplantation (HSCT) shares many similarities with *de novo* autoimmune disorders, being associated with the presence of autoantibodies. However, data on their implication in paediatric HSCT recipients are scarce. In this single-centre study of paediatric patients with ALL surviving longer than 3 months, our objectives were to evaluate autoantibody expression and investigate the correlation with cGvHD and immune reconstitution using serially monitored parameters.

Methods: We investigated circulating autoantibodies along with cellular and humoral parameters [T- and B-cell subsets, NK-cells, and immunoglobulin levels] in 440 samples from 74 patients serially during long-term follow-up (median 8 years, range 0.4-19.3). Evaluations comprised of patient and transplant characteristics, NIH-defined cGvHD details, and outcome such as relapse, overall survival (OS) and mortality, analysing these parameters for associations.

Results: Autoantibodies were detected in 65% of patients. Anti-nuclear antibodies were the most common, occurring in 75% of patients. When comparing demographic data and transplant characteristics, there were no significant differences between patients with and without autoantibody expression; 5-year OS was excellent, at 96%. Patients with autoantibodies showed significantly better immune reconstitution, with overall higher numbers of T cells, B cells, and serum immunoglobulins. In autoantibody-positive patients with cGvHD, autoantibody production positively correlated with significant expansion of CD56+ NK cells (p=0.023) and with signs of B-cell perturbation, higher $CD21^{low}$ B cells (p=0.044) in comparison to autoantibody-positive patients without cGvHD.
Furthermore, analysis of the association between autoantibody positivity and cGvHD activity at the time of evaluation demonstrated features of dysregulated B-cell homeostasis, evidenced by reduced $CD27^{+}$memory B cells (p = 0.028) and increased CD21^low B cells (p = 0.013) in patients with active cGvHD compared with those without cGvHD. We subsequently evaluated the potential role of autoantibody expression in the setting of increased CD21^low B cells (cutoff >7%), a well-established marker of cGvHD. Unexpectedly, a significantly higher prevalence of elevated CD21^low B cells associated with active cGvHD was observed in the autoantibody-negative group compared with the autoantibody-positive group (82% vs. 47%, p = 0.0053).
Analysis of immune parameters in the majority of survivors (89%) demonstrated normalization of the B-cell compartment, characterized by significantly increased levels of

class-switched CD27⁺IgD⁻ B cells ($p < 0.0001$) and immunoglobulin G4 ($p < 0.0001$). Overall mortality was significantly associated with elevated CD21^low B cells ($p = 0.039$) and CD56⁺ NK cells ($p = 0.019$). In multivariate analysis, improved overall survival was independently associated with lower CD56⁺ NK cell levels ($p = 0.041$) and higher CD27⁺ memory B-cell levels ($p = 0.014$).

Conclusions: Our findings indicate that autoantibody profiles are not reliable biomarkers for the diagnosis of cGvHD in children and adolescents, nor for predicting disease severity, clinical course, or outcomes. We identified a number of indicators of aberrant immune homeostasis associated with active cGvHD in paediatric ALL patients after HSCT. These findings confirm published results and suggest that candidate B cell subpopulations may serve as a surrogate measure for characterisation of cGvHD in paediatric HSCT for malignant diseases.



Disclosure: Anita Lawitschka: Neovii, Sanofi, Novartis, Therakos, Amgen, Medac, Vertex

B003

DUPILUMAB: EFFECTIVE AND SAFE ADDITION TO THE THERAPEUTIC ARMAMENTARIUM FOR PAEDIATRIC SKIN GVHD – A SINGLE CENTRE EXPERIENCE

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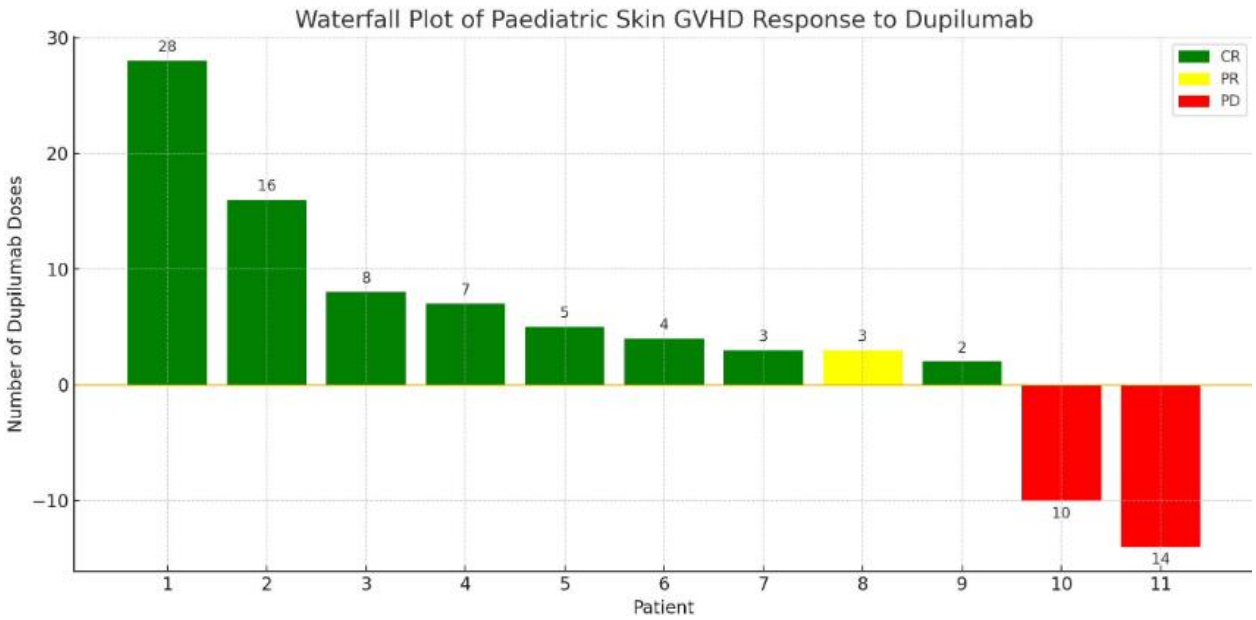
Background: Skin graft versus host disease (GVHD) in children remains difficult to manage, particularly in steroid-dependent or refractory cases. Dupilumab, an IL-4Rα blocker, which targets Th2-driven pathways, improves cutaneous symptoms, and reduces steroid exposure, offering a promising therapeutic option.

Methods: We retrospectively reviewed paediatric patients receiving dupilumab for skin GVHD between January 2023 and October 2025. Severe acute(a) skin GVHD (stage III/IV) and chronic GVHD was treated with steroids and, steroid sparing second line agents, including dupilumab and others, such as, ruxolitinib, belumosudil, calcineurin inhibitors and extra corporeal photopheresis (ECP) when it was steroid dependent or refractory. Dupilumab was administered at 300 mg subcutaneously every two weeks until clinical improvement, then monthly until complete remission. Concomitant systemic therapies were tapered in responders, and additional interventions were used only if lesions progressed during dupilumab therapy.

Results: Eleven patients (median age 12 years, range 13 months–19 years; male-to-female ratio 2.6:1) received dupilumab post haematopoietic stem cell transplant (HSCT). Of them, eight (72%) underwent HSCT for non-malignant disorders. Nine patients (81%) received myeloablative conditioning, and eight received serotherapy (alemtuzumab, n=6; anti-thymocyte globulin, n=2). Donors included unrelated (n=8, HLA matched 4/8, HLA mismatched 4/8), matched sibling (n=2), haploidentical (n=1), with stem cell source being peripheral blood (n=5), bone marrow (n=2), and cord blood (n=4). Chronic, skin only GVHD was present in five (45%), skin aGVHD in two (19%), and overlap skin GVHD in four (36%) patients. All exhibited extensive eczematous type of skin GVHD (Stage-3/Grade-2: 10/11; Stage-4/Grade-4: 1/11). Nine (81%) were steroid-dependent and two (19%) steroid-refractory. Patients had a median of three prior systemic therapies (range 2–5). Overall response rate was 81% (eight complete response (CR), one partial response (PR)), with median time to improvement of 13 days (range: 5–40 days). Two patients had skin GVHD progression (PD) whilst on dupilumab (Figure-1). No significant adverse events were recorded.



Conclusions: Dupilumab is effective and well tolerated in steroid-dependent or refractory skin GVHD, demonstrating rapid clinical improvement and steroid-sparing potential. Early incorporation may further enhance outcomes in paediatric patients. Its use over other second line immunosuppressive agents may be considered, in particular, in malignant HSCT. However, larger prospective trials are needed to inspect its role in skin GVHD post HSCT.

Clinical Trial Registry: -

Disclosure: nothing to disclose

B004

REAL-WORLD RESULTS ON THE USE OF BELUMOSUDIL IN PATIENTS WITH RELAPSED/REFRACTORY CHRONIC GVHD: THE ITALIAN RETROSPECTIVE ANALYSIS

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Background: Chronic GVHD (cGVHD) is one of the most debilitating complications following allogeneic stem cell transplantation (SCT), resulting in increased mortality, morbidity and reduced quality of life. The first-line treatment still relies on steroids. Multiple new therapeutic options are capable of acting on inflammatory pathways responsible for cGVHD and are being used in subsequent therapeutic lines for patients with relapsed/refractory (r/r) cGvHD. Belumosudil is a selective ROCK2 inhibitor with immunomodulatory and anti-fibrotic properties. While the drug received approval in the United States in 2021 and in other

several Countries thereafter, it has not yet authorized in Europe and the only way to access the drug in Italy is through a compassionate use.

Methods: This observational, retrospective, multicentre study included 80 patients treated with belumosudil by 29 SCT centers in Italy between June 2023 and April 2025. The study aimed to evaluate the efficacy of belumosudil, accessed via compassionate use, in patients with r/r cGVHD, after failure of at least two systemic lines of therapy. Clinical data, encompassing baseline demographics, cGVHD severity, prior and concomitant treatments, NIH response, patient-reported outcomes (PROs), and adverse events (AEs) were collected from medical records. The cohort was characterized by a high proportion of patients with severe disease (86%), extensive prior treatment (median of 3 lines), and significant previous exposure to ruxolitinib (84%). Patients also presented with a prolonged history of cGVHD (median: 42.6 months). The median follow-up time from belumosudil treatment was 9.1 months (range: 1-20).

Results: The overall response rate (ORR) ORR at 3, 6, and 12 months was 52.6%, 57.6%, and 55.0%, respectively. The best overall response (BOR) was 62.5%, comprising 1.3% complete remission (CR) and 61.2% partial response (PR). Median time to response was 3 months, while duration of response was 83.4% at 12 months. Responses were observed across all organs evaluated, with the highest rates recorded in mouth, gastrointestinal tract, and liver, while for lung involvement only 10% of patients showed a NIH response. Failure-free survival was 89.1% and 67.5% at 6 and 12 months, respectively. Treatment was generally well tolerated: 28 non-infectious AEs were observed, with 36% being grade ≥3. Drug discontinuation due to any cause occurred in 26% of cases, with 11% due to AEs. Evaluation of the NIH Severity Index Score (SIS) was used as a tool to assess PROs: this demonstrated a significant improvement (≥ -2 points) in 33%, 36%, and 29% of patients at 3, 6, and 12 months, respectively. Moreover, NIH objective clinical responses showed a moderate concordance with the SIS ones (51.6%, 54.4%, and 46.1% at 3, 6, and 12 months, respectively).

Conclusions: The present real-world data confirm belumosudil as a valuable therapeutic option for patients, who were extensively pretreated, with moderate-to-severe forms of cGVHD. Our findings are consistent with those reported in previous clinical trials and real-world studies, thereby confirming the drug's efficacy and safety in advanced, heavily pretreated cGVHD patients.

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Omeros, Sanofi, Italfarmaco. FL has received honoraria from and/or has been a member of the speakers bureau for Novartis, Sobi, Miltenyi, Gilead, Amgen, Medac, and BMS, and has participated in an advisory board for Amgen, Novartis, Sanofi and Vertex. All the other authors declare no conflicts of interest related to this manuscript.

B005

KEY RESULTS FROM THE CHRONOS MULTICENTRE RETROSPECTIVE COHORT STUDY DESCRIBING PATIENT OUTCOMES IN THIRD-LINE ACUTE GASTROINTESTINAL GVHD

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Background: Treatment options for acute graft-versus-host disease (aGvHD) refractory to corticosteroids and ruxolitinib are poorly characterized, none being approved for this indication. CHRONOS study aimed to describe response rates, duration of response, and survival following third-line systemic therapy in this high-risk setting.

Methods: CHRONOS is a multicentre, non-interventional, retrospective cohort study including aGvHD adults with gastrointestinal (GI) symptoms who failed both corticosteroids and ruxolitinib, and who initiated a third-line systemic treatment between 30-May-2019 and 30-September-2024, in 22 European sites. Inclusion criteria were adult aGvHD patients with GI involvement, who only previously received corticosteroids and ruxolitinib. Main exclusion criteria were hyperacute GvHD, overlap chronic GvHD, relapsed malignancy, cytomegalovirus colitis, uncontrolled cardiac disease or significant respiratory disease. Data were collected via electronic case report forms with rigorous data curation ensuring highest standards of data quality and completeness. Primary endpoints were D28 (closest assessment date) all-organ

overall response rate (ORR) and GI-specific ORR (GI-ORR) after third-line treatment initiation, based on MAGIC criteria for aGvHD assessment. Secondary endpoints included D56 response (closest assessment date), duration of response (DOR), real-world progression-free survival (rwPFS) of the underlying malignancy, overall survival (OS), and incidence of events of special interest (Grade≥2 infectious events, Grade 3-4 neutropenia and thrombocytopenia) up to 12 months.

Results: Fifty-nine patients were included from 16 sites in Austria, Belgium, France, and Spain. Median age was 59 years (IQR, 49-64); 54% (n=32) were male. Most patients presented with Grade III/IV (93%, n=55) aGvHD; 97% (n=57) were steroid-resistant and 95% (n=56) resistant to ruxolitinib. Among the 13 third-line therapies used, the three most administered were extracorporeal photopheresis (n = 17), etanercept (n = 14), and vedolizumab (n = 10), with an overall median time from initial aGvHD diagnosis of 32 days (IQR: 20–53 days). At Day 28, ORR was 36% (21/59; 95% CI, 24%–49%), including 20% CR (n=12), 7% VGPR (n=4), and 9% PR (n=5). GI-ORR was 37% (22/59; 95% CI, 25%–51%), including 22% GI-CR (n=13), 10% GI-VGPR (n=6), and 5% GI-PR (n=3). Response rates declined by Day 56: all-organ ORR of 20% (12/59; 95% CI: 11%– 33%) and GI-ORR of 22% (13/59; 95% CI: 12%-35%). 29% (95% CI: 11%–49%) of D28-responders lost their all-organ response within the next 30 days, and 52% (95% CI: 29%–72%) within 90 days. Same results were observed for the GI-aGvHD-responders. Median rwPFS and OS were 86 days (95% CI: 54–128). Median OS was 186 days in responders (95% CI: 115 days-not reached) *versus* 45 days in non-responders (95% CI: 28–86 days). Up to M12, 41 patients died, mostly from aGvHD (n=25) and infectious complications (n=9). Grade≥2 infectious events occurred in 58% of patients, grade 3 to 4 thrombocytopenia and neutropenia in 64% and 32% respectively.

Conclusions: These findings illustrate the absence of standardization and the limited benefit of available third-line interventions, emphasizing the need for novel treatments. Survival outcomes were poor, particularly among non-responders, and infectious events were frequent. By establishing clear benchmarks, this study will facilitate the evaluation of novel therapeutic approaches.

Disclosure: [17], Imi Faghmous[18], Behzad Kharabi Masouleh[17], Emilie Plantamura[17], Florent Malard[19], Mohamad Mohty[19]

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B006

PHASE 2 STUDY OF EXTRACORPOREAL PHOTOPHERESIS WITH UVADEX™ PLUS STANDARD STEROID TREATMENT FOR HIGH-RISK ACUTE GRAFT-VERSUS-HOST DISEASE

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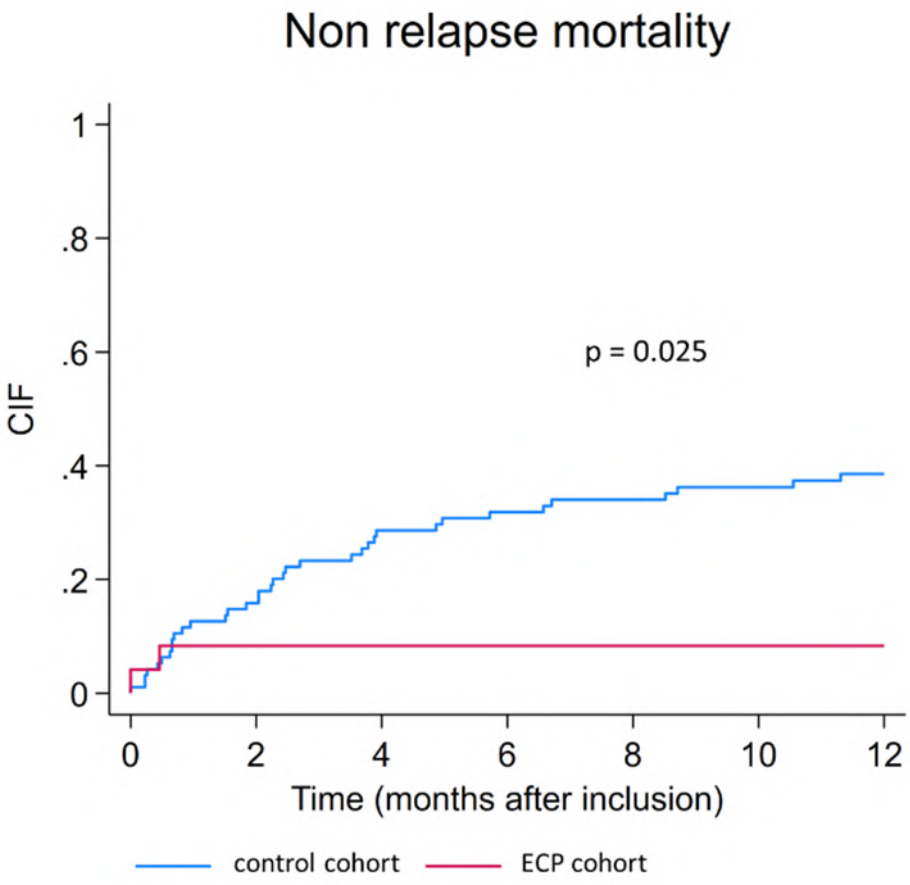
Background: Acute graft-versus-host disease (aGVHD) is a major cause of morbidity and mortality after allogeneic stem cell transplantation; one year non-relapse mortality (NRM) following the diagnosis of grade II-IV GVHD is 25% (Holtan, *BMT*, 2022). Ann Arbor (AA) scores, derived from biomarkers associated with gastrointestinal damage, have been shown to correlate with resistance to standard therapy and increased non-relapse mortality; AA 2/3 scores are considered high-risk with 1-year NRM of 40% (Al Malki, *Blood Adv*, 2023). Extracorporeal photopheresis (ECP) is used for steroid-resistant GVHD, but prospective studies evaluating its efficacy as a first-line treatment for aGVHD are lacking.

Methods: We conducted a multicenter phase 2 trial combining ECP with standard corticosteroid therapy in patients with newly diagnosed aGVHD (clinical grade 2–4) and AA2/3. Patients were recruited from three centers in Germany and one center in Austria. ECP was administered (using the Therakos™ CELLEX™ Photopheresis System) three times per week in weeks 1–2, twice per week thereafter until Day 28, and once per week until Day 56. Methylprednisolone (2 mg/kg/day or equivalent) was given from Day 0 to Day 3, then tapered according to clinical response. Treatment per protocol lasted 2 months, with a follow-up period of 1 year. The primary endpoint was the rate of complete response (CR) at Day 28. Secondary endpoints included rates of NRM, relapse, and overall survival at 12 months. Results were compared with a contemporary matched control cohort (n=72) from the Mount Sinai Acute GVHD International Consortium (MAGIC) database.

Results: 52 patients were screened and 24 enrolled (n = 17 AA2; n = 7 AA3). Acute GVHD was grade II (17, 71%), III (6, 25%), and IV (1, 4%). Lower GI GVHD was present in 14 (58%) of patients. Median age was 59 years (range 44–63), and patients were transplanted

for acute leukemia (12, 50%), myelodysplastic or myeloproliferative neoplasms (9, 38%), and lymphoma or other malignancies (3, 12%). ECP treatment was well tolerated; adverse events of CTCAE grade ≥3 occurred in 19 patients (79%), mostly infections (15/19, 79%). One severe adverse event (port catheter infection) was considered related to ECP procedure. The addition of ECP to high dose methylprednisolone was more effective than methylprednisolone alone in comparative analyses performed after propensity score matching to achieve balance between groups for GVHD target organ involvement and severity, Ann Arbor score, and age: D28 OR (92% vs 63%, p=0.008); D28 complete response (88% vs 55%, p=0.009), 1y NRM (8% vs 35%, p=0.025) and 1y survival (88% vs 61%, p=0.018). One patient died from relapse and two from non-relapse causes.

Conclusions: The addition of ECP to standard corticosteroid first-line treatment in patients with GVHD that is high risk by biomarker score was feasible. Although the sample size was relatively small the excellent short-term patient outcomes such as Day 28 response rate translated into significantly improved long-term outcomes such as one-year NRM and survival when compared to a contemporary matched cohort as well as published NRM rates. A larger randomized controlled trial is warranted.



Clinical Trial Registry: EudraCT No.: 2019-000894-22

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B007

CLINICAL OUTCOMES AMONG PATIENTS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE TREATED WITH AXATILIMAB: ANALYSIS OF AN EXPANDED ACCESS PROGRAM

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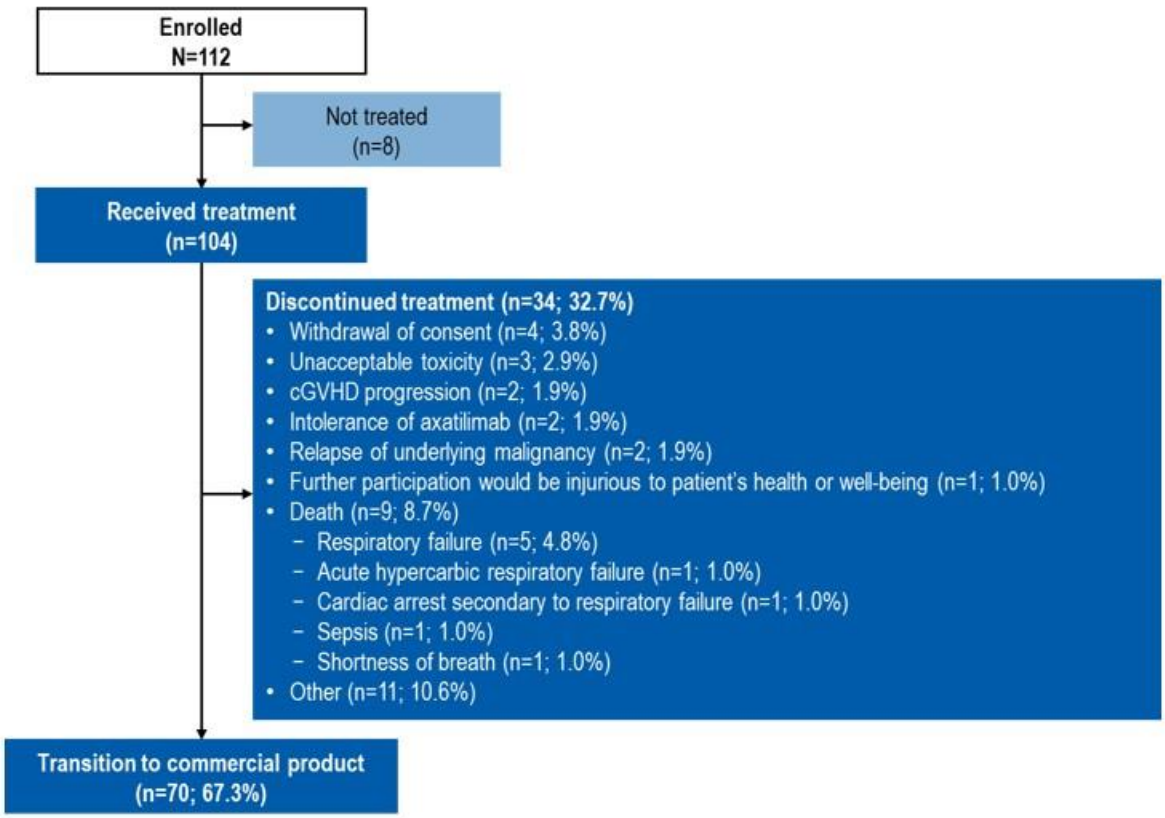
Background: Chronic graft-versus-host disease (cGVHD) is associated with significant morbidity and nonrelapse mortality. Axatilimab, a monoclonal antibody targeting colony-stimulating factor 1 receptor (CSF-1R), depletes the CSF-1R–dependent monocytes and macrophages that potentiate inflammation and fibrosis in cGVHD. The US Food and Drug Administration (FDA) approved axatilimab 0.3 mg/kg every 2 weeks (Q2W) for patients with cGVHD after ≥2 prior lines of systemic therapy (LOT). Axatilimab was previously available through an expanded access program (EAP) in the US sponsored by Incyte Corporation (NCT05544032). This analysis evaluated the safety and clinical benefit of axatilimab among patients in the EAP.

Methods: Patients aged ≥6 years with refractory or recurrent cGVHD and ≥2 prior LOT received axatilimab 0.3 mg/kg Q2W until loss of benefit, withdrawal, or commercial availability of axatilimab. Concomitant cGVHD treatments were permitted. Clinician assessment of clinical benefit was evaluated in the EAP at each resupply (every two 28-day cycles of axatilimab 0.3 mg/kg Q2W). Treatment-emergent adverse events (TEAEs) were assessed until 30 days after treatment end or transition to commercial product. The first EAP site was activated on April 15, 2024, and the last patient stopped treatment in the EAP on July 11, 2025, following axatilimab commercial availability. The data cutoff was October 24, 2025.

Results: Of the 112 enrolled patients, 104 patients received axatilimab (**Figure**). Most treated patients (64.4%) had severe cGVHD, and 45.2% of patients had ≥4 organs involved at baseline (**Table**). Patients received a median of 4 prior LOT (range, 1–7), including belumosudil (80.8%), ruxolitinib (76.0%), and prednisone (74.0%). The most common concomitant cGVHD therapies were belumosudil (76.0%), prednisone (63.5%), and

ruxolitinib (54.8%); fewer patients received concomitant calcineurin inhibitors (21.2%) and sirolimus (16.3%). Prior to EAP closure, median (range) duration of axatilimab treatment in the EAP was 143 (19–372) days. Though most patients (73.1%) maintained stable cGVHD severity per National Institutes of Health 2014 criteria, clinicians reported clinical benefit in 90 patients (86.5%) from axatilimab during the EAP. At EAP closure, 70 patients (67.3%) transitioned to commercial product. Seventy-six patients (73.1%) experienced TEAEs of any severity, with 4 patients (3.8%) having infusion-related reactions. Thirty-seven patients (35.6%) had treatment-related TEAEs, most commonly (>3%) increased aspartate aminotransferase (n=12 [11.5%]), increased alanine aminotransferase (n=9 [8.7%]), fatigue (n=5 [4.8%]), and increased gamma-glutamyl transferase (n=4 [3.8%]). Fifteen patients (14.4%) had treatment-related serious TEAEs, most commonly pyrexia (n=2 [1.9%]). Three patients (2.9%) discontinued treatment due to unacceptable toxicity, and 2 patients (1.9%) discontinued treatment due to intolerance to axatilimab.

Figure. Patient Disposition



cGVHD, chronic graft-versus-host disease.
Percentages are calculated using the 104 patients who received treatment as the denominator.

Table. Baseline Patient Demographics and Clinical Characteristics

Characteristic	Patients (N=104)

Table. Baseline Patient Demographics and Clinical Characteristics

Age, median (range), y	51 (6–82)
<17 y, n (%)	11 (10.6)
Male, n (%)	57 (54.8)
Severe cGVHD, n (%)	67 (64.4)
Number of organs involved, median (range)	3 (1–7)
≥4 involved organs, n (%)	47 (45.2)
cGVHD organ involvement, n (%)	
Skin	75 (72.1)
Eyes	65 (62.5)
Lungs	51 (49.0)
Mouth	49 (47.1)
Joints	42 (40.4)
Gastrointestinal tract	33 (31.7)
Liver	23 (22.1)
Genital tract	7 (6.7)
Number of prior cGVHD treatments, median (range)	4 (1–7)
≥3, n (%)	93 (89.4)

cGVHD, chronic graft-versus-host disease.

Conclusions: The US EAP represents the largest real-world experience of axatilimab treatment at the FDA-approved dose of 0.3 mg/kg Q2W in patients with cGVHD. Most patients (86.5%) experienced clinical benefit from axatilimab treatment per clinician assessment, and the majority (67.3%) transitioned to commercial product upon EAP closure, suggesting ongoing clinical benefit. Axatilimab safety was consistent with that observed in clinical trials, with no new or unexpected toxicities. Only 5 patients (4.8%) discontinued treatment due to unacceptable toxicity or intolerance to axatilimab. This analysis provides additional evidence of the real-world effectiveness and safety of axatilimab for cGVHD.

Clinical Trial Registry: NCT05544032
Clinicaltrials.gov

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B008

TWO-AGENT GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS WITH CYCLOPHOSPHAMIDE AND RUXOLITINIB: EXPERIENCE BEYOND THE CLINICAL TRIALS

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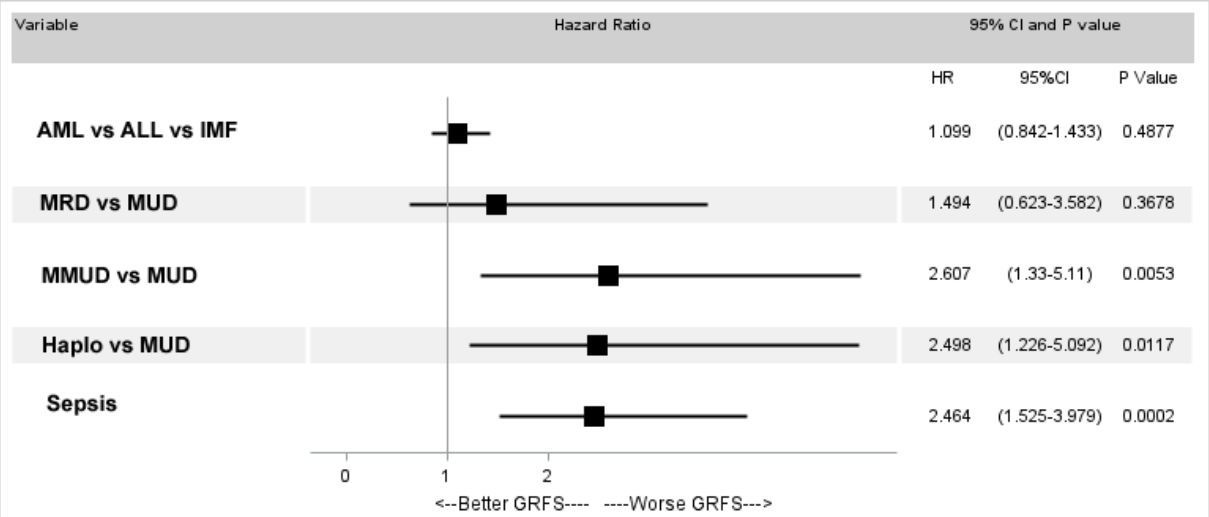
Background: We have previously reported promising efficacy and safety of calcineurin-free cyclophosphamide (PTCy) and ruxolitinib (PTCyRuxo) graft-versus-host disease (GVHD) prophylaxis in myelofibrosis (NCT02806375) and in acute leukemia (NCT04669210). Now we evaluated long-term results of this regimen in routine clinical practice.

Methods: The study comprised 225 standard risk adult recipients of hematopietic cell transplantation (HCT) with acute myeloid or lymphoblastic leukemia and myelofibrosis transplanted between 2015 and 2025. Disease characteristics are presented in the table. HCT was performed from a haploidentical donor in and unrelated donor in . Peripheral blood stem cells were a graft source in 97% of patients. All patients received FB2-FB4 conditioning with ruxolitinib 15-30 mg/day on days -7 to -2 and GVHD prophylaxis with PTCY 50 mg/kg on days +3,+4 and ruxolitinib 15 mg/day on days 5-21, and 10 mg/day on days 22-15. Median follow up was 17 months (range 1-117). Four-year outcomes are presented.

Parameter	Percent (n), Total n=225
Age, median (range), years	44 (18-75)

Males Females	50% (112) 50% (113)
Acute myeloid leukemia Primary myelofibrosis Acute lymphoblastic leukemia	53% (119) 29% (66) 18% (40)
Matched related donor (MRD) Mismatched related donor (Haplo) Matched unrelated donor (MUD) Mismatched unrelated donor (MMUD)	11% (24) 23% (53) 29% (65) 37% (83)
Graft CD34+ mln/kg, median (range)	6.4 (1.0-11.9)
PBSC BM	96% (216) 4% (9)
FB2 conditioning FB3 conditioning FB4 conditioning	17% (39) 76% (170) 7% (16)

Results: Cumulative incidence of engraftment was 93% (95%CI 90-97%) with a median of 18 days (range 12-229). Myelofibrosis negatively impacted engraftment and time to engraftment (89%, 34 days vs 96%, 17 days in acute leukemia, p<0.0001). Cumulative incidence of acute GVHD grade II-IV was 18% (95%CI 13-23%), grade III-IV 5% (95%CI 3-8%). Significant difference was observed in the incidence of grade II-IV acute GVHD according to the donor type: 8% MUD, 4% MRD, 21% Haplo, 28% MMUD, p=0.006. Incidence of moderate and severe chronic GVHD was 27% (95%CI 20-35%), while severe – 10% (95%CI 6-16%). No difference in the incidence of chronic GVHD was observed according to a donor type (p=0.20). Non-relapse mortality (NRM) was 19% (95%CI 13-26%), cumulative incidence of relapse (CIR) was 19% (95%CI 12-27%). NRM was lower in AML patients (10% vs 26%, p=0.02), while there was no differences in CIR (p=0.71). Overall survival was 71% (95%CI 61-78%), event-free survival 62% (95%CI 52-70%), GVHD-relapse-free survival (GRFS) 49% (95%CI 40-58%). The significant parameter for GRFS was the type of a donor, with best results in MUD HCT (69% vs 46% in MRD, 34% in MMUD, 44% in Haplo, p=0.01). After graft infusion 27% of patients had early cytokine release syndrome. Grade 3-4 toxicities included mucositis in 35%, hepatic toxicity in 6%, acute kidney injury 0.6%, bloodstream infections in 38%, sepsis in 23%, pneumonia in 28%, soft tissue infection in 8%. Veno-occlusive disease (VOD) was observed in 1.3%, transplant-associated microangiopathy in 0.6%. Cytomegalovirus reactivation was documented in 49%, herpes type 6 reactivation in 40%. Only sepsis had a negative impact on survival (p<0.0001). In the multivariate analysis MMUD (HR 2.6, 95%CI 1.2-5.1) and Haplo donors (HR 2.5, 95%CI 1.2-5.1) were associated with worse GRFS compared to MUD, while no differences were observed for MRD donors (HR 1.5, 95%CI 0.6-3.6).



Conclusions: Application of PTCy-ruxolitinib prophylaxis in the large patient cohort outside of clinical trials demonstrated reproducible results to the initial studies. We observed very low incidence of severe GVHD. The study also confirmed low incidence of VOD and TA-TMA as initially observed. Even with this effective prophylaxis there is an impact of 10/10-HLA compatibility on HCT outcomes.

Clinical Trial Registry: NCT02806375, NCT04669210

Disclosure: The study was supported by RSF grant №23-15-00327.

B009

ABATACEPT REDUCES ACUTE GVHD INCIDENCE AND IMPROVES GRFS IN PEDIATRIC PATIENTS TRANSPLANTED FROM AN HLA-MISMATCHED DONOR: A REAL-WORLD, MULTICENTER, RETROSPECTIVE STUDY

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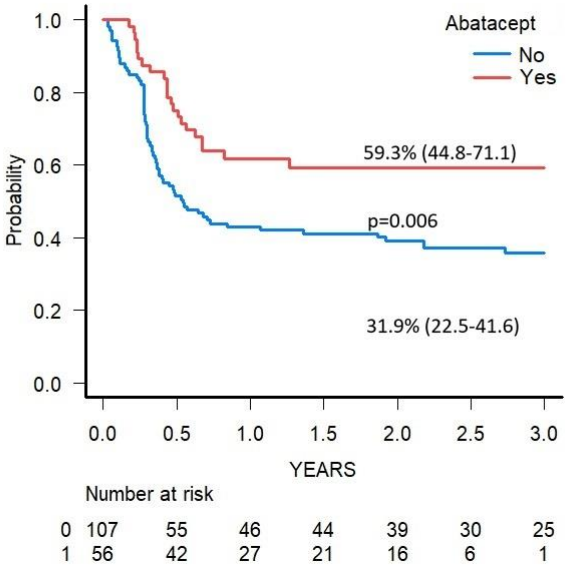
Background: The use of HLA-mismatched donors has been associated with an increased risk of both acute and chronic GvHD (respectively 30-60% and 29-70%), resulting in higher TRM (20-28%) (Jagasia, Blood 2012; Kröger, NEJM 2016)
New promising strategies for prevention of GvHD involve modulation of interactions between T-cells and antigen-presenting cells (APCs). In this regard, abatacept (ABA, CTLA4-IgG1) is a fusion protein that selectively inhibits T-cell co-stimulation by binding ligands CD80 and CD86 on APCs, thus blocking CD28-mediated signaling.

Methods: We retrospectively collected data from 8 pediatric centers from Italy and Norway on all consecutive patients transplanted from an HLA-mismatched donor who received abatacept during the transplant period. ABA was added, on an off-label basis, to standard GvHD pharmacological prophylaxis following EBMT guidelines (CSA, MTX, ATLG) at the dose of 10 mg/kg (max 750 mg/dose). Besides the classical administration schedule (day -1,+5,+14,+28), extended administration with additional doses was performed in many patients.
Classical clinical outcomes (GvHD, TRM, relapse, OS, EFS and GFRFS) were calculated, and compared to a historical cohort of acute leukemia patients receiving a transplant from a MMUD donor (Bertaina, Blood 2018).

Results: Between February 2021 and January 2025, ABA was administered to 100 pediatric/young adult patients undergoing unmanipulated HSCT from mismatched donors (91 MMUD and 9 PTCy haploidentical transplants). Twenty-eight patients received 4 doses of ABA, while 72 >4 (median 6 doses, range 5-13). Most patients, except 23 with non-malignant diseases, received a myeloablative conditioning regimen. Details on patients and transplants characteristics are reported in Table 1.
With a median follow-up for surviving patients of 19 months (range, 3-50), cumulative incidence of grade II-IV and grade III-IV aGvHD for MMUD transplants were 24.4% (95% CI 16.6-35.0) and 6.9% (95% CI 3.1-14.8), respectively. Cumulative incidence of grade II-IV aGvHD was higher in patients who received only four doses of abatacept (38.1% vs 18.7%, p=0.05). Twenty-three patients out of the 92 at risk, developed mild to moderate cGvHD (no cases of severe cGvHD were recorded), the cumulative incidence being 29.3% (95% CI 20-41.8), with no difference according to the number of doses of ABA received.
In malignant diseases, both TRM and relapse incidence were lower in patients receiving extended-course ABA (4.9 vs 15.3%, p=0.19, and 7.1% vs 39.7%, p=0.009), this resulting into an improved 3-yr EFS as compared to patients receiving 4 doses of the drug (88.2% vs 44.9%, p=0.001). Compared to the historical controls, patients receiving ABA showed an improved 3-yr GRFS (59.3% vs 31.9%, p=0.006, Fig.1).
OS and EFS of non-malignant patients were 95.8% and 92.9%, respectively.
Regarding safety, we did not observe an increased incidence of infections, with the only exception of increased EBV reactivation, 24 patients requiring treatment with rituximab. However, no cases of PTLD were recorded.

	N	% - range
Age at HSCT (years, range)	8.5	(1-23.0)

Diagnosis		
ALL	30	30
AML	17	17
Other malignant diseases	7	7
SAA/RCC	18	18
Other non-malignant diseases	28	28
Mismatch		
5/10	9	9
8/10	5	5
9/10	86	86
Locus of MM (96 loci for 91 unrelated donors)		
Class I	76	79
Class II	20	21
Source of Stem Cell infused		
BM	64	64
PBSC	36	36
Table I. Patients and transplant characteristics		



Conclusions: Our data indicate that ABA, added to a standard GvHD prophylaxis (including serotherapy), is a safe and effective approach for preventing acute GvHD in pediatric patients undergoing mismatched HSCT for both malignant and non-malignant diseases, especially if administered up to day + 60, without increased risk of relapse or TRM.

Disclosure: Nothing to declare.

B011

A MULTICENTRE STUDY ON IN VIVO T-CELL DEPLETION PLATFORMS IN REDUCED-INTENSITY ALLOGENEIC STEM CELL TRANSPLANTS FOR HAEMATOLOGICAL MALIGNANCIES

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Background: Graft-versus-host disease (GVHD) is a major complication of allogeneic stem cell transplantation (allo-SCT). Reduced-intensity conditioning (RIC) and GVHD prophylaxis with in vivo T-cell depleting agents such as alemtuzumab or ATG have broadened access to allo-SCT for older or co-morbid patients with high-risk haematological malignancies. The role of ATG in RIC allografts is not well characterised and comparative studies with alemtuzumab remain pertinent. The primary aim of this study was to assess 2-year GVHD-free, relapse-free survival (GRFS) in patients who received alemtuzumab compared with ATG during RIC allo-SCT. Secondary endpoints include cumulative incidence (CI) of acute grade III/IV GVHD (aGVHD), CI of moderate and severe chronic GVHD (cGVHD), CI of non-relapse mortality (NRM), CI of relapse (CIR), overall survival (OS) and progression-free survival (PFS).

Methods: Retrospective multicentre study of 399 patients from five centres who underwent RIC allo-SCT for haematological malignancy and received either alemtuzumab (n=261) or ATG (n=138). The median age was 60.25 years (range 16.5-76.9), with 57.6% males. Disease lineage was either myeloid (n=300), lymphoid (n=97), mixed phenotype (n=1) or undifferentiated (n=1). Donor types included unrelated (n=318) and sibling (n=81). Median follow-up estimated using the reverse Kaplan-Meier method was 37.9 months. PFS and OS were calculated using univariate and multivariate Cox proportional hazards models. CIR, NRM and CI of GVHD were assessed with Fine-Gray competing-risks regression for both univariate and multivariate analyses. Multivariable models adjusted for age, sex, disease lineage, cytogenetic risk, cytomegalovirus serostatus, donor type, conditioning regimen and centre.

Results: In univariate analysis, choice of GVHD prophylaxis had no significant effect on GRFS, PFS, NRM, CIR or CI of moderate/severe cGVHD. ATG use was associated with better OS (HR 0.69, 95% CI 0.5-0.95, p=0.024) but more grade III/IV aGVHD (HR 3.5, p=0.0073) when compared with alemtuzumab.
In multivariate analysis, choice of GVHD prophylaxis had no effect on GRFS, PFS, OS, CIR, NRM or CI of moderate/severe cGVHD. ATG was associated with more grade III/IV aGVHD when compared with alemtuzumab (HR 6.24, 95% CI 1.28-30.4, p=0.024). Age and cytogenetic risk were significant co-variates for GRFS, PFS, OS and NRM.

Conclusions: Alemtuzumab-based GVHD prophylaxis is associated with lower incidence of grade III/IV aGVHD compared with ATG in RIC allo-SCT. No differences were observed in GRFS, PFS, OS, CIR or NRM after adjustment for confounding covariates. These findings support the continued use of alemtuzumab in RIC allo-SCT.

Disclosure: Nothing to declare.

B012

RESULTS OF ABATACEPT ADDITION TO POST TRANSPLANT CYCLOPHOSPHAMIDE-BASED GVHD PROPHYLAXYS IN ALLOGENEIC HEMATOPOYETIC STEM CELL TRANSPLANTATION

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Background: Graft-versus-host disease (GVHD) remains a leading cause of morbidity and mortality.Abatacept (ABA) inhibits T-cell activation and has recently been approved by the FDA for GVHD prophylaxis in combination with MTX and a calcineurin inhibitor. However, clinical data on its use alongside high-dose post-transplant cyclophosphamide (PTCY) regimens remain limited. Since February 2020, our center has incorporated ABA in patients undergoing HSCT with high risk GVHD (female donor, mismatched donor) and presenting HCT-CI score ≥3 and/or age ≥55 years. Initially, three doses of abatacept were administered on days +5, +14, and +28. Following an interim analysis, a fourth dose was added on day+56, based on existing literature, in an effort to reduce the incidence of chronic GVHD.

Methods: In this single center, retrospective analysis, 45 consecutive patients who underwent allo-HSCT between February 2020 and March 2025 were included. ABA was administered intravenously at a dose of 10mg/kg on days +5, +14, and +28. A subset of patients received an additional dose on day +56. Patients were stratified into two cohorts based on the administration of the day +56 dose: +56 cohort (n=17) and non+56 cohort (n=28).

Results:

Variable	+56 cohort	Non +56 cohort	p
Median age, years (IQR)	63 (57–65.5)	63 (57–65.5)	–
HCT-CI, median (range)	4 (0–13)	4 (0–13)	–
Graft source	PB (100%)	PB (100%)	–
GVHD prophylaxis	ABA+PTCY+TAC+MMF	ABA+PTCY+TAC+MMF	–
AML diagnosis	47.1%	56.3%	–
CR pre-HSCT	58.8%	50%	–
CR MRD+ AML	23.6%	11.8%	–
High/very high risk	23.5%	10.7%	0.3
Haplo donor	82.4%	85.7%	0.2
Reduced-intensity conditioning	88.2%	93.4%	0.5
Outcomes (overall cohort)			
Median follow-up, months (range)	15.7 (7.4–31.1)		
1-year PFS	66% (95% CI 0.5–0.7)		
1-year OS	72% (95% CI 0.5–0.8)		
1-year relapse CI	16.6% (95% CI 0.07–0.2)		
1-year NRM	23.3% (95% CI 0.12–0.3)		
GVHD outcomes			
aGVHD II–IV day +100	11.7%	10.7%	0.4
aGVHD II–IV day +180	18.5%	32.1%	0.4
Mod–sev cGVHD at 1 year	13.3%	28.9%	0.3
Immunosuppression stopped by day +100	47.1%	7.7%	0.007

The median age of the study population was 63 years (IQR 57–65.5), with a median HCT-CI of 4 (range 0–13). Baseline characteristics were generally balanced between cohorts, although a higher proportion of patients with high or very high disease risk were included in the +56 cohort. All patients received PBSC grafts and uniform GVHD prophylaxis including ABA. Haploidentical donors predominated, and reduced-intensity conditioning regimens were used in the majority of cases. Two patients in the +56 cohort received clofarabine–melphalan due to persistent disease prior to transplant. With a median follow-up of 15.7 months, estimated 1-year progression-free survival and overall survival in the overall cohort were 66% and 72%, respectively. The 1-year cumulative incidence (CI) of relapse was 16.6%, and non-relapse mortality was 23.3% (Table 1). The CI of grade II–IV acute GVHD at day +100 and day +180 was 11.7% vs 10.7% and 18.5% vs 32.1% in the +56 vs non+56 cohorts, respectively, without statistically significant differences. Grade III–IV acute GVHD incidence across the entire cohort was low (2.2% at day +100 and 6.9% at day +180). The CI of chronic GVHD at day +180 and day +365 was 13.3% vs 14.3% and 20.6% vs 28.5% in the +56 vs non+56 cohorts, respectively. Moderate-to-severe chronic GVHD at one year was numerically lower in the +56 cohort. Notably, immunosuppression discontinuation by day +100 was significantly more frequent in the +56 cohort (47.1% vs 7.7%, p=0.007). No ABA-

related adverse events were observed, and neutrophil and platelet engraftment were comparable between cohorts.

Conclusions: In this real-world PBSC allo-HSCT cohort receiving PTCY-based GVHD prophylaxis, the addition of abatacept was associated with low rates of acute and chronic GVHD and favorable overall outcomes. Administration of an additional ABA dose at day +56 enabled earlier immunosuppression discontinuation without an apparent increase in GVHD incidence. These findings support the feasibility of ABA incorporation into PTCY-based platforms and warrant prospective validation.

Disclosure: Nothing to declare

B013

BELUMOSUDIL FOR ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE: A SINGLE-CENTER REAL-WORLD STUDY OF EFFICACY AND SAFETY

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Background: Graft-versus-host disease (GVHD) remains a serious complication following allogeneic hematopoietic stem cell transplantation. Although corticosteroids serve as the cornerstone of first-line therapy, a considerable proportion of patients require additional treatment due to inadequate response, steroid dependence, intolerance, or the need to preserve graft-versus-leukemia (GVL) effects in high-risk settings. Belumosudil, a selective ROCK2 inhibitor approved for chronic GVHD (cGVHD), promotes immune homeostasis by rebalancing effector and regulatory T-cell responses. Importantly, preclinical studies indicate that inhibition of the ROCK1/2 pathway mitigates acute GVHD (aGVHD) by downregulating dendritic cell costimulation and T-cell trafficking, while notably preserving GVL activity. This mechanistic insight provides a strong rationale for evaluating belumosudil in aGVHD. However, real-world evidence regarding its use in aGVHD, as well as across different lines of therapy for cGVHD, remains limited. This study aimed to assess the real-world effectiveness of belumosudil in a heterogeneous cohort of patients with GVHD.

Methods: In this retrospective study, patients receiving belumosudil for GVHD after allo-HSCT were identified. Data on baseline characteristics, treatment history, clinical outcomes, and safety were collected.

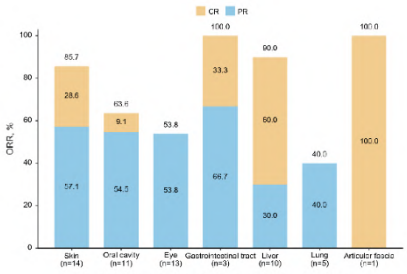

Figure 1. ORR by organ system in the cGVHD population

Results: A total of 32 patients with GVHD were analyzed, with a median follow-up of 9.2 months. The aGVHD cohort (n=8) had high-grade disease (62.5% grade III-IV) with universal gastrointestinal involvement.The cGVHD cohort (n=24) included 15 patients receiving belumosudil as second-line therapy (one prior treatment line) and 9 patients treated in later lines (≥2 prior lines), the latter group exhibiting a higher disease burden (33.3% vs. 20.0% severe cGVHD; median of 3 vs. 2 organs involved). In the aGVHD group, the day-28 overall response rate (ORR) was 100%, with 75% achieving complete response (CR) and a median time to response of 13.5 days; responses were maintained through day 56 in all surviving patients (5/5 CR). 7/8 patients responded in GI-GVHD. Among cGVHD patients, the best overall response rate reached 95.8%, including a CR rate of 16.7%. Notably, response rates were higher in the second-line therapy group (ORR 100%) compared to later-line therapy (ORR 88.9%). Responses deepened over time, with ORR increasing from 90.5% at 3 months to 95.8% at 6 months, and reaching 100% at 9 months among evaluable patients, reflecting sustained therapeutic benefit. All affected organs showed response(figure 1).Median time to response was 21 days, and median duration of response was 220 days (range 120–519). Immunosuppressant dose reductions were achieved in 79.1% of patients. Five fatal events occurred (four in aGVHD and one in cGVHD), all judged unrelated to belumosudil. No grade≥3 treatment-related adverse events were observed.

Conclusions: This study provides the first real-world evidence of belumosudil's efficacy in aGVHD, demonstrating promising therapeutic potential with a 100% day-28 ORR.The findings in cGVHD further validate its robust clinical activity, particularly when used in earlier treatment lines, supported by high response rates and a favorable steroid-sparing profile. The results support that belumosudil is highly effective and well-tolerated in the management of GVHD.

Disclosure: We have no potential conflict of interest and source of funding.

B014

REAL-WORLD SINGLE-CENTER EXPERIENCE OF ANTI-THYMOCYTE/ ANTI-T-LYMPHOCYTE GLOBULINS IN POST-TRANSPLANT CYCLOPHOSPHAMIDE CONDITIONINGS OF HAPLOIDENTICAL AND UNRELATED ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: SAFETY, EFFICACY, AND ENDOTHELIAL INJURY PROFILE

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Background: Different types of globulins, such as thymoglobulin (ATG) and Grafalon (ATLG), in combination with post-transplant cyclophosphamide (PTCY), have been incorporated into graft-versus-host disease (GvHD) prophylaxis regimens for haploidentical and unrelated allogeneic hematopoietic cell transplantation (allo-HCT) over the last few years. Nevertheless, no studies have compared the safety and efficacy of ATLG to ATG combined with PTCY in allo-HCT recipients. Moreover, the differential impact of these two agents on endothelial injury markers, such as soluble C5b-9, following HCT remains unexplored.

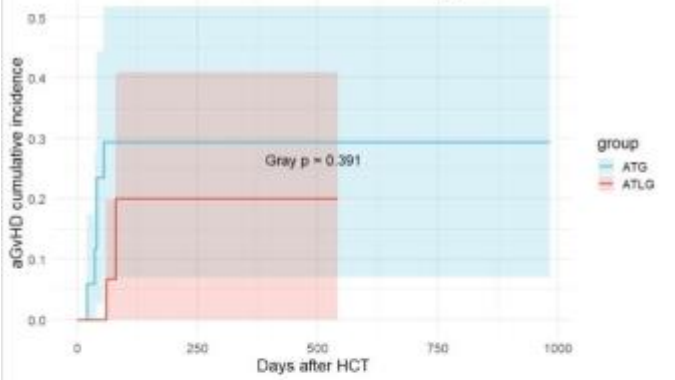
Methods: Therefore, we prospectively studied consecutive adult patients who underwent allo-HCT from a haploidentical or unrelated donor at our JACIE-accredited centre and received either ATLG (15 mg/kg for 3 days) or ATG (5 mg/kg for 2 days) along with PCTY as GvHD prophylaxis. The following parameters were analyzed: GvHD prophylaxis (ATLG or ATG), age, gender, HCT indication, disease risk index, donor type, endothelial activation and stress index (EASIX) score on the day of HCT, acute (aGvHD) and chronic (cGvHD) development, overall survival (OS), progression-free-survival (PFS), transplant-related mortality (TRM), and GvHD, relapse-free survival (GRFS). Patients' samples for sC5b-9 measurement were collected and stored before ATLG/ ATG administration and post-allo-HCT, and the difference between post and pre-HCT values was compared within the two arms.

Results: We studied 34 allo-HCT recipients (ATLG: 17, ATG: 17). The main indication for HCT in both groups was acute myeloid leukemia [41.2% versus (vs) 41.2%, p=0.66]. ATLG patients were older [median age interquartile range (IQR): 58 (48-63) vs 45 (27-55), p=0.006] and had higher baseline EASIX scores [6.25 (2.8-12.3) vs 1.3 (0.8-1.9), p<0.01]. The remaining clinical pre-HCT characteristics were comparable between the two groups. The 90-day cumulative incidence of aGvHD was 20% [95% confidence interval (95% CI): 0-41] for those treated with ATLG and 29.4% (7–51.8) for ATG patients (p=0.39, Figure 1A). Similarly, the 90-day cumulative incidence of grade≥ II aGvHD was comparable between the two groups [ATLG: 13.3% (0-31.1) vs ATG: 17.6% (0-36.4), p=0.62, 1B]. Regarding cGvHD, the 1-year cumulative incidence was 27.8% (3.6–52) in the ATLG arm and 48.4% (20.2-76.6) in ATG (p=0.37, 1C). Importantly, all cGvHD cases were classified as mild, whereas cGvHD development was correlated with prior aGvHD (p<0.001). Furthermore, we observed

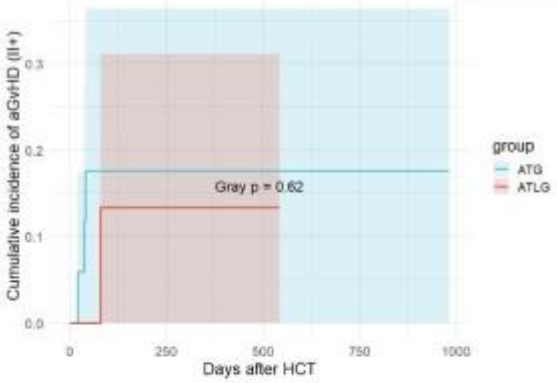
zero prevalence of graft failure. With a median follow-up of 9.7 (6.8-16.2) months [ATLG: 8.5 (6.7-10.3) vs ATG: 15.4 (7.2-23.6), p=0.04], 12-month OS was not statistically different among the two groups (ATLG: 75% (95% CI: 53.5-100) vs ATG: 92.3 % (78.9-100), HR: 2.23, p=0.38, 1D). Similarly, 12-month PFS was comparable (ATLG: 75% (53.5-100) vs ATG: 80.1 (62.2-100), HR: 0.97, p=0.97, 1E). Additionally, the 24-month cumulative incidence of TRM was 7.1% (95% CI: 0-21.1) in the ATLG group and 20% (0–59.2) in ATG (p=0.285, 1F). GRFS was found to be 52.8% (29.8-93.6) in the ATLG cohort and 58.8% (39.5-87.5) in ATG (p=0.66, 1G). The mean sC5b-9 difference was comparable between the two groups [ATLG: 161.4 ($\pm$308) vs ATG: 57.2 ($\pm$152), p=0.54, 1H].

Conclusions: Endothelial injury markers and clinical outcomes were similar between ATLG/ ATG and PCTY, with an excellent survival and safety profile.

Cumulative incidence of aGvHD **Figure 1A**



Cumulative incidence of aGvHD (Grade II+) **Figure 1B**



Cumulative incidence of cGvHD **Figure 1C**

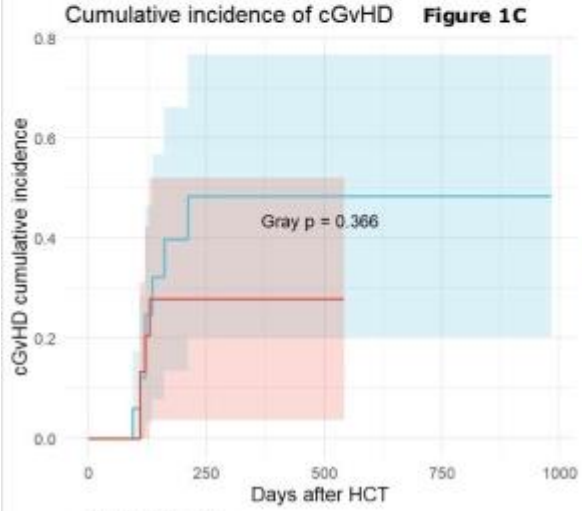
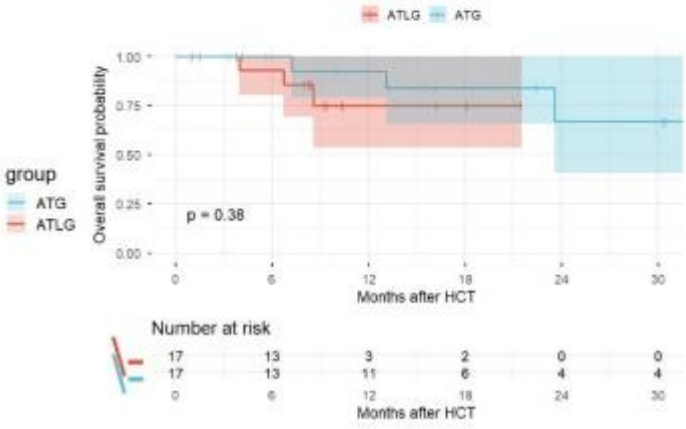


Figure 1D

Overall Survival: ATLG vs ATG



PFS: ATLG vs ATG **Figure 1E**

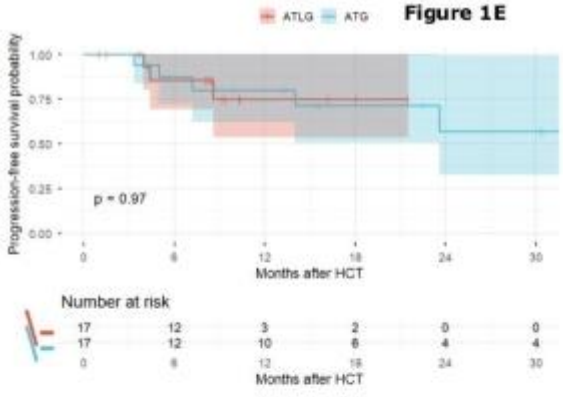


Figure 1F

Cumulative incidence of TRM

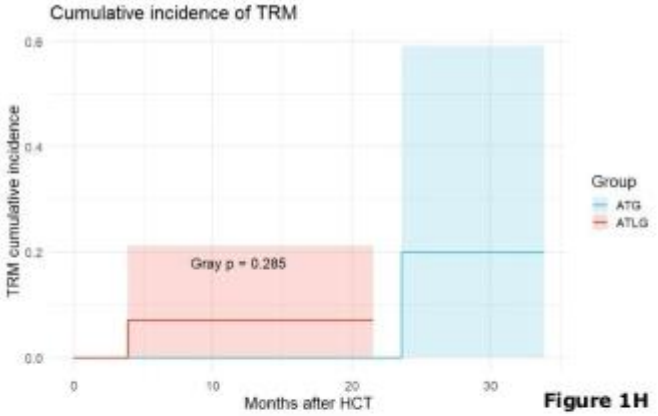
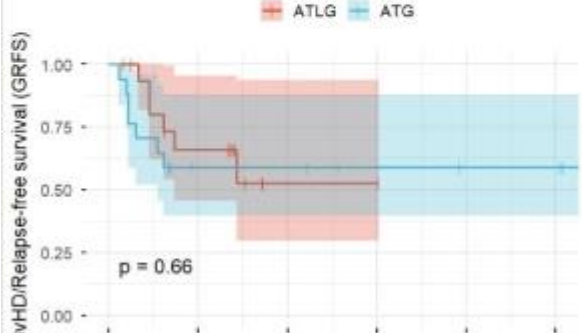
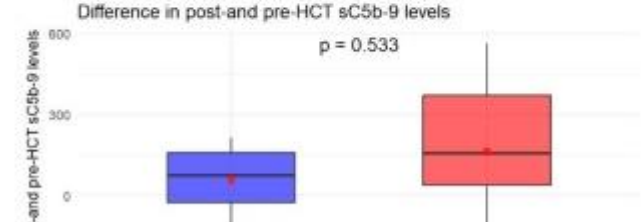


Figure 1H

GRFS: ATLG vs ATG **Figure 1G**



Difference in post-and pre-HCT sC5b-9 levels



Disclosure: This study was funded in part by an investigator-driven grant from Neovii Pharmaceuticals. Neovii Pharmaceuticals was not involved in the collection and interpretation of data, in the writing of the abstract, or in the decision to submit it for consideration in EBMT 2026. The authors have no other conflicts of interest to declare.

B015

ASSOCIATION BETWEEN ORAL CHRONIC GRAFT-VERSUS-HOST DISEASE AND THE GRAFT-VERSUS-LEUKEMIA EFFECT AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A PROSPECTIVE, SINGLE-CENTER OBSERVATIONAL STUDY

Nicolas Labrue[1], Ghada Abichou[2], Sami Benachour[2], Rinzine Sammut[2], Thomas Cluzeau[2], Christine Voha[2], ***Michael Loschi***[2]
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Background: Oral cGVHD compromises quality of life but may reflect the Graft-versus-Leukemia (GVL) effect due to shared T-cell mechanisms. We hypothesized that oral involvement serves as a clinical surrogate for beneficial immune surveillance and improved disease control.Consequently, the study aims to determine if oral cGVHD correlates with improved post-transplant outcomes, such as Overall Survival, Disease-Free Survival and Non-Relapse Mortal.

Methods: We conducted a prospective monocentric study including 54 consecutive patients who underwent allo-HSCT between October 2023 and May 2025. Oral evaluations were performed at pre-transplantation visit and at month +1, +3 +6, and +12 post-transplant. Oral cGVHD was graded according to the NIH Modified Oral Mucosal rating Scale (M-OMRS) consensus criteria by a dental practitioner. Clinical outcomes were compared between patients with and without oral cGVHD. Univariate and multivariate analyses were conducted using standard statistical methods with SPSS 2018 software. To focus on the impact of oral cGVHD, the following patient exclusions occurred post-transplant:frailty, early death, and patient withdrawal/refusal. These exclusions primarily concerned patients who were either too frail to develop sustained chronic GVHD or who did not survive long enough to reach the cGVHD assessment points.

Results:

Graft characteristics	Number (%)
Disease comorbidity	45 (83)
Complete Chimerism	50 (96,2)
Stem cell source Peripheral blood	51 (94,44)

Graft characteristics	Number (%)
Stem cell source cord blood	2 (3,70)
Stem cell source Bone marrow	1 (1,85)
CMV Donor-/recipient+ mismatch	17 (31,44)
Relationship to recipient unrelated	36 (66,66)
Relationship to recipient related	18 (34,34)
MAC	13 (24,07)
RIC	41 (75,99)

Among the 54 patients (median age 57,6 years, sex ratio 1/1) with a median follow up of 15,11 months, 52 (96,3%) developed aGVHD, and 46 (85%) cGVHD, including oral involvement in 35 cases (76%). two cases of oral cGVHD weren't associated with a systemic form. Oral cGVHD scores were mild in 35,1% of the cases, moderate and severe equal at 31,4% of the cases according to the NIH M-OMRS assessment.The most frequency underlying disease was AML in 20 cases and Myelofibrosis in 12 cases. Twenty-four patients were in RC1 state while 15 were RC2, 2 were RC3 and 1 RC4. One patient with myelofibrosis was in partial remission and 11 had a stable disease. At 15 months OS was significantly higher in patients with oral cGVHD compared to those without (100% vs 66%, p=0.01). DFS was also significantly improved (98% vs. 48%, p=0.003). Importantly, oral cGVHD was not associated with increased NRM, at 15 months it was significantly lower in patients with oral cGVHD compared to those without (0% vs. 24%, p=0.002), indicating a strong negative correlation between the presence of oral cGVHD and the incidence of NRM.

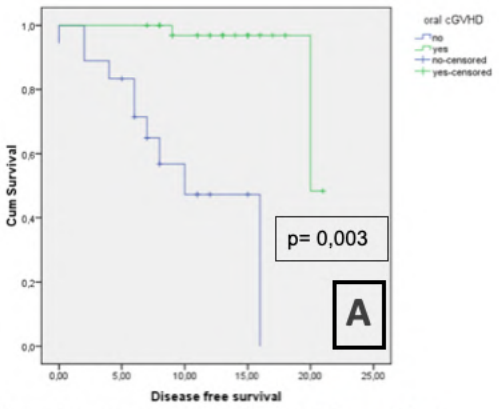

Figure A : Impact of oral cGVHD on Disesase Free Survival

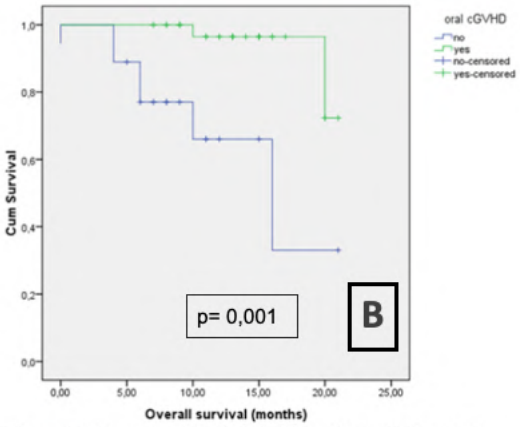

Figure B : Impact of oral cGVHD on Overall Survival

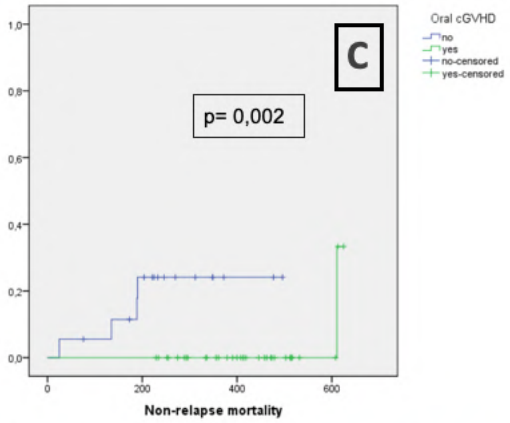

Figure C : Impact of oral cGVHD on Non Relapse Mortality

Conclusions: This prospective study identifies oral cGVHD as a promising proxy for the GVL effect. Crucially, the presence of oral cGVHD correlated with significantly improved OS and DFS, without increasing NRM. these results suggest that mild to moderate oral cGVHD indicates a favorable balanced immune state. This methodology likely contributed to the high incidence of acute GVHD (96.3%) and chronic GVHD (85%) observed in the final cohort, as patients with early, non-relapse mortality (often without established cGVHD) were disproportionately excluded from the primary outcome analysis. The short median follow-up of 15.11 months is a primary limitation of the current data, which requires further validation. Ongoing analyses, including salivary biomarkers and long-term data updates, aim to validate early diagnostic tools and optimize post-transplantmanagement strategies.

Clinical Trial Registry: **NCT07271498**
clinicalTrial.org

Disclosure: Dr Loschi Michael's conflict of interest: Alexion, Astellas, AstraZeneca, BMS Celgene, Gilead, GSK, Incyte Biosciences, Janssen, Kartos, Medac, MSD, Neovii, Novartis, Pfizer, Sanofi Winthrop, Sobi, Telios, Takeda, Morphosys.

Pr Cluzeau Thomas' conflict of interest: Aprea, Novartis, Alexion, BMS Celegene, Amgen, Syros, Kartos, Arog, Sanofi Winthrop, Pfizer, Novartis

B016

THE COMBINATION OF RUXOLITINIB AND EXTRACORPOREAL PHOTOPHERESIS IS A HIGHLY EFFECTIVE SECOND LINE TREATMENT FOR CHRONIC GRAFT-VERSUS-HOST DISEASE

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is potentially curative for hematologic malignancies, but its success is limited by graft-versus-host disease (GVHD). Chronic GVHD (cGVHD) affects one third to half of long-term survivors and is a major cause of late non-relapse morbidity and mortality. Standard first-line therapy with prolonged glucocorticoids frequently leads to steroid-refractory (SR) or steroid-dependent (SD) disease and long-tem toxicity. Ruxolitinib is an established second-line agent in SR cGVHD, while extracorporeal photopheresis (ECP) is an effective immunomodulatory option with a relative lack of toxicity and immunosuppression. Both are recommended as preferred second-line therapies, but data on their combined use in larger, well-characterized cGVHD cohorts remain limited. We therefore evaluated the efficacy and safety of combined ECP and ruxolitinib (RUX+ECP) treatment and explored clinical predictors of response.

Methods: We performed a single-center retrospective study of 80 patients with SR or SD cGVHD, treated between 2017 and 2025 at Central Hospital of Southern-Pest, National Institute of Hematology and Infectious Diseases, Department of Hematology and Stem Cell Transplantation, Innovative Cell Therapy Center, Budapest, Hungary. SR cGVHD was defined as progression despite ≥1mg/kg/day prednisone for 1–2 weeks or lack of improvement on ≥0.5mg/kg/day for 1–2 months, SD cGVHD as flare when tapering prednisone below 0.25mg/kg/day. All patients received ruxolitinib 5–10 mg twice daily combined with ECP, initiated twice weekly and then tapered individually. Responses were assessed by NIH consensus criteria as complete response (CR), partial response (PR), or no response (NR). Statistical analyses were performed using GraphPad Prism 10.6.1.

Results: Median age at start of treatment was 45.5 years (IQR 31.25–53). Underlying diseases were predominantly AML (38/80,47.5%) and B/T-ALL (19/80,23.8%). Myeloablative conditioning was used in 59 patients (73.8%) and reduced-intensity conditioning in 21 (26.2%). Donor types included matched unrelated donors in 32 patients (40.0%), HLA-identical related donors in 27 (33.8%), and haploidentical related donors in 21 (26.2%). Overall, 32 patients (40.0%) achieved CR and 36 (45.0%) PR, yielding an overall response rate of 68/80 (85.0%), 12 patients (15.0%) were non-responders. Median time to response was 30 days (IQR 21–60). Neither baseline cGVHD severity (χ^2=0.62, df=2, p=0.73) nor

donor type (χ^2=1.7, df=2, p=0.42) significantly influenced response to RUX+ECP. A prior history of acute GVHD (aGvHD) likewise had no statistically significant impact on response (92.3% vs 81.4% responders without vs with prior aGVHD; χ^2=1.61, df=1, p=0.20; Fisher's exact test p=0.31).

Conclusions: Here we report the largest cohort to date to evaluate the efficacy and safety of RUX+ECP in cGVHD. In this SR or SD cGVHD population, we observed an overall response rate of 85%, which compares favorably with historical cohorts treated with ruxolitinib monotherapy (60–75%). Response rates were consistently high across the patient population, independent of donor types, baseline cGVHD severity or the history of aGVHD, suggesting that the benefit of this combination extends across clinically diverse risk groups. No relevant safety signal emerged. These findings support RUX+ECP as a highly active and broadly applicable second-line strategy in cGVHD and warrant confirmation in prospective, controlled studies.

Disclosure: Therakos Advancing ECP Immunomodulation Investigator Award 2024 -Andrea Varkonyi and Nikolett Wohner

B017

OUTCOMES IN TCRAB-DEPLETED HAPLOIDENTICAL TRANSPLANTATION WITH UPFRONT CD45RA-DEPLETED MEMORY T-CELL ADD-BACK: ANALYSIS OF 127 ADULTS WITH HEMATOLOGICAL MALIGNANCIES TREATED AT NATIONAL UNIVERSITY CANCER INSTITUTE, SINGAPORE

Victor Wei Teik Ling[1], *Boo Yang Liang*[1,2], *Michelle Limei Poon*[1], *Lip Kun Tan*[1], *Joanne Lee*[1,3], *Evelyn Aun*[1], *Ian Wu*[1,4], *Balamurugan Vellayappan*[1], *Teck Guan Soh*[1,5], *Christopher Thow*[1], *Jamie Chew*[1], *Yin Jie Koh*[1], *Liang Piu Koh*[1]
[1]*National University Cancer Institute, Singapore, Singapore,* [2]*Hospital Sultanah Aminah, Johor Bharu, Malaysia,* [3]*Center for Clinical Haematology, Mount Elizabeth Novena Medical Center, Singapore, Singapore,* [4]*Sengkang General Hospital, Singapore, Singapore,* [5]*KK Women's and Children's Hospital, Singapore, Singapore*

Background: In haploidentical hematopoietic cell transplantation (haplo-HCT), effective prevention of graft-versus-host disease (GVHD) through T-cell depletion (TCD) must be balanced against increased risks of infection and relapse. We hypothesised that combining a TCRαβ-depleted allograft with upfront infusion of CD45RA-depleted memory T cells (αβTCD+T_MDLI) could improve GVHD-free, relapse-free survival (GRFS).

Methods: Mobilized peripheral blood stem cells (PBSC) were separated into two fractions (8-9:1-2 ratio) and depleted using the CliniMACS device (Miltenyi Biotec) with TCRαβ and CD45RA reagents, respectively. Most patients (n=119) received reduced-intensity conditioning comprising fludarabine, thiotepa, and melphalan combined with either total lymphoid irradiation (TLI 6-7.5 Gy; n=22), low-dose total body irradiation (TBI 2 Gy; n=105), or anti-thymocyte globulin (ATG; n=1). Eight patients received alternative

conditioning regimens. GVHD prophylaxis (tacrolimus n=117; sirolimus n=2; MMF n=4) was administered for 30 days post-transplant.

Results: Between 2017-2025, 127 patients (median age 56 years, range 18-75) with high-risk malignancies underwent αβTCD+TMDLI: AML (n=67, 53%), ALL (n=22, 17%), MDS/MPN (n=15, 12%), lymphoproliferative disorders/others (n=23, 18%). The grafts contained median 7.33×10^6 $CD34^+$ cells/kg, 2.06×10^6 $CD3^+CD45RO^+$ memory T cells/kg, 8.2×10^6 $TCR\gamma\delta^+$ cells/kg, with negligible $TCR\alpha\beta^+$ and $CD3^+CD45RA^+$ naïve T cells. Engraftment was robust with median neutrophil and platelet recovery at days 12 (range 7-22) and 11 (range 7-43), respectively. No primary graft failure occurred; two secondary graft failures after day +90 (COVID-19 vaccine-related and sepsis-induced) were successfully rescued with second transplants from different donors. Five patients with high-level donor-specific antibodies achieved successful engraftment after desensitization.
Cumulative incidence (CI) of grade II-IV and III-IV acute GVHD at 180 days was 27.0% (95% CI 19.6-34.9) and 5.5% (95% CI 2.4-10.5), respectively. Two-year CI of chronic GVHD was 6.8% (95% CI 2.9-12.8). At 2 years, non-relapse mortality (NRM) was 18.5% (95% CI 11.9-26.2) and relapse was 15.8% (95% CI 9.3-23.8). With median follow-up of 22 months, the 3-year overall survival, event-free survival, and GRFS were 68% (95% CI 56.9-77.1), 66% (95% CI 55.9-74.3) and 58% (95% CI 47.8-67.0), respectively.
Multivariate analysis identified low/intermediate disease risk index (DRI) and the use of TBI 2Gy as independent prognostic factors associated with superior OS, EFS, GRFS, and lower NRM. Relapse was influenced solely by DRI. Letermovir prophylaxis correlated with improved outcomes in univariate, but not multivariate analysis. Outcomes significantly improved in transplants performed after 2020, coinciding with universal adoption of TBI 2Gy and letermovir prophylaxis.

Conclusions: RIC haplo-HCT using TCRαβ-depleted grafts with upfront CD45RA-depleted memory T-cell achieves reliable engraftment, remarkably low rates of severe acute and chronic GVHD, translating into promising GRFS. Optimal outcomes occur in patients with low/intermediate-risk DRI receiving TBI 2Gy conditioning.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

B018

MESENCHYMAL STROMAL CELLS FOR THE TREATMENT STEROID REFRACTORY GRAFT-VERSUS-HOST DISEASE IN CHILDREN

Krzysztof Czyzewski[1], *Joanna Cisek*[1], *Monika Richert-Przygonska*[1], *Robert Debski*[1], *Katarzyna Peszynska-Zelazny*[1], *Lukasz Ledzinski*[2], *Anna Klarkowska*[2], *Jan Styczynski*[1]
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Background: Corticosteroids remain the first-line therapy for both acute and chronic graft-versus-host disease (GVHD). However, approximately 50% of patients with acute GVHD are

refractory to high-dose corticosteroids, and 50–60% of patients with moderate to severe chronic GVHD require steroid-sparing treatment strategies. Mesenchymal stromal cells (MSCs) derived from Wharton's jelly represent a therapeutic option for subsequent lines of treatment in steroid-refractory (SR) GVHD. MSCs are multipotent, non-hematopoietic stromal cells with immunoregulatory and immunosuppressive properties mediated through the secretion of cytokines, chemokines, and extracellular vesicles. MSC therapy is generally safe, with a low incidence of adverse events. The aim of this study was to evaluate the safety and efficacy of MSC therapy in pediatric patients with steroid-refractory GVHD based on a single-center experience.

Methods: We performed a retrospective analysis of pediatric patients with steroid-refractory graft-versus-host disease (SR-GVHD) following allogeneic hematopoietic stem cell transplantation (allo-HSCT) who received cryopreserved, commercially available, third-party donor Wharton's jelly–derived mesenchymal stromal cells (WJ-MSCs).

Results: Twenty children (13 boys, 7 girls) with median age 5.3 years (age range 3 months - 16.7 years), diagnosed for ALL (n=6), primary immunodeficiencies (n=6), AML (n=3), MDS (n=1), BMF (n=4: SAA n=2, BDA n=1, FA n=1) recipients of allo-HSCT (10 MUD-PB, 7 MUD-BM, 2 MSD-PB, 1 MSD-BM) were included into the study. In all patients SR-GVHD was diagnosed (15 acute GVHD, grade 2-4: 6-skin+gastro-intestinal, 4-skin, 2-gastro-intestinal, 1-lungs+skin, 1-hepatic+gastro-intestinal, 1-skin+hepatic+gastro-intestinal; 5 chronic GVHD, grade moderate-severe: 2-skin, 1-sclerodermatous, 1-skin+eye, 1 lungs+skin+gastro-intestinal). The total number of 85 MSCs intravenous infusions were performed (median: 3, range: 1-10). The median number of infused MSCs was $1.36x10^6$/kg b.w. (range 0.85-2.99) in 1-4 weeks intervals. In 19/20 patients before MSC administration combined therapy with corticosteroids was performed including 1-3 agent/therapy (ciclosporine, tacrolimus, mycophenolate mofetil, vedolizumab, ruxolitinib, basiliximab, extracorporeal photophereses). The median time from GVHD diagnosis to first infusion of MSC was 96 days (range 15-305 days); 75% (15/20) achieved a response (55% complete response, 20% partial response), while 25% (5/20, all acute GVHD) did not respond to MSC therapy. Overall, 80% (12/15) of patients with complete/partial response are alive (2 patient died due to leukemic relapse, 1 due to infection). Among 5 non-responding patients, 3 died due to GVHD progression, 1 due to infection and 1 due to toxic encephalopathy. In two patients, mild abdominal pain occurred 1-2 days after infusion (not after all infusions). No other adverse events were observed in the other patients.

Conclusions: Cryopreserved Wharton's jelly mesenchymal stromal cells area safe and effective therapeutic option in pediatric patients with steroid refractory acute or chronic GVHD. Overall, 75% of patients achieved clinical response.

Disclosure: Krzysztof Czyzewski: lectures fees and participation in scientific conferences supported by the Polish Stem Cell Bank. Other authors – nothing to declare.

B019

BEYOND STATIC SNAPSHOTS: A DYNAMIC PREDICTION MODEL FOR ACUTE GRAFT-VERSUS-HOST DISEASE INTEGRATING SERIAL MEASUREMENTS OF SIX INFLAMMATORY BIOMARKERS

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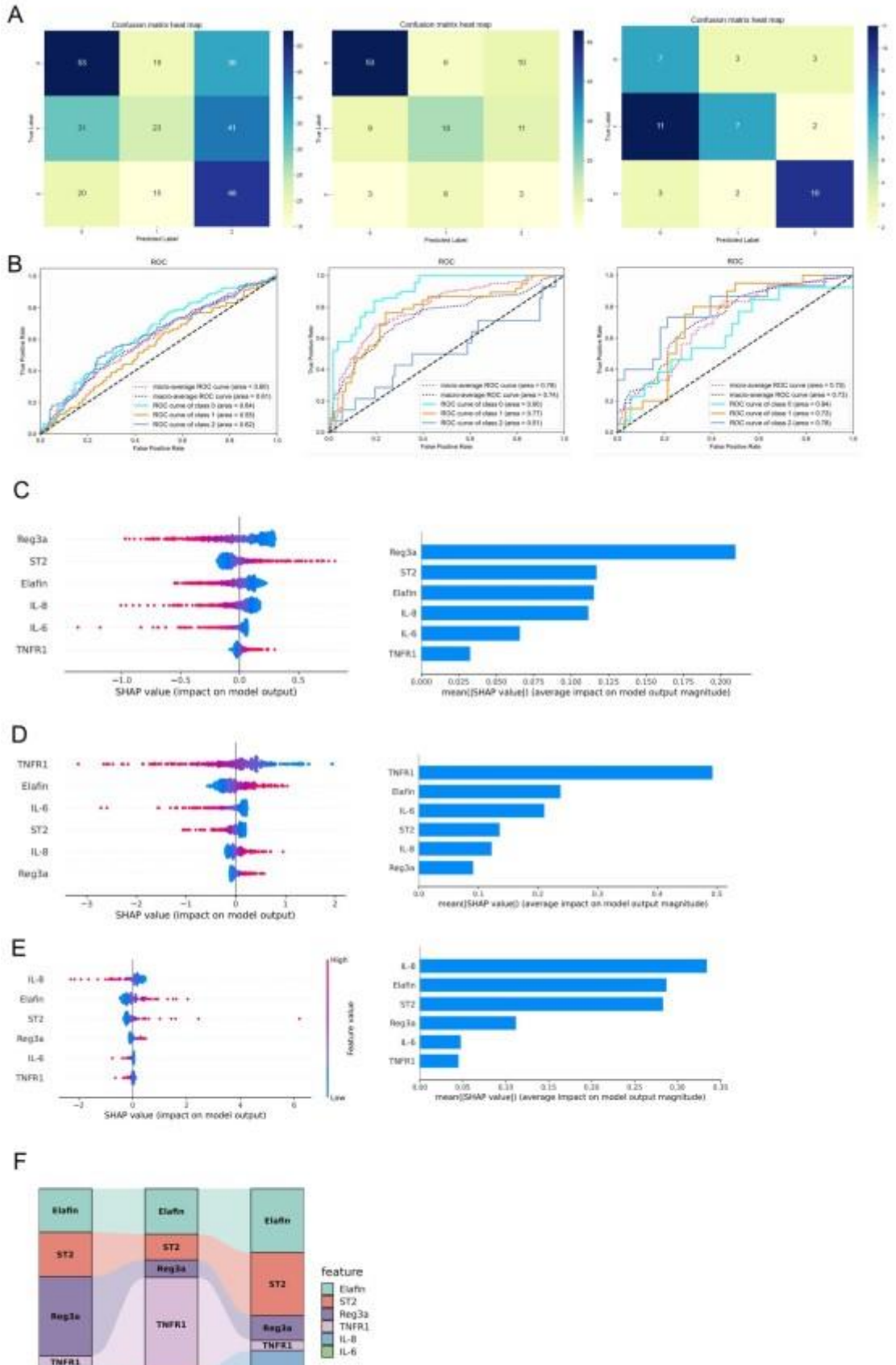
Background: Acute graft-versus-host disease (aGVHD) is a life-threatening complication following allogeneic hematopoietic cell transplantation (allo-HSCT), with non-relapse mortality (NRM) rates exceeding 50% in severe cases. This high mortality underscores the urgent need for accurate and timely predictions to guide risk-adapted therapies. Although several prognostic models exist, including clinical grading and biomarker-based tools, they have notable limitations. Therefore, we propose a dynamic prediction model that integrates distinct pathophysiological signals from multiple biomarkers measured serially after transplantation.

Methods: This single-center, retrospective cohort study enrolled patients undergoing HID-HSCT at the Stem Cell Transplantation Center, Institute of Hematology and Blood Diseases Hospital, Chinese Academy of Medical Sciences, between January 2019 and January 2025. Six inflammatory biomarkers—IL-6, IL-8, TNFR1, ST2, REG3α, and Elafin—were measured at three time points: on the day of stem cell infusion (day 0) and on days +7 and +14 post-infusion. The dataset was randomly divided into training and testing sets at a 7:3 ratio. Machine learning (ML) models were developed based on the six biomarkers at different time points, and their performance was assessed. We evaluated a total of twelve ML classifiers, optimizing them via 10-fold cross-validation repeated ten times and grid search. Model performance was assessed using the area under the ROC curve (AUC), accuracy, sensitivity, specificity, and F1-score. Interpretability of the optimal "black-box" model was achieved using SHapley Additive exPlanations (SHAP) to determine global feature importance and provide local explanations for individual predictions.

Results: This retrospective study included 1,278 patients who underwent HID-HSCT and completed biomarker testing. Ultimately, 951 patients were enrolled and completed follow-up. Among the algorithms tested, logistic regression demonstrated the most robust and consistent performance. Predictive accuracy varied over time, with the highest discriminative ability observed on day +7 (AUC=0.78), compared to day 0 (AUC=0.62) and day +14 (AUC=0.51). SHAP analysis revealed distinct, time-dependent biomarker importance: at day 0, REG3α, ST2, and Elafin (reflective of initial tissue damage) were most influential; by day +7, TNFR1, IL-6, and Elafin (indicating systemic inflammation) dominated; and at day +14, IL-8, Elafin, and ST2 (GVHD-associated tissue injury and adaptive immune responses) became primary contributors. This shift underscores the evolving biological processes post-

transplant.


A
B
ROC
C
Reg3a
ST2
Elafin
IL-8
IL-6
TNFR1
SHAP value (impact on model output)
mean(|SHAP value|) (average impact on model output magnitude)
D
E
High
Low
Feature value
F
feature

Conclusions: Our study validated a dynamic, time-aware machine learning model for predicting Grade II–IV aGVHD following HID-HSCT using six classic inflammatory biomarkers—IL-6, IL-8, TNFR1, ST2, REG3α, and Elafin—measured at multiple post-transplant time points. By establishing a time-aware modeling framework, this study demonstrates how dynamic biomarker importance reflects physiological transitions after transplantation—from initial tissue injury to subsequent immune activation. Such an approach enables earlier identification of patients at risk, providing clinicians with actionable insights for timely and individualized intervention.

Disclosure: Nothing to declare.

B020

THE ROLE OF ADDING ANTITHYMOCYTE GLOBULIN TO STANDARD GVHD PROPHYLAXIS IN HLA ONE-LOCUS–MISMATCHED UNRELATED BONE MARROW TRANSPLANTATION: A RANDOMIZED MULTICENTER PHASE III TRIAL

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Background: ATG has been reported to improve GRFS in HLA-mismatched unrelated PBSCT; however, its role in BMT remains unclear. We conducted a prospective, randomized, multicenter phase III trial to evaluate the efficacy of adding ATG-Thymoglobulin (ATG-T) to standard GVHD prophylaxis with tacrolimus and methotrexate.

Methods: Patients with hematologic malignancies scheduled to undergo HLA one-locus mismatched unrelated BMT were enrolled. Patients were randomly assigned in a 1:1 ratio to receive standard GVHD prophylaxis with or without ATG-T at a dose of 2.5 mg/kg. The target enrollment was 130 patients; however, only 102 were enrolled, and 97 were eligible for analysis (47 in the ATG-T group and 50 in the control group). The primary endpoint was GRFS.

Results: At one year, GRFS was 42.6% (95% CI, 28.3–57.8) in the ATG-T group and 36.0% (95% CI, 22.9–50.8) in the control group, with no significant difference (P=0.509, Figure 1). The incidence of grade III–IV acute GVHD was 10.6% in the ATG-T group and 12.0% in the control group (P=0.833). The incidence of severe or steroid-requiring moderate chronic GVHD was 14.9% and 14.0%, respectively (P=0.900). The relapse rate was 34.0% (95% CI, 20.9–49.3) in the ATG-T group versus 28.0% in the control group (P=0.520). Overall survival was 78.7% in the ATG-T group and 68.0% in the control group (P=0.233), with no significant difference observed.

Conclusions: Although the target enrollment was not met, limiting the strength of the conclusions, the addition of ATG-T to standard GVHD prophylaxis did not demonstrate improvement in one-year GRFS. No significant differences were observed in secondary endpoints either, suggesting that the impact of low-dose ATG in HLA one-locus mismatched unrelated BMT may be limited.

Clinical Trial Registry: CRB3200006

Disclosure: Junya Isada: Received lecture fees from Sanofi.
Yoshinobu Kanda: Received lecture fees from Sanofi.
Emiko Sakaida: Received lecture fees from Bristol Myers Squibb, Novartis, Pfizer, Sanofi, and Janssen.

B021

3X3 COMPARISON OF TACROLIMUS, SIROLIMUS AND MYCOPHENOLATE MOPHETIL (MMF) VS POSTRASPLANT CYCLOPHOSPHAMIDE (PT-CY), TACROLIMUS AND MMF VS PT-CY, SIROLIMUS AND MMF. A RETROSPECTIVE ANALYSIS (GETH-TC)

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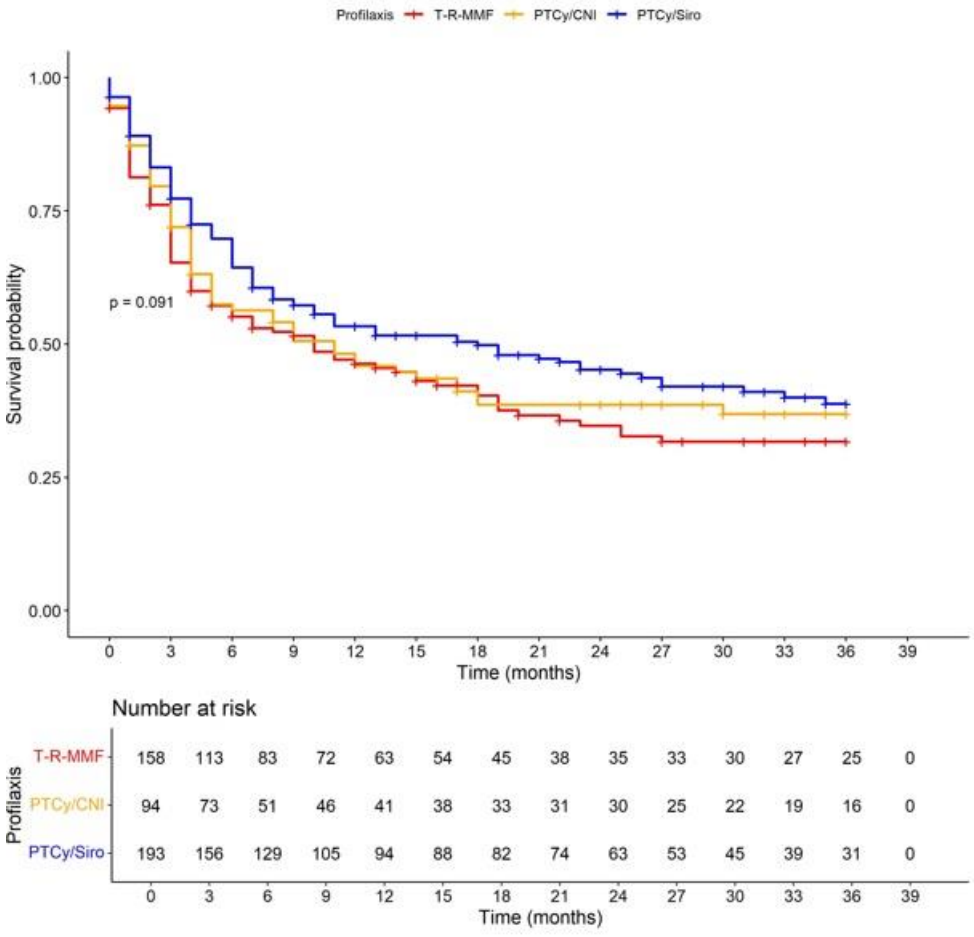
Background: Calcineurin inhibitor (CNI) based prophylaxis combined with an antimetabolite has been the historical standard for preventing graft-versus-host disease (GVHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Post-transplant cyclophosphamide (PTCy) has reshaped this paradigm decreasing acute and chronic GVHD without impairing overall survival (OS). In parallel, sirolimus has emerged as an effective alternative to CNIs, lowering aGVHD and improving survival outcomes. Therefore, PTCy-

based strategies incorporating sirolimus instead of tacrolimus have generated meaningful interest.

Methods: A multicenter, retrospective study included 445 adult patients undergoing reduced-intensity conditioning allo-HSCT between September`19 and December`22 was performed to compare 3 GVHD-prophylaxis regimens based on: tacrolimus-sirolimus-MMF (G1, n=158), PTCy-CNI-MMF (G2, n=193), and PTCy-sirolimus-MMF (G3, n=94). Outcomes evaluated included overall survival (OS), GVHD-free relapse-free survival (GRFS), incidence of acute and cGVHD, relapse, transplant-related mortality (TRM), and CMV reactivation. To quantify differences for the different outcomes, Cox proportional hazards models were fitted with G1 as reference group. We accounted transplant centre as a clustering factor. Hazard ratios (HRs) therefore represent population-averaged effects with standard errors corrected for intra-centre correlation. Results are reported as HRs with 95% confidence intervals (CI) and two-sided p-values.

Results:



Characteristic	**No PT Cy N= 158 (35.5%)**	**PT Cy CNI N=96 (21%)**	**PT Cy Siro N=203 (44.5%)**	P
Age at transplant (years), median (range)	61 (20-72)	57.5 (19-72)	*58.6 (19-72)*	0.004
Male, n (%)	97 (61,4%)	54 (57.4%)	118 (61.1%)	0.798
HCT-CI (%) 0 1,2 >3	 3 (1.9%) 64 (40.5%) 91 (57.6%)	 7 (7.4%) 41 (43.6%) 46 (49%)	 37 (19.2%) 55 (28.5%) 101 (52.3%)	<0.001
Diagnosis n (%) Acute myeloid leukemia Myelodysplactic syndrome Acute lymphoblastic leukemia Non-Hodgkin lymphoma Hodgkin Lymphoma Chronic myelomonocytic leukemia Primary myelofibrosis MDS/MNP Multiple mieloma/ Plasma cell leukemia CML Others	 53 (33.5%) 39 (24.7%) 3 (1.9%) 22 (13.9%) 9 (5.7%) 15 (9.5%) 10 (6.3%) 0 (0%) 2 (1.3%) 5 (3.2%) 0 (0%)	 35 (38.8%) 24 (25.1%) 7 (7.4%) 9 (9.5%) 3 (3.2%) 3 (3.2%) 5 (5.3%) 0 (0%) 1 (1.1%) 4 (4.2%) 2 (2.2%)	 73 (37.8%) 21 (10.9%) 10 (5.2%) 34 (17.6%) 15 (7,8%) 8 (4.1%) 10 (5.2%) 1 (0.5%) 11 (5.7%) 2 (1%) 8 (3.9%)	0.001
Disease risk index (DRI), n (%) Very high/High Intermediate Low	 81 (51.2%) 62 (39.2%) 15 (9.5%)	 33 (35.9%) 54 (58.7%) 5 (5.4%)	 52 (27%) 113 (58.5%) 28 (14.5%)	<0.001

Related donor Unrelated dolor	98 (62%) 60 (38%)	11 (11.7%) 83 (88.3%)	117 (60.6%) 76 (39.4%)	<0.001
Identical HLA 1 Mistmatched	122 (77.2%) 36 (22.8%)	73 (77.7%) 21 (22.3%)	175 (90.7%) 18 (9.3%)	0.001
Conditioning regimen, n (%) Flu-Bu Flu-Bu-Thio Others	129 (81.6%) 26 (16.5%) 3 (1.9%)	8 (8.5%) 73 (77.7%) 13 (14%)	7 (3.6%) 149 (77.2%) 37 (19.2%)	<0.001
Graft source, n (%) Peripheral blood Bone Marrow	158 (100%) 0 (0%)	88 (93.6%) 6 (6.4%)	191 (99%) 2(1%)	0.001

Baseline characteristics were balanced *(Table 1)*, although G3 contained the highest proportion of HCT-CI = 0, and G1 the highest percentage of high/very-high DRI.
Cumulative incidence (CI) of grades II-IV aGVHD were 31% for G1, 27% [HR 0.73 (95% CI 0.60–0.88) p=0.001] for G2 and 28% [HR 0.77 (95% CI 0.53–1.11) p=0.20] for G3. By contrast, no significant diferentes were observed for grades III-IV aGvHD between the different groups with a CI of 14, 15 and 14%, respectively. Similarly, no significant differences were observed in terms of mod/severe cGvHD, with CI of 40% for G1, 37% [HR 1.33 (95% CI 0.81–2.17) p=0.30] for G2 and 28% [HR 0.86 (95% CI 0.69–1.07) p=0.20] for G3. Significantly lower rates of mucositis, CMV reactivation, and hemorrhagic cystitis were observed among patients included in G1.
OS at 3 years was 64% for G1, 67% [HR 0.80 (95% CI 0.59–1.07) p=0.13] for G2 and 62% [HR 0.97 (95% CI 0.72–1.32) p=0.90] for G3, while GRFS at 3 years was 32% for G1, 37% [HR 0.90 (95% CI 0.74–1.09) p=0.30] for G2 and 39% [HR 0.77 (95% IC 0.71–0.84) p<0.001] for G3.
In multivariate analysis, age [HR 1.03 (95% CI 1.01-1.04), p<0.001], HLA mismatched [HR 1.4 (95% CI 1.12-1.74), p=0.003] and unrelated donor [HR 1.31 (95% CI 1.14-1.5), p<0.001] significantly influenced on OS while GvHD prophylaxis: for G2 [HR 0.79 (95% CI 0.76-0.94, p=0.007] and for G3 [HR 0.81 (95% CI 0.70-0.94), p=0.004] together with age [HR 1.01 (95% CI 1.0-1.02), p<0.046], HLA mismatched [HR 1.62 (95% CI 1.15-2.27), p=0.006] and unrelated donor [HR 1.28 (95% CI 1.04-1.56), p<0.017] significantly influenced on GRFS.

Conclusions: As compared to tacrolimus-sirolimus-MMF, the use of PTCy-CNI-MMF and PTCy-sirolimus-MMF decreases the risk of GRFS while increases the risk of mucositis, CMV reactivation, and hemorrhagic cistitis. No differences in terms of survival are observed between these strategies to prevent GvHD.

Disclosure: Nothing to declare

B022

ST2 AND REG3A IN GRAFT VERSUS HOST DISEASE

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Background: Serological biomarkers offer a non-invasive way to predict chronic graft-versus-host-disease (cGvHD) occurrence/outcomes. Suppression of tumorigenicity (ST2) and Regenerating islet-derived protein 3-alpha (REG3a) have been shown to predict onset of acute graft-versus-host disease (aGvHD) and correlate with gastrointestinal cGvHD severity at onset. There is little published evidence of their role in predicting cGvHD. ST2 is a member of the interleukin family (IL)-1 receptor family, binding to IL-33 with capacity to regulate its function.1 REG3a is a c-type lectin secreted by Paneth cells, and a biomarker of GI GvHD.2 Our study aims to evaluate the association of ST2/REG3a levels with aGvHD/cGvHD incidence.

Methods: Consecutive patients who underwent elective alloSCT between January 2022 to 2024 were included in this study and were followed up regularly to evaluate for aGvHD/cGVHD. Patient serum was collected on day (D)100 following allogeneic stem cell transplant (alloSCT); ST2/REG3a concentrations were measured using enzyme-linked immunosorbent assay (ELISA). GvHD severity was graded according to Mount Sinai Acute GVHD International Consortium (MAGIC) criteria for aGVHD and National Institutes of Health (NIH) criteria for cGVHD. Data was compared using 2-tailed Welch's t-test and analysed using GraphPad.

Results: 101 patients were analysed during this study period. Table 1 shows patient characterstics. The median follow-up period was 23.8 months. Median time of onset for aGvHD and cGvHD were 51 and 204 days respectively.
ST2 levels at D100 post-alloSCT were elevated in patients with Grade II-IV aGvHD compared to patients with Grade I or less (52682 pg/L versus 37181 pg/L; p=0.004). Therefore, patients with grade II–IV aGVHD were excluded from subsequent analyses of cGVHD outcomes to avoid confounding (n=32). There was no significant difference in D100 ST2 levels between patients with cGVHD and those without cGVHD (33059 pg/L versus 38619 pg/L; p=0.25). D100 ST2 levels were not significantly different between patients with moderate-severe cGVHD and patients unaffected by cGVHD (37221 pg/L versus 38619 pg/L; p=0.84) and those with and without involvement of the gastrointestinal (GI) tract (60532 pg/L; 33399 pg/L; p=0.11).

REG3a levels at D100 did not differ between patients with and without grade II–IV aGVHD (23 ng/L versus 30 ng/L; p=0.27) or between those with and without cGVHD (34 ng/L versus 28.4 ng/L; p=0.61), and were not associated with cGVHD severity (37 ng/L versus 28 ng/L; p=0.55) or gastrointestinal involvement (23 ng/L versus 32.8 ng/L; p=0.45).

	Patients (N)	**Percentage (%)**

Male sex, n, %	70	69.3
Diagnosis, n, %		
Acute leukaemia	60	59.4
Myelodysplastic syndrome	13	12.9
Myeloproliferative neoplasm	13	12.9
Lymphoma	10	9.9
Others	5	5
GVHD prophylaxis, n, %		
Post transplant cyclophosphamide	84	83.2
Methotrexate	9	8.9
Alemtuzumab	5	5
Others	3	3
Acute GVHD, n, %		
Grade 2-4	32	31.7
Chronic GVHD, n, %	23	22.8
Chronic GVHD NIH grade, n, %		
Mild	8	8
Moderate	12	11.9
Severe	3	3

Conclusions: In our study, ST2 and REG3a levels are not associated with subsequent development of cGVHD regardless of GI tract involvement. ST2 in the early-post transplant period correlates with aGVHD in alloSCT recipients, reaffirming it as a credible biomarker in this setting. This could be explained by aGVHD/cGVHD being mediated by different pathophysiology - tissue damage, inflammatory cytokine release and T-cell autoinflammatory activity in aGVHD; tissue fibrosis/sclerosis from self-tolerance loss and autoreactive Th17/B cells activity in cGVHD.3,4
While associations between ST2 and REG3a with cGvHD occurrence were not demonstrated, this may be limited by cohort size. Future studies examining potential linkages between ST2, REG3a and cGVHD should consider the impact of prior aGVHD.

Disclosure: Nothing to declare.

B023

GRAFT-VERSUS-HOST DISEASE IN THE CENTRAL NERVOUS SYSTEM - EMERGING PROBLEM OF MODERN HSCT TECHNOLOGY

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Background: Hematopoietic stem cell transplantation (HSCT) and CAR-T cell therapy are increasingly being used to treat both oncological and non-oncological diseases. The early and late complications of these treatments are also being studied. One important aspect is the recognition of the existence of acute and chronic graft-versus-host disease (GVHD) in the central nervous system (CNS). The aim of this study is to describe and systematize the immune neurological complications of cell therapy in children.

Methods: Retrospective analysis of 444 patient records after HSCT and 21 after CAR-T cell therapy over a 7-year period. The results of clinical, laboratory, and instrumental examinations were reviewed. The study revealed 11 patients with immune neurological complications, aged 2 to 18 years.

Results: Eight patients developed neurological immune complications after HSCT: five before day 100 (45 ± 12.8), which were considered "possible acute CNS-GVHD," and three after day 100 (200 ± 47), considered "chronic CNS-GVHD." The average age of the children was 10.4 ± 2.4; there were five boys and three girls. Two children developed complications after the second HSCT, and one - three months after CAR-T therapy. Six children underwent haploidentical HSCT, one from a matched related donor, and one - from a matched unrelated donor. All patients experienced neurological disorders: seizures (3/8), impaired consciousness (3/8), mental disorders (3/8), focal symptoms (5/8), and eye pain as the only symptom in one child. 6/8 patients had changes in magnetic resonance imaging of the CNS, 3/8 had albuminocytologic dissociation, 5/8 had macrophage activation syndrome, 1/8 had thrombotic microangiopathy, and 1/8 had mixed chimerism. 7/8 children had GVHD affected

organs outside the CNS, grades 2-4. All patients met the criteria for "possible CNS-GVHD". All patients received many lines of immunosuppression for the treatment of CNS-GVHD. Thus, 4/8 patients underwent plasmapheresis, 5/8 received high-dose (2g/kg) intravenous immunoglobulin (IVIG), 5/8 - rituximab and cyclophosphamide, 1 child - etanercept. Three out of eight patients received mycophenolic acid for the long maintenance therapy, one child received IVIG, and one received ruxolitinib. Three patients experienced complete regression of neurological symptoms, while two experienced partial regression. Three patients died: one from non-CNS involvement of GVHD, one from sudden unexpected death in epilepsy (SUDEP), and one from complications of CNS-GVHD. Two patients developed grade 1 immune effector cell-associated neurotoxicity syndrome (ICANS) early after CAR-T therapy, but they had a good clinical response to anti-cytokine therapy. Two children experienced late complications: one developed demyelinating disease (an undulating course, with a partial response to immunosuppressive therapy) after CAR-T and subsequent HSCT; the other developed toxic encephalopathy grade 4 (the child died from complications).

Conclusions: Immune-mediated neurological complications are possible after cell therapy. They significantly worsen outcomes, leading to persistent neurological deficits and, through the need for increased immunosuppressive therapy, indirectly affecting the course of the underlying disease and secondary complications (including infectious ones). Further study of these complications and the development of optimal therapeutic strategies are needed.

Clinical Trial Registry: Not applicable.

Disclosure: No conflict of interest.

B024

SKIN RESPONSES USING MODIFIED CRITERIA AMONG PATIENTS WITH SCLEROTIC CHRONIC GRAFT-VERSUS-HOST DISEASE TREATED WITH AXATILIMAB IN THE AGAVE-201 TRIAL

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Background: The 2014 National Institutes of Health (NIH) criteria for therapeutic response in chronic graft-versus-host disease (cGVHD) assess cutaneous responses using the NIH skin score based on percent body surface area involved and gross changes in sclerotic features.

Clinical or functional improvements in sclerotic skin features following cGVHD treatment may not be captured by the current 2014 NIH criteria for patients with deep sclerosis. In the pivotal, phase 2 AGAVE-201 trial (NCT04710576), axatilimab, a monoclonal antibody targeting colony-stimulating factor 1 receptor, was evaluated among patients with cGVHD after ≥2 prior lines of therapy. Overall efficacy and safety results of the trial were previously reported. The objective of this analysis was to assess improvements in sclerotic skin and associated symptoms after 6 months of axatilimab treatment in AGAVE-201 among patients who would not be considered clinical skin responders per the 2014 NIH criteria.

Methods: This analysis included patients in AGAVE-201 with an NIH skin feature score of 3, documented percent body surface area of sclerosis/fasciitis (sBSA), and clinician-rated 0–10 skin/joint tightening score at baseline and Cycle 7 Day 1 (C7D1). Modified response criteria were developed by the NIH Skin Taskforce (unpublished). Partial response (PR) was defined as ≥20% improvement in current sBSA with ≥10% absolute improvement (or resolution to 0%) and ≥2-point improvement from baseline in skin/joint tightening. Progression was defined as >20% worsening in current sBSA with >10% absolute worsening or ≥2-point worsening from baseline in skin/joint tightening. Stable disease was defined as not meeting response or progression criteria.

Results: In AGAVE-201, 180/193 patients (93.3%) with skin involvement at baseline had sclerotic features and 149 of these patients (82.8%) had a skin feature score of 3, indicating a high degree of sclerotic skin involvement. For this analysis, improvements per the modified response criteria were assessed at C7D1 in all 69 patients who met the inclusion criteria (**Table**). PR per the modified criteria occurred in 5 patients (7.2%), progression in 2 patients (2.9%), and stable disease in 62 patients (89.9%). Assessment of individual response criteria within the PR composite definition demonstrated additional clinical benefit. Improvement of ≥20% in sBSA occurred in 15 patients (21.7%), with ≥10% absolute improvement (or resolution) in 10 patients (14.5%). Improvement of ≥1 point and ≥2 points in skin/joint tightening occurred in 41 patients (59.4%) and 24 patients (34.8%), respectively.

Table. Responses per Modified Criteria and Individual Disease Assessments

Response, n (%)	**Axatilimab 0.3 mg/kg Q2W (n=24)**	**Axatilimab 1 mg/kg Q2W (n=23)**	**Axatilimab 3 mg/kg Q4W (n=22)**	**Axatilimab all doses (N=69)**
Partial response	4 (16.7)	1 (4.3)	0	5 (7.2)
Stable disease	19 (79.2)	21 (91.3)	22 (100)	62 (89.9)
≥20% improvement in sBSA	7 (29.2)	3 (13.0)	5 (22.7)	15 (21.7)

Table. Responses per Modified Criteria and Individual Disease Assessments

≥10% absolute improvement in % sBSA, or resolution	7 (29.2)	1 (4.3)	2 (9.1)	10 (14.5)
≥2-point improvement in skin/joint tightening	10 (41.7)	9 (39.1)	5 (22.7)	24 (34.8)
≥1-point improvement in skin/joint tightening	18 (75.0)	13 (56.5)	10 (45.5)	41 (59.4)
Progression	1 (4.2)	1 (4.3)	0	2 (2.9)

Q2W, every 2 weeks; Q4W, every 4 weeks; sBSA, percent body surface area of sclerosis/fasciitis.

Conclusions: These data demonstrate that axatilimab was associated with sBSA and skin/joint tightening improvement at C7D1 in a subset of patients with sclerotic cGVHD who had a skin feature score of 3 and would not have met the 2014 NIH criteria for clinical response. These data highlight the need for additional, sensitive assessments of treatment benefit in clinical trials for patients with sclerotic cutaneous involvement.

Clinical Trial Registry: NCT04710576
Clinicaltrials.gov

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Corporation, Janssen, OnQuality, Protagonist Therapeutics, Sanofi, and Treeline Biosciences; and has received royalties from UpToDate. Daniel Wolff received honoraria from Behring, Gilead, Incyte Corporation, Mallinckrodt, Novartis, Sanofi, and Takeda and received research funding from Novartis. Emily Baumrin has no disclosures to report. Britnie Thomas, Zhenyi Xue, and Valkal Bhatt are employees and shareholders of Incyte Corporation. Steven Z. Pavletic received research funding from Eli Lilly, Pharmacyclics, Sanofi, and Sobi and has served as a consultant for CSL Behring, Sanofi, and Therakos.

B028

A MODIFIED PEDIATRIC DAY 100 SCORE TO PREDICT MODERATE TO SEVERE CGVHD, TRANSPLANT-RELATED MORTALITY, AND OUTCOME AFTER HEMATOPOIETIC CELL TRANSPLANTATION

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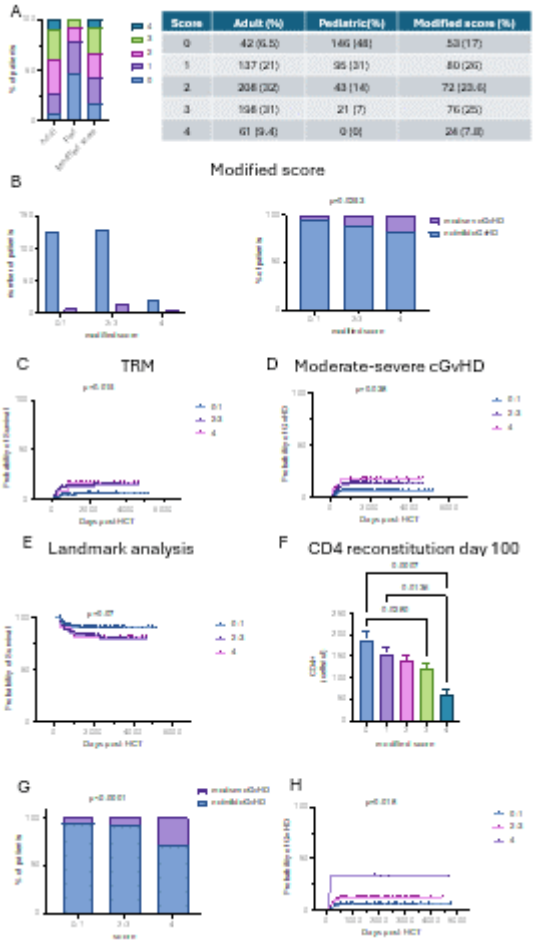
Background: Chronic graft-versus-host disease (cGVHD) is one of the most devastating complications following HCT in pediatric patients, as it has a profound impact on mortality and long-term quality of life. Classical predictors of cGVHD include HLA matching, donor–recipient age, use of peripheral blood as the stem cell source. However, no patient-specific predictive tool currently exists to estimate the individual risk of developing cGVHD in children. In the adult setting, Metafuni et al. in 2022 validated a simple and practical score that can predict the likelihood of moderate/severe cGVHD at day +100 post-HSCT. This score is based on 4 readouts: gamma-glutamyl transferase (GGT) >75 UI/l, creatinine >1 mg/dl, cholinesterase <4576 UI/l, and albumin <4 g/dl and stratifies patients according to the score: 0-1 low risk; 2-3 intermediate risk; 4 high risk of cGvHD.
We developed a pediatric score derived from the adult model to assess its feasibility and its ability to predict the risk of chronic GVHD in individual pediatric patients.

Methods: We retrospectively studied a cohort of 305 pediatric patients who underwent HCT at Fondazione IRCCS San Gerardo dei Tintori from 2011 to 2025. Composition of the cohort is shown in Table1. To establish the cut-off of albumin, GGT, creatinine and cholinesterase in the pediatric population we used ROC curves as done by Metafuni and colleagues. We exploited the new cut-offs to calculate the score. Patients' outcomes and cGvHD data were then correlated with the score.

Characteristic	Number of patients
Indication for HCT: **-ALL:** **-AML** **-other malignancies**	 -128 -57 -42

-hemoglobinopathies	-25
-metabolic diseases	-20
-aplastic anemia/Fanconi anemia	-23
-other non malignant diseases	-10
Age (median)	9 years (6mo-21 years)
Donor:	
-MSD	-76
-MRD	-8
-MUD 10/10	-107
-MUD 9/10	-62
-MMD	-43
Source:	
-BM	-262
-PB	-39
-CB	-4
Conditioning:	
-Busulfan based	-80
-Fludarabin based	-34
-TBI	-103
-Treosulfan based	-85
GvHD prophylaxis:	
-CSA + MTX	-201
-CSA + MTX + MMF	-24
-CSA + MTX + Rituximab	-26
-CSA, MMF, PTCy	-43
T cell depletion:	
-ATG-G	-89
-ATLG	-118



Results: We first applied the adult score to the pediatric population (Fig1A) but the distribution of the patients was significantly different from the adult cohort. We exploited ROC curves to estimate the proper cut-offs for our cohort: GGT >39 UI/l (AUC 0.54, specificity 0.55 sensitivity 0.55), creatinine >0.55 mg/dl (AUC 0.52, specificity 0.57 sensitivity 0.43), cholinesterase <6225 UI/l (AUC 0.53, specificity 0.53 sensitivity 0.53, and albumin <4 g/dl (AUC 0.46, specificity 0.41 sensitivity 0.53) and with the modified score the distribution of patients is similar to the adult cohort (Fig1A). We then compared the number and percentage of patients that developed moderate/severe cGvHD and we observed that patients with score>2 have a significant increase in cGvHD (Fig1B). Importantly, a score>2 predicts a higher transplant-related mortality (Fig1C) and higher cumulative incidence of cGvHD (Fig1D). In landmark survival analysis (cut-off 225 days, median onset of cGvHD) we observe a trend towards worse overall survival for score >2 (Fig1E). We also observe a significant delay in CD4 T cell reconstitution in patients with score >2 (Fig1F). Finally, we observe that in patients wothout aGvHD (grade 0-1), the score is even more predictive (Fig1G-H).

Conclusions: We demonstrated that this score, appropriately adapted for the pediatric population, reliably identifies patients who, at day +100 post-HSCT, are at higher risk of developing cGVHD and consequently face an increased risk of mortality. This seems

particularly true for patients who do not have prior aGvHD. These results need validation in a larger pediatric cohort. This score could support the implementation of targeted preventive interventions from day +100 for high-risk patients, to mitigate progression to cGVHD.

Clinical Trial Registry: na

Disclosure: The authors have not conflict of interest related to the study

B029

SERUM CHOLINESTERASE AS A LOW-COST, ROUTINELY AVAILABLE BIOMARKER FOR ACUTE INTESTINAL GRAFT-VERSUS-HOST DISEASE IN CHILDREN

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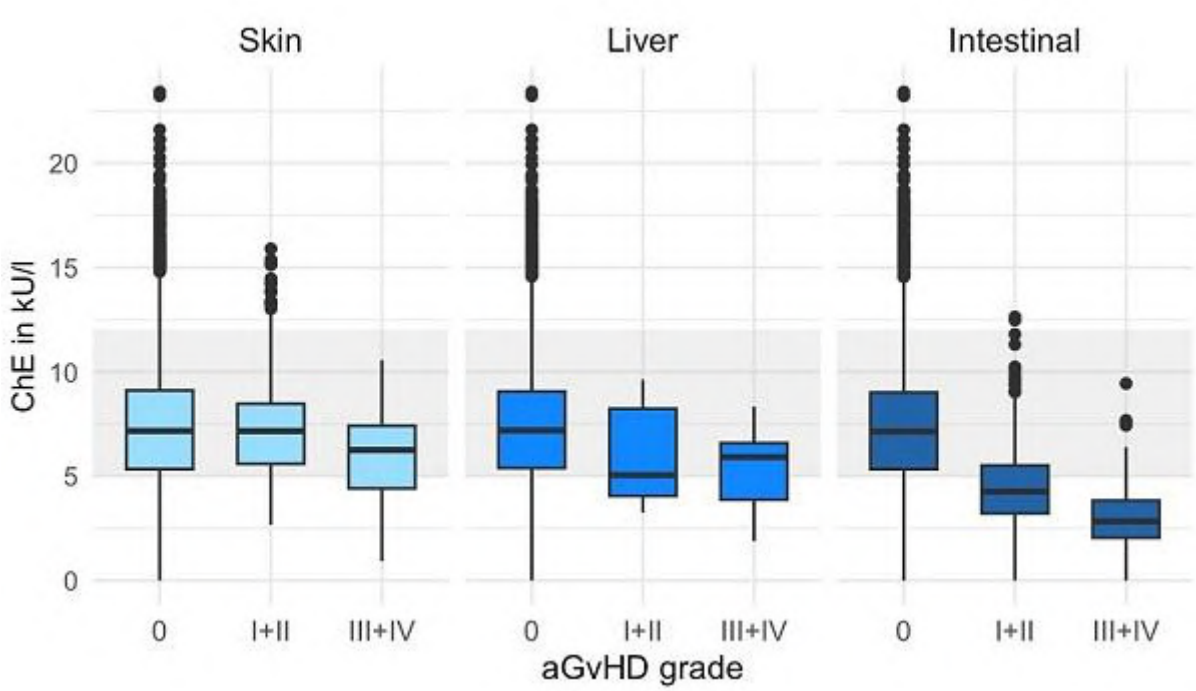
Background: Acute graft-versus-host disease (aGvHD) of the intestine is a dreaded complication following allogeneic stem cell transplantation. Currently, disease severity is determined by stool frequency or volume, parameters that are often difficult to measure in pediatric patients. Early diagnosis and accurate staging are crucial for initiation of therapy, response assessment and timely adjustment of treatment intensity. To support clinical decision making, we sought for a cheap and readily-available biomarker reflecting disease severity in aGvHD of the intestine.

Methods: We evaluated all patients who developed aGvHD after receiving an allogeneic stem cell transplantation at our center between January 2014 and December 2023. Serum levels of albumin, immunoglobulin G (IgG) and cholinesterase (ChE) were measured at least twice a week and the GvHD stages were prospectively documented in the electronic patient records. Files were retrospectively analyzed and the correlation of serum protein values and the severity of aGvHD was analyzed using a cumulative link mixed model as part of a mixed ordinal logistic regression analysis.

Results: In total, 139 patients (32%) developed grade I-IV aGvHD, 33 of whom suffered from intestinal aGvHD. 9756 assessments of GvHD severity were identified in the patient charts and correlated with 7818 measurements of ChE. Patients with intestinal aGvHD displayed a relevant stage-dependent decrease in ChE-levels. Almost all ChE levels of patients with severe intestinal aGvHD were out of normal range, while ChE levels remained largely constant in patients suffering skin or liver aGvHD (Fig. 1). Two other serum proteins, albumin and IgG, showed only a limited decline, as they are supplemented regularly based on predefined thresholds.
The odds of reaching a higher intestinal aGvHD stage was decreased by more than 50% with each rise of ChE by one unit, demonstrating the significant association of a higher ChE-value with a lower score for intestinal aGvHD, with a coefficient in odds of 0.468 (confidence interval 0.444 – 0.493, $p < 0.0001$).

Patients with steroid-responsive intestinal aGvHD showed a rapid increase in ChE concentration after treatment initiation, while patients with steroid-refractory aGvHD continued to show below-normal serum ChE concentration levels for weeks.



Conclusions: We see a correlation between serum ChE levels and the clinical severity of intestinal aGvHD. With every rise in ChE-unit, patients have a significantly reduced risk of being scored into a higher stage of intestinal aGvHD. In patients with response to steroids, ChE levels rapidly normalized under treatment demonstrating that ChE is a potential indicator for treatment response in intestinal aGvHD.
ChE is a commonly available and inexpensive parameter with a short turnaround time. The course of individual ChE levels could be particularly valuable for assessing disease severity changes under treatment in pediatric patients and helpful in deciding whether early therapeutic escalation is necessary or de-escalation possible.
These findings need to be corroborated prospectively by including ChE measurements in a prospective multicenter trial with a pediatric patient cohort at risk for intestinal GvHD, thus validating consecutive ChE measurements as a useful marker for the course of disease in aGvHD.

Disclosure: Nothing to declare.

B030

HUMANIZED ANTI-CD25 MONOCLONAL ANTIBODY FOR GVHD PROPHYLAXIS IN ELDERLY HAPLOIDENTICAL ALLOGENEIC STEM CELL TRANSPLANTATION: A PHASE II STUDY

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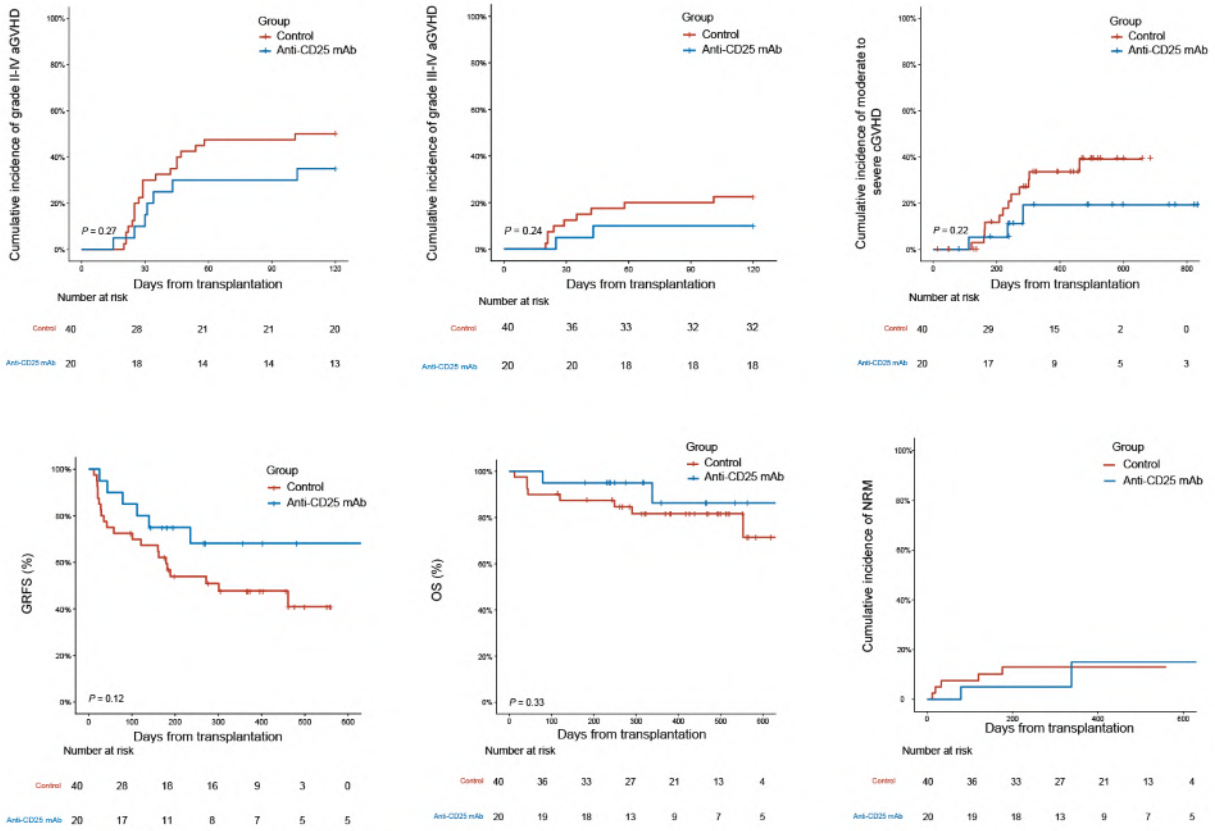
Background: Older age was associated with high risk of aGVHD after allogeneic HSCT, morbidity and mortality attributed to aGVHD was even higher. Optimization of GVHD prophylaxis is essential in elderly haploidentical HSCT. Anti-CD25 monoclonal antibody (mAb) was safe and effective in treating steroid-refractory GVHD. In this prospective, phase II clinical trial, we aim to investigate the efficacy and safety of addition of humanized anti-CD25 mAb in ATG-based GVHD prophylaxis system in elderly patients undergoing haploidentical HSCT (NCT05923814).

Methods: Eligible patients were over 50 years old and undergoing haploidentical allogenic HCT between 2023–2025. A historical control group was established from patients in the same center. Institutional Review Board approval was obtained in accordance with the Declaration of Helsinki. The standard GVHD prophylaxis protocol includes rATG+CNI+short-term MTX+mycophenolate mofetil. Patients in experimental group received humanized anti-CD25 mAb (50 mg/day, +1d, +4d) and reduced rATG (8mg/kg, Thymoglobuline). The control group was administered a standard rATG dose (10mg/kg). The primary endpoint was the cumulative incidence of grade 2–4 acute GVHD by day 100 post-HCT and cumulative incidence of chronic GVHD. Acute GVHD were diagnosed and graded based on MAGIC algorithm. Chronic GVHD were scored based on NIH criteria.

Results: We enrolled 20 patients in CD25 group and 40 patients in control group. Baseline characteristics were balanced between the two groups. The median age was 58 years (range, 50-67) in CD25 group and 56 years (range, 50-66) in control group. Neutrophil engraftment occurred at a median of 14 days vs 16 days respectively, and no adverse effect of early-used CD25 mAb on engraftment was documented. The cumulative incidence of grade 2–4 acute GVHD was 30% for CD25 group and 47.5% for control group (P=0.27). Even no statistical significance was observed, CD25 group showed 17.5% advantage in reducing aGVHD. Furthermore, addition of anti-CD25 reduced the severe grade 3-4 aGVHD incidence by **12.5% (10% vs 22.5%, P=0.24)**. Anti-CD25 prophylaxis group also exhibited lower rate in chronic GVHD requiring systemic immunosuppression (19.3% vs 33.6%, P=0.21). Otherwise, no significant differences were observed in post-HSCT infectious complications, including pneumonia, sepsis, invasive fungal infection, respiratory viral infection, CMV viremia, and EBV viremia. At a median follow-up of 467 days (range:382-519), no patient died of aGVHD in CD25 group, and two patients (10%) died of infection. The causes of deaths in control group was relapse (4/8, 50%), infection (2/8, 25%), acute GVHD (1/8, 12.5%), and hemorrhagic stroke (1/8, 12.5%). The CD25 group showed potentially improved one-year GRFS **(**68.2**% vs 40.9%)** with a **27.3%** advantage. No significant

difference was observed in one-year OS (86.4% vs 81.7%), one-year NRM (15% vs 13%) and one-year relapse incidence (5% vs 9%).



Conclusions: Our study revealed that the addition of short-course anti-CD25 prophylaxis (day +1, +4) in the rATG system proved feasible and safe. However, we did not observe its significant advantage in reducing severe acute or chronic GVHD. The benefit of extensive administration of anti-CD25 mAb warrants further investigation.

Clinical Trial Registry: NCT05923814
https://clinicaltrials.gov/

Disclosure: Nothing to declare.

B031

ABSOLUTE LYMPHOCYTE COUNT AT ANTI-T-LYMPHOCYTE GLOBULIN DOES NOT PREDICT GVHD INCIDENCE AND GVHD/RELAPSE FREE SURVIVAL AFTER MATCHED UNRELATED DONOR TRANSPLANTATION: A TWO-CENTER VALIDATION STUDY

Radwan Massoud[1], *Margherita Ursi*[2,3], *Enrico Maffini*[3], *Francesco Barbato*[2], *Francesco De Felice*[3], *Sadia Falcioni*[3], *Marcello Roberto*[3], *Gabriele Fontana*[2], *Federica Ardizzoia*[2], *Michele Loffredo*[2], *Enrica Tomassini*[3], *Luca Zazzeroni*[3], *Salvatore Nicola Bertuccio*[3], *Daria Messelodi*[3], *Gianluca Storci*[3], *Evgeny Klyuchnikov*[1], *Ina Rudolph*[1], *Silke Heidenreich*[1], *Claudia Langebrake*[1], *Adrin Dadkhah*[1], *Nico Gagelmann*[1], *Garielle Zeck*[1], *Rolf Krause*[1], *Christian Niederwieser*[1], *Catherina Lueck*[1], *Christine Wolschke*[1], *Francis Ayuk*[1], *Nicolaus Kröger*[1], *Francesca Bonifazi*[2,3]

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Background: Allogeneic stem cell transplantation (allo-SCT) is a curative strategy for hematological malignancies but remains limited by graft-versus-host disease (GVHD). In matched unrelated donor (MUD) transplantation, in vivo T-cell depletion with anti-thymocyte globulin (ATG; Thymoglobulin®) or anti-T-lymphocyte globulin (ATLG; Grafalon®) is widely used for GVHD prophylaxis, although optimal dosing strategies remain undefined. While several studies have demonstrated that recipient absolute lymphocyte count (ALC) influences ATG exposure and clinical outcomes, corresponding data for ATLG are lacking. We therefore evaluated the prognostic impact of ALC at ATLG initiation in two independent cohorts receiving a fixed ATLG dose.

Methods: This retrospective two-center study included 368 adult patients undergoing first 10/10 MUD peripheral blood stem cell transplantation, comprising a University Medical Center Hamburg-Eppendorf (UKE) cohort (n=251) and a University Hospital of Bologna cohort (n=117). All patients received a fixed cumulative ATLG dose of 30 mg/kg (Grafalon®), administered according to center-specific schedules (UKE: test dose on day -4 followed by fractionated dosing until day -1; Bologna: five equal doses from day -6 to day -2). Patients were stratified into low- and high-ALC groups based on the median ALC at the first ATLG dose; ALC was also analyzed as a continuous variable. Endpoints included acute and chronic GVHD, non-relapse mortality (NRM), relapse, overall survival (OS), progression-free survival (PFS), and GVHD-free, relapse-free survival (GRFS).

Results: Median ALC at ATLG initiation differed significantly between centers (UKE: 0.23 × 10^9/L; Bologna: 0.70 × 10^9/L). ALC was not associated with the incidence of acute or chronic GVHD or with GRFS in either cohort and showed no consistent association with OS, PFS, or NRM. In the UKE cohort, 1-year acute GVHD grades II–IV incidence was 33% versus 38% (p=0.40), and 1-year GRFS was 37% versus 36% (p=0.59) for low versus high ALC, respectively. Corresponding values in the Bologna cohort were 19% versus 14% for acute GVHD (p=0.80) and 58% versus 59% for GRFS (p=0.69). Divergent associations were

observed for relapse: in the UKE cohort, higher continuous ALC was associated with increased relapse incidence (sHR 1.20, p=0.034), whereas in the Bologna cohort, higher categorical ALC was associated with a lower 1-year relapse incidence (7% vs. 23%, p=0.03).

Conclusions: ALC on the first day of ATLG administration does not represent a consistent prognostic biomarker across centers when a fixed cumulative dose of 30 mg/kg is used. In the Bologna cohort, the association between higher ALC and lower relapse incidence is biologically plausible and compatible with a pharmacodynamic model in which higher recipient lymphocyte counts bind more ATLG, resulting in reduced effective immunosuppression and preserved graft-versus-leukemia activity. In contrast, the opposite association observed in the UKE cohort appears more likely influenced by center-specific factors and residual confounding. Nevertheless, the biological rationale for ALC-guided and schedule-optimized ATLG dosing remains compelling, and earlier administration when lymphocyte counts are higher may optimize exposure. Prospective studies integrating pharmacokinetic monitoring with harmonized administration schedules are required to define optimal ATLG dosing strategies.

Clinical Trial Registry: NA

Disclosure: NO

B033

SAFETY AND FEASIBILITY OF 0.6 MG/KG EVERY 4 WEEKS DOSING OF AXATILIMAB IN PATIENTS TREATED IN THE AGAVE-201 STUDY

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Background: Axatilimab, a monoclonal antibody targeting colony-stimulating factor 1 receptor, is approved by the US Food and Drug Administration at a dose of 0.3 mg/kg (up to a maximum dose of 35 mg) every 2 weeks (Q2W) for patients with chronic graft-versus-host disease (cGVHD) after ≥2 prior lines of therapy, based on results from the pivotal AGAVE-201 study (NCT04710576). Patients treated with axatilimab 0.3 mg/kg Q2W in AGAVE-201 were able to transition to 0.6 mg/kg every 4 weeks (Q4W) dosing based on the investigator's discretion and per study protocol criteria. The objective of this analysis was to describe the safety and feasibility of transition from axatilimab 0.3 mg/kg Q2W to 0.6 mg/kg Q4W dosing in AGAVE-201.

Methods: Patients treated with axatilimab 0.3 mg/kg Q2W in AGAVE-201 who had their Cycle 7 assessment and achieved a partial or complete response per National Institutes of

Health criteria that was sustained for ≥20 weeks or had not progressed were able to change their dosing schedule to 0.6 mg/kg Q4W (without dose capping) per the study protocol and investigator discretion. Patients who received additional systemic therapies were excluded from this post hoc analysis. The data cutoff was March 30, 2025.

Results: In the first 6 treatment cycles, 59 of the 80 patients (73.8%) randomized to axatilimab 0.3 mg/kg Q2W had a response to treatment, 19 of whom (32.2%) transitioned to 0.6 mg/kg Q4W dosing. Overall response rate in the first 6 treatment cycles among the 19 patients who switched to 0.6 mg/kg Q4W was 94.7% (95% CI, 74.0%–99.9%); 1 patient with stable disease was eligible to switch, per investigator discretion. Patients were on treatment for a median (range) of 20.9 (2–32) months after switching doses, and 16 of 19 patients (84.2%) maintained the 0.6 mg/kg Q4W dose. The safety with axatilimab was generally similar before and after the dosing change. With 0.6 mg/kg Q4W, 10 patients (52.6%) had grade ≥3 treatment-emergent adverse events (TEAEs); pneumonia was the only grade ≥3 TEAE reported in >1 patient (n=2). TEAEs led to treatment interruptions in 4 patients (21.1%) and discontinuations in 3 patients (15.8%) after switching. The most common TEAEs after switching were fatigue and upper respiratory tract infection (each n=5 [26.3%]); 1 patient (5.3%) had an infusion-related reaction (rash). Incidences of on-target TEAEs were generally similar before and after the switch, including elevations in alanine aminotransferase (n=3 before, n=1 after) and amylase (n=0 before, n=1 after).

Conclusions: Transition to 0.6 mg/kg Q4W (without dose capping) is feasible and well tolerated in patients treated with axatilimab 0.3 mg/kg Q2W in AGAVE-201. The Q4W dosing strategy at the 0.6 mg/kg dose identified no new safety signals. Patients had a prolonged treatment duration (median, 20.9 months [1.7 y]), and 84% of patients continued treatment, suggesting ongoing clinical benefit. These data show the safety and feasibility of 0.6 mg/kg Q4W dosing in alignment with the AGAVE-201 protocol.

Clinical Trial Registry: NCT04710576
Clinicaltrials.gov

Disclosure: Nosha Farhadfar has served as a consultant for Omeros and Sanofi; served as a member of advisory committee for Incyte Corporation; served as a speakers bureau member for Incyte Corporation; served as a medical monitor for Blood and Marrow Clinical Trial Network (BMT CTN); and served as a DSMB member for Chronic GVHD Consortium. María Sola Soto has received honoraria from Sanofi. Saurabh Chhabra has received honoraria from Ascentage Pharma, Bristol Myers Squibb, Legend Biotech, Pfizer, Sanofi, and Sobi and institutional research funding from AbbVie, Ascentage Pharma, AstraZeneca, C4 Therapeutics, CARSgen Therapeutics, Cullinan Therapeutics, Cynata Therapeutics, Johnson & Johnson, and Takeda. Valkal Bhatt, Emily Andersen, and Zhenyi Xue are employees and shareholders of Incyte Corporation. Zachariah DeFilipp has served as a consultant for Forte Biosciences Inc., Incyte Corporation, Inhibrx, MaaT Pharma, Medexus Pharmaceuticals Inc., Mesoblast Ltd., RegImmune Corp., Sanofi, and Therakos and received research funding from Incyte Corporation, Kura Oncology, Regimmune, and Taiho Oncology.

B034

ASSESSMENTS OF BONE HEALTH AMONG PATIENTS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE RECEIVING AXATILIMAB IN THE AGAVE-201 TRIAL

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Background: Bone mineral density (BMD) loss is a common complication of allogeneic hematopoietic stem cell transplantation, often related to pretransplantation chemotherapy, radiation exposure, and immunosuppressive therapy for chronic graft-versus-host disease (cGVHD). BMD loss results from gonadal hormonal deficiencies, disturbances in calcium and vitamin D homeostasis, and osteoblast and osteoclast dysfunction. Colony-stimulating factor 1 (CSF-1), a CSF-1 receptor (CSF-1R) ligand, is a key regulator in bone-remodeling pathways, as shown in CSF-1–knockout and CSF-1–deficient mice, which present with severe skeletal phenotypes. Axatilimab is a high-affinity monoclonal antibody that targets CSF-1R signaling to deplete monocytes and macrophages, key drivers of inflammation and fibrosis in patients with cGVHD. Thus, the potential effects of axatilimab on bone health are of clinical interest. The objective of this analysis is to evaluate bone-health associated parameters in patients with refractory cGVHD who received axatilimab in the pivotal, phase 2 AGAVE-201 trial (NCT04710576).

Methods: In AGAVE-201, patients were randomized to intravenous axatilimab 0.3 mg/kg every 2 weeks (Q2W), 1 mg/kg Q2W, or 3 mg/kg every 4 weeks (Q4W). Bone turnover markers, specifically bone-specific alkaline phosphatase (BAP) and C-telopeptide of cross-linked type 1 collagen (CTX), were assessed at baseline, throughout treatment, and at treatment end. Changes in bone biomarkers were summarized using descriptive statistics. The data cutoff was March 30, 2025.

Results: Of the 241 patients enrolled, 239 received axatilimab (0.3 mg/kg Q2W, n=79; 1 mg/kg Q2W, n=81; 3 mg/kg Q4W, n=79). Among all 241 patients, the median (range) baseline age was 53 (7–81) years; 151 patients (62.7%) were male, and median (range) follow-up was 31.2 (0–46.5) months. Prior bone-related medications included vitamin D (50.6%), calcium combinations (14.9%), calcium (13.7%), bisphosphonates (11.6%), and calcium carbonate (1.7%). Concomitant bone-related medications included vitamin D (56.8%), calcium combinations (19.1%), bisphosphonates (18.3%), calcium (17.8%), and calcium carbonate (2.9%). Concomitant corticosteroid use at baseline was reported in 65.3% of patients, with a mean daily dose of 19.4 mg. Bone-related medical conditions in patients' medical histories included osteoporosis (19.5%), osteopenia (16.2%), osteonecrosis (7.9%), osteoarthritis (4.1%), bone pain (1.2%), osteolysis, osteoporotic fracture (both 0.8%), bone fissure, bone surgery, decreased bone density, osteochondrosis, and osteosclerosis (each 0.4%). Changes from baseline in BAP and CTX at Cycle 6 Day 1 and end of treatment were

minimal (Table). Across all doses, bone-related treatment-emergent adverse events (TEAEs) were grade 1 or 2 and included osteopenia (n=6 [2.5%]), osteoarthritis (n=5 [2.1%]), bone pain, osteonecrosis (both n=4 [1.7%]), musculoskeletal pain (n=2 [0.8%]), bone infarction, coccydynia, increased vitamin D, and osteochondroma (each n=1 [0.4%]). Fractures of any grade occurred in 17 patients (7.1%), with ≥2 fractures occurring in 3 patients (1.3%).

Table. Baseline and Changes in Bone Biomarkers Among Patients in AGAVE-201

		Axatilimab 0.3 mg/kg Q2W (n=79)		Axatilimab all doses (N=239)	
Parameter	Visit	n	Mean (SE)	n	Mean (SE)
BAP, U/L	Baseline	77	27.1 (3.08)	233	26.2 (1.47)
	Change from baseline to C6D1	53	0.9 (1.08)	135	−0.2 (1.52)
	Change from baseline to EOT	32	−1.0 (2.07)	110	−0.4 (0.88)
CTX, µg/L	Baseline	77	0.4 (0.04)	233	0.4 (0.02)
	Change from baseline to C6D1	53	−0.0 (0.03)	136	−0.1 (0.02)
	Change from baseline to EOT	33	−0.0 (0.05)	112	−0.1 (0.02)

BAP, bone-specific alkaline phosphatase; C6D1, Cycle 6 Day 1; CTX, C-telopeptide of cross-linked type 1 collagen; EOT, end of treatment; Q2W, every 2 weeks.

Conclusions: In AGAVE-201, axatilimab was associated with minimal changes in bone turnover markers in patients with cGVHD. Bone-related TEAEs were rare, with only a small number of patients having multiple fractures; this is notable given that 65.3% of patients received concomitant corticosteroids. These findings may indicate that axatilimab had minimal effects on bone metabolic markers, although additional analyses, including bone density measurements in this population with refractory cGVHD, are needed.

Clinical Trial Registry: NCT04710576
Clinicaltrials.gov

Disclosure: Doris M. Ponce served on an advisory board or as a consultant for CareDx, Ceramedix, Evive Biotechnology, Incyte Corporation, and Sanofi and received research funding from Incyte Corporation, Sanofi, and Takeda. Gabriela B. Thoennissen is an employee of Incyte Biosciences International Sàrl and a shareholder of Incyte Corporation. Jordan Fortunato and Zhenyi Xue are employees and shareholders of Incyte Corporation. Amandeep Salhotra received research funding from Bristol Myers Squibb, Orca Bio, and Rigel Pharmaceuticals; served as a speakers bureau member for Sanofi; and served on an advisory board for Incyte Corporation and Servier.

B035

OUTCOMES OF PATIENTS DIAGNOSED WITH STEROID-REFRACTORY OR DEPENDENT ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE RESISTANT OR INTOLERANT TO SECOND-LINE RUXOLITINIB: A RETROSPECTIVE STUDY FROM THE GETH-TC

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Background: Acute and chronic graft-versus-host disease (aGvHD, cGvHD) represents a major cause of morbimortality after allogeneic hematopoietic cell transplant (Allo-HCT). After steroid failure, ruxolitinib represents a standard of care in steroid-refractory or dependent-GvHD (SR/SD-GvHD), in acute and chronic. However, the prognosis and clinical management of patients resistant or intolerant to second-line (2L) ruxolitinib is uncertain.

Methods: This retrospective study included patients from EBMT centers within the Spanish Group of Hematopoietic Stem Cell Transplantation and Cellular Therapy. Inclusion criteria: 1) patients undergoing allo-HCT; 2) diagnosed with acute or chronic SR/SD-GvHD, 3) failure (resistance or intolerance) to 2L ruxolitinib. The primary endpoint was the overall response rate (ORR) after third-line (3L) treatment. Secondary endpoints were overall survival (OS) and non-relapse mortality (NRM).

Results: Sixty-six patients treated with ruxolitinib 2L were included. Patients underwent Allo-HCT between 2008-2022. Table 1 summarises patient's characteristics.

Thirty patients were diagnosed with SR/SD-aGVHD and received ruxolitinib as a 2L. The gut was the most affected organ with score 3-4 (18 patients, 60%), followed by the skin (6; 20%), and the liver (4; 13%). Ruxolitinib discontinuation was due to GVHD progression (11 patients; 37%), suboptimal response (7; 23%), infection (2; 7%), toxicity (1; 3%), other reasons (3; 11%) and death (4; 13%). Out of 30 patients, 23 received a 3L, which consisted on extracorporeal photopheresis (ECP) (7 patients; 23%), infliximab (4; 13%), mesenchymal stromal cells (MSC) (3; 10%), vedolizumab (2; 6%), fecal microbiota transplantation (2; 6%) and five patients other therapies. The 28-day ORR after 3L was 33%, including 6 patients (20%) with CR and 4 (13%) with PR. Twenty-six patients (86%) died during the study period. The most common cause of death was GVHD progression (12 patients; 46%). With a median OS of 4 months, the estimated 3-month OS was 58.6% (95%CI 40.8%-76.4%); and the 2 year NRM was 82%.
Regarding SR/SD-cGVHD, 36 patients received ruxolitinib as a 2L. Skin (23 patients; 63%), liver (13; 36%) and ocular (13; 36%) were the most frequently affected organs at cGvHD diagnosis. The most common cause of ruxolitinb discontinuation was no response in 19 patients (53%). Twenty-six patients received a 3L, which consisted on ECP (11; 42%), mTOR inhibitor (6; 19%), calcineurin inhibitors (3; 11%), MSC (1; 4%), alpha 1-antitrypsin (1; 4%), T regulatory cells (1; 4%), belumosudil (1; 4%), and other therapies in 2 patients. Out of 26 patients, 18 (69%) were evaluable for response. The 6-month ORR after 3L was 66%, including 3 patients (16%) with CR and 9 patients (50%) with PR. Thirteen patients died during the study period. The most common cause of death was infection (8; 61%). With a median follow up of 4 years, the estimated 2 year-OS was 79,7% (95% CI 66.2%-93.2%) and the 2-year NRM was 23% (95%CI 9.2%-37.4%).

Table 1. Patient's characteristics (n=66)	
Characteristics	**Patients**
Median age, *years* (range)	50 (20 - 69)
Male gender, *n* (%)	32 (48%)
Diagnosis, *n* (%) Acute leukemia/MDS HL/NHL/MPN	 51 (77%) 15 (23%)
Conditioning regimen, *n* (%) MAC RIC Data not available	 37 (56%) 27 (41%) 2 (3%)
Graft source, *n* (%) Peripheral blood Bone marrow	 59 (90%) 2 (3%)

Cord blood Data not available	2 (3%) 3 (4%)
Type of donor, *n* (%) MRD MUD MMUD Haploidentical	 26 (40%) 29(44%) 3(4%) 8(12%)
GvHD prophylaxis, *n* (%) CNI-based PT-Cy Other Data not available	 33 (50%) 19 (29%) 13 (19%) 1 (2%)
SR/SD-aGVHD, *n* (%) MAGIC score 3 MAGIC score 4	30 (45%) 14 (47%) 8 (27%)
SR/SD-cGvHD, *n* (%) NIH score moderate NIH score severe	36 (55%) 12 (33%) 18(50%)

N number, *MDS* myelodysplastic syndrome, *MPN* myeloproliferative neoplasm, *MAC* myeloablative conditioning, *RIC* reduced intensity conditioning, *MRD* matched related donor, *MUD* matched unrelated donor, *MMUD mismatched unrelated donor, GVHD* graft-versus-host disease, *CNI-based* calcineurin inhibitor based, *PT-Cy* Post-Transplant Cyclophosphamide, *MAGIC* Mount Sinai Acute GVHD International Consortium, *NIH score* National Institutes of Health Consensus score.

Conclusions: This nationwide cohort shows that, aGvHD patients failing to 2L ruxolitinib associate with low response rates (33%) and dismal survival. Conversely, cGvHD patients failing to 2L ruxolitinib associate with an encouraging ORR >60%. The advent of novel therapies for cGvHD could help to improve these outcomes.

Disclosure: Nothing to declare.

B036

IMPACT OF POST-TRANSPLANT CYCLOPHOSPHAMIDE DOSE REDUCTION ON THE INCIDENCE OF COMPLICATIONS AND RELAPSE AFTER ALLOGENEIC TRANSPLANTATION

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Background: Graft-versus-host disease (GVHD) is one of the main complications of allogeneic hematopoietic stem cell transplantation (allo-HSCT), significantly affecting morbidity, mortality, and quality of life. Post-transplant cyclophosphamide (PTCy) has been established as an effective strategy for GVHD prophylaxis. However, the standard dose (100 mg/Kg) may be associated with delayed engraftment, a higher risk of infections, and other complications such as thrombotic microangiopathy (TMA) or sinusoidal obstruction syndrome (SOS). A reduced cyclophosphamide dose (80 mg/Kg) has been evaluated in terms of efficacy and safety in several studies, both with matched and alternative donors. The objectives were to evaluate the efficacy and safety of reducing the post-transplant cyclophosphamide dose to 80 mg/Kg as a strategy for GVHD prophylaxis in matched and alternative donors.

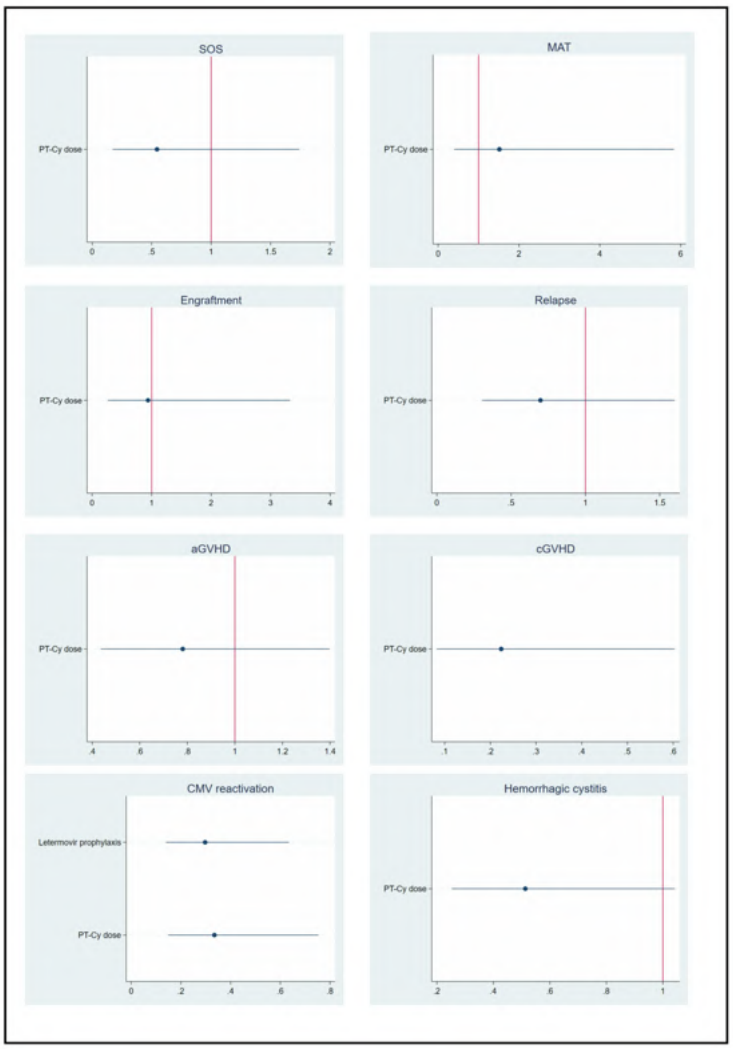
Methods: A retrospective observational study was conducted in a cohort of 200 patients who underwent allo-HSCT at Clinica Universidad de Navarra between February 2016 and May 2025. Two groups were compared according to the PTCy dose administered: standard dose (100 mg/Kg) and reduced dose (80 mg/Kg). All patients had a minimum follow-up of 6 months, and relevant clinical and laboratory data were collected. Statistical analysis was performed using STATA v12.

Results: Baseline characteristics are shown in Table 1. Of the 200 patients included, 130 (65%) received the standard dose and 70 (35%) received the reduced dose.
Reduced-dose PTCy showed no significant association with engraftment (OR 0.94, p=0.92), nor with MAT (OR 1.52, p=0.55), SOS (0.56 p=0.31) or relapse (OR 0.70, p=0.40).
Similarly, reduced-dose PTCy was not significantly associated with acute GVHD of any grade (OR 0.78; p=0.41) nor clinically relevant acute GVHD (grade ≥2) (OR 0.57; p=0.13). In contrast, reduced-dose PTCy was significantly associated with a lower risk of chronic GVHD (OR 0.22; 95% CI 0.08-0.60; p< 0.01).
Regarding hemorrhagic cystitis, a lower incidence was observed in patients receiving reduced-dose PTCy compared with standard-dose PTCy (18.6% vs. 30.8%), although this association was not statistically significant (OR = 0.51; p=0.06).
Reduced-dose PTCy was associated with a significantly lower likelihood of CMV reactivation compared with the standard dose (OR 0.16; 95% CI 0.08–0.30; p<0.01). Overall, 56% of patients (n=111) received CMV reactivation prophylaxis with letermovir. In the multivariable logistic regression model, both letermovir prophylaxis (OR 0.30; 95% CI 0.14–0.63; p < 0.01) and reduced-dose PTCy (OR 0.34; 95% CI 0.15–0.75; p < 0.01) were independently associated with a lower likelihood of CMV reactivation.

Table 1. Baseline characteristics.

	Dose 100 mg/kg (n = 130)	Dose 80 mg/Kg (n = 70)	Total (n = 200)	*P* value
Age, median (RIC)	21 (10-43)	27 (15-43)	22 (11-43)	0.20
Adults, n (%)	78 (60)	51 (73)	129 (64)	
Pediatrics, n (%)	52 (40)	19 (27)	71 (36)	
Sex, n (%)				< 0.01
Male	68 (52)	50 (71)	118 (59)	
Female	62 (48)	20 (29)	82 (41)	
Diagnosis, n (%)				0.03
ALL	58 (45)	22 (47)	91 (46)	
AML	30 (23)	12 (17)	42 (21)	
MDS	8 (6)	6 (9)	14 (7)	
CML	8 (6)	-	8 (4)	
MF	-	2 (3)	2 (1)	
HL	6 (5)	2 (3)	8 (4)	
AMS	5 (4)	7 (10)	12 (6)	
Other	15 (11)	8 (11)	23 (11)	
Karnofsky, n (%)				<0.01
100	119 (92)	70 (100)	189 (95)	
≤ 90	11 (8)	-	11 (5)	
HTC-CI, n (%)				0.96
0-1	85 (65)	46 (66)	131 (65)	
≥ 2	45 (35)	24 (34)	69 (35)	
Disease status, n (%)				< 0.01
RC 1	36 (28)	39 (56)	75 (38)	
RC ≥ 2	46 (35)	23 (33)	69 (34)	
EE	10 (8)	5 (7)	15 (8)	
EP	14 (11)	-	14 (7)	
Chronic	24 (18)	3 (4)	27 (13)	
Donnor type, n (%)				<0.01
MSD	3 (2)	4 (6)	7 (3)	
MUD	7 (5)	19 (27)	26 (13)	
MMUD	22 (17)	15 (21)	37 (19)	
Haplo	98 (75)	32 (46)	130 (65)	
Source, n (%)				0.10
SP	116 (89)	66 (94)	182 (91)	

MO SCU	14 (11) -	3 (4) 1 (2)	17 (8) 1 (1)	
Conditioning regimen AMA AIR	 78 (60) 52 (40)	 53 (76) 17 (24)	 131 (66) 69 (34)	0.03
Preconditioning EASIX score, median (IQR)	0.71 (0.36-2.21)	0.81 (0.44-1.82)	0.74 (0.40-1.96)	0.53



Conclusions: The reduced PTCy dose appears to be an effective and safe strategy, lowering the risk of CMV reactivation and chronic GVHD without increasing relapse or other adverse

events. It also showed a trend toward reduced hemorrhagic cystitis, although this did not reach statistical significance, likely due to limited sample size.

Disclosure: The author declares no conflicts of interest related to this work.

B037

MISSED AND DELAYED GENITAL GVHD: ORAL INVOLVEMENT AS A CLINICAL BIOMARKER FOR EARLY DETECTION

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Background: Chronic Graft-versus-Host disease (cGvHD) remains a leading cause of morbidity and mortality after allogeneic Haematopoietic Stem Cell Transplantation (allo-HSCT). Genital location affects both sexes, but in women it is underdiagnosed and causes more sexual dysfunction. The added presence of physiological changes due to Premature Ovarian Failure (POF) further compound sexual morbidity, as several symptoms overlap with those of genital cGvHD.
The study aimed to assess the incidence of genital GvHD and to evaluate potential delays in its diagnosis compared with oral cGvHD.

Methods: This retrospective, single-center observational study included 121 consecutive female recipients of allo-HSCT treated between January 2011 and March 2022. The study was censored at 4.4 years, as this corresponds to the latest time point at which genital cGVHD developed in the series.Consequently, all patients who did not reach this follow-up duration and had not developed genital cGVHD were excluded from the analysis (36 of 121 in total). Statistical analyses were therefore performed on a cohort of 85 patients, whose clinical and demographic characteristics are detailed in Table 1.

Table 1. Baseline characteristics of patients analyzed with and without cGvHD

(n = 85)	**Genital cGVHD YES** 13 (15%)	**Genital cGVHD NO** 72 (85%)	**p value**
Age of Recipient (median, range)	42 (29-65)	48 (19-72)	0,059

Age of Donor (median, range)	37 (22-53)	38 (17-70)	0,6
Types of Donors [n (%)] Identical related donor (IRD) Non-identical related donor (NIRD) Non-identical unrelated donor (NURD) Haploidentical donor	 6 (46%) 7 (54%) 0 0	 25 (35%) 21 (29%) 17 (24%) 9 (13%)	0,057
Baseline Disease al Diagnosis [n (%)] Myelodysplastic syndrome Acute leukemias Lymphoproliferative syndromes Myeloproliferative neoplasms Aplastic anemia	 3 (23%) 9 (69%) 0 0 1 (7,7%)	 16 (22%) 42 (58%) 10 (14%) 1 (1,4%) 3 (4,2%)	0,6
Pre-Transplant Risk Index [n (%)] Low Medium High	 11 (85%) 1 (7,7%) 1 (7,7%)	 39 (54%) 22 (31%) 11 (15%)	0,13
Donor/Recipient Gender [n (%)] Male/Female Female/Female	 6 (46%) 7 (54%)	 41 (57%) 31 (43%)	0,5
CMV Donor/Recipient Status [n (%)] P/P (positive/positive) N/N (negative/negative) N/P (negative/positive) P/N (positive/negative)	 4 (31%) 4 (31%) 4 (31%) 1 (7,7%)	 32 (44%) 7 (9,7%) 27 (38%) 6 (8,3%)	0,2
Conditioning regimen [n (%)] RIC (reduced intensity) MA (myeloablative)	 1 (7,7%) 12 (92%)	 31 (43%) 41 (57%)	0,026
Source of Hematopoietic Progenitors [n (%)] PB (peripheral blood) BM (bone marrow)	 12 (92%) 1 (7,7%)	 68 (94%) 4 (5,6%)	0,6
Median Infused Cells (10^6/Kg) CD3 CD34	 243(21,1-616) 5,2(1,4-7,2)	 214,6(17,5-858) 5,6 (1,7-7)	 0,2 0,6
GvHD Prophylaxis [n (%)] CsA/MTX	 13 (100%)	 45 (63%)	0,031

CsA/MMF + Cypost CsA;CsA/MTX;CsA/MMF+Thymoglobulin	0 0	14 (20%) 12 (17%)	
Previous aGvHD YES	2 (15%)	12 (17%)	>0,9
aGvHD Grades 0 (GRADE 0 and 1) 1 (GRADE 2) 2 (GRADES 3 and 4)	11 (85%) 1 (7,7%) 1 (7,7%)	60 (83%) 6 (8,3%) 6 (8,3%)	>0,9
cGvHD Global Grades 0 1 2 3	0 0 3 (23%) 10 (77%)	33 (46%) 12 (17%) 12 (17%) 15 (21%)	<0,001
Genital cGvHD Grades 0 1 2 3	0 4 (31%) 0 9 (69%)	72 (100%)	<0,001
Oral cGvHD YES	8 (67%)	22 (31%)	0,023
Oral cGvHD Grades 0 1 2 3	5 (35%) 5 (38%) 2 (15%) 1 (7,7%)	49 (68%) 19 (26%) 2 (2,8%) 2 (2,8%)	0,053
POF Yes No	9 (69%) 4 (31%)	25 (35%) 47 (65%)	0,019
Survival Lives Dead	12 (92%) 1 (7,7%)	40 (56%) 32 (44%)	0,012

Results: After a median follow-up of 3.1 (range, 0.8–6.9),13 of 85 evaluable patients (15%) developed genital cGvHD, with a median time from HCT to diagnosis of 28 months (IQR, 4.7–55.3), whereas oral cGvHD was diagnosed earlier, at a median of 8.2 months (IQR, 3.4–48.9).
In multivariable analysis, oral cGvHD, premature ovarian failure (POF), and myeloablative conditioning were independently associated with the development of genital (Figure 1A).Genital cGvHD severity was also significantly associated with POF (p = 0.02): 89% of

patients with severe genital cGvHD had POF, compared with 25% of those with mild disease (Figure 1B).

Survival analyses demonstrated that patients who developed cGvHD had a significantly higher overall survival compared with those who did not (p = 0.02; Figure1C). Stratification by disease severity revealed a higher probability of survival among patients with mild cGvHD (p = 0.037; Figure 1D). When analyses were restricted to genital involvement, patients with genital cGvHD also exhibited superior overall survival (p = 0.022; Figure 1E).

A

Genital cGvHD

VARIABLES	*Odds Ratio*	*CI*	*p*
Myeloablative conditioning regimen	6.2394	0.9380-124.8153	0.1062
cGvHD	6.0033	1.5244-28.0619	0.0140
POF	4.3851	1.0304-23.8308	0.0585

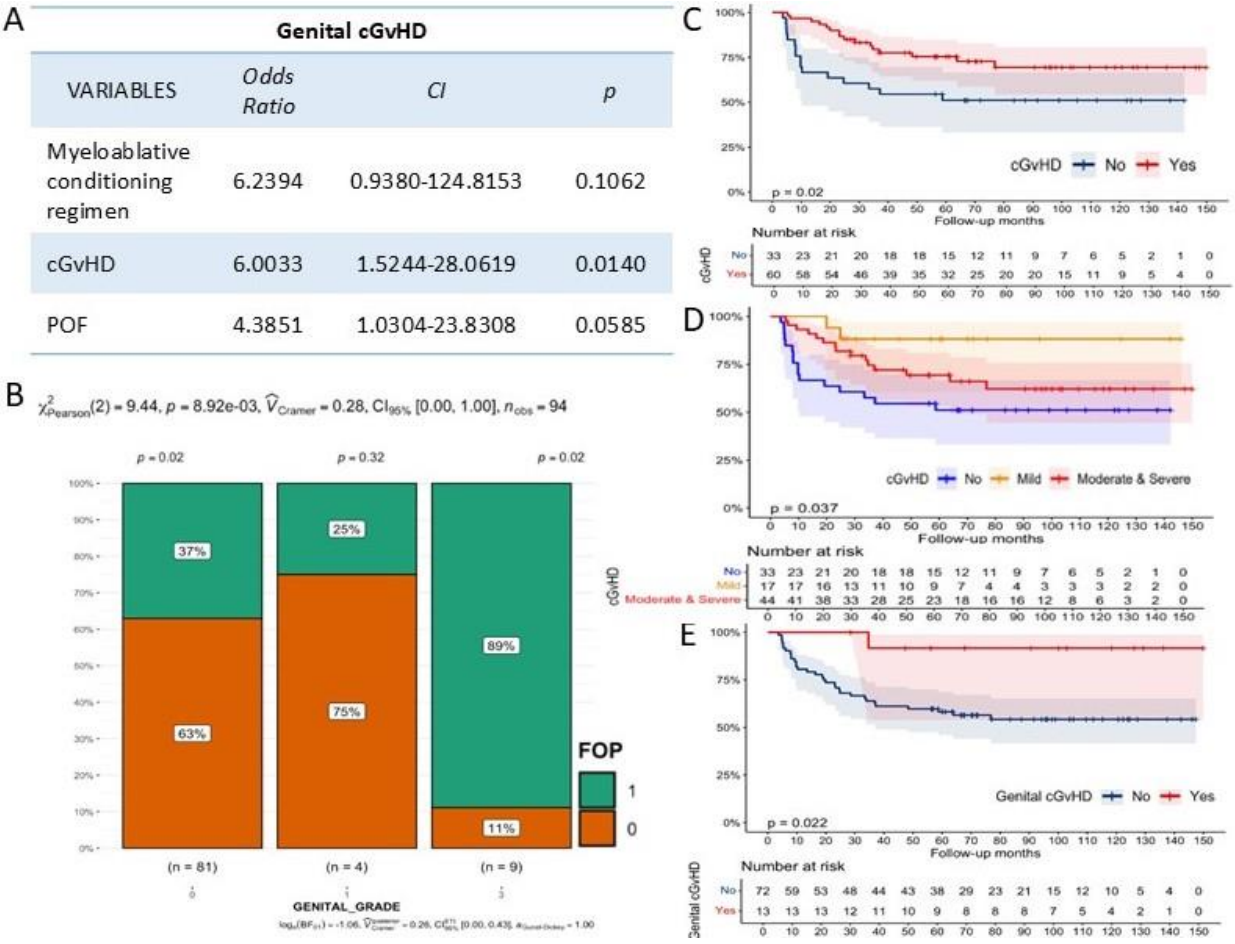

Figure 1A: Multivariate analysis of genital cGvHD.
Figure 1B: between POF and genital cGvHD and its grades 0, 1, and 3. Statistical test: Pearson's chi-square
Figure 1C: Overall survival (OS) according to the presence or absence of global cGVHD. Kaplan-Meier graphs. Log-rank stadistical test.
Figure 1D: Overall survival (OS) in patients with genital cGVHD, stratified by mild versus moderate–severe disease, compared with patients without GVHD.
Figure 1E: Overall survival (OS) according to the presence or absence (yes/no) of genital cGVHD.

Conclusions: In conclusion, genital cGVHD appears to be underdiagnosed and diagnosed later in our cohort compared with previously published studies. The presence of oral cGVHD may serve as an early clinical biomarker for the development of genital cGVHD. Therefore, once oral cGVHD is confirmed, early referral of HSCT recipients to specialised gynaecology units is warranted to enable timely diagnosis of genital cGVHD, as delays in treatment may worsen long-term sequelae and adversely affect quality of life.

Disclosure: No Disclosure.

B039

REDUCED-DOSE POST TRANSPLANTATION CYCLOPHOSPHAMIDE (PTCY) IN HEMATOPOIETIC STEM CELL TRANSPLANTATION: LEARNINGS FOR THE FUTURE

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Background: Post-Transplant cyclophosphamide (PTCy) has been widely accepted as the graft-versus-host disease (GVHD) prophylaxis following hematopoietic stem cell transplantation (HSCT) in the setting of haploidentical transplants and also matched related or unrelated donor transplants. PTCy has been effective in preventing GVHD without increasing the risk of relapse. However, prolonged cytopenias, cardio-toxicity, viral infections and hemorrhagic cystitis are adverse events that warrant caution. While standard dose PTCy (100mg/kg) has been used historically, recent data suggest a reduced dose might be equally effective with favourable outcomes while reducing the associated toxicities.

Methods: This was a retrospective analysis reviewed from the data of patients who underwent HSCT with PTCy prophylaxis between January 2021 to March 2025 at Rajiv Gandhi Cancer Institute and Research Centre, New Delhi, India.

Results: A total of 173 patients (Standard dose (SD): 113 and Low-dose (LD): 60) who underwent HSCT with PTCy prophylaxis were included. Median follow-up was 11 months. The median age, hematopoietic comorbidity index (HCT-CI) scores were similar across both the cohorts. Acute Myeloid Leukemia/Myelodysplastic Syndrome was the most common disease in most cases (32.7% [SD] vs. 50%[LD]). Peripheral blood was the most common stem cell source (100%). Myeloablative conditioning was employed in most cases (SD: 67.3% vs. LD: 48.3%). Donors were haploidentical (SD: 65.5% vs. LD: 71.7%) in most cases, followed by matched sibling donors (MSD) (SD: 27.4% vs. LD: 20%) and matched unrelated donors (MUD) (SD: 7.1% vs. LD: 8.3%).
Neutrophil (14 days; range-10-31) and platelet engraftment (14 days: range-11-30) were earlier in the low dose PTCy arm when compared to the standard dose (Neutrophil: 16 days (range:11-30) and platelets: 17 days (range:10-44)). The incidence of bloodstream infections was similar in both the cohorts. There was a signal for lower rates of invasive

fungal infections (IFI) in the low-dose PTCy cohort. Acute GVHD grade 1 was significantly higher in the low-dose PTCy cohort but there was no increase in grade 2-4 rates in either cohort. Deaths due to Cardiac toxicity, veno-occlusive disease and primary graft failure were seen in two, three and five patients all in the SD cohort.
One-year PFS was 79.7% with standard-dose PTCy and 82.2% with low-dose PTCy, while 2-year PFS for the standard-dose group was 66.5% (p-value = 0.549). One-year OS was similar between groups (74.0% vs 71.1%, p-value = 0.696), but only the standard-dose cohort maintained a 2-year OS of 69.6%, as the low-dose group reached a median OS of 18 months due to limited follow-up.

Conclusions: Our study suggests that reduced-dose PTCy is feasible in our setting and was associated with earlier engraftment, which is an important landmark during HSCT. Overall, no statistically significant differences in PFS or OS were observed between standard-dose and low-dose PTCy, indicating that both regimens provided comparable long-term disease control and survival within the limitations of follow-up duration, retrospective nature and cohort size. Prospective, randomised controlled trials would be needed to confirm our findings.

Disclosure: None

B042

A SINGLE TRANSPLANT PROGRAM EXPERIENCE IN TERMS OF GVHD PROPHYLAXIS: IS LESS DOSES OF METHOTREXATE BETTER THAN MORE?

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Background: Methotrexate (MTX) represents the standard prophylaxis for GVHD in matched allogeneic stem cell transplantation (HSCT). However, the optimal dosing schedule among the available MTX regimens is still debated. Based on this background, a retrospective study comparing two MTX schedules was performed within the Transplant Program of AORN Cardarelli in Naples to assess their impact on acute and chronic GVHD incidence and grading, infections, gastrointestinal (GI) toxicity and grade, overall survival (OS), time to discharge, engraftment, non-relapse mortality (NRM), and time to relapse (TTR).

Methods: To compare the safety and efficacy of administering 4 (N=59) versus 3 (N=29) MTX doses (15 mg/m² on day +1, and 10 mg/m² on days +3, +6, and +11 only in the four-doses group), we conducted a target trial emulation (TTE) using two real-world cohorts of patients affected by AML/MDS and ALL. Baseline imbalances between groups were evaluated through standardized mean differences (SMD), with SMD ≥|0.10| indicating meaningful imbalance. Variables exceeding this threshold were used to create weights via the propensity

score calculation and generate a weighted pseudo-population (inverse probability of treatment weighting, IPTW) in which the two arms were balanced. Weighted logistic regression models assessed acute and chronic GVHD and their grade, infections, and GI toxicity and grade, and results expressed as odds ratio (OR); weighted Cox models evaluated time to discharge, engraftment, and OS. NRM and TTR were analysed using Fine-Gray competing-risk models, considering death due to relapse or other causes as the competing event for NRM, and NRM as the competing event for TTR. Results from survival models were expressed as hazard ratio (HR).

Results: After IPTW adjustment, baseline characteristics were well-balanced (all SMD<|0.07|) between groups (Table 1).
In the weighted pseudo-population, GI toxicity and its maximum grade were significantly lower in the three-doses group (OR 0.17, 95% CI 0.06-0.47, p<0.01; maximum grade: OR 0.17, 95% CI 0.04-0.77, p=0.01). No significant differences were observed in aGVHD (OR 1.19, 95% CI 0.39-3.65, p=0.79; maximum grade: OR 1.10, 95% CI 0.11-10.48, p=0.93) and cGVHD (OR 2.64, 95% CI 0.93-7.45, p=0.18; maximum grade: OR 1.17, 95% CI 0.32-4.24, p=0.85), time to discharge (HR 1.19, 95% CI 0.75-1.89, p=0.45), or engraftment (HR 1.40, 95% CI 0.91-2.14, p=0.13).
Overall, 28.4% of patients died, with a NRM of 7.9% and the median survivals were not reached. In the pseudo-population, no significant differences emerged between the two regimens for OS, NRM or TTR (HR 0.76, 95% CI 0.25-2.28, p=0.62; SHR 1.38, 95% CI 0.21-8.96, p=0.74; SHR 0.55, 95% CI 0.16-1.91, p=0.35).

	Baseline population				Weighted pseudo-population			
	4 doses	**3 doses**	**p value**	**Test SMD**	**4 doses**	**3 doses**	**p value**	**Test SMD**
N	59	29			57.21	28.64		
Age (mean (SD))	44.6 (14.4)	46.9 (16.4)	0.516	0.144	45.32 (15.05)	44.85 (14.40)	0.900	-0.0308
Sex n (%): F M	30 (50.8) 29 (49.2)	13 (44.8) 16 (55.2)	0.761	0.121	28.4 (49.7) 28.8 (50.3)	12.7 (44.5) 15.9 (55.5)	0.724	0.0518
Diagnosis n (%): ALL AML/MDS	17 (28.8) 42 (71.2)	6 (20.7) 23 (79.3)	0.577	0.189	15.2 (26.6) 42.0 (73.4)	6.2 (21.9) 22.4 (78.1)	0.709	0.0465
Donor n (%): MUD 8/8 Sibling	24 (40.7)	22 (75.9)	0.004	0.764	30 (52.4)	16.9 (59.1)	0.656	-0.0672

	35 (59.3)	7 (24.1)			27.2 (47.6)	11.7 (40.9)		
Conditioning regimen n (%): -low intensity -high-moderate intensity	14 (23.7) 45 (76.3)	16 (55.2) 13 (44.8)	0.007	0.679	17.4 (30.4) 39.8 (69.6)	8.6 (30.2) 20 (69.8)	0.983	0.0026

Table 1. Baseline characteristics

Conclusions: Data concerning the impact of three versus four doses of MTX, as prophylaxis of GVHD in matched allogeneic HSCT at single adult Transplant Program, showed that the omission of the fourth dose of MTX did not significantly affect the transplant outcomes in terms of engraftment, NRM, TTR, OS, aGVHD and cGVHD occurrence and grading. The reduction of MTX doses may reduce severe mucosal damage and the consequent GI toxicity, incidence and maximum grade.

Disclosure: Nothing to declare

B043

SYSTEMIC TREATMENT WITH THE ROCK2 INHIBITOR BELUMOSUDIL IN OCULAR CHRONIC GRAFT VERSUS HOST DISEASE

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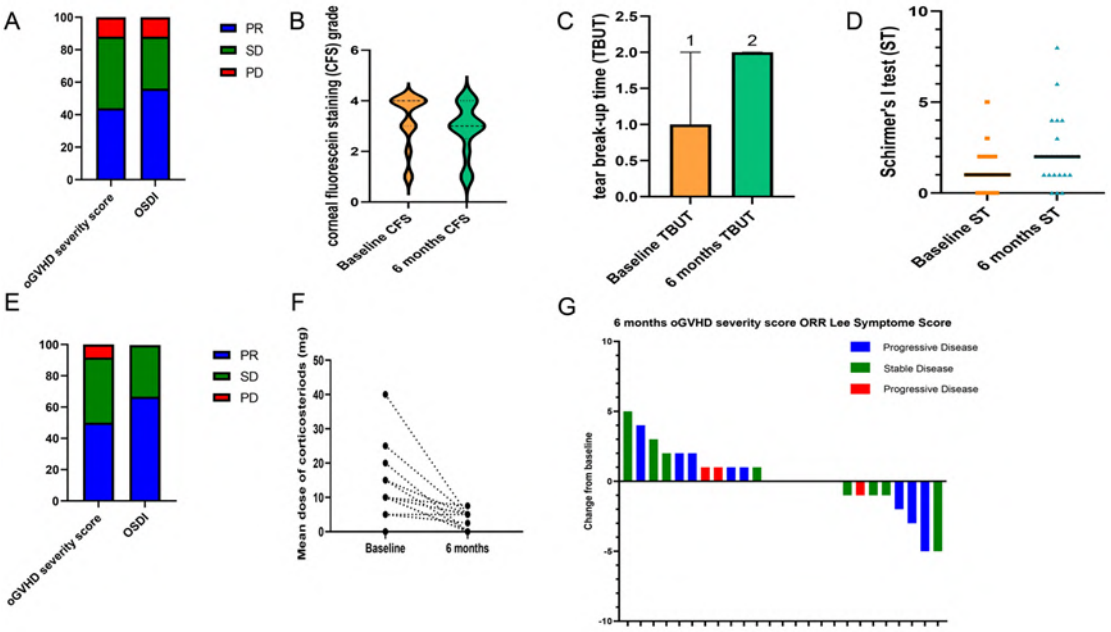
Background: To evaluate the efficacy of oral belumosudil on ocular surface disease (OSD) in patients with steroid-refractory chronic graft-versus-host disease (cGVHD).

Methods: We retrospectively analyzed patients with steroid-refractory cGVHD and ocular involvement (oGVHD) who received systemic belumosudil. Ocular assessments were performed at baseline and at the 6-month primary efficacy endpoint, including: the International Chronic Ocular GVHD Consensus Group severity score, NIH eye score (0-3), corneal fluorescein staining (CFS) grade (0-4), tear break-up time (TBUT), Schirmer's I test without anesthesia (ST), and the Ocular Surface Disease Index (OSDI). The 6-month overall

response rate (ORR), organ-specific responses, and adverse events were evaluated per NIH consensus criteria.

Results: Among 67 steroid-refractory cGVHD patients treated with belumosudil (200 mg daily), 38 had oGVHD with NIH eye score 2(1-3) and oGVHD severity score 9(1-10) respectively. Of these, 25 patients completed both baseline and 6-month assessments. The cohort had high-risk features: 48.0% (12/25) had severe NIH-grade systemic disease and 64.0% (16/25) had conjunctival fibrosis.
At 6 months, the oGVHD severity score improved in 44.0% (11/25), was stable (SD) in 44.0% (11/25), and progressed (PD) in 12.0% (3/25). OSDI improved in 56.0% (14/25), was SD in 32.0% (8/25) and PD in 12.0% (3/25) (Fig 1A).
Objective signs showed improved from baseline: CFS decreased from 4 (1-4) to 3 (1-4) (Fig 1B) , TBUT increased from 1.0 s (0.8-4.78) to 2.0 s (0-5) (Fig 1C), and ST improved from 1.0 mm (0-5) to 2.0 mm (0-22) (Fig 1D).
Greater benefit was observed in the 12 patients (48.0%) who achieved systemic ORR at 6 months. In this subgroup, the oGVHD severity score improved in 50.0% (6/12), was stable in 41.7% (5/12) and progressed in 8.3% (1/12). OSDI improved in 66.6% (8/12), was stable in 33.3% (4/12) and none worsened (Fig 1E). Objective signs also improved: CFS decreased from 4 (1-4) to 3 (1-4), TBUT increased from 1.0 s (0.8-2.0) to 2.0 s (0.5-3.0), and ST improved from 1.0 mm (0-2.0) to 2.0 mm (0-6.0).
Visual acuity remained stable across all groups. Corticosteroid dose reduction was achieved in 48.0% (12/25) of patients (Fig 1F). The eye Lee Symptom Scale score remained unchanged (7 [2-12] vs. 7 [1-15]) (Fig 1G). Treatment was well-tolerated with no drug-related discontinuations or severe hematologic toxicities.



Conclusions: Systemic belumosudil treatment demonstrated a high response rate, significant improvements in international oGVHD severity scores and ocular surface

parameters, and favorable tolerability in steroid-refractory oGVHD patients. Notably, the greatest ocular benefit was closely associated with systemic overall response, indicating that systemic response may serve as a predictor for ocular outcomes in cGVHD management.

Disclosure: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this study.

B044

DONOR- AND DOSE- SPECIFIC ENDOTHELIAL ACTIVATION AND CLINICAL OUTCOMES AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE

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Background: Post-transplant cyclophosphamide (PTCy) is widely used for GVHD prophylaxis across donor types. Although experimental data suggest that PTCy induces endothelial stress, clinical characterization of early endothelial activation in allo-HCT remains limited. At our institution, PTCy-based prophylaxis has been progressively implemented since 2013; tacrolimus (TK) is routinely combined, and mycophenolate mofetil (MMF) is added in haploidentical transplants (haplo-HCT). In 2021, PTCy dosing was reduced to 40 mg/kg/day in 10/10 HLA-matched donors to mitigate early toxicity.
Given the central role of endothelial dysfunction in post-transplant complications, this study describes endothelial activation patterns and compares clinical results of allo-HCT performed with PTCy across donor types.

Methods: Ninety-five consecutive adults receiving allo-HCT with PTCy between August 2022 and January 2025 were included. Endothelial activation was monitored using serial EASIX scores from baseline to day +180. Biomarkers of endothelial injury (VWF, thrombomodulin [TM], TNFR1) and inflammatory/GVHD signaling (REG-α, ST2) were quantified from cryopreserved plasma collected at admission, day 0, +7, +14, and +21.

Results: Among 95 patients, 50 (52.6%) received grafts from HLA-matched donors (PTCy40-TK), 25 (26.3%) from 9/10 mismatched unrelated donors (MMUD, PTCy50-TK), and 20 (21.1%) underwent haplo-HCT (PTCy50-TK-MMF). All CMV-positive recipients received letermovir, and all patients received G-CSF from day +7.
As reported in Table 1, baseline characteristics were balanced. Engraftment was slightly faster in HLA-matched allo-HCT. TA-TMA was only documented in MMUD recipients (20%; p=0.016), whereas VOD was infrequent. Haplo-HCT showed the highest burden of early toxicity, including graft failure (10.0%), cardiac events (20% vs. 0–2%; p=0.001) and infectious complications such as bloodstream infections (45%), BK hemorrhagic cystitis

(10%), and invasive fungal infections (20%).
Acute GVHD rates were comparable across HLA-matched, MMUD, and haplo-HCT cohorts: grade II–IV (24%, 24%, 20%; p=0.915) and grade III–IV (10%, 12%, 15%; p=0.829). Two-year moderate–severe cGVHD incidence was similarly low (12.6%, 13.2%, 10.9%; p=0.678). Overall survival did not differ significantly (2-year: 73.2%, 84.0%, 70.0%; p=0.953), with low rates of non-relapse mortality (2-year: 0%, 8%, 5%). However, relapse incidence at two years remained substantial (38.8%, 16.7%, 29.9%; p=0.094), reflecting the high-risk features of the population transplanted during this period.
Endothelial activation increased during the early post-transplant period in all transplant settins (Figure 1). However, Haplo-HCT displayed the highest EASIX values across all time points, with a sharp post-PTCy increase from 1.24 (day 0) to 4.67 (day +7), peaking at 7.38 (day +14), and remaining elevated at 7.61 (day +21). TNFR1 and TM trajectories mirrored EASIX profiles, reinforcing the greater endothelial stress in haplo-HCT. ST2 and REG-α medians were also higher in haplo-HCT, with ST2 presenting pronounced peaks between days +7 and +14, and REG-α remaining persistently elevated. Moreover, espite receiving reduced PTCy dosing, HLA-matched transplants consistently showed the lowest endothelial activation.

Baseline Information and Main Results	HLA-Matched (n=50) PTCY40-TK	9/10 MMUD (n=25) PTCY50.-TK	Haplo-HCT (n=20) PTCY50-TK-MMF	P value
Median age, years, (range)	58 (18-74)	54 (22-74)	50 (19-75)	0.647
Sex Male Female	30 (60.0) 20 (40.0)	9 (36.0) 16 (64.0)	15 (75.0) 5 (25.0)	0.026
Diagnosis Acute Myeloid Leukemia Myelodisplastic Syndrome Acute Lymphoblastic Leukemia Myeloproliferative Neoplasm Lymphoproliferative Diseases Others	20 (40.0) 8 (16.0) 10 (16.0) 1 (2.0) 5 (10.0) 6 (12.0)	10 (40.0) 5 (20.0) 8 (32.0) 0 1 (4.0) 1 (4.0)	7 (35.0) 3 (15.0) 4 (20.0) 0 5 (25.0) 0	0.665
Conditioning Intensity Myeloablative Reduced	21 (42.0) 29 (58.0)	14 (56.0) 11 (44.0)	10 (50.0) 10 (50.0)	0.501

Early HCT Information Median days to neutrofil engraftment Median days to platelet engraftment Graft Failure	15 (14-16) 16 (13-21) 0	16 (15-18) 19 (16-25) 1 (4.0)	17 (15-19) 17 (15-27) 2 (10.0)	0.090 0.140 0.399
Cumulative Incidence Infectious (CIF) Complications Bacterial Bloodstream Infections (Day 100) CMV Reactivation (All letermovir, Day 100) Grade II-IV BK virus Hemorrhagic Cystitis Invasive Pulmonary Fungal Infections	26.0 (14.7-38.7) 6.0 (1.5-15.0) 4.0 (0.7-12.2) 2.0 (0.2-9.3)	36.0 (14.7-38.7) 0 8.0 (1.3-22.9) 8.0 (1.3-22.9)	45.0 (22.4-65.3) 0.5 (0.3-21.1) 10.0 (1.6-27.8) 20.0 (9.5-42.1)	0.127 0.521 0.29 0.097
Post-transplant events SOS TA-TMA CIF Cardiac Events (at day 100) CIF Grades II-IV aGVHD at day 100 CIF Grades III-IV aGVHD at day +100 CIF Moderate/Severe cGVHD	1 (4.0) 1 (4.0) 2.0 (0.2-9.3) 24.0 (13.2-36.6) 10.0 (3.6-20.2) 12.6 (5.0-23.8)	0 5 (20.0) 0 24.0 (9.4-42.1) 12.0 (2.9-28.0) 13.2 (3.1-31.0)	0 0 20.0 (6.0-39.9) 20.0 (9.5-42.1) 15.0 (3.6-34.0) 10.0 (1.6-27.8)	0.399 0.016 0.915 0.829 0.678
Death Causes of Death Disease relapse Infectious complications GVHD Other	13 (26.0) 13 (26.0) 0 0 0	7 (28.0) 4 (16.0) 1 (4.0) 0 2 (8.0)	5(25.0) 4 (20.0) 0 1 (5.0) 0	0.924
2-Year Overall Survival 2-year Cumulative Incidence of Disease Relapse 2-year Non-Relapse Mortality	73.2 (58.3-83.5) 38.8 (25.0-54.3) 0	84.0 (62.8-93.7) 8.0 (1.3-22.9) 0	70.0 (55.1-92.1) 29.9 (6.0-39.9) 0	0.953 0.093 0.073

Conclusions: Endothelial activation after allo-HCT with PTCy appears influenced by donor type and PTCy dosing. Haplo-HCT showed the highest endothelial stress and the greatest burden of early infectious and cardiovascular complications, despite similar GVHD rates and survival outcomes across groups. Results support the conduction of studies evaluating whether early biomarker dynamics can predict post-transplant complicationss.

Clinical Trial Registry: No applicable.

Disclosure: Nothing to declare.

B045

EFFICACY OF CNI-FREE GVHD PROPHYLAXIS IN PEDIATRIC PATIENTS UNDERGOING HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER PRIOR MONOCLONAL ANTIBODY THERAPY

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HCT) is an effective therapy for children with high-risk acute lymphoblastic leukemia (ALL) in remission. Furthermore, it represents a key therapeutic strategy for patients with relapsed or refractory ALL who achieve remission following treatment with monoclonal antibodies (e.g., blinatumomab or inotuzumab ozogamicin). However, in this setting, allo-HCT carries a substantial risk of endothelial damage, leading to complications such as sinusoidal obstruction syndrome (SOS) and transplant-associated thrombotic microangiopathy (TA-TMA). This risk is further compounded by graft-versus-host disease (GVHD) prophylaxis regimens based on calcineurin inhibitors (CNIs), particularly in patients with a history of intensive prior therapy, including a second allo-HCT. These challenges underscore the need for developing CNI-free GVHD prophylaxis protocols for this vulnerable group of patients.

Methods: This single-center retrospective cohort study enrolled 63 pediatric patients (<18 years) with ALL who received haploidentical HCT following prior treatment with inotuzumab ozogamicin and/or blinatumomab. Patients were stratified into two cohorts according to the GVHD prophylaxis regimen: with or without calcineurin inhibitors (Table 1). The GVHD prophylaxis backbone for all patients consisted of post-transplant cyclophosphamide (PTCy) administered on days +3 and +4. In the CNI-based group (n=24), all patients received a combination of tacrolimus and an mTOR inhibitor. In the CNI-free group (n=39), prophylaxis comprised mTOR inhibitor only.

Patients and HCT characteristics	CNI N=24	CNI-free N=39	p value

Age, years, median	7.9 (3.92)	8.7 (4.25)	0.457
Gender Female Male	 7 (29.2%) 17 (70.8%)	 12 (30.8%) 27 (69.2%)	1.000
HCT number First Second	 20 (83.3%) 4 (16.7%)	 34 (87.2%) 5 (12.8%)	0.721
Graft source Bone marrow PBSC	 19 (79.2%) 5 (20.8%)	 33 (84.6%) 6 (15.4%)	0.735
Conditioning regimens Myeloablative Reduced intensity	 15 (62.5%) 9 (37.5%)	 7 (17.9%) 32 (82.1%)	**0.001**
Remission status before HCT No remission Remission	 7 (29.2%) 17 (70.8%)	 13 (33.3%) 26 (66.7%)	0.947
MRD Negative Positive	 12 (50.0%) 12 (50.0%)	 20 (51.3%) 19 (48.7%)	1.000
Therapy used prior HCT Blinatumomab Blinatumomab and inotuzumab ozogamicin Inotuzumab ozogamicin	 15 (62.5%) 3 (12.5%) 6 (25.0%)	 15 (38.5%) 6 (15.3%) 18 (46.2%)	0.226

Results: With a median follow-up of 374 days (range, 15–2092), the incidence of acute GVHD did not differ significantly between the CNI-based and CNI-free groups (60% vs. 67%, p=0.86). Similarly, comparable rates were observed for grade 2-4 aGVHD (40% [95% CI 19 – 61%] vs. 53% [95% CI 34 – 70%], p=0.3) and grade 3-4 aGVHD (25% [95% CI 9 – 46%] vs. 27% [95% CI 12 – 43%], p=0.84) (Fig.2). There were no significant differences in the frequency and severity of organ involvement, including skin (p=0.79), gastrointestinal tract (p=0.74), or liver (p=1.0). Engraftment rates were comparable (83% vs. 77%, p=0.71), with a uniform median time to engraftment of 21 days. Notably, the incidence of SOS/TA-TMA showed a non-significant trend towards being higher in the CNI-based group (33% vs. 15%, p=0.097). One-year overall survival (57% vs. 59%, p=0.5), cumulative

incidence of relapse (45% vs. 53%, p=0.4), and non-relapse mortality (12% in both groups, p=0.95) were not significantly different. In multivariate analysis, ALL remission (HR 0.35; 95%CI 0.14-0.89; p=0.028) and use of a reduced-intensity conditioning (HR 0.24; 95%CI 0.06-0.92; p=0.037) were associated with better overall survival outcomes, while the use of intotuzumab ozogamicin before HCT significantly reduced OS (HR 5.6; 95%CI 1.8-17.9; p=0.004). Only positive MRD status before HCT was associated with significant increase of relapse probability (90% [95% CI 25 – 99%] vs. 30% [95% CI 13 – 50%]). We observed a trend towards a higher incidence of chronic GVHD in the CNI-free group (33% vs. 15%, p=0.13).

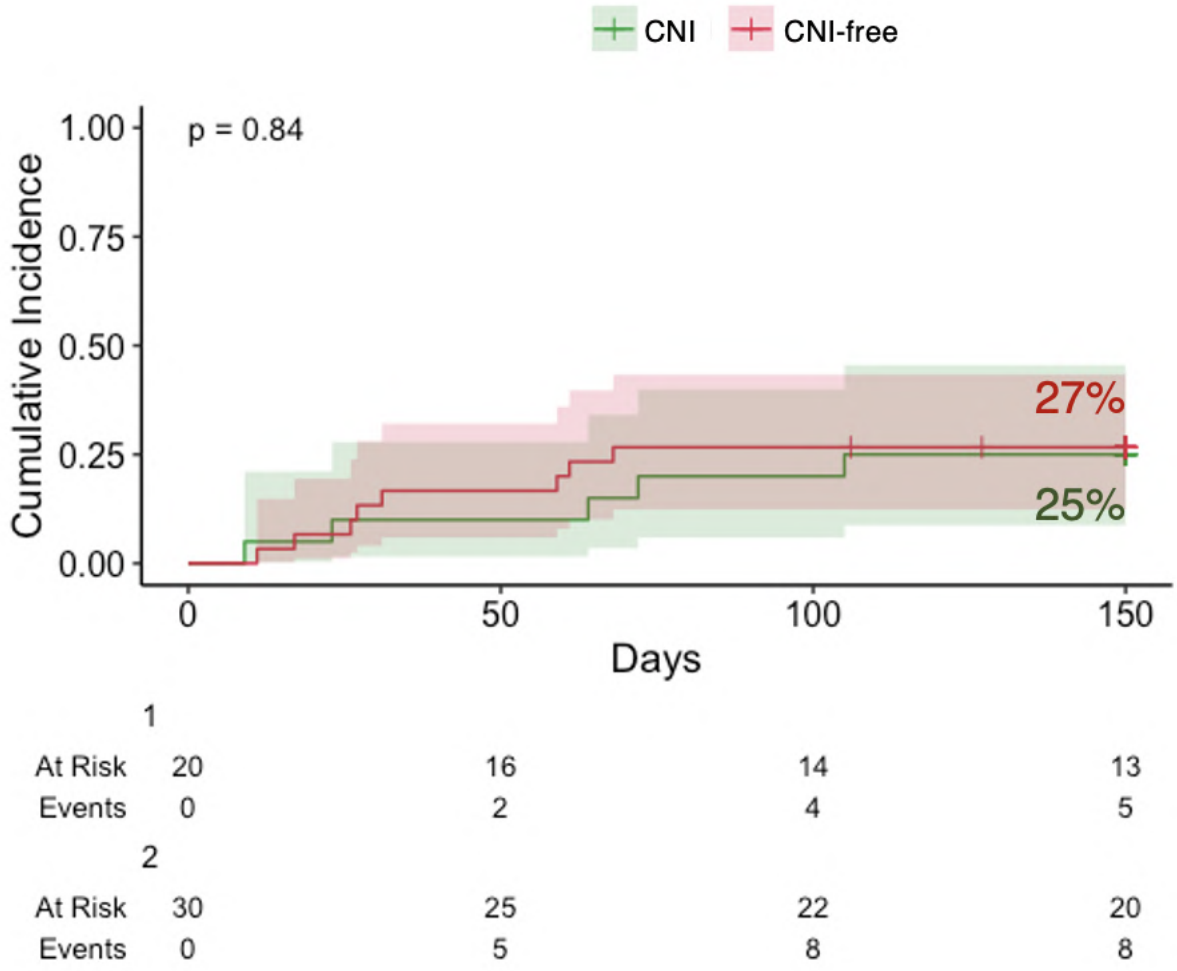

Fig. 1 Cumulative incidence of grades 3–4 acute GVHD, by GVHD prophylaxis regimen

Conclusions: Our findings suggest that CNI-free prophylactic regimens yield comparable survival outcomes and provide similar control over acute GVHD relative to standard CNI-based protocols. Future research should focus on elucidating the risk factors for chronic GVHD in this setting and developing targeted strategies to reduce its incidence.

Disclosure: Nothing to declare.

B046

VIRAL INFECTION WITHIN STEROID REFRACTORY/DEPENDENT GVHD PATIENTS TREATED WITH RUXOLITINIB: A SINGLE CENTER ANALYSIS

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Background: Graft-versus-host disease (GVHD) is a major complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) and a leading cause of non-relapse mortality. While corticosteroids remain first-line therapy, up to 50% of patients develop steroid-refractory or steroid-dependent (SR/D) GVHD. Ruxolitinib, a selective JAK1/2 inhibitor, has demonstrated superior responses in both acute and chronic SR/D GVHD (REACH2/REACH3 trials). Its immunosuppressive effect increases the risk of bacterial, viral, and fungal infections. Herein we analyzed viral reactivation incidence and its impact on overall survival (OS) in patients who developed GVHD requiring treatment in our centre.

Methods: All allo-HSCT patients transplanted between 2018 and 2024 that developed GVHD were considered eligible for this study. Among 308 transplanted patients, 160 (52%) experienced GVHD. Acute myeloid leukemia (AML) was the most frequent indication for allo-HSCT. Conditioning intensity was evenly distributed between myeloablative (MAC) and reduced-intensity regimens (RIC). Nearly half of the patients (48.1%) received grafts from matched unrelated donors, followed by HLA-identical siblings and haploidentical donors. Peripheral blood stem cells were the predominant graft source. GVHD prophylaxis was primarily based on ATG. GVHD cases were subsequently stratified into two groups: steroid-sensitive (SS) GVHD and SR/D GVHD, the latter treated with ruxolitinib as second-line therapy. Finally, we evaluated the incidence of viral reactivations in both groups, with specific attention to CMV, EBV, HHV-6, and adenovirus. Overall survival (OS) was estimated using Kaplan–Meier analysis.

Results: Baseline demographic and transplant-related characteristics are summarized in Table 1. The 8-year OS was 53% in patients with SS-GVHD and 61% in those with SR/D-GVHD, with no significant difference ($p = 0.1229$). In the SR/D-GVHD cohort, 8-year overall survival (OS) was 56% in patients who experienced at least one viral infection versus 70% in those without viral infections ($p = 0.7624$). Similar findings were observed when restricting

the analysis to CMV reactivation: 8-year OS was 49% in SR/D-GVHD patients with CMV reactivation and 74% in those without (p = 0.2588; Figure 1A). Among patients with CMV reactivation, 8-year OS did not differ significantly between SS-GVHD and SR/D-GVHD patients treated with ruxolitinib (52% vs 49%, respectively; p = 0.7192; Figure 1B). Relapse incidence was comparable between the SS-GVHD and SR/D-GVHD groups (Table 1) and was 33% among SR/D-GVHD patients with CMV reactivation. In this subgroup, the main causes of death were relapse (50%), infections (30%), and acute GVHD (20%), with no significant differences compared with the SS-GVHD and SR/D-GVHD groups.

Conclusions: Viral infections remain a relevant complication after allo-HSCT, particularly in patients with GVHD requiring intensified immunosuppression. In our cohort, viral reactivations, including CMV, were frequent among SR/D-GVHD patients treated with ruxolitinib but were not associated with a significant impairment in long-term overall survival. Notably, CMV reactivation did not translate into increased infection-related mortality, with relapse remaining the leading cause of death across all groups. Overall, these findings suggest that ruxolitinib can be used as second-line therapy for SR/D-GVHD without an apparent detrimental impact on survival, even in the context of common viral reactivations, when appropriate monitoring and pre-emptive strategies are applied.

	Total patients with acute or chronic GvHD (160)	SS GvHD (97)	SR/D GvHD treated with Ruxolitinib (63)	P valu
Male (%) Female (%)	101 (63%) 59 (37%)	68 (70%) 29 (30%)	33 (52%) 30 (48%)	<0.0
Median age at HSCT (range)	58 (19-74)	56 (19-74)	59 (20-73)	0.78
Diagnosis AML (%) MDS (%) ALL B/T (%) NHL/HL (%) MF (%) Other (%)	 61 (38.1%) 19 (11.9%) 15 (9.4%) 17 (10.6%) 25 (15.6%) 23 (14.4%)	 42 (43.3%) 11 (11.3%) 6 (6.2%) 6 (6.2%) 16 (16.5%) 16 (16.5%)	 19 (30.2%) 8 (12.7%) 9 (14.3%) 11 (17.4%) 9 (14.3%) 7 (11.1%)	 0.03
Donor type Sibling (%) MUD (%) Haploidentical (%)	 41 (25.7%) 77 (48.1%) 42 (26.2%)	 24 (24.7%) 49 (50.6%) 24 (24.7%)	 17 (27%) 28 (44.4%) 18 (28.6%)	 0.6
SC source PBSC (%) BM (%)	 147 (91.9%) 13 (8.1%)	 89 (91.7%) 8 (8.3%)	 58 (92%) 5 (8%)	 1
Conditioning regimen MAC (%) RIC (%)	 89 (55.6%) 71 (44.4%)	 56 (57.7%) 41 (42.3%)	 33 (52.4%) 30 (47.6%)	 0.43

GVHD prophylaxis ATG based (%) PTCY based (%) Other (%)	 94 (58.7%) 40 (25%) 26 (16.3%)	 56 (57.7%) 22 (22.7%) 19 (19.6%)	 38 (60.3%) 18 (28.6%) 7 (11.1%)	0.18
Median follow up (range)	24.3 months (0.5-115.3)	21.6 months (0.5-90.1)	29.5 months (1.5-115.3)	0.26
CMV reactivation (%)	56 (35%)	32 (33%)	24 (38%)	0.55
CMV therapies (%)	47/56 (84%)	27/32 (84%)	20/24 (83%)	0.93
EBV reactivation (%)	20 (12%)	7 (7%)	13 (20%)	0.01
HHV6 reactivation (%)	26 (16%)	20 (20%)	6 (10%)	0.006
Median days to CMV reactivation (range)	134 (8-1595)	127 (8-352)	156 (34-1595)	0.08
Median days to EBV reactivation (range)	144 (28-1703)	89 (31-195)	196 (28-1703)	<0.0
Death (%)	58 (36%)	39 (40%)	19 (30%)	0.23
Incidence of Relapse (%)	45 (28%)	31 (32%)	14 (22%)	0.17
Cause of death Relapse (%) Infections (%) aGVHD (%) cGVHD (%) Toxicity (%) Other (%)	 33 (57%) 13 (22.4%) 5 (8.6%) 2 (3.4%) 1 (1.7%) 4 (6.9%)	 23 (59%) 9 (23.5%) 1 (2.5%) 2 (5%) 1 (2.5%) 3 (7.5%)	 10 (52.7%) 4 (21%) 4 (21%) 0 (%) 0 (%) 1 (5.3%)	 <0.0

Figure 1A

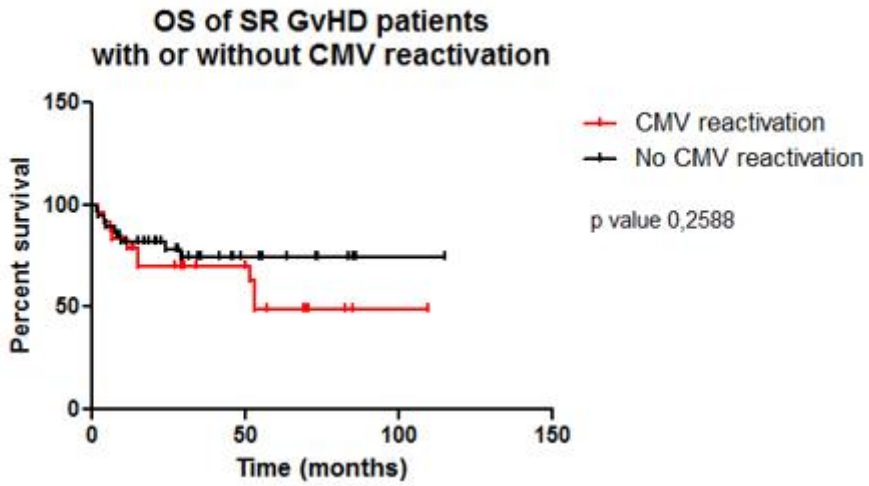
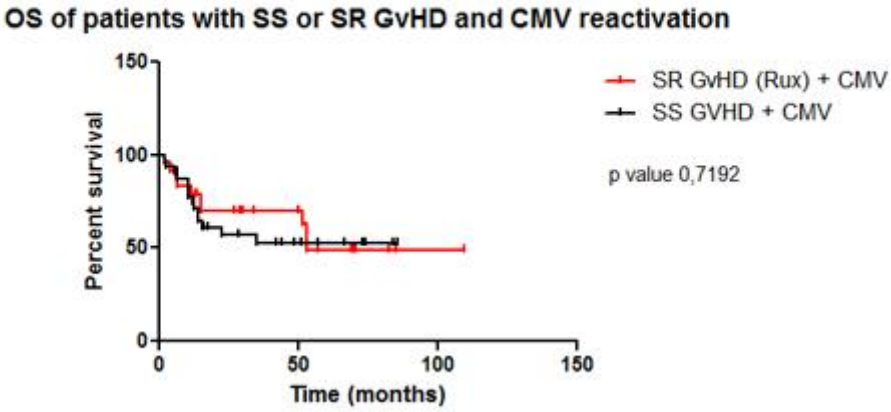


Figure 1B



Disclosure: Not applicable.

B047

BENEFITS OF A MULTIDISCIPLINARY COMMITTEE FOR THE TREATMENT OF CHRONIC GVHD: CASE REPORTS AS A PARADIGM FOR COLLABORATIVE CARE

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Background: Chronic graft-versus-host disease (cGVHD) affects more than one third of patients undergoing allogeneic hematopoietic stem cell transplantation and can involve multiple organs.
This multisystem involvement may benefit from collaboration among different specialists who can provide tailored solutions for each of the potential complications of the disease. In this context, the Ramón y Cajal Hospital in Madrid, Spain, has a dedicated multidisciplinary committee for the management of this condition. This committee is composed of specialists in Hematology, Pulmonology, Ophthalmology, Dermatology, Rehabilitation, and Pharmacy, and is open to the inclusion of other departments in the future.

Methods: Based on our center`experience, we present four illustrative cases of patients with cGVHD who have particularly benefited from management by our committee.

Results: Table 1 summarizes the main information regarding medical history, cGVHD characteristics, and the committee's approach for each patient.
Below, we describe how the committee's intervention contributed to clinical improvement in each case.

	Medical history					cGVHD		
	Age	**Gender**	**Underlying disease**	**Relevant comorbidities**	**Years since HCT**	**Month of onset**	**Lee Score at the time of assessment**	**Treatment at th**
Patient 1	47	Male	MDS	-COPD -Smoker	6	+14	14 points: - 5 skin - 6 eyes - 2 mouth - 1 breath	- Ruxolitinib 5mg - Belumosudil 20 - Lungs: fluticaso bromide, and vila azithromycin - Eyes: Insulin ey times a day, auto retinol palmitate lubricants and m
Patient 2	32	Male	MonoMAC syndrome	- CKD3b - Lymphedema left lower limb -Previous pulmonary cGVHD	4	+17	5 points: - 4 skin - 1 eyes	- Cyclosporine A - Ursodeoxycholi - Lungs: montelu and vilanterol - Clobetasol nail - Eyes: cyclospor serum, acetylcyst

Patient 3	31	Male	AML	- Mild iron overload	3	+17	27 points: - 15 skin - 5 eyes/mouth - 1 digestion - 1 muscle - 2 energy - 2 mental	- Belumosudil 20 - Famotidine - Atarax - Beclomethason
Patient 4	51	Female	AML	- Severe combined immunodeficiency - Recurrent lung infections	3	+13	7 points - 1skin - 3 eyes - 3 breath	-Cyclosporine A 5 -Belumosudil 200 -Ruxolitinib 10mg -Prednisone 10m -Lungs: montelu budesonide, iprat tiotropium and ol -Infectious proph cotrimoxazole, is -Eyes: cyclospori eye serum, lubric - Ursodeoxycholi

Patient 1. Ocular worsening: Despite all treatments administered, the patient showed no improvement. He was referred to the ophthalmologist on the committee, who realized that the autologous serum was only increasing inflammation; therefore, it was replaced with plasma, since this provides additional regenerative and anti-inflammatory factors that are not present in serum, which improved the patient's clinical condition.
Patient 2. Ankle sclerosis with impaired dorsiflexion; asthma: Rehabilitation proposed several options that are not commonly considered by hematologists, such as performing an ankle MRI to better determine the cause, using botulinum toxin, and prescribing specific exercises. Additionally, this patient's previous diagnosis of pulmonary cGVHD was re-evaluated, reconsidered as bronchial asthma, and the pulmonary treatment was adjusted accordingly.
Patient 3. Sclerodermiform cutaneous cGVHD: With the treatment administered up to that point, the patient had multiorgan cGVHD with good evolution in all areas except the skin, presenting the lesions shown in Figure 1b. Together with the Dermatology Department, tocilizumab was initiated—monthly at first and later every three months—with clinical improvement beginning after the second dose. A 12-point decrease in the "skin" domain of the Lee score was achieved, along with recovery of sweating and body hair. Grade III neutropenia developed as an adverse effect but resolved with a single dose of G-CSF.

Patient 4. Severe pulmonary cGVHD: The patient had difficulty achieving respiratory improvement, due to recurrent infections, and lung transplantation had been proposed as primary option. She was re-evaluated, and recovery was optimized through respiratory physiotherapy, FAM therapy, optimization of bronchodilator therapy with closed triple therapy (LABA/LAMA/ICS), and temporarily increasing azithromycin to 600 mg for six days, followed by a return to the previous dose of 250 mg three days per week. Prednisone was gradually discontinued, and immunoglobulins were administered every three weeks. The patient achieved pulmonary improvement, avoiding need for transplantation.

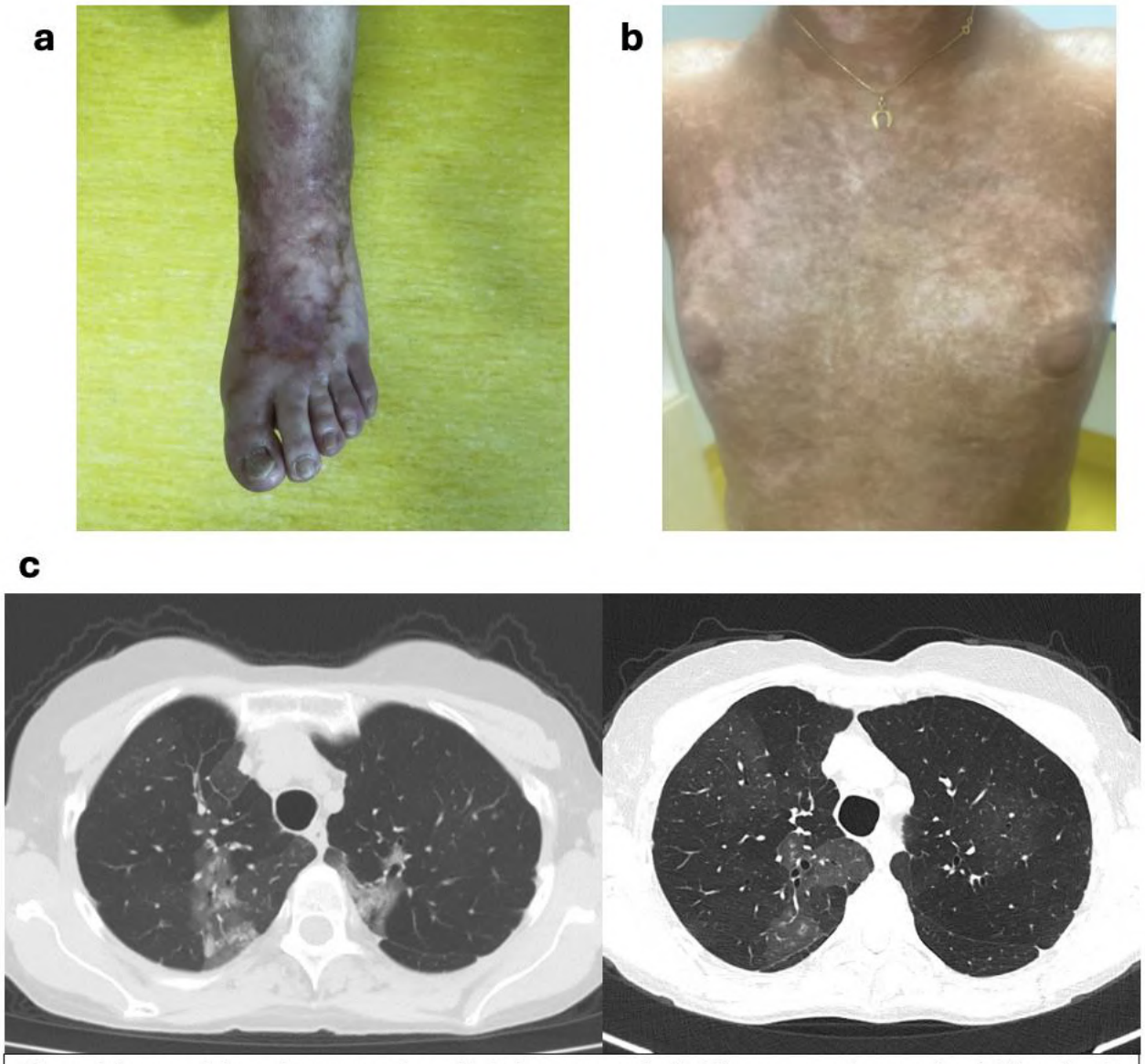

Figure 1: Images of the patients were taken with their consent and with full assurance of anonymity. **a)** Skin sclerosis on the dorsum of the left foot of patient 2. **b)** Skin of patient 3 with poikiloderma, hair loss, and lichen planus-like, sclerodermiform lesions, associating onychodystrophy. **c)** Chest CT scan of patient 4 before (left) and after (right) the committee's intervention, showing improvement of the pulmonary complications derived from cGVHD (bronchiolitis obliterans with radiological improvement of the micronodular involvement and consolidation areas).

Conclusions: The GVHD committee at our hospital reflects a collaborative effort among various specialists focused on the management of patients with this condition. We believe that this kind of multidisciplinary approach provides clear clinical benefit among patients with GVHD, particularly in cases with several organs involved.

Disclosure: Nothing to declare

B048

EFFICACY AND SAFETY OF BELUMOSUDIL-ECP (EXTRACORPOREAL PHOTOPHERESIS) COMBINATION THERAPY IN REFRACTORY CHRONIC GRAFT-VERSUS-HOST DISEASE (CGVHD) AND CORRELATION WITH CYTOKIN KINETIC: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Chronic GVHD, a key complication of allogeneic transplantation affecting quality of life even at mild stages, remains inadequately controlled by corticosteroids, while novel approaches such as the ROCK2 inhibitor belumosudil and ECP, especially in combination, show encouraging therapeutic potential.

Methods: At our institution, Fondazione Policlinico Gemelli, between February 2024 and November 2025, we enrolled nine patients (2 females and 7 males) with moderate to severe chronic GVHD (according to the NIH grading system) refractory to at least two prior lines of therapy (median 4 lines). All patients received belumosudil (400 mg daily for those on proton pump inhibitors, 200 mg for others) in combination with extracorporeal photopheresis (ECP; two procedures per month, intensified to twice every two weeks in case of flare). Cytokine parameters (IL-2, IL-6, and sST2) were measured at therapy initiation and on the day of the first ECP each month. **Patient characteristics' are summarized in Table 1.**

Table 1. Patient characteristics

Patient	Age (years)	Underlying disease	Donor type	GVHD prophylaxis	Prior therapy lines	cGVHD grade at belumosudil start	Organs involved
1	25	HL	URD 8/8	CSA-MMF + PT-Cy	>5	Severe	Skin, intestine
2	55	HL	APLO	CSA-MMF + PT-Cy	>5	Severe	Skin, intestine
3	21	AML	Sibling	CSA-MTX	1	Severe	Lung
4	27	B-ALL	Sibling	CSA-MMF + PT-Cy	3	Moderate	Joint/fascia, mouth, skin

5	57	MPN	URD 8/8	CSA-MMF + PT-Cy	2	Moderate	Liver, eye, skin
6	64	AML	APLO	CSA-MMF + PT-Cy	3	Severe	Lung, skin
7	41	NHL	Sibling	CSA-MMF + PT-Cy	3	Severe	Skin
8	33	HL	APLO	CSA-MMF + PT-Cy	4	Moderate	Skin, oral cavity
9	53	MPN	MUD 8/8	CSA-MMF + PT-Cy	3	Severe	Skin

Results: At belumosudil initiation, six patients remained on corticosteroids, one on ruxolitinib, four on cyclosporine, and two on mycophenolate mofetil. Median treatment duration was 14 months (range, 4–22).

One patient discontinued therapy after 4 months due to disease progression and subsequently underwent lung transplantation; the remaining eight continued treatment.

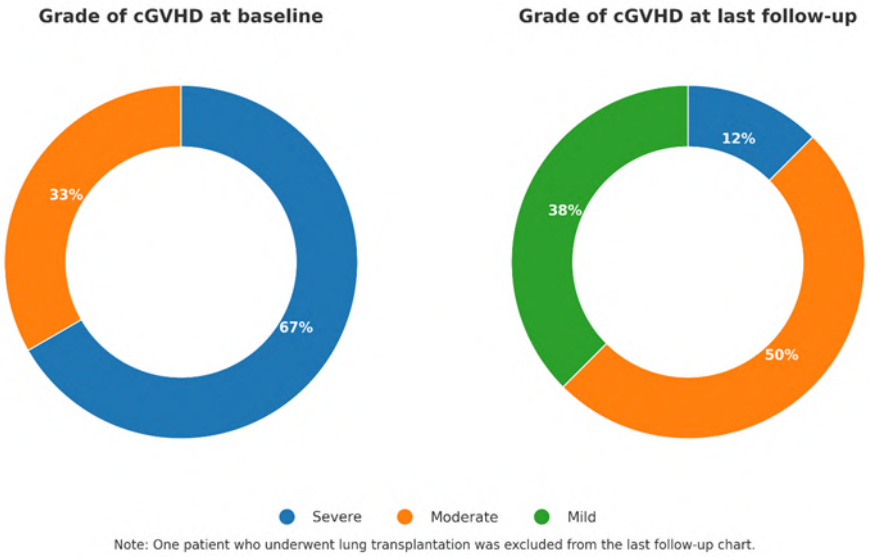
Among these eight patients, **six** reached the 12-month treatment evaluation: **five** achieved a **partial response** (three improved from severe to mild cGVHD; two maintained moderate cGVHD but were able to discontinue or significantly reduce concomitant immunosuppressive therapy), and **one** achieved **stable disease** (this patient had isolated pulmonary involvement, with no improvement but also no further deterioration, unlike prior treatment lines).

The remaining **two patients** were evaluated at 6 months of treatment (as they had not yet reached one year) and both achieved **partial responses**—one improving from severe to moderate cGVHD, and the other maintaining moderate disease with reduction of concomitant immunosuppression.

Among patients treated for more than one year, **two experienced a cGVHD flare** requiring reintroduction of low-dose corticosteroids, which are still ongoing; both presented with pulmonary reactivation.

cGVHD outcomes in our patient cohort at last follow-up are summarized in **Figure 1**.

During combination therapy, **three infectious episodes** occurred, **two** of which were severe and required hospitalization. According to cytokine analyses, median sST2 and IL-6 values appeared to decrease during the first months of treatment in patients who experienced clinical improvement.



Conclusions: The combination of belumosudil and ECP was well tolerated, with no patients discontinuing treatment due to intolerance. In our small cohort, this regimen resulted in favorable clinical responses among heavily pretreated patients. Notably, patients with predominant pulmonary cGVHD appeared to be less responsive to therapy. Larger studies with extended follow-up are warranted to confirm the efficacy and safety of this approach and to further investigate potential correlations between cytokine dynamics and cGVHD progression.

Disclosure: Nothing to declare

B049

BELUMOSUDIL TREATMENT FOR CHRONIC GRAFT-VERSUS-HOST DISEASE: REAL-WORLD CLINICAL DATA FROM FRANCE

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Background: Corticosteroids are the first-line treatment for post-transplant chronic graft-versus-host disease (cGvHD); however, adverse effects and steroid refractoriness in ~50% of patients have driven the development of novel agents. Belumosudil, an oral, selective Rho-associated coiled-coil containing protein kinase 2 (ROCK2) inhibitor, is approved as a third-line cGvHD treatment. In France, belumosudil became accessible to patients on 13 March 2022 via a compassionate use programme, providing an opportunity to evaluate its use in clinical practice.

Methods: On 26 September 2023, a compassionate access programme with a protocol for therapeutic use and patient follow-up for belumosudil was implemented. Thereafter, 143 patients with cGvHD who received belumosudil were enrolled under this programme until 25 March 2025. The inclusion criteria were age ≥12 years, weight ≥40 kg, Karnofsky score (≥16 years) or Lansky score (<16 years) ≥60, moderate-to-severe cGvHD diagnosis per National Institutes of Health (NIH) criteria, and prior treatment with 2–5 systemic lines of therapy (LOTs). Patients received belumosudil at a dose of 200 mg daily, which was increased to 200 mg twice daily if administered concurrently with a potent CYP3A inducer or proton-pump inhibitor. Organ-specific responses were assessed to evaluate efficacy.

Results: The median age of the 143 patients was 59.0 (IQR, 44.0–66.0) years, with 136 (95.1%) adults (aged ≥18 years) and 7 (4.9%) children (aged 12–18 years). Forty-nine (34.3%) patients were female and 94 (65.7%) were male. Of 143 patients, 34 (23.8%) had moderate cGvHD and 109 (76.2%) had severe cGvHD. The median number of prior LOTs was 3.0 (IQR, 2.0–4.0). Nine (6.3%) patients had not received ruxolitinib or systemic corticosteroids in prior LOTs. Sixteen (11.2%) patients received treatment concomitantly with a potent CYP3A inducer, and 83 (58%) received treatment concurrently with a proton-pump inhibitor. Fifty-one (35.7%) patients had confirmed belumosudil administration, evidenced by at least one follow-up or treatment discontinuation form.
Organ-specific response data were available for 38 of these 51 patients at 3 months. Responses were observed in patients with inflammatory and fibrotic cGvHD manifestations, including prototypic fibrotic changes in the lungs. At 3 months, among 34.3% of patients showing lung manifestations, 5.3% experienced symptom disappearance and 7.9% showed improvement; among 21% showing gastrointestinal symptoms, 7.9% experienced symptom disappearance and 7.9% showed improvement; among 15.8% showing musculoskeletal involvement, 7.9% showed improvement; among 76.4% showing skin manifestations, 7.9% experienced symptom disappearance and 39.5% showed improvement; and among 39.5% showing oral cavity manifestations, 5.3% experienced symptom disappearance and 18.4% showed improvement. These results were sustained at 9 and 12 months. However, considering the low number of sheets collected and discontinuation sheets received at these timepoints, interpretation of efficacy results and quality of life could not be performed. No new adverse event was reported beyond those previously published for belumosudil.

Conclusions: Organ-specific responses were observed across organs in all dose groups, including organs with the most fibrotic changes. This analysis confirmed the safety profile of belumosudil, agreeing with previously published data. As of July 2025, 281 patients have been recruited, and the overall analysis might reveal better efficacy outcomes with belumosudil.

Disclosure: **David Michonneau** has received research grants from CSL Behring, Novartis and Sanofi. He has also received consulting fees from CSL Behring, Incyte, Jazz Pharmaceuticals, Novartis, Sanofi and Therakos. **Florent Malard** has received honoraria from AstraZeneca, Bristol Myers Squibb (BMS), Jazz Pharmaceuticals, Merck Sharp & Dohme, Novartis, Priothera, Sanofi and Therakos. **Michael Loschi** has received consultancy fees from Novartis. He has received honoraria from Alexion, BMS Celgene, Gilead, GlaxoSmithKline, Novartis, Pfizer, Sanofi, Sobi and Takeda. He has received research funding from Janssen Pharmaceuticals. **Anne Huynh** has participated in advisory boards and/or congress activities and has received support from Jazz Pharmaceuticals, Novartis, Pierre Fabre and Sanofi. **Leonardo Magro** has received honoraria from Gilead, Jazz Pharmaceuticals, Novartis, Sanofi and Therakos. **Maud D'Aveni** has nothing to disclose. **Nicolas Vallet** has received grants or contracts from Sanofi. **Darko Kiprijanovski** and **Chaimae Ighidi** are employees of Sanofi and hold stocks or stock options in the company.

B050

MORTALITY BY ORGAN-SPECIFIC FIBROTIC MANIFESTATIONS IN PATIENTS WITH CHRONIC GRAFT-VERSUS-HOST DISEASE IN THE UNITED STATES

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Background: Fibrotic manifestations of cGVHD can affect multiple organs including lung, skin, gastrointestinal tract, and joint/fascia, leading to significant morbidity and mortality; however, the real-world impact of organ-specific fibrotic manifestations on mortality has not been well characterized. This study evaluated the impact of organ-specific fibrosis on all-cause mortality.

Methods: Patient electronic medical records de-identified in a HIPAA-compliant manner from a multisite academic medical center in the US were analyzed to identify adults (aged ≥18 years) with first allogenic hematopoietic stem cell transplantation (aHSCT) and cGVHD diagnosis between 1 January 2015 and 31 May 2024. A large language model (LLM) with tailored prompts was leveraged to identify lung, skin, gastrointestinal (GI), and joint/fascia fibrosis from unstructured patient notes using predefined fibrosis-suggestive and -specific terms developed with clinical expert input. Fibrosis presence was assessed from 90 days before through the day of their first identified cGVHD diagnosis in the health care system (baseline) and post-cGVHD diagnosis (follow-up). Landmark analyses at 1-year post-cGVHD diagnosis evaluated the impact of fibrosis on all-cause mortality. Differences in overall survival were assessed by Cox hazard regression and the log-rank test.

Results: Of 925 patients meeting inclusion criteria, median age at diagnosis was 60 years, 91% were White, 57% male, with acute myeloid leukemia (34%) and myelodysplastic syndrome (23%) being most common pre transplant diagnoses. Mean follow-up was 33.1 months. 1/2 Internal Overall, 49% of patients had evidence of selected fibrosis at some point in their medical record with fibrosis of skin being the most common (31%) followed by fibrosis of lung (17%), joint and fascia (16%) and GI (5%). Of 674 patients alive and contributing data at 1-year landmark timepoint, 259 patients had evidence of fibrosis. Patients with fibrosis at one-year landmark had more severe cGVHD at baseline (30% vs 19%) and were prescribed more systematic treatments compared to patients with no fibrosis including ruxolitinb and ECP. Whilst median survival was not reached for landmark cohort, survival at 36 month was lower for those with lung fibrosis compared to those without fibrosis at landmark (77.6% vs 89.7%, p-value 0.039) corresponding to a hazard ratio of 1.72 (95% CI 1.02-2.90).

Conclusions: This real-world evidence study demonstrates that fibrotic manifestations in cGVHD are prevalent. Those developing lung fibrosis had lower overall survival compared to patients without. These findings support the need for early identification and intervention.

Disclosure: Funding: This study was funded by Sanofi.
Disclosures Kevin Hall: Consultant: CSL-Behring, Sanofi. Honorarium for presentation: Sanofi Lauren Rota, Kathy Marshall, Shaum Kabadi, Alyshah Abdul Sultan, Nataly Bleibdrey, Robert Schwenk: Employees of Sanofi and may hold shares and/or stock options in the company. Mithun Manoharan and Allison Smither: Employee of nference.

B051

SAFETY AND TOLERABILITY OF A CANNABIS-BASED OIL EXTRACT IN MULTIPLE MYELOMA PATIENTS UNDERGOING AUTOLOGOUS STEM CELL TRANSPLANTATION – A PHASE I STUDY

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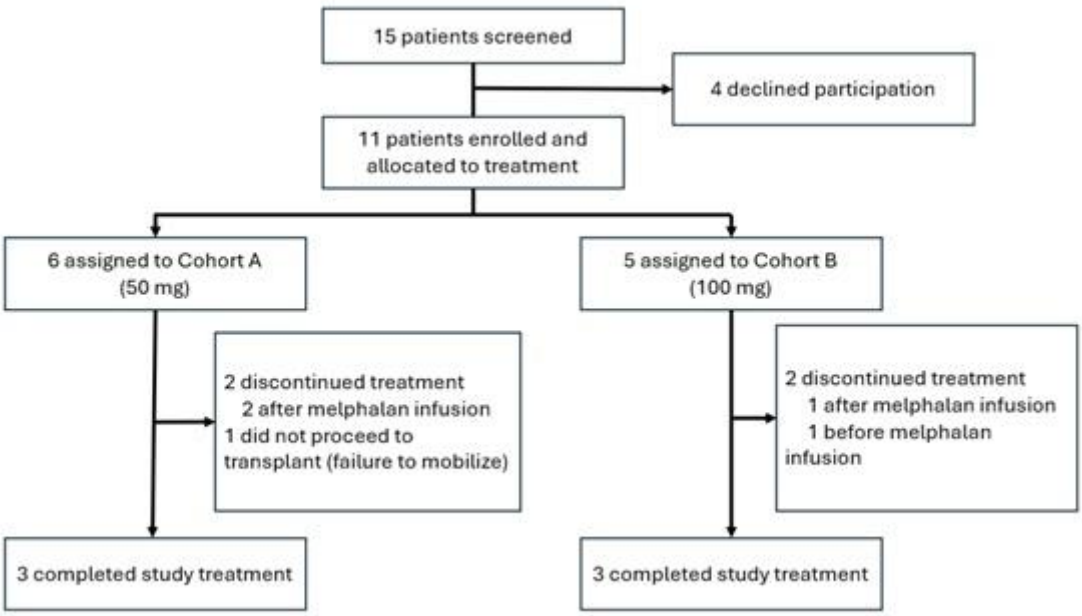
Background: Patients submitted to autologous stem cell transplantation face a heavy burden of symptoms such as nausea, mucositis and pain. Cannabidiol-based (CBD) products may alleviate such symptoms. However, CBD safety in the setting of high-dose chemotherapy is not well established. Objective: to assess the safety of a cannabis-based oil in patients undergoing aHSCT with high-dose melphalan (HDM) for multiple myeloma and plasma cell dyscrasias.

Methods: We planned a classical 3+3 dose-finding study with escalating doses of a CBD-rich extract (160 mg/mL; CBD 96 mg/mL; THC 2.4 mg/mL; GreenCare Pharma®), followed by an expansion cohort of 15 patients at the maximum tolerated dose (MTD). Patients received

50 mg, 100 mg, 200 mg or 300 mg in cohorts A, B, C and D, respectively. Patients with prior severe psychiatric disorders or using clobazam or valproate were considered ineligible. The extract was administered from 7 days prior to graft infusion to 15 days after hospital discharge. Predefined dose-limiting toxicities (DLTs) included elevation of hepatic enzymes and severe psychiatric toxicities (unwanted psychotropic effects, hallucinations, delusions, psychosis, major depressive episodes or mania/hypomania).

Results: From June 2024 to May 2025, fifteen patients were screened, 11 were recruited and 10 patients undergoing aHSCT received at least one dose of CBD and were included in the analysis. Participants median age was 63 years [range 42-67], 3/10 were female and 9/10 received 200 mg/m² of melphalan, while one participant received 140 mg/m². Median exposure to the study drug was 35 days [range 7–43]. No DLTs were observed among the 11 participants. Engraftment occurred after a median of 11 days [range 11–14] from graft infusion in all transplanted patients. Severe nausea attributed to extract occurred in 1 patient prior to HDM, leading to withdrawal from the protocol. After HDM, 8 of 9 evaluable patients reported severe nausea attributed to extract, and 3 of them discontinu
ed therapy. Therefore, severe nausea was 8.89 times more likely after HDM (95% CI 1.36–57.8). Among transplanted patients, 6 experienced a documented infection during aHSCT, and all had grade 3 febrile neutropenia. No patient required ICU admission, and all participants were alive after 224 days of follow-up [range 173-224].



Conclusions: Most patients either complained of nausea or discontinued therapy shortly after HDM. This transplant period is characterized by a high incidence of dysgeusia, chemotherapy-induced nausea and vomiting and oral mucositis, which may have contributed to poor tolerability of the oil-based CBD formulation. Difficulties in maintaining patients on-protocol, together with budgetary constraints, led investigators to terminate the study early. Considering aHSCT outcomes, there were no concerns regarding safety, rates of engraftment

and infection/febrile neutropenia were within the expected range.
In the present study, CBD-rich oil was not associated with DLTs but was poorly tolerated, particularly in the post-HDM period, due to nausea and taste intolerance. Future research in this setting should consider alternative CBD formulations, such as capsules or transdermal patches.

Clinical Trial Registry: NA

Disclosure: The present study was partially funded by Green Care Pharma.

B052

PROPHYLACTIC TOCILIZUMAB FOR THE PREVENTION OF ACUTE GRAFT-VERSUS-HOST DISEASE IN MATERNAL HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION: A PROSPECTIVE SINGLE-ARM STUDY

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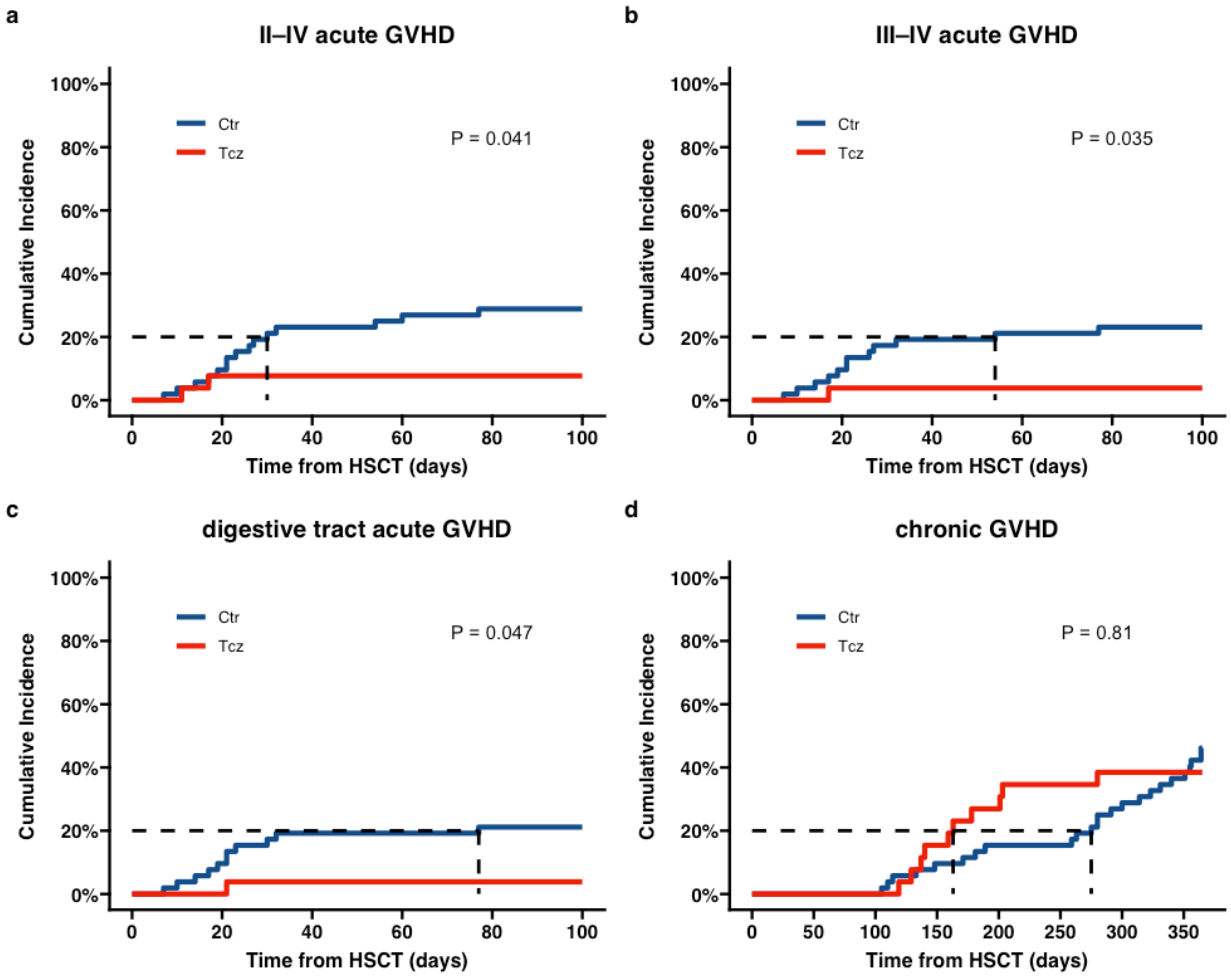
Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is increasingly performed worldwide, and maternal donors represent an important alternative donor source, particularly in regions with limited availability of HLA-matched donors. However, maternal donors are associated with a higher risk of acute graft-versus-host disease (aGVHD), potentially related to heightened alloimmune priming and early inflammatory activation. Tocilizumab (TCZ), an IL-6 receptor antagonist, has shown efficacy in steroid-refractory aGVHD and in prophylaxis after HLA-matched transplantation. However, its role as upfront prophylaxis in maternal haploidentical transplantation remains unclear. We therefore conducted a prospective study to assess the safety, efficacy, and immunologic impact of prophylactic TCZ in maternal haplo-HSCT.

Methods: From March 2021 to April 2024, 26 patients who received haplo-SCT from maternal donors in the Bone Marrow Transplantation Center of the First Affiliated Hospital of Zhejiang University School of Medicine were enrolled in tocilizumab prevention trial. All patients received a myeloablative BUCY-based conditioning regimen. Anti-thymocyte globulin Fresenius (ATG-F 10mg/kg) or anti-thymocyte globulin-Genzyme (ATG-G 6mg/kg) was applied. One intravenous dose of TCZ (8 mg/kg) was given the day before stem cell transfusion along with standard GVHD prophylaxis (cyclosporin plus short-term methotrexate and mycophenolate mofetil). Outcomes were compared with a matched historical control cohort receiving identical conditioning and prophylactic regimens except for TCZ. The trial was registered at Clinicaltrials.gov (NCT04688021).

Results: Twenty-six patients received prophylactic TCZ and were compared with 54 matched historical controls with balanced baseline characteristics. The median onset of aGVHD was 17 days (range, 12–30) in the TCZ group and 21 days (range, 14–38) in controls. By day 100

post-transplant, the cumulative incidence of grade II–IV and grade III–IV aGVHD was significantly reduced in the TCZ group compared with controls (7.7% vs 28.8% and 3.9% vs 23.1%, respectively; P = 0.041 and P = 0.035; Figure 1). Organ-specific analysis further demonstrated a marked reduction in GI aGVHD (3.8% vs 21.2%; P = 0.047), whereas no significant differences were observed in skin or liver involvement.After a median follow-up of 27 months, 1-year overall survival and relapse-free survival were 88.5% and 73.1%, respectively, while transplant-related mortality and relapse incidence were 11.5% and 15.4%. Transplant-related deaths were attributable to cGVHD (n = 1) and sepsis (n = 2), with no excess mortality observed in the TCZ group.Median neutrophil recovery occurred at 16 days in the TCZ group versus 14 days in controls, whereas platelet recovery was comparable. The cumulative incidence of cGVHD did not differ between groups. Rates of severe infections were consistent with historical experience, and no infusion-related adverse events attributable to TCZ were observed.Early cytokine profiling showed a transient elevation of serum IL-6 after transplantation, consistent with pharmacodynamic receptor blockade. Immune monitoring demonstrated early $CD8^+$ T-cell expansion with delayed $CD4^+$ T-cell recovery, resulting in a temporary reduction in the $CD4^+/CD8^+$ ratio that normalized by day 180.



Conclusions: In conclusion, prophylactic tocilizumab is safe, biologically rational, and clinically promising for reducing aGVHD after maternal haploidentical HSCT. Larger multicenter randomized trials are warranted to validate these findings.

Clinical Trial
Registry: NCT04688021;https://register.clinicaltrials.gov/prs/beta/studies/S000AHXY00000045/recordSummary

Disclosure: The authors declare no competing financial or non-financial interests related to this work. This study was supported by the National Natural Science Foundation of China (Grant No. 81500114).

B053

ABATACEPT FOR GVHD PROPHYLAXIS IN PEDIATRIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE FROM SAUDI ARABIA

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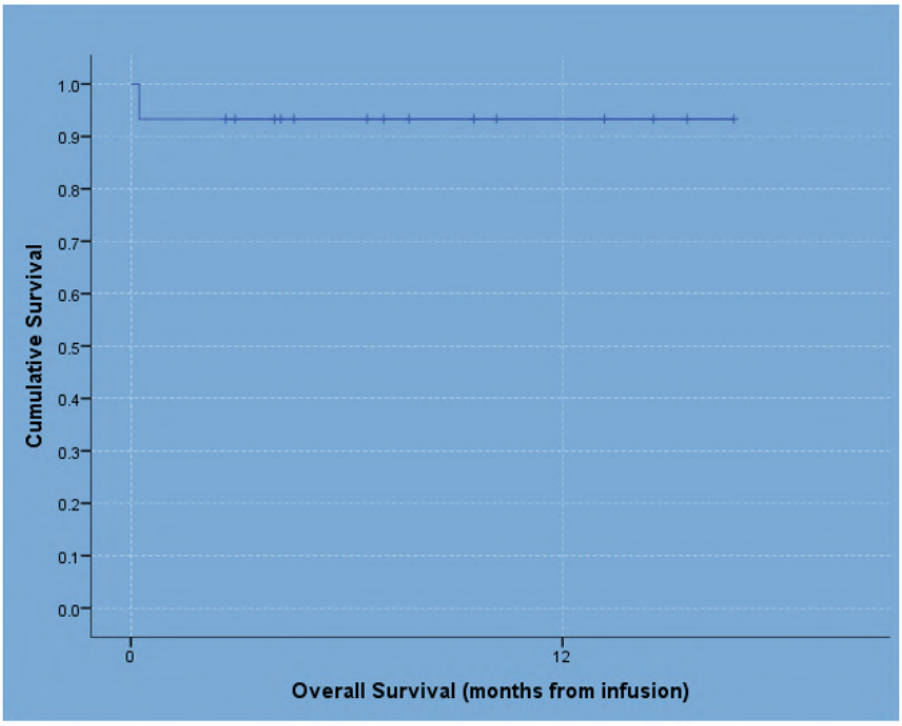
Background: Graft-versus-host disease (GVHD) remains a major complication of allogeneic hematopoietic stem cell transplantation (HCT), particularly in the setting of HLA disparity. It continues to pose a significant clinical challenge and contributes to transplant related mortality despite over five decades of advancements in GVHD prophylaxis. In 2021, the FDA approved abatacept (Orencia) in combination with calcineurin inhibitors (CNIs) and methotrexate (MTX) for acute GVHD prophylaxis in adults and children ≥2 years undergoing matched or 1 allele-mismatched unrelated donor HCT. While its efficacy and safety have been demonstrated in multicenter trials, data in pediatric populations, especially from the Middle East, remain limited.

Methods: We retrospectively analysed 15 consecutive pediatric patient (less than 14 years) who underwent allogeneic HCT between 2024–2025 and received abatacept-based GVHD prophylaxis. Median age at infusion was 2.8 years (range 0.3–12.3); 12 (80%) were males. Fourteen patients (93.3%) had non-malignant disorders. Stem cell sources included bone marrow in 13 (86.7%) and peripheral blood in 2 (13.3%). Donors were matched related in 8 (53.3%), mismatched related in 5 (33.3%), and haploidentical in 2 (13.3%). Myeloablative conditioning was used in 14 (93.3%) patients. Median CD34+ cell dose was 7.1 × 10^8/kg of body weight.

Results: Fourteen patients (93.3%) achieved complete hematopoietic recovery, with median time neutrophil and platelet engraftment of 14 days (range 12–19) and 22 days (range 14–42) respectively. Among 12 evaluable patients at day +120, acute GVHD (only skin) occurred in 2 (16.7%; Grade II and III), while chronic GVHD (moderate-sk in) was observed in 2 (16.7%) and was not preceded by acute GVHD. Transplant-related toxicities included hypertension (50%) and isolated cases (8.3% each) of seizure, SOS/VOD, interstitial pneumonia, hemorrhagic cystitis, encephalopathy, and mucositis. Infectious complications occurred in 10 (83.3%) patients: 8 (66.7%) bacterial, 5 (41.7%) viral and 4 (33.3%) fungal. CMV reactivation was documented in 4 (33.3%). At a median follow-up of 7.0 months (95% CI: 4.9–9.2), overall survival was 93.3% ± 6.4%. One patient (6.7%) died early post-transplant (day+10); this child had severe combined immunodeficiency with a history of recurrent bacteremia and PICU admissions prior to HCT. All surviving patients maintained

engraftment and demonstrated stable immune reconstitution at last follow up.



Conclusions: In this single-center pediatric cohort, abatacept-based prophylaxis was associated with low rates of acute and chronic GVHD compared to historical cohorts using ATG based -regimen. It showed favorable survival outcomes, despite frequent infectious complications. These findings support the safety and efficacy of abatacept in pediatric HCT, though larger studies with longer follow-up are warranted to confirm its role in diverse transplant settings.

Disclosure: Nothing to declare

B054

PET-CT AND CHRONIC GVHD: A DIAGNOSTIC TOOL AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION ? A PROSPECTIVE INTERVENTIONAL STUDY WITHIN CHU CAEN NORMANDY, FRANCE

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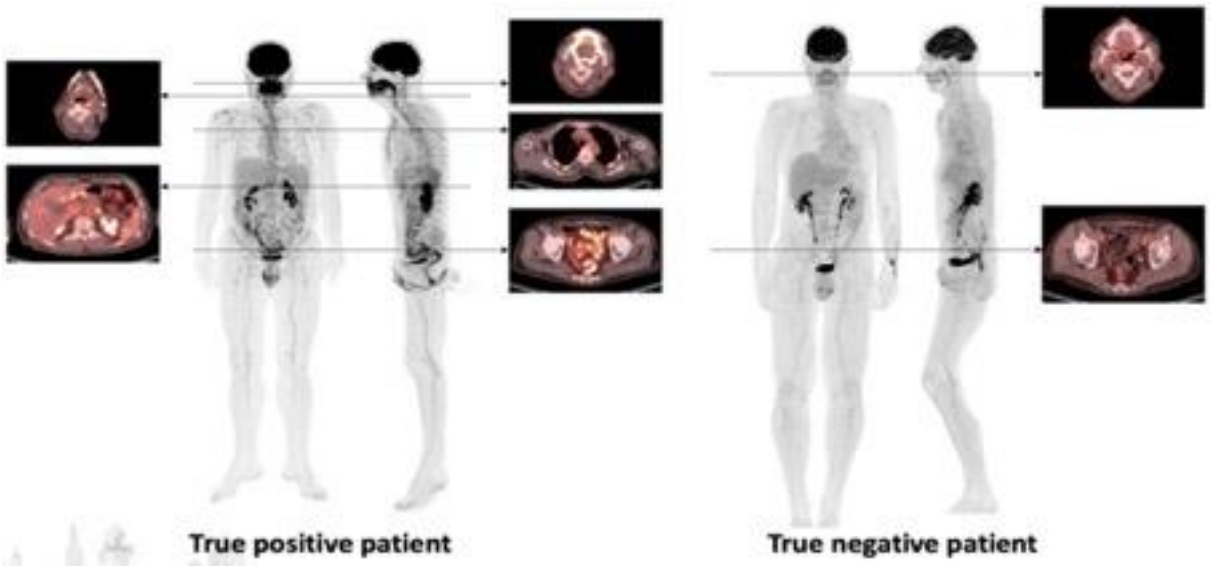
Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a curative treatment for numerous malignant and benign hematologic diseases, but its benefit is often offset by graft-versus-host disease (GVHD), the leading cause of non-relapse morbidity and mortality. Chronic GVHD (cGVHD) develops in 30–70% of patients. Diagnosis is primarily clinical and must be confirmed by histology, which remains the gold standard despite its invasiveness. FDG PET-CT has shown potential value in acute GVHD due to its non-invasive nature, but its role in chronic GVHD remains unclear. This study aimed to assess the diagnostic accuracy of FDG PET-CT for cGVHD after immunosuppressive withdrawal.

Methods: In this prospective study conducted at the Institut d'Hématologie de Basse-Normandie, 42 patients transplanted between 2015 and 2019 were screened. Thirty-five patients ultimately underwent FDG PET-CT for diagnostic evaluation; seven were excluded due to consent withdrawal, disease progression, loss to follow-up, death, refusal, or non-interpretable imaging. FDG PET-CT was completed approximately one month after discontinuation of immunosuppressive therapy. PET results were blinded to clinicians and used for research purposes only. Patients were monitored monthly for 6 months, and cGVHD was assessed using the 2014 NIH criteria. PET findings were compared with clinical diagnosis and histological confirmation when available.

Results: The median age was 56 years. Conditioning regimens were myeloablative (14.3%), reduced-intensity (71,4%), and sequential (14,3%). Graft sources included peripheral blood stem cells (88,6%), bone marrow (8.6%), and cord blood (2.8%). GVHD prophylaxis varied according to conditioning regimen. FDG PET/CT was performed at a median of 161 days post-transplant. Among the 35 patients, 27 (77%) developed cGVHD. FDG PET/CT was positive in 15 patients (43%). Diagnostic performance showed a sensitivity of 44,4% ($CI_{95\%}$[0,28 ; 0,62]), specificity of 62,5%($CI_{95\%}$[0,31 ; 0,86]), positive predictive value of 80%, and negative predictive value of 25%. From this data, the likehood ratios (LR) calculated are 1,19 ($CI_{95\%}$[0,44 ; 3,19]) for the positive one (LR+) and 0,89 ($CI_{95\%}$[0,47 ; 1,68]) for the negative one (LR-).

Conclusions: FDG PET-CT demonstrated limited diagnostic accuracy for chronic GVHD after immunosuppressive withdrawal. Given its low sensitivity and limited predictive value, FDG PET-CT does not appear suitable for routine evaluation of suspected chronic GVHD in this setting. Alternative non-invasive biomarkers or imaging strategies should be explored.



Disclosure: Nothing to declare.

B055

REAL-WORLD EFFICACY AND TOXICITY PROFILE OF RUXOLITINIB IN PEDIATRIC ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE: A MULTICENTER RETROSPECTIVE STUDY

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Background: Ruxolitinib has been the first drug approved for acute and chronic GvHD in patients≥12 years with inadequate response to corticosteroids or other systemic therapies. The pediatric population affected by GvHD is highly heterogeneous, thus real-world studies are essential to identify potential predictors of response and toxicity in this setting.

Methods: We retrospectively analyzed 51 pediatric patients (0-18 years) treated with ruxolitinib for GvHD between 2016 and 2024 in 3 Italian centres (acute n=29; chronic n=17; overlap n=1; acute and chronic n=3; overlap and chronic n=1). GvHD was steroid-resistant in 51%, steroid-dependent in 38%, and steroid-naïve in 11% of cases. Kaplan–Meier and cumulative incidence analyses were used to evaluate time to treatment failure.

Results:

In acute GvHD the overall response (OR) and complete response (CR) rates were 78% and 50%, respectively. Multi-organ involvement was associated with a significantly lower response to ruxolitinib compared to isolated skin aGvHD (OR 59% vs 100%, p=0.007).

In chronic/overlap GvHD the OR and CR rates were 78% and 26%, respectively. OR was significantly associated with the number of prior immunosuppressive lines, being higher in patients who had received two or fewer lines before ruxolitinib (p = 0.03). Ruxolitinib enabled steroid tapering in 75% of patients with both acute and chronic/overlap GVHD, with complete steroid discontinuation—without the need for additional immunosuppressive therapy—achieved in 38% and 58% of cases, respectively.

Patients with aGvHD grade III–IV had the highest and earliest failure incidence (p 0.005), in particular they experienced a 60 days- and 90 days-CIF of 46.9% and 74.7% respectively, concerning ruxolitinib discontinuation for non-response or initiation of additional immunosuppression. When including ruxolitinib discontinuation due to toxicity as a failure event, failure-free survival was significantly lower in aGvHD grade III–IV (9% at 6 months, p < 0.005), with children aged 6–12 years being the most affected (p = 0.019).

No significant differences in overall response rates were observed across age groups; however, patients aged 6–12 years showed a lower complete response rate compared to those aged ≥12 years with aGvHD (p 0.02).

Response rates were comparable between patients starting ruxolitinib at reduced age-adjusted doses and those receiving standard doses, while toxicity was slightly higher in the latter group (43% vs 33%). All steroid-naive patients (n=6) responded to Ruxolitinib.

Ruxolitinib was discontinued due to toxicity in 20/51 patients (39%). The most common toxicity was hematologic. 30/51 patients (59%) had infections requiring specific therapy during Ruxolitinib treatment, while 16/51 patients (31%) had viral reactivations.

Conclusions: Our study supports the efficacy of ruxolitinib in pediatric patients with both acute and overlap/chronic GvHD, including children <12 years. Lower complete response rates observed in children aged 6–12 years with aGvHD warrant further investigation. The comparable response observed even in patients receiving lower-than-age-recommended starting doses suggests that a dose-escalation strategy may help mitigate toxicity without compromising efficacy. The higher failure-free survival in patients with lower grade aGvHD suggests an early-stage ruxolitinib initiation.

Disclosure: Nothing to declare.

B056

"EFFECT OF REDUCING THE DOSES OF CYCLOPHOSPHAMIDE ON OUTCOMES AND ON IMMUNE RECOVERY"

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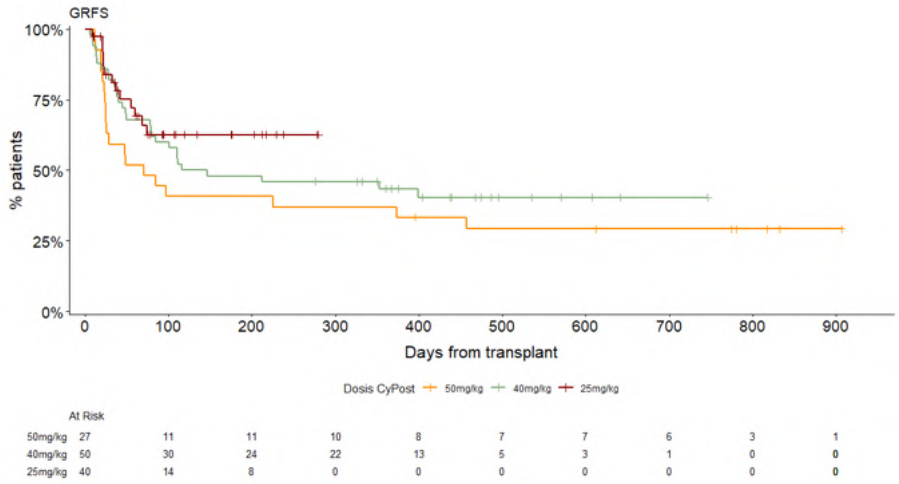
Background: Post-transplant cyclophosphamide (PTCy) 50 mg/kg on days +3 and +4 has become one of the standard graft-versus-host disease (GvHD) prophylaxis after allogeneic stem cell transplantation. Although effective, it may cause early toxicity. Reduced-dose PTCy regimens aim to preserve efficacy while minimizing adverse effects.

Methods: Single-center retrospective study of adult patients, consecutively undergoing allogeneic hematopoietic stem cell transplantation (HSCT) between May2023 and Sept2025. Patients received PTCy according to one of three regimens: a) 50 mg/kg on days +3 and +4 combined with tacrolimus or sirolimus and mycophenolate mofetil (MMF); b) 40 mg/kg on days +3 and +4 combined with tacrolimus and MMF; or c) 25 mg/kg on days +3 and +4 combined with sirolimus and MMF. The primary endpoints included overall survival (OS), GvHD-free-survival, GVHD-free/relapse-free survival (GRFS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM), cumulative incidence and severity of acute (aGvHD) and chronic graft-versus-host disease (cGvHD). Quantification of major leukocyte subsets in blood was assessed by flow cytometry at days +100 and +180 after HSCT. Analyses were performed in *R* (R Core Team, 2021) using Kaplan–Meier and Cox models.

Results: A total of 117 patients were included (a=27, b=50 and c=40). No significant differences were observed among the groups regarding HCT-CI, underlying disease, stem cell source or infusion-related parameters. A statistically significant reduction in the incidence of haemorrhagic cystitis (33% vs 22% vs 10%; p=0.01) and sinusoidal obstruction syndrome/veno-occlusive disease (22% vs 0% vs 10%; p=0.005) was observed in patients receiving reduced-dose PTCy.
In contrast, no significant differences were found in terms of OS at day 200 [55% vs 68% vs 72% (p=0.3)], GvHD-free-survival at day 200 [55% vs 62% vs 73% (p=0.3)], GRFS at day 200 [41% vs 48% vs 63% (p=0.2)], CIR at day 200 [8% vs 15% vs 0% (p=0.16)], NRM at 100 days [41% vs 25% vs 27% (p=0.16)], aGvHD grades 2-4 at day 100 [40% vs 30% vs 47% (p=0.17)], aGvHD grades 3-4 at day 100 [39% vs 20% vs 25% (p=0.16)], overall cGvHD at day 275 [8% vs 10% vs 11% (p=0.97)] and moderate to severe cGvHD at day 275 [6% vs 8% vs 10% (p=0.95)].
Regarding immune cell reconstitution, patients who received a reduced dose of PTCy showed higher T-cell counts (129 [55–353] vs. 298 [135–489] vs. 460 [244–1099], p=0.02) at day +100 after HSCT, across all major T-cell subsets. However, by day +180 after the transplant, these differences remained significant only for CD4+ T cells (195 [100–217] vs. 263 [166–339] vs. 311 [247–459], p=0.03). These findings suggest a dose-dependent effect of PTCy on post-transplant immune reconstitution of the T-cell compartment.



Conclusions: Cyclophosphamide dose reduction appears to be safe and effective, showing no inferiority to the standard-dose regimen in terms of efficacy and safety. Moreover, lower PTCy doses were associated with reduced early post-transplant toxicity and a more favourable pattern of immune reconstitution. These results suggest that optimized, reduced-dose PTCy regimens may improve post-transplant outcomes without compromising disease control or GvHD prevention.

Disclosure: Nothing to declare.

B057

RUXOLITINIB UTILIZATION IN STEROID-REFRACTORY GVHD DURING THE PTCY ERA: A COMPARATIVE ANALYSIS WITH AN HISTORICAL ATG COHORT

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Background: Acute and chronic Graft-Versus-Host Disease (GVHD) remain major contributors to morbidity and mortality following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite the adoption of post-transplant cyclophosphamide (PTCy)–based prophylaxis, which is standard in haploidentical transplantation and more recently also in matched unrelated donor transplantation, acute GVHD (aGVHD) still occurs in approximately 30–50% of patients (pts) and chronic GVHD (cGVHD) in 30–70%.

Corticosteroids represent the standard first-line therapy; however, up to 50% of pts develop steroid-refractory (SR) disease. Since 2018, ruxolitinib has been validated as an effective second-line agent in the REACH2 and REACH3 trials. Here, we describe real-world clinical use patterns of ruxolitinib for SR-GVHD during the PTCy era in comparison with ATG-based GVHD prophylaxis.

Methods: A single-center retrospective study was performed including patients who underwent allo-HSCT between 2018 and 2024 and subsequently developed steroid-refractory acute or chronic GVHD treated with ruxolitinib. Major transplant-related outcomes were compared between patients receiving PTCy-based versus ATG-based GVHD prophylaxis.

Results: A total of 250 patients were included. Five-year overall survival (OS) from transplantation was 54.2%, with no significant difference between ATG- and PTCy-based GVHD prophylaxis (51.2% vs 55.4%, respectively; p=0.228). Five-year non-relapse mortality (NRM) was 23.7% overall and was higher in the PTCy group compared with the ATG group (36.2% vs 18.1%; p=0.02).
Acute GVHD occurred in 44.4% of patients (111/250), with 22.5% presenting with grade III–IV disease. Among patients with acute GVHD, 52.3% developed steroid-refractory disease. Ruxolitinib was administered in 69.0% of SR-aGVHD cases. Among ruxolitinib-treated patients, 55.0% had received ATG-based prophylaxis, 32.5% PTCy-based prophylaxis, and 12.5% cyclosporine plus MTX/MMF. The median duration of ruxolitinib treatment was 101 days (range 13–382). Median overall survival for ruxolitinib-treated SR-aGVHD patients was 50 months, and 100-day failure-free survival (FFS) was 86.7%.
Chronic GVHD developed in 22.8% of patients (57/250), with 80.7% classified as moderate to severe. Steroid-refractory disease occurred in 59.6% of cGVHD cases, and ruxolitinib was used in 67.6% of these patients. Among ruxolitinib-treated SR-cGVHD cases, 73.9% had received ATG-based prophylaxis, 17.4% PTCy-based prophylaxis, and 8.7% cyclosporine plus MTX. The median duration of ruxolitinib treatment was 237 days (range 16–1044). Median overall survival was not reached, and 1000-day FFS from transplantation was 85.0%.

Patients characteristics	N	%		
Total	250	100		
Male	155	62,0		
Female	95	38,0		
Diagnosis				
AML	117	46,8		
MDS	28	11,2		
ALL	27	10,8		
NHL B	10	4,0		
NHL T	12	4,8		
HL	2	0,8		
CLL	2	0,8		
MM	8	3,2		
AA	2	0,8		
LNH/LC cell dendritiche	3	1,2		
Myelofibrosis	29	11,6		
MDS/MPN	2	0,8		
Others*	8	3,2		
Donor				
MUD	119	47,6		
Related full-match	59	23,6		
UCB	1	0,4		
Haplo	71	28,4		
HSC source				
PBSC	230	92,0		
BM	19	7,6		
UBC	1	0,4		
Conditioning				
MAC	128	51,2		
RIC	122	48,8		
GVHD prophylaxis		0,0		
ATG- based	137	54,8		
PTCy-based	75	30,0		
Others (CyA+MTX/MMF)	38	15,2		
Acute GVHD			**% on GVHD cases**	
Any grade	111	44,4	100,0	
Grade III-IV	25	10,0	22,5	
SR	58	23,2	52,3	**% on SR GVHD**
SR treated with Ruxo	40	16,0	36,0	69,0
Chronic GVHD				
Any grade	57	22,8	100,0	
Moderate-Severe	46	18,4	80,7	
SR	34	13,6	59,6	
SR treated with Ruxo	23	9,2	40,4	67,6

Conclusions: In this real-world cohort, ruxolitinib demonstrated sustained efficacy in the treatment of steroid-refractory acute and chronic GVHD across different GVHD prophylaxis strategies. Although PTCy-based prophylaxis is associated with lower rates of chronic GVHD in the contemporary transplant setting, clinically relevant SR-cGVHD remains a significant unmet need. Our findings indicate that ruxolitinib retains clinical activity and durability of response in this context, supporting its role as an effective second-line therapy for SR-GVHD irrespective of the upfront prophylaxis strategy.

Disclosure: None.

B058

CLINICAL FEATURES AND OUTCOME OF CHRONIC GVHD IN PEDIATRIC PATIENTS: A MULTICENTER STUDY ON BEHALF OF THE SPANISH GROUP FOR HEMATOPOIETIC TRANSPLANTATION AND CELL THERAPY(GETH-TC)

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Background: Chronic graft-versus-host disease (cGVHD) is a major cause of morbidity and the leading cause of non-relapse mortality among long-term survivors after pediatric allogeneic hematopoietic stem cell transplantation (HSCT). However, the incidence and outcomes in children remain poorly characterized. The impact of cGVHD in pediatric patients may be greater due to longer life expectancy. This study aims to describe clinical features and outcome of pediatric patients diagnosed with cGVHD following HSCT.

Methods: Retrospective analysis of pediatric patients who underwent allogeneic HSCT between January 2018 and December 2023 in transplant units of the GETH-TC and were diagnosed with cGVHD.

Results: A total of 63 patients were included from 5 hospitals. Median age at HSCT was 9.6 years (IQR 5.2–13.1), with a median follow-up of 3.63 years (IQR 2.3–5.4). The median time from HSCT to cGVHD diagnosis was 0.54 years (IQR 0.36–0.94).Underlying disease was malignant in 74% (ALL 46%, AML 14%) and non-malignant in 26% (including inborn errors of immunity 12.7% and metabolic disorders 3.2%).
Most patients received myeloablative conditioning (87%), based on TBI for 12.8 % and chemotherapy for the rest. Serotherapy was administered to 47.6%. Peripheral blood was the predominant stem cell source (65%), followed by bone marrow (32%). Donor types included haploidentical (43%), MSD(16%), MUD(22%), and MMUD (16%). Graft manipulation (mainly αβ T-cell depletion) was performed in 24%. Prior acute GVHD occurred

in 86%.
At cGVHD onset, severity was mild in 27%, moderate in 51%, and severe in 22%, with maximum severity reaching severe in 45%. The most frequently involved organs were skin (74.6%), mucosa (39.7%), lung (36.5%), liver (34.9%), eye (33.3%), gut (23,8%), fascia (4.8%). Autoimmunity was described in 4.8% and pleural or pericardial effusion in 1.6%
Complications were reported in 35 patients (56.5%), including viral infections (37.1%) and bone-related problems (48.6%).
Treatment response:72.6% of patients required more than one line, with 8 receiving up to five lines of treatment.
Thirteen patients died. Two due to leukemia relapse and for the rest, the causes of death were: infectious complications in 5, including influenza and pneumococcal septic shock; thrombotic microangiopathy and infection; pulmonary haemorrhage; respiratory failure due to progressive pulmonary cGVHD; complications after lung transplantation; surgical complications. One patient died of causes not related to HCT.
Overall survival at 12 months post-cGVHD diagnosis was 88.7% (95%CI: 77.7–94.4), and at 24 months, 85.2% (95%CI: 73.5–92.0).
Of the 50 patients that are alive, with median follow-up of 4.64 years, 16 present active cGVHD and 22 still receive immunosuppression.

Conclusions: This series provides a valuable clinical picture of pediatric cGVHD in recently transplanted patients. Despite the high overall survival, the probability of achieving freedom from cGVHD and immunosuppression remains low and the burden of treatment and associated complications is high.
The most frequent cause of death remains infectious complications, which reminds us of the importance of optimal infectious prophylaxis for these patients, including flu and pneumococcal vaccination.
This results highlight the importance of developing transplant strategies that avoid chronic GVHD, and we believe also provide valuable information to inform families.

Disclosure: None.

B059

CHARACTERISTICS OF CLINICAL TRIALS IN GRAFT-VERSUS-HOST DISEASE: LANDSCAPE OF STUDY DRUGS AND ASSESSMENT OF OUTCOME MEASURES

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Background: Graft-versus-host disease (GvHD) has a significant impact on survival and quality of life of patients after allogeneic hematopoietic stem cell transplantation (HCST), and patients frequently do not respond to currently available treatments, calling for further advances through clinical trials.

Methods: Based on study registration records from ClinicalTrials.gov (from database inception to 2025-10-31), completed and ongoing GvHD treatment studies were evaluated with respect to general trial characteristics, eligibility criteria, treatments, and endpoints.

Results: Of the 1,063 interventional treatment studies identified by an initial database search, 382 clinical trials investigated treatments for manifest GvHD (3.4% early phase 1, 16.0% phase 1, 19.1% phase 1/2, 39.0% phase 2, 2.4% phase 2-3, 11.3% phase 3, and 2.9% phase 4 trials; 6.0% missing). The median enrollment count was 25 patients and 31.4% of trials were randomized, with significant differences ($p<0.001$) based on study phase (median number of 17, 30, and 105 patients included and randomization in 14.8%, 31.5%, and 74.4% for phases 1, 2, and 3, respectively). Overall, 43.2% of trials investigated acute GvHD and 48.2% chronic GvHD (3.1% either and 5.5% not specified), with significantly ($p=0.039$) more phase 2 trials (48.4% vs 32.7%) and significantly ($p<0.001$) longer study durations for chronic GvHD (median duration for primary outcome of 3.2 vs 2.0 years and for the overall study of 4.0 vs 2.9 years). Concerning the period of study initiation, 31.2% were started in 2006-2015 and 59.9% in 2016-2025. Studies from the later period were significantly more likely to have parallel study groups (34.5% vs 26.1%, $p=0.002$), to be shorter in overall duration (3.0 vs 4.0 years, $p<0.001$), and to recruit in multiple ($n>5$) centers (33.2% vs 16.8%, $p<0.001$). Registered studies were predominantly conducted only in the United States (48.7%) and to a lesser extent only in Europe (12.4%). Over time, there was a rise in registered trials per year (>30 trials per year in 2024 and 2025). The most frequent treatments studied were corticosteroids (n=64), followed by mesenchymal stem cells (n=52), ruxolitinib (n=31), extracorporeal photopheresis (n=26), fecal microbiota transplantation (n=17), rituximab (n=15), belumosudil and cyclosporin (n=13 each), itacitinib (n=11), axatilimab and donor regulatory T-cells (n=10 each), and ibrutinib (n=9). In terms of primary endpoints, response was most frequently assessed (56.4%), followed by safety (27.5%), dosing (12.3%), patient-reported outcomes (6.4%), a composite of either efficacy or treatment failure (5.1%), pharmacokinetics and survival (2.7% each), feasibility (1.9%), and other measures (12.6%). The relevant point in time for overall response rate assessment was earlier for acute (median: 4 weeks, Q1–Q3: 4–7.5 weeks) than for chronic GvHD (median 26 weeks, Q1–Q3: 24–52 weeks). Of all completed trials (n=228), 38.6% had been withdrawn or terminated prematurely (n=37/81 or 45.7% due to slow accrual).

Conclusions: Acute and chronic GvHD remain major areas of clinical research, with their distinct clinical courses reflected in differences in trial design and outcome measures. Recent shifts toward multicenter designs, shorter study durations, and more frequent evaluation of targeted therapies suggest evolving priorities and growing methodological maturity in GvHD trial planning.

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Hanna Knaus, Axel Schulenburg, and Margit Mitterbauer have no conflicts of interest to disclose.

B060

IMPACT OF ANTI-T-LYMPHOCYTE GLOBULIN DOSING ON GRAFT VERSUS HOST DISEASE IN MATCHED SIBLING PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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Background: Anti-T-lymphocyte globulin (ATLG) is routinely used for graft-versus-host disease (GVHD) prophylaxis in allogeneic stem cell transplantation; however, the optimal ATLG dose in matched sibling donor peripheral blood stem cell transplantation (MSD-PBSCT) remains undefined. Lower doses may result in insufficient GVHD prevention, whereas higher doses may increase immunosuppression and compromise graft-versus-leukaemia effects. We evaluated the impact of two ATLG dosing strategies on transplant outcomes, with a primary focus on GVHD-free, relapse-free survival (GRFS) and moderate-to-severe chronic GVHD (cGVHD).

Methods: We conducted a single-centre retrospective cohort study including 165 consecutive adult patients with haematological malignancies who underwent MSD-PBSCT between 2011 and 2022. Patients received either ATLG 15 mg/kg (ATLG-15, n=71) or 30 mg/kg (ATLG-30, n=94; Grafalon®). Primary endpoints were moderate-to-severe cGVHD and GRFS. Secondary endpoints included overall survival (OS), progression-free survival (PFS), non-relapse mortality (NRM), relapse incidence, acute GVHD, and engraftment. Propensity score matching (PSM) was performed to reduce baseline imbalances, and a predefined subgroup analysis was conducted in AML/MDS patients not receiving total body irradiation (TBI).

Results: At 2 years, the cumulative incidence of moderate-to-severe cGVHD was significantly lower in the ATLG-30 group compared with ATLG-15 (28% vs. 43%, p=0.045). In multivariable analysis, ATLG-30 was independently associated with improved GRFS (HR 0.47, 95% CI 0.25–0.88; p=0.02). Two-year GRFS was 36% in the ATLG-30 group versus 24% in the ATLG-15 group (p=0.10). No significant differences were observed between groups in 2-year OS (77% vs. 72%, p=0.2), PFS (65% vs. 60%, p=0.4), NRM (6% vs. 13%, p=0.11), or cumulative incidence of relapse (28% vs. 25%, p=0.64). Neutrophil (median 11 vs. 12 days, p=0.004) and platelet engraftment (median 12 vs. 15 days, p=0.0002)

occurred earlier with ATLG-15, without a survival advantage.
In the PSM cohort, ATLG-30 remained associated with superior GRFS (p=0.047) and showed a consistent trend toward reduced moderate-to-severe cGVHD (p=0.067). Among AML/MDS patients without TBI (n=108), ATLG-30 was associated with a significantly lower incidence of moderate-to-severe cGVHD (19% vs. 38%, p=0.039).

Conclusions: In MSD-PBSCT, ATLG 30 mg/kg was associated with a clinically meaningful reduction in moderate-to-severe chronic GVHD and improved GRFS, without adversely affecting relapse or non-relapse mortality. These findings support a quality-of-survival benefit of higher ATLG dosing in this setting and warrant prospective validation in multicentre studies.

Clinical Trial Registry: NA

Disclosure: NA

B061

SAFETY AND EFFICACY OF ABATACEPT IN THE MANAGEMENT OF STEROID-REFRACTORY CHRONIC GRAFT-VERSUS-HOST DISEASE. A SINGLE CENTER EXPERIENCE

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Background: Despite therapeutic advances, steroid-refractory chronic graft-versus-host disease (cGVHD) remains a major clinical challenge, particularly in patients with significant cytopenias who have limited treatment options. Abatacept, a CTLA-4–Ig fusion protein that binds CD80/CD86 on antigen-presenting cells and inhibits T-cell activation, is currently FDA-approved only for the prophylaxis of acute GVHD. Its role as salvage therapy in steroid-refractory cGVHD requires further evaluation. This study assessed the efficacy and safety of abatacept in this setting.

Methods: We conducted a retrospective analysis of consecutive patients with NIH-defined moderate or severe steroid-refractory cGVHD who received abatacept at our center between 2024–2025. Abatacept was administered at 10 mg/kg weekly for the first three doses and every four weeks thereafter. Patient characteristics, organ involvement, previous therapies, cytopenias, treatment response, steroid tapering, and adverse events were recorded.

Results: Nine patients were included (median age 44.8 years, range 20–58). Underlying diagnoses were B-ALL (n=4), AML (n=3), and NHL (n=2). Stem-cell donors were matched sibling (n=5), matched unrelated (n=3), and haploidentical (n=1). The median interval from transplant to abatacept initiation was 18.6 months (3.4–61). Prior to treatment, 3 patients had moderate and 6 had severe cGVHD. Organ involvement included skin (9/9), oral mucosa

(5/9), gastrointestinal tract (4/9), eyes (4/9), liver (1/9), and lungs (2/9). One patient had steroid- and rituximab-refractory autoimmune hemolytic anemia. Patients had received a median of 3 prior systemic lines (1–5) and all were on corticosteroids (mean dose 0.66 mg/kg). Only three had previously received ruxolitinib, discontinued due to toxicity and five were undergoing ECP.
cGVHD Responses at 1, 3, and 6 months and cytopenias evolution are summarized in Table 1.

Table 1. Response to Treatment**.**

Timepoint	Anemia ≥GIII	Neutropenia ≥GIII	Thrombocytopenia ≥GIII	≥1 Cytopenia ≥GIII	cGVHD Response	Mean PDN Dose (mg /kg)
Baseline	1/9	3/9	6/9	7/9	-	0.66
1 month (n=9)	1/9	1/9	6/9	7/9	5/9 PR 4/9 SD	0.38
3 months (n=6)	1/6	1/6	2/6	2/6	2/6 CR 2/6 PR 2/6 SD	0.22
6 months (n=6)	0/6	0/6	0/6	0/6	2/6 CR 2/6 PD after PR 2/6 PR after SD	0.12

PDN: Prednisolone, CR: Complete Response, PR: Partial Response, SD: Stable Disease, PD: Progressive Disease

During six-month follow-up, six lower respiratory tract infections occurred, alongside other infectious episodes (Clostridium difficile colitis, febrile neutropenia, bacteremia). Mean hospitalization duration was 9 days (0–20). Abatacept was discontinued in one patient due to recurrent grade 3 infections. Two patients died within two months: one because of relapsed B-ALL (MRD-positive pre-transplant) and one because of septic shock in the context of poor performance status and recurrent infections prior to abatacept inanition.
Among the five patients with longer follow-up (median 10 months, range 9–16), none remains on abatacept: four switched to ruxolitinib (three due to progression, one as treatment continuation), while one patient in sustained CR is off any therapy. One patient with Richter's transformation relapsed.

Conclusions: Abatacept appears to be a safe and effective therapeutic option for steroid-refractory cGVHD. Moreover, abatacept seems to enable meaningful steroid sparing. In patients with severe cytopenias who cannot tolerate other established therapies, abatacept may serve as a viable alternative or bridging therapy until hematologic recovery.

Disclosure: Nothing to declare.

B064

OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION FOR MYELOFIBROSIS WITH PERI-TRANSPLANT-RUXOLITINIB PROPHYLAXIS

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Background: While the innovation of the JAK-inhibitor ruxolitinib has expanded the treatment possibilities for myelofibrosis (MF), allogeneic stem cell transplantation (alloHCT) still represents the only curative treatment. Relapse after alloHCT is frequent and complications like graft-versus-host disease (GvHD), transplant-related toxicity and infections remain serious concerns.

Methods: We retrospectively analyzed data from 68 adults with MF (Table 1) after first alloHCT between 04/2008 and 04/2025. Peri-transplant-ruxolitinib prophylaxis was added 08/2023 and administered 2x5mg/d from d-7 to d-2 and from d+4 to d+21 before dose reduction to 1x5mg/d and discontinuation on d+28. Statistical analyses were performed with R (Version 4.3.2). Primary endpoint was GvHD-relapse-free survival (GRFS). Secondary endpoints were overall survival (OS) and disease-free survival (DFS).

Results: Peri-transplant-ruxolitinib prophylaxis was added in 20.6%. Median follow-up time after alloHCT was 23.3 months (range 0.2-182.6). Patients receiving peri-transplant-ruxolitinib displayed a tendency towards longer GRFS (2-year GRFS with ruxolitinib: 51.0%, 2-year GRFS without ruxolitinib: 18.5% (n.s.)), OS (2-year OS 92.9% vs. 63.0% (n.s.)) and DFS (2-year DFS 79.6% vs. 57.4% (n.s.)) (Figure 1). In multivariate cox regression analysis including patient-, disease- and treatment-specific characteristics, peri-transplant-ruxolitinib and a higher transplant conditioning intensity (TCI) positively and significantly impacted GRFS (addition of peri-transplant-ruxolitinib: HR 0.276, p=0.017, TCI intermediate vs. low: HR 0.375, p=0.0155), while year of alloHCT, age at alloHCT and hematopoietic cell transplantation-specific comorbidity index (HCT-CI) showed no significant impact.
Driver mutations at primary diagnosis were present in: *CALR* n=11 (16.2%), *JAK2* n=30 (44.1%) and *MPL* n=7 (10.3%). Pre-alloHCT treatments included ruxolitinib (73.5%), hydroxyurea (42.6%) and supportive therapies (17.6%, e.g erythropoietin, anagrelide and phlebotomy). All patients received peripheral blood stem cell grafts, mostly from 10/10 matched unrelated donors (MUD, 67.7%) (Table 1) after conditioning with fludarabine, thiotepa and melphalan (FTM, 44.1%), fludarabine, carmustin and melphalan (FBM, 30.9%) or thiotepa, fludarabine and treosulfan (TFTreo, 25.0%). GvHD prophylaxis consisted of a backbone of cyclosporine A (CsA) + mycophenolate (MPA) in 85.3% or everolimus + MPA in 14.7% of patients and was combined with serotherapy (anti-T-lymphocyte globulin (ATLG) or alemtuzumab) in 80.9% of cases.
Prevalence of GvHD requiring systemic treatment (acute GvHD (aGvHD) or chronic GvHD

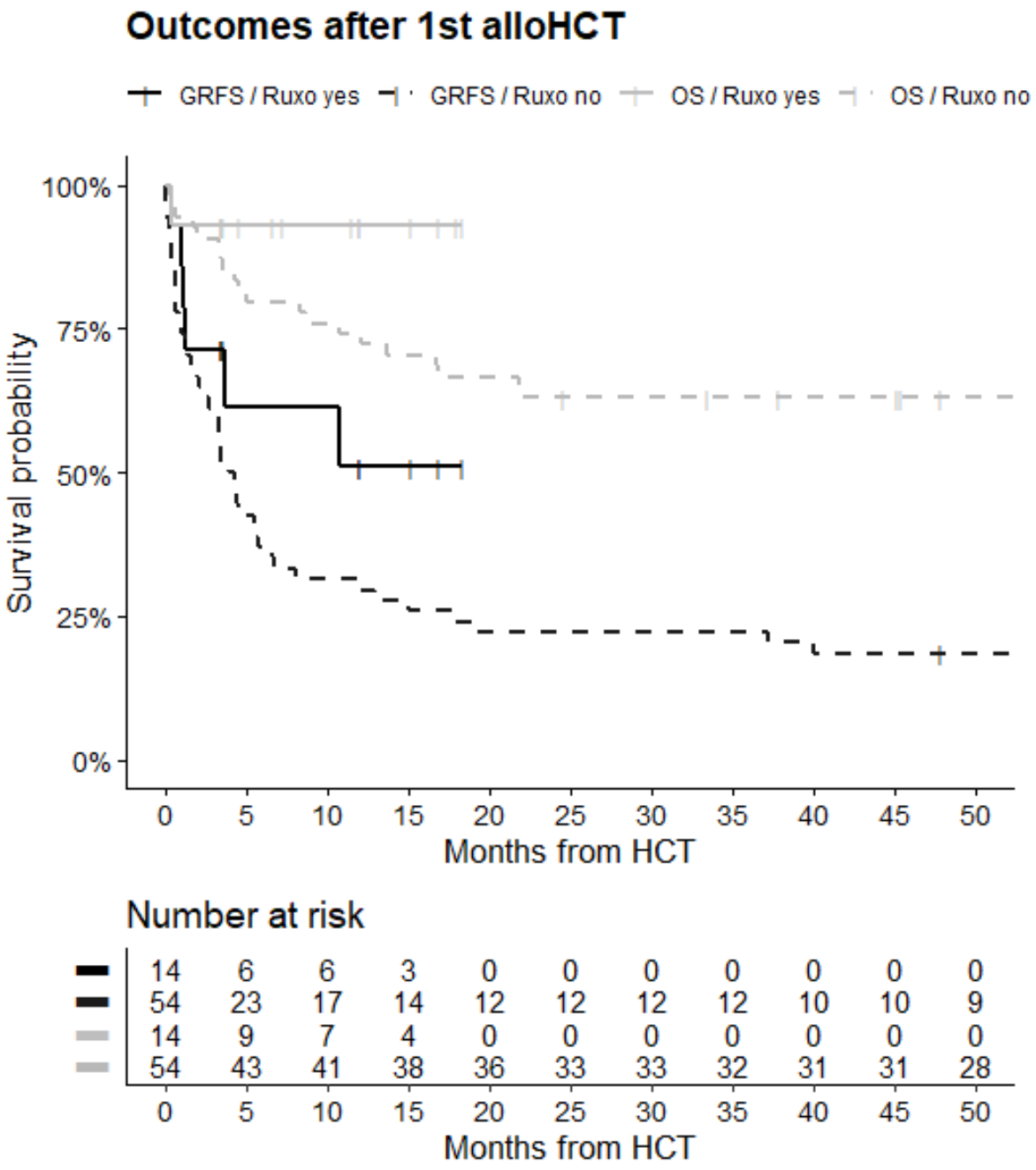
(cGvHD)) was 50.0% in the entire cohort (with ruxolitinib: 28.6%, without ruxolitinib: 55.6%) and distributed equally between aGvHD (overall: 36.8%, with ruxolitinib: 28.6%, without ruxolitinib: 35.2%) and cGvHD (overall: 32.4%, with ruxolitinib: 7.1%, without ruxolitinib: 38.9%). Ruxolitinib as treatment for steroid refractory GvHD was administered in 50% of those cases.
After alloHCT 77.9% of patients achieved complete remission (CR). At last follow-up 26 (38.2%) patients were deceased. Death prior to d+30 post alloHCT occurred in 7 (10.3%) patients (with ruxolitinib: n=1 (7.1%), without ruxolitinib: n=6 (11.1%)) and 15 (22.1%) patients died within the first year (with ruxolitinib: n=1 (7.1%), without ruxolitinib: n=14 (25.9%)). Leading causes of death were primary disease (30.8%), GvHD (30.8%) and infections (23.1%), followed by graft failure (7.7%), and toxicity (7.6%).

Table 1: Patient, alloHCT and treatment characteristics of 68 patients.

Age at HCT in years (median, range)	62 (18-76)
Sex	
female, n (%)	25 (36.8%)
male, n (%)	43 (63.2 %)
Time from diagnosis to alloHCT (months), median (range)	31.5 (0.3-383.5)
HCT-CI at alloHCT, median (range)	3 (0-7)
Disease	
Primary Myelofibrosis, n (%)	37 (54.4%)
Secondary Myelofibrosis, n (%)	31 (45.6%)
Donor match	
MRD, n (%)	12 (17.6%)
MUD, n (%)	46 (67.6%)
MMRD, n (%)	2 (2.9%)
MMUD, n (%)	8 (11.8%)
TCI Score	
low, n (%)	21 (30.9%)
intermediate, n (%)	47 (69.1%)

Table 1: Patient, alloHCT and treatment characteristics of 68 patients.

Abbreviations: HCT, hematopoietic stem cell transplantation; HCT-CI, Hematopoietic Cell Transplantation-specific Comorbidity Index; PV, polycythemia vera; ET, essential thrombocytosis; MRD, matched related donor; MUD, matched unrelated donor; MMRD, mismatched related donor; MMUD, mismatched unrelated donor; TCI, transplant conditioning intensity.



Conclusions: While MF patients are at risk for early death due to GvHD, relapse and infections after alloHCT, the addition of peri-transplant-ruxolitinib prophylaxis represents a promising strategy to optimize outcomes in this group.

Clinical Trial Registry: Not applicable.

Disclosure: The authors declare no conflicts of interest.

B065

IMPACT OF PULMONARY FUNCTION TESTING ON BRONCHIOLITIS OBLITERANS SYNDOME AND OUTCOME AFTER HEMATOPOIETIC STEM CELL TRANSPLANT

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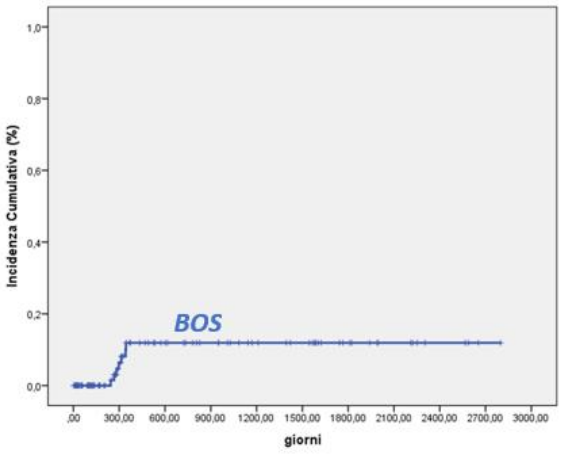
Background: Bronchiolitis obliterans syndrome (BOS) is a progressive small airway disease that can develop after hematopoietic stem cell transplantation (HSCT), often with poor therapeutic response and progression to respiratory failure. Diagnosis relies on pulmonary function test (PFT). We investigated the role of PFT as a prognostic marker in BOS and graft-versus-host disease (GvHD) after HSCT.

Methods: We performed a retrospective study of patients undergoing allogeneic HSCT from January 2018 to May 2025 at the Cardinale G. Panico Hospital (Tricase, Italy). Inclusion required baseline pre-transplant spirometry and informed consent. We used modified criteria from the 2005 NIH consensus definitions for BOS. Mid-expiratory flow at 75% of forced vital capacity (MEF75), 50% (MEF50), 25% (MEF25), and the mid-expiratory flow range between 75% and 25% (MEF75–25) ≤60% predicted were evaluated as additional markers of small airway obstruction and as potential predictors of BOS. Statistical analyses were conducted using Statistical Package for the Social Sciences, version 20.0 (SPSS 20.0). Associations with BOS, acute GvHD and chronic GvHD were examined through univariate testing, with significant variables entered into multivariate logistic regression. Odds ratios were calculated and significance was set at $\alpha = 0.05$. Time-to-event outcomes were analyzed using Kaplan–Meier estimates.

Results: The baseline characteristics of patients are shown in Table 1. Among 105 included patients (median age 56 years), 60% had a past or current smoking history, and 6% had pre-transplant chronic obstructive pulmonary disease (COPD). Acute leukemia was the most common indication for HSCT. Overall, 69% of patients received a matched unrelated donor transplant. BOS was diagnosed in 7 (7%) patients, at a median of 297 days (243-344) after HSCT, during a median follow-up of 492 days (391-1937) from the time of HSCT. All patients with BOS had evidence of chronic GVHD at another site. Univariate analysis showed that patients' clinical features, hematologic disease, smoking history, and pre-transplant COPD diagnosis were not significantly associated with BOS. Transplant-related variables likewise showed no significant impact on BOS onset (Table 1). The median Forced Expiratory Volume in 1 second (FEV1) was 98% of the predicted value (75–112) in patients with BOS and 103% (49–153) in those without BOS, with no statistically significant difference. Pre–alloHSCT PFTs showed no significant differences in median FEV_1, Tiffeneau index, MEF75, MEF50, or MEF75–25 between patients who developed BOS and those who did not (Table 1). MEF25 ≤ 60% was present in 86% of BOS cases compared to 47% of non-BOS patients, indicating a

significant association (p = 0,05, table 1). We analyzed the role of pre-transplant PFTs in the development of acute and chronic GvHD. MEF75 ≤ 60% was observed in 19% and 3% of patients with and without acute GvHD, respectively (p = 0.004). None of the examined pre-transplant PFT values showed a statistically significant correlation with the onset of chronic GvHD.



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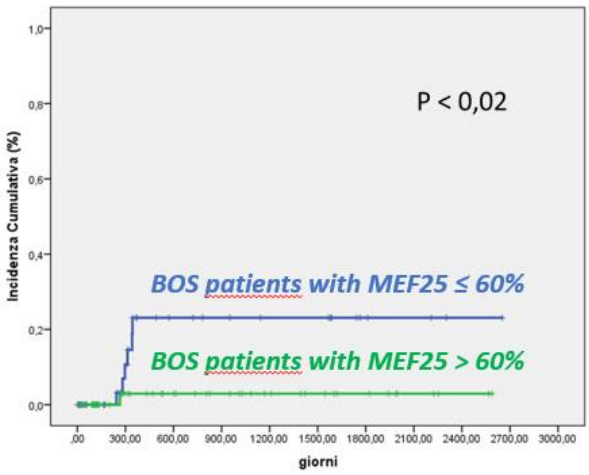

1B

	Total (n = 105)	With BOS (n = 7, 7%)	Without BOS (n = 98, 93%)	P value
Male patients, n (%)	64 (61)	2 (29)	62 (63)	0,75
Age (yr), median (range) 1. > 65 yr, n (%)	56 (17-71) 17 (16)	55 (20-61) 0	56 (17-71) 17 (17)	0,67
Smoking, n (%) 1. Current, n (%)	56 (60) 14 (15)	4 (57) 0	52 (60) 14 (16)	0,89
Pre-HSCT COPD, n (%)	6 (6)	0	6 (6)	0,493
Acute leukemia, n (%) Lymphoma, n (%) Others, n (%)	61 (58) 22 (21) 22 (21)	5 (71) 0 2 (29)	56 (57) 22 (22) 20 (20)	0,366
Complete remission at HSCT, n (%)	65 (62)	6 (86)	59 (60)	0,14

Matched-unrelated donor, n (%)	72 (69)	2 (29)	70 (71)	0,45
Myeloablative Conditioning regimen, n (%)	63 (60)	4 (57)	59 (60)	0,176
Antithymocyte globulin prophylaxis, n (%)	64 (61)	5 (71)	59 (60)	0,56
FEV_1 (%), median (range) ≤ 80 %, n (%)	103 (49-153) 9 (9)	98 (75-112) 1 (14)	103 (49-153) 8 (8)	0,59
FEV_1/FVC (Tiffeneau index), median (range) ≤ 70 %, n (%)	80 (58-96) 5 (5)	82 (75-89) 0	80 (58-95) 5 (5)	0,53
MEF75 (%), median (range) ≤ 60 %, n (%)	100 (37-149) 6 (6)	108 (91-125) 0	99 (37-145) 6 (6)	0,43
MEF50 (%), median (range) ≤ 60 %, n (%)	85 (28-174) 14 (14)	89 (64-98) 0	85 (28-174) 14 (15)	0,27
MEF25 (%), median (range) ≤ 60 %, n (%)	61 (12-203) 51 (50)	52 (48-103) 6 (86)	63 (12-203) 45 (47)	0,05
MEF75-25 (%), median (range) ≤ 60 %, n (%)	78 (21-168) 20 (20)	74 (60-95) 1 (14)	81 (21-168) 19 (20)	0,71

Conclusions: We identified novel pre-transplant PFT abnormalities associated with the development of BOS and acute GvHD. These findings may help identify a high-risk population and guide preventive or early therapeutic interventions.

Disclosure: Nothing to declare.

B066

LOW-DOSE WEEKLY CIDOFOVIR AS AN EFFECTIVE PROPHYLACTIC ALTERNATIVE TO LETERMOVIR FOR PRE-ENGRAFTMENT CMV IN ALLOGENEIC HSCT

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Background: Letermovir has redefined cytomegalovirus (CMV) prophylaxis in hematopoietic stem cell transplantation (HSCT) but remains inaccessible in many resource-limited regions. For high-risk patients in the pre-engraftment phase, the myelosuppressive toxicity of

ganciclovir limits its prophylactic use, creating an urgent need for effective, available alternatives. This study performs a head-to-head comparative analysis of low-dose weekly cidofovir as a prophylactic strategy against the benchmark efficacy and safety profile of letermovir.

Methods: In a setting where letermovir is unavailable, we prospectively evaluated weekly low-dose cidofovir (2.5 mg/kg, initiated Day +3, or Day +6 with PTCy) as pre-engraftment CMV prophylaxis in high-risk allogeneic HSCT recipients (R+/D-, haploidentical with PTCy, prior CMV infection). Monitoring included twice-weekly CMV PCR. Outcomes were compared to published letermovir data, focusing on breakthrough reactivation rates, need for secondary therapy, engraftment kinetics, nephrotoxicity, and survival.

Results: Among 32 high-risk patients receiving cidofovir prophylaxis, the breakthrough CMV reactivation rate was 31% (10/32), comparable to the 35-40% range reported with letermovir. Of these 10, 70% (7/10) were controlled by escalating cidofovir to a treatment dose (5 mg/kg/week), avoiding alternative antivirals. One patient (3.1%) required escalation to ganciclovir for disease. Notably, no significant nephrotoxicity or adverse impact on median time to neutrophil (Day +14) or platelet engraftment was observed, mirroring letermovir's favorable myelosuppression profile. There was no attributable mortality.

Conclusions: In a direct efficacy comparison, low-dose weekly cidofovir demonstrates breakthrough rates and a safety profile akin to letermovir for pre-engraftment CMV prophylaxis. For geographical regions where letermovir is unavailable or cost-prohibitive, this protocol provides a highly effective, practical, and cost-conscious prophylactic alternative, potentially mitigating early CMV-related graft compromise without the myelosuppressive risks of ganciclovir. It warrants consideration as a strategic option in global transplant practice.

Disclosure: Nothing to declare.

B067

DESCRIPTION OF CHRONIC GRAFT VERSUS HOST DISEASE USING AN INNOVATIVE ARTIFICIAL INTELLIGENCE NATURAL LANGUAGE PROCESSING ON ELECTRONIC MEDICAL RECORDS FROM 8 CENTERS IN FRANCE

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Background: Chronic Graft Versus Host Disease (cGVHD) is the most frequent and serious complication after allogenic hematopoietic stem-cell transplantation (allo-HSCT). In Europe, there is no agreed-upon standard of care or preferred therapeutic agents for patients who failed second line of systemic therapy (LOT). Therapeutic management beyond the first LOT remains poorly described. Conventional real-world data collection through manual chart review is time-consuming and costly, while some treatments are not captured in claims data. Thus, we used another approach.
We developed an innovative artificial intelligence natural language processing (AI-NLP) approach to identify and analyze cGVHD cases directly from electronic medical records (EMRs).

Methods: The AI-NLP scanned all EMRs of patients who received an allo-HSCT in 8 French centers, identifying those with cGVHD and at least 1 year of follow-up after cGVHD onset. Relevant information was extracted to structure, derive and infer the variables.
To ensure NLP derived data completeness and accuracy, a 3-step quality control process was performed: review by clinical research associate, comparison with the French Branch of the European Bone Marrow Transplant (EBMT) registry, validation by investigator experts.

Results: Among 513 screened allo-HSCT patients' EMRs, 235 patients developed a cGVHD, and 41 had at least 3 LOTs.
Of these 41 patients, 63.4% were men, mean age at allo-HSCT was 48.3 years, main reason for allo-HSCT was acute myeloid leukaemia (29.3%), myelodysplastic syndrome (19.5%). Median delay from allo-HSCT to cGVHD was 346.6 days. Seventeen patients (77.3%) had severe cGVHD.
The most frequently affected organs were skin (92.7%), gastrointestinal tract (43.9%), lungs (43.9%), liver (43.9%), mouth (39%), eyes (36.6%).
Treatments in LOT 1 were corticosteroids alone for 17 patients (41.5%). Other treatments alone or in association were ciclosporin for 15 patients (36.6%), ruxolitinib for 10 patients (24.4%), and other drugs for 4 patients (9.8%).
Treatments in LOT 2 (alone or in association) were ruxolitinib for 18 patients (43.9%), tacrolimus for 14 patients (34.1%), ciclosporin for 13 patients (31.7%), and other drugs for 5 patients (12.2%).
Treatments in LOT 3 (alone or in association) were ruxolitinib for 28 patients (68.3%), tacrolimus for 14 patients (34.1%), ciclosporin for 14 patients (34.1%), belumosudil for 8 patients (19.5%), and other drugs for 5 patients (12.2%).
At LOT 3:

- Overall response was available for 15 patients; 5 (33.3%) achieved complete response, 7 (46.7%) partial response.
- Mean time to response (time from the LOT initiation to the first documented cGVHD overall partial or complete response) was 191.7 days (11 patients).
- Mean failure free survival (time from the LOT initiation to the date of initiation of a new cGVHD treatment, recurrence/relapse of the underlying disease or death, whichever comes first) was 319.9 days (14 patients).

Conclusions: This is a first insight into the real-world management of cGVHD in France, using AI-NLP to generate a comprehensive, robust and accurate structured dataset, issued from information in electronic medical records of transplanted patients, with minimal burden on the medical teams in the participating centers. These initial analyses describe the therapeutic management and response of patients with cGVHD beyond second-line treatment.

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Sandrine Colas, Darko Kiprijanovski, Noémie Allali are Sanofi employees and may hold shares/stocks in the company.
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B068

EFFECTIVENESS AND SAFETY OF BELUMOSUDIL FOR CUTANEOUS CHRONIC GRAFT-VERSUS-HOST DISEASE: A RETROSPECTIVE STUDY FROM CHINA

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Background: cGVHD (chronic graft-versus-host disease) is a major cause of morbidity and mortality after allo-HCT. Cutaneous cGVHD is present in upto 80% of patients with cGVHD and clinical presentations vary widely. Belumosudil (BEL), an oral selective Rho-associated coiled-coil–containing protein kinase 2 (ROCK2) inhibitor, was approved as a second-line treatment for steroid-refractory in August 2023 in China. It has been reported with 37% skin-specific ORR in the ROCKstar trial and 40% in Chinese phase II study. The current study aims to assess the efficacy and safety of BEL in cutaneous cGVHD patients at our center.

Methods: In this study, we retrospectively analyzed the clinical data of 21 cutaneous cGVHD adult patients in our center from March 1, 2024 to December 1, 2025. The overall response rate (ORR) and organ-specific responses, especially skin-specific ORR, were assessed using the NIH consensus response criteria. In addition, duration of treatment, OS, recurrence, and safety were also reviewed.

Results: A total of 21 patients were included in this retrospective study, with a median age of 35 years (range, 14-63). Ethnicities included Han (12, 57.1%), Uyghur (8, 38.1%), and Kazakh (1, 4.8%). The cutaneous manifestations of cGVHD were non-sclerotic in 19 patients and sclerotic in 2. Skin presentations with an incidence rate greater than 10% included maculopapular/lichen-planus like eruptions in 14 patients (67%), pruritus in 11 (52%), erythema in 10 (48%), and hyperpigmentation in 5 (24%). At baseline, 2 (9.5%), 14 (66.7%), and 5 (23.8%) patients had mild, moderate, and severe cGVHD, respectively. Treatments comprised second-line (12, 57.1%) and third-line or later (9, 42.9%) therapies. The median duration of treatment was 6.1 months (range, 0.4-21.3), with 12 patients treated for over 6 months. The skin-specific ORR for BEL was 81.0% (17/21) with CR 42.9% (9/21) and PR 38.1% (8/21), with ORR of 83.3% (5/6) for patients with skin-only organ involvement and 73.3% (11/15) for patients with multi-organ involvement. The ORR was 76.2% (16/21) for whole group, the ORRs for second-line and third-line or later therapy subgroups were 83.3% (10/12), and 66.7% (6/9), respectively. According to the NIH Grading, ORR was 100%(2/2), 78.6%(11/14) and 60% (3/5) for mild, moderate, or severe cGVHD. The other organ-specific ORRs are mouth 66.7% (4/6), ocular 87.5% (7/8), hepatic 75%(3/4),Joint 100% (1/1), and lung 0% (1patient PD and 3 patients with stable symptoms). Dose reduction of glucocorticoids and CNIs were common, mainly after 2 weeks of BEL administration. All patients survived without relapse. No new treatment-related adverse events (AEs) or serious AEs occurred.

Characteristic	All patients (n=21)	Characteristic
Age, years, median (range)	35 (14-63)	Non-sclerotic/Sclerotic
Race(Han/Uyghur/Kazakh)	12/8/1	Lines of belumosudil therapy
Sex (Male)	14 (66.7%)	2
Indication for transplant		≥3
AML	10 (47.6%)	Previous treatments
MDS	7 (33.3%)	Systemic corticosteroids
Others	4 (19.1%)	CNI
Donor type (MSD/HID)	2/19	Ruxolitinib
Previous acute GVHD	13 (61.9%)	MTX

Chronic GVHD severity (Mild/Moderate/Severe)	2/14/5	Others(MMF/Basiliximab/MSC/Rituxim
Organs involved at enrollment		Concomitant medications
1/2/3/4	6/9/4/2	MMF
Skin	21 (100%)	Ruxolitinib
Eyes	8 (38.1%)	cGVHD-to-belumosudil interval, mont
Mouth	7 (33.3%)	Follow-up time, months, median
Liver	5 (23.8%)	Duration of belumosudil treatment, m
Lungs	3 (14.3%)	≥6months
Joints	1 (4.8%)	<6months

Conclusions: Belumosudil demonstrated clinical efficacy in patients with cutaneous cGVHD, particularly in those with skin-only involvement and lower baseline NIH severity scores. The superior response observed with second-line use compared to later-line therapies suggests a benefit of earlier intervention.

Disclosure: Nothing to declare.

B069

EARLY RUXOLITINIB USE IN MODERATE-TO-SEVERE PULMONARY CHRONIC GRAFT-VERSUS-HOST DISEASE: A CASE SERIES

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Background: Pulmonary involvement is a severe manifestation of chronic graft-versus-host disease (cGVHD) and is associated with significant morbidity and reduced quality of life after hematopoietic stem cell transplantation (HSCT). The introduction of targeted therapies, including Janus kinase inhibitors, has improved outcomes in steroid-refractory cGVHD. We

report three cases of moderate-to-severe pulmonary cGVHD successfully treated with early ruxolitinib.

Methods: Patient medical records and diagnostic images were reviewed for case descriptions.

Results:

Case 1: A 62-year-old man underwent haploidentical HSCT for acute myeloid leukemia with NPM1 and FLT3-ITD mutations. Comorbidities included type 2 diabetes mellitus and chronic kidney disease stage G2. Conditioning consisted of FluBuCy RIC with post-transplant cyclophosphamide (PTCy). A total of 7.4 × 10^6 $CD34^+$ cells/kg from peripheral blood were infused. Neutrophil and platelet engraftment occurred on days +14 and +16, respectively.

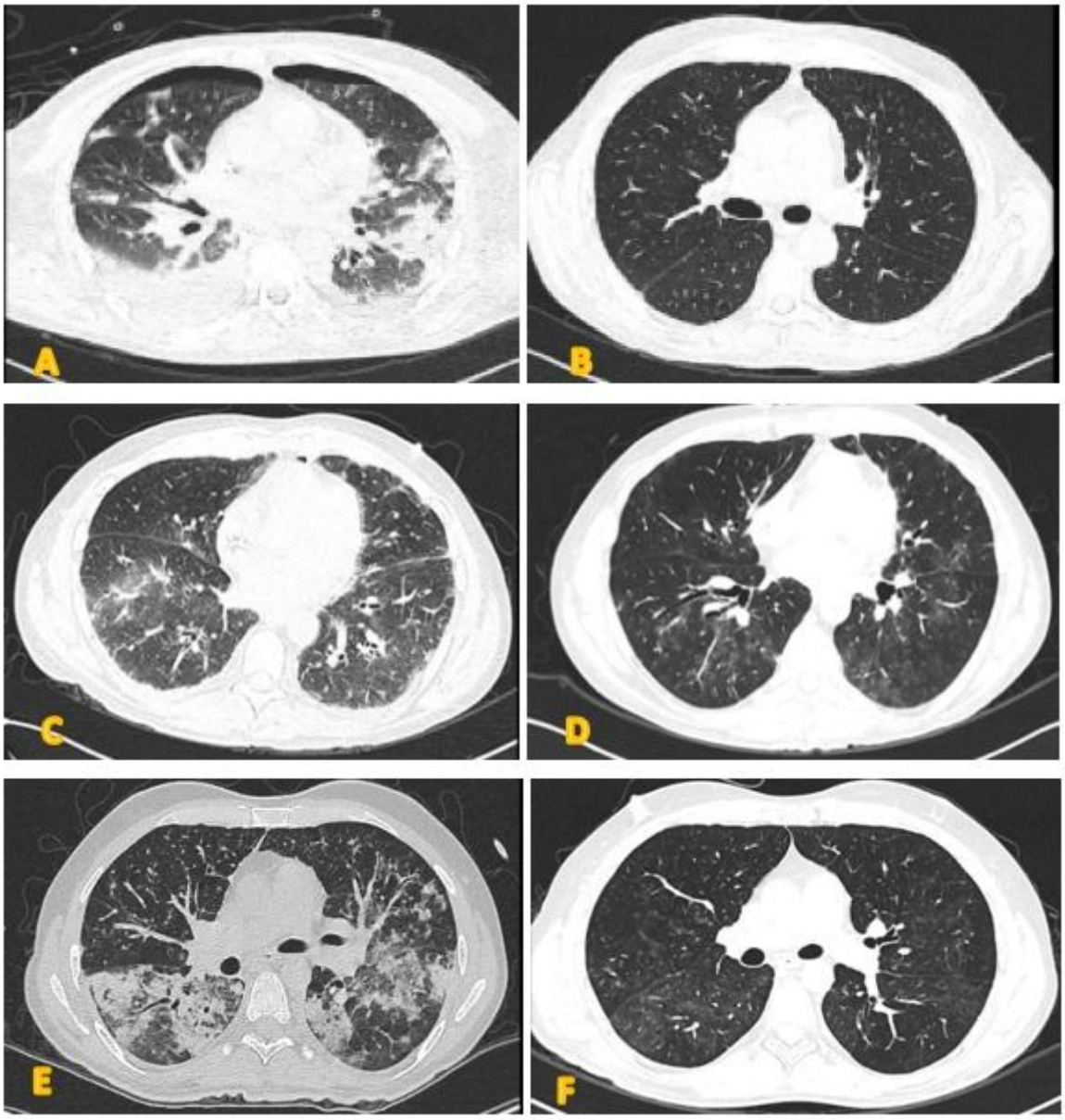
Moderate cGVHD involving skin and eyes developed on day +164 and was treated with systemic corticosteroids, without successful tapering. On day +310, the patient presented with progressive dyspnea and fatigue, evolving to respiratory failure. Chest CT revealed multilobar pneumonia. Despite broad-spectrum antibiotics, mechanical ventilation, and intravenous corticosteroids, clinical response was limited. Ruxolitinib was initiated at 5 mg twice daily, leading to rapid improvement, ventilator withdrawal within 72 hours, and hospital discharge. Follow-up CT showed radiologic resolution with spirometric improvement.

Case 2: A 59-year-old man underwent haploidentical HSCT for high-risk acute lymphoblastic leukemia with CNS involvement and persistent MRD. Comorbidities included treated latent tuberculosis and catheter-related thrombosis. Conditioning consisted of FluBuCy MAC with PTCy, followed by infusion of 7.84 × 10^6 $CD34^+$ cells/kg. Engraftment occurred on days +14 and +18.

He developed grade II cytokine release syndrome and febrile neutropenia. Acute GVHD (MAGIC II, skin stage 3) occurred on day +26, with steroid dependence. On day +137, he presented with cough and hypoxemia. CT angiography showed bilateral ground-glass opacities and interstitial thickening, without pulmonary embolism. Despite systemic steroids, FAM therapy, and antibiotics, respiratory failure progressed, requiring high-flow oxygen. Ruxolitinib 5 mg twice daily was started, resulting in marked clinical improvement within 10 days and subsequent discharge. Follow-up imaging demonstrated pulmonary recovery.

Case 3: A 32-year-old man underwent haploidentical HSCT for acute myeloid leukemia with KMT2A rearrangement. Conditioning consisted of FluBuCy MAC with PTCy, followed by infusion of 7.84 × 10^6 $CD34^+$ cells/kg. Engraftment occurred on days +13 and +15. Acute GVHD (MAGIC I, skin stage 1) developed on day +66.

On day +135, the patient presented with exertional dyspnea and nonproductive cough. Chest CT revealed an organizing pneumonia pattern. Bronchoscopy was negative for infection. Antibiotics, FAM therapy, and ruxolitinib 5 mg once daily were initiated, leading to symptomatic improvement within two weeks and radiologic response on follow-up imaging.



Patient	Time Point	FEV1/FVC (%)	FEV1 (% predicted)	FVC (% predicted)
1	Pre-HSCT	104	34	121
1	Post-HSCT	95	94	99
2	Pre-HSCT	96.9	121	120

2	Post-HSCT	100	95	93
3	Pre-HSCT	110	92.9	83.4
3	Post-HSCT	85	89	90

Conclusions: These cases illustrate the high effectiveness of early ruxolitinib initiation in pulmonary chronic GVHD, including severe presentations requiring respiratory support. Early JAK inhibition may represent a valuable therapeutic strategy in this setting.

Disclosure: The authors declare no conflicts of interest.

P123

FAECAL MICROBIAL TRANSPLANTATION FOR GRAFT-VERSUS-HOST DISEASE

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Background: Graft-versus-Host disease (GVHD) is a potentially fatal complication of bone marrow transplantation (BMT), and its frequency and severity are linked to a poorly diverse gut microbiome. Faecal Microbial transplantation (FMT) transfers diverse microbial populations from a healthy donor into recipients and therefore offers promise as a novel therapy for GVHD. We have completed a pilot clinical trial of FMT after BMT, using the Australian Red Cross Lifeblood Microbiome product in patients with GVHD at the Royal Brisbane and Women's Hospital, Australia.

Methods: 9 patients with steroid refractory (SR) or steroid dependent (SD) gastrointestinal GVHD were treated with a one-time instillation of Lifeblood faecal microbiota transplant via naso-duodenal tube. This product is manufactured from healthy donors and subject to screening for drug resistant organisms. Participants were able to receive all other standard of care treatments including Ruxolitinib. Correlative scientific analysis includes shotgun metagenomic sequencing of donor and recipient faecal microbiome, to determine the impact of donor microbial diversity on recipient outcomes, as well as unbiased metabolomic and proteomic analysis as biomarkers for response.

Results: At 7 days post FMT 2 (22.2%) patients achieved a complete response (CR) and 3 (33.3%) patients a partial response, giving an overall response rate (ORR) of 55.5%. CR rates subsequently increased to 3 (33.3%) at day 14 and 4 (44.4%) at day 28.
No aspiration events occurred. 1 patient experienced a blood stream infection after instillation of FMT with a coliform organism potentially related to the FMT product, however this patient had cultured this organism from prior episodes of sepsis.
All participants had poorer diversity of gut microbial species, reflected by Shannon Index, at

baseline when compared to donors. Achievement of CR was associated with return of gut microbial diversity to near donor levels.
Instillation of FMT was associated with upregulation of serum IL-15 and downregulation of programmed cell death protein 1 and CD-40 ligand.

Conclusions: Use of FMT in highly immunosuppressed patients with SR and SD GVHD is safe and feasible using a single donor FMT product. FMT for SR and SD gut GVHD produced sustained CR in 44.4% of patients and was associated with increases in gut microbial diversity.

Clinical Trial Registry: ACTRN12622000797774

Disclosure: Nothing to declare.

P124

GRADE YOUR GVHD YOURSELF - DEVELOPMENT OF AN APP TO DOCUMENT CHRONIC GRAFT -VERSUS-HOST DISEASE BY PATIENTS AND CAREGIVERS

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Background: The NIH consensus on chronic graft-versus-host disease (cGVHD) recommends complementary use of patient-reported outcome measures (PROMs). However, physician-based severity scoring is limited to outpatient visits, potentially delaying detection of disease onset or worsening. In contrast, patient-reported documentation allows continuous symptom monitoring, enabling earlier identification of flares and deterioration while more accurately reflecting the true symptom burden.

Methods: We developed an APP incorporating existing PROMs to capture symptoms of cGVHD to enable longitudinal monitoring of the symptom burden of patients. The APP allows symptom-documentation 24/7. Data are automatically transferred into the data base of the German-Austrian-Swiss GVHD registry. During pilot testing, patient-reported symptom burden was compared with physician-documentated cGVHD assessments and paper-based PROMs collected during outpatient visits.

Results: The pilot test (PT) of the cGVHD APP was recently completed including ten patients during routine follow-up after allogeneic stem cell transplantation (alloSCT), demonstrating general feasibility. Recruitment in the extension phase is ongoing, with 11 additional patients currently under follow-up. The APP showed sufficient content validity compared to paper-

based PROMs with no relevant symptoms being missed. Patients highlighted the need for a weekly reminder function as well as the availability of the APP results for their outpatient-clinic appointments to discuss the symptom load with their physician.
Moreover, a short cut function to report the absence of symptoms was requested. During PT, APP and paper-based PROM results from the same timeframe were compared across seven domains (skin, eyes, mouth, lung, nutrition, energy, psychological stress) using four severity grades (none-mild, mild-moderate, moderate-quite severe, quite severe-extreme). Overall, a high level of agreement was observed, with concordance in 28 of 42 assessments (67%) and a difference of only one severity grade only in the remaining 14 assessments.

Conclusions: PROM-based remote documentation of cGVHD symptom burden via the APP is feasible in routine clinical practice and has the potential to enhance patient follow-up. Initial results demonstrate a high level of agreement between APP-based PROMs and physician-based assessment, suggesting that, following appropriate validation, the APP could complement physician evaluation; however, confirmation in a larger patient cohort is still required.

Disclosure: Bernhard Holzner & Gerhard Rumpold hold IPRs on the data collection software used in the study.
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P125

TREATMENT PATTERN AND EFFECTIVENESS OF BELUMOSUDIL FOR CHRONIC GVHD: A SINGLE-CENTRE, RETROSPECTIVE STUDY IN CHINA

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Background: Belumosudil, a novel selectively ROCK2 inhibitor, targets to both the inflammatory and fibrotic processes in chronic graft-versus-host disease (cGVHD). Study KD025-213 demonstrated favorable efficacy and safety of belumosudil for steroid refractory cGVHD. However, real-world evidence of belumosudil, especially in early-line treatment settings, remains limited in China.

Methods: This retrospective study enrolled adult patients treated with belumosudil between April 2023 and November 2025, all of whom had cGVHD after receiving allogeneic stem cell transplantation (allo-HSCT). Patients were stratified by the line of belumosudil therapy (first-line, second-line, and third-or-later-line). Treatment outcomes were assessed using the NIH consensus response criteria for overall response rate (ORR), including complete remission (CR) and partial remission (PR). Changes in cGVHD symptom burden were measured using Lee Symptom Scale (LSS). Failure-free survival (FFS), and overall survival (OS) were also evaluated. Adverse events were recorded throughout the study. The data cutoff date was November 14, 2025.

Results: A total of 36 patients were included and 17 (47 %) were female. Other baseline characteristics were shown in Table 1. Nine (25%), 6 (17%) and 21 (58%) patients received belumosudil as first-line, second-line and third-or-later-line therapy, respectively. The most common indication for transplant was acute myeloid leukemia (AML) (50%) regardless of the line of therapy. Senventy-eight percent of patients had severe cGVHD at baseline. Fifty-three percent of patients had lung involvement, 42% had skin involvement and 39% had eye involvement. All the 27 pretreated patients had prior corticosteroid and 89% of them had prior ruxolitinib. Belumosudil (200mg/d) was initiated at a median of 2 months (range, 0.03-108) after cGVHD diagnosis with a treatment duration of 8±5 months and a median follow-up of 9 months (range, 1-19). Thirty-five patients received combination regimens: 69% combined with corticosteroids, 71% with ruxolitinib, and 3% with calcineurin inhibitor. The ORR for belumosudil was 72% (95%CI, 55-86), comprising a 31% CR, and a 42% PR. The ORRs for the first-line, second-line, third-or-later-line therapy subgroups were 78% (95% CI, 40 -97), 100% (95% CI, 54-100) and 62% (95% CI, 38-82). Twenty (57%) patients archived clinically meaningful symptom improvement (defined as ≥ 7 LSS score reduction from baseline). The 1-year FFS rate was 92% (95% CI, 83-100) and 1-year OS rate was 94% (95% CI, 87-100). Specifically, within the first-line and second-line therapy subgroups, both of these survival metrics were 100% (95% CI, 100-100). Treatment-emergent adverse events (TEAEs) occurred in 12 patients (33%), and the most common TEAE was pneumonia (14%). Two patients (6%) experienced grade ≥3 TEAEs: one had elevated transaminases (>5×ULN) and the other developed grade 3 pneumonia. Two patients, who received combination regimens, died from relapse of leukemia and severe bacterial infection, respectively. No drug-related deaths were reported.

Conclusions: In this retrospective study of Chinese cGVHD patients, belumosudil demonstrated favorable effectiveness and safety profile, with particularly promising clinical outcomes observed in patients receiving it as first-line and second-line therapy.

Table 1. Baseline characteristics

Variables	Total (n=36)	First-line (n=9)	Second-line (n=6)	Third-or-later-line (n=21)
Age, year, Mean±SD	44±12	48±11	50±9	40±13
History of aGVHD, n (%)	28 (78)	4 (44)	4 (67)	20 (95)
Time from cGVHD diagnosis to enrollment, months, median (range)	2 (0.03, 108)	1(0.03, 8)	2 (0.47, 3)	4 (0.23, 108)
cGVHD severity, n (%)				
Mild	1 (3)	0	1 (17)	0

Moderate	7 (19)	5 (56)	1 (17)	1 (5)
Severe	28 (78)	4 (44)	4 (66)	20 (95)
No. of organs involved, median (range)	2 (1, 6)	1 (1, 2)	2 (1, 3)	2 (1, 6)
LSS, median (range)	15 (0, 42)	10 (6, 38)	17 (8, 26)	16 (0, 42)
Combination regimens, n (%) [N=35]				
Corticosteroids	24 (69)	6 (67)	5 (83)	13 (65)
Ruxolitinib	25 (71)	3 (33)	3 (50)	19 (95)
Calcineurin Inhibitor	1 (3)	1 (11)	0	0

Disclosure: Nothing to declare.

P126

ANTI-T-LYMPHOCYTE GLOBULIN (ATLG) VS. ANTI-THYMOCYTE GLOBULIN (ATG) IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A PRELIMINARY COMPETING-RISK ANALYSIS

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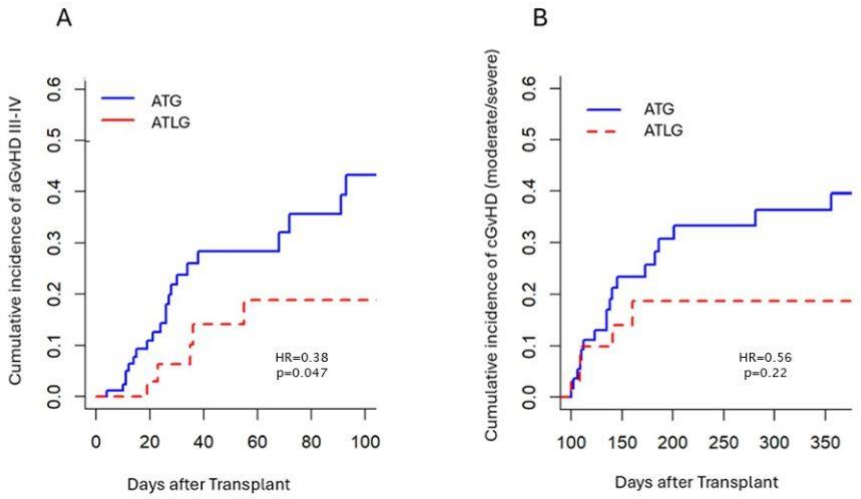
Background: Anti-T-lymphocyte globulin (ATLG, Grafalon®, formerly ATG-Fresenius S) and anti-thymocyte globulin (ATG, Thymoglobulin®, formerly ATG-Genzyme) are widely used as part of GvHD prophylaxis prior to allogeneic hematopoietic stem cell transplantation (AHSCT). However, comparative data on their impact on graft-versus-host disease (GvHD) and post-transplant outcomes remain limited. Therefore, we conducted a retrospective, real-world, single-centre analysis comparing ATLG and ATG in an AHSCT cohort.

Methods: All adult patients undergoing first allogeneic AHSCT at our centre between 2010 and 2014 who received either ATG or ATLG as part of the GvHD prophylaxis were included, regardless of indication. Group assignment was based on availability of the respective preparation. The study was approved by the institutional ethics committee and patient consent for analysis of clinical data was obtained upon registration in the EBMT database. Primary endpoints were grade III-IV acute GvHD (aGvHD; according to Glucksberg

classification) and moderate to severe chronic GvHD (cGvHD; according to NIH criteria). Secondary endpoints included overall survival (OS), GvHD-free, relapse-free survival (GFRS) and non-relapse mortality (NRM). Time-to-event analysis for GvHD and NRM were performed using a competing risk approach, with death (for GvHD) or relapse (for NRM) considered as respective competing events. For competing risk endpoints, cumulative incidences were estimated, and group comparisons were performed using Gray's test. Hazard ratios (HR) were calculated using Fine-Gray regression. For OS and GRFS, survival probabilities were estimated using Kaplan-Meier method and group comparisons were performed using the log-rank test. A p-value of < 0.05 was considered statistically significant. The statistical analysis was conducted using R, Version 4.5.2.

Results: This analysis represents preliminary data from the first evaluation period (2010-2012). A total of 190 patients was included (ATLG: n=131, ATG: n=59), with a median follow-up of 12.6 month. Patients treated with ATLG showed a significantly lower cumulative incidence of aGvHD within 100 days after AHSCT compared with those receiving ATG (HR 0.38, 95% CI [0.15; 0.99], p=0.047). In contrast, no significant difference in the cumulative incidences of cGvHD between day 100 and day 365 was observed (HR 0.56, 95% CI0.23-1.41, p=0.22). Regarding survival outcomes, OS did not differ significantly between ATLG and ATG (p=0.17). Median OS was numerically longer in the ATLG group (1002 days) compared with the ATG group (222 days). GRFS also showed a numerically longer (341 days vs. 159 days) but not statistically significant median duration with ATLG (p=0.093). NRM did not differ significantly between groups (p=0.30), with rates of 31.2% in the ATLG group and 44.2% in the ATG group.

Figure 1: Cumulative incidence of grade III-IV acute GvHD (A) and moderate to severe chronic GVHD (B) after AHSCT
GvHD prophylaxis using ATG is represented by blue solid lines and using ATLG by red dashed lines.



Conclusions: Preliminary 3-year data from this real-world cohort suggest that ATLG is associated with a significant reduction in severe acute GvHD within the first 100 days after

AHSCT compared with ATG. The final results from the entire 5-year cohort will provide a more reliable assessment not only of the GvHD incidence, but also of long-term survival.

Disclosure: JF received honoraria from Medac. All other authors declare no conflicts of interest.

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REAL-WORLD IMPACT OF RUXOLITINIB IN GRAFT-VERSUS-HOST DISEASE: EXPERIENCE FROM A NATIONAL REFERRAL CANCER CENTER IN MEXICO

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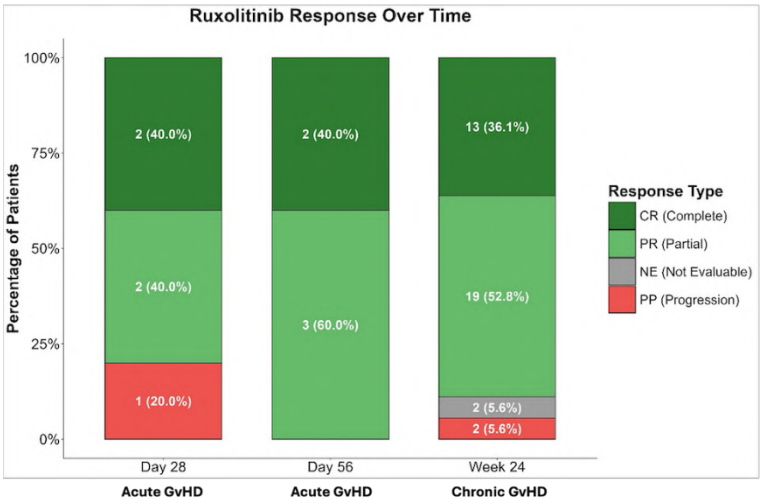
Background: Real-world evidence on the use of ruxolitinib for graft-versus-host disease is limited in Latin America, particularly within resource-limited healthcare systems such as those in Mexico.

Methods: We conducted a retrospective observational study of patients with acute and chronic graft-versus-host disease treated with ruxolitinib at the National Cancer Institute of Mexico between 2018 and 2025. Clinical and treatment data were collected from electronic medical records. Continuous variables were summarized as medians and interquartile ranges and compared using non-parametric tests, while categorical variables were compared using Chi-square or Fisher's exact test. Overall survival was estimated using the Kaplan–Meier method, and univariate logistic regression was used to explore factors associated with treatment response. A p-value <0.05 was considered statistically significant.

Results: A total of 36 patients with graft-versus-host disease treated with ruxolitinib were included. Median age at transplantation was 28 years (IQR 23–42), and most patients had acute leukemia as the underlying diagnosis. Among patients with acute GVHD, classic onset was observed in 85.7% of cases. In acute GVHD, skin was the most frequently involved organ, whereas gastrointestinal and hepatic involvement were uncommon. In chronic GVHD, the most frequently involved organs were the skin, liver, and oral mucosa, followed by ocular involvement.
In patients with acute GVHD, ruxolitinib induced rapid clinical responses, with an overall response rate of 80% at day 28 (CR 40%, PR 40%) and 100% at day 56 (CR 40%, PR 60%), with minimal progression. Overall survival in this subgroup remained favorable during follow-up.
In chronic GVHD, response assessment at week 24 demonstrated an overall response rate of 88.9%, including 36.1% CR and 52.8% PR, while progression or non-evaluable outcomes were infrequent. Long-term overall survival remained stable at approximately 80%, with

superior survival observed among patients achieving complete response compared with those with partial response.
Adverse events differed by GVHD type. In acute GVHD, toxicity was mainly infectious, whereas in chronic GVHD infections (52%) and cytopenias (40%) were the most frequent complications. No statistically significant factors associated with response were identified in univariate analyses, although concomitant calcineurin inhibitor use showed a trend toward improved response. In patients with acute GVHD, steroid discontinuation was achieved in 85.7% (6/7) of those receiving concomitant corticosteroids, and overall 83.3% (30/36) of patients were able to discontinue steroids during follow-up.

Variable	Total (N= 36)
Age, median (IQR), years	28 (23–42)
Sex, n (%) (female / male)	22 (61.1) / 14 (38.9)
Underlying diagnosis, n (%) (acute leukemia / other)	28 (77.8) / 8 (22.2)
GVHD presentation, n (%)	Chronic: 36 (100); Acute: 7 (19.4)
Organs involved in acute GVHD, n (%): skin / GI / liver	18 (85.7) / 3 (14.3) / 1 (4.8)
Organs involved in chronic GVHD, n (%): liver / skin / oral / eyes	23 (63.9) / 22 (61.1) / 22 (61.1) / 20 (55.6)
Steroid-refractory or steroid-dependent GVHD, n (%)	24 (66.7)
Steroid discontinuation, n (%)	Acute: 6/7 (85.7); Overall: 30/36 (83.3)
Concomitant calcineurin inhibitor use, n (%)	15 (41.7)



Conclusions: In this real-world experience from a national referral cancer center in Mexico, ruxolitinib was associated with high response rates, favorable survival outcomes, and an acceptable safety profile in patients with acute and chronic graft-versus-host disease. These findings provide valuable evidence from a resource-limited setting, where access to specialized treatments may be restricted. Despite healthcare system limitations, outcomes were comparable to those reported in other settings, highlighting the clinical value of ruxolitinib and supporting its use in routine clinical practice across Latin America.

Disclosure: Nothing to declare.

P128

ETANERCEPT AS SECOND-LINE THERAPY FOR STEROID-REFRACTORY GVHD: FEASIBILITY, SAFETY, AND OUTCOMES

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Background: Graft versus host disease (GVHD) remains a significant cause of morbidity and mortality following allogeneic haematopoietic stem cell transplantation (alloHSCT). As supported by the 2024 European Society for Blood and Marrow Transplantation (EBMT) consensus recommendations, ruxolitinib is now first line for steroid refractory acute GVHD (SR-aGVHD) and chronic GVHD (SR-cGVHD). There is, however, no consensus treatment for SR-aGVHD beyond ruxolitinib with numerous agents trialed globally.

Methods: This retrospective cohort study evaluated etanercept as second-line therapy for SR-aGVHD following alloHSCT at a single metropolitan transplant centre in Australia between April 2020 and October 2025. All patients received calcineurin inhibitor–based GVHD

prophylaxis in combination with either antithymocyte globulin or post-transplant cyclophosphamide.
Eligible patients had glucocorticoid- and ruxolitinib-refractory disease. Failure to respond was defined according to EBMT guidelines: disease progression within 3–5 days of initiating therapy, incomplete response by 7–14 days or recurrence following dose reduction of the preceding treatment. The study timeframe reflected the availability of ruxolitinib through compassionate access programs and the Pharmaceutical Benefits Scheme (PBS), Australia's government-subsidised prescription medication program.

Results: A total of 9 patients (age range: 21–70 years; 5 female and 4 male) received etanercept as 2nd-line therapy following ruxolitinib for SR-aGVHD. The median interval between ruxolitinib and etanercept initiation was 22 days (range: 5-97 days). 66.7% presented with MAGIC Grade IV disease, predominantly involving the lower gastrointestinal tract (77.8%). At 30 days after initiating etanercept, 42.9% with SR-aGVHD achieved a ≥50% reduction in corticosteroid dose across skin, liver, and gastrointestinal GVHD phenotypes. All patients surviving to one year weaned off corticosteroids completely. Overall survival was 77.8% at 30 days and 62.5% at 1 year. Within 100 days post-transplant, only one patient had CMV reactivation despite no letermovir prophylaxis as is standard practice in Australia. Overall, 3 of 9 (33.3%) had CMV reactivation within three months of etanercept initiation. All were CMV-seropositive recipients with cumulative immunosuppression, including pulse steroids, prior to etanercept.

Conclusions: In this small, high-risk cohort, etanercept administered as a second-line agent following ruxolitinib for steroid-refractory GVHD demonstrated feasible use with treatment-related toxicity analogous to other immunosuppressants. Its introduction occurred early in the disease course as a rescue escalation rather than as prolonged salvage, as is reflected in etanercept's administration schedule as a subcutaneous injection given over an eight-week finite course. Among patients with SR-aGVHD, a meaningful steroid-sparing effect was observed, with over one-third achieving substantial corticosteroid reduction by 30 days and all 1-year survivors ultimately discontinuing steroids. Survival outcomes were acceptable given the predominance of MAGIC Grade IV GVHD with lower gastrointestinal involvement, though interpretation remains limited by the small sample size and absence of a comparator group. These findings suggest that etanercept may offer clinical benefit for selected patients with SR-aGVHD, warranting further evaluation in larger studies. Although those who received etanercept for SR-aGVHD and SR-cGVHD following ruxolitinib were both examined, meaningful analysis for SR-cGVHD was limited by small numbers at time of write up and our study is ongoing.

Disclosure: Nothing to declare.

P130

IN VIVO T CELL DEPLETION IN COMPLETE REMISSION ACUTE LEUKEMIA PATIENTS RECEIVING PERIPHERAL STEM CELL TRANSPLANTATION FROM HLA IDENTICAL SIBLING WITH MYELOABLATIVE CONDITIONING REGIMEN

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Background: A large metanalysis showed that the incidence of extensive chronic GVHD (cGVHD) was highest using conventional graft versus host disease (GVHD) prophylaxis after allogeneic hematopoietic cell transplantation (HCT) with peripheral blood stem cell (PBSC) from HLA identical sibling (SIB). At least 3 randomized studies showed the benefit to add ATG/ATLG reducing this complications. ATG/ATLG could blunt the graft versus leukemia effect and could be an obstacle spreading it in clinical practice.

Methods: From 2010 and 2025, we retrieved in our data set acute leukemia (AL) patients with the same characteristics of randomized trial with ATLG. ATG (Thymoglobuline) was administered at total dose of 5 mg/kg days -2 and -1. All patients were conditioned with transplant conditioning intensity (TCI) regimens intermediate/high and PBSC. Patients were in complete (CR) and donors were HLAid sibling. Before 2021, patients did not receive ATG.

Results: 89 patients were identified. Main patient characteristics were depicted in Table 1. The median follow-up was 5 years.
For the whole population, the 2-y OS, PFS, cumulative incidence of relapse (CIR), and 1-year non-relapse mortality were 63%, 55%, 33% and 14%. The 6-month CI of grade 2-4 and 3-4 acute GVHD were 25% and 10%. The CI of moderate-severe chronic GVHD was 19%.
In univariate analysis, we founded a trend to better 2-y OS (66% with ATG vs 62% without ATG) and 2-y PFS (62% with ATG vs 52% without ATG), and 2-y CIR was lower with ATH (21% vs 36%). Similarly, the 1-year NRM was lower with ATG (11% vs 15%). The 6M CI of aGVHD was similar while the 1-y CI of moderate/severe cGVHD was statistically higher without ATG than with ATG (0% vs 31%, p 0.01).

Conclusions: This retrospective single center study, with confounding factors due to the retrospective nature and low number of patients, show that ATG use, in HLAid sibling setting, improves the outcomes of AL. Only the CI of moderate/severe cGVHD was significant lower in ATG cohort.

Disclosure: Nothing to declare

P131

ECP BASED COMBINATIONS FOR TREATING ACUTE AND CHRONIC GRAFT VERSUS HOST DISEASE

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Background: We present our experience using ECP in combination with ruxolitinib for steroid refractory aGvHD, and ECP in combination with belumosudil vs belumosudil alone for refractory cGvHD.

Methods: Patients treated with ruxolitinib or belumosudil were identified from pharmacy records. All other data were collected from medical records.
For aGvHD the outcomes presented are response rate and overall survival. For cGvHD accurate retrospective evaluation of response as per NIH criteria is very difficult. We therefore present two outcomes: Firstly, successful time on therapy defined as treatment duration until cGvHD progression, death, relapse of underlying disease, start of new systemic cGvHD treatment, or discontinuation due to toxicity; and secondly, the ability to successfully wean systemic corticosteroids.

Results: Twelve patients with steroid refractory / dependent aGvHD were treated with ECP in combination with ruxolitinib. Median age was 55 years. Five out of twelve patients had grade 2 aGvHD, four had grade 3 aGvHD, and three had grade 4 aGvHD. The skin was involved in nine patients, the lower GI tract in eight patients, the liver in three patients, and the upper GI tract in three patients.
Ten out of twelve patients (83%) achieved a partial or complete response, and nine patients (75%) successfully discontinued corticosteroids. Median overall survival has not yet been reached. Overall survival is 66% at 8 months median follow-up. Deaths were from aGvHD (two patients), cGvHD (one patient), and infection (one patient). Treating death as a competing risk, 33% of patients developed cGvHD. There have been no relapses of the underlying haematological disease.
The median time spent on ruxolitinib was 4.5 months, and the median time spent on ECP was 6 months. The median time until patients were on a physiological dose (5mg or less) of prednisolone was 6 weeks.
For cGvHD nine patients were treated with beluosudil, and eight with ECP plus belumosudil. Patient characteristics were balanced between the groups apart from cGvHD severity. In the belumosudil group four patients (44%) had severe cGvHD. In the ECP plus belumosudil group six (75%) had severe cGvHD. Median successful time on therapy as defined in the methods section was 4 months in the belumosudil group vs 13 months in the ECP plus belumosudil group. In the belumosudil group four patients were on systemic corticosteroids when belumosudil started and one (25%) was able to wean to a physiological dose of prednisolone. In the ECP plus belumosudil group five patients were on corticosteroids and three (60%) were able to wean to a physiological dose of prednisolone.
In the belumosudil group six patients (66%) discontinued treatment; three due to cGvHD

progression and three due to toxicity. In the ECP plus belumosudil group four patients (50%) discontinued treatment; one due to cGvHD resolution, two due to cGvHD progression, and one due to leukaemia relapse.

Conclusions: ECP combined with ruxolitinib for steroid refractory aGvHD appears to be a safe and efficacious combination. ECP combined with belumosudil to treat refractory cGvHD appears more efficacious than belumosudil alone. Further evaluation in prospective studies is warranted.

Disclosure: Sasha Ollerenshaw: Nothing to declare.
Arun Alfred: Therakos, Kyowa Kirin.
Jennifer Clay: Nothing to declare.
Anjum Khan: Novartis.
Katja Kimberger: Amgen, KITE, Autolus, Therakos.
Suzanne Liebersbach: Nothing to declare.
Francesca Padday: Nothing to declare.
Janette Sampson: Nothing to declare.
Simon Bulley: Janssen, Sanofi, Therakos, Hartley Taylor, Vertex Pharmaceuticals, McKinsey & Company, BDO Services.

P132

BELUMOSUDIL FOR REFRACTORY CHRONIC GRAFT VERSUS HOST DISEASE IN CHILDREN AND YOUNG ADULTS: REPORT OF 4 CASES

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Background: Although significant progress has been obtained in donor selection, conditioning regimens, and graft versus host disease prophylaxis in recent years, chronic graft versus host disease (cGVHD) remains a serious complication and a major factor determining quality of life after hematopoietic stem cell transplantation (HSCT). cGVHD is an immune-mediated inflammatory disorder which causes fibrosis and sclerosis. Despite the medicines we currently use, there is still a need for new drugs. Belumosudil, an oral selective inhibitor of Rho–associated coiled–coil–containing protein kinase 2 (ROCK2). It mainly inhibits Th17 cells, reduces collagen/extracellular matrix production and cytokine production. It has been approved for the treatment of adults and pediatric patients aged >12 years with cGVHD after at least two systemic therapies.

Methods: We describe four cases of cGVHD who have been receving belumosudil. The assessment of the severity of the cGVHD, and treatment response were made based on the NIH 2014 criteria. Written consent was obtained.

Results: The first three patients underwent allo-HSCT for hematological malignancies, and the last one for thalassemia major. One of our patients was 5 years old, and off-label

approval was obtained before the medication was used. After myeloablative conditioning regimens, cyclosporin (CSA) and methotrexate were used for GVHD prophylaxis. All patients had severe cGVHD and had been received at least 4 lines of immunosuppressive treatment before starting belumosudil. Additionally, they underwent extracorporeal photopheresis. Belumosudil was used at a dose of 200 mg/day. No serious adverse event were reported. The findings of the patients related to cGVHD and details regarding to belumosudil treatment are shown in Table 1.

Table 1:Patient Characteristics

Age/ gender	Donör type	GVHD organ/ Grade	Previosuly used treatments	Belumosudil start date	Currently used treatments	Treatment response
21/ F	MUD 9/10	Skin-3 Eye-3 Mouth-2 Lung-2	Steroid CNI RUXO MMF Ibrutinib	08-08-2024	Belumosudil CNI	From the first month of treatment, hyperpigmentation and sclerosis began to decrease.
17 / F	MUD 10/10	Skin-3 Joints-3 Liver-2 Lung-3	Steroid CNI RUXO MMF Ibrutinib	23-07-2025	Belumosudil RUXO	An apparent improvement in skin and joint findings has been observed.
15 / F	MUD 10/10	Skin-3 Joints-3 Eye-3 GIS-3 Mouth-2	Steroid CNI RUXO MMF	30-07-2024	Belumosudil RUXO Steroid	There was complete recovery in GIS findings. Sclerosis disappeared. Joint contractures continue.
5 / F	MSD 10/10	Skin-3	Steroid CNI RUXO MMF	08-08-2024	Belumosudil RUXO	Ulcers on the skin were healed. Hyperpigmented areas on the upper and lower extremities were decreased. The lesions on the trunk have completely healed.

F:Female, M:Male, MUD: Matched unrelated donor, MSD:Matched sibling donor, CSA: cyclosporin, MTX: methotrexate, CNI: calcineurin inhibitor, RUXO: ruxolitinib, MMF: mycophenolate mofetil, GIS: gastrointestinal system

Conclusions: In all four patients who have been using belumosudil for severe cGVHD, marked clinical improvement was seen especially in the skin, fascia and joints. Additionally, steroid treatment could be discontinued in three patients. Belumosudil may effective for pediatric patients with severe cGVHD, especially the sclerotic subtype with acceptable toxicity profile. However, prospective studies involving a larger patient population are needed on this subject.

Disclosure: The Authors declare no conflict of interest.

P134

OCULAR GRAFT VERSUS HOST DISEASE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A 10-YEAR SINGLE CENTER EXPERIENCE

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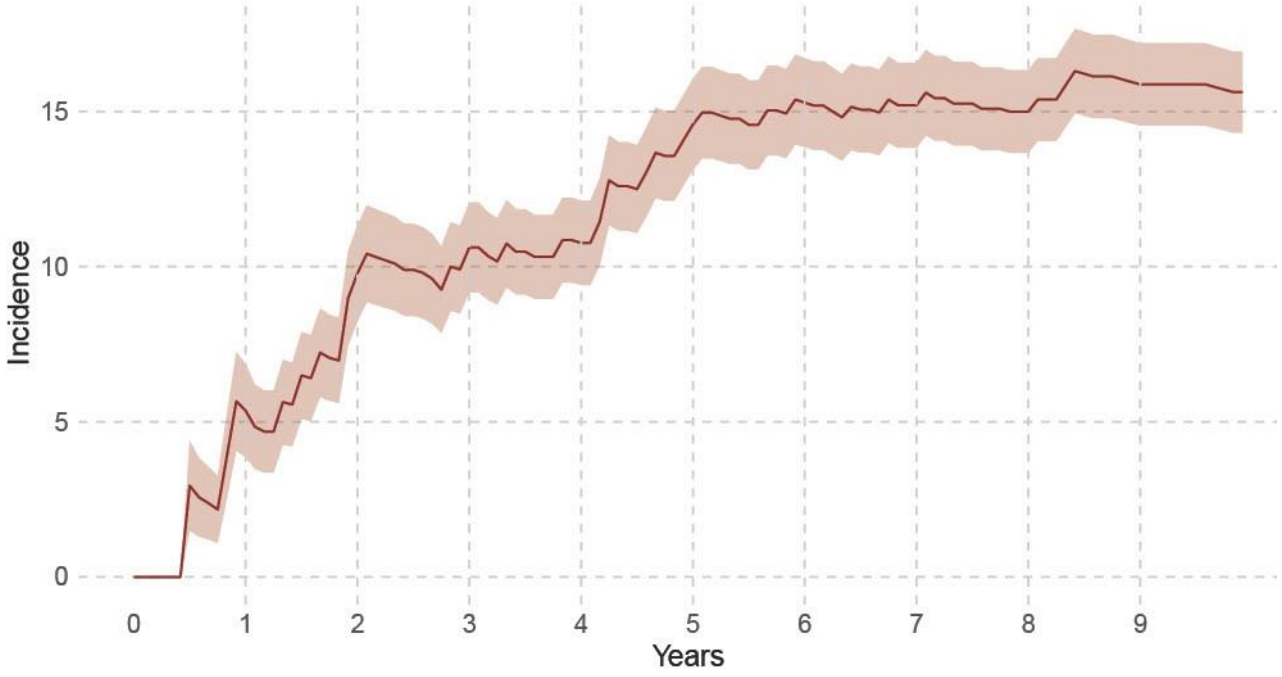
Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is currently the only curative option for several hematologic diseases. Among allo-HSCT associated ocular complications, ocular graft-versus-host disease (oGVHD) severely affects patient quality of life.
This study aimed to review oGVHD incidence, clinical presentation, risk factors, therapy, and outcome in 192 consecutive patients who underwent allo-HSCT at our center between January 2015 and January 2025.

Methods: Data were retrieved from hospital records upon patient informed consent. Ocular GVHD was diagnosed according to NIH 2014 criteria and treated by a dedicated in-hospital ophthalmology team. Slit-lamp examination, corneal fluorescein staining and tear breakup time were the main diagnostic tools.

Results: Thirty-two (16.7%) patients were affected by oGVHD, which occurred after a median time of 12 (1-72) months from allo-HSCT. At diagnosis, 18 (56%) patients were receiving systemic immunosuppression. oGVHD was isolated in 7 (22%) cases, associated to one or more additional GVHD-involved sites in 10 (31%) and 15 (47%) cases, respectively. Symptoms reported at presentation were ocular dryness (59% of patients), ocular hyperemia (31%), burning sensation (19%), ocular discharge (19%), photophobia (18%), decreased visual acuity (25%), foreign body sensation (13%), and ocular pain (1%). At onset, all patients were affected by keratoconjunctivitis sicca. Ocular adnexal involvement was observed in 24 (75%) cases. Four (12.5%) patients further developed corneal ulcers that were subsequently complicated by bacterial infections in 3 cases.
oGVHD severity was mild in 14 (44%) patients, moderate in 6 (19%), and severe in 12 (37%). Female recipient (OR 4.46, 95% CI 1.42–14.08, $p<0.05$), prior skin acute GVHD (OR 3.64, 95% CI 1.62–8.18, $p<0.05$), and female-to-male allo-HSCT (OR 4.37, 95% CI 1.08–17.7, $p<0.05$) independently increased the risk of oGVHD by multivariate analysis (AUC 0.766). Patients received at least one topical treatment which was eventually modified. Steroid drops were used in 22 patients, cyclosporin A 1% drops in 19, autologous serum drops in 6, amniotic membrane extract fresh drops in 9, and therapeutic contact lens in 12. The median number of topical treatments was 2.6 (1-4). Two patients underwent ocular surgery due to corneal ulceration with infectious keratitis.
Clinical remission with first-line topical therapy (steroid drops) occurred in 13/32 (41%) patients. Topical 0.1% cyclosporine A was used in 19 (59%) patients, who obtained a significant reduction of oGVHD severity in 12 (63%) cases. Nine (28%) patients received

amniotic membrane extract fresh drops (AMED), obtaining a significant oGVHD improvement in 7 (77%) cases at 1 month. Despite treatment, visual acuity decreased significantly (median Δ dpt last follow-up vs baseline −1.45/10, $p<0.05$), with 3 (9%) patients experiencing total blindness.



Conclusions: oGVHD was a relatively frequent complication of allo-HSCT, mostly occurring within the first year, with a moderate to severe presentation pattern in 56% of cases. Patients underwent a median of 2.6 lines of treatments, reporting on average a significant loss of visual acuity, and total blindness in 9% of cases. Overall, these findings indicate that a close interaction between transplant physicians and ophthalmologists is needed to provide early oGVHD assessment and prompt intervention.

Disclosure: Nothing to declare

P135

COMPARATIVE OUTCOMES OF THREE DIFFERENT ATLG REGIMENS IN ALLO-HSCT FOR PATIENTS WITH HEMATOLOGICAL MALIGNANCIES: A RETROSPECTIVE STUDY

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Background: Anti–T-lymphocyte globulin (ATLG) is a rabbit-derived polyclonal antibody widely used for GVHD prophylaxis after allogeneic HSCT. However, the optimal dosing and combination strategy—balancing GVHD prevention with immune recovery and infection risk—remains uncertain.

Methods: We retrospectively analyzed 191 allo-HSCT recipients at Hebei Yanda Ludaopei Hospital and Beijing Ludaopei Hospital (July 2023–January 2025). All patients received ATLG-based GVHD prophylaxis and were assigned to three cohorts: ATLG 25 mg/kg, ATLG 20 mg/kg, or ATLG 20 mg/kg combined with anti-CD25 antibody on day +1 and/or +4. Primary endpoints were day-100 acute GVHD. Secondary endpoints included day-180 CMV/EBV reactivation, hemorrhagic cystitis, CIR, NRM, LFS, and OS.

Results: **Patient Characteristics and Outcomes**
A total of 191 allo-HSCT recipients were assigned to the CD25+ATLG20 (n = 61), ATLG20 (n = 92), and ATLG25 (n =38) groups. baseline variables—including disease status, sex, graft characteristics including $CD34^+$, MNC, and $CD3^+$ cell doses and letermovir use—were well balanced. With a median follow-up of 15.3 months (range, 0.4–28.3), long-term outcomes were comparable across groups. CIR remained low (3.39% for CD25+ATLG20 vs. 11.57% for ATLG20 vs. 6.59% for ATLG25; P=0.225). NRM showed no significant differences, though lower rates were observed with ATLG20-based regimens (9.8% and 8.9%) compared with ATLG25 (21.2%; P=0.106). LFS (86.9%, 79.5%, 71.9%; P=0.189) and OS (88.6%, 82.9%, 72.2%; P=0.109) followed a similar pattern, with CD25+ATLG20 showing numerically favorable but non-significant improvements.
Acute GVHD and Viral Reactivation
The day-100 cumulative incidence of grade II–IV aGVHD did not differ significantly among the CD25+ATLG20, ATLG20, and ATLG25 groups (26.7%, 28.5%, and 39.5%, respectively; P = 0.329) (Figure 1A). In contrast, a significant difference was observed in severe grade III–IV aGVHD. The CD25+ATLG20 group had the lowest incidence (5.0%), markedly lower than both ATLG20 (12.0%) and ATLG25 (26.3%) groups (P = 0.007)(Figure 1B). This finding indicates that ATLG 20 mg/kg provided aGVHD control comparable to 25 mg/kg, while adding CD25 antibody reduced severe aGVHD. In multivariable Fine–Gray regression for II–IV aGVHD (Table 1), the combined CD25+ATLG20 approach was associated with a markedly reduced risk of severe (grade III–IV) aGVHD (HR 0.14, 95% CI 0.04–0.53; P = 0.004), and remained the only protective factor in the multivariable model.
The day-180 cumulative incidence of CMV reactivation was 36.44% in the CD25+ATLG20 group, 32.21% in the ATLG20 group, and 43.24% in the ATLG25 group (P = 0.598). EBV reactivation was similarly low and not significantly different (15.2%, 11.0%, and 7.9%; P = 0.450). Neither ATLG dose escalation nor the addition of CD25 antibody increased viral susceptibility or early toxicity.

Figure 1. Cumulative incidence of aGVHD among CD25+ATLG20, ATLG20, and ATLG25 groups

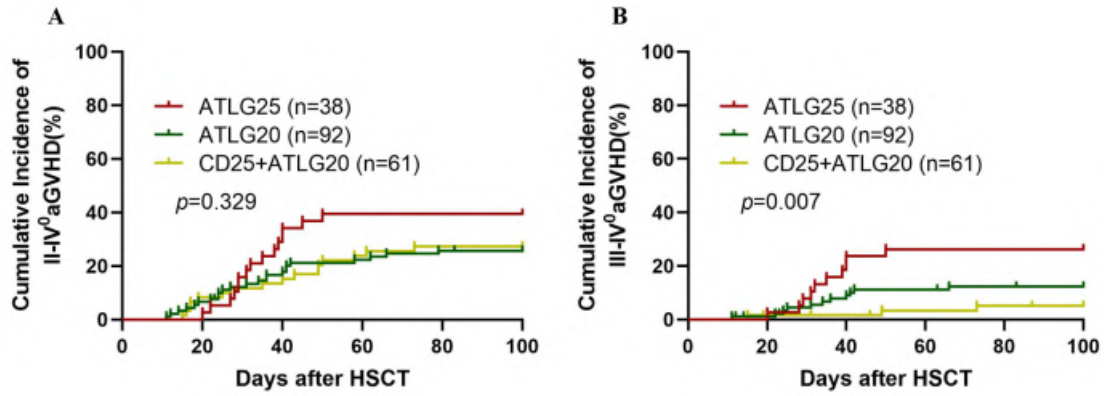

Table 1. Multivariable Fine–Gray regression for aGVHD

Characteristic	II-IV0aGVHD		III-IV0aGVHD	
	HR (95%CI)	p-value	HR (95%CI)	p-value
CR1	1(reference)			
≥CR2	0.95(0.52-1.74)	0.86	1.21(0.47-3.12)	0.69
NR/PR	1.39(0.57-3.41)	0.47	1.46(0.33-6.45)	0.62
BU-based vs. TBI-based	0.91(0.50-1.65)	0.75	0.53(0.18-1.56)	0.25
CD34+ (≤6 vs. >6)	1.53(0.88-2.64)	0.13	1.92(0.77-4.81)	0.16
MNC (≤9 vs.>9)	0.82(0.47-1.43)	0.49	1.72(0.74-3.97)	0.21
CD3+ (≤2 vs.> 2)	1.30(0.78-2.19)	0.32	1.65(0.74-3.67)	0.22
ATLG25	1(reference)			
ATLG20	0.64(0.33-1.25)	0.19	0.45(0.18-1.15)	0.096
CD25+ATLG20	0.58(0.29-1.16)	0.12	0.14(0.04-0.53)	0.004
age (≤14Y vs. >14Y)	1.56(0.74-3.32)	0.25	1.28(0.40-4.13)	0.68

Conclusions: In this real-world cohort, ATLG at 20 mg/kg achieved aGVHD prophylaxis comparable to the 25-mg/kg dose across all efficacy and safety endpoints. Only the addition of CD25 monoclonal antibody to ATLG20 was associated with a significantly lower incidence of severe grade III–IV aGVHD, without increased viral reactivation or toxicity.

Disclosure: Nothing to declare

P137

BELUMOSUDIL IN SEVERE PROGRESSIVE OCULAR CHRONIC GRAFT-VERSUS-HOST DISEASE: A CASE SERIES

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Background: Belumosudil is a selective ROCK2 inhibitor approved by the U.S. Food and Drug Administration for the treatment of chronic graft-versus-host disease (cGVHD) after failure of at least two prior systemic therapies. Through modulation of IL-21 and IL-17 secretion, upregulation of regulatory T cells, inhibition of pro-fibrotic pathways and TGF-β signaling, and reduction of choroidal neovascularization, belumosudil may represent a promising therapeutic option for ocular cGVHD.

Methods: We report a case series of five patients with severe, progressive ocular cGVHD treated with belumosudil for six months. All patients had undergone allogeneic hematopoietic stem cell transplantation more than 10 years before treatment initiation. Ocular cGVHD was graded as severe in all cases (NIH ocular score 3). Ophthalmologic assessments were performed according to NIH recommendations. Belumosudil was administered at a dose of 200 mg twice daily.

Results: Common ocular manifestations included corneal ulceration, eyelid thickening and irregularity, meibomian gland dysfunction, reduced tear meniscus, diffuse epithelial keratopathy, filamentary keratitis, early lens opacities, and severe dry eye with corneo-conjunctival epitheliopathy. All patients experienced significant impairment of daily activities, with vision loss reported in two cases. Concomitant cGVHD involvement included oral involvement in three patients and pulmonary involvement in two patients. All patients had previously received long-term topical cyclosporine, and two were on oral cyclosporine, without clinical benefit. The overall response rate for ocular cGVHD was 100%. All patients showed symptomatic improvement, confirmed by serial ophthalmologic evaluations performed every two months. After six months of therapy, three patients improved from NIH ocular score 3 to 1, and two patients from score 3 to 2.

Conclusions: Belumosudil demonstrated significant clinical activity in patients with severe, progressive ocular cGVHD and may represent an effective therapeutic option in this difficult-to-treat population.

Disclosure: Nothing to declare.

P138

EFFECTS OF EXTRACORPOREAL PHOTOPHERESIS (ECP) ON LEUKEMIA-SPECIFIC AND ANTI-LEUKEMIC IMMUNE CELL SUBSETS IN LEUKEMIA PATIENTS AFTER STEM CELL TRANSPLANTATION (HSCT) WITH ACUTE OR CHRONIC GRAFT-VERSUS-HOST-DISEASE

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Background: Acute (a) or chronic (c) Graft-versus-Host-Disease (GvHD) are frequent, potentially life-threatening complications after HSCT and can be treated with ECP. How ECP influences the function and dynamics of leukemia-specific immune subsets remains unclear. We analyzed leukemia-specific subsets defined by CD107a$^+$ (DEG) or IFNγ$^+$ (INC) responses and "antitumor-directed" (Integrinβ7$^+$, γδ$^+$) T cells and TH cells in aGvHD, cGvHD, no-GvHD patients, and healthy donors (H). We correlated these profiles with clinical characteristics to identify ECP-, GvHD-, or relapse-associated signatures at baseline (d0) and after 3 months of ECP (d90).

Methods: ECP was performed using the TherakosTM CELLEXTM system. Flow cytometric analyses were performed on patient blood samples at d0 (pre ECP) and d90 (after ECP), focusing on leukemia-specific (DEG+/INC+), antitumor directed and Thelper cells. Statistical analyses were conducted.

Results: noGvHD d0 vs Healthy controls:

- TH cells H vs. noGvHD: TH17↑ TH1↑ TH2↑
- Integrinß7$^+$T^{4-}↓ and γδ$^+$ T^{4+}↓ in H

noGvHD d0 vs. d90:

- Degranulating cells: CIK cells ↓ NK cells ↓ Tem cells ↓
- INFγ producing cells: CIK↓ NK↑
- TH cells: TH17↑ TH1 and TH2 stable

cGvHD d0 vs. d90 under ECP:

- Degranulating cells: CIK cells ↓ NK cells↑ Breg↑ Tem↓ Tcm↑
- INFγ producing cells: CIK cells ↓ NK cells ↓ Tcm↑
- TH cells: TH17 stable, TH1↑ TH2↓

aGvHD d0 vs. d90 under ECP:

- Degranulating cells: CIK cells ↓ NK cells ↓
- INFγ producing cells: CIK cells↑ NK cells↑ Tem cells↑
- TH cells: TH17, TH1 and TH2 stable

cGvHD vs. noGvHD d0:

- Degranulating cells cGvHD vs. noGvHD: CIK cells↓ NK cells↓ Tcm↓ Tem↓ Breg↑
- INFγ producing cells cGvHD vs. noGvHD: CIK cells↓ NK cells↓ Tcm↓ Tem↑
- TH cells cGvHD vs. noGvHD: TH17↓ TH1↓ TH2↓

aGVHD vs. noGvHD d0:

- Degranulating cells aGvHD vs. noGvHD: CIK cells↑ NK cells↑ Breg ↑ Tcm↓ Tem↓
- INFγ producing cells aGvHD vs. noGvHD: CIK cells↓ NK cells↓ Tcm↓ Tem↓
- TH cells aGvHD vs. noGvHD: TH17↓ TH1↓ TH2↓

cGvHD under ECP vs. noGvHD d90:

- Degranulating cells cGvHD vs. noGvHD: CIK cells↑ NK cells↑ Breg↑ Tcm↓ Tem↓
- INFγ producing cells cGvHD vs. noGvHD: CIK cells↑ NK cells↑ Tcm↑
- TH cells cGvHD vs. noGvHD: TH17↓ TH1↑ TH2↓

aGvHD under ECP vs. noGvHd d90:

- Degranulating cells aGvHD vs. noGvHD: CIK cells↑ NK cells↑ Tem↑
- INFγ producing cells aGvHD vs. noGvHD: CIK cells↑ NK cells↑ Tcm↓ Tem↑
- TH cells aGvHD vs. noGvHD: TH17↓ TH1↑ TH2↓

Conclusions: At d0, both GvHD groups showed reduced degranulating and IFNγ-producing CIK, NK, and Tcm cells and lower TH17, TH1, and TH2 levels compared with noGvHD. Both groups also had decreased DEG/IFNγ$^+$ Tem and increased DEG-Breg cells. Intβ7$^+$T4$^-$ and γδ$^+$T4$^+$ subsets were lowest in healthy donors.
At d90, aGvHD and cGvHD patients showed higher degranulating and IFNγ-producing CIK andNK cells than noGvHD, along with reduced TH17/TH2 and increased TH1 levels. cGvHD patients additionally showed reduced DEG-Tcm and increased DEG-Breg cells.
Overall, noGvHD patients showed stable, GVHD patients under ECP variable immune subset compositions. Correlations of findings with clinical parameters will be presented.

Disclosure: FUNDING: This work was funded by an external collaborative research (ECR) grant provided by Therakos EMEA Limited.

P140

REDUCED-DOSE POST-TRANSPLANT CYCLOPHOSPHAMIDE FOR GVHD PROPHYLAXIS IN HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION: REAL-WORLD OUTCOMES FROM A LATIN AMERICAN TRANSPLANT CENTER

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Background: Post-transplant cyclophosphamide (PTCy), administered at high doses of 50 mg/kg/day on days +3 and +4, is a standard of care for graft-versus-host disease (GVHD) prophylaxis in haploidentical hematopoietic cell transplantation (HCT). Although highly effective, PTCy is associated with toxicities that may be dose-dependent, prompting dose-adjustment strategies aimed at reducing cardiovascular and infectious complications. We report the experience of a transplant center in Mexico using dose-adjusted PTCy as GVHD prophylaxis in haploidentical HCT.

Methods: Patients aged ≥16 years who underwent haploidentical hematopoietic cell transplantation between 2024 and 2025 at IMSS UMAE 25, Monterrey, Mexico, were included. Descriptive analyses were performed using measures of central tendency and percentages. Overall survival (OS) and relapse-free survival (RFS) were estimated using the Kaplan–Meier method, while non-relapse mortality (NRM) and graft-versus-host disease (GVHD) were analyzed using cumulative incidence functions.
Objective: Describe outcomes of patients receiving PTCy at 40 mg/kg/day on days +3 and +4 following haploidentical HCT at a single transplant center in Mexico.

Results: Patients aged ≥16 years who underwent haploidentical hematopoietic cell transplantation between 2024 and 2025 at IMSS UMAE 25, Monterrey, Mexico, were included. Descriptive analyses were performed using measures of central tendency and percentages. Overall survival (OS) and relapse-free survival (RFS) were estimated using the Kaplan–Meier method, while non-relapse mortality (NRM) and graft-versus-host disease (GVHD) were analyzed using cumulative incidence functions.
Results: A total of 21 patients were included (16 men and 5 women), with a median age of 27 years (range 16-50). The main indication for transplantation was malignancy (ALL 11, AML 3, MDS 2, NHL 1, PMF 1). Nine donors were male and 12 were female. The median CD34+ count was 11.27/kg (range 3-28.6), all obtained from peripheral blood by apheresis. Conditioning was performed using the MAC variant in 80% of cases. Engraftment was successful in 91% of cases; one patient experienced primary failure requiring a second transplant. The median chimerism at day 30 was 99% (0-99). The median neutrophil engraftment was on day 14 (range 12-20), and the median platelet engraftment was on day 15 (range 13-50).

The median follow-up was 200 days (range 20-455). Overall survival was 69%, and relapse-free survival was 90%. Only 8 (38%) patients developed GVHD during the follow-up period.

The cumulative incidence of acute GVHD was 24% (19% GII-IV) and of chronic GVHD was 12% (6% NIH moderate/extensive) at 400 days of follow-up.

CMV reactivation occurred in 10 patients (47%), none with clinical disease; BK virus reactivation in 4 patients (19%); hemorrhagic cystitis in 5 patients (23%), none in its severe form; and pneumonia in 5 patients (23%). Non-Relapse Mortality was 23% (1 patient graft failure, 3 Klebsiella sepsis, and 1 patient severe graft-versus-host disease).

Conclusions: The reduction of PTCy dose in our patient group demonstrated comparable efficacy to the conventional dose against GVHD prevention and a low incidence of severe/extensive forms.

Disclosure: No conflict of interest.

P142

CLINICAL CHARACTERISTICS AND SURVIVAL OUTCOMES OF GRAFT-VERSUS-HOST DISEASE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE-CENTRE COHORT ANALYSIS

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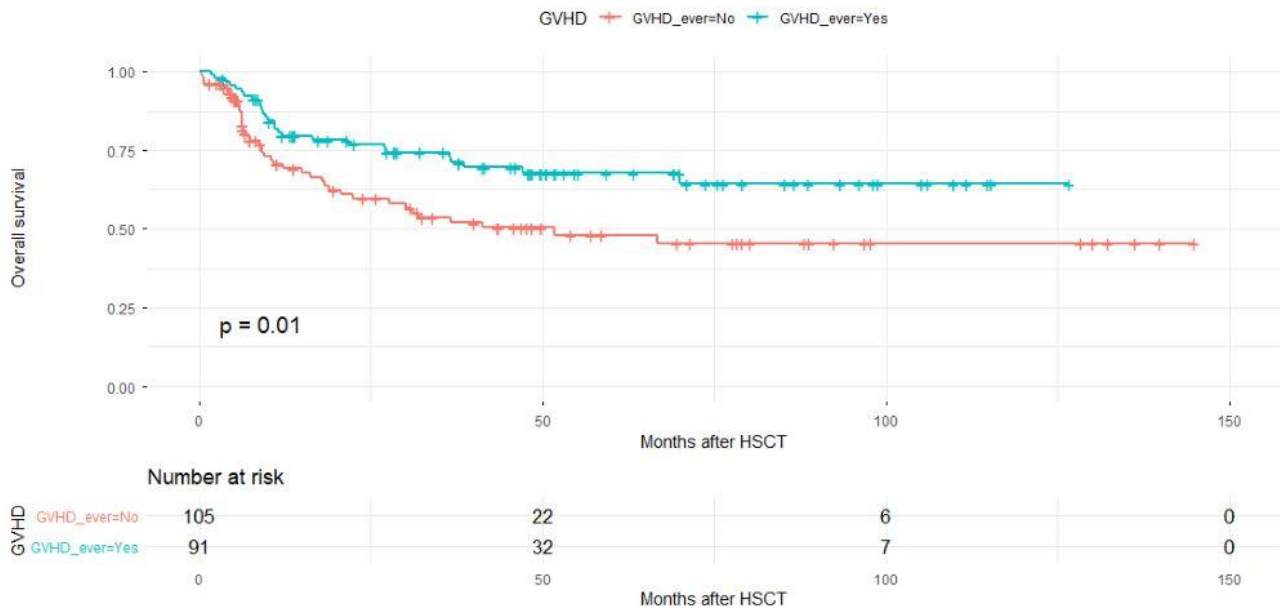
Background: Graft-versus-host disease (GVHD) remains an important complication after allogeneic haematopoietic stem cell transplantation (allo-HSCT), with a complex relationship to post-transplant outcomes. Characterising the clinical presentation of GVHD and its association with survival remains clinically relevant. We aimed to describe the incidence of GVHD in a real-world allo-HSCT cohort and to evaluate its association with overall survival (OS) and its relationship with selected baseline donor and recipient characteristics.

Methods: We conducted a retrospective cohort study including 235 adult patients who underwent allo-HSCT. OS was estimated using the Kaplan–Meier method. Survival outcomes were compared by GVHD status using the log-rank test. GVHD was defined based on documented clinical diagnosis and classified as acute or chronic. Acute GVHD severity was graded according to standard criteria (grades I–IV), while chronic GVHD was categorised as mild, moderate or severe. Baseline characteristics, including organ involvement, recipient sex, donor sex, and donor–recipient sex combinations, were summarised descriptively. Associations between categorical variables and GVHD occurrence were evaluated using Fisher's exact test.

Results: With a median follow-up of 49.8 months (range 0.8–140), patients who developed GVHD showed significantly improved overall survival compared with those without GVHD (Figure 1). Two- and five-year OS rates were 76.9% and 67.8% in patients with GVHD versus 59.6% and 48.1% in those without GVHD (log-rank p = 0.01).Among the 235

patients, 91 (38.7%) developed GVHD. Of these, 34 (37.4%) presented with acute and 57 (62.6%) with chronic GVHD. Acute GVHD was predominantly low-grade, with grade I being 58.1% of cases. Higher-grade acute GVHD was less frequent, with grades III–IV observed in 19.3% of patients. Chronic GVHD was mainly mild (40.7%) to moderate (53.7%), while severe chronic GVHD was uncommon, accounting for only 5.6% of cases.
Regarding organ involvement, hepatic GVHD was the most frequent manifestation, observed in 45.1% of cases, followed by skin involvement in 20.9%. Multiorgan GVHD was present in approximately one fifth of patients (22.0%), while mucosal (5.5%), pulmonary (4.4%) and gastrointestinal (2.2%) involvement were less frequent.
The distribution of donor–recipient sex combinations was balanced across the cohort. No significant differences in GVHD occurrence were observed among the four donor–recipient sex combinations (female donor–female recipient, female donor–male recipient, male donor–female recipient, and male donor–male recipient; Fisher's exact test, p = 0.65). Donor–recipient sex discordance was not associated with GVHD development. The classical female donor–male recipient combination was not associated with a higher frequency of GVHD when compared with other sex combinations.



Conclusions: In this cohort, GVHD occurrence was associated with improved overall survival, supporting the clinical relevance of the graft-versus-leukaemia effect. Acute GVHD was predominantly low grade, and chronic GVHD was mainly mild to moderate, with severe forms being uncommon. Hepatic and skin involvement were the most frequent clinical manifestations. No significant associations were observed between GVHD and donor–recipient sex combinations. These findings highlight the prognostic relevance of GVHD while emphasising the absence of detectable associations with baseline donor–recipient sex characteristics in this cohort.

Disclosure: Nothing to declare.

P143

DUPILUMAB AS EFFECTIVE TREATMENT IN ADULT AD-LIKE GVHD: A CASE REPORT

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Background: Atopic dermatitis (AD)-like graft-versus-host disease (GVHD) is a chronic form of cutaneous GVHD that may occur following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Both for acute and chronic GVHD, systemic corticosteroids are considered first-line therapy, but responses may be temporary. Second-line options—including Ruxolitinib, extracorporeal photopheresis, Sirolimus, Mycophenolate mofetil and Rituximab—are variably effective but could often be toxic. Targeted therapies such as Dupilumab are emerging as promising options for cutaneous, AD-like chronic GvHD in pediatric patients. Dupilumab is a human IgG4 monoclonal antibody targeting the interleukin-4 receptor α subunit (IL-4Rα), thereby inhibiting IL-4 and IL-13 signalling and selectively modulating the Th2 axis involved in cutaneous inflammation and pruritus.

Methods: We report a case of an adult, 55-year-old woman, who underwent cord blood allo-HSCT for Acute Myeloid Leukaemia and was treated with Dupilumab for AD-like GVHD.

Results: The patient had a history of atopy (seasonal allergic rhinoconjunctivitis, skin reactions to fish and shellfish, family history of atopy) and was affected by high-risk Acute Myeloid Leukaemia FAB M4 diagnosed in 2009. After a suboptimal response to multiple induction and consolidation chemotherapy regimens (FLAIE, IDA-AraC, HD-AraC, MEC-My) and persistence of minimal residual disease, she underwent an allo-HSCT. In 2010, she received a cord blood unrelated donor transplantation (4/6 mismatched, ABO major incompatible, infused dose TNC/kg 3.61×10^7) after a myeloablative conditioning therapy including Thiotepa, Fludarabine and Busulfan with a GVHD prophylaxis including anti-thymocite globulin, mycophenolate mofetil and cyclosporine. No acute GHVD signs occured. One year after transplant, the patient developed erythematous-scaling skin lesions with an eczematous appearance at the base of the neck, in the elbow folds and breast region, associated with dry, pruritic skin, excoriations and facial erythema. Histological picture was compatible with Atopic Dermatitis, with a transient response to topical corticosteroid therapy, emollients and cyclosporine. Following the loss of therapeutic response, a new skin biopsy led to a diagnosis of chronic cutaneous GVHD; therefore the patient was treated with cyclosporine and extracorporeal photopheresis, continued for nearly ten years with moderate clinical benefit, despite seasonal flare-ups. After immnosuppressive therapy was interrupted, in 2022 a new worsening of skin condition was observed. New histological evaluation documented moderate-to-severe Atopic Dermatitis with GVHD features. Resuming cyclosporine resulted in an unsatisfactory clinical response; therefore, in light of the evidence of a concomitant EBV infection, the patient received two administrations of rituximab, resulting in both a reduction in EBV viral load and an improvement in the cutaneous findings.

Subsequently, second-line biologic therapy with Dupilumab was started in December 2023, at a dosage of 300 mg s.c. every two weeks, obtaining a good disease control, with disappearance of skin lesions. Dupilumab was well tolerated, with no drug-related toxicities reported.

Conclusions: As reported in pediatric setting, Dupilumab seems to be a promising, well-tolerated option also in adult patients with steroid-refractory cutaneous GvHD with AD-like features. Its use may reduce immunosuppressive burden and improve quality of life.

Disclosure: Nothing to declare.

P146

VERY LATE ONSET ACUTE GVHD AFTER COVID19 VACCINE AND INFECTION: A CASE REPORT

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Background: Late onset acute graft-versus-host disease (aGVHD) is defined by the presence of acute GVHD beyond 100 days post allogeneic hematopoietic stem cell transplantation (allo-HSCT).
These findings present clinical and pathological features of aGVHD without any representative chronic GVHD findings. Of note, they usually present more severe symptoms, frequently unresponsive to immunosuppressive therapy. Cutaneous late onset aGVHD is the most common form, characterized by pruritic and erythematous rash with basal keratinocyte apoptosis, perivascular lymphocytic infiltration and dyskeratosis.

Methods: We report a case of a 63-year-old female affected by Myelofibrosis post Polycythemia Vera (PPV-MF), JAK2 mutated, who received an allo-HSCT in 2014 and developed a late onset aGVHD 8 years post-transplant.
In 2001 our patient was diagnosed with Polycythemia Vera, and she started treatment with hydroxyurea and phlebotomies. In 2009 she experienced an increasing spleen volume, and she underwent bone marrow (BM) biopsy which documented the evolution to PPV-MF, and she started Ruxolitinib with improvement of symptoms.
In April 2014 she underwent haploidentical allo-HSCT. GVHD prophylaxis included post-transplant cyclophosphamide, mofetil mycophenolate (MMF) and cyclosporine. At day +24 she developed grade I cutaneous aGVHD, which responded to increased cyclosporine and prolonged MMF until day +35. BM evaluations, performed up to two and a half years after allo-HSCT, confirmed CR, JAK2 negative and complete donor chimerism.
In April 2022, 8 years after allo-HSCT, she developed a widespread pruritic erythroderma some weeks after COVID-19 vaccination and subsequent infection. She underwent skin biopsy which documented apoptotic keratinocytes and lymphocityc infiltration, histopathological features consistent with aGVHD rather than lichenoid or sclerotic chronic GVHD. Furthermore, we performed BM evaluation, 8 years after allo-HSCT, which

documented Myelofibrosis JAK2 mutated and mixed chimerism with 30,9% donor and 69,1% recipient.

Results: Corticosteroid therapy was eventually initiated, without clinical improvement, thus cyclosporine and extracorporeal photopheresis were introduced, however, these interventions also proved ineffective. An improvement in the cutaneous findings was finally obtained with the JAK1/JAK2 inhibitor ruxolitinib, a particularly effective treatment in steroid-refractory aGVHD.
During this therapy our patient developed pancytopenia, so we performed another BM biopsy, which showed persistence of JAK2 mutation and chimerism improvement with 89,5% donor and 10,5% recipient. Despite being evaluated for a second allo-HSCT, she withdrew consent and, today, 3 years after, she continues Ruxolitinib with hematological recovery.

Conclusions: This case shows a very rare entity of late onset aGVHD occurred 8 years after transplantation, triggered by COVID-19 vaccination and infection. Despite its complexity was aggravated by the concurrent Myelofibrosis relapse and chimerism loss, Ruxolitnib appears to be an effective treatment.

Disclosure: Nothing to declare.

P147

COMPOSITION OF PERIPHERAL BLOOD IMMUNE-CELLS IN PATIENTS WITH LEUKEMIA AFTER ALLOGENEIC STEM-CELL-TRANSPLANTATION(HSCT) IN PATIENTS WITH VS. WITHOUT CHRONIC(C) OR ACUTE(A) GRAFT-VERSUS-HOST-DISEASE(GVHD) AND HEALTHY DONORS

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Background: aGvHD/cGvHD are common and potentially life-threatening autoimmune complications after HSCT, mediated by immune cells. Treatment aims to suppress excessive immune activity while maintaining graft versus leukemia effects. The impact of treatment on the provision of inflammatory or inhibitory immune cell subsets is poorly understood. We compared myeloid, adaptive and innate immune cell compositions in aGvHD/cGvHD vs non-GvHD HSCT patients or healthy controls before treatment (baseline) and correlated findings with clinical patients' characteristics. Finally, we deduced knowledge about immune cells involved in patients after HSCT that did not develop GvHD ('NoGvHD') vs GvHD patients.

Methods: Flow cytometric cell analyses of blood samples (H=10, NoGvHD=19, cGvHD=18, aGvHD=6) were observed at baseline. Statistical analysis was performed.

Results: Cells in cGvHD compared to NoGvHD

- Myeloid: ↓ DCtol/MDSCs, ↑ myeloid dysfunction
- Adaptive: ↑ effector-memory, ↓ regulatory/anti-tumor subsets
- Innate: ↑ differentiated/exhausted NK/CIK

Cells in aGvHD compared to NoGvHD

- Myeloid: ↓ inhibitory monocytes/DCtol
- Adaptive: ↑ strong late T-cell proliferation, ↓ Tregs/B cells
- Innate: ↓ NK56bri, ↑ destabilized/exhausted NK/iNKT

Cells in aGvHD compared to cGvHD

- Myeloid: acute collapse (aGvHD) vs. chronic dysfunction (cGvHD)
- Adaptive: extreme effector proliferation (aGvHD) vs. persistent activation (cGvHD)
- Innate: loss of early NK regulators (aGvHD) vs. NK56dim dominance (cGvHD)

Cells in NoGvHD compared to GvHD development

- Myeloid: ↑ tolerogenic DC/MDSC
- Adaptive: ↑ T/Treg, ↓ activation/proliferation
- Innate: ↓ NK/CIK exhaustion

Cells in skin aGvHD compared to no-skin aGvHD

- Myeloid: ↓ tolerogenic signatures
- Adaptive: ↑ activation/homing markers, ↓ regulatory subsets
- Innate: ↑ NK/CIK exhaustion, ↑ TH1/TH17 skewing

Cells in overlap cGvHD compared to non-overlap cGvHD

- Myeloid: ↓ tolerogenic myeloid cells
- Adaptive: ↑ PD-L1/TIGIT, ↓ Tregs
- Innate: ↑ NK/CIK exhaustion

Cells in severe cGvHD compared to mild cGvHD

- Myeloid: ↑ activated/CTLA-4^{+} MDSC/DC
- Adaptive: ↑ proliferating/gut-homing T cells, ↓ Th1/Treg
- Innate: ↑ NK/CIK exhaustion

Cells in multi organ cGvHD compared to single organ cGvHD

- Myeloid: ↑ inflammatory monocytes/MDSCs
- Adaptive: ↑ γδ⁺/Intβ7⁺ activation, ↓ Tregs
- Innate: ↑ checkpoint-positive NK/CIK, ↓ NK56bri

Cells in DLI-exposed compared to non-DLI exposed cGvHD

- Myeloid: ↓ tolerogenic myeloid function
- Adaptive: ↑ activation/gut-homing, ↓ Tregs
- Innate: ↑ NK/CIK exhaustion

Conclusions: Post-HSCT, NoGvHD patients who did not develop GVHD maintain regulatory myeloid and adaptive features with limited T/NK activation, whereas GvHD patients, with especially skin aGvHD, severe cGvHD, multi-organ cGvHD, or DLI-treated cGvHD, showed myeloid suppression, T-cell hyperactivation, and NK/CIK exhaustion, reflecting distinct inflammatory and tissue-homing immune signatures.

Disclosure: This work was funded by an external collaborative research (ECR) grant provided by Therakos EMEA Limited.

P148

DYNAMIC MODULATION OF NATURAL KILLER (NK) AND CYTOKINE INDUCED KILLER (CIK) CELLS BY EXTRACORPOREAL PHOTOPHERESIS IN CHRONIC GRAFT-VERSUS-HOST DISEASE AFTER HEMATOPOETIC STEM CELL TRANSPLANTATION

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Background: NK cells are central to immune reconstitution after Hematopoetic Stem Cell Transplantation**(**allo-SCT) and contribute to Chronic Graft vs Host Disease(cGvHD) pathophysiology. Altered NK maturation and inhibitory phenotypes have been linked to persistent inflammation in cGVHD. Extracorporeal Photopheresis (ECP) is widely used in steroid-refractory cGvHD, but its effects on NK-cell subset composition remain poorly defined. Aims**:** To compare NK and checkpoint-expressing NK/CIK subsets between patients without GvHD ('No-GvHD', controls) and cGVHD patients receiving ECP at baseline and after 12 weeks.

Methods: ECP was administered using the THERAKOS™ CELLEX™ Photophoresis system. Peripheral Blood samples from cGvHD (n=14) and no-GvHD (n=14) allo-SCT recipients were analyzed at baseline and after 12-weeks follow-up. NK and CIK subsets were quantified by flow cytometry. Statistical analyses were performed.

Results: 1. cGVHD displayed vs no-GvHD (baseline):
↑ **Cytokine-producing NK** ($CD56^{bri}$) cells
↓**TIGIT-expressing NK** cells
↓**KLRG1-expressing and TIM3-expressing CIK** cells
2.After 12 weeks from baseline, cGVHD patients displayed vs no-GvHD:
↓**Cytotoxic NK** ($CD56^{dim}CD16^{+}$, $CD56^{dim}CD57^{+}$) cells
↓**TIGIT-expressing and KLRG1-expressing NK** cells
↓**KLRG1-expressing CIK** cells
3. cGVHD patients displayed after 12 weeks ECP treatment:
↓**Cytokine-producing NK** ($CD56^{bri}$) cells
↑**TIGIT-expressing ,KLRG1-expressing NK cells** and **$2B4^{+}$ expressing NK** cells
↓**TIGIT -expressing** and **KLRG1-expressing CIK** cells

Conclusions: cGVHD patients showed reduced cytotoxic NK signatures at follow-up compared with no-GVHD controls. During ECP, NK cells shifted toward increased inhibitory/stimulatory phenotypes and reduced cytokine-producing subsets, while CIK cells displayed an opposite trend. These data suggest differential NK/CIK remodeling as part of ECP's immunomodulatory mechanism. Clinical correlations will be presented at the meeting.

Disclosure: *FUNDING: This work was funded by an external collaborative research (ECR) grant provided by Therakos EMEA Limited*

P149

REPORT ON THE EFFICACY OF MESENCHYMAL STROMAL CELLS (MSC–OBTINIX™) IN STEROID AND RUXOLITINIB-REFRACTORY GVHD (SRR-GVHD) WITHIN A COMPASSIONATE USE PROGRAM: AN ITALIAN SINGLE-CENTER EXPERIENCE

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Background: Graft-versus-host disease (GVHD) remains a major complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) and a leading cause of morbidity and mortality. Although corticosteroids represent first-line therapy and ruxolitinib is currently the standard second-line treatment for steroid-refractory disease, a substantial proportion of patients develop GVHD that is refractory to both agents (SRR-GVHD). In this setting,

therapeutic options are limited, and clinical management remains poorly defined, representing a significant unmet medical need. Mesenchymal stromal cells (MSCs), due to their immunomodulatory and anti-inflammatory properties, have emerged as a potential therapeutic strategy for patients with multi-refractory GVHD.

Methods: We conducted a retrospective single-center analysis of patients with refractory acute and chronic GVHD treated with third-party mesenchymal stromal cells (MSCs-Obnitix™). Clinical and transplant-related variables, prior GVHD therapies, and MSC dosing were collected. Response was assessed according to EBMT criteria one week after the last MSC infusion, and post-treatment complications were recorded. Descriptive analyses were performed to explore associations between baseline characteristics and outcomes.

Results: Three patients with an average age of 55 years at the time of transplantation were included in the analysis (Table 1).
The first patient, female, affected by primary myelofibrosis, developed acute gut GvHD which persisted after day +100 post HSCT. She was initially treated with corticosteroids and ruxolitinib achieving only a partial response followed by an exacerbation of symptoms. One week after the infusion of the fourth and final dose of MSCs, she showed a marked clinical improvement, with a reduction in daily stool volume from 1500 to 200ml (Image 1).
The second patient, male, affected by T lymphoblastic lymphoma, developed acute gut GvHD on day +49 post HSCT. After achieving an only partial response to steroids, ruxolitinib and vedolizumab, he experienced a marked clinical improvement along the course of MSCs infusion, with a progressive resolution of the fecal volume (from 3000 ml/day to about 300 ml/day).
The third patient, male, affected by B lymphoblastic leukemia, developed acute cutaneous GvHD on day +15 that evolved to chronic on day +280 post HSCT characterized by lichenoid lesions and diffuse pruritus. The treatment with corticosteroids, ruxolitinib, imatinib, tacrolimus and belumosudil resulted in only limited benefit. A notable amelioration was achieved after the last dose of the MSC-based treatment, with pruritus improving to CTCAE grade 2, BSA involvement decreasing from 80% to 50% and full resolution of the oral lichenoid manifestations.
MSCs infusions were well tolerated and no complications or adverse events were observed in any of the patients.

	Patient 1	**Patient 2**	**Patient 3**
Sex	F	M	M
Age	58	58	48
Diagnosis	MF	T-ALL	B-ALL
Sorror score	0	5	1

Donor type	MUD	Haplo	Sibling
GvHD prophylaxis	ATG, MMF, cyclosporine	PTCY, MMF, tacrolimus	ATG, MTX, cyclosporine
Type of GVHD	Acute, severe	Acute, severe	Chronic, moderate
Involved organs	GI tract	GI tract	Skin
Symptoms	Diarrhea	Diarrhea	Lichenoids lesions, diffuse pruritus
Previous therapy for GvHD	Corticosteroids, ruxolitinib	Corticosteroids, ruxolitinib, sirolimus, vedolizumab	Corticosteroids, ruxolitinib, imatinib, tacrolimus, belumosudil
Pre-MSC severity	Fecal output of 1500 ml/day	Fecal output of 3000 ml/day	CTCAE grade 3, BSA involved of 80%
Post-MSC severity	Fecal output of 200 ml/day	Fecal output of 300 ml/day	CTCAE grade 2, BSA involved of 50%, oral lichen resolution

Table 1

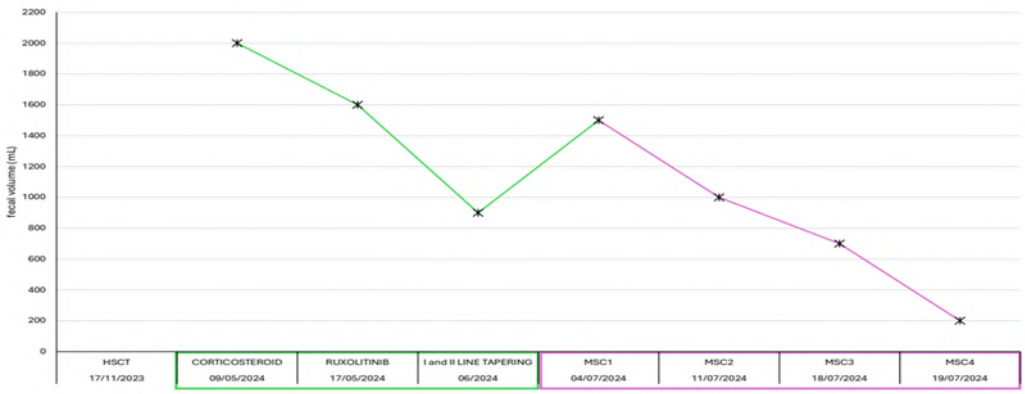

Image 1

Conclusions: Our data show that MSC cell therapy provides a clear improvement in GVHD-related clinical manifestations, both gastrointestinal and cutaneous, and notably without

evident adverse events.
Based on our observations, MSCs may represent a valuable therapeutic option for patients with therapy-refractory acute and chronic GvHD. In all treated cases, MSCs were associated with meaningful clinical improvements, without any treatment-related toxicities or complications. Although limited by the sample sample size, these results encourages further exploration of MSCs as a backbone to current treatment options.

Disclosure: Nothing to declare.

Infections and vaccination – Basic and Translational

B070

IMMUNOGENICITY AND REACTOGENICITY OF REPEATED COVID-19 VACCINATION IN IMMUNOCOMPROMISED PATIENTS (AUTO-COVID-VACC): PRELIMINARY RESULTS FROM A MULTICENTRE, PROSPECTIVE, NON-INTERVENTIONAL STUDY

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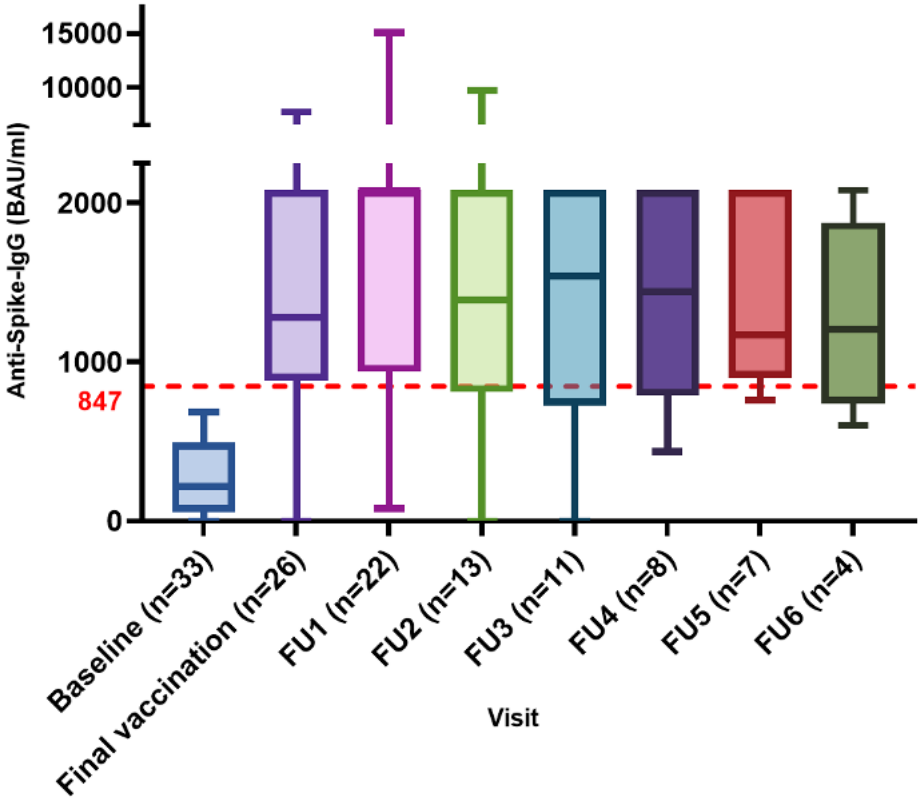
Background: Immunocompromised patients are at an ongoing high risk for severe COVID-19 infections. Vaccination has been proven to be an effective measure in preventing severe SARS-CoV-2 infections, while data on B-cell and T-cell responses are lacking in this population.

Methods: This multicentre, prospective, non-interventional study aimed to determine the immunogenicity and reactogenicity of a COVID-19 vaccination strategy in immunocompromised patients with a focus on patients after autologous HSCT and CAR-T cell recipients. Immunocompromised patients received up to eight COVID-19 vaccinations in 4-week intervals depending on their individual anti-SARS-CoV-2-spike-IgG level as standard of care (SOC). Patients after autologous HSCT and CAR-T cell recipients received a minimum of three vaccinations to re-complete basic immunization. Blood samples were drawn immediately before each vaccination and during a 6-months follow-up.

At each study visit, the humoral and cellular immunity was analysed. Humoral immunity was investigated by measuring anti-SARS-CoV-2-spike-IgG, anti-SARS-CoV-2-nucleocapsid-IgG and Omicron-BA.1-specific neutralising serum activity. Cellular immunity was measured by T-cell-specific IFN-y and IL-2 secretion upon SARS-CoV-2-spike-protein stimulation using IFN-y release assay, FluoroSpot- and FACS analysis. All invasive procedures were performed as SOC.

Results: The study has enrolled 49 patients. Antibody responses were measured in all patients after each visit. Anti-spike-IgG levels show a steady incline in most patients following repeated vaccinations and remained stable during follow-up (Figure 1).
With regard to cellular response, preliminary results show an increase in T-cell immune response in most patients following vaccinations. However, CAR-T cell recipients have lower T-cell responses compared to patients after autologous HSCT during the vaccination and follow-up phase.
Two female patients (31 and 55 years old) with an aggressive B-cell lymphoma, who received CAR-T cell therapy, failed to reach an anti-spike-IgG level ≥847 BAU/ml, which was defined as an adequate immune response in this study, after eight vaccine doses. However, in one of these patients T-cell response increased, while antibody levels declined despite repeated vaccinations.

Figure 1 – SARS-CoV-2 antibody titres before vaccination, at the last vaccination visit and during the follow-up phase



Anti-spike-IgG levels were measured by the LIAISON SARS-CoV-2 TrimericS IgG test on the LIAISON XL (DiaSorin, Vicenza, Italia).
BAU = Binding antibody units, FU = Follow-Up

Conclusions: Our preliminary findings show a boosted B-cell response following repeated vaccinations in most patients. However, even with minimal antibody response, T-cell response may still offer protection. Results will be used to optimize vaccination and booster schedules for immunocompromised patients and to increase rates of protection against severe COVID-19. Further, results may identify risk and treatment factors leading to low immune responses in immunocompromised patients vaccinated against COVID-19, as well as the impact of repeated vaccinations on B-cell and T-cell responses.

Clinical Trial Registry: ClinicalTrials.gov #NCT05597761

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B071

IMPACT OF EBV-DRIVEN POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE (EBV-PTLD) ON DONOR T-CELL CHIMERISM IN ALLOGRAFT RECIPIENTS RECEIVING THYMOGLOBULIN AS GVHD PROPHYLAXIS

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Background: EBV-PTLD is a well-recognized complication of allogeneic transplant when thymoglobulin is used for GVHD prophylaxis. A single case report described T-cell chimerism loss in this context (Guo et al., World J Radiol 2024). We investigated the association between PTLD and donor T-cell chimerism in a large cohort.

Methods: We analysed 405 patients who underwent allograft from matched sibling (n=37), matched unrelated (n=364), or mismatched (n=4) donors between 2015–2023. GVHD prophylaxis consisted of thymoglobulin 4.5 mg/kg in divided doses (days −3 to −1), predominantly with methotrexate and cyclosporine (n=395). Myeloablative conditioning (MAC) was used in 105 (25%). $CD3^+$ chimerism was measured using short tandem repeat analysis and categorised as complete (100%), near-complete (95–100%), mixed (51–94%), or predominant recipient (<50%). PTLD was diagnosed according to WHO criteria. Comparisons were made between D30 and D100 CD3 chimerism, with D60 substituted where D30 data were missing. Severe, moderate and minor chimerism loss were defined as ≥50%, 20–50% and 10–20% respectively. Clinically significant EBV reactivation (csEBVR) was defined as requiring intervention: reduction in immunosuppression and/or rituximab.

Results:

Chimerism (%): median(IQR)	No EBV (n=125)	csEBV(n=144)	PTLD (n=61)	p-value
$CD3^+$baseline	100 (98-100)	100 (98-100)	100 (99-100)	0.45
$CD3^+$day 100	99(95-100)	98(90-100)	96(75-100)	0.89
Severe loss (≥50%), n (%)	5(4)	8(5)	10(16)	0.009
Moderate loss (20-50%), n (%)	6(5)	17(12)	5(8)	.084

Minor Loss (10-20%), n(%)	12(11)	9(7)	5(9)	0.419
$CD3^-$ day 100**:** **data** available in 110	100(99-100)	100(98-100)	100(98-100)	0.89

csEBVR occurred in 161 patients (40%), managed with immunosuppression reduction alone (n=54) and/or rituximab (n=107). Of these, 70 developed PTLD (43%) at a median of 47 days post-allograft (IQR 36–64). Diagnosis was by CT (n=15) or PET (n=55), with biopsy confirmation in 36 cases (51%). Treatment comprised immunosuppression reduction plus rituximab (n=68) or chemotherapy (n=4). PTLD resolved in 68 patients; two died (one PTLD, one respiratory failure).
Serial $CD3^+$ chimerism data were available in 330 patients, including 61 with PTLD. Severe, moderate and minor $CD3^+$ chimerism loss occurred in 26 (7%), 29 (8%) and 23 (7%) patients, respectively. Patients were stratified into no csEBVR (n=126), csEBVR without PTLD (n=145), and PTLD (n=61). Severe chimerism loss occurred in 4%, 5.5% and 16.4%, respectively (p=0.009), with a similar trend for moderate loss (4.8%, 12.4%, and 24.6%:p=0.084): no difference in minor loss (table 1).
$CD3^-$ chimerism (available in 110/329 cases) remained stable with median day-100 chimerism of 100% in patients with (n = 36: IQR 98-100) and without (n=74: IQR 99-100%) PTLD. In all but one patient $CD3^-$ chimerism remained above 80%; the outlying patient had moderate $CD3^+$chimerism loss and developed secondary graft failure.
In multivariable logistic regression adjusting for age, conditioning intensity, and diagnosis, PTLD remained independently associated with severe (OR 3.74, 95% CI 1.41–8.84, p=0.007) and moderate chimerism loss (OR 2.04, 95% CI 1.00–4.15, p=0.048). After adjustment for age, conditioning regimen, and diagnosis, survival analysis showed that <50% donor $CD3^+$ chimerism conferred increased mortality (adjusted HR 2.31, 95% CI 1.27–4.21, p=0.006), while PTLD was not independently associated with mortality after chimerism adjustment (HR 1.37, p=0.210).

Conclusions: EBV-driven PTLD is independently associated with loss of donor T cell engraftment, conferring four times the risk of major chimerism loss. While the causal mechanism remains unclear, subsequent $CD3^+$ chimerism status—rather than PTLD itself—is a strong independent predictor of survival. These findings highlight the critical importance of intensive chimerism monitoring in EBV-driven PTLD post allograft

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Ad board Kite Gilead

Infections and vaccination - Clinical

OS05-07

LOW T-CELL RESPONSES TO PHYTOHEMAGGLUTININ ARE ASSOCIATED WITH INCREASED RELAPSE AND MORTALITY AT 1-YEAR POST-CAR-T CELL THERAPY

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Background: T-cell responses to phytohemagglutinin (PHA), a polyclonal activator used as positive control in interferon-γ (IFN-γ) release assays, provide an accessible measure of global T-cell function. Low or indeterminate PHA-induced IFN-γ responses in the QuantiFERON TB assay have been associated with reduced overall survival, higher non-relapse mortality, and worse outcomes in hematopoietic cell transplant recipients. Assessing T-cell function in chimeric antigen receptor (CAR)-T cell therapy (CARTx) recipients could serve as a global marker of T cell activity and immune competence to identify patients at high risk for adverse outcomes.

Methods: We prospectively enrolled adult CMV-seropositive patients treated with CD19, CD20, or BCMA-targeted CARTx for hematologic malignancies at Fred Hutch Cancer Center from August 2021 through March 2023. We assessed CMV cell-mediated immunity using an IFN-γ release assay (T-SPOT®.CMV) pre- and at week 2 and 4 post-CARTx. T-cell responses to PHA were quantified. A low PHA value at two weeks post CARTx was defined as below the median value of the cohort (185 spot counts) and indeterminate responses as those that fail the positive control. Cox regression was used to assess the association of PHA T-cell responses and other clinically relevant variables (included in Table 1) with 1-year disease relapse and overall mortality. Data on CAR-T cell expansion, including peak PCR values and persistence, were collected when available (n=23) and compared by PHA category (high versus low) at week 2 post-CARTx

Results: 89 patients were enrolled; demographic and clinical characteristics are summarized in Table 1. Disease relapse occurred in 35% (n=31) of patients, and 27% (n=24) died within 1 year. Low and indeterminate PHA T-cell responses (combined) at week 2 post-CARTx were associated with lower peak and persistence of CAR-T cells (Figure 1A-B). Concordant with this observation, low and indeterminate PHA T-cell responses at week 2 post-CARTx were independently associated with increased disease relapse (low PHA: adjusted hazard ratio [aHR], 5.22; 95% confidence interval [CI], 1.98-13.8; p<0.001; indeterminate PHA: aHR, 4.45; 95% CI, 1.48-13.4; p=0.01, respectively). Low PHA T-cell responses at week 4 post-

CARTx remained significantly associated with an increased risk of overall mortality (aHR 3.14; 95% CI, 1.11-8.90; p= 0.003), in addition to the use of corticosteroids for >3 days (aHR, 7.14; 95% CI, 1.96-26.0; p=0.003).

Table 1. Demographic and clinical characteristics of the included patients

Characteristic	Total (N=89)
Age at time of CARTx (years), median (IQR)	65.0 (57.0-71.0)
Female sex, n (%)	40 (45%)
Underlying hematologic malignancy, n (%)	
ALL	3 (3%)
CLL	4 (4%)
Lymphoma	60 (67%)
Multiple Myeloma	19 (21%)
Waldenstrom macroglobulinemia	3 (3%)
Number of prior chemo treatment regimens ≥6, n (%)	24 (27%)
CARTx target, n (%)	
BCMA	19 (21%)
CD19/CD20	70 (79%)
CAR-HEMATOTOX score ≥2, n (%)	29 (33%)
PHA at 2-week post infusion, Median (IQR)	237.0 (110.0-456.0)
PHA at 4-week post infusion, median (IQR)	448.0 (238.0-554.0)
Any steroid use >3 days after day 14, n (%)	7 (8%)
ALC value at 2-week post infusion, median (IQR)	450.0 (260.0-910.0)
Maximum ICANS grade≥2 or CRS grade≥2, n (%)	42 (47%)

Characteristic	Total (N=89)
High risk disease for relapse/progression post CART infusion, n (%)	27 (30%)

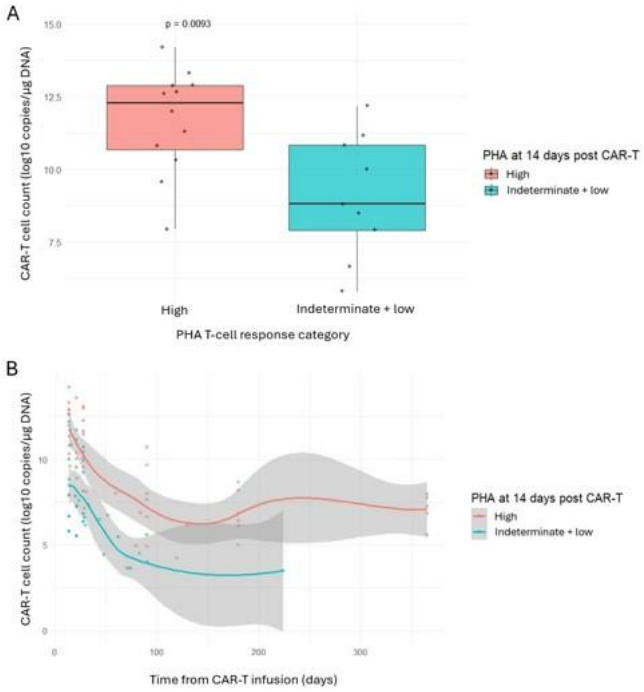

Figure 1. *A)* Distribution of peak CAR-T cell counts (log_{10}) according to PHA response at 14 days post-CARTx. *B)* CAR-T cell counts kinetics from day 14 through 1 year after CARTx, stratified by PHA response at 14 days post-CARTx. In both panels, the 'Indeterminate+low' category includes participants with values below the median (n=8) in addition to indeterminate responses (n=1) at week 2 post-CARTx.

Conclusions: PHA T-cell responses could represent a promising and accessible marker of T-cell function, correlating with CARTx efficacy, disease response, and survival. Low PHA responses following CARTx identify patients at higher risk of disease relapse and mortality, highlighting their potential as an early biomarker of impaired global T-cell function.

Disclosure: Eleftheria Kampouri: advisory boards Merck/MSD, speaker at symposia by Takeda Nordic, Biotest.
Joshua A. Hill reports consultancy for Moderna, Allovir, Gilead, Takeda, CSL Behring, Karius, Geovax, and Sanofi and research funding from Revvity (previously Oxford Immunotec), Gilead, Takeda, Merck, Geovax, and Sanofi.

OS09-01

CYTOMEGALOVIRUS CELL-MEDIATED IMMUNITY GUIDED LETERMOVIR PROPHYLAXIS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: AN OPEN-LABEL, MULTICENTER, RANDOMIZED, PHASE 3 TRIAL

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Background: Findings of retrospective studies suggested that cytomegalovirus (CMV)-specific cell-mediated immunity (CMV-CMI) might reduce clinically significant CMV infections (cs-CMVi) after letermovir withdrawn in allogeneic hematopoietic stem cell transplantation (allo-HCT). In this study, we aimed to evaluate the efficacy and safety of CMV-CMI guided letermovir prophylaxis for decreasing the late-onset cs-CMVi in patients following allo-HCT.

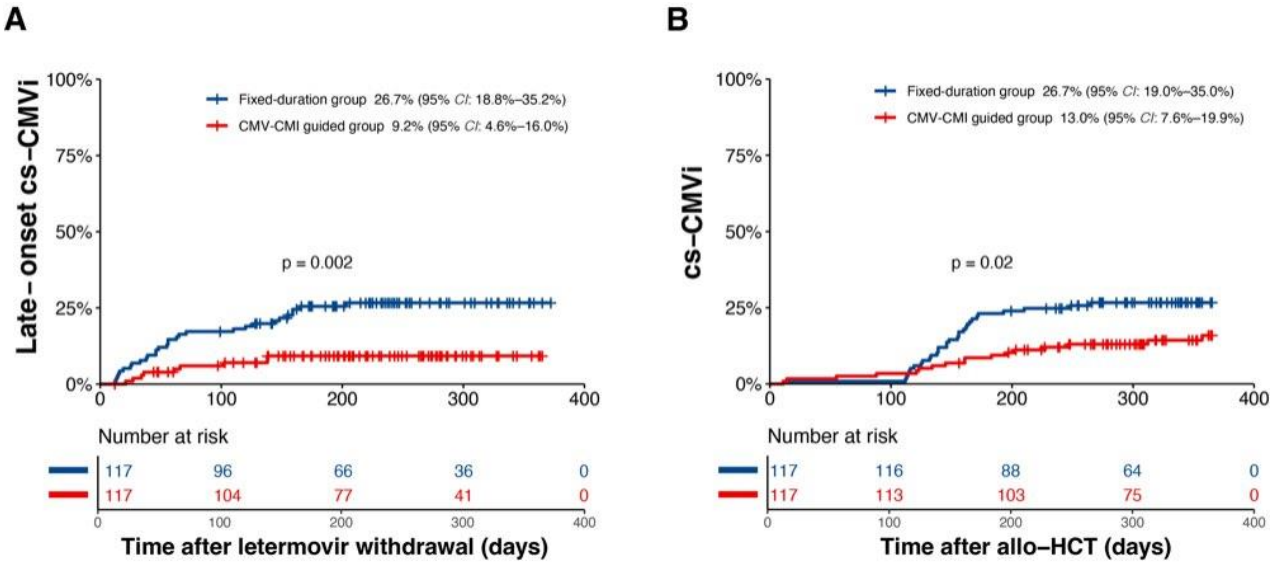
Methods: We conducted an open-label, randomized phase 3 trial at seven transplantation centers in China. Eligible patients (aged 18–70 years) underwent their first allo-HCT and received letermovir for CMV prophylaxis were enrolled. Randomization was performed using an electronic data capture (EDC) system with a stratified randomization ratio of 1:1, based on patient age and transplantation type at the transplantation day. The participants were divided into two groups: the CMV-CMI guided group (n=125), where letermovir was discontinued after achieving the CMV-CMI recovery, with a maximum treatment duration of 270 days post-transplantation; and the fixed-duration group (n=125), where letermovir was discontinued at day 100 after allo-HCT. Letermovir was given orally or intravenously at a dose of 480 mg daily from day 1, or 240 mg daily when in conjunction with cyclosporine A. CMV-CMI was evaluated with CMV-ELISPOT at at the 3rd, 5th, 6th, and 9th month post-HCT. The primary endpoint of this study was the cumulative incidence of late-onset cs-CMVi after letermovir withdrawal. This study was registered with ClinicalTrials.gov, NCT06449586, and is complete.

Results: Between July 2024 and May 2025, 250 patients were randomly assigned to the CMV-CMI guided group (n=125) or the fixed duration group (n=125). Median follow-up was 355 days (IQR 283, 436). The median age of the cohort was 42 (IQR 32, 54) years old, and 80.5% of the recipients received haploidentical related donor (HID) grafts were included in the study. The primary endpoint, cumulative incidence of late-onset cs-CMVi after letermovir withdrawal was significantly lower in the CMV-CMI guided group (9.2% [95% *CI:* 4.6%–

16.0%]) compared to the fixed duration group (26.7% [95% *CI:* 18.8%–35.2%], *P*=0.002) within the first year after allo-HCT. Additionally, the cumulative incidence of cs-CMVi within the first year after allo-HCT was also lower in the CMV-CMI guided group (13.0% [95% *CI:* 7.6%–19.9%]) compared to the fixed duration group (26.7% [95% *CI:* 19.0%–35.0%], *P*=0.02). In the multivariate analysis, reduced intensity conditioning (HR 2.97, 1.25–7.03; *P*=0.01) was a risk factor for late-onset cs-CMVi. Conversely, CMV-CMI guided strategy (HR 0.43, 0.21–0.88; *P*=0.02) was a protective factor against late-onset cs-CMVi. The most common adverse events among participants in the CMV-CMI guided group versus the fixed duration group were acute graft versus host disease (20 [16.9%] *vs*. 28 [23.7%]), poor appetite (14 [11.6%] *vs*. 18 [15.2%]) and EBV reaction (15 [12.7%] *vs*. 14 [11.8%]). There were no treatment-related deaths.

Conclusions: The CMV-CMI-guided strategy of letermovir use for CMV prophylaxis after allo-HCT is effective and safe in reducing the cumulative incidence of late-onset cs-CMVi after letermovir withdrawal.

	HR (95%CI)	***p*-value**
Letermovir prophylaxis		
fixed-duration	Reference	
CMV-CMI guided	0.43 (0.21–0.86)	0.017
Conditioning intensity		
MAC	Reference	
RIC	3.65 (1.74–7.65)	<0.001
Systemic steroid exposure No Yes	 Reference 0.61 (0.28–1.34)	 0.220



Clinical Trial Registry: This study was registered with ClinicalTrials.gov, NCT06449586, and is complete.

Disclosure: Nothing to declare

OS09-02

PREDICTORS OF PROTECTIVE ANTIBODY LEVELS IN ALLOGENEIC HCT RECIPIENTS FOLLOWING A STANDARDIZED POST-TRANSPLANT VACCINATION SERIES INCLUDING TWO DOSES OF MMR

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Background: Without vaccination, levels of antibodies against vaccine-preventable diseases decline after allo-HCT so that by 1-5 years after HCT, a substantial fraction of patients have the specific antibody levels undetectable or under the limit for protection. For measles, it is known that <80% achieve protective levels after one MMR dose. Little is known about the factors influencing the likelihood of achieving protective antibody levels after routine post-HCT vaccination, which in Alberta includes two doses of MMR, and whether the immunity achieved by the vaccination is durable and reaches the immunity of the general population.

Methods: Antibody levels to measles, hepatitis B and tetanus were measured before allo-HCT, and at 3 and 5 years after allo-HCT in recipients receiving a uniform vaccination series that included 2 doses of the MMR vaccine, 3 doses of the hepatitis B vaccine and 3 doses of a

tetanus containing vaccine, with the entire series typically completed by 2.5 years post-transplant. Donor antibody levels were measured at the time of donation. Univariable and multivariable analyses were undertaken to elucidate predictors of non-protective antibody levels in recipients.

Results: *Measles*
At 3 years post-transplant, 178 of 196 recipients (91%) had protective antibody levels versus 67 of 81 donors (83%) at the time of donation (p=0.06). Antibody levels were durable with 49 of 53 (92%) recipients with available levels at 5 years remaining with protective levels. In univariable analyses, non-protective antibody levels at 3 years post-transplant was associated with donor age <50 (i.e. born after 1970) (p=0.02), lower IgG levels at 6 months post-transplant (p=0.05), and possibly non-protective antibody levels in donors (p=0.06).
Hepatitis B
At 3 years post-transplant, 149 of 198 recipients (75%) had protective antibody levels versus 44 of 89 donors (49%) at the time of donation (p <0.01). Antibody levels were somewhat durable with 45 of 65 (69%) recipients with available levels at 5 years remaining with protective levels. In multivariable analyses, non-protective antibody levels at 3 years post-transplant was associated with receipt of immunosuppression beyond 1-year post-transplant (OR 0.21, p=0.02), recipient age >50 (OR 0.24, p=0.04), and possibly non-protective donor antibodies (OR 0.31, p=0.07).
Tetanus
At 3 years post-transplant, 226 of 259 recipients (87%) had protective antibody levels versus 93 of 109 donors (85%) at the time of donation (p=0.62). Antibody levels were somewhat durable with 57 of 76 (75%) recipients with available levels at 5 years remaining with protective levels. In multivariable analyses, non-protective antibody levels at 3 years post-transplant was associated with receipt of immunosuppression beyond 1-year post-transplant (OR 0.03, p<0.01) and receipt of rituximab in the first-year post-transplant (OR 0.05, p=0.03).

Conclusions: After 2 doses of MMR vaccination, 91% of allo-HCT recipients experience protective antibody levels against measles, with the proportion protected exceeding the proportion of donors protected. Protective antibody levels to measles at 3 years appear to be durable to at least 5 years post-transplant. Donors with probable natural immunity to measles through exposure (born before 1970) are associated with protective antibody levels in recipients.

Disclosure: Nothing to declare.

OS09-03

OUTCOME OF ADULT PATIENTS WITH HIV UNDERGOING AUTOLOGOUS OR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: A RETROSPECTIVE MULTICENTER STUDY OF THE IDWP

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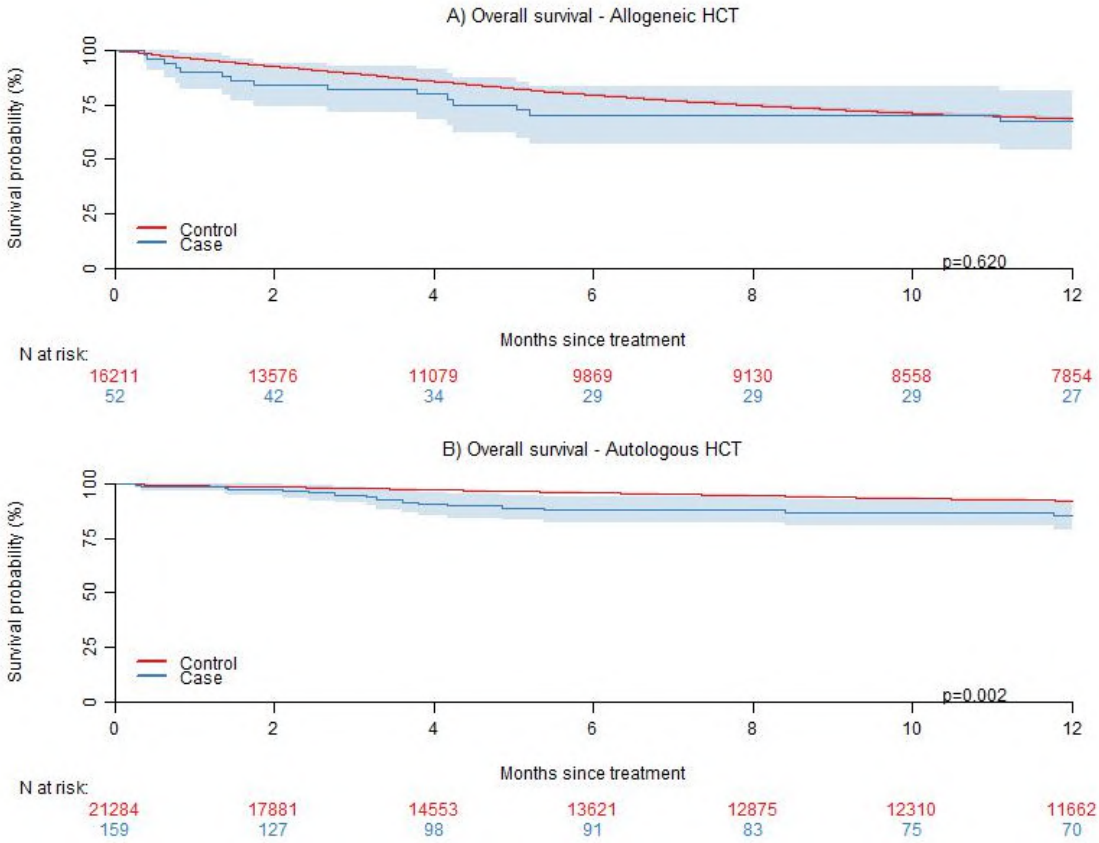
Background: With the improved life expectancy of people living with HIV (PLWH), the prevalence of hematological diseases and, therefore, the need for hematopoietic cell transplantation (HCT) is increasing. Despite initial reluctance, advance in supportive care has progressively improved HCT outcomes and expanded the number of patients considered eligible, including for allogeneic HCT. Despite these advances, uncertainty remains regarding safety and efficacy of HCT in PLWH with very limited data.

Methods: We retrospectively evaluated outcomes of autologous and allogeneic HCT in adult PLWH and compared them with negative controls in the EBMT registry. PLWH were defined as adults with HIV from EBMT member centres who received their first autologous or allogeneic

HCT between 2010 and 2023 and were HIV-positive at the time of transplant. The primary endpoint was 100-day non-relapse mortality (NRM). Secondary endpoints were 1-year NRM, relapse incidence (RI), progression-free survival (PFS), overall survival (OS), in HIV-positive and negative patients.

Results: Baseline characteristics were well balanced between cases and controls (Table 1). Among HIV-positive patients we identified 159 who underwent autologous HCT and were compared with 21,284 controls. The median age of cases was 48.5 (range 39.9-55.5) years, and 139 (87.4%) were male. Diagnosis was Non-Hodgkin B cell lymphoma in 96 (60.4%), and 87 (54.7%) were in complete remission (CR) at HCT. The conditioning regimen was BEAM in 79 (53.7%). NRM at 100 days was not significantly different among HIV-positive patients and negative controls (2% [95%CI 1-2%] and 3% [95%CI 0-6%], p=0.237). OS was significantly higher for HIV-negative controls than HIV-positive cases (92% [95%CI 92-92%] vs 85% [95%CI 79-92%] at 1 year, p=0.002) (figure 1a). PFS was similar between HIV cases and controls (81% [95%CI 74-89%] vs 80% [95%CI 79-80%] at 1 year, p=0.920).
We identified 52 HIV-positive adults who underwent allogeneic HCT and compared them with 16,211 controls. The median age was 44.1 (36.4-55) years and 36 (69.2%) were male. Diagnosis was acute myeloid leukemia in 21 (40.4%) and 38 (73.1%) underwent allogeneic HCT in CR. Myeloablative conditioning was used in 30 (57.7%) and graft source was peripheral blood in 44 (84.6%). The most frequent donor type was a matched unrelated donor in 16 (30.8%). The 100-day NRM did not differ significantly between groups (9% [95%CI 8-9%] for controls and 12% [95%CI 3-21%] for cases, p=0.776). One-year OS was also similar between HIV-positive patients and negative controls (68% [95%CI 54-81%] vs 68% [95%CI 68-69%], p=0.620) (figure 1b). PFS and RI were also not significantly different between the two groups.



	GROUP	control auto-HCT	case auto-HCT	control allo-HCT	case allo-HCT
		21284	159	16211	52
Patient sex	male female	12610 (59.2%) 8674 (40.8%)	139 (87.4%) 20 (12.6%)	9067 (55.9%9 7144 (44.1%)	36 (69.2%9 16 (30.8%)
Age at HCT (years)	median (IQR)	57.9 (49.1-64)	48.5 (39.9-55.5)	50.9 (37-60.8)	44.1 (36.4-55)
Disease	acute leukemia multiple myeloma lymphoma MDS/MPN	11347 (53.3%) 9937 (46.7%)	17 (10.7%) 142 (89.3%)	12879 (79.4%) 751 (4.6%) 2581 (15.9%)	31 (59.6%) 13 (25%) 8 (15.4%)

Disease status at HCT	complete remission other	8240 (38.7%) 13044 (61.3%)	87 (54.7%) 72 (45.3%)	12706 (78.4%) 3505 (21.6%)	38 (73.1%) 14 (26.9%)
conditioning (alloHCT)	RIC MAC			6716 (42.2%9 9210 (57.8%)	22 (42.3%9 30 (57.7%)
conditioning (autoHCT)	BEAM other	6380 (34.4%) 12168 (65.6%)	79 (53.7%) 68 (46.3%)		

Conclusions: This is one of the largest reported series of HCT for PLWH. We observed a modestly lower OS for autologous HCT in the HIV group though rates remained acceptable. No differences were detected in any other outcomes. Overall, these findings support the inclusion of carefully selected HIV-positive patients in standard transplant pathways for both autologous and allogeneic HCT, highlighting the need for continued data collection and reinforcing that HIV infection is no longer a contraindication to HCT.

Clinical Trial Registry: NA

Disclosure: Nothing to declare

OS09-04

PRITELIVIR DEMONSTRATED SUPERIOR EFFICACY COMPARED TO INVESTIGATOR'S CHOICE TREATMENT FOR REFRACTORY HERPES SIMPLEX VIRUS INFECTIONS IN IMMUNOCOMPROMISED PATIENTS: PRIOH-1, PHASE 3 SAFETY AND EFFICACY

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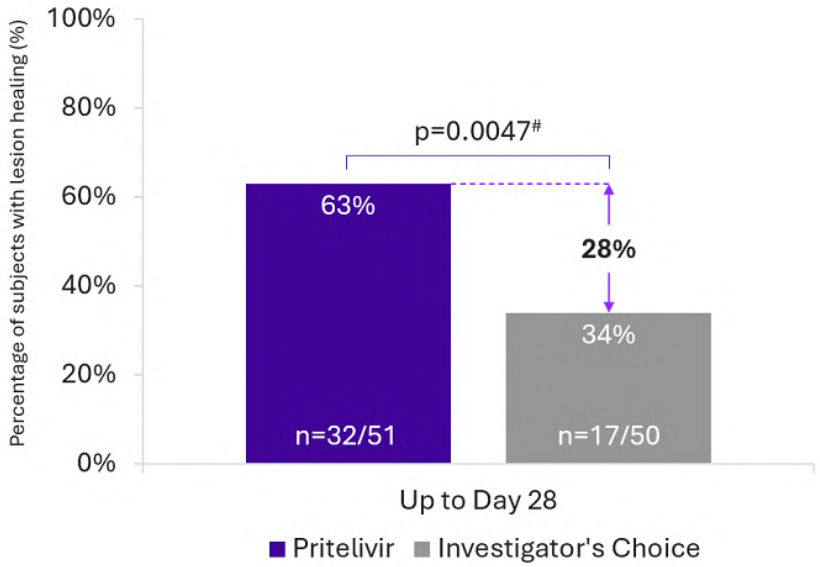
Background: Pritelivir is a novel oral helicase-primase inhibitor, active against HSV-1 and HSV-2, including strains resistant to nucleoside analogues and foscarnet. PRIOH-1 evaluated the safety and efficacy of pritelivir vs. investigator's choice therapy (ICT) in immunocompromised (IC) patients with refractory herpes simplex virus (HSV) infection, with or without resistance (R±R).

Methods: In this randomized (1:1), controlled, open label trial, 101 IC patients (≥16 years) with R±R HSV mucocutaneous infection received oral pritelivir (100 mg daily; 400 mg loading dose) or ICT (IV foscarnet, IV/topical cidofovir, or topical imiquimod) for up to 28 days, extendable to 42 days. Eligibility criteria included hematopoietic cell transplant, solid organ transplant, HIV, malignancy, or chronic use of immunosuppressive treatment with refractory/clinical failure (defined as no clinical improvement of lesions after ≥7 days of standard of care nucleoside analogue therapy or confirmed acyclovir resistance). The primary endpoint was complete lesion healing within 28 days. Secondary endpoints included safety and tolerability.

Results: The mean age of patients was 52.6 years (range 19-84 years) and 52.5% were male. Refractory HSV was diagnosed in 71.3%, and acyclovir resistant infection in 28.7%. HSV-1 and HSV-2 were identified in 31.7% and 45.5% of patients, respectively. Immunocompromised conditions included transplant (43.6%), oncology and other indications (including autoimmune, primary immunodeficiency disorders, and use of chronic immunosuppressive agents) (33.7%), and HIV infection (22.8%). Pritelivir demonstrated superior lesion healing of 62.7% vs. 34.0% for ICT up to 28 days, resulting in an adjusted treatment difference of 28.4%, p=0.0047 [95% CI: 9.6, 47.3] (Fig.1). The most common TEAEs are presented in Table 1. The majority of events are lower for pritelivir vs. ICT. Pritelivir was associated with fewer renal, electrolyte events and drug-related TEAE discontinuations (2.0%) compared with ICT (20.0%).

Conclusions: Pritelivir met the Phase 3 primary endpoint, demonstrating statistically superior efficacy compared with ICT, with a favorable safety and tolerability profile. These findings support pritelivir as a promising oral agent to address the unmet needs of refractory HSV infections in IC patients.

Figure 1 Summary of lesion healing rate: primary efficacy endpoint (28 days)



#Stratified Cochran Mantel Haensel (CMH) test adjusted for protocol versions (4.0 and earlier, 5.0 and later)

Table 1 Incidence of TEAEs (≥ 10%): Pritelivir vs. investigator's choice (ICT)

MedDRA preferred term	Pritelivir (N=51)	ICT (N=50)
Any TEAE (n%)	40 (78.4%)	44 (88.0%)
Headache	7 (13.7%)	6 (12.0%)
Nausea	4 (7.8%)	12 (24.0%)
Diarrhoea	6 (11.8%)	7 (14.0%)
Vomiting	3 (5.9%)	5 (10.0%)
Hypokalaemia	0	7 (14.0%)
Hypomagnesaemia	1 (2.0%)	6 (12.0%)
Thrombocytopenia	1 (2.0%)	6 (12.0%)

Clinical Trial Registry: NCT03073967

Disclosure: Genovefa Papanicolaou: Research funding paid by Aicuris to institution
Yeon Joo Lee: Research funding paid by Aicuris to institution

Anna Wald: Grant provided by Aicuris to institution
Roy Chemaly: Honorarium paid by Aicuris for Medical Affairs consultations

OS09-05

LETERMOVIR USE IN PEDIATRIC HSCT PATIENTS UNDER 12 YEARS OLD: UPDATED DATA FROM A RETROSPECTIVE MULTICENTER STUDY OF THE PDWP AND IEWP OF THE EBMT

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Background: Letermovir is widely used in adult allogeneic haematopoietic stem cell transplantation (HSCT) for CMV prophylaxis and has recently been authorised for paediatric use. However, data remain limited for children under 12 years treated in real-world settings. We report outcomes of letermovir prophylaxis in a large multicentre paediatric HSCT cohort.

Methods: We performed an updated multicentre retrospective analysis (2019–2025) within the PDWP and IEWP of the EBMT. A total of 146 HSCT recipients under 12 years (median age 7.2 years; range 0.1–11.9) received letermovir as primary (n=115) or secondary (n=31) prophylaxis (Table 1). Letermovir was administered orally (82.2%), intravenously (13.7%), or via both routes (4.1%). Conditioning regimens included treosulfan-based (44.5%), TBI-based (32.2%), busulfan-based (15.1%), and other (8.2%). In-vivo T-cell depletion (TCD) was used in 34.2% of patients (ATG 27.4%, Campath 6.8%), and ex-vivo TCD in 11.6%.

Table 1: Patient and transplant characteristics

Characteristics	Primary prophylaxis N = 115	Secondary prophylaxis N = 31	Overall N = 146
Diagnosis for HSCT (groups), n (%)			
ALL, AML, MDS and Lymphoma	60 (52.2%)	16 (51.6%)	76 (52.1%)
Haemoglobinopathies	17 (14.8%)	1 (3.2%)	18 (12.3%)
PID, DOM and histiocytosis	21 (18.3%)	11 (35.5%)	32 (21.9%)
Others	17 (14.8%)	3 (9.7%)	20 (13.7%)
Donor, n (%)			
Haploidentical HSCT	31 (27.0%)	8 (25.8%)	39 (26.7%)
Identical sibling	11 (9.6%)	5 (16.1%)	16 (11.0%)
UD 10/10	40 (34.8%)	11 (35.5%)	51 (34.9%)
Others	33 (28.7%)	7 (22.6%)	40 (27.4%)
Stem cell source, n (%)			
BM	45 (39.1%)	10 (32.3%)	55 (37.7%)
PB	63 (54.8%)	19 (61.3%)	82 (56.2%)
CMV donor to patient, n (%)			
D:Negative; P:Negative	1 (0.9%)	1 (3.6%)	2 (1.4%)
D:Negative; P:Positive	47 (42.3%)	9 (32.1%)	56 (40.3%)
D:Positive; P:Negative	14 (12.6%)	1 (3.6%)	15 (10.8%)
D:Positive; P:Positive	49 (44.1%)	17 (60.7%)	66 (47.5%)

Unknown	4	3	7

Results: With a median follow-up of 1 year (95% CI: 0.9–1.1), the 1-year cumulative incidence of CMV reactivation was 23.8% (95% CI: 16–30) overall, 21.4% (95% CI: 13.6–29.2) during primary prophylaxis, and 32.6% (95% CI: 13.1–45) during secondary prophylaxis (Figure 1). One-year overall survival was 87.3% (95% CI: 79.5–92.2), with comparable outcomes between primary 88.2% (95% CI: 79.5–93.4) and secondary 83.9% (95% CI: 61.9–93.8) prophylaxis.

Among CMV-seropositive recipients with seronegative donors (n=56), CMV reactivation occurred more frequently than in seropositive donor-recipient pairs (32.1% versus 17.8%). In the seropositive recipient with seronegative donors group, seven patients died without prior CMV-reactivation (1-year incidence 13.3% [95% CI: 5.1–25.4]). Among the patients with seropositive donors (n=82), 14 patients experienced CMV reactivation (17.8% [95% CI: 10.2–27]) and 7 died without reactivation (9.1% [95% CI: 3.6–17.7]).

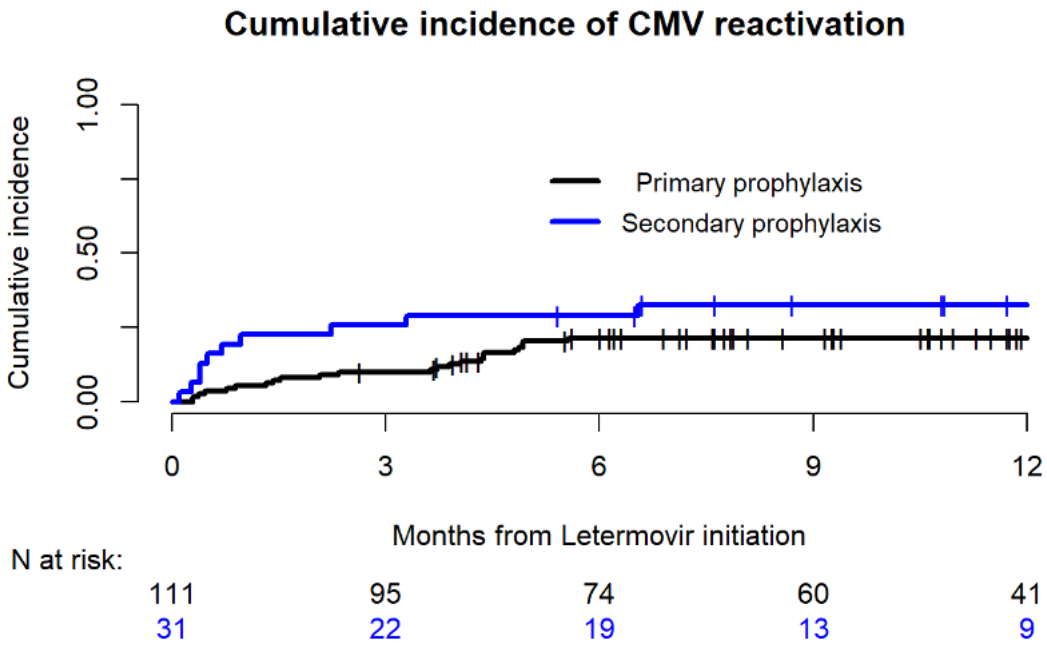
Of the 17 CMV-seronegative patients, two received grafts from CMV-negative donors and letermovir as secondary prophylaxis; both are alive at last follow-up, one with and one without CMV reactivation.

Causes of death included relapse (5), non-CMV infections (3), GvHD (2), hypovolaemic shock (1), pulmonary vascular event (2), and veno-occlusive disease (1). Among patients with CMV reactivation, one death was attributed to relapsed disease.

Letermovir was well tolerated with only two patients experiencing mild gastrointestinal toxicity, and no additional significant adverse events reported.

CMV reactivations were managed using standard antiviral strategies, including valganciclovir (n=10), ganciclovir (n=8), foscarnet (n=7), and cidofovir (n=1) or continued letermovir alone (n=8). All but one patient achieved complete viral clearance by end of follow-up. There were no CMV-related deaths in the cohort.

Figure 1: Cumulative incidence of CMV reactivation



Conclusions: In this large real-world pediatric HSCT cohort in children under 12 years of age, letermovir demonstrated high efficacy and excellent tolerability in both primary and secondary prophylaxis. Breakthrough reactivations were infrequent and generally manageable, supporting routine use of letermovir in paediatric HSCT recipients.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

OS09-06

IMPACT OF CMV INFECTION IN PATIENTS WITH LYMPHOMA AFTER CAR-T THERAPY. AN INTERNATIONAL STUDY ON BEHALF OF IDWP, LWP, AND CTIWP OF EBMT

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Background: CMV is among the most frequent infections early after CAR-T therapy, but only incidental CMV disease cases have been reported. The impact of CMV on non-relapse mortality (NRM) and survival after CAR-T treatment is largely unexplored.

Methods: In this registry-based study, we analysed CMV infection (CMVi) (defined as a positive CMV-PCR) in adult patients with lymphoma who received their first CAR-T infusion between 2019-2024, and in whom at least one CMV-PCR test was performed after CAR-T infusion and the result reported as negative or positive. CMV-PCR monitoring was not standardized across centers, and testing frequency was heterogeneous and center-dependent . The primary endpoint was the impact of CMVi on NRM at 1 year after CAR-T. Because most CMVi occur early, a 50-day landmark analysis was performed, comparing outcomes between patients who developed CMVi by day 50 and those who did not.

Results: 1,429 patients were reported from 22 countries. Baseline characteristics are shown in Table 1.
A CMVi developed in 205 patients, with a median time of 23 days after CAR-T (min-max:0-1282). 73% occurred ≤ 50 days after CAR-T. The cumulative incidence at 100 days was 10% (95%CI 9-12%), higher in CMV seropositive than in seronegative patients (19% (95%CI 15-23%) vs 1% (95%CI 0-3%), p<.001).
The NRM at 1 year was 8% (95%CI 7-10%) for all patients, and 11% (95%CI 6-17%) for those with CMVi. In the Cox model, CMVi was associated with higher NRM (HR 2.51, 95%CI 1.56, 4.01; p <.001) (Figure 1).
In the Kaplan-Meier(KM) landmark analysis at 50 days, the overall survival(OS) at 1 year was significantly lower in those with vs without CMVi (62% (95%CI 52-71%) vs 74% (95%CI 71-76%) p=.003). In the Cox model, CMVi was associated with lower survival (HR 2.11; 95%CI 1.65,2.70; p<.001), as were male sex (HR 1.29; 95%CI 1.07,1.55; p=.0008), relapse/progression at CAR-T (HR 1.59; 95%CI 1.30,1.94; p<.001), ECOG ≥2 (HR 2.68; 95%CI 2.05,3.51; p<.001), and year of CAR-T (lower for 2023-2024 (HR 1.46, 1.67) vs 2019-2020; p<0.03).
In the KM landmark analysis at 50 days, the relapse/progression rate at 1 year was no different in those with vs without CMVi (36% vs 37%, p .75). In the Cox model, CMVi was associated with higher risk of relapse/progression (HR 1.36; 95% CI 1.01-1.84; p=.043), as were male sex (HR 1.23;p=.021), relapse/progression at CAR-T (HR 1.71;p<.001), ECOG ≥2 (HR 1.81;p<.001), use of tisagenlecleucel(Kymriah®) (HR 1.37;p=.006), and year of CAR-T infusion (higher for 2022-2024 (HR 1.92, 2.60, 3.35) vs 2019-2020, p<.001).
In a Cox model landmark analysis at 50 days, CMVi was associated with a significantly lower OS at 1 year (HR 1.43; 95%CI 1.04,1.96, p=.026) but did not significantly affect NRM (HR 1.43 95%CI 0.78,2.63, p=.2) or relapse/progression (HR 1.0; 95%CI 0.71,1.41; p>.9).

Table 1 Baseline characteristics of CAR T patients

Total Number of patients	**1,429**
Age at infusion, median (Min-Max)	**63.8** (18.1-86.3)

Table 1 Baseline characteristics of CAR T patients

Sex (male/ female)	**875** (61.2%) / **554** (38.8%)
CMV serology at CAR T: seropositive / seronegative	**431 / 246** (missing 752)
ECOG status prior to CAR T nº (%) • 0 / 1 /2 / 3 / 4	(Available data on 1351) **617/ 618 / 95 / 19 / 2**
Type of lymphoma • DLBC / MCL • Other large B-cell lymphomas • Follicular lymphoma • Primary mediastinal large B-cell	(Available data on 1,419) **914** (63.9%) / 160 (11.2%) **156** (10.9%) **60** (4.2%) **38** (2.6%)
Lymphoma status at CAR T. nº (%) • CR / PR • Relapse-progression / Stable disease	(Available data on 1,369) **152** (11.1%) / **355** (25.9%) **748** (54.6%) / **114** (8.3%)
Type of CART used • axicabtagene ciloleucel (Yescarta@) / tisagenlecleucel (Kymriah®) • brexucabtagene autoleucel (Tecartus@)/ lisocabtagene maraleucel (Breyanzi@)	**989(** 69.2%) / **245** (17.1%) **161**(11.3%) / **34** (2.4%)
Lymphodepleting prior to CAR T • Fludarabine + cyclophosphamide / Others	(Available data on 1,375) **1325** / 50
Prior HCT: Autologous / Allogeneic	**321** (22.5%) / **27** (1.9%)

Figure 1

Cox model NRM - time-varying cmv

Variables, N=1353	HR	95% CI	p-value
CMV	**2.51**	1.56, 4.01	**<0.001**
Sex			
Female	—	—	
Male	**1.50**	1.06, 2.12	**0.023**
Year of therapy			
2019/2020	—	—	
2021	**2.30**	1.17, 4.50	**0.016**
2022	**2.17**	1.08, 4.37	**0.031**
2023	**2.71**	1.35, 5.43	**0.005**
2024	**3.17**	1.46, 6.89	**0.004**
Age at treatment	**1.33**	1.14, 1.56	**<0.001**
Disease stage at CT			
CR + PR	—	—	
Rel/prog	**1.42**	1.00, 2.03	**0.050**
Stable	0.94	0.47, 1.89	0.9
NA	1.83	0.79, 4.27	0.2
CAR-T product			
Yescarta	—	—	
Breyanzi	1.99	0.82, 4.83	0.13
Kymriah	**0.59**	0.35, 1.01	**0.053**
Tecartus	**1.72**	1.12, 2.64	**0.013**
Previous transplant			
No	—	—	
Yes	0.98	0.67, 1.42	>0.9
ECOG score			
ECOG 0-1	—	—	
ECOG 2+	**3.56**	2.28, 5.55	**<0.001**
Missing	1.33	0.65, 2.69	0.4
frailty(treatment_cic)			0.023

Abbreviations: CI = Confidence Interval, HR = Hazard Ratio

Conclusions: In this large series of lymphoma patients treated with CAR-T, CMVi was associated with a significantly higher NRM, relapse/progression and lower OS at 1 year after CAR-T infusion. In the 50-day landmark analysis, CMVi continued to adversely affect OS, although its impact on NRM and relapse/progression was no longer significant.

Disclosure: No conflict of interest

OS09-07

INTRAVENOUS BRINCIDOFOVIR EFFECTIVELY REDUCES CMV DNAEMIA IN ANTIVIRAL EXPERIENCED IMMUNOCOMPROMISED PATIENTS: RESULTS OF A PHASE 2A CLINICAL TRIAL

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Background: Cytomegalovirus (CMV) infection and disease remain major causes of morbidity and mortality among immunocompromised patients, and limited existing treatment options are either associated with renal or bone marrow toxicities or can rapidly select for resistance. Brincidofovir (BCV) is a lipid conjugate of cidofovir that overcomes cidofovir's dose-limiting nephrotoxicity while enhancing antiviral activity against CMV and other double-stranded DNA viruses. Here, we report data from CMV Cohorts of the Phase 2a ATHENA study (BCV-PA01: NCT04706923) that evaluated multiple ascending doses of intravenous (IV) BCV for safety, tolerability and antiviral activity against adenovirus or CMV.

Methods: Eligible immunocompromised patients ≥2 months of age with CMV plasma levels ≥ 500 IU/ mL, with or without evidence of tissue invasive CMV disease, were enrolled. Dosing consisted of IV BCV 0.4 mg/kg twice weekly (BIW; max 20 mg) in Cohort A and 0.5 mg/kg BIW (max 25 mg) in Cohort B for ≤14 weeks. Treatment emergent and treatment related adverse events (TEAEs/TRAEs) and virologic response (measured as change in plasma CMV DNAemia) were assessed throughout the study. CMV was quantified weekly using the Eurofins CMV qPCR (plasma) 5500 assay with a limit of quantitation (LOQ) of 96 IU/mL (2.0$\log_{10}$).

Results: Of 19 treated patients (primarily hematopoietic cell transplant recipients), 18 (9 in each Cohort) received more than one dose of BCV and were evaluated for virologic response. Most patients (7/9 per Cohort) had failed ≥1 prior CMV antiviral (n=12 GCV or valGCV, 4 foscarnet, 4 letermovir, and 2 maribavir). Mean baseline CMV DNAemia was 3.99 $\log_{10}$ IU/mL in Cohort A and 3.39 $\log_{10}$ IU/mL in Cohort B. Most patients in Cohort A (8/9) and Cohort B (6/9) received 4 weeks of treatment with BCV. At this timepoint, CMV DNAemia decreased to <LOQ for 2/9 (22%) and 5/9 (56%) subjects in Cohort A and B, respectively. This difference is likely influenced by higher baseline viral load in Cohort A as the mean decline in CMV DNAemia was approximately 1.3 $\log_{10}$ IU/mL for both cohorts (Figure 1). Within 8 weeks, CMV DNAemia decreased to <LOQ for 4/9 (44%) and 8/9 (89%) subjects in Cohort A and B,

respectively. The average decrease in CMV DNAemia after 8 weeks was -1.67 log_{10} IU/mL in Cohort A and -1.80 log_{10} IU/mL in Cohort B (Figure1). As expected for this population, TEAEs were common (Table 1), and possible drug related AEs included mild diarrhea (1 in Cohort A and 1 in Cohort B), liver enzyme elevations (2 in Cohort B), and an allergic reaction (1 Cohort B). There were two deaths in Cohort A, both considered unrelated to IV BCV.

Figure 1. Plasma CMV (DNA log IU/mL) Change from Baseline

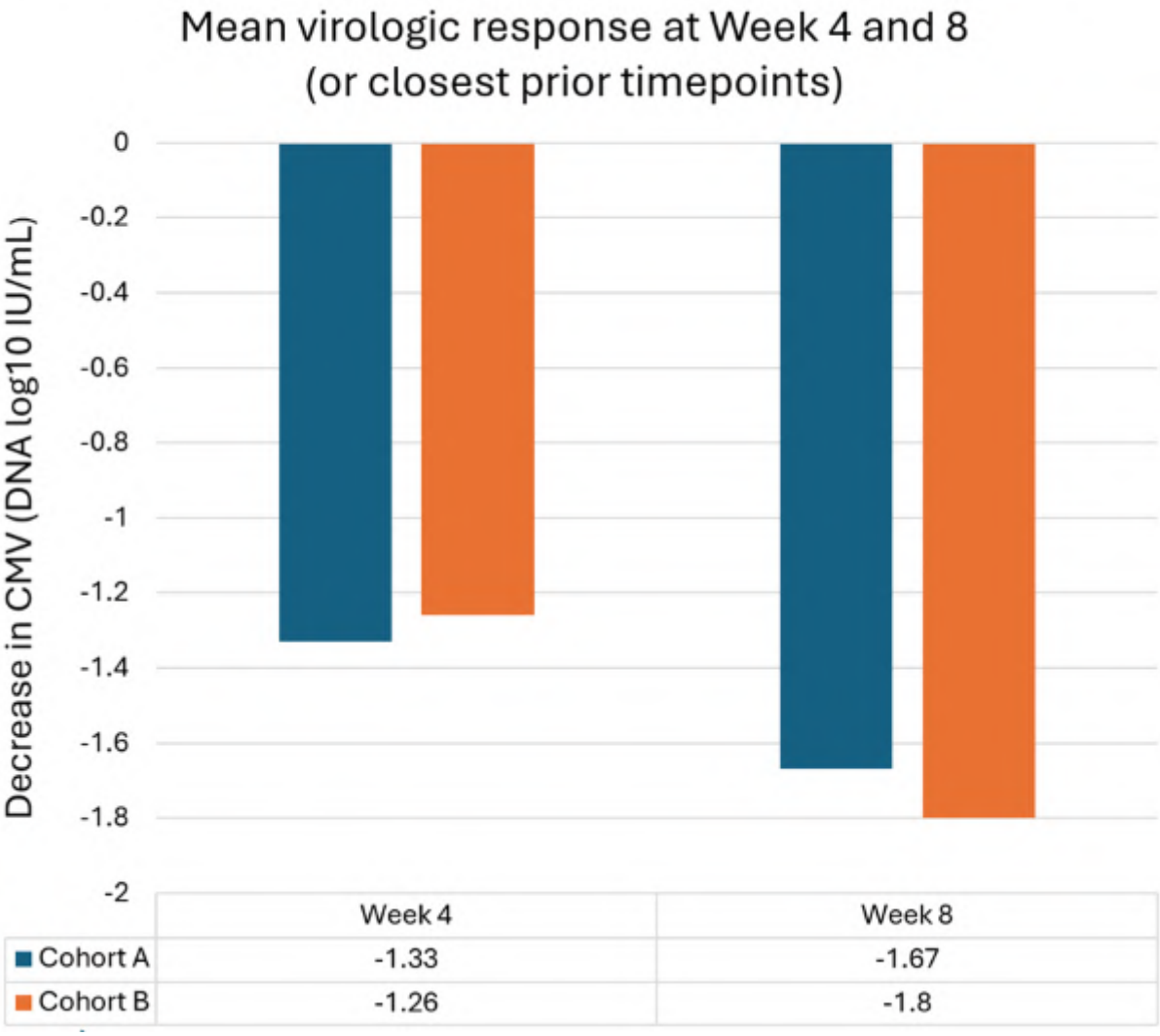

Table 1. Treatment Emergent Adverse Events

	Cohort A – 0.4 mg/kg BIW n=9 (%)	Cohort B – 0.5 mg/kg BIW n=10 (%)

Table 1. Treatment Emergent Adverse Events

TEAEs, Total	7 (77.7%)	7 (70%)
TRAEs	3 (33%)	5 (50%)
Serious TEAE (SAEs)	1 (11.1%)	6 (60%)
Treatment Related SAE	0	1 (10%)*
TEAEs leading to discontinuation	1 (11.1%)	6 (60%)
Drug Related TEAEs leading to discontinuation	1 (11.1%)	4 (40%)
Death	2 (22.2%)	0
		*Allergic Reaction

Conclusions: IV BCV was effective in reducing CMV DNAemia and was reasonably well tolerated in this population of pre-treated immunocompromised patients with CMV viremia. IV BCV is a potential treatment option for these patients with limited treatment options. These data support further study of IV BCV for treatment of CMV infections in immunocompromised patients.

Clinical Trial Registry: Clintrials.gov NCT04706923

Disclosure: Fareed Khawaja, Genovefa Papanicolaou, Michael Grimley, Carlos Gomez, Kris Mahadeo, Caitlin Elgarten, Gabriela Maron, and Roy Chemaly served as clinical investigators on NCT04706923. Roy Chemaly also serves as an advisor to Symbio. Randall Lanier, Inger Nielsen-Orzeck, Rochelle Maher, and Nkechi Azie were employed by Symbio during the conduct of NCT04706923.

OS09-08

MARIBAVIR FOR CLINICALLY SIGNIFICANT CYTOMEGALOVIRUS INFECTION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE INTERNATIONAL REAL-WORLD STUDY OF IDWP OF EBMT

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Background: Despite letermovir prophylaxis, refractory or resistant (R/R) Cytomegalovirus (CMV) infections occur. Maribavir (MBV) was approved in Europe in November 2022 for the treatment of R/R CMV in adults who undergone allogeneic hematopoietic stem cell (allo-HCT) or solid organ transplantation, but real-world data in allo-HCT recipients remain scarce.

Methods: We conducted a retrospective multicenter study in EBMT centers, including adult and pediatric allo-HCT recipients who received MBV for CMV infection or disease after its approval in Europe (including off-label use). Compassionate use was excluded. The primary endpoint was clinical outcome after MBV initiation; secondary endpoints included reasons for discontinuation, overall survival (OS), and non-relapse mortality (NRM) at 12 weeks.

Results: One hundred six adults and 9 pediatric patients were included. Eight patients had more than one MBV course for a total of 123 MBV courses with a median duration of 7.8 (min-max 0.6-26.6) weeks. Acute leukemia was the most common disease (n=61, 53%) and most of the patients underwent a haploidentical HCT (n=41, 36%). The graft-versus-host disease prophylaxis was post-transplant cyclophosphamide-based in 63 (55%); 60 (52%) had received prophylaxis with letermovir. Treatment with MBV was given as: first line pre-emptive (PET) in 24 (20%), second line PET in 60 (49%), third or more line PET in 22 (18%), first line treatment for CMV disease in 1 (1%), second line in 6 (5%) and third line or more in 10 (8%) courses. A test for resistance before starting MBV was reported for 8 courses. Mutations identified were: UL54 in one, UL54 and UL97 in two, UL56 in two, UL97 in two, and UL56 + UL97 in another one.
Among the 106 PET courses, 87 (83%) had CMV resolution, 11 (10%) progressed on MBV, 6 (6%) had response and rebound, and in 2 cases (1%) response was not evaluable due to

death or lost to follow-up. A CMV viremia requiring antiviral treatment within 12 weeks from MBV initiation was observed in 17 courses. In 5 cases a CMV end organ disease (EOD) developed. One patient had a proven CMV pneumonia, two had proven CMV gastrointestinal disease (GID), one had a probable CMV retinitis and another had a probable CMV encephalitis.
Among the 17 courses given for CMV disease, all were proven: 12 patients had CMV GID, two had a CMV GID and pneumonia, one had a pneumonia, in one case a CMV skin disease (biopsy-proven), and in one case a combination of CMV cystitis, GID, hepatitis and pneumonia. Response was not evaluable in 3 cases, 12 (71%) responded to MBV and progression was observed in two cases.
OS and NRM were 82% (95% CI 74–89%) and 16% (95% CI 9-22%) at 12 weeks.
Discontinuation was due to planned therapy completion (n=88, 72%); failure (n=14, 13%) including no response (n=8, 6%) or response and rebound (n=6, 5%), death (n=13, 11%), side effects (n=4, 3%), supply problem (n=3, 2%), other (n=1, 1%).

Conclusions: This large real-world study confirms MBV as an effective and well-tolerated option for CMV infection and disease in allo-HCT recipients

Clinical Trial Registry: NA

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OS19-01

TOXOPLASMOSIS SCREENING, PROPHYLAXIS AND TREATMENT PRACTICES ACROSS EBMT CENTERS: A SURVEY ON BEHALF OF THE INFECTIOUS DISEASES WORKING PARTY

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Background: Toxoplasmosis is a potentially life-threatening complication after allogeneic stem cell transplantation (allo-HSCT). In 2024, new ECIL guidelines were published on the management of *Toxoplasma gondii* infection and disease in this setting.

Methods: On behalf of the Infectious Diseases Working Party (IDWP), we conducted a survey addressing current practices in EBMT centers and alignment with ECIL guidelines.

Results: Overall, 140 EBMT centers performing allo-HSCT participated in the survey. Responses and ECIL recommendations are reported in table 1.
PCR technique for *T. gondii* detection is widely available (132/140, 94%), reimbursed for toxoplasmosis screening and diagnostic purpose in 87/140 (62%) centers, only for disease diagnosis in 17/140 (12%), not reimbursed in 35/140 (25%). Screening after allo-HSCT is offered in 67/140 (48%) centers, beginning either on the day of transplant (38/66, 57%) or after engraftment (28/66, 42%) and continued variably: more frequently until engraftment (19/63, 30%), during first 3mo after allo-HSCT (18/63, 28%), during immunosuppressive therapy (14/63, 22%), until CD4+>200/µL (13/63, 20%).
Prophylaxis is offered in 127/140 (91%) of centers, in most cases to all recipients in 90/127 (71%), whereas in 20/127 (16%) it is restricted to IgG-positive, in 9/127 (7%) only in presence of additional risk factors.
Prophylaxis is generally started after engraftment (94/126, 75%) and variably continued: at least 6mo in 31/126 centers (25%), 1y in 22/126 (17%), until CD4+>200/µL in 38/126 (30%), >400 CD4+/µL in 24/126 (19%), until immunosuppression discontinuation in 23/126 (18%). In 99/100 (99%) of centers, prophylaxis is trimethoprim-sulfamethoxazole. If trimethoprim-sulfamethoxazole is contraindicated, most employed alternatives are atovaquone ± pyrimethamine (45/126, 36%) or nothing (27/126, 21%).
In asymptomatic patients, anti-toxoplasma therapy is initiated after a single positive blood PCR in 19/67 (28%) centers, in 2/67 (3%) only if the patient is considered high-risk, in 7/67 (10%) only if the PCR-value is very high. In 24/67 (36%) two consecutive positive PCR-results are required. Specific assessments are variably performed: cerebral MRI (49/67, 73%), lung CT (42/67, 63%), ophthalmic examination (43/67, 64%), lumbar puncture (20/67, 30%) and bone marrow assessment (10/67; 15%).
Anti-toxoplasma therapy relies on trimethoprim-sulfamethoxazole, pyrimethamine-sulfadiazine and pyrimethamine-clindamycin with similar distribution for infection (73/134, 54%; 49/134, 37%; 10/134, 7%) and disease (66/132, 50%; 54/132, 41%; 9/132, 7%). The preferred regimen for neuro-toxoplasmosis is pyrimethamine-sulfadiazine (61/129, 47%) or trimethoprim-sulfamethoxazole (45/129, 35%).
Treatment for infection is continued in 71/132 (54%) centers until two negative PCRs, in 10/132 (8%) until one. A fixed duration criteria is often considered (< 4w in 5/133, 4% of centers; 4-7w in 32/133, 24%; 8-12w in 16/133, 12%) and more frequently applied while treating toxoplasmosis disease (< 4w in 7/131, 5% centers; 4–7w in 64/131, 49%; 8–12w in 41/131, 31%; >12w in 19/131, 15%). Imaging resolution of pathologic finding is often required (88/131, 67%) before treatment discontinuation.

Toxoplasmosis management – Survey results (n = 140). Number of centers are presented	**ECIL guidelines recommandations, graded for the level of proof and**

			strength of recommandation [Aerts et al., Lancet Inf Dis 2024]
Screening	Screening with qPCR	Yes- 67/140 (48%); no- 73/140 (52%).	qPCR screening recommended for seropositive recipients. A-B II
	Start	Day 0 - 38/66 (58%); after engraftment -28/66 (42%).	PCR screening should start from day 0. A II
	Frequency	<1x week - 17/66 (26%); 1x week - 33/66 (50%); 2x week - 4/66 (6%); > 2x week - 12/66 (18%).	The screening should be at least once per week until day 100, then at least every 2 weeks until day 180, adapted to the schedule of patient follow-up and the intensity of immunosuppression. B II
	Duration (one or more possible answers)	Until engraftment - 19/63 (30%) ; during first 3 months - 18/63 (28%); until IS discontinuation - 14/63 (22%); until CD4+ count > 200/µL - 13/63 (20%); during first 6 months - 9/63 (14%); other 5-63 (8%).	
Prophylaxis	Prophylaxis administration	Yes 127/140 (91%), No 13/140 (9%) For all patients - 90/127 (71%); Only for IgG-positive - 20/127 (16%); Only for IgG-positive patients plus additional risk factors - 9/127 (7%); No specified – 7/127 (6%).	All seropositive recipients before allo-HCT should receive primary toxoplasma prophylaxis. A II
	First-line Drug	TMP- SMZ 99/100 (99%). Posology : 80/400 mg 1 pill every day - 8/99 (8%); 160/800 mg 1 pill 3x days/week - 70/99 (70%); 160/800 mg 1 pill every day- 3/112 (3%); other	First choice: oral or intravenous TMP-SMZ (80–400 mg) per day or 160 mg-800 mg, three times per week regimen. A II

		schedule - 18/99 (18%); Other than TMP- SMZ - 12/99 (12%).	
	Alternative if TMP-SMZ contraindicated	Atovaquone ± pyrimethamine - 45/126 (36%); dapsone ± pyrimethamine - 21/126 (17%); pyrimethamine monotherapy - 15/126 (12%); other - 11/126 (9%); unknown - 8/126 (6%); none, 27/126 (21%).	Alternate options: Pyrimethamine–sulfadiazine with folinic acid. No grade; oral atovaquone 1500 mg/day. C III; dapsone, azithromycin, or clindamycin only in combination with pyrimethamine and folinic acid. No grade
	Start	Before/during conditioning without discontinuation - 14/126 (11%); During pre-engraftment phase - 7/126 (5%); after engraftment - 94/126 (75%); more than 1 month after allo-HCT - 6/126 (5%); other - 13/126(10%).	Prophylaxis should ideally be started as soon as feasible after transplant, but no later than neutrophil engraftment. A II Given the potential for marrow toxicity, it is advised not to start TMP-SMZ prophylaxis during the pre-engraftment period. B II
	Criteria Stop (one or more possible answers)	CD4+ count > 200/µL - 38/126 (30%) centers; ≥6 to < 12 months from the day of allo-HCT - 31/126(25%) centers; CD4+ count > 400/µL - 24/126 (19%) centers; IS discontinuation - 23/126 (18%) centers; ≥12 to < 24 months from the day of allo-HCT - 22/126 (17%) centers; ≥3 to < 6 months from IS discontinuation -	At least 6 months; During immunosuppression ; Until the CD4 cell count significantly increases, when IS is discontinued. B II

		14/126 (11%) centers; ≥6 to < 12 months from IS discontinuation - 12/126 (10%) centers; other 45/126 (36%).	
Toxoplasma gondii Infection/asymptomatic patient with positive blood PCR	Pre-emptive therapy	PCR positive in asymptomatic patient is sufficient for starting treatment - 19/67 (28%); PCR positive in asymptomatic patient is sufficient for starting treatment, only when a single value is very high - 7/67 (10%); only after a second positive PCR or evidence of increasing toxoplasma DNA copies over time - 24/67 (36%); only if the patient is considered high-risk - 2/67 (3%); case by case decision - 15/67 (22%).	Resampled for qPCR within 48–72 h. Concomitantly and without delaying the treatment by waiting for the second qPCR result, the patient should be assessed for any toxoplasma disease. A II If the second qPCR is negative, it is the clinician's choice to either continue the treatment or to stop treatment. However, this patient should at least receive an efficient toxoplasmosis prophylaxis and be monitored with qPCR. B III
	First line	TMP-SMZ - 73/134 (54%); pyrimethamine/sulfadiazine - 49/134 (37%); pyrimethamine/clindamycin - 10/134 (7%); pyrimethamine/atovaquone - 1/134 (1%); other - 1/134 (1%).	If already under TMP-SMZ prophylaxis: increase the dose or switch to an alternative. If not under TMP-SMZ as prophylaxis: start TMP-SMZ prophylactic, intermediate, or therapeutic dose or pyrimethamine plus sulfadiazine

			/clindamycin. No grade
	PCR monitoring frequency	Less than 1x week - 21/133 (16%); 1x week - 82/133 (62%); 2x week - 19/133 (14%); More than 2x week - 11/133 (8%).	qPCR monitor at least once per week. B III
	Duration of treatment (one or more possible answers)	PCR-guided: Until one negative PCR - 10/132 (8%); until two negative PCRs - 71/132 (54%); not based on PCR result(s) - 51/132 (39%). Fixed-duration: < 4 weeks - 5/133 (4%), 4-7 weeks - 32 /133(24%), 8-12 weeks -16/133 (12%); not based on fixed duration - 80/133 (60%).	After starting, pre-emptive treatment should be continued until at least the second negative qPCR, 7 days apart. B II
Toxoplasmosis disease	First line	TMP-SMZ - 66/132 (50%); pyrimethamine–sulfadiazine-54/132 (41%); pyrimethamine–clindamycin - 9/132 (7%); pyrimethamine–atovaquone - 2/132 (2%); pyrimethamine–azithromycin - 1/132 (1%). In case of neurotoxoplasmosis: Pyrimethamine–sulfadiazine 61/129 (47%) - TMP-SMZ 45/129 (35%); pyrimethamine–atovaquone - 1/129 (1%); pyrimethamine–azithromycin - 2/129 (2%); pyrimethamine–clindamycin -16/129 (12%); other - 4/129 (3%).	Pyrimethamine plus folinic acid plus sulfadiazine (A II) or clindamycin (A II) or atovaquone (C II); TMP-SMZ with or without clindamycin whether either pyrimethamine is not available or oral route is not feasible, irrespective of previous trimethoprim–sulfamethoxazole prophylaxis A II ; Atovaquone might also be used in combination with sulfadiazine. C II

	PCR monitoring frequence	<1x week - 25/129 (19%); 1x week - 75/129 (58%); 2x week - 21/129 (16%); ≥2x week - 8 /129 (6%).	
	Duration of treatment (one or more possible answers)	PCR-guided: Until one negative PCR - 7/130 (5%); until two negative PCRs - 52/130 (40%); not based on PCR result - 71/130 (55%). Fixed-duration: < 4 weeks- 7/131 (5%); 4-7weeks - 64/131 (49%); 8-12 weeks - 41/131 (31%); >12 weeks - 19/131 (15%).	Minimum duration of therapy is 6 weeks or until clinical resolution, or both, and two negative PCR tests in blood, 7 days apart, or one qPCR negative in a previously qPCR-positive cerebrospinal fluid; longer courses might be required if clinical disease or radiological findings are extensive or response is incomplete at 6 weeks. B II
		Complete resolution of radiological/ophthalmological findings required before treatment discontinuation Yes - 88/131 (67%); No - 43/131 (33%).	

Table 1 - Survey responses and ECIL recommendations. Allo-HCT – hematopoietic stem cell transplantation IS- Immunosuppression; TMP-SMZ – trimethoprim-sulfamethoxazole

Conclusions: This survey highlights significant variability across EBMT centers in toxoplasmosis management, underscoring the need for ongoing harmonization, in line with recent ECIL guidelines. Notably, pre-emptive strategy with PCR screening is offered in 48% of centers and pyrimethamine-based regimens remain less commonly used than trimethoprim–sulfamethoxazole in toxoplasmosis infection and disease treatment.

Disclosure: Nothing to declare

OS19-02

PROGNOSIS OF INVASIVE ASPERGILLOSIS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: After allogeneic hematopoietic stem cell transplantation (allo-HSCT), triazole antifungals significantly improve short-term survival in patients with invasive aspergillosis (IA). However, few recent cohorts have described the long-term prognosis of these patients.

Methods: To address this issue, we retrospectively analyzed all consecutive patients receiving an allo-HSCT from 2012 to 2023 at Saint-Louis Hospital, Paris, France. Transplant characteristics were extracted from the EBMT Promise registry. We identified patients diagnosed with proven or probable IA according to the 2020 EORTC/MSGERC criteria. Clinical data were collected from electronic medical records. The primary objective was to compare overall survival (OS) between allo-HSCT recipients with vs. without proven or probable IA. To account for the delay between transplantation and aspergillosis diagnosis, we performed a Mantel-Byar test.

Results: Among the 1,495 allo-HSCT recipients, 61 (4%) developed IA after transplantation. The characteristics of IA patients were generally similar to those without IA, except for higher rates of late (>D30) neutropenia and steroid-resistant acute GvHD in IA patients ($p = 0.003$ and < 0.001, respectively). Notably, pre-transplant IA was not associated with an increased risk of post-transplant IA. IA was diagnosed a median of 95 days after allo-HSCT (Q1-Q3 = [25 – 230]).
We detailed the clinical, mycological, and CT scan findings of IA cases, with pulmonary IA representing the large majority (n = 58). Among patients with pulmonary IA, 21 only had positive respiratory samples, 21 only had positive blood samples and 13 had both. Twenty-one patients developed breakthrough IA, defined as IA occurring while receiving anti-mold triazole therapy. The characteristics of breakthrough and non-breakthrough IA are presented in the **Table**. First-line treatments were mainly liposomal amphotericin B and voriconazole. Treatment response was observed in 50% of the patients after first-line therapy and 60% after second-line (including oral continuation after first-line response, treatment toxicity, or failure). Despite these encouraging response rates, IA remained associated with a very poor prognosis after allo-HSCT. Median OS was 165 days after IA diagnosis (95% CI = [70 – 286]). Death was directly attributable to IA in 23% of cases and possibly related in 19%. Patients who died due to IA had significantly shorter survival than those who died from other causes: OS was 33 days (95% CI = [13–62]) vs 189 days (95% CI = [81–286]), $p < 0.001$. Other causes of death were mainly relapse (23%) and GvHD (27%).
When analyzing IA as a time-dependent variable after allo-HSCT, the 2-year OS was 9% (95% CI = 4–17) in patients with IA, compared with 68% (95% CI = 66–77) in those without IA (**Figure**, $p < 0.001$). Multivariate analysis demonstrated that IA as a time-dependent variable was strongly associated with increased post-allo-HSCT mortality (HR 3.20, 95% CI = [2.32-4.41], ($p < 0.001$)).

Table	Breakthrough IA (n = 21)	No breakthrough IA (n = 40	p
Neutropenia	9 (43%)	23 (58%)	0.03
Systemic steroids	12 (57%)	15 (38%)	0.14
Systemic immunosuppressive treatment (except steroids)	15 (71%)	37 (93%)	0.02
Pulmonary lesions on CT scan (n = 58) - Consolidations - Nodules - Other lesions	 10 (50%) 10 (50%) 0	 12 (32%) 17 (46%) 9 (24%)	0.05
Mycological criteria* - Positive only in respiratory samples - Positive only in blood samples - Positive both in respiratory and blood samples	 8 (42%) 5 (26%) 6 (32%)	 13 (35%) 17 (46%) 7 (19%)	0.3
***Aspergillus* species identification in culture (n = 32)** - *Aspergillus fumigatus* - *Aspergillus fumigatus associated with other species* - *Aspergillus non fumigatus*	 10 (67%) 0 5 (33%)	 10 (63%) 2 (2%) 5 (25%)	0.6
First line treatment - Liposomal amphotericin B - Liposomal amphotericin B + isavuconazole - Liposomal amphotericin B + caspofungine - Caspofungine - Isavuconazole - Posaconazole - Voriconazole - No treatment	 10 (48%) 1 (5%) 1 (5%) 1 (5%) 2 (9.5% 2 (9.5%) 3 (14%) 1 (5%)	 10 (30%) 0 0 2 (5%) 0 4 (10%) 22 (55%) 0	0.007
Survival after IA diagnosis (median, [$_{95}$CI]), days	180 days [49 – 697]	123 days [55 – 306]	0.88

* Positive galactomannan, positive *Aspergillus* PCR or culture positive for *Aspergillus*

Conclusions: Despite recent therapeutic advances, IA remains associated with substantial long-term mortality in allo-HSCT recipients. Although part of this mortality is directly caused by IA, the infection mainly reflects clinical frailty characterized by profound immunosuppression (e.g. systemic corticosteroid therapy, prolonged neutropenia) or relapse of the underlying hematological malignancy.

Disclosure: Nothing to declare

OS19-03

INFECTION RATES ACROSS THE FIRST-YEAR POST-TRANSPLANT IN PTCY AND NON-PTCY-BASED GVHD PROPHYLAXIS: A POST-HOC ANALYSIS OF A RANDOMIZED PHASE II STUDY

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Background: A prior randomized phase II trial (NCT03246906) of graft-vs-host disease (GVHD) prophylaxis with sirolimus and cyclosporine combined with either post-transplant cyclophosphamide (PTCy) or mycophenolate mofetil (non-PTCy) showed superior GVHD-free relapse-free survival and extremely low rates of moderate to severe chronic GVHD (3% vs. 33% at 1-year post-transplant) but delayed neutrophil engraftment and higher rates of early (day 0-100 post-transplant) grade ≥3 (CTCAE) infections with PTCy (Ueda Oshima, *JCO* 2025). There was no definitive difference in 1-year non-relapse mortality (NRM) between arms. In this post-hoc analysis, we hypothesized that the lower rates of chronic GVHD and associated reduced need for immunosuppression later post-transplant leads to overall lower infection burden across the first-year post-transplant in PTCy-treated patients.

Methods: We retrospectively evaluated all infections by CTCAE version 4.03 and by BMT CTN Infection Grading System between day 0 and 365 post-transplant in patients treated on the trial. The number of unique infections per patient in each arm was calculated by time intervals post-HCT: Day 0-30, 30-100, 100-180, 180-365, and 0-365. Poisson regression was used to compare infection rates between arms across the first year post-transplant. Time at risk for infection was taken as the beginning of the appropriate interval to the earliest of relapse, death, last contact, or end of the relevant interval. For each time interval, the rate of infection per patient and rate ratios (RR), which measures the average infection rate for the PTCy arm relative to the non-PTCy arm, were calculated for different severities of BMT CTN and CTCAE infections.

Results: In the first year post-transplant (days 0-365), 266 and 175 unique infections occurred in 72 PTCy and 72 non-PTCy treated patients, and PTCy-treated patients had higher rates of infection compared to non-PTCy for all infection severity categories (Table 1, Figure

1). When examining specific time periods, the early (days 0-30) and late (days 180-365) post-transplant period showed higher rates of infection in PTCy patients across all infection severities, with the magnitude of difference in PTCy vs. non-PTCy being most pronounced in days 180-365 particularly for severe infections (BMT CTN 2+: RR 3.02, 95% CI 1.16-9.34, p=0.0339 and CTCAE 2+: RR 3.45, 95% CI: 1.35-10.55, p=0.0156; Table 1). For time intervals days 30-100 and 100-180, infection rates with PTCy were numerically higher for every infection severity (Table 1).

Time Interval	Grade	RR	conf.low	conf.high	p.value
Day 0-30	ALL				
	BMT 1+	1.64	1.24	2.19	0.0007
	BMT 2+	1.65	1.24	2.20	0.0006
	CTCAE 2+	3.47	1.93	6.71	0.0001
	CTCAE 3+	1.68	1.23	2.32	0.0014
		1.86	1.28	2.73	0.0013
Day 30-100	ALL				
	BMT 1+	1.32	0.93	1.89	0.1182
	BMT 2+	1.32	0.93	1.89	0.1182
	CTCAE 2+	1.13	0.61	2.08	0.6962
	CTCAE 3+	1.20	0.79	1.81	0.3934
		1.57	0.83	3.08	0.1725
Day 100-180	ALL				
	BMT 1+	1.74	0.99	3.12	0.0564
	BMT 2+	1.74	0.99	3.12	0.0564
	CTCAE 2+	2.24	0.88	6.36	0.1032
	CTCAE 3+	1.81	0.99	3.41	0.0594
		2.29	1.07	5.30	0.0387
Day 180-365	ALL	1.81	1.08	3.12	0.0270
	BMT 1+	1.90	1.12	3.30	0.0188
	BMT 2+	3.02	1.16	9.34	0.0339
	CTCAE	2.97	1.57	5.98	0.0013
		3.45	1.35	10.55	0.0156

	2+ CTCAE 3+				
Day 0-365	**ALL BMT** **1+ BMT** **2+ CTCAE** **2+ CTCAE 3+**	 1.57 1.58 2.06 1.64 1.90	 1.30 1.31 1.46 1.32 1.44	 1.90 1.92 2.94 2.04 2.52	 <0.0001 <0.0001 <0.0001 <0.0001 <0.0001

Table 1. Poisson Model
RR = Rate Ratio represents the average infection rate for the PTCy group relative to the non-PTCy group

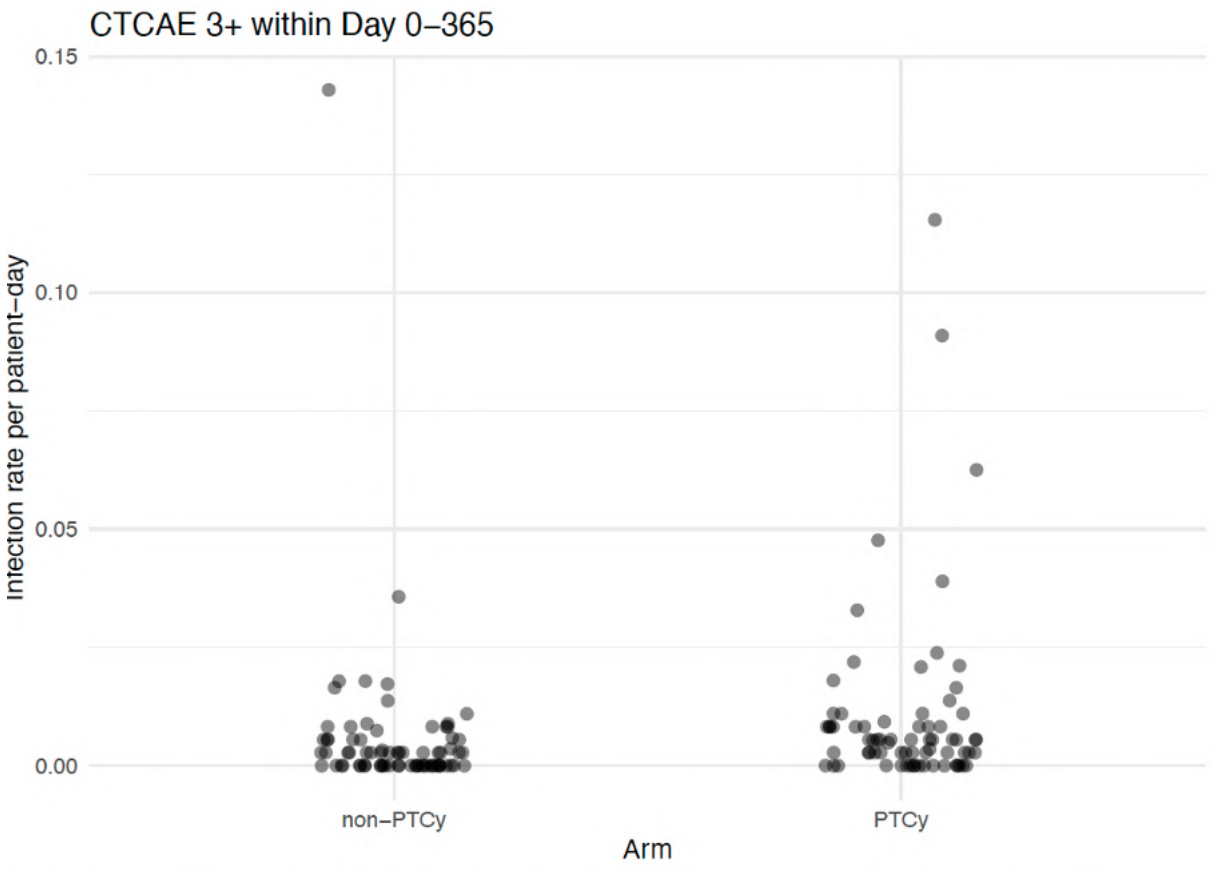

Figure 1. Jittered dot plot of infection rate per patient by arm day 0-365 post-transplant for

CTCAE grade 3+ infections. Each gray dot represents the infection rate per patient per days at risk (Note: overlapping gray dots appear black).

Conclusions: Despite significantly lower rates of GVHD and immunosuppressive treatment, PTCy-treated patients had higher rates of infection even beyond the initial pre-engraftment period and throughout the entire first year post-transplant compared to non-PTCy-treated patients. This suggests continued compromise to immune reconstitution extending beyond initial delay in neutrophil engraftment with PTCy. Targeted infection surveillance and prevention, as well as further optimization of PTCy-based GVHD prophylaxis, is needed to better balance GVHD reduction with infection risk.

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OS19-04

VACCINATION STRATEGY IN PATIENTS UNDERGOING CAR-T THERAPIES – AN IDWP AND CTIWP EBMT SURVEY

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Background: Vaccine studies focused on the population undergoing therapies with chimeric antigen receptor T-cells (CAR-T) are limited and, in most centres, the vaccination strategies are adopted from the transplantation protocols.
To optimize the vaccine-preventable protection, some authors propose immunizing patients against some pathogens prior to lymphodepleting therapy. Immunisation with killed/inactivated/recombinant vaccines (non-live; NLV) is recommended ≥3 months after CAR-T and with live attenuated vaccines (LAV) ≥12 months.

Methods: To obtain an overview of current vaccination practices, we launched a survey across EBMT-affiliated CAR-T centres. The differences between the center's prioritized vaccines were investigated using Fisher's exact test.

Results: The response rate was 38% (99/261) from adult centres (n=73), paediatric centres (n=9) and mixed centres (n=17). 56/99 (57%) centres reported a specific vaccination protocol for CAR-T recipients. Vaccinations before lymphodepleting therapy are performed in 18/99 (18%; in 5% routinely) centres (mainly against influenza and SARS-CoV-2 viruses). The vaccination strategies do not differ by CAR-T type (anti-CD19 or anti-BCMA). The fixed timing for beginning immunisation with NLV at 3-6 months and >6 months post-CAR-T is used in 34/88 (39%) and 17/88 (19%) centres, respectively. For LAV, a fixed timing of >12 months post-CAR-T is used in 42/99 (42%) centres. The immune reconstitution-dependent (CD4+ or CD19+ or CD20+ >0.2x10^9/L) strategy for NLV and LAV initiation is declared by 41/99 (41%) centres. Regarding the time elapsed since the last immunoglobulin supplementation as a strategy for NLV initiation, no specific time is reported by 72/88 (82%) centres, and 2-3 months by 12/88 (14%). For the LAV initiation, no particular time is declared by 69/99 (70%) centres, while 5-6 months, >6-12 months and >12 months by 13/99 (13%), 10/99 (10%), and 7/99 (7%) centres, respectively. Assessment of the specific vaccine-preventable humoral immunity before initiation of post-CAR-T vaccination is performed in 27/99 (27%) centres (mainly for hepatitis B virus (HBV), and varicella-zoster virus). Post-vaccine antibody response assessment in patients immunised after CAR-T therapy is performed in 29/99 (30%) centres (mainly for pneumococcal and HBV vaccines). To assess the durability of protection, the post-vaccine antibody maintenance after seroconversion is monitored in 20/99 (20%) centres.
The prioritized vaccines recommended in >80% of CAR-T centres, regardless of patients' age and the centre's geographical location, include influenza and pneumococcal vaccines (Table 1). The significant differences between the numbers of centres recommending specific vaccines in children vs adults were observed regarding papillomavirus (p=0.021) and zoster (p=0.004) vaccines, and between the CAR-T centres' regions (Western Mediterranean and Central Europe and Benelux versus West Asia–Southeast Asia) regarding vaccines against hepatitis A virus (p=0.012), HBV (p=0.049), and mumps, measles, rubella (p=0.005). Almost all responders (95%) expressed a need for vaccination guidelines for patients undergoing CAR-T cell therapy.

Table 1 Vaccines recommended in the CAR-T centres according to the treated population (paediatric, adult, or both) and the centres' geographic location.

Type of recommended vaccine	**Patient population**				**Regions**		
	Total number of centres n = 99	**Paediatric centres** n = 9	**Adult centres** n = 73	**Both** n = 17	**WME** n = 29	**CEB** n = 27	**WASEA** n = 8
	Number of CAR-T centres (%)						

Influenza	97 (98%)	8 (89%)	72 (99%)	17 (100%)	29 (100%)	25 (93%)	8 (100%)
Streptococcus pneumoniae	82 (83%)	8 (89%)	59 (81%)	15 (88%)	24 (83%)	22 (81%)	8 (100%)
HiB	71 (72%)	8 (89%)	50 (68%)	13 (76%)	21 (72%)	20 (74%)	8 (100%)
SARS-CoV-2	87 (88%)	7 (78%)	65 (89%)	15 (88%)	28 (97%)	22 (81%)	5 (62%)
DTaP	67 (68%)	8 (89%)	46 (63%)	13 (76%)	18 (62%)	20 (74%)	8 (100%)
Poliomyelitis (inactivated)	55 (56%)	7 (78%)	40 (55%)	8 (47%)	16 (55%)	14 (52%)	7 (88%)
HBV	61 (62%)	8 (89%)	40 (55%)	13 (76%)	19 **(66%)**	17 **(63%)**	8 **(100%)**
HAV	24 (24%)	2 (22%)	17 (23%)	5 (29%)	8 **(28%)**	7 **(26%)**	6 **(75%)**
aRZV*	70 (71%)	3 **(33%)**	54 **(74%)**	13 (76%)	25 (86%)	19 (70%)	8 (100%)
RSV	25 (25%)	1 (11%)	17 (23%)	7 (41%)	5 (17%)	11 (41%)	3 (38%)
Neisseria meningitidis	56 (57%)	7 (78%)	39 (53%)	10 (59%)	21 (72%)	14 (52%)	5 (62%)
HPV*	30 (30%)	7 **(78%)**	19 **(26%)**	4 (24%)	12 (41%)	6 (22%)	4 (50%)
MMR* (Live-attenuated)	45 (45%)	5 (56%)	33 (45%)	7 (41%)	14 **(48%)**	11 **(41%)**	8 **(100%)**

***Vaccines with statistically significant differences in percentages of recommended vaccines**

aRZV - adjuvant recombinant zoster vaccine; **DTaP** – diphtheria, tetanus, acellular pertussis; **HAV** - hepatitis A virus; **HBV** - hepatitis B virus; **HiB** - Haemophilus influenzae type B; **HPV** - human papillomavirus; **MMR** - mumps, measles, rubella; **RSV** - respiratory syncytial virus; **SARS-CoV-2** - severe acute respiratory syndrome coronavirus 2

Regions: **WME** = Western Mediterranean Europe (Italy, Spain); **CEB** = Central Europe and

Benelux (Germany, Austria, Switzerland, Belgium, Netherlands); **WASEA** = West Asia–Southeast Asia (Israel, Saudi Arabia, Singapore)

Conclusions: Real-world data from cellular therapy centres provided an overview of current trends and discrepancies in local vaccination practices. It is a perfect platform for developing future prospective studies that would provide background for CAR-T-cell-oriented vaccine recommendations.

Disclosure: Nothing to declare

OS19-05

INCIDENCE AND OUTCOME OF INFECTIONS AFTER TREATMENT WITH CAR-T CELLS VERSUS BISPECIFIC ANTIBODIES IN PATIENTS AFFECTED BY HEMATOLOGICAL MALIGNANCIES

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Background: Novel immunotherapies such as chimeric antigen receptor T-cells (CAR-T) and bispecific antibodies (BsAbs) have significantly improved long-term outcomes in heavily pre-treated hematological malignancies. Both therapies are associated with cytopenia, hypogammaglobulinemia, and prior extensive treatment exposure, factors known to increase infectious risk. Although infection incidence after CAR-T and BsAbs has been increasingly investigated, comparative data between these approaches remain limited, with controversial results. Recent evidence shows that infectious risk is high with both CAR-T cells and bispecific antibodies, with severe infections occurring predominantly early after CAR-T therapy, whereas bispecific antibodies are associated with a sustained and cumulative infectious burden over time, particularly with continuous treatment. [1–3]

Methods: We conducted a retrospective analysis of all consecutive patients who received CAR-T cell therapy or bispecific antibodies at our institution, evaluating the incidence and spectrum of viral, bacterial, and fungal infections, as well as infection-related outcomes such as hospitalization rate and duration, ICU admission, and infection-related mortality. We retrospectively analyzed 237 patients treated with CAR-T (n=110), bispecific antibodies (BsAbs, n=81) or both (n=46). Table 1 describes patients characteristics.

Results: Across the 3 groups of CAR-T, bispecifics, or both, at least one infectious event occurred in 49%, 57% and 61% of patients, respectively. A total of 95, 109, and 46 infectious events were recorded in the CAR-T, bispecific antibody, and dual-therapy cohorts, respectively. Among infection episodes, early infections (<100 days) accounted for 34.7% after CAR-T and 20.0% after bispecific antibodies (p=0.018), while late infections predominated in the bispecific cohort (80.0% vs 65.3%). Across all groups, viral infections were the most frequent (46–49%), followed by bacterial (28–33%) and fungal infections (3–

10%). Infection-related hospitalization and mortality were significantly higher in patients treated with bispecific antibodies compared with CAR-T recipients (p=0.044 and p=0.009, respectively). Overall infection incidence and ICU admission did not differ significantly between groups.

Variable	**CAR-T (n=110)**	**Bispecifics (n=81)**	**Both therapies (n=46)**	
Sex (Male)	63 (57.3%)	47 (58.0%)	35 (76.1%)	0.069
Age at treatment (mean ± SD)	57.9 ± 13.1	61.7 ± 15.9	58.3 ± 12.0	0.074
Charlson Comorbidity Index (mean ± SD)	3.84 ± 1.40	4.14 ± 1.88	3.65 ± 1.46	0.386
ECOG PS (median, IQR)	0 (0–2)	0 (0–3)	0 (0–1)	0.174
Prior therapy lines (mean ± SD)	3.34 ± 1.15	3.54 ± 1.41	3.17 ± 0.82	0.401
Prior transplant	24 (21.8%)	8 (9.9%)	4 (8.7%)	0.030
Underlying disease				0.001
– Lymphoma	98 (89.1%)	73 (90.1%)	40 (87.0%)	
– Acute Leukemia	1 (0.9%)	8 (9.9%)	2 (4.4%)	
– Multiple Myeloma	11 (10.0%)	0	4 (8.7%)	
CAR-T product type				
– Tisagenlecleucel	44 (40.0%)			
– Axicabtagene ciloleucel	34 (30.9%)			
– Brexucabtagene autoleucel	16 (14.6%)			
– Idecabtagene vicleucel	11 (10.0%)			
– Lisocabtagene maraleucel	2 (1.8%)			

– Other / investigational	3 (2.7%)			
CAR-HEMATOTOX score, median (IQR)	3 (3–4)			
CAR-HEMATOTOX score ≥1 n (%)	101 (91.8%)			

Conclusions: Despite the limitations of this retrospective analysis, in a cohort predominantly composed of lymphoma patients we reported a later onset of infections and poorer infection-related outcomes after treatment with BsAbs compared with CAR-T, likely attributable with continuous exposure and sustained immunosuppression associated with ongoing BsAb therapy.

Disclosure: No significant COI to be declared.

OS19-06

MANAGEMENT OF BLOODSTREAM INFECTION SECONDARY TO BACTERIAL TRANSLOCATION DURING THE NEUTROPENIC PHASE OF STEM CELL TRANSPLANT. A NO–CENTRAL LINE REMOVAL STRATEGY IN 73 EPISODES

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Background: Bacteremia secondary to bacterial translocation from injured mucosa during the neutropenic phase after stem cell transplant (SCT) is a frequent event. It has been well described and is classified by the CDC as mucosal barrier injury laboratory-confirmed bloodstream infections (MBI-LCBI) (1). However, controversy persists over whether the central line (CL) should be removed. In our transplant center, by protocol, we did not remove the CL in cases of MBI-LCBI. We present our experience with this approach.

Methods: From Jan 2023 to Oct 2025, we identified all bloodstream infections (BSI) that occurred during the neutropenic phase of SCT. Patients aged 18 years or older who met the CDC criteria for MBI-LCBI (1) and had a CL were included. We assessed: 1) resolution of infection after 7 days of treatment, 2) ICU transfer, 3) recurrence of BSI with the same organism, 4) overall mortality at 30 days, and 5) the percentage of CL that was finally removed.
In each episode of fever and neutropenia, a set of blood cultures was obtained, and empiric antibiotic (meropenem or ceftazidime/avibactam) was initiated within the first hour. Later, the therapy was de-escalated to cefepime according to the results and evolution. The CL was removed only in cases of thrombosis, exit site infection, or persistence of BSI.

Results: During the study period, 112 bloodstream infections were identified. A total of 73 of them (65.1%), occurring in 71 patients, met the inclusion criteria. (See Table 1 for the characteristics of the group). The median time to the first bacteremia was 7 days after transplant (-2 to 20), and for the second, it was 13 days (+12 to 15). In 5 episodes, the BSI was polymicrobial. Pathogens identified were E. coli (43.5%), Klebsiella spp. 32.0%, Enterococcus spp. 10.2%, Streptococcus spp. 10.2%, and others Gram negatives, 4.0%. The pattern of drug resistance was ESBL 26,9%, carbapenemase 17.9% and VRE 2.5%.
The 30-day mortality rate was 2.8%. Persistent infection with the same bacterium was observed in 2.7% of cases, catheter removal was required in 4.1% of instances, and 12% of episodes necessitated transfer to the ICU. Finally, 69 out of 71 patients (97,2%), corresponding to the 73 episodes, were alive at D+30.

Table 1 **Characteristics of patients**

Age	50.3 (20-75)
Gender	Men: 37, Women: 34
Type of Transplant	
	Autologous: 21 (29.5%)
	Allogeneic: 08 (11.2%)
	Haploidentical: 42 (59.1%)
Diagnosis	
	AML/MDS: 26 (36.6%)
	ALL: 13 (18.3%)
	Lymphomas: 14 (19.7%)
	Myeloma: 11 (15.5%)
	Other: 07 (9.85%)

Table 1 **Characteristics of patients**

Neutrophil number	100 (0-300)
Total patients	71

Conclusions: 1-More than 50% of bacteremia occurring during the neutropenic phase of SCT meet the CDC criteria of MBI-LCBI.
2- Given that the central line (CL) is not the source of the infection, a strategy involving early initiation of antibiotics and salvage of the catheter is feasible and seems safe.
3- This strategy saves resources and avoids invasive procedures in patients at risk of complications
Reference: (1) CDC. NHSN Patient Safety Component Manual: CLABSI. https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf

Disclosure: Nothing to disclose

OS19-07

THIRD PARTY FUNGUS-SPECIFIC T CELL THERAPY FOR INVASIVE FUNGAL INFECTION AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: The global immune deficit that follows allogenic stem cell transplantation (HSCT) predisposes to multiple infections including invasive fungal infections (IFIs) with yeasts and moulds. The incidence of IFIs after transplant is 5 to 15% depending on factors including the severity of post-transplant neutropenia and the intensity of immune suppression. Despite optimal antifungal drug therapy, mortality for IFIs after transplant varies from 20% for primary invasive Candidiasis to over 60% for breakthrough mould infections. Defects in innate and adaptive immunity contribute to the development and progression of post-HSCT IFIs.

Methods: We generated a bank of cryopreserved fungus-specific T cells (FSTs) from the G-CSF primed apheresis product of allogeneic stem cell donors. Fungus-specific T cells were predominantly CD4+ and targeted fungal antigens mainly through HLA DR restriction. In a phase 1 trial, we treated 8 patients with possible, probable or proven IFI with one or more

infusions of FSTs with which they shared an HLA DR antigen. A 9th patient was treated off study but on the trial protocol. Patients received traditional antifungals at the discretion of their treating physicians.

Results: From August 2020 to September 2025, nine patients aged 24-71 years received FSTs 24 to 224 days (median 40) after HSCT for AML (n=3), MDS (1), ALL (2), T-LBL (1), NHL (1) and Vexas syndrome (1). Transplants were performed using haploidentical (n=4), matched unrelated (3), matched sibling (1) and mismatched related donors (1). GVHD prophylaxis consisted of post-transplant cyclophosphamide/tacrolimus/MMF (n=5) and thymoglobulin/ciclosporin/methotrexate (4). All patients had fungal lung disease, with additional disease in sinuses (n=4), brain (3), orbit (1) and blood (1). IFIs were proven (n=5), probable (3) and possible (1). Fungi identified were *Lomentospora prolificans (2), Candida albicans (2), Scedosporium aurantiacum, Clavispora lusitaneae, Candida parapsilosis, Purpureocillium lilacinum and Naganishia spp.* Three patients had infections with multiple fungal species. All infections occurred as breakthrough in patients receiving prophylactic antifungals. Two patients received 2 FST infusions. FST doses were $1x10^6/m^2$ (5), $10x10^6/m^2$ (3) and $100x10^6/m^2$ (3). There were no acute infusion related toxicities. Of eight currently evaluable patients including two with deep CNS infections, seven cleared or effectively controlled IFIs. One patient transplanted for Vexas syndrome developed persistent Lomentospora prolificans fungemia and died despite receiving FSTs in conjunction with antifungals including olorofim. One patient cleared his IFI but died with disseminated atypical Mycobacteria. GVHD occurred in 4 patients (1 pre-FST only, 1 pre- and post-FST, 2 post-FST only). Post-FST only GVHD was mild, did not require systemic steroids and fully resolved. At a median of 753 days (range 12-1772) post FST infusion, 7 patients are alive and well, 4 off all antifungal treatment.

Conclusions: FSTs infused after HSCT appear safe and were not associated with infusion related toxicity or excess GVHD. Eight of nine patients resolved IFIs including those with severe sinopulmonary and deep CNS mould infections. Fungus-specific adoptive T cell therapy may complement traditional antifungal drug treatment in immunodeficient HSCT patients with IFIs and result in improved outcomes without adversely affecting transplant safety. A larger study is required to confirm these encouraging preliminary findings.

Clinical Trial Registry: ACTRN12618001540202, http://www.ANZCTR.org.au/ACTRN12618001540202.aspx

Disclosure: David Gottlieb discloses patents in the field of adoptive immunotherapy, not related to fungus-specific T cells.

OS19-08

PRE-TRANSPLANT ASPERGILLOSIS IS ASSOCIATED WITH REDUCED POST-TRANSPLANT SURVIVAL OF CHILDREN WITH LEUKEMIA: SUBGROUP ANALYSIS OF A PROSPECTIVE STUDY ON BEHALF OF IDWP, PDWP AND ALWP-EBMT

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Background: Invasive aspergillosis (IA) is an important infectious cause of morbidity and mortality in patients with hemato-oncological malignancies and those undergoing allogeneic stem cell transplantation (allo-SCT). Although IA may be a cause of transplant-ineligibility, a recent prospective study in patients with acute leukemia undergoing alloSCT showed that more than two thirds of patients with pre-SCT IA were alive one year after allo-SCT. We analyzed the pediatric population from this cohort to assess the influence of pre-SCT IA in children undergoing allo-SCT.

Methods: The data of children with acute leukemia undergoing allo-SCT and recruited in a prospective EBMT-IDWP study were analyzed to assess the impact of a prior history of probable or proven IA (pre-SCT P/P-IA) on 1-year overall survival (OS) and non-relapse mortality (NRM), relapse incidence and occurrence of infectious complications, and graft-versus-host disease (GvHD). Kaplan-Meier estimator was applied to estimate the OS, whilst the cumulative incidence method was used for NRM, relapse incidence and GvHD. Risk factors analysis was performed by using the Cox regression model. All the analyses were performed by using the RStudio software.

Results: Among the 449 children included between 2016 and 2021, the incidence of pre-SCT P/P-IA was 6.5% (N=29). The interval between diagnosis of P/P-IA and allo-SCT was median 125 days (range 17 – 1391 days). The incidence of 1-year NRM was significantly higher in children with pre-SCT P/P-IA (28% NRM, 95% CI 11-44%) versus children without pre-SCT P/P-IA (9% NRM, 95% CI 6-11%) (p = 0.003) (Figure 1A). Consequently, 1-year OS was lower in children with pre-SCT P/P-IA (62% OS, 95% CI 44-80%) versus children without pre-SCT P/P-
IA (83%, 95% CI 79-86%) (p<0.001) (Figure 1B). In the multivariate model, among the variables analyzed for OS (sex, age, underlying disease, disease status, pre-SCT P/P-IA, recipient-donor (R/D) sex, donor age, TBI, conditioning (RIC/MAC), stem cell source, donor type,T-cell depletion, R/D CMV, diagnosis-SCT interval), pre-SCT P/P-IA (HR 2.26, C.I. 1.28-3.97, *p* 0.005), stem cell source (PB+CB) (HR 2.01, C.I. 1.38-2.93, $p < 0.001$)), and longer diagnosis-SCT interval (HR 1.53, C.I.1.05-2.24, p=0.028) were significantly associated with a worst OS. Causes of death in children with pre-SCT P/P-IA compared to children without pre-SCT P/P-IA were more often related to bacterial infections (6.9% versus 1.7%), viral infections (3.4% versus 2.1%) and infection-related disease with unknown etiology (6.9% versus 0.7%).

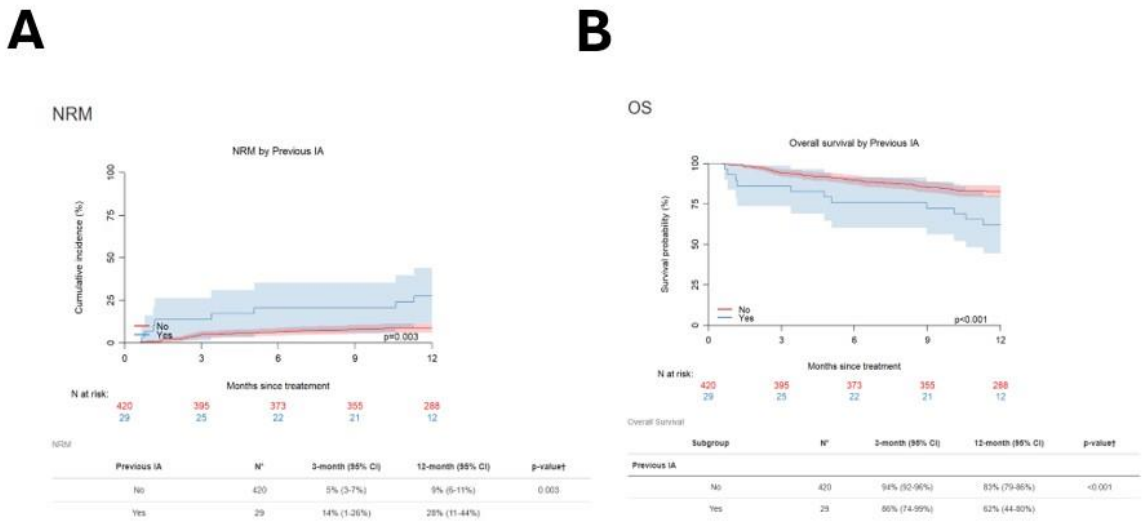

Figure 1A-B: Cumulative incidence of (A) 1-year non-relapse mortality (NRM) and (B) overall survival (OS) in children with and without invasive aspergillosis (IA) prior to allogenic stem cell transplantation.

Conclusions: In children, pre-SCT P/P-IA is significantly associated with worse allo-SCT outcomes. In addition, we observed a lower overall survival in the pediatric population with pre-SCT P/P-IA compared to the previously published cohort including both children and adults with pre-SCT P/P-IA undergoing allo-SCT. Nonetheless, allo-SCT represents a valuable

therapeutic option also in patients with prior IA, being successful in more than half of the patients.

Disclosure: Nothing to declare

B072

RISK STRATIFICATION SYSTEM FOR CMV MONITORING AFTER AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Autologous hematopoietic cell transplantation (auto-HCT) is a standard consolidation therapy for hematologic malignancies. However, the incidence and clinical impact of cytomegalovirus (CMV) infection post-auto-HCT remain poorly defined, as current guidelines do not recommend routine CMV monitoring in recipients of unmodified grafts. We aimed to characterize CMV reactivation patterns and identify pre- and post-transplant risk factors to develop a predictive model for targeted CMV monitoring.

Methods: We retrospectively analyzed 1,000 CMV-seropositive (all ages), non-CD34-selected auto-HCT recipients transplanted between 2011 and 2021 at Fred Hutchinson Cancer Center who underwent CMV monitoring between days +20 and +60. To assess the impact of CMV serostatus, 846 concurrently transplanted CMV-seronegative recipients were also analyzed. Preemptive therapy (PET) was initiated at ≥5 antigen-positive cells per slide or viremia ≥150 IU/mL, or at any positive antigenemia/viremia ≥50 IU/mL during high-dose steroid use (≥1 mg/kg) or anti-thymocyte globulin (ATG) administration. Clinically significant CMV infection (csCMV) was defined as viremia requiring PET or CMV disease. Time-to-event and Cox proportional hazard analyses were performed for CMV infection, CMV disease, and high-risk CMV infection (viremia ≥500 IU/mL, antigenemia ≥7, or CMV disease).

Results: By day 100 post-HCT, 29% (95% CI 26.6–32.3%) experienced any CMV viremia, while high-risk infection occurred in 4.4% (95% CI 3.2–5.8%). csCMV incidence was 12.7% (95% CI 10-14%), with CMV disease diagnosed in 1% of patients. Reactivation was most frequent in non-malignant disorders treated with ATG and in lymphomas (Figure 1A). Pre-HCT CMV reactivation (7.8% of 190 tested) predicted markedly post-HCT high-risk infection rates (33% vs 5%). By day 100, 24 deaths (2.4%) occurred among CMV-seropositive and 15 (2%) among CMV-seronegative patients; CMV contributed to death in 3 cases. CMV serostatus did not affect non-relapse mortality at day 100 (Figure 1B) or overall survival at 3 years.
In univariable models, HIV infection was associated with CMV disease (HR 16.1; 95% CI 2.03- 128) and pre-HCT CMV viremia (among patients with available data) was associated with increased risk of post-HCT CMV infection (HR 11.6; 95% CI 3.63-36.8). Multivariable

models identified elevated pre-HCT creatinine (>1.5 mg/dL), hypoalbuminemia (<3.4 g/dL), and lymphoma diagnosis as significant predictors of high-risk CMV reactivation (Figure 1C). A risk model incorporating these factors stratified patients by cumulative incidence of high-risk infection (1.4% with no risk factors vs. 9.4% with ≥2), Figure 1D. Adding pre-HCT CMV variable to the model further increased incidence of high-risk infection (30% with ≥2 risk factors). Post-HCT systemic steroid use (>0.5 mg/kg) was a significant predictor of high-risk infection (HR 4.7; 95% CI 1.86-11.9).

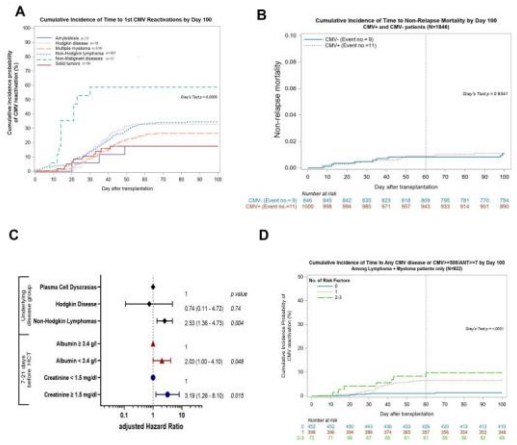

Figure 1. A) Cumulative incidence by 100 days post-transplant of CMV viremia by underlying disease (amyloidosis – solid purple line, Hodgkin disease – dotted line, multiple myeloma – long dashed line, non-Hodgkin lymphoma– short dashed line, non-malignant diseases – medium dashed line, and solid tumor – red solid line); B) Cumulative incidence of non-relapse mortality by day 100 post-transplantation among CMV seronegative (solid line) and CMV seropositive (dotted line) HCT recipients. Analyses of risk factors among patients diagnosed with plasma cell dyscrasias and lymphomas: C) Multivariable Cox regression model for high-risk CMV infection (≥500 IU/mL, ≥7 antigen-positive cells per slide, or CMV disease) among HCT recipients. D) Risk stratification model based on a number of risk factors (0 to 3, hypoalbuminemia, renal dysfunction, lymphoma diagnosis) for high risk infection.

Conclusions: We identified key pre- and post-transplant risk factors for CMV reactivation and developed a risk stratification model to guide targeted PCR monitoring, enabling more precise prevention and diagnostic stewardship after auto-HCT. CMV monitoring should be performed in patients with pre-HCT viremia, ATG exposure, HIV infection, or those receiving post-HCT steroid treatment, regardless of the underlying disease. Among patients with lymphoma and myeloma, PCR monitoring is recommended for those with at least two risk factors including hypoalbuminemia, renal dysfunction, or lymphoma diagnosis.

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Other authors: nothing to declare.

B073

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REAL-WORLD USE, EFFECTIVENESS AND SAFETY OF MARIBAVIR IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS WITH REFRACTORY/RESISTANT CMV OR INTOLERANCE TO ANTI-CMV AGENTS: INTERIM ARISE RESULTS

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Background: Maribavir was approved in Europe in 2022 for treatment of post-transplant refractory/resistant (R/R) cytomegalovirus (CMV) infection/disease. Real-world data are needed to characterize its use, effectiveness and safety in routine practice. We report interim data from hematopoietic cell transplant (HCT) recipients in the ARISE study.

Methods: ARISE is a multinational, retrospective cohort study evaluating the use, effectiveness and safety of maribavir in adult (≥18 years) HCT or solid organ transplant recipients with R/R CMV or intolerance to anti-CMV agents. This analysis includes allogeneic HCT recipients who initiated maribavir between the start of country-specific commercial availability/early access program and 4 months before data abstraction (i.e., the eligibility period). The primary objective was to describe CMV clearance at maribavir discontinuation (i.e., last negative CMV quantitative PCR before maribavir discontinuation). Secondary objectives included maribavir treatment patterns, safety and healthcare resource utilization (HCRU). Outcomes were summarized using descriptive statistics and Kaplan-Meier (KM) analysis.

Results: This interim analysis included 89 allogeneic HCT recipients (R/R, n=56; intolerant, n=33) from nine European countries. Mean (SD) age at transplant was 50.5 (17.1) years, 52.8% were male, and 74.2% recipients had CMV-positive serostatus at transplant. Median (Q1-Q3) duration of follow up was 14.6 (9.1-21.2) months. Median (Q1-Q3) time from transplant to maribavir initiation and from maribavir initiation to end of follow up was 143 (70-189) days and 228 (122-512) days, respectively. Among evaluable patients at maribavir discontinuation (n=74), CMV clearance was achieved in 38/47 (80.9%; 95% CI: 66.7-90.9) HCT recipients with R/R CMV and in 25/27 (92.6%; 95% CI: 75.7-99.1) recipients with intolerance to anti-CMV agents. Median (Q1-Q3) time to CMV clearance from maribavir initiation was 50 (26–71) and 44 (18-56) days in the R/R and intolerant groups, respectively; KM analysis shown in Figure. Median (Q1-Q3) duration of maribavir treatment courses (n=94) was 49.5 (22-61) days. Maribavir was initially administered at home in 51/96 (53.1%) treatment courses. Adverse events of special interest and HCRU are shown in the Table. Before and after maribavir initiation, respectively, incidence rates per person-year for myelosuppression were 0.623 and 0.181 in the R/R group, and 1.409 and 0.218 in the intolerant group, while for nephrotoxicity were 0.147 and 0.052 in the R/R group, and 0.634 and 0.054 in the intolerant group. Hospitalization rates per person-year before and after

maribavir initiation were 1.36 and 0.91 in the R/R group and 1.27 and 0.46 in the intolerant group, respectively. All-cause mortality was 41.1% in the R/R group and 42.4% in the intolerant group.

Figure. Time to CMV clearance from start of maribavir therapy

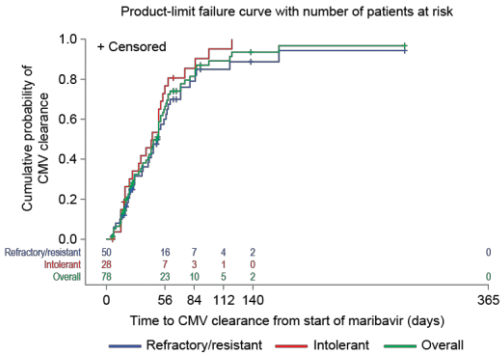

Table. Adverse events of special interest (AESI) and health care resource utilization, n (%)

	R/R (n=56)		Intolerance to anti-CMV agents (n=33)	
	Prior to maribavir initiation	After maribavir initiation	Prior to maribavir initiation	After maribavir initiation
Overall AESIs	21 (37.5)	10 (17.9)	23 (69.7)	9 (27.3)
Myelosuppression	17 (30.4)	7 (12.5)	19 (57.6)	7 (21.2)
Nephrotoxicity	4 (7.1)	2 (3.6)	9 (27.3)	2 (6.1)
Taste disturbance	4 (7.1)	2 (3.6)	1 (3.0)	1 (3.0)
ER visits	2 (3.6)	4 (7.1)	1 (3.0)	4 (12.1)
Inpatient hospitalizations	28 (50.0)	20 (35.7)	16 (48.5)	10 (30.3)

Table reports number (%) of patients with ≥1 events.
CMV, cytomegalovirus; ER, emergency room; R/R, refractory/resistant CMV

Conclusions: Interim results of this European retrospective study support the real-world effectiveness and safety of maribavir in adult HCT recipients with refractory/resistant CMV or

intolerance to anti-CMV agents. CMV clearance rates at maribavir discontinuation appeared to be higher than previously observed in the HCT population within the phase 3 SOLSTICE trial. The lower incidence of myelosuppression and nephrotoxicity after versus before maribavir initiation is in line with the lower hematologic and renal toxicity of maribavir compared with ganciclovir/valganciclovir and foscarnet in the overall SOLSTICE transplant population.

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B074

INFECTION BURDEN IN MISMATCHED UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION USING REDUCED-DOSE POST-TRANSPLANTATION CYCLOPHOSPHAMIDE AS GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS: RESULTS FROM THE OPTIMIZE TRIAL

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Background: Favorable one year overall survival was noted in the mismatched unrelated donor (MMUD) ACCESS trial (NCT04904588) (PMID 40523209). However, 60% of adult

patients experienced 275 clinically significant infections (CTCAE Grades 2-5) within the first 100 days (D100), with similar frequences in infections for patients receiving either myeloablative (MAC, 56%) or non-myeloablative/reduced intensity conditioning (NMA/RIC, 64%). Using combination reduced dose post-transplant cyclophosphamide (PTCy 25 mg/kg Days 3 and 4), tacrolimus, and mycophenolate mofetil as graft-versus-host disease (GvHD) prophylaxis, the OPTIMIZE (NCT06001385) trial aims to improve D100 infection free survival (IFS). As part of the trial's secondary objectives, we describe infections in the initial cohort of patients enrolled in OPTIMIZE.

Methods: Infection data was aggregated from 157 adult patients (n=75 MAC, n=82 RIC/NMA), who were fully evaluable for the primary endpoint and comprised patients enrolled in both stages of the 2-stage trial design, stratified by conditioning intensity. Infection surveillance and prophylaxis were according to institutional guidelines. Infections were graded using Blood and Marrow Transplant Clinical Trial Network (BMT CTN) criteria. Infection density was calculated as number of infections per 100 days at risk for enrolled patients. Infections occurring within 30 days after acute GvHD diagnosis were considered GvHD-related. Infection density with 95% confidence intervals (CI) were estimated using Poisson regression models; $p<0.05$ was considered statistically significant for differences in infection density by post-HCT time or conditioning intensity.

Results:

Figure 1. Infectious Sequelae in Patients Enrolled in OPTIMIZE

A Density of BMT CTN Grade 2-3 infections within 100 days by conditioning intensity

Strata	Post-HCT time	No. patients at risk[1]	Cumulative days at risk	Cumulative infections Grade 2-3	Cumulative infections Grade 3	Infection Density (per 100 days at risk) (95% CI) Grade 2-3	Infection Density (per 100 days at risk) (95% CI) Grade 3
Total	Days 0-30	157	4867	65	14	1.34 (1.04-1.69)	0.29 (0.16-0.47)
	Days 31-100	157	15586	36	5	0.23 (0.16-0.31)[#]	0.03 (0.01-0.07)[#]
MAC	Days 0-30	75	2325	41	10	1.76 (1.28-2.36)[‡]	0.43 (0.22-0.75)
	Days 31-100	75	7432	23	1	0.31 (0.2-0.45)[#]	0.01 (0-0.06)[#]
RIC/ NMA	Days 0-30	82	2542	24	4	0.94 (0.61-1.37)[‡]	0.16 (0.05-0.37)
	Days 31-100	82	8154	13	4	0.16 (0.09-0.26)[#]	0.05 (0.02-0.11)

[1] For the calculation of days at risk, participants were considered at risk for infection while on-study.
[‡] Indicates $p<0.05$ in comparing infection density between MAC and RIC/NMA at the given post-HCT time.
[#] Indicates significant pairwise comparisons (adjusted $p<0.05$) within each stratum to the Day 0-30 timepoint. P-values are adjusted using the Sidak method and result from generalized Poisson models with random intercepts for each subject.

B Site of BMT CTN Grade 2-3 infection within 100 days by conditioning intensity

Site	MAC Days 0-30 No. Infections	MAC Days 0-30 No. Patients	MAC Days 31-100 No. Infections	MAC Days 31-100 No. Patients	RIC/NMA Days 0-30 No. Infections	RIC/NMA Days 0-30 No. Patients	RIC/NMA Days 31-100 No. Infections	RIC/NMA Days 31-100 No. Patients
All Sites	41	26	23	18	24	16	13	12
Blood	25	20	7	5	11	9	9	9
CNS	2	2	1	1	1	1	0	0
Genital Area	2	1	0	0	0	0	0	0
GI tract, Lower	3	3	4	4	4	4	2	2
GI tract, Upper	2	2	2	1	1	1	0	0
Resp tract, Lower	3	3	4	4	4	4	0	0
Sinus and/or Resp tract, Upper	3	3	3	2	1	1	0	0
Skin	4	3	2	2	0	0	0	0
Urinary tract, Lower	0	0	2	2	1	1	2	2
Urinary tract, Upper	0	0	0	0	1	1	1	1
Unknown	0	0	1	1	0	0	0	0

C BMT CTN Grades 2-3 Infection and pathogen type frequencies by conditioning regimen

Regimen	Pathogen type	Overall No. infections	Overall No. patients	Days 0-30 No. infections	Days 0-30 No. patients	Days 31-100 No. infections	Days 31-100 No. patients
All	Overall	101	75	65	55	36	32
	Gram-positive bacteria	16	14	11	10	5	5
	Gram-negative bacteria	13	11	11	9	2	2
	Respiratory virus	8	7	4	4	4	3
	Non-respiratory virus	46	31	26	21	20	17
	Yeast	1	1	1	1	0	0
	Unknown/non-specific	17	11	12	10	5	5
MAC	Overall	64	44	41	34	23	20
	Gram-positive bacteria	9	8	6	6	3	3
	Gram-negative bacteria	6	5	5	4	1	1
	Respiratory virus	7	6	3	3	4	3
	Non-respiratory virus	30	18	19	15	11	9
	Yeast	0	0	0	0	0	0
	Unknown/non-specific	12	7	8	6	4	4
RIC/NMA	Overall	37	31	24	21	13	12
	Gram-positive bacteria	7	6	5	4	2	2
	Gram-negative bacteria	7	6	6	5	1	1
	Respiratory virus	1	1	1	1	0	0
	Non-respiratory virus	16	13	7	6	9	8
	Yeast	1	1	1	1	0	0
	Unknown/non-specific	5	4	4	4	1	1

D Site of BMT CTN Grade 2-3 infection associated with acute GvHD by conditioning intensity

Site	Grade 2-4 Acute GvHD MAC No. Infections	Grade 2-4 Acute GvHD MAC No. Patients	Grade 2-4 Acute GvHD RIC/NMA No. Infections	Grade 2-4 Acute GvHD RIC/NMA No. Patients	Grade 3-4 Acute GvHD MAC No. Infections	Grade 3-4 Acute GvHD MAC No. Patients	Grade 3-4 Acute GvHD RIC/NMA No. Infections	Grade 3-4 Acute GvHD RIC/NMA No. Patients
All Sites	9	7	3	3	4	3	0	0
Blood	6	4	3	3	3	2	0	0
GI tract, Lower	1	1	0	0	1	1	0	0
Sinus and/or Resp tract, Upper	1	1	0	0	0	0	0	0
Urinary tract, Upper	1	1	0	0	0	0	0	0

Median patient age was 46 (19-64) and 66 (22-78) years for MAC and RIC/NMA strata, respectively. Cytomegalovirus (CMV) serostatus was similar by conditioning intensity. By D100, 37% enrollees, 44% receiving MAC and 30% receiving NMA/RIC, experienced 101 BMT CTN Grade 2-3 infections (n=64 MAC, n=37 RIC/NMA). Infection density was

statistically higher between Days 0-30 versus Days 31-100 overall and within each conditioning intensity stratum (Figure 1A). Notably, MAC Days 0-30 infection density was significantly higher than RIC/NMA (p=0.044), but not between Days 31-100 (Figure 1A). The most common sites of BMT CTN Grades 2-3 infection were blood (n=52), lower gastrointestinal (GI) tract (n=13), and lung (n=11) (Figure 1B). Non-respiratory viruses were the most frequent pathogen type in patients receiving either MAC (n=30 infections) or RIC/NMA (n=16 infections) (Figure 1C). Gram-positive (n=16) and gram-negative (n=13) bacteria were the next most common pathogen types. CMV (MAC n=18, RIC/NMA n=8), Clostridioides difficile (MAC n=4, RIC/NMA n=3), and Escherichia coli (MAC n=4, RIC/NMA n=5) were the most frequent isolates for each of the respective pathogen types (data not shown). The most common site for the 12 acute GvHD-related BMT CTN Grades 2-3 infections was blood (n=9) (Figure 1D), and CMV (n=6) was the most common isolate (data not shown). Grades 3-4 acute GvHD-associated infections were similar by site (Figure 1D) and pathogen (data not shown).

Conclusions: Taken together, these preliminary results suggest potential difference in impact of PTCy dose reduction between MAC and RIC in the MMUD setting with respect to infection burden. Whether these preliminary observations translate into higher IFS for patients enrolled on OPTIMIZE will be addressed with data forthcoming on the study's primary endpoint.

Clinical Trial Registry: OPTIMIZE NCT06001385
https://clinicaltrials.gov/study/NCT06001385

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B075

RISK STRATIFICATION FOR EARLY EBV REACTIVATION AFTER PEDIATRIC ALLO-HSCT: DEVELOPMENT OF A CLINICAL SCORING SYSTEM

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Background: Epstein–Barr virus (EBV) reactivation is a clinically significant complication after pediatric allogeneic hematopoietic stem cell transplantation (allo-HSCT). Early

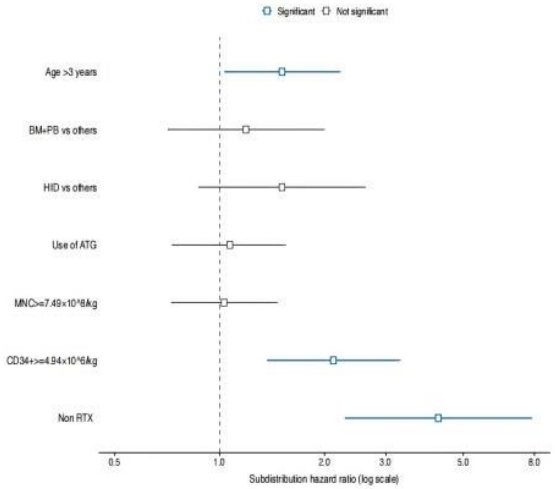
identification of high-risk patients is essential for optimizing monitoring intensity and pre-emptive therapy. This study aimed to develop and validate a simple clinical risk score to predict early EBV reactivation in children undergoing allo-HSCT.

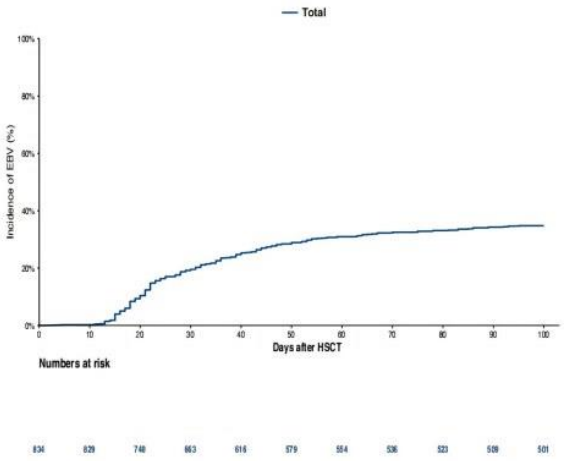
Methods: A total of 834 pediatric patients receiving allo-HSCT at Children's Hospital of Soochow University were retrospectively analyzed. Patients transplanted between 2010–2020 (n=488) served as the training cohort, and those transplanted between 2021–2024 (n=346) as the validation cohort. EBV reactivation was defined as two consecutive EBV DNAemia measurements exceeding 500 copies/mL. EBV reactivation within 100 days post-transplant was evaluated using competing-risk models. Variables with $P<0.05$ in multivariable Fine–Gray analysis were incorporated into a weighted risk-scoring system and validated temporally.

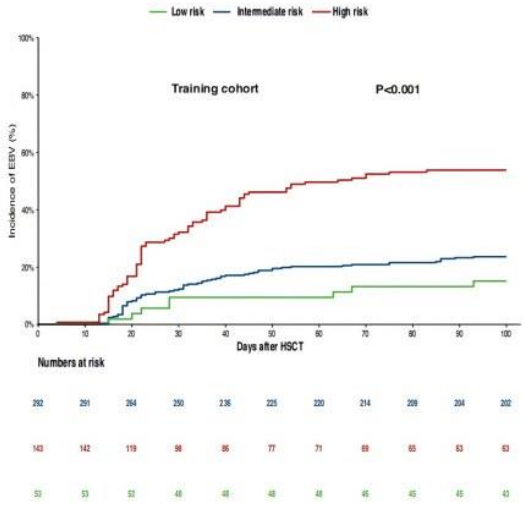
Results: Baseline characteristics differed significantly between the two cohorts, reflecting temporal evolution in transplant practices. The validation cohort exhibited higher rates of rituximab use (39.1% vs. 18.0%), ATG-containing conditioning (96.5% vs. 58.8%), haploidentical donors (75.1% vs. 50.8%), and PB grafts (44.2% vs. 22.5%), along with a greater proportion of older children (>11 years: 30.3% vs. 19.7%). Cord blood use markedly declined (2.0% vs. 26.0%). CMV and EBV serostatus were similar between cohorts. The overall cumulative incidence of EBV reactivation by day 100 in the entire cohort was 37.7%. Multivariable analysis identified three independent predictors of EBV reactivation: age >3 years, omission of rituximab in conditioning, and $CD34^+$ cell dose $>4.94\times10^7$/kg. A weighted score (2, 4, and 2 points) stratified patients into low- (0–3), intermediate- (4–6), and high-risk (7–8) groups, with corresponding 100-day EBV incidences of ~15.1%, ~23.6%, and ~53.8% ($P<0.001$). Findings were consistent in the validation cohort (5.0% vs 32.9% vs 56.8%, $P<0.001$), demonstrating temporal robustness.

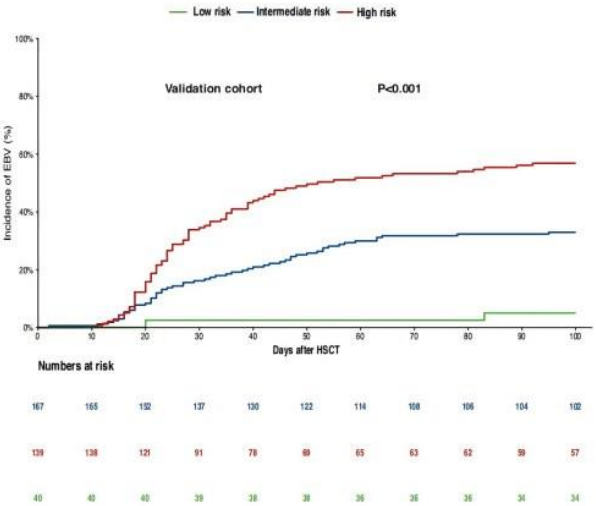
Factor	Univariable analysis
	HR (95% CI)
Male vs female	1.010 (0.731–1.400)
Age >3 year	1.700 (1.170–2.480)
Malignant vs non-malignant	0.913 (0.643–1.300)
MAC vs (RIC/NMA)	0.884 (0.610–1.280)
BM+PB vs others	2.120 (1.520–2.950)
ABO matched vs mismatched	1.160 (0.847–1.590)
HLA matched vs mismatched	1.200 (0.849–1.690)
HID vs others	2.180 (1.560–3.060)
EBV serostatus positive(R)	1.050 (0.418–2.630)

CMV serostatus positive (R)	0.573 (0.246–1.340)
ATG, yes vs no	1.460 (1.040–2.050)
Ara-c, yes vs no	0.880 (0.639–1.210)
TBI, yes vs no	1.040 (0.579–1.880)
MNC≥7.49×10^8/kg	1.390 (1.010–1.900)
CD34+≥4.94×10^6/kg	2.580 (1.840–3.620)
RTX, no vs yes	3.350 (1.830–6.120)









Conclusions: We developed and validated a practical three-factor score that reliably discriminates EBV reactivation risk after pediatric allo-HSCT and may support individualized surveillance and prophylactic strategies. The absence of external validation remains a limitation, underscoring the need for future multicenter prospective studies.

Clinical Trial Registry: None.

Disclosure: No conflict of interest.

B076

ADENOVIRUS IN THE ERA OF INCREASING ALTERNATE DONOR HSCT: OUTCOMES, PREDICTORS, AND THERAPEUTIC RESPONSE OVER THE LAST DECADE

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Background: Adenoviral reactivation represents a serious infectious complication in children undergoing hematopoietic stem cell transplantation (HSCT), particularly with increasing reliance on alternate donor transplantation. Immunosuppression, delayed immune recovery, and intensive conditioning regimens are recognized contributors to increased susceptibility. This study aimed to determine the incidence, risk factors, management, and clinical outcomes associated with adenoviral reactivation in children undergoing alternate donor HSCT.

Methods: This retrospective observational study included patients up to 25 years of age who underwent alternate donor HSCT between July 2014 and June 2025. Indications included hemoglobinopathies, inborn errors of immunity (IEI), inborn errors of metabolism (IEM), bone marrow failure syndromes (BMFS), and malignancies. Clinical data was obtained from medical records, including transplant type, conditioning regimen, graft-versus-host disease (GVHD) prophylaxis, virological monitoring, and therapeutic interventions. All patients underwent weekly multiplex polymerase chain reaction (PCR) surveillance for cytomegalovirus (CMV), Epstein–Barr virus (EBV), and adenovirus until Day 100 post-transplant. Adenoviral reactivation prompted a 50% reduction in immunosuppression and initiation of weekly cidofovir at 5 mg/kg.

Results: A total of 1,245 HSCTs were performed during the study period, of which 700 (56.2%) were alternate donor transplants. Adenoviral reactivation occurred in 77 patients, reflecting an incidence of 11%. The median age at transplantation was 8.4 years (range: 7 months–22 years), with a male-to-female ratio of 1.2:1. Underlying diagnoses included hemoglobinopathies (n=27), IEI (n=18), malignancies (n=16), BMFS (n=11), and IEM (n=5).
Haploidentical HSCT using post-transplant cyclophosphamide (PTCY) demonstrated the highest association with adenoviral reactivation (59.7%), followed by TCR α/β–depleted

haploidentical grafts (19.5%) and matched unrelated donor transplants (13%) (p<0.001). Myeloablative conditioning was significantly associated with higher incidence compared with reduced-intensity conditioning **(67.5%, p=0.004)**. The median time to detection was 45 days post-HSCT, with viral load ranging from 135 to 7.95×10^7 copies/ml. Acute GVHD occurred in 59.7% of the cohort, and 53.2% required escalation of immunosuppression in the week preceding reactivation. Lymphopenia was common, with 57.1% demonstrating Day-30 absolute lymphocyte count below 500/µL.
One-third of patients cleared the virus following immunosuppression modification alone, while 66% received a median of 3 doses of cidofovir (range: 1–11). Co-infections were prevalent: CMV (61%), BK virus (15.6%), and EBV (13%). Overall survival was 62.3%, with a median follow-up of 27.5 months.

Conclusions: Adenoviral reactivation occurred in 11% of alternate donor HSCT recipients with a mortality rate of 31.1%. Myeloablative conditioning and PTCY-based haploidentical transplantation were significant risk factors. Early immune reconstitution, particularly achieving adequate lymphocyte recovery by Day 30, appears critical in reducing risk. Strengthened post-transplant surveillance and optimized immune-modulatory strategies may improve outcomes in this high-risk group.

Disclosure: Nothing to declare

B077

IMPACT OF INTERLEUKIN-6 DYNAMICS ON INFECTION SEVERITY AND CLINICAL OUTCOMES IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES UNDERGOING INTENSIVE THERAPY AND ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Infectious and inflammatory complications remain a major cause of morbidity and non-relapse mortality in patients with hematological malignancies undergoing intensive chemotherapy or allogeneic stem cell transplantation (allo-SCT). Early recognition of clinically relevant inflammatory events is challenging in immunocompromised patients, as clinical signs and routinely used biomarkers such as C-reactive protein (CRP) often show delayed or nonspecific responses. Interleukin-6 (IL-6) is a rapidly responding proinflammatory cytokine and may provide earlier and prognostically relevant information during severe inflammatory events. This study evaluated the diagnostic and prognostic relevance of IL-6 dynamics in a real-world cohort of high-risk hematological patients.

Methods: We conducted a retrospective, monocentric cohort analysis including 81 patients with hematological malignancies treated between 2020 and 2024. All patients experienced

clinically significant inflammatory events graded CTCAE ≥3, defined by a documented IL-6 increase to ≥100 pg/ml. Patients were treated with intensive chemotherapy or in the peri-transplant setting after allo-SCT. Serial IL-6 measurements were analyzed in relation to inflammatory kinetics, initiation or escalation of antibiotic therapy, microbiologically documented infections, intensive care unit (ICU) admission, and overall survival (OS). IL-6 dynamics were compared with CRP and procalcitonin (PCT) where available. Predictive performance for ICU admission and mortality was assessed using receiver operating characteristic (ROC) analyses.

Results: Eighty-one patients (median age 59.8 years) were analyzed; 72/81 (88.9%) were in the allo-SCT setting. IL-6 elevation preceded conventional biomarkers, rising approximately 24–48 hours before a clinically relevant CRP increase. IL-6 kinetics were rapid, with a median of 24.0 hours from the last IL-6 value <100 pg/ml to the first rise ≥100 pg/ml and 24.9 hours from first rise to peak, illustrating distinct kinetic patterns between resolving and fatal inflammatory courses (Figure 1A).
IL-6 peak levels identified patients at risk for severe clinical deterioration: IL-6 peak predicted ICU admission with an AUC of 0.763; an optimal cut-off of 1736 pg/ml yielded 74.2% sensitivity and 71.9% specificity (negative predictive value 80.5%) (Figure 1B).
IL-6 clearance was the strongest outcome discriminator. All patients with documented IL-6 normalization below 100 pg/ml survived, whereas all patients without IL-6 decline died, and most required ICU care. IL-6 peak showed the highest prognostic accuracy for mortality (AUC 0.80), followed by later IL-6 measurements (AUC 0.78), while early single measurements were less informative. Rapid IL-6 increases (ΔIL-6 >1346 pg/ml early or >2600 pg/ml to peak) were associated with fatal outcome. Mortality increased with delayed or absent IL-6 decline (<72 h: 11.1%; >72 h: 26.9%; no decline: 100%).

Conclusions: IL-6 dynamics provide early and clinically meaningful information during severe inflammatory events in patients with hematological malignancies undergoing intensive therapy or allo-SCT. IL-6 rises earlier than CRP, defined IL-6 cut-offs identify patients at imminent risk for ICU admission, and IL-6 clearance versus non-clearance stratifies distinct survival phenotypes. To validate these findings, an ongoing analysis of approximately 500 patients after allo-SCT with longitudinal IL-6 data is underway, aiming to confirm the dissertation-derived thresholds and develop clinically applicable IL-6–guided decision algorithms in the post-transplant setting.

Clinical Trial Registry: 2025-3378
https://www.medizin.hhu.de/die-fakultaet/gremien-und-beauftragte-der-medizinischen-fakultaet/kommissionen/ethikkommission

Disclosure: The authors declare no conflicts of interest.

B078

PRE-TRANSPLANT CLOSTRIDIOIDES DIFFICILE INFECTION: A TIMING-DEPENDENT PREDICTOR OF GI GVHD AND EARLY MORTALITY IN ALLOGENEIC HSCT RECIPIENTS

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Background: *Clostridioides difficile* infection (CDI) is a frequent complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT), yet its impact on post-transplant outcomes remains controversial. Therefore, this study aimed to evaluate the risk factors for CDI and its association with early post-transplant complications and overall clinical outcomes.

Methods: This retrospective, single-center study included patients who underwent allo-HSCT at our center between January 2021 and December 2023 and experienced diarrhea in the peri-transplant period (from conditioning to discharge from laminar flow). Stool screening for *C. difficile* was routinely performed for all patients who developed diarrhea during the peri-transplant period. CDI was defined as the occurrence of diarrhea (three or more unformed stools within a 24-hour period) accompanied by a positive stool test result for *C. difficile*.

Results: A total of 593 patients was included in the study. Among these diarrheic recipients, 64 patients developed CDI. The cumulative incidence of CDI was 12.1% (95% CI, 9.5%-15.1%), with a median onset of day -1 (range, -7 to +26) relative to HSCT. Multivariate analysis revealed that older age was independently associated with a lower risk of CDI (HR, 0.97; 95% CI, 0.96-0.99; P = 0.006). No significant association was found between overall CDI and gastrointestinal acute graft-versus-host disease (GI aGVHD), severe infection or 100-day non-relapse mortality (NRM) in both univariate analysis or multivariate analysis. However, the timing of CDI dramatically influenced prognosis. When patients were stratified by the median onset time of CDI, pre-transplant CDI was suggestive of a trend toward an increased risk of grade 1-4 GI aGVHD, grade 2-4 GI aGVHD in the univariate model (Table 1). Multivariate analysis confirmed pre-CDI as an independent risk factor for grade 1-4 (HR, 2.46; P=0.022) and grade 2-4 (HR, 2.32; P=0.048) GI aGVHD (Table 1). Moreover, pre-transplant CDI conferred a substantially elevated risk of severe fungal infection (HR, 7.65; P=0.007) and 100-day NRM (HR, 3.26; P=0.044).

Table 1

Variables	Univariate		Multivariate	
	HR (95%CI)	p	HR (95%CI)	p
Grade 1-4 GI aGVHD				
CDI before HSCT		0.033		0.022
No	Reference		Reference	
Yes	2.29 (1.07, 4.92)		2.46 (1.14, 5.30)	
CDI after HSCT		0.307		-
No	Reference		-	
Yes	0.36 (0.05, 2.58)		-	
Grade 2-4 GI aGVHD				
CDI before HSCT		0.07		
No	Reference		Reference	0.048
Yes	2.16 (0.94, 4.95)		2.32 (1.01, 5.34)	
CDI after HSCT		0.357		-
No	Reference		-	
Yes	0.39 (0.05, 2.86)		-	

Conclusions: Our study demonstrates that the timing of onset is a critical determinant of the adverse impact of CDI on severe complications and mortality in diarrheic allo-HSCT recipients. Further prospective studies are warranted to investigate targeted prevention or pre-emptive management of pre-transplant CDI to improve transplant outcomes.

Disclosure: Nothing to declare.

B079

HHV-6B INFECTION ADVERSELY IMPACTS OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A MULTICENTER, CASE-CONTROL STUDY

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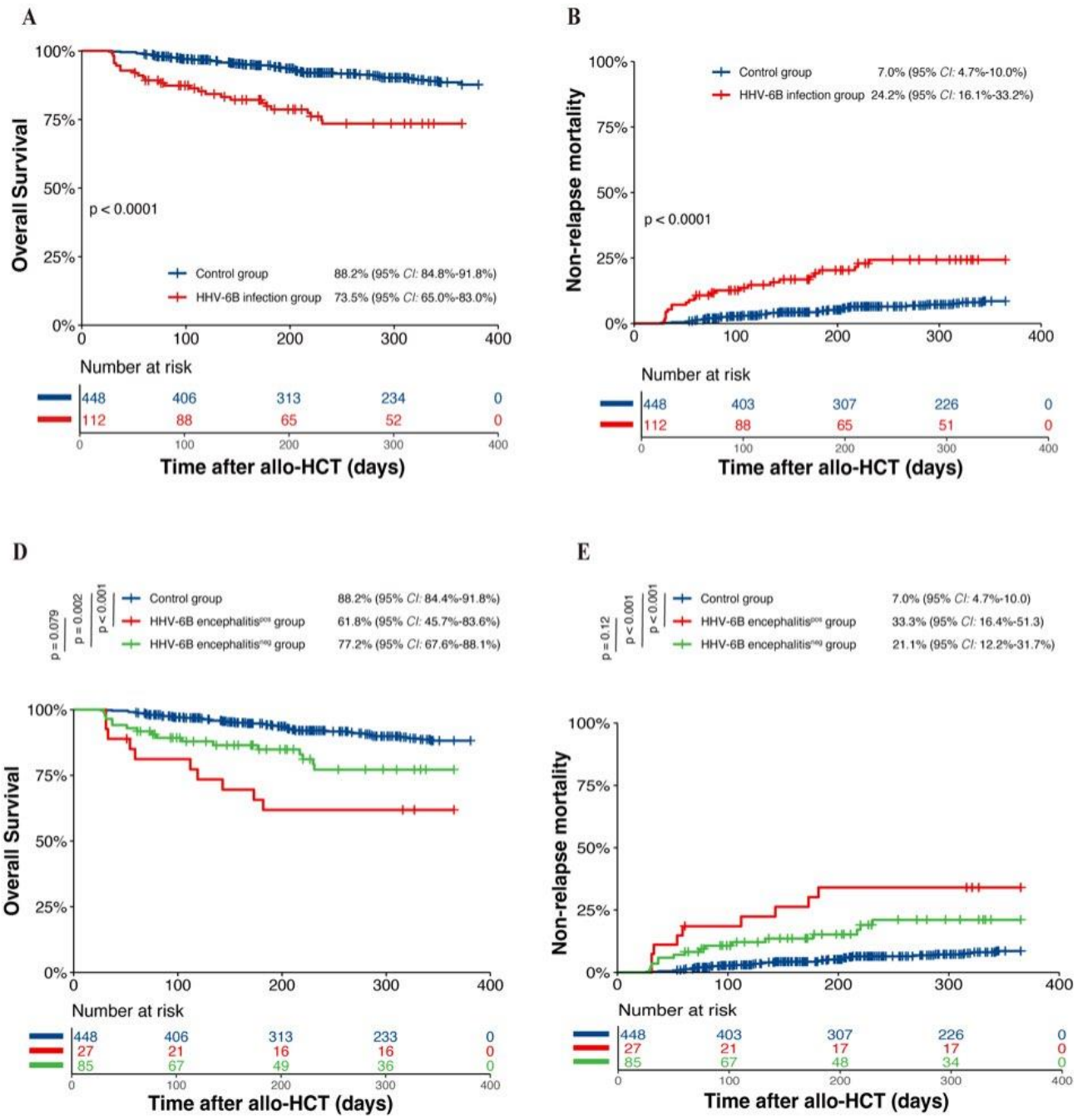
Background: Latent human herpesvirus 6B (HHV-6B) can reactivate in patients with hematologic diseases who have undergone allogeneic hematopoietic stem cell transplantation (allo-HCT). Its impact on post-transplant outcomes, particularly in haploidentical (HID) allo-HCT–dominant cohorts, however, is unclear.

Methods: In this multi-center retrospective study, we conducted a case-control study from December 2019 to January 2025 to evaluate clinical outcomes and risk factors of adult patients receiving allo-HCT with different type of HHV-6B reactivation. 112 patients were included in the HHV-6B reactivation group, with a one-to-four ratio matched to the control group. 27 patients diagnosed with HHV-6B encephalitis were classified as HHV-6B encephalitis^{pos} group, and the rest 85 patients in the HHV-6B reactivation group were defined as HHV-6B encephalitis^{neg} group.

Results: After inverse propensity weighting, the 1-year OS was significantly lower in the HHV-6B group (74.4% [95% *CI*: 65.4–84.6%]) compared to controls (88.7% [95% CI: 85.3–92.1%], *P*<0.001), while the 1-year NRM was significantly higher in the HHV-6B group (20.3% [95% *CI*: 16.0–24.5%]) compared to controls (6.7% [95% CI: 5.0–8.3%], *P* < 0.001). The 1-year relapse rates were comparable between groups (3.4% [95% *CI*: 1.5–5.3%] *vs*. 4.8% [95% CI: 3.4–6.2%], *P*=0.27). However, the 1-year OS and NRM rates were not statistically different between the encephalitis^{pos} and encephalitis^{neg}groups (OS: 61.8% [95% *CI*: 45.7%–83.6%] *vs.* 77.2% [95% *CI*: 67.6%–88.1%], *P*=0.079; NRM: 33.9% [95% *CI*: 13.1%–49.7%] *vs*. 21.1% [95% *CI*: 10.6%–20.3%], *P*=0.12). Propensity score–weighted multivariable logistic regression identified hematopoietic cell transplantation–specific comorbidity index (OR, 2.075; 95% *CI*: 1.002–4.295; *P*=0.04), donor-specific antibody (OR, 2.336; 95% *CI*: 1.087–5.02; *P*=0.03), platelet engraftment failure (OR, 4.190; 95% *CI*: 1.147–15.306; *P*=0.03), and steroid-refractory acute graft-versus-host disease (OR, 3.024; 95% *CI*: 1.548–5.904; *P*=0.001) as risk factors for HHV-6B infection. Landmark Cox regression analyses using a 180-day cut-off showed that HHV-6B infection (HR, 1.825; 95% *CI*: 0.879–3.788; *P*=0.016), platelet engraftment (HR, 3.812; 95% *CI*: 1.625–8.945; *P*=0.002) and grade II–IV aGvHD (HR, 2.632; 95% *CI*: 1.243–5.574; *P*=0.011) were associated with reduced OS within the first 180 days post-transplant, but not thereafter. Based on a nomogram for HHV-6B infection prediction, 107 patients were categorized as high risk (HR; ≥80th percentile), and 453 as low risk (LR). This stratification correctly identified 87% of patients without HHV-6B infection and 49.5% with infection. Patients in the HR group had a significantly higher likelihood of HHV-6B infection compared to the LR group (odds ratio, 6.55; 95% *CI*: 4.1–10.4; *P*<0.001).

	HR (95%CI)	***p*-value**

Group		
non-HHV-6B infectio	Reference	
HHV-6B infection	1.825 (0.879–3.788)	0.016
Grades II–IV aGvHD		
No	Reference	
Yes	2.632 (1.243–5.574)	0.011
Platelet engraftment		
No	Reference	
Yes **TA-TMA** No Yes	3.812 (1.625–8.945) Reference 2.299 (0.941–5.618)	0.002 0.068



Conclusions: These findings suggest that HHV-6B reactivation is not merely a by-product of severe immune suppression but a contributor to early post-transplant complications and mortality in haploidentical transplantation.

Disclosure: Nothing to declare

B080

VIROLOGIC OUTCOMES BY BASELINE CMV VIRAL LOAD IN HCT RECIPIENTS TREATED WITH MARIBAVIR: POST HOC ANALYSIS OF PHASE 2 AND 3 TRIALS

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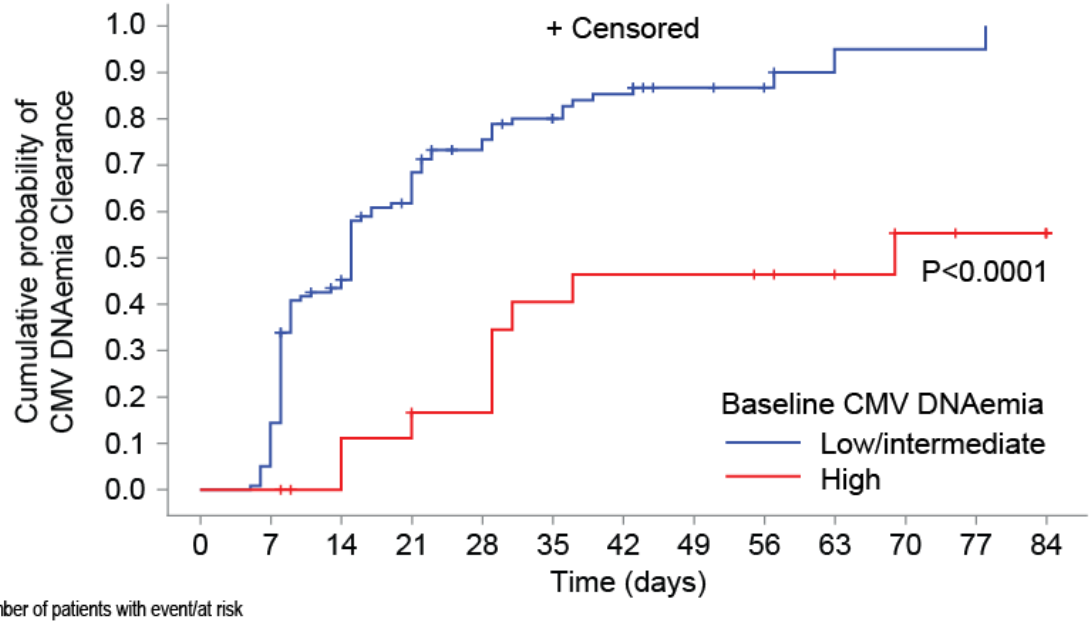
Background: In hematopoietic cell transplant (HCT) recipients, cytomegalovirus (CMV) viral load is a predictor of CMV disease and mortality in the context of severe immunosuppression. Higher baseline CMV DNAemia (viral load) has been associated with delayed DNAemia clearance in addition to host factors. Maribavir is an oral benzimidazole riboside antiviral approved for refractory CMV infection post transplant. This analysis examined virologic and safety outcomes by baseline DNAemia in HCT recipients with refractory CMV infection treated with maribavir in clinical trials.

Methods: We conducted an exploratory, post hoc analysis of two maribavir trials in HCT recipients with refractory CMV infection: a phase 2, dose-ranging study (1263-202; SHP620-202; NCT01611974) and a phase 3 study versus investigator-assigned therapy (SOLSTICE; NCT 02931539). Patients received maribavir for up to 24 weeks in study 202 and 8 weeks in SOLSTICE. Analyses were restricted to maribavir-treated patients. Baseline plasma CMV DNAemia was categorized as low/intermediate (study 202: <10,000 copies/mL; SOLSTICE: <91,000 IU/mL) or high (study 202: ≥10,000 copies/mL; SOLSTICE: ≥91,000 IU/mL). Efficacy endpoints included DNAemia clearance by week 8 and at any time on study. Safety endpoints included the incidence of adverse events (AEs), treatment-emergent AEs (TEAEs), and AEs leading to treatment interruption or discontinuation, or death. Outcomes were summarized descriptively by DNAemia category. Time to CMV DNAemia clearance at any time during the study was assessed by DNAemia category using Kaplan-Meier analysis with log-rank testing.

Results: A total of 138 maribavir-treated HCT patients were included, of whom 118 (85.5%) had low/intermediate and 20 (14.5%) had high baseline plasma CMV DNAemia. Median (range) age was 55.0 (19-77) and 60.5 (26-69) years in the low/intermediate and high DNAemia groups, respectively; 52.5% and 55.0% were male. By week 8, a higher proportion of patients with low/intermediate versus high baseline DNAemia achieved DNAemia clearance (64.4% vs 40.0%, respectively). DNAemia clearance was observed beyond week 8 (Figure). At any time during the study, DNAemia clearance was achieved in 82.2% of the low/intermediate DNAemia group and 45.0% of the high DNAemia group. Time to first DNAemia clearance was significantly shorter for patients with low/intermediate versus high

baseline DNAemia (P<0.0001; Figure). Overall, AE incidence was similar between DNAemia groups; however, AEs leading to treatment interruption or discontinuation, or death, occurred more frequently among patients with high versus low/intermediate baseline DNAemia (Table).

Figure. Inverse Kaplan-Meier curve for time to first confirmed undetectable CMV DNAemia at any time during the study up to Week 12 (Day 84) by baseline DNAemia category



Number of patients with event/at risk

Low/intermediate (n=118)	0/118	17/112	36/63	25/40	7/24	4/17	4/11	1/6	0/5	2/2	0/1	0/1	1/0
High (n=20)	0/20	0/20	2/18	1/16	0/14	4/10	1/9	0/9	0/8	0/7	1/4	0/3	0/3

DNAemia categories were determined using the definition from the respective studies: low/intermediate: study 202: <10,000 copies/mL; SOLSTICE: <91,000 IU/mL; high: study 202: ≥10,000 copies/mL; SOLSTICE: ≥91,000 IU/mL.

Table. Safety data for HCT recipients with refractory CMV by baseline DNAemia category

	Low/intermediate DNAemia (n=118)	High DNAemia (n=20)
Patients with AEs, n (%)	118 (100)	20 (100)
Number of AEs, n	1859	277

Patients with TEAEs, n (%)	117 (99.2)	20 (100)
Number of TEAEs, n	1224	261
Mild, n (%)[a]	699 (57.1)	116 (44.4)
Moderate, n (%)[a]	395 (32.3)	102 (39.1)
Severe, n (%)[a]	115 (9.4)	34 (13.0)
Maximal, n (%)[a]	15 (1.2)	9 (3.4)
Patients with AEs resulting in death, n (%)	28 (23.7)	9 (45.0)
Patients with serious TEAEs, n (%)	57 (48.3)	16 (80.0)
Patients with discontinuations of study drug due to AEs, n (%)	27 (22.9)	10 (50.0)
Patients with study drug interruptions due to AEs, n (%)	11 (9.3)	6 (30.0)

[a]Percentages calculated from the total number of TEAEs.
AE, adverse event; TEAE, treatment emergent adverse event

Conclusions: In this post hoc analysis of maribavir-treated HCT recipients with refractory CMV infection, a higher proportion of patients with low/intermediate baseline CMV DNAemia achieved DNAemia clearance, and more rapidly, than those with high baseline DNAemia, without an increase in overall AE frequency. These data reflect a population with complex treatment needs, especially in those with high DNAemia, and further research is warranted to determine if early identification and initiation/switch to maribavir could improve clinical outcomes in patients with refractory post-HCT CMV infection.

Clinical Trial Registry: NCT01611974, https://clinicaltrials.gov/study/NCT01611974
NCT02931539, https://www.clinicaltrials.gov/study/NCT02931539

Disclosure: GAP: Consulting/other fees: Genentech, MSD, Pulmocide, Regeneron, Scynexis, Symbio, Takeda; Investigator (funds paid to my institution): AiCuris, Merck; Honoraria for speaking engagement: Merck, Merck Sharp & Dohme Europe. RKA: Study/grant support: Aicuris, Astra-Zeneca, Merck, Takeda, and United Therapeutics. MB: Consulting: Merck, Takeda, AiCuris, Symbio, Moderna, EvrysBio; Research support: Moderna, Merck. WC, JG, TB: Employees of Takeda and hold equity interest in Takeda.

B081

PROGNOSTIC IMPLICATIONS OF CMV INFECTION/DISEASE AND HHV-6 ENCEPHALITIS IN CORD BLOOD TRANSPLANT RECIPIENTS RECEIVING FOSCARNET

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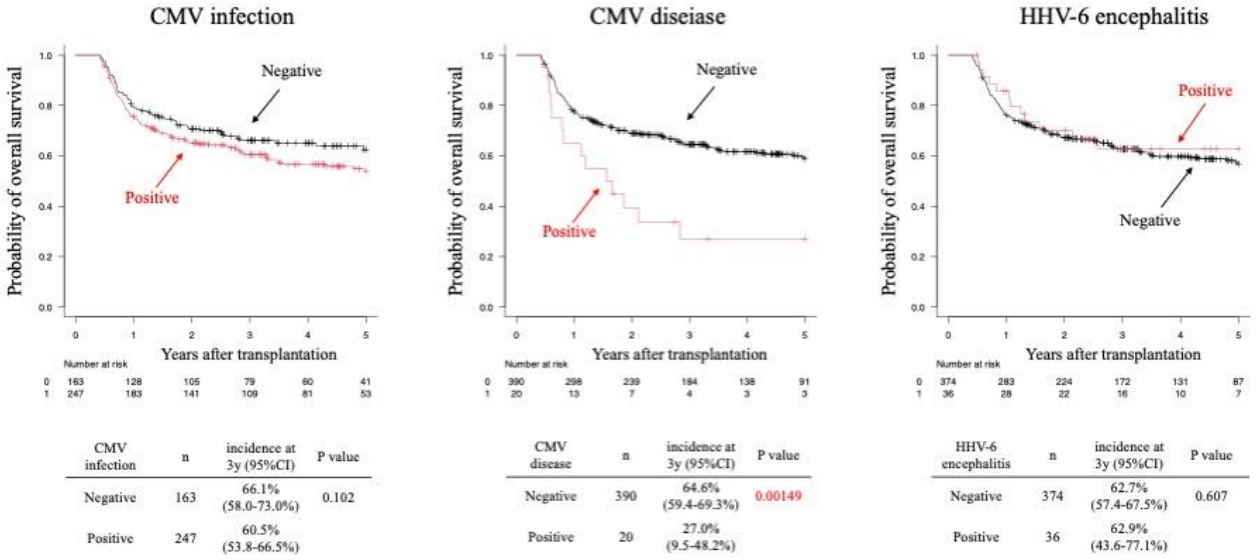
Background: Cytomegalovirus (CMV) infection remains an important post-transplant complication despite improved management. Human herpesvirus 6 (HHV-6) encephalitis is another severe infectious disease with high incidence in cord blood transplantation (CBT). Foscarnet (FOS) is an effective therapeutic agent against CMV infection and HHV-6 encephalitis; however, large-scale studies evaluating prophylactic FOS use in CBT are limited.

Methods: We retrospectively analyzed patients who underwent first single-unit CBT between 2016 and 2022 and received prophylactic FOS (120 mg/kg/day). FOS was planned from day 7 to day 50 post-transplant, with modification at physician discretion. Prophylactic administration of letermovir was not performed. Tacrolimus and mycophenolate mofetil were used for GVHD prophylaxis.
Primary endpoints were the cumulative incidence of CMV infection and its impact on relapse, non-relapse mortality (NRM), and overall survival (OS). Secondary endpoints included the incidence of CMV disease and HHV-6 encephalitis, as well as their impact on clinical outcomes. Multivariate analyses included age, disease, year of transplant, conditioning regimen, remission status, performance status, HCT-CI, HLA mismatch, total body irradiation use, and development of grade II-IV acute graft-versus-host disease (aGVHD).
Landmark analyses using events by day 150 were performed to assess the impact of CMV infection, CMV disease, HHV-6 encephalitis, and aGVHD.
The log-rank test was used to compare OS. Cumulative incidence was compared using Gray tests. Death was considered as a competing event. Fine-Gray or Cox proportional hazards models were used for multivariate analysis.
Reasons for early discontinuation of FOS (<30 days) were also assessed.

Results: A total of 491 patients were included. The cumulative incidence of CMV infection by day 150 was 53.5%. CMV infection was more common in patients aged ≥60 years (51.0% vs. 37.1%, p<0.01) and those who received reduced-intensity conditioning (20.4% vs. 11.3%, p<0.01).
In univariate analysis, CMV infection was not significantly associated with 3-year cumulative incidence of relapse (15.7% vs. 16.2%, p=0.77) or OS (60.5% vs. 66.1%, p=0.102), but was associated with higher NRM (23.9% vs. 15.5%, p=0.023). However, multivariate analysis showed no independent association between CMV infection and relapse, NRM, or OS. The cumulative incidence of CMV disease by day 150 was 4.1%. Among the 20 cases that developed CMV disease within 150 days, the disease types were gastrointestinal disease (15 cases), pneumonia (3 cases), and encephalitis (2 cases). Although CMV disease did not significantly affect relapse, it was associated with markedly higher NRM (57.9% vs. 18.5%, p<0.01) and inferior OS (27.0% vs. 64.6%, p<0.01). The cumulative incidence of HHV-6 encephalitis by day 150 was 9.2%. HHV-6 encephalitis had no significant impact on NRM (23.4% vs. 20.4%, p=0.965) or OS (62.9% vs. 62.7%, p=0.607). FOS was discontinued within 30 days in 204 patients (41.5%), mainly due to renal dysfunction (155; 75.5%), which improved in 122 patients (79.2%) after cessation.

		CMV reactivation		
Characteristic	**Group**	**Negative n = 186 (%)**	**Positive n = 304 (%)**	***P***
Age	<60	117 (62.9)	149 (49.0)	0.003
	60≦	69 (37.1)	155 (51.0)	
Disiase	AML	127 (68.3)	212 (69.7)	0.403
	ALL	34 (18.3)	43 (14.1)	
	MDS	25 (13.4)	49 (16.1)	
Conditioning regimen	Myeloablative	165 (88.7)	242 (79.6)	0.009
	Reduced intensity	21 (11.3)	62 (20.4)	
Remission status	CR	56 (30.1)	87 (28.6)	0.759
	non-CR	130 (69.9)	217 (71.4)	
Performance status	0,1	170 (91.4)	275 (90.5)	0.872
	2	16 (8.6)	29 (9.5)	

Characteristic	Group	CMV reactivation Negative n = 186 (%)	Positive n = 304 (%)	*P*
HCT-CI	0	66 (35.5)	113 (37.2)	0.928
	1,2	77 (41.4)	121 (39.8)	
	≧3	43 (23.1)	70 (23.0)	
HLA mismatch	≦2	64 (34.4)	116 (38.2)	0.44
	3≦	122 (65.6)	188 (61.8)	
TBI	Absent	133 (71.5)	204 (67.1)	0.317
	Present	53 (28.5)	100 (32.9)	



Conclusions: In CBT with prophylactic FOS, CMV infection was associated with higher NRM, with CMV disease showing a more pronounced impact and adversely affecting OS. Although prophylactic FOS did not sufficiently prevent HHV-6 encephalitis, its occurrence did not affect outcomes.

Disclosure: (Honoraria)
Hisashi Yamamoto: Meiji Seika Pharma Co., Janssen Pharmaceutical KK., Asahi Kasei Pharma Co., Otsuka Pharmaceutical Co., Takeda Pharmaceutical Co., JCR Pharmaceuticals Co., Nippon Shinyaku Co., MSD KK., Chugai Pharmaceutical Co., AstraZeneca plc, Novartis Pharma Co.,
Kyosuke Yamaguchi: Nippon Shinyaku Co.,
Daisuke Kaji: Janssen Pharmaceutical KK., Bristol Myers Squibb KK., Pfizer Japan Inc., Chugai Pharmaceutical Co., AbbVie GK, Genmab KK., Taisho Pharmaceutical Co., Ono Pharmaceutical Co., SymBio Pharmaceuticals, AstraZeneca plc, Gilead Sciences, Inc., Nippon Shinyaku Co., Daiichi Sankyo Co., Sumitomo Pharma, Takeda Pharmaceutical Co., Nippon Kayaku Co.,
Aya Nishida: Nippon Shinyaku Co., Astellas Pharma Inc., Asahi Kasei Corporation, JCR Pharmaceuticals Co., Kyowa Kirin Co., Otsuka Pharmaceutical Co., Amgen KK.,
Shinsuke Takagi: Pfizer Japan Inc., Sumitomo Pharma, MSD KK., Nippon Shinyaku Co., Kissei Pharmaceutical Co., Novartis Japan, Kyowa Kirin Co., Astellas Pharma Inc., Meiji Seika Pharma Co.,
Yuki Mori: Asahi Kasei Pharma Co., Novartis Japan, Kyowa Kirin Co., GlaxoSmithKline KK., JCR Pharmaceuticals Co., Meiji Seika Pharma Co.,
Go Yamamoto: Janssen Pharmaceutical KK., Bristol Myers Squibb KK., Pfizer Japan Inc., Chugai Pharmaceutical Co., Genmab KK., AstraZeneca plc, Gilead Sciences, Inc., Nippon Shinyaku Co., Daiichi Sankyo Co., Takeda Pharmaceutical Co., BeOne Medicines, Kyowa Kirin Co., Fuji Pharma Co., CSL Behring,
Atsushi Wake: AbbVie GK, Alexion Pharma, Amgen KK, Asahi Kasei Pharma Co., Astellas Pharma Inc., AstraZeneca plc, Bristol Myers Squibb KK., Chugai Pharmaceutical Co., Daiichi Sankyo Co., Eisai Co., GlaxoSmithKline KK., Janssen Pharmaceutical KK., Kyowa Kirin Co., Meiji Seika Pharma Co., Mundi Pharma Co., Nihonkayaku Co., Novartis Pharma Co., Ono Pharmaceutical Co., Otsuka Pharmaceutical Co., Pfizer Japan Inc., Sanofi KK., SymBio Pharmaceuticals, Takeda Pharmaceutical Co.,
Naoyuki Uchida: CSL Behring, JCR Pharmaceuticals Co., Merck & Co., Asahi Kasei Pharma Co., Astellas Pharma Inc., AstraZeneca plc, AbbVie Inc., Otsuka Pharmaceutical Co., Kyowa Kirin Co., SymBio Pharmaceuticals, Daiichi Sankyo Co., Chugai Pharmaceutical Co., Nippon Kayaku Co., Novartis Japan, Janssen Pharmaceutical KK, Takeda Pharmaceutical Co.
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B082

BRONCHOALVEOLAR LAVAGE PRACTICES IN ALLO-HCT RECIPIENTS WITH LOWER RESPIRATORY TRACT INFECTIONS: A SURVEY OF INFECTIOUS DISEASES WORKING PARTY (IDWP) EBMT

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Background: Bronchoscopy (BS) with bronchoalveolar lavage (BAL) is widely used for diagnosing lower respiratory tract infections (LRTI). Lack of standardisation in BAL procedures makes it difficult to compare the diagnostic performance of BAL across studies.

Methods: We conducted a survey to identify BS/BAL practices in allogeneic hematopoietic cell transplantation (allo-HCT) recipients with LRTI in EBMT transplant centres.

Results: The response rate was 113/653 (17%) from adult centres (n=57), paediatric centres (n=26), and mixed centres (n=30).
In 111/113 (98%) centres, BAL is performed in patients with clinical symptoms of LRTI and CT findings, especially when undetermined aetiology after non-invasive tests (92/113; 81%). Specific contraindications are a risk for patients being/remaining intubated after BAL (45/111; 41%) and thrombocytopenia <20 x10^9/l, refractory to platelet transfusion (21/111; 19%).
Less than 100 ml of fluid is instilled in 27/82 adult centres (33%), while 100-200 ml is instilled in 52/82 (63%). 34/97 (35%) centres systematically analyse bronchial aspirate in addition to BAL fluid (BALf).
A microbiologist/infectious diseases expert is involved in the decision on which tests to perform in 65/111 (59%) centres, while a routine set of microbiological tests is applied in 46/111 (41%).
Standard tests performed in BALf either routinely or on demand include: PCR multiplex pneumonia panels covering respiratory viruses either alone or together with bacteria (101/109; 93%), PCR assays in single-plex or oligoplex formats (89/106 centres; 84%), and detection of genotypic resistance markers when appropriate (41/106 centres; 39%).
Standard bacterial culture is performed routinely in 99/104 (95%) centres. Legionella, Mycoplasma, Mycobacterium tuberculosis, and other mycobacteria are routinely tested in 61/104 (59%), 76/105 (72%), 60/102 (59%), and 38/101 (38%) centres, respectively, and only on clinical suspicion in 41/104 (39%), 25/105 (24%), 41/102 (41%), and 56/101 (55%), respectively.
Fungal tests (excluding Pneumocystis) in BAL are performed routinely in 95/103 (92%) centres and include galactomannan (94/102, 92%), culture (79/102; 77%), Aspergillus PCR-qualitative (57/102; 56%), Mucorales PCR-qualitative (39/102; 38%), panfungal PCR-

qualitative (32/102; 31%), Aspergillus PCR-quantitative (25/102; 24%). Pneumocystis jirovecii pneumonia (PJP)-directed tests are performed routinely in BALf in 80/101 (79%) centres, mainly PCR (66/99; 67%). A significant number of centres also apply PJP PCR on bronchial aspirate (66/98; 67%), endotracheal aspirate (51/98; 52%), and sputum (39/98; 40%).
Genotypic and phenotypic antifungal susceptibility testing is performed in 35/101 (35%) and 67/101 (66%) centres either in the centre or sent to a reference centre.
CMV PCR is routinely tested in 80/101 (79%) centres. In 53/99 (53%) centres, the treatment for CMV is based on a PCR flexible threshold in BALf, depending on a clinical situation, whereas in 34/99 (34%) centres, it is based on any positive result without a threshold. The practices concerning tests for EBV, HHV6, and Toxoplasma are summarized in the table.
Respiratory viruses, including Adenovirus, Human metapneumovirus, Influenza, Parainfluenza, Respiratory syncytial virus, and SARS-CoV-2, are routinely tested in 85-96% of centres, regardless of season, in 76/97 centres (78%).

Table 1.
Criteria for testing and treatment of specific pathogens in allo-HCT patients

Pathogens	EBV	HHV6	Toxoplasma
Criteria for testing in BALf in patients with LRTI			
Routinely	43/100 (43%)	34/100 (34%)	24/99 (24%)
Only in patients with interstitial pneumonitis	12/100 (12%)	14/100 (14%)	10/99 (10%)
Only in patients with interstitial pneumonitis and other negative tests	22/100 (22%)	31/100 (31%)	29/99 (29%)
Never	23/100 (23%)	21/100 (21%)	36/99 (36%)
Treatment approach in a specific scenario*			
Always treated	19/78 (24%)	17/77 (22%)	35/65 (54%)
Treated if other plausible co-pathogens were not detected in BAL	18/49 (37%)	22/52 (42%)	8/29 (28%)
Treated if PCR is positive both in BALf and in plasma	10/49 (20%)	12/52 (23%)	5/29 (17%)

Treated based on viral load in BALf - any positive result without the threshold	4/49 (8%)	4/52 (8%)	5/29 (17%)
Treated based on viral load in BALf - we use a specific fixed threshold	2/49 (4%)	2/52 (4%)	2/29 (7%)
Treated based on viral load in BALf - we use a flexible threshold depending on the clinical situation	30/49 (61%)	36/52 (69%)	20/29 (69%)
*Specific clinical scenario: treatment of allo-HCT patient on immunosuppressive therapy with interstitial pneumonitis based on pathogen detection in BALf			

Conclusions: The results of this study reveal differences in practices and highlight the need to harmonize them to enable comparison and optimization of BS/BAL performance.

Clinical Trial Registry: -

Disclosure: Nothing to declare.

B083

MOST PATIENTS DON'T NEED COMPLETE REVACCINATION AFTER AUTOLOGOUS PERIPHERAL BLOOD STEM CELL TRANSPLANTATION

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Background: Autologous peripheral blood stem cell transplantation (ASCT) is a well established treatment modality esp. in patients (pts.) with Multiple Myeloma and Malignant Lymphoma. The preceding conditioning therapy induces profound immunosuppression, which is assumed to result in the loss of acquired immunity, included vaccine-induced protection. Consequently, complete revaccination is currently recommended for patients similar to pts. undergoing allogeneic transplantation, although the supporting evidence is considerably weaker. To our knowledge, no published data are available regarding the actual loss of immunization after autologous transplantation. Given that the duration and degree of immunosuppression are markedly shorter and less pronounced compared to allogeneic transplantation, we hypothesized that immunization titers might be preserved. To test this, we prospectively assessed antibody titers before and after ASCT.

Methods: Serological testing before and after autologous transplant was performed for tetanus-antitoxin, poliovirus-antibodies (type 1 and 3) and antipneumococcal-IgG. Tetanus-antitoxin (IgG) was measured by EIA with a detection limit of 0.03 IE/ml and a protection threshold of 0,1 IE/ml. Poliovirus-antibodies were assessed by neutralisation assay (WHO),

with a protective titer defined as ≥ 1:8. Anti-pneumococcal-IgG was determined by EIA, with a positive threshold of > 3,3 mg/l.

Results: Forty-five patients (pts) were included in the analysis. The median age was 59 years (range, 19–74). Underlying diagnoses included multiple myeloma in 27 pts, non-Hodgkin lymphoma in 13 pts, Hodgkin lymphoma in 4 pts, and germ cell tumor in 1 pt.

In 26 pts, antibody titers against tetanus, poliomyelitis and pneumococci were assessed both before and at a median of 8 months (range, 4–19) after autologous stem cell transplantation (ASCT). Before ASCT, most pts had protective antibody titers against tetanus (24/26 pts.) and pneumococci (22/26pts.). These titers were preserved after ASCT in all but one pt. In contrast, only 13/26 pts had protective antibody titers against poliomyelitis before ASCT, and 3 of these 13 pts lost the protective titers after ASCT.

In 19 pts, only post-ASCT antibody titers were available. Protective titers were observed in 14/19 pts against tetanus and in 12/19 pts against pneumococci, but in only 7/19 pts against poliomyelitis.

Conclusions: Our findings showed a high percentage of patients with protective antibody titers against tetanus and pneumococci, but not against poliomyelitis, both before and after ASCT. Therefore, we conclude that routine complete revaccination of all patients after ASCT is not necessary. A more tailored approach—assessing post-transplant antibody titers and vaccinating only when indicated—may be more appropriate.

Disclosure: No disclosure.

B084

OUTCOME OF CMV PNEUMONIA AFTER HEMATOPOIETIC CELL TRANSPLANTATION IN THE ERA OF MODERN TRANSPLANTATION AND CMV PREVENTION PRACTICES

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Background: The incidence of early cytomegalovirus (CMV) pneumonia has decreased significantly with the introduction of routine PCR surveillance and next letermovir prophylaxis in allogeneic hematopoietic cell transplantation (HCT) recipients; however, late episodes of the CMV disease still occur and contribute to transplant-related mortality. The aim of this study was to assess CMV pneumonia-related mortality in the modern era of changing transplantation and CMV prevention and diagnostic practices and to evaluate the impact of antiviral therapies and immunoglobulin administration on patient outcomes.

Methods: We retrospectively analyzed the incidence of proven or probable CMV pneumonia (defined according to published criteria) among patients who underwent transplantation between 1986 and 2022 at Fred Hutchinson Cancer Center. In the subset of patients transplanted after 2000, we evaluated recipient, donor, transplant, viral, and treatment-related factors associated with overall and CMV-attributable mortality using Cox regression models. Attributable mortality was defined as death that occurred within 6 months after the day of CMV disease onset with active CMV disease at autopsy and/or respiratory failure, with no other cause directly contributing to the death (Clin Inf Dis 61:31, 2015).

Results: A total of 448 patients were identified, with decreasing numbers over the last 20 years: 133 cases between 2000–2011 and 26 cases between 2012–2022 (Figure 1A). Of these, 141 patients received antiviral treatment, and were included to the detailed analysis. None of the patients with early disease received letermovir prophylaxis. Co-pathogens were detected in bronchoalveolar lavage in 58 cases (41%), and 45 patients (32%) required mechanical ventilation at the time of diagnosis. Furthermore, 28 (20%) were diagnosed with an additional lung condition, such as organizing pneumonia (11%), idiopathic pneumonia syndrome (IPS; 7%), or diffuse alveolar hemorrhage (DAH; 1%).
Outcomes improved significantly after 2000, with the lowest incidence of CMV-related mortality observed in the most recent era at 11% (95% CI, 2.8–27.1%) (Figure 1B). In univariable analysis, female sex, lymphopenia, elevated bilirubin prior to CMV onset, mechanical ventilation, high-dose steroids (>2 mg/kg), and a diagnosis of DAH/IPS were associated with increased overall and CMV-attributable death risk. However, only mechanical ventilation, elevated bilirubin, and female sex remained significant in multivariable models adjusted for year of transplantation (Figure 1C). Over the past two decades, mechanical ventilation rates at the time of diagnosis remained high (2000-2011: 26.3%; 2012-2022: 50%), while there were no patients with elevated bilirubin in the more recent period (62.4%; 0%). The addition of IVIG or CMV-specific immunoglobulin was not associated with benefit in overall survival compared to antiviral therapy alone (Figure 1C, 1D).

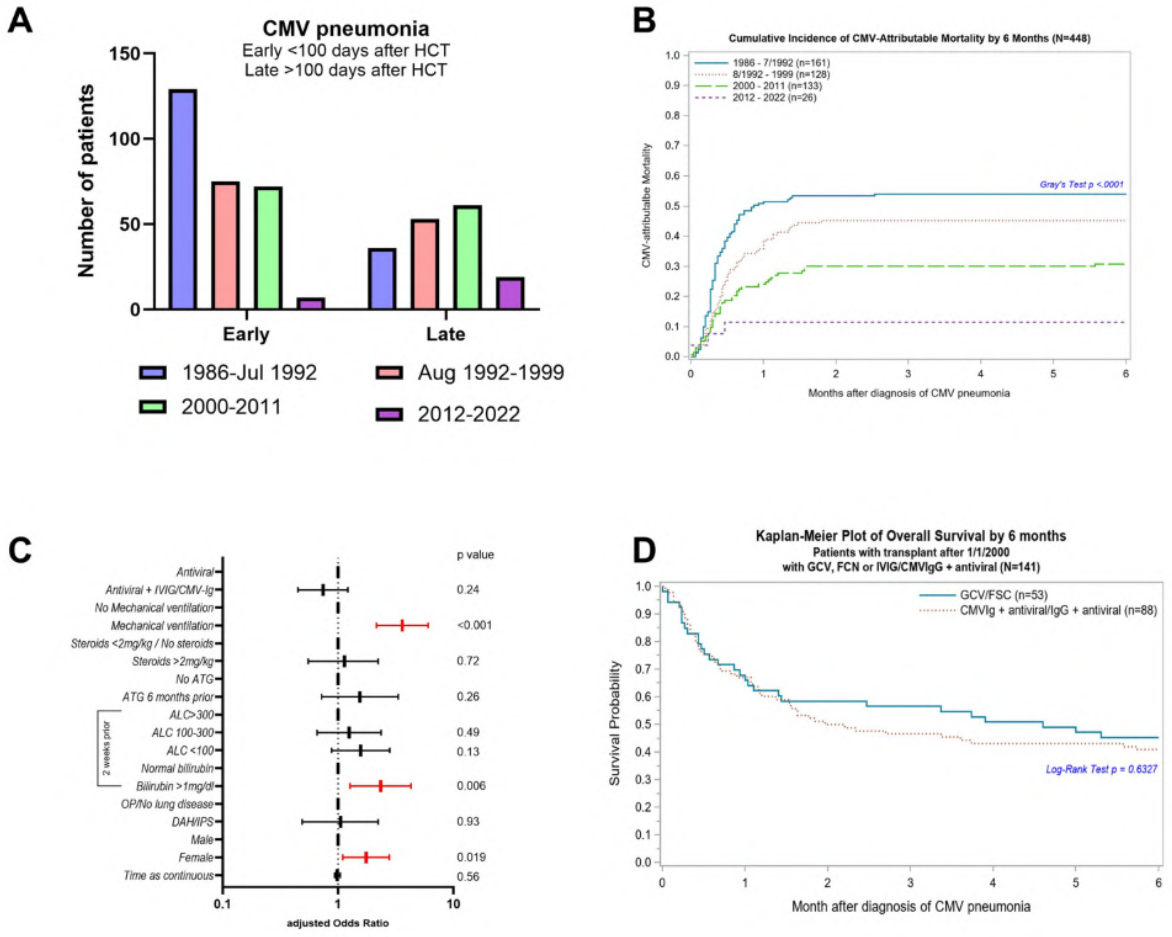

Figure 1. A) Distribution of early and late cases of CMV disease across four time periods; (B) cumulative incidence curves for CMV-attributable mortality in these periods; (C) multivariable model for overall mortality among patients transplanted after 2000 and treated with antiviral therapy; and (D) 6-month overall survival in this subset of patients.

Conclusions: CMV pneumonia incidence and mortality have continued to decline in the modern era, although late cases remain clinically relevant. The prognosis for patients requiring mechanical ventilation at the time of diagnosis remains poor, despite the improvement of transplant and supportive care techniques. The addition of IVIG or CMV-specific immunoglobulin to antiviral therapy did not show a clear survival benefit in this cohort, suggesting limited evidence to support their routine use.

Disclosure: M.Boeckh research support: Merck, Moderna, consulting: Merck, Moderna, AiCuris, Takeda, EvrysBio, Symbio
other authors have nothing to disclose.

B086

EBV REACTIVATION AND PTLD IN THE LETERMOVIR ERA: BEYOND ANTIVIRAL PROPHYLAXIS

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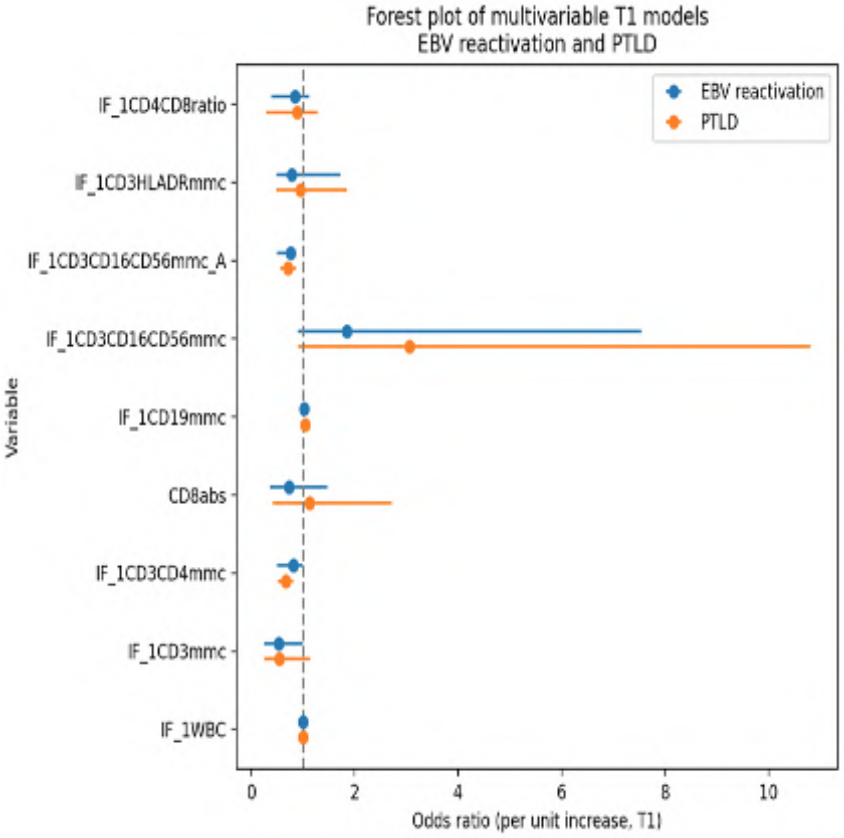
Background: Epstein–Barr virus reactivation (EBV-R) and post-transplant lymphoproliferative disorders (PTLD) remain major complications after allo-HSCT. Although EBV-PTLD occurs in 1–3% of unselected recipients, incidence increases to 8–10% in high-risk settings, including in vivo T-cell depletion, specific donor types, and severe aplastic anaemia. Emerging evidence suggests a possible rise in EBV-R and PTLD in the letermovir era, especially after haploidentical transplantation, potentially related to impaired early immune reconstitution. Consistently, our centre has observed a progressive increase in both EBV-R and PTLD over time.

Methods: We retrospectively analyzed 196 allo-HSCT from June 2019 to May 2025, with ≥6 months' follow-up, to assess EBV-R and PTLD incidence. Clinical and transplant variables were compared annually, including EBV/CMV serostatus, conditioning intensity, GVHD prophylaxis, letermovir use, GVHD, corticosteroid exposure, infections, relapse, and immune reconstitution at day +30. EBV-R was defined as EBV-DNA>10,000 copies/mL, and suspected PTLD per ECIL-6 criteria. Statistical analyses included χ^2, Spearman's test, Mann–Whitney U tests, ROC-guided logistic regression, and Kaplan–Meier analyses to identify risk factors and cumulative risks.

Results: EBV-R occurred in 30/196 patients (15.3%) and PTLD in 14/196 (7.1%). EBV-R and PTLD rates increased over time, peaking in 2023 at 22.7% and 18.2%, respectively, although year-to-year differences were not statistically significant. Baseline transplant characteristics and transplant-related complications did not differ between EBV-R and PTLD groups, except for immune reconstitution parameters, including NK-cells (p=0.0019), activated NK/T-cells (p=0.0266), and the CD4/CD8 ratio (p=0.0266).
In univariate analyses, EBV-R was associated with ATG exposure (p<0.001), PTCy use (p<0.001), and higher Fujimoto risk score (p=0.0056), with a trend for letermovir exposure (p=0.085), and differed by transplant type (p<0.001). PTLD was significantly associated with EBV reactivation (r=0.65,p<0.001), ATG use (r=0.24,p=0.0006), PTCy (r=−0.21,p=0.0028), transplant type (r=−0.16,p=0.023), and Fujimoto risk (r=0.14,p=0.047), but not with CMV reactivation.
Given the median onset of EBV-R/PTLD at 42 days (IQR 38.3–54.5), analyses focused on day 30. At this timepoint, EBV-positive patients showed higher WBC counts and lower CD3+,

CD4+, CD8+, and activated NK/T-cells, with increased counts of NK- and B-cells (all p≤0.002). ROC analysis identified NK-cells (AUC 0.72), WBC (AUC 0.69), and B-cells (AUC 0.68) as predictors of EBV-R.
Similarly, PTLD patients showed higher WBC counts (p=0.019), lower CD3+ (p<0.001), CD4+ (p<0.001), and CD8+ (p=0.007), and increased NK- (p<0.001) and B-cells (p<0.001). ROC analysis identified NK-cells (AUC 0.80,p<0.001), B-cells (AUC 0.70,p=0.001), and WBC (AUC 0.70,p=0.0017) as the strongest predictors of PTLD.
In multivariable models, higher early CD4+ (OR 0.82, p=0.05) and activated NK/T-cells (OR 0.71,p<0.01) were independently protective against both EBV-R and PTLD, whereas higher B-cell counts (p=0.05) increased the risk of both outcomes (Fig.1).



Conclusions: IIn this real-world allo-HSCT cohort, EBV-R and PTLD increased over time and were associated with ATG, PTCy, and donor type. Day-30 immune reconstitution was a key risk factor. EBV-R/PTLD were marked by poor T-cell recovery, increased NK- and B-cells, and a protective effect from higher early $CD4^{+}$ and activated NK/T-cells. Early immune monitoring may enable risk stratification and identify patients at risk for EBV-R and PTLD.

Clinical Trial Registry: None.

Disclosure: No COI

B087

IMPACT OF EBMT 2025 DEFINITIONS ON THE IDENTIFICATION OF CATHETER-RELATED BLOODSTREAM INFECTIONS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Central venous catheters (CVC) play a central role in the care of patients undergoing allogeneic hematopoietic stem cell transplantation (Allo-HSCT). Catheter-related bloodstream infections (CRBSI) are a significant complication, sometimes underestimated. Recently, the EBMT Infectious Working Party has published refined definitions of bloodstream infections (BSI) in the presence of CVC addressing their variability across the literature (*Clin Microbiol Infect 2025*). While IDSA guidelines require rigorous laboratory proof, like paired cultures, to definitively diagnose catheter-related infections (CRBSI) in general populations. In contrast, EBMT guidelines adopt these standards for transplant patients, allowing "presumed" diagnoses when strict testing isn't feasible and prioritize the distinction between gut-origin infections (MBI-BSI) and catheter infections.
The aim of this study is to compare previously described definitions of CRBSI (IDSA, Infectious Diseases Society of America, 2009) with the new EBMT definitions.

Methods: We retrospectively analyzed all patients undergoing Allo-HSCT consecutively at our center, between 2015 and 2024. All positive blood cultures were evaluated. Only first episodes of bacteremia were considered; subsequent episodes in the same patient were excluded.

Results: The study analyzed 432 patients (median age 56 years; 62.3% male) undergoing Allo-HSCT, with acute myeloid leukemia (37%) being the most frequent underlying disease. A total of 265 probable BSI episodes were evaluated, of which 224 were classified as definite BSI, occurring at a median of 7 days post-transplant. While Gram-negative bacilli accounted for 51% of definite BSIs, with *Escherichia coli* (27%) being the most frequent pathogen, the comparison of CRBSI definitions revealed significant differences. Only 28 episodes met the strict criteria for both IDSA and EBMT definite CRBSI, predominantly driven by CoNS (68%). In contrast, the EBMT probable CRBSI criteria identified an additional 46 episodes, capturing clinically relevant pathogens such as *Staphylococcus aureus* (11%) and *Candida parapsilosis* (4%) that were absent in the definite group. In the probable EBMT CRBSI category, a total of 27 CVC was removal to infectious issues: persistent bacteremia (n=5), persistent fever (n=8), signs of local infection (n=12) and sepsis/septic shock (n=2). The frequency of pathogen groups according to IDSA and EBMT definitions is shown in Table 1.
The cumulative incidence from Allo-HSCT at day +15, day +30, and day +90 for definite BSI

was 36%, 41%, and 46%, respectively. The cumulative incidence for probable EBMT CRBSI was 9%, 10%, and 12%, respectively; for definite IDSA/EBMT CRBSI, 5%, 5%, and 7%, respectively; and for probable/definite EBMT CRBSI, 14%, 15%, and 19%, respectively. Consequently, applying the combined probable and definite EBMT definitions increased the cumulative incidence of CRBSI at day +90 to 19%, compared to only 7% using the strict definite criteria.

	PROBABLE CRBS EBMT 2025 n=46	DEFINITE CRBSI IDSA 2009 n=28	PROB/DEFINITE CRBSI EMBT 2025 n=74
Microorganism group			
Gram-positive coccus	44 (96)	21 (75)	65 (88)
Gram-negative bacilli	0	6 (21)	6 (8)
Other	2 (4)	1 (4)	3 (4)
Most common identified species			
CoNS	39 (85)	19 (68)	59 (80)
Intes. GNB	0	6 (20)	6 (8)
Other GNB	0	1 (4)	1 (1)
S. aureus	5 (11)	0	5 (7)
Candida parapsilosis	2 (4)	0	2 (2)
Other	0	1 (4)	1 (1)

Table 1. Representation of pathogens identified according to EBMT and IDSA criteria.
CoNS: coagulase-negative staphylococcus; Intes: intestinal; GNB: Gram-negative bacilli.

Conclusions: BSI remains a significant complication after Allo-HSCT. The implementation of the EBMT 2025 definitions leads to an increased identification of CRBSI. Their use allows the

identification of frequent and clinically important pathogen groups that were not captured by previous definitions.

Disclosure: No disclosure.

B089

INCREASED INCIDENCE OF INFECTIONS WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE AS GVHD PROPHYLAXIS IN MATCHED SIBLING AND UNRELATED DONOR STEM CELL TRANSPLANTATION

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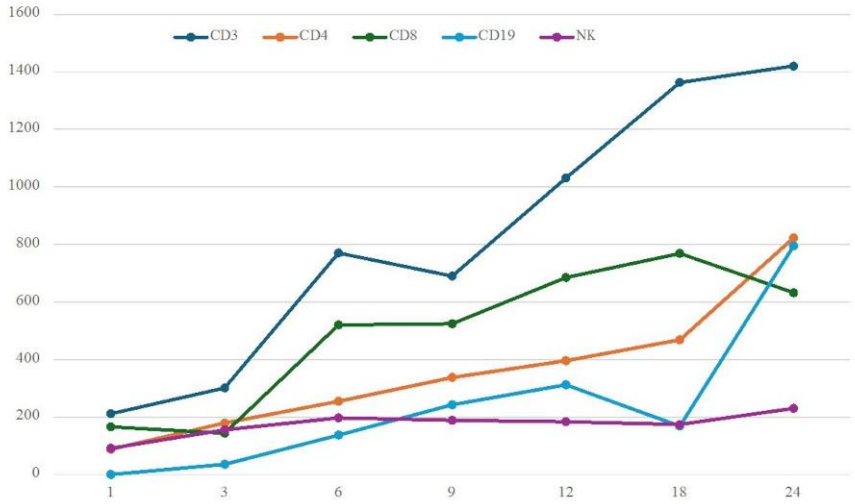
Background: Besides haploidentical procedures, post-transplant cyclophosphamide (PTCy) has become the standard-of-care GvHD prophylaxis in stem cell transplantation (SCT) from matched sibling (MSD) and matched during post-transplant period. The aim of this study was to assess immune reconstitution and infectious complications in a cohort of patients who received PTCy for matched sibling or unrelated donor SCT.

Methods: Between 02/2021 and 05/2025, 133 consecutive patients, aged 17-79 years (median; 56), underwent SCT from MSD (n=33), MUD (n=100) or MMUD (n=20), with PTCy (40 mg/kg/day for MSD and 50 mg/kg/day for MUD/MMUD, on days +3 and +4) in combination with calcineurin inhibitor/mycophenolate mofetil as GvHD prophylaxis. Underlying diseases included AML (n=79), MDS (n=23), other myeloid neoplasms (n=8), ALL (n=18), and lymphomas (n=5). Conditioning was myeloablative (n=92) or reduced-intensity (n=41), based on chemotherapy (n=113) or TBI (n=20). Immune reconstitution was monitored by flow cytometry at 3-monthly intervals. Infections were categorized according to site and type of pathogen.

Results: Engraftment (ANC >500/uL) was observed in 127/133 (95.5%) patients at a median of 15 (12-44) days. With a median follow-up of 23 (6-58) months, overall survival at 2 years was 72.9% (95% CI; 65.2-81.6). Non-relapse mortality (NRM) and cumulative incidence or relapse (CIR) at 2 years were 18.5% (95% CI; 12.6-27.1) and 13.3% (95% CI; 8.3-21.4), respectively. The rates of grade II-IV or III-IV acute GvHD at 180 days, and of moderate/severe chronic GVHD at 24 months were 44.6% (95% CI; 36.8-54.0), 5.3% (95% CI; 2.6-10.9), and 26.8% (95% CI; 19.8-36.2), respectively. T cell reconstitution (median absolute CD4+ count >200 and >400/uL) was encountered at 6 and 18 months, respectively. Overall, 251 infections were observed in 104/133 (78.2%) patients. Infections were classified as bacteremias (n=84, 33.5%), bacterial site-specific other than C. difficile (n=71, 28.3%), C. difficile (n=10, 4%), viral (n=73, 29%), and fungal (n=12, 4.8%), and protozoan (n=1, 0.4%). Viral infections were CMV reactivation (n=19), CMV enteritis (n =6),

BKV cystitis (n=24), and COVID-19 or other respiratory (n=13 and 11, respectively). Fungal pathogens were yeasts (n=7), molds (n=4), and mucor (n=1). Infections were identified as contributing factors in 19/21 recorded fatalities.

Image 1: Immune reconstitution in month 1, 3, 6, 9, 12, 18 and 24 after transplantation.



Months from alloSCT	1	3	6	9	12	18	24
CD3	212	301	770	690	1030.5	1363	1420
CD4	88	179	255	337.5	396	468.5	823
CD8	166	144	520	524	685	768.5	632
CD19	0	36	137	243	312	168.5	795
NK	92	156	197	188.5	183.5	174	230

Conclusions: Although PTCy significantly reduced the incidence of both severe acute and chronic GvHD, infections remain prevalent among patients and represent a major cause for morbidity and mortality. Optimization of the PTCy immunosuppression regimen may facilitate hematopoietic and immune reconstitution, thereby reducing the incidence of infections.

Disclosure: Nothing to disclose.

B090

EFFICACY AND SAFETY OF MARIBAVIR IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS BY BASELINE NEUTROPENIA STATUS: A POST HOC ANALYSIS OF PHASE 2 AND 3 CLINICAL TRIALS

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Background: Recipients of hematopoietic cell transplantation (HCT) are susceptible to myelotoxicity associated with anti-cytomegalovirus (CMV) agents such as ganciclovir or valganciclovir. In the phase 3 SOLSTICE trial (NCT02931539), lower rates of myelosuppression were observed with maribavir compared with ganciclovir/valganciclovir in HCT recipients with refractory CMV infections. This exploratory post hoc analysis of clinical trial data assessed the efficacy and safety of maribavir in patients with post-HCT refractory CMV infection, according to baseline neutropenia status.

Methods: Data from maribavir-treated HCT recipients in SOLSTICE and a phase 2, dose-ranging study (1263-202; SHP620-202; NCT01611974) were stratified by baseline neutrophil count: ≤1000/mm^3 (moderate-to-severe neutropenia); >1000/mm^3 to 1500/mm^3 (mild neutropenia); >1500/mm^3 (no neutropenia). Patients enrolled in the SOLSTICE study were required to have a baseline absolute neutrophil count of ≥1000/mm^3, and thus only participants from study 202 were included in the moderate-to-severe neutropenia cohort. Participants with confirmed CMV DNAemia clearance at the end of study week 8 were considered responders regardless of whether maribavir was discontinued before the end of the stipulated 8 weeks of therapy. Responder rates and incidence of adverse events (AEs) were summarized descriptively, and time to CMV clearance at any time during the studies was assessed by neutropenia category using Kaplan-Meier (KM) analysis with log-rank test.

Results: In total, 139 maribavir-treated HCT recipients with baseline moderate-to-severe (n=12), mild (n=11), or no neutropenia (n=116) were included in this analysis. Baseline demographics for this population are summarized in the Table. At the end of week 8, 10/12 (83.3%) and 7/11 (63.6%) participants with moderate-to-severe or mild neutropenia versus 68/116 (58.6%) with no neutropenia were considered responders to maribavir. Responder rates at any time during the study were 11/12 (91.7%), 9/11 (81.8%), and 87/116 (75.0%) in patients with moderate-to-severe, mild or no neutropenia, respectively. Time to CMV DNAemia clearance, as assessed by KM analysis, was similar across the three neutropenia categories (P=0.1644), as well as between those with and without neutropenia (P=0.0979; Figure). Treatment-emergent AEs were observed in 100% of participants with moderate-to-severe or mild neutropenia, and in 99.1% of participants without neutropenia. Adverse events led to discontinuations in 25.0%, 9.1%, and 28.4% of participants with moderate-to-severe, mild or no neutropenia, respectively.

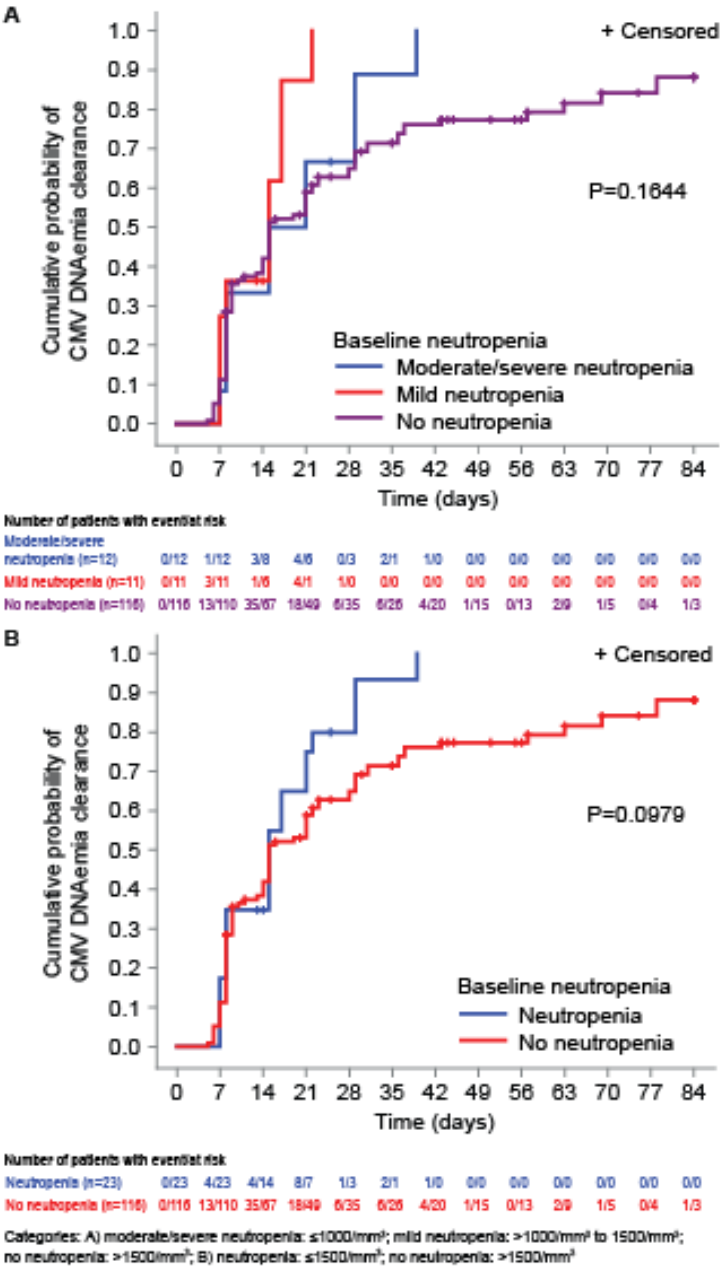
Table. Baseline demographics and safety data for HCT recipients with refractory CMV by baseline neutropenia category

	Neutrophil count ≤1000/mm^3 (n=12)	Neutrophil count >1000/mm^3 to 1500/mm^3 (n=11)	Neutrophil count >1500/mm^3 (n=116)
Age, years (median [range])	45.5 (24–65)	60.0 (19–73)	58.0 (19–77)
Male, n (%)	7 (58.3)	3 (27.3)	64 (55.2)
Race, n (%) Asian Black or African American White Other Missing	 1 (8.3) 4 (33.3) 6 (50.0) 1 (8.3) 0	 2 (18.2) 1 (9.1) 8 (72.7) 0 0	 8 (6.9) 8 (6.9) 85 (73.3) 13 (11.2) 2 (1.7)
Patients with AEs, n (%)	12 (100)	11 (100)	116 (100)
Number of AEs, n	148	110	1891
Number of TEAEs, n (%)[a]	123 (83.1)	82 (74.5)	1293 (68.4)
Mild, n (%)[b]	50 (40.7)	47 (57.3)	727 (56.2)
Moderate, n (%)[b]	55 (44.7)	26 (31.7)	420 (32.5)
Severe, n (%)[b]	14 (11.4)	9 (11.0)	126 (9.7)
Maximal, n (%)[b]	4 (3.3)	0	20 (1.5)

Patients with AEs resulting in death, n (%)	3 (25.0)	2 (18.2)	32 (27.6)
Patients with serious TEAEs, n (%)	5 (41.7)	6 (54.5)	62 (53.4)
Patients with study drug discontinuations due to AEs, n (%)	3 (25.0)	1 (9.1)	33 (28.4)
Patients with study drug interruptions due to AEs, n (%)	2 (16.7)	1 (9.1)	14 (12.1)

[a]Percentages calculated from the total number of AEs.
[b]Percentages calculated from the total number of TEAEs.
AE, adverse event; TEAE, treatment-emergent adverse event

Figure. Inverse Kaplan-Meier Curves of time to first confirmed undetectable plasma CMV DNAemia at any time during the study up to Week 12 (Day 84) by baseline neutropenia category



Categories: A) moderate/severe neutropenia: ≤1000/mm³; mild neutropenia: >1000/mm³ to 1500/mm³; no neutropenia: >1500/mm³; B) neutropenia: ≤1500/mm³; no neutropenia: >1500/mm³

Conclusions: This post hoc analysis of phase 2 and 3 clinical data in HCT recipients with refractory CMV infection showed no statistically significant differences in time to CMV DNAemia clearance and broadly similar overall AE profiles in maribavir-treated patients with and without baseline neutropenia. Although these findings are based on small sample sizes, especially in the neutropenia groups, they support the use of maribavir as a therapeutic

option in HCT recipients with refractory CMV infection, regardless of neutropenia, and warrant further research.

Clinical Trial Registry: NCT01611974, https://clinicaltrials.gov/study/NCT01611974 NCT02931539, https://www.clinicaltrials.gov/study/NCT02931539

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B091

THE ORAL MICROBIOME IN PEDIATRIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: Oral mucositis (OM) is a frequent and debilitating complication during hematopoietic stem cell transplantation (HSCT), contributing significantly to pain, impaired nutrition, prolonged hospitalization, and increased infection risk. OM is also a well-recognized risk factor for bloodstream infections (BSI) due to mucosal barrier injury that facilitates microbial translocation. Although oral microbial dysbiosis has been proposed as a contributing factor in OM development and oral bacteria have been implicated as sources of BSI, most prior work has focused on adults, leaving a critical gap in pediatric populations. This prospective study was designed to characterize the pediatric oral microbiome during HSCT, explore whether specific microbial signatures are associated with the incidence and severity of OM, and determine whether oral organisms could be linked to BSI episodes occurring during transplant.

Methods: Ten pediatric subjects undergoing HSCT were followed longitudinally throughout their transplant course. Oral health assessments—including gingivitis scores, plaque index, tongue coating, and OM grading—were recorded at serial time points. Site-specific oral samples from plaque, buccal mucosa, and tongue, as well as microbial DNA from BSI-positive blood cultures, were collected for 16S rRNA gene sequencing. Microbial beta-diversity was assessed using Bray–Curtis dissimilarity, and PERMANOVA was applied to evaluate whether community composition varied by oral site or OM severity. Amplicon sequence variants generated through the DADA2 pipeline provided high-resolution, strain-level microbial fingerprints, allowing us to precisely track specific microbial species across different oral niches and determine whether the same organisms appeared in the bloodstream during BSI events.

Results: All subjects demonstrated progression of OM and dynamic changes in oral health indices as they moved through conditioning, the neutropenic phase, and subsequently engraftment. Distinct microbial communities were observed across oral sites (P = 0.001), reflecting the unique ecological environments of plaque, mucosa, and tongue. As OM severity increased, significant shifts in community composition occurred within each niche (plaque P = 0.023; buccal mucosa P = 0.006; tongue P = 0.041), suggesting that mucosal injury is associated with measurable restructuring of the oral microbiome.
Six of the ten subjects experienced BSI events (including two events in one subject). Sequencing revealed polymicrobial bloodstream profiles containing microbial species typically residing in the oral cavity. High-resolution ASV matching demonstrated overlap between oral microbial species and those detected in blood culture samples, supporting an oral source for BSI in multiple cases. These findings suggest that OM-associated microbial disruption may facilitate translocation of oral microbes into the bloodstream during HSCT.

Conclusions: Distinct, site-specific microbial signatures were identified in pediatric HSCT recipients, and these communities shifted significantly with the development and progression of OM. High-resolution microbial tracking provided molecular evidence linking bloodstream pathogens to the oral cavity, emphasizing the oral microbiome as an important—and potentially modifiable—source of infectious risk during HSCT. These data lay the groundwork for future mechanistic microbiome studies and support the development of targeted oral health or microbiome-directed interventions to reduce OM severity and prevent BSI in children undergoing HSCT.

Disclosure: i have no conflict of interest to declare

B092

SURVEY BY THE INFECTIOUS DISEASES WORKING PARTY OF EBMT ON THE USE OF RECOMBINANT HERPES ZOSTER VACCINE AFTER AUTOLOGOUS AND ALLOGENEIC HAEMOPOIETIC STEM CELL TRANSPLANTATION

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Background: For many years, the only existing vaccine for Herpes Zoster (HZ) was a live-attenuated vaccine that wasn’t recommended in immunocompromised patients. The

recombinant HZ vaccine (RZV, Shingrix®) was shown to be safe and effective in a randomized observer-blind, phase-III trial in adults after autologous HSCT (auto-HSCT)(Bastidas et al, JAMA 2019). In that study, the first dose of vaccine was administered between 50-70 days after transplant, and the second dose 1-2 months thereafter. Patients with antiviral prophylaxis for HZ of more than 6 months were excluded. However, there are few data about the use of this vaccine after auto-HSCT in the real world. Moreover, information about Shingrix® after allogeneic HSCT (allo-HSCT) is limited.
This survey shows a current picture of the use of RZV in transplant centres of the EBMT network, its reimbursement, and the management of prophylaxis.

Methods: A 20-item questionnaire regarding RZV, approved by the scientific board of IDWP-EBMT, was sent to all centres performing HSCT on February 10th, 2025.

Results: 187 adult HSCT centres responded to this survey. Results are shown in Table 1. Most European centres get reimbursed for the vaccine.
Allo-HSCT: 107/157 centres have RZV in their routine schedule. 98/105 centres (93.3%) started RZV based on time after transplant either alone (54/105;51.4%) or in combination with other factors (44/105;41.9%). Other factors more commonly mentioned are corticosteroids, other immunosuppression and chronic Graft vs Host Disease (GvHD).
10/17 centres (58.8%) that started vaccination 3-6 months after transplant provided prophylaxis regardless of RZV, while 20/44 centres (45.4%) that started 6-12 months and 11/36 centres (30.5%) that started >1 year after transplant provided prophylaxis regardless of RZV
Auto-HSCT:103/170 centres have RZV in their routine schedule. Only 25/103 centres (35.4%) use the 2-dose interval (30-59 days) as recommended in the phase III study.
9/12 centres (75%) that started the vaccine <3 months and 29/42 centres (69%) that started 3-6 months after transplant provided prophylaxis regardless of RZV. 18/37 centres (48.6%) that gave RZV 6-12 months after transplant, and 5/8 centres (62.5%) that gave RZV >1 year after transplant provided antiviral prophylaxis regardless of RZV.

Table 1

	Allo-HSCT	**Auto-HSCT**
Number of centres	157	179
Reimbursement	107/157 (68.2%)	115/172 (66.9%)
RZV used in the routine vaccination schedule	107/157 (68.2%)	103/170 (60.6 %)
RZV start based on time after transplant	98/105 (93.3%)	99/103 (96.1%)
< 3 months	0	12/99(12.1%)
3-6 months after transplantation	18/98 (18.4%)	42/99(42.4%)

6-12 months after transplantation	44/98 (44.9%)	37/99 (37.4%)
>1 year after transplantation	36/98 (36.7%)	8/99 (8.1%)
RZV start based on other factors	51/105 (48.6%)	NA
Posology of RZV 1 dose 2 doses >2 doses	 3/101 (3.0%) 95/101 (94.1%) 3/101 (3.0%)	 2/100 (2.0%) 96/100 (96%) 2/100 (2.0%)
Interval between doses		
<30 days 30-59 days 60-90 days >90 days	2 (2.1%) 38 (39.6%) 54 (56.3%) 2 (2.1%)	4 (4%) 35 (35.4%) 57 (57.6%) 3 (3%)
Antiviral drug prophylaxis		
Stopped prophylaxis after RZV administration	60/104 (57.7%)	39/101 (38.6%)
based on time after last dose	45/60 (75%)	33/39 (84.6%)
<14 d 15-30 d >30 d	12 /45(26.7%) 18/45 (40.0%) 15/45 (33.3%)	9/33 (27.3%) 12/33 (36.4%) 12/33 (36.4%)
Based on other factors alone	15/60 (25%)	6/39 (15.4%)
RZV does not influence decision on prophylaxis	44/104 (42.3%)	62/101 (61.4%)

Conclusions: This survey shows that most transplant centres that responded have incorporated RZV into their vaccination schedules after HSCT. Despite the paucity of data, more responding centres use RZV after allo-HSCT (68.2%) than after auto-HSCT (60.6%).
In auto-HSCT, most centres started the vaccination either 3-6 months or 6-12 months post-transplant, while in the phase III study RZV was administered 50-70 days post-transplant. Interestingly, most centres continue prophylaxis regardless of vaccination
In allo-HSCT, most centres started RZV based on time after HSCT, alone or together with other factors, mostly the absence of chronic GvHD and/or immunosuppressive treatment. Most centres started vaccination at 6 months or later. Although 58% of centres stopped prophylaxis after vaccination, in 42% of centres, vaccination with RZV didn't influence the decision on prophylaxis.
Centres that gave RZV earlier after allo-HSCT were more likely to report that vaccination didn't affect decision on prophylaxis, although this trend was not as pronounced in auto-HSCT.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare.

B093

ANAKINRA TO REDUCE FEVER DURING NEUTROPENIA AND MUCOSITIS IN MULTIPLE MYELOMA PATIENTS RECEIVING AUTOLOGOUS STEM CELL TRANSPLANTATION AFTER HIGH-DOSE MELPHALAN – A RANDOMIZED CONTROLLED TRIAL

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Background: The recombinant human IL-1 receptor antagonist anakinra is effective in ameliorating murine chemotherapy-induced mucositis and fever during neutropenia. In this phase 2b AFFECT-2 trial, multiple myeloma (MM) patients receiving high-dose melphalan (HDM) followed by autologous stem cell transplantation (ASCT) were randomized between placebo or anakinra to reduce the incidence of fever during neutropenia and mucositis severity.

Methods: MM patients admitted for ASCT after single dose HDM 200mg/m2 were 1:1 randomized between once daily anakinra 300 mg iv or placebo for 15 days starting at day of HDM infusion. Patients with uncontrolled infections, bowel disease or impaired renal function with eGFR <40 ml/min were excluded. Ninety patients were required to detect a reduction from 80% to 50% in our primary outcome incidence of fever during neutropenia, with a two-sided test, α of 0.05 and power of 80%. Fever during neutropenia was defined as a tympanic temperature ≥38.5°C and ANC < 0.5 × 10^9 /l or expected to fall below 0.5 × 10^9 /l in the next 48 hours.
During hospital admission vital functions, clinical oral and intestinal mucositis scores, antibiotic use and feeding method were registered daily. Plasma for citrulline concentration (biomarker for intestinal mucositis), C-reactive protein (CRP) and exploratory cytokine analysis was collected thrice-weekly. Blood cultures were collected daily between 4 and 12 days after ASCT and in case of fever. Positive blood cultures were classified into laboratory confirmed blood stream infections (LCBI) and mucosal barrier injury related LCBI (MBI-LCBI) according to the American Center of Disease Control. Patients received oral ciprofloxacin prophylaxis and ceftazidime iv in case of neutropenic fever.
Primary outcome was analyzed with Chi square test. Continuous outcomes were tested with independent samples T-tests or zero count inflated model if appropriate. Repeated measurements were analyzed with linear mixed models.

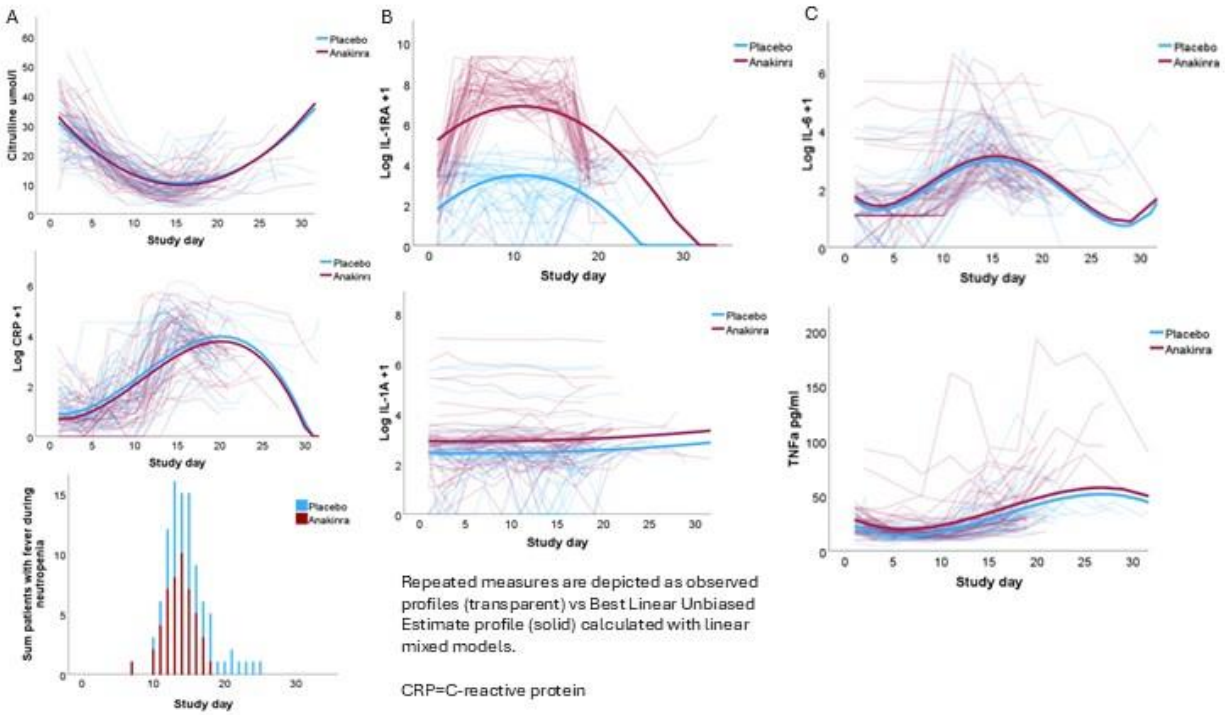
Results: 87 patients were enrolled were enrolled between October 2019 and March 2023. The intention-to-treat population consisted of 82 patients who received ≥1 dose of study medication. Basic characteristics were comparable between groups.
Fever during neutropenia occurred in 18 patients in the anakinra group (40.9%) and 21

patients in placebo group (55.3%), *P*= 0.194, OR 0.56 (CI 0.23-1.35).
Daily clinical mucositis scores, feeding method, hospital stay and empirical antibiotic therapy use were not significantly different between groups.
Incidence of LCBI was low, table 1.
Citrulline concentration declined throughout hospitalization in both groups to <10 umol/l around 10 days after ASCT reflecting severe gut mucositis. At the same time, CRP peaked and fever during neutropenia occurred, figure 1A.
Anakinra administration resulted in higher IL-1 receptor antagonist (IL-1RA) concentrations than in the placebo group. IL-1a concentrations were consistent and tended to be higher in the anakinra group, figure 1B. IL-6 peaked together with CRP and fever, TNFa peaked around repopulation, figure 1C.

Nr of patients with BSI per type	**Anakinra**	**Pathogens**	**Placebo**	**Pathogens**
LCBI type 1, n	5	*Pseudomonas aeruginosa, Acinetobacter radioresistens, Enterococcus faecalis, Granulicatella adiacens, Streptococcus pneumoniae*	2	*Sphingomonas species, Staphylococcus aureus*
LCBI type 2, n	2	*Micrococcus luteus, Staphylococcus epidermidis*	2	*Staphylococcus epidermidis*
MBI-LCBI type 1, n	0		0	
MBI-LCBI type 2, n	2	*Streptococcus mitis*	2	*Streptococcus mitis, Streptococcus gallolyticus*
Total, n	9		6	

In both groups 1 patient had a LCBI 1 and MBI-LCBI 2 during hospitalization.

Figure 1. Citrulline, CRP and cytokine profiles next to incidence of fever during neutropenia during hospitalization.



Conclusions: Anakinra did not prevent development of fever during neutropenia nor severe mucositis, also reflected by rise of IL-6 and TNFa despite high IL-1RA. Severe intestinal mucositis coincided with fever during neutropenia whilst incidence of LCBI was low.

Clinical Trial Registry: Clinicaltrials.gov NCT04099901

Disclosure: This trial was funded by KWF Dutch Cancer Society.

B094

THE IMPACT OF CMV-SEROPOSITIVITY ON OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN THE ERA OF LETERMOVIR IN AML AND MDS PATIENTS

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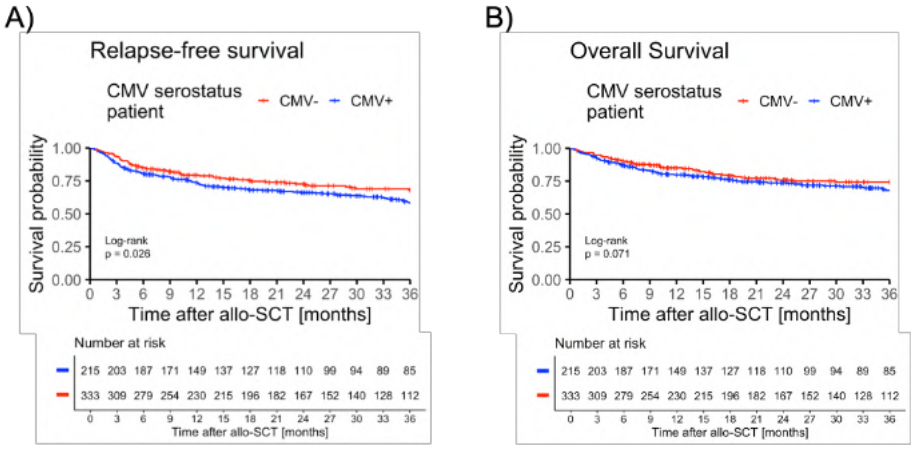
Background: Until the approval of letermovir for the prophylactic treatment of cytomegalovirus (CMV) positive patients after allogeneic stem cell transplantation (allo-SCT), CMV infections were frequent and relevant problems after allo-SCT. Furthermore, the CMV serostatus has been linked to survival outcomes and relapse incidence. However, the introduction of letermovir has changed the field and the current impact of CMV positivity on outcomes after allo-SCT remains unclear.

Methods: A total of 548 patients with acute myeloid leukemia (AML) and myelodysplastic neoplasia (MDS) who underwent allo-SCT between 2018 and 2024 at our center were divided in 2 groups according to their CMV serostatus. We retrospectively analyzed associations between patient and donor CMV status and clinical outcomes, including overall survival (OS), relapse-free survival (RFS), incidence of relapse, non-relapse mortality (NRM), and graft-versus-host-disease (GvHD).

Results: 333 patients (61%) were CMV seropositive (CMV+) and 215 patients (39%) were CMV seronegative (CMV-). Both groups were well balanced regarding diagnosis and associated risk factors like prevalence of a complex karyotype, age at allo-SCT, gender, Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) score, remission before allo-SCT, and immunosuppressive regimens. 66% in the CMV+ group versus 20% in the CMV- group had a CMV+ donor. 97% of the CMV+ patients received primary prophylaxis with letermovir.
With a median follow-up of two years for the whole cohort, CMV+ patients trended towards lower two-year overall survival (OS) rate (74% vs. 76%, p=0.071) higher relapse incidence (20% vs. 13%, p=0.075) and a significantly lower RFS rate (66% vs. 73%, p=0.026). A subgroup analysis of CMV+ patients showed a trend towards higher relapse incidences for those transplanted from CMV+ donors (incidence of relapse at 2 years for CMV+ donors: 23% vs. 12% for CMV- donors, p=0.056). In multivariate analysis for RFS including variables found to be significant in univariate analyses (age >60 years, HCT-CI score, Eastern Cooperative Oncology Group performance score and complex karyotype), the patients' CMV serostatus trended towards significance (HR: 1.33, p=0.062), while the CMV serostatus of the donor did not affect RFS (univariate: HR: 1.1, p=0.45).
During the entire follow-up, 94 patients had a CMV infection with subsequent preemptive therapy, 31 of those occurred during prophylaxis with letermovir. A preemptive therapy against CMV did not influence survival outcomes (yes vs. no, two-year OS rate: 72% vs. 75%, p=0.48; two-year RFS rate: 68% vs. 71%, p=0.82). Incidence of acute or chronic GvHD and duration of immunosuppression did not significantly differ between CMV+ and CMV- patients.
Cellular immune reconstitution measured by CD4+ and CD8+ T-cells on day +100 revealed a faster reconstitution in CMV+ patients (median CD4+/µl: 137 vs. 108 for CMV-, p=0.028, median CD8+/µl: 230 vs. 201 for CMV-, p=0.016).



Conclusions: Our findings suggest that, even in the letermovir era, the CMV serostatus may still affect RFS. Furthermore, we found no evidence that prophylaxis with letermovir or CMV infection are relevant risk factors for relapse in our large cohort of AML and MDS patients. However, further studies are needed to confirm these findings and to evaluate the possible impact of donor CMV serostatus and the underlying mechanisms.

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MS has served as a consultant for Pfizer, MSD, Bristol-Myers Squibb (BMS), Incyte, Takeda, Astellas and Amgen; as a speaker for Pfizer, Medac, MSD, Astellas, Jazz Pharmaceuticals, Amgen, Novartis, Gilead, Celgene, BMS, AbbVie, and Incyte; has received research funding from Pfizer; and has received travel support from Medac and Pfizer.

B095

MARIBAVIR FOR TREATMENT OF REFRACTORY/RECURRENT CYTOMEGALOVIRUS INFECTION IN ALLOGENEIC HSCT RECIPIENTS

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Background: There is a lack of real-world data on maribavir therapy in recipients of allogeneic hematopoietic stem cell transplantation (allo-HCT). The study aimed to assess the outcomes of maribavir therapy in allo-HSCT recipients with refractory or recurrent cytomegalovirus (CMV) infection in a real-world clinical setting.

Methods: A single-center study included 51 patients, both adults (42/51, 82.4%) and children (9/51, 17.6%), following allo-HCT with refractory (42/51, 82.4%) or recurrent (9/51, 17.6%) CMV infection. Patient characteristics are presented in Table 1.

	Study group (n=51)
Age, median (range)	40 (0.2 – 66)
Sex Male Female	 29 (56.8%) 22 (43.2%)
Indications for allo-HCT Standard Salvage	 39 (76.5%) 12 (23.5%)
Donor type Haploidentical MMUD MUD MRD	 21 (41.2%) 15 (29.4%) 8 (15.7%) 7 (13.7%)
Stem cell source PBSC BM	 43 (84.3%) 8 (15.7%)
Conditioning regimen RIC MAC	 26 (51.0%) 25 (49.0%)
Post-transplant cyclophosphamide GVHD prophylaxis	49 (96.0%)
Second allo-HCT BOOST	7 (15.7%) 2 (3.9%)
CMV DNA levels at the start of 1st line treatment, median (range) IU/ml Copies/ml	 3520 (100 - 4656000) 5780 (500 - 7760000)

Duration of 1st line treatment, median (range), days	13.5 (2 - 60)

No analysis for CMV drug resistance mutations was performed. The median time from the first allo-HSCT to CMV infection onset was 36 days (range: 9–342). First-line therapy was ganciclovir in 44 cases (86.3%). Therapy was administered preemptively in 46 cases (90.2%), while 3 patients (5.8%) were treated for CMV pneumonia and 2 (4%) for CMV gastrointestinal disease. Maribavir was used as second-line therapy in 38 patients (74.5%) and as a subsequent line in 13 (25.5%). The median follow-up time from the start of maribavir therapy was 147 days (range: 2–1165).

Results: The median time from CMV infection onset to the initiation of maribavir was 18 days (range: 9–486). The median CMV DNA level at the start of therapy was 5370 IU/mL (300–4,156,259) or 1760 copies/mL (72–559,000). A response to maribavir therapy was achieved in 39 patients (76.5%). The median time to CMV clearance after starting maribavir was 15 days (range: 1–84). The achieved response was maintained at the 8-week mark in 30 patients (58.8%). CMV clearance was maintained at the 16-week mark in 13 patients (25.5%). The six-month cumulative incidence of recurred CMV infection from the start of maribavir was 33.4% (95% CI: 20 – 47.5). At the 4-week mark, the following Grade 3-4 adverse events were recorded: thrombocytopenia in 28 patients (54.9%); neutropenia, leukopenia, and anemia in 16 patients each (31.4%); and acute kidney injury with hyperkalemia in 1 patient (1.9%). However, their association with maribavir was not documented. The six-month overall survival from the start of maribavir therapy was 72.5% (95% CI: 57.2–83.2), and the six-month failure-free survival was 44.5% (95% CI: 29.5–58.4). During maribavir therapy, reactivation of other herpesviruses was also noted: Human Herpesvirus 6 in 32 patients (62.7%), Epstein-Barr Virus in 12 (23.5%), Herpes Simplex Virus types 1 and 2 in 10 (19.6%), as well as 2 cases of herpes zoster (3.9%).

Conclusions: Maribavir therapy demonstrated efficacy in achieving CMV clearance, comparable to the results of clinical trials. However, maintaining this response and preventing CMV recurrence remain challenging. Careful monitoring and management of other herpesvirus infections are essential during maribavir therapy.

Disclosure: COI: Maribavir was obtained through extended access program.

B096

EFFECTIVENESS OF A STRUCTURED PREVENTION STRATEGY FOR HBV REACTIVATION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION USING HBSAG-POSITIVE DONORS

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Background: Donor scarcity frequently necessitates the use of HBsAg-positive donors, yet no unified guidelines exist for managing allogeneic hematopoietic stem cell transplantation (allo-HSCT) from such donors. Building on our retrospective evidence supporting a structured HBV management protocol, we conducted a prospective single-center evaluation of this strategy.

Methods: Between May 2020 and February 2025, 47 patients undergoing allo-HSCT from HBsAg-positive donors at our center were prospectively enrolled. Donors with detectable HBV DNA received entecavir 0.5 mg/day until completion of stem cell collection. HBsAg-positive recipients received long-term antiviral prophylaxis. HBsAg-negative recipients received HBIG at months 0, 1, and 2, followed by HBV vaccination at 1 year. Antiviral therapy was initiated immediately upon HBV reactivation (HBVr). The primary endpoint was the cumulative incidence of HBVr; secondary endpoints included HBV-related hepatitis, non-relapse mortality (NRM), and liver-related mortality. The study was approved by the Ethics Committee of the First Affiliated Hospital of Zhejiang University School of Medicine (ChiCTR2000032614).

Results: After a median follow-up of 1309 days (95% CI, 1043–1540), 12 patients developed HBVr, including 4 with HBV-related hepatitis. HBVr occurred at a median of 464 days post-HSCT (IQR, 307–623). The 3-year cumulative incidences of HBVr and HBV-related hepatitis were 30% (95% CI, 16–44) and 10% (95% CI, 3.1–22), respectively. The 3-year NRM was 9.4% (95% CI, 2.9–21), and no liver-related deaths occurred.
Among 10 HBsAg-positive and 37 HBsAg-negative recipients, HBVr occurred in 3 and 9 patients, respectively. The 3-year cumulative incidences of HBVr, HBV-related hepatitis, and NRM were 37%, 23%, and 0% in HBsAg-positive patients, and 28%, 6.1%, and 12% in HBsAg-negative patients, respectively, with no significant differences (all $p>0.05$) (Fig.1A-C). Following HBVr, antiviral therapy was modified in HBsAg-positive recipients, whereas HBsAg-negative recipients initiated antiviral treatment with entecavir or tenofovir.
HBsAg-negative recipients were further stratified into $HBcAb^+/HBsAb^+$ (n=17), $HBcAb^+/HBsAb^-$ (n=4), and $HBcAb^-$ (n=16) groups. Within this cohort, 21 recipients received hepatitis B vaccination at 1 year after allo-HSCT. $HBcAb^+/HBsAb^-$ patients had a significantly higher 3-year HBVr incidence (100%, 95% CI, 100–100) compared with $HBcAb^-$ (6.7%, 95% CI, 0.37–27; $p<0.001$) and $HBcAb^+/HBsAb^+$ patients (27%, 95% CI, 7.5–52; $p=0.007$) (Fig.1D).
Among the 9 HBsAg-negative recipients who developed HBVr, HBsAb titers declined consistently prior to reactivation, with a median titer of 0.45 mIU/mL (IQR, 0–1) at the time of HBVr (Fig.1E). In the overall HBsAg-negative cohort, serial monitoring demonstrated a marked decline in HBsAb levels after HSCT, reaching persistently low levels by 6 months post-transplantation (Fig.1F).

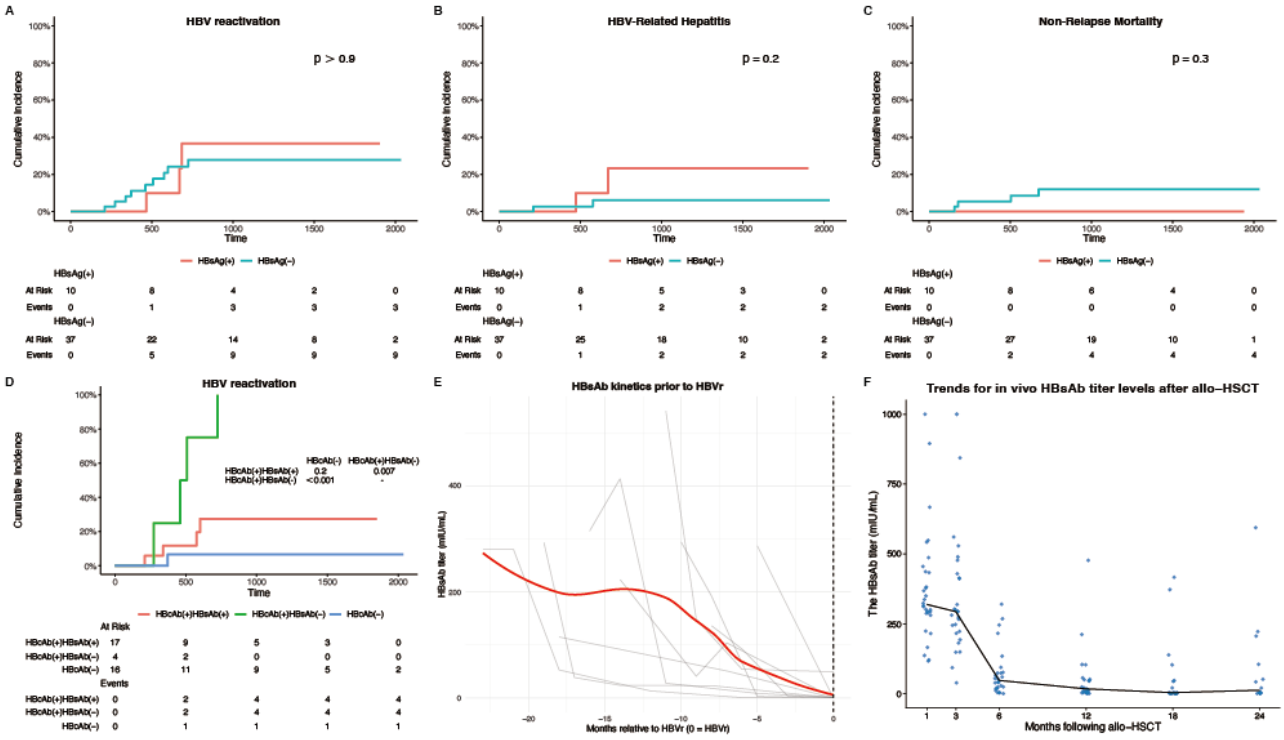

Figure 1. HBV-related outcomes and HBsAb dynamics following allo-HSCT from HBsAg-positive donors

Conclusions: This prospective study demonstrates that a novel HBV management strategy is feasible and associated with excellent hepatic safety, with no liver-related mortality observed. Although HBVr occurred, it was clinically manageable. Substantial heterogeneity in HBVr risk was observed among HBsAg-negative recipients with different baseline serologic profiles, providing important insights for the future refinement of risk-stratified preventive strategies. Dynamic declines in HBsAb levels may serve as an early biomarker of HBVr risk. Collectively, these findings support broader implementation and further refinement of structured HBV management when using HBsAg-positive donors in allo-HSCT.

Clinical Trial Registry: The study was registered in the Chinese clinical trial registry (ChiCTR2000032614).
Website: https://www.chictr.org.cn/showproj.html?proj=52966

Disclosure: No conflict of interest.

B097

LETERMOVIR PRIMARY PROPHYLAXIS IS A PROTECTIVE FACTOR FOR SURVIVAL IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS. DATA

FROM THE FIRST PROSPECTIVE MULTICENTER STUDY IN LATIN AMERICA

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Background: Letermovir (LET) primary cytomegalovirus (CMV) prophylaxis in Allogeneic Hematopoietic Cell Transplant Recipients (aHCT) is not available in many Latin American countries and has limited access. Therefore, data on its use are currently scarce.
The aim of the study was to describe and compare the incidence of clinically significant infection (cs-CMVi), CMV disease (CMV-d), CMV-related rehospitalization, and mortality between patients who received LET primary prophylaxis or were managed with preemptive therapy (PET). We further aimed to identify risk factors for overall mortality at day +200 post-HCT.

Methods: A prospective observational multicenter cohort study was conducted in 9 referral centers in Argentina between January 2020 and September 2025. Adult CMV-seropositive aHCT recipients who received LET until day 100 post-HCT or were managed with PET were included. Weekly CMV plasma viral load was monitored from pre-engraftment and follow-up to day +200 post-HCT. Baselines and clinical characteristics, risk factors for cs-CMVi and CMVd, and outcome variables were evaluated. A propensity score (PS) to balance baseline covariates was used. Adjusted conditional multivariate logistic regression analysis to PS was used to identify independent risk factors for 200-day mortality.

Results: Five hundred and fifty-one patients were included (PET: 346 and LET: 205), with median ages of 41 years (IQR: 28-53) in the PET group and 46 years (IQR: 33-60) in the LET group ($p < 0.001$). The most frequent underlying diseases were acute myelogenous leukemia (33.2%) and acute lymphoblastic leukemia (28.49%), with no differences between groups. CMV seronegative donors, alternative donors, post-transplant Cyclophosphamide administration and T-cell depletion were compared in PET vs. LET groups: 12.43% vs. 30.73% ($p<0.001$), 56.94% vs. 87.32% ($p<0.001$), 51.73% vs. 80.98% ($p<0.001$), and 12.14% vs. 15.61% ($p=0.24$), respectively. High risk stratification for the development of CMV-d was 88.15% in the PET group compared to 97.07% in the LET group ($p=0.003$). cs-CMVi, CMV-d, and CMV-related rehospitalization at day 100 post-HCT were compared between the PET and LET groups: 54.34% vs. 7.32% ($p<0.001$), 7.51% vs. 0% ($p=0.001$), and 37.86% vs. 10.24% ($p<0.001$), respectively. Mortality at day 200 post-HCT was 21.68% in the PET group vs. 16.10% in the LET group (0.11). Multivariate analysis adjusted for PS identified the following risk factors for mortality: graft failure, OR 16.57, CI 95%, 5.23-55.52

(p<0.001), GvHD with high dose of corticosteroids, OR 1.90, CI 95%, 1.19-3.04 (p=0.007), and lymphopenia < 300/ mm^3, OR 1.78, CI 95%, 1.10-2.89 (p=0.019). LET primary prophylaxis was a protective factor for survival, OR 0.51, CI 95%, 0.29-0.89 (p=0.018).

Conclusions: Our cohort largely comprised patients at high risk of developing cs-CMVi and CMV-d. Notwithstanding that, LET primary prophylaxis effectively prevented CMV-related complications, reduced rehospitalizations and was a protective factor for survival. These data support the use of this antiviral for primary prophylaxis in seropositive aHCT patients in Latin American countries.

Disclosure: Fabián Herrera has participated in advisory boards and/or received speaker honoraria and grants from Merck, Sharp & Dohme (MSD) and Takeda. Diego Torres has participated in advisory boards and/or received speaker honoraria from MSD. Lucas Tula has participated in advisory boards and/or received speaker honoraria from MSD and Takeda. María Laura Pereyra has participated in advisory boards and/or received speaker honoraria from Takeda. Julieta Dalmaroni has participated in advisory boards and/or received speaker honoraria from MSD. Rosana Jordán has participated in advisory boards and/or received speaker honoraria from MSD. All other authors report no potential conflicts of interest.

B098

SAFETY OF OMITTING ANTIBACTERIAL PROPHYLAXIS IN ADULT ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS: EXPERIENCE FROM A SINGLE CANADIAN CENTER

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Background: Graft-versus-host disease (GVHD) and infectious complications remain major contributors to non-relapse mortality (NRM) following allogeneic hematopoietic cell transplantation (alloHCT). Guidelines from major societies (IDSA, NCCN) recommend antibacterial prophylaxis (pATB) for patients at increased infectious risk however, although pATB reduces fever and bacteremia, it has not shown improved survival, and emerging evidence suggests fluoroquinolone (FQ) exposure may disrupt the intestinal microbiome and increase acute GVHD. Rising antimicrobial resistance and higher rates of *Clostridioides difficile* infections have led many centers to reconsider routine prophylaxis. After demonstrating that pATB increase GI GVHD and impaired survival, our center ceased pATB and evaluated infectious complications and early transplant outcomes.

Methods: We conducted a retrospective single-center study of consecutive adults undergoing alloHCT from November 2022 to March 2025 without routine pATB. Patients

receiving experimental graft manipulation or a second alloHCT were excluded. Collected variables included demographics, donor type, graft source, and conditioning intensity. All patients had central venous access. First-line therapy for febrile neutropenia (FN) in stable, non–high-risk patients was cefepime. Outcomes included FN rates, bacteremia, bacterial distribution, infection-related mortality (IRM), acute GVHD (including GI involvement), use of carbapenems or vancomycin, and *C. difficile* infection. Descriptive statistics summarized safety outcomes.

Results: We analyzed 204 consecutive alloHCT recipients (median age 56.5 years). Acute leukemias (49.0%), MDS/MPN (27.9%), and lymphomas (13.2%) were most common indications. Matched unrelated donors accounted for 62.7%, and peripheral blood stem cells for 85.8% (Table 1).
FN occurred in 185 (90.7%) patients, and 86 (46,5%) of these had documented bacteremia. Isolated gram-positive and gram-negative bacteria were present in 37.2% and 36% of these FN episodes, respectively, and 26.7% had polymicrobial infections. Fluoroquinolone resistance among gram-negative isolates occurred in 14/54 (25.9%) evaluable cases, whereas cefepime resistance was identified in only two patients. Carbapenems were required in 64 (34.6%) FN episodes, and vancomycin in 93 (50.3%). Among 31 cases of *Clostridioides difficile* infection, 13 were detected prior to any antibiotic exposure, and one patient had a recent pre-transplant episode (Table 2).
aGVHD developed in 96 patients (47.1%), with upper GI involvement in 21.6% and lower GI in 11.3%; eight patients (3.9%) had grade III–IV lower-GI disease. There were 35 relapses and 39 deaths, including 17 NRM events attributed to GVHD (n=3), organ toxicity (n=3), COVID-19 (n=2), PTLD (n=2), hepatic failure (n=1), endothelial injury (n=1), bleeding (n=1), and bacterial infections (n=4). Infection-related deaths predominantly occurred in patients with FQ resistant isolate or identifiable high-risk features. Median follow-up was 12.6 months, with 12-month NRM of 7.8% and IRM of 2.2%.

Conclusions: In this alloHCT cohort managed without pATB, FN rates, and bacteremia were within expected ranges and effectively managed with cefepime. Fluoroquinolone resistance was found in 25,9% of gram-negative bacteriemia. Many *C. difficile* infections occurred independently of antibiotic exposure. Severe acute GI-GvHD and NRM rates were low. Severe infection-attributable mortality was uncommon and non preventable by pATB. Overall, these results suggest that omission of antibacterial prophylaxis is safe in well-monitored alloHCT recipients and supports ongoing antimicrobial stewardship. Further comparative studies are needed to refine patient selection.

Figure 1. alloHCT characteristics

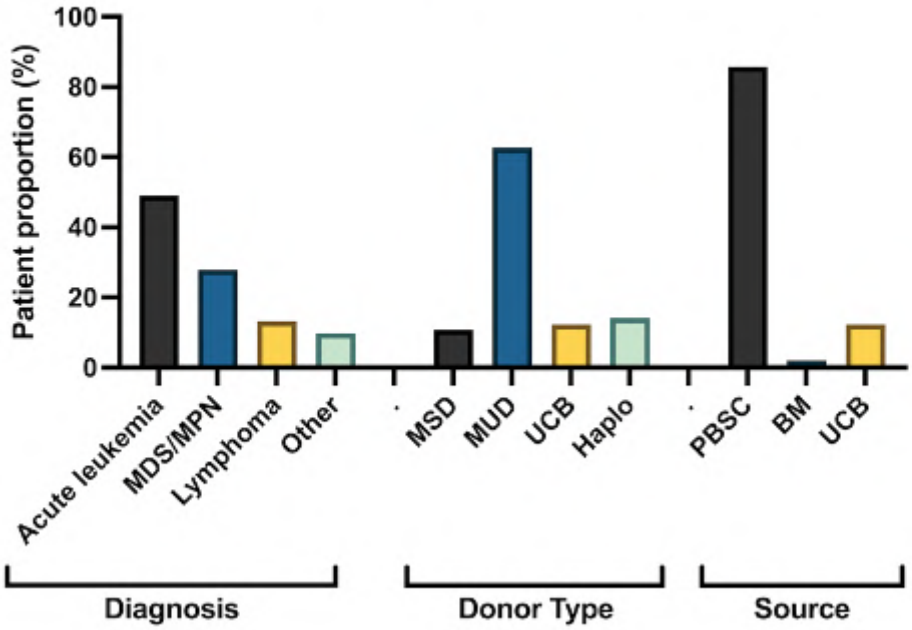

Table 2. Infectious outcomes, antimicrobial use and GvHD rates

Domain	Variable	Results
Febrile Neutropenia (FN)	FN episodes, n (%)	185/204 (90.7)
Bacteremia among FN	Bacteremia, n (%)	86/185 (46.5)
	Gram-positive isolate, n (%)	32/86 (37.2)
	Gram-negative isolate, n (%)	31/86 (36.0)
	Mixed (both), n (%)	23/86 (26.7)
Antimicrobial resistance	Gram-negative fluoroquinolone resistance, n (%)	14/54 (25.9)
Therapy for FN	Cefepime as first-line, n (%)	163/185 (88.1)
	Carbapenem use, n (%)	64/185 (34.6)
	Vancomycin use, n (%)	93/185 (50.3)
Other infectious outcomes	*C. difficile* infection, n (%)	31/204 (15.2%)
Acute Graft-versus-Host Disease (aGvHD)	Any grade aGvHD, n (%)	96/204 (47.1)
	Upper aGvHD, n (%)	44/204 (21.6)
	Lower aGvHD, n (%)	23/204 (11.3)

Variables with denominator 185 refer to patients with febrile neutropenia; variables with denominator 204 refer to the full allo-HCT cohort.

Disclosure: The authors declare no conflict of interest.

B099

EARLY ADMINISTRATION OF LETERMOVIR PROPHYLAXIS POST-ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IS ASSOCIATED WITH DELAYED ENGRAFTMENT

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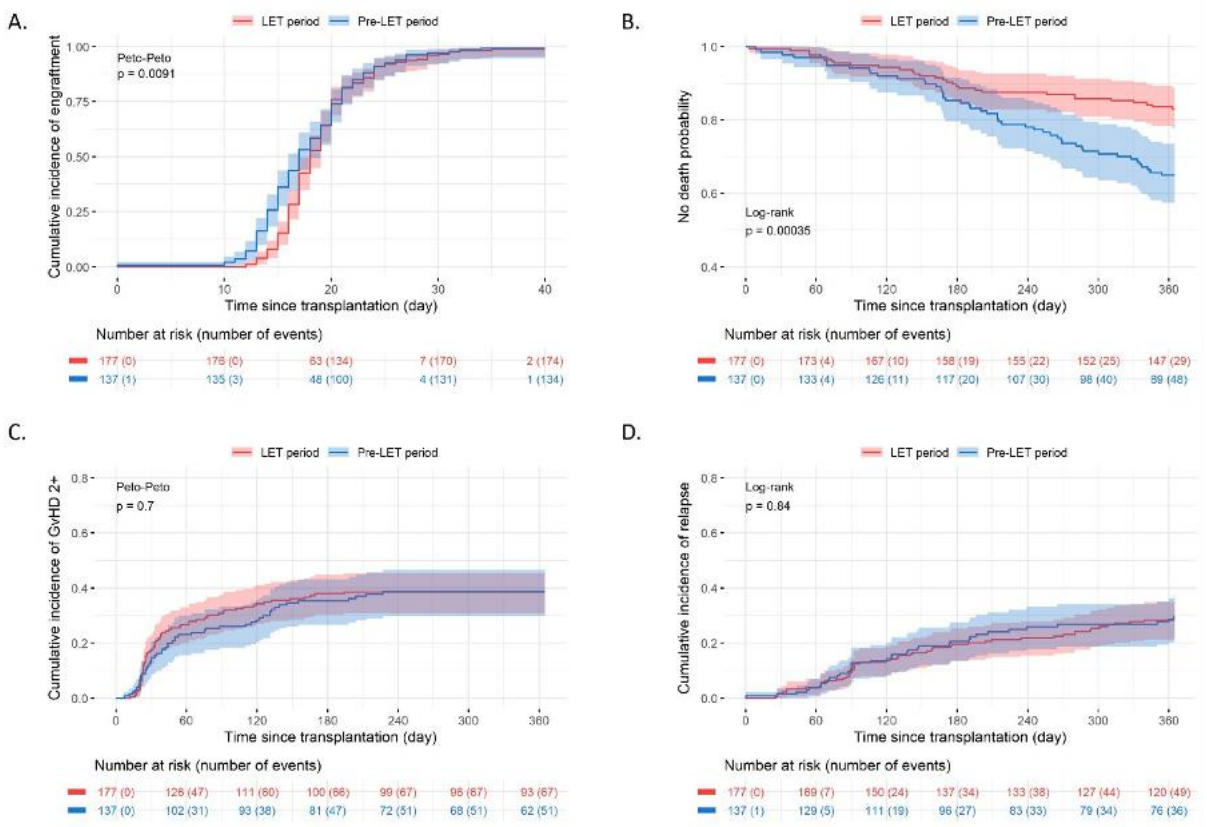
Background: Since its introduction as primary prophylaxis in allogeneic hematopoietic cell transplant recipients (allo-HCTR), multiple studies have confirmed the broad beneficial influence of letermovir on both virological and hematological outcomes. However, its impact on hematologic reconstitution and especially engraftment remains poorly described.

Methods: We conducted a retrospective cohort study including all consecutive adult allo-HCTR (16.11.2015-31.12.2023) in our center. Letermovir prophylaxis was administered after 01.05.2019 from day (d) 1 to d100 posttransplant in CMV-seropositive patients (R+). We assessed the differences in cumulative incidences (Log-rank or Peto-Peto tests, as appropriate) in the time-to-engraftment, all-cause mortality, hematological relapse and grade≥2 acute GvHD by 1-year posttransplant, in CMVR+ allo-HCTR in the pre- and post-letermovir periods.

Results: Overall, 137 (65%) and 177 (60%) allo-HCTR were considered as CMV R+ during the pre- and post-letermovir periods, respectively. Patient characteristics were similar between the 2 periods except for higher rates in the post-letermovir period of peripheral blood versus bone marrow stem cells for HCT sources, and of cyclophosphamide-based regimens for GvHD prophylaxis. In CMV R+, engraftment was significantly delayed in the letermovir period (median 17d versus 18d post-HCT in the pre- and post-letermovir periods, respectively, p = 0.009, Figure 1A). As already reported, 1-year all-cause mortality was significantly decreased during the letermovir period ($p < 0.001$, Figure 1B), whereas cumulative incidences at 1-year of acute GvHD and hematologic relapse were similar (Figure 1C-1D). In multivariate Cox regression analysis, letermovir prophylaxis was negatively associated with engraftment (hazard ratio 0.71, $p = 0.008$).



Conclusions: In our cohort, engraftment is slightly but significantly delayed in allo-HCTR+ receiving letermovir compared to the pre-letermovir period, despite the reduction in post-HCT CMV reactivation incidence and improved survival. In the literature, few studies report on engraftment but 5/9 studies also find delayed engraftment in letermovir-receiving patients. This effect is independent of other tested covariables and could be due to the drug itself or virus-mediated. Additional studies are needed to confirm this association and explore its clinical significance.

Disclosure: No conflict of interest related to this work.

B100

EXHALED-BREATH VOLATILE MARKERS OF INVASIVE PULMONARY ASPERGILLOSIS IN PEDIATRIC CANCER AND STEM CELL TRANSPLANT PATIENTS: A PILOT STUDY

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Background: Invasive pulmonary aspergillosis (IPA) remains a major clinical challenge in pediatric cancer and stem cell transplant patients and has a high mortality. Early and accurate diagnosis is complicated by a lack of specificity of CT chest imaging, limited sensitivity of bronchoalveolar lavage (BAL) diagnostics and the invasiveness of lung sampling procedures. Exhaled breath analysis might offer a non-invasive alternative by detection of volatile organic compounds (VOCs). In this pilot we aimed to identify mold-associated VOCs in the exhaled breath of pediatric cancer and stem cell transplant patients with IPA.

Methods: Between March 2022 and December 2024, a prospective case–control study was conducted at the Princess Máxima Center for Pediatric Oncology. Exhaled breath samples were collected from immunocompromised children with probable or proven IPA, taken at initial diagnosis and after completion of antifungal treatment. They were compared to exhaled breath samples collected from immunocompromised children without IPA. Sparse partial least square discriminant analysis was used to develop a VOC model consisting of the most relevant VOCs discriminating between groups. The performance of the model was tested by calculation of the area under the receiver operating characteristic curve (AUROCC). VOCs were explored and annotated for metabolic origin using Kyoto Encyclopedia of Genes and Genomes, FungiDB, and the Human Metabolome Database.

Results: Thirty-three children were enrolled (21 pulmonary IPA cases, 12 controls), yielding 45 breath samples. Discriminative VOCs between cases and controls were, 3-methyl-1-butanol, α-pinene, and ethyl acetate, achieving an AUROC of 0.93 (95% CI: 0.82–1.00) in the training set and 1.00 (95% CI: 1.00–1.00) in the test set. Longitudinal analysis showed declining levels of these VOCs following antifungal therapy. Pathway annotation linked these compounds to fungal amino acid degradation (3-methyl-1-butanol), central carbon metabolism (ethyl acetate), and terpenoid biosynthesis (α-pinene), consistent with known *Aspergillus* metabolic pathways.

Conclusions: This study identified three candidate VOCs as potential biomarkers associated with pulmonary aspergillosis in pediatric cancer and stem cell transplant patients. Their strong diagnostic performance and decrease following antifungal treatment suggest potential roles in both non-invasive diagnosis and therapeutic monitoring. Validation in larger, independent cohorts is needed to confirm these results and support the development of breath-based diagnostic tools for IPA.

Disclosure: Nothing to declare.

B101

CMV INFECTION AFTER ALLOGENEIC HSCT IN SERONEGATIVE RECIPIENTS TRANSPLANTED FROM A SEROPOSITIVE DONOR: A MONOCENTRIC RETROSPECTIVE STUDY

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Background: CMV infection is a significant cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (alloHSCT). The incidence of CMV infection has been reported as high as 30% in seronegative recipients transplanted from a seropositive donor (D+/R-). Since 2017, letermovir (LMV) prophylaxis is recommended after alloHSCT in R+ to decrease the incidence of clinically significant CMV infection (CS-CMVi). However, its use in D+/R- has not been studied.

Methods: In this monocentric retrospective cohort, we compared among D+/R-, patients receiving or not LMV prophylaxis after alloHSCT (based on the physician in charge's personal decision). CMV PCR was prospectively collected in blood twice weekly from transplantation until D+100. CS-CMVi was defined as CMV infection requiring pre-emptive treatment (according to locally defined threshold) or CMV disease. Transplant characteristics were extracted from the EBMT Promise registry. Clinical data were collected from electronic medical records. The primary outcome was the cumulative incidence of CS-CMVi at D+100 in both groups. Survival curves were generated using Kaplan–Meier and multivariable analysis was conducted using a time-dependent Cox proportional hazards model. All statistics were performed in R.

Results: We included 163 D+/R- patients transplanted from January 2012 to March 2025 in Saint-Louis hospital, Paris, France: 18 patients received LMV while 145 did not. Patient characteristics are presented in the table.
Between alloHSCT and D+100, CMV PCR was positive at least once in 34/145 patients (23.4%) in the no-LMV group vs 0/18 in the LMV group ($p<0.01$). However, the incidence of CS-CMVi was not statistically different (24/145 (16.5%) in the no-LMV group vs 0/18 in the LMV group, $p= 0.07$). First line pre-emptive treatment was given for a median of 23 days (min: 15, max: 68) and was ganciclovir in 23/24 patients (96%). Eight patients (33.3%) needed second-line foscarnet treatment due to cytopenia (n= 7) or virological failure (n= 1). CMV contributed to death in one patient. There was no significant difference in the D+100-overall survival (88%, 95%CI [88-96] in the no-LMV group vs 93%, 95%CI [62-97] in the LMV group, $p= 0.45$).
Excluding patients from the LMV group, we aimed to identify risk factors for CMV PCR positivity. In univariate analysis, only TBI significantly increased the risk of positive CMV PCR, while the underlying hematological disease, intensity of conditioning, anti-thymocyte globulin (ATG), donor type, stem cell source, sex matching and graft-versus-host disease

(GVHD) as a time-dependent covariate, did not. In multivariate analysis including GVHD as a time-dependent covariate, ATG and TBI, only TBI remained significant (HR 2.4, 95%CI [1.1-5.4], p= 0.03).

	Overall population n = 163	Letermovir n=18 (%)	No Letermovir n=145 (%)	p
Age mean (years)	43.2	42.5	43.3	
Male sex	115 (70.6)	8 (44.4)	107 (73.8)	0.28
Hematological disease Acute leukemia MDS Lymphoproliferative disorder MPN Aplastic anemia SCD	 69 (42.3) 41 (25.2) 29 (17.8) 7 (4.3) 8 (4.9) 9 (5.52)	 7 (38.8) 3 (16.6) 3 (16.6) 3 (16.6) 0 (0) 2 (11.1)	 62 (42.7) 38 (26.2) 26 (17.9) 4 (2.8) 8 (5.5) 7 (4.8)	
HLA-matching MRD MUD 9/10MMUD Haplo-identicak	 49 (30.1) 78 (47.9) 20 (12.3) 16 (9.8)	 4 (22.2) 7 (38.8) 5 (27.8) 2 (11.1)	 45 (31) 71 (49) 15 (10.3) 14 (9.6)	0.19
Source of stem cells				0.17
Bone marrow	26 (16)	5 (27.8)	21 (14.5)	
Peripheral blood	137 (85)	13 (72.2)	124 (85.5)	
Conditioning intensity				0.88
Reduced-intensity	114 (69.9)	13 (72.2)	101 (69.6)	
Myelo-ablative	49 (30.1)	5 (27.8)	44 (30.3)	
ATG	97 (55.8)	7 (38.8)	90 (62)	0.07
Alemtuzumab	11 (6.7)	4 (22.2)	7 (4.8)	0.02
TBI (all doses)	38 (23.3)	2 (11.1)	36 (24.8)	0.24
TBI ≤ 8 Gy	17 (10.4)	2 (11.1)	15 (10.3)	0.92
GvHD prophylaxis				
CNI alone	10 (6.1)	3 (16.6)	7 (4.8)	0.08

CNI + MMF	99 (60.7)	11 (61.1)	88 (60.7)	0.97
CNI + MTX	54 (33.1)	4 (22.2)	50 (34.5)	0.42
PTCy + CNI + MMF	19 (11.7)	5 (27.8)	14 (9.6)	0.04

Conclusions: In our cohort, the incidence of positive CMV PCR in D+/R- alloHSCT patients was lower than historically reported. LMV significantly reduced the incidence of CMV PCR positivity, and was associated with a trend towards a significant reduction in the incidence of CS-CMVi, maybe due to the small size of the cohort. TBI was the only factor significantly associated with a CMV PCR positivity.

Disclosure: Alienor Xhaard: MSD, Takeda
All other authors: nothing to declare

B103

CYTOMEGALOVIRUS REACTIVATION IN A SINGLE CENTER PAEDIATRIC COHORT UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATION AND USE OF LETERMOVIR

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Background: Viral reactivations, especially cytomegalovirus (CMV), are a common complication in paediatric patients undergoing hematopoietic stem cell transplantation (HSCT). In recent years, letermovir has been authorized for the prophylaxis in seropositive HSCT recipients and has shown to reduce CMV reactivations.
Objective: To evaluate, under real-world conditions, the effectiveness of letermovir use in paediatric patients.

Methods: Retrospective observational study of pediatric patients undergoing HSCT from May 2010 to July 2025 at a tertiary hospital. The collected variables included: age, donor/recipient CMV serology, prophylaxis with letermovir, myeloablative or reduced-intensity conditioning, administration of serotherapy and donor type (HLA- identical sibling [MSD], haploidentical with post-transplant cyclophosphamide, other related donors [MMFD] and matched unrelated donor [MUD]. The efficacy variables studied were CMV reactivation, CMV disease, treatment with foscarnet or ganciclovir, and other viral reactivations.

Results: A total of 134 patients were included; the median age at transplant was 7.5 years old (range 3.5 months – 18 years). Underlying diseases included: haemoglobinopathies 78, malignant diseases 41, bone marrow failures 9, immunodeficiencies 6. Donor type were as follows: MSD 84, Haploidentical 33, MMFD 6, MUD 11. Conditioning was myeloablative in 125

patients (93%) and reduced intensity in 9. Serotherapy was administered in 93 patients (69%).
Eighty-four % of recipients and 78% of donors were CMV-seropositive; 7% of recipients were CMV-negative while donors were positive. Twelve patients (9%) with negative serology (donor and recipient) were excluded, leaving 122 patients for further analysis.
A total of 79/122 patients (65%) experienced CMV reactivation. Among those without prophylaxis, the reactivation and treatment rates were 33% in MSD recipients without serotherapy, 73% with serotherapy, 63 % in haploidentical donors, 83% in MMFD (all but 1 with serotherapy) and 56 % in MUD.
Sixteen (13%) patients received letermovir: 11 had a haploidentical transplant, 2 a MUD and 3 a MSD. Among these patients, only 2/16 (13%) required foscarnet/ganciclovir due to progressive increase in viral load, 2 developed HHV-6 encephalitis and one macrophage activation syndrome caused by HHV-6. All patients stopped letermovir before day 200 post-transplant. 2 patients suffered CMV- reactivation, one of them with enteritis involvement. Regarding the safety profile, no significant toxicities were reported. One patient experienced grade 1 vomiting related to administration. No treatments were discontinued due to toxicity. Only one patient in the cohort without letermovir developed possible HHV-6 encephalitis (versus metothrexate toxicity).

Conclusions: CMV reactivation is a common complication following HSCT. Letermovir could be effective for prophylaxis in seropositive paediatric patients without significant toxicity. In our series, patients who received serotherapy reactivated CMV more frequently. However, further studies with larger sample sizes and longer follow-up are needed to assess its effectiveness, as well as its impact on CMV reactivation after discontinuing prophylaxis and other viral reactivations, such as HHV-6, which could potentially be covered by preemptive treatment with foscarnet and/or ganciclovir.

Disclosure: Nothing to declare

B104

PRESERVATION OF ADAPTIVE IMMUNITY AFTER NONMYELOABLATIVE HEMATOPOIETIC CELL TRANSPLANTATION IN ADULTS WITH SICKLE CELL DISEASE (PROTECT STUDY)

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Background: Recipients of allogeneic hematopoietic cell transplantations (HCT) generally lose vaccination-derived immunity, necessitating revaccination. Patients with sickle cell disease (SCD) undergoing matched sibling donor (MSD) transplantation with nonmyeloablative alemtuzumab/total body irradiation (TBI) conditioning develop mixed lymphoid chimerism, potentially preserving their own immunity. We hypothesized that mixed

chimerism after nonmyeloablative MSD transplantation results in preservation of immunity, rendering revaccination potentially unnecessary.

Methods: Preservation of previously developed immunity against measles, rubella, and *Streptococcus pneumoniae* vaccinations was prospectively evaluated in SCD patients undergoing nonmyeloablative transplantation (mixed chimerism; n=24) as compared to patients undergoing haploidentical HCT with a more intensive conditioning regimen (full donor chimerism; n=14). To confirm that the preservation of pre-transplant immunity was recipient-derived, we evaluated immunity against HBV vaccination in subgroup of patients undergoing MSD (n=6) or haploidentical (n=6) transplantation and in non-transplant control SCD patients (n=6). None of the donors had been infected by or vaccinated against HBV. All patients received HBV vaccinations in an accelerated schedule in the months before transplantation. Additionally, immune reconstitution was assessed by measuring lymphocyte subsets (CD3+, CD4+, CD8+, CD19+, and natural killer cells), and total IgG levels at baseline and multiple timepoints after transplantation.

Results: After a follow-up of 24 months, immunity preservation was higher in MSD recipients than in haploidentical recipients for measles (86% vs 70%, p=0.36) and rubella (95% vs 67%, p=0.053), as shown in Figure 1A/B. Pneumococcal immunity remained intact in 95% of MSD recipients compared to only 17% of haploidentical recipients (p=0.005; Figure 1C). Of the patients vaccinated with HBV prior to HCT, three patients (50%) in the MSD cohort and two patients (33%) in the haploidentical cohort lost protective anti-HBs titers, with results in the MSD cohort likely confounded by rituximab treatment shortly after transplantation. In the non-transplant control cohort, one patient remained seronegative and another patient with initial response lost protection against HBV. Immune reconstitution after HCT followed similar trajectories in both groups, with CD3+, CD4+, CD8+, and CD19+ counts falling below reference values after 3 months and recovering to normal levels between 12 and 24 months. However, throughout follow-up, MSD recipients maintained significantly higher total IgG levels, most pronounced at +3 months (16.1 vs 8.1 g/L, p<0.001).

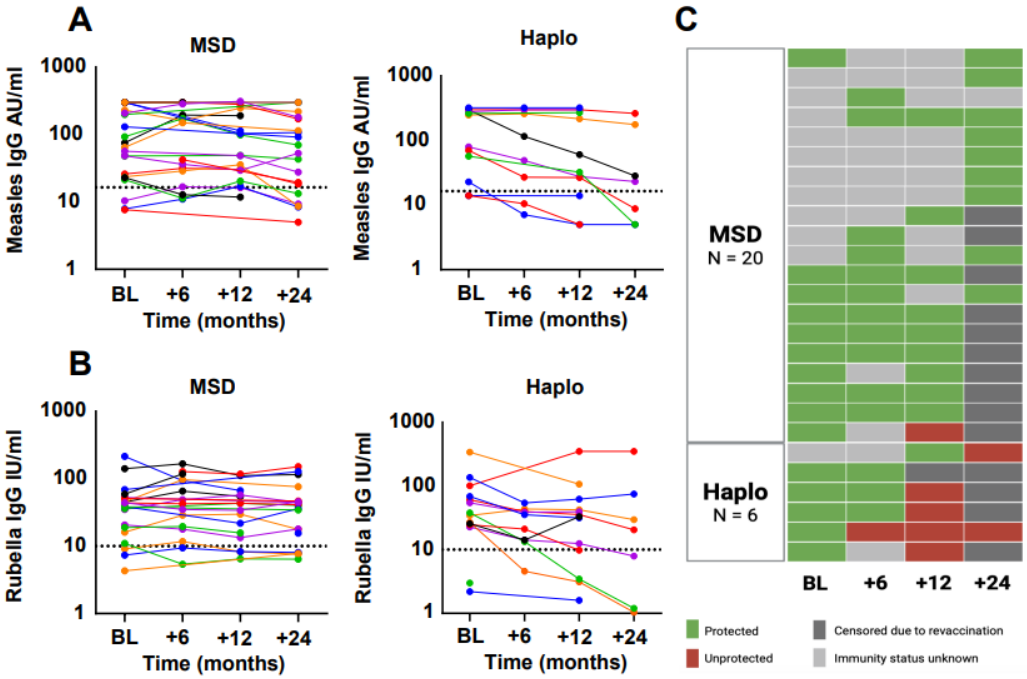

Figure 1. Course of measles (A) and rubella (B) specific IgG titers in the months following hematopoietic cell transplantation (HCT) for MSD (left) and haploidentical (right) groups. Protective threshold is indicated by the dotted line. Measles seropositivity cutoff value > 16.5 AU/mL. Rubella cutoff value > 10 IU/mL. Each line represents an individual subject. (C) Course of immunity against Streptococcus pneumoniae infection at baseline, +6, +12 and +24 months after HCT for MSD and haploidentical transplant recipients. Each row represents an individual subject. Subjects without any data regarding pneumococcal immunity and subjects with only baseline available are not shown. For the single value ELISA, subjects with a titer above 37 mg/L are considered immune. For the multiple subvariant test, subjects with antibody titers above 1.0 µg/mL for 6 or more pneumococcal serotypes are considered immune. Abbreviations: BL = baseline, MSD = matched sibling donor.

Conclusions:
Our results suggest that nonmyeloablative MSD transplantation leading to mixed chimerism results in better preservation of pre-transplant immunity compared to haploidentical transplantations with full donor chimerism. MSD recipients demonstrated high preservation of immunity across important pathogens, whereas haploidentical recipients showed considerable variability in immune preservation, both across pathogens and between patients. The comparable preservation of anti-HBV response between the transplant groups and the non-transplant controls indicates that the preservation of pre-transplant immunity is recipient-derived rather than donor-derived, as all the donors were not exposed to HBV (vaccination). These findings suggest that standard early revaccination programs may be omitted or delayed in adults with SCD undergoing nonmyeloablative MSD transplantation. Whether revaccination in this specific group can fully be abandoned should be subject of future research.

Clinical Trial Registry: The trial was registered with clinicaltrials.gov (NCT05200338).

Disclosure: AG: 2024: Advisory Board Astra Zeneca (RSV vaccination)
BB: Novartis, Sanquin, GBT/Pfizer, BMS (research funding); GBT/Pfizer, BMS/Celgene, (advisory board consultancy); Novo Nordisk, Sanofi (honoraria for lectures and podcasts).
EN: Novartis (research funding, consultancy, speakers bureau), Vertex (speakers bureau).

B105

CAN RECTAL SWABS PREDICT POST-HCT *PSEUDOMONAS AERUGINOSA* INFECTIONS? – A PRELIMINARY SINGLE-CENTER ANALYSIS

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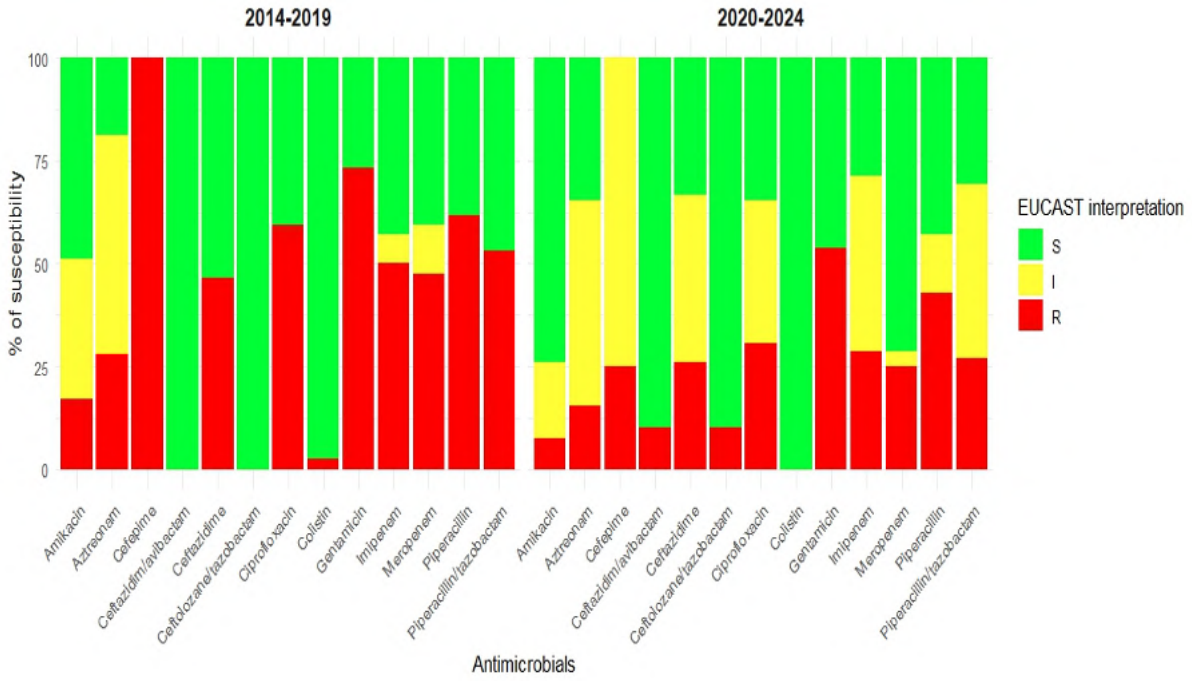
Background: Patients undergoing hematopoietic cell transplantation (HCT) are at high risk for severe infections due to immunosuppression. Colonization with multidrug-resistant organisms increases the risk of invasive infections, particularly early post-transplant. Data on Pseudomonas aeruginosa (PSAE) colonization in HCT recipients remain limited.

Methods: We retrospectively included all adult patients who underwent autologous or allogeneic HCT at ASST GOM Niguarda, Milan, between January 1, 2014, and December 31, 2024. Clinical and microbiological data were obtained through comprehensive chart review. As part of routine clinical practice, rectal surveillance cultures were performed in all patients before transplantation and subsequently on a weekly basis post-transplant. Patients with documented PSAE colonization during the transplantation hospitalization were selected for further analysis. All invasive PSAE infections diagnosed during the study period were identified. The cumulative incidence of PSAE infection was calculated at 30 days post-transplant for non-colonized patients and at 30 days post-colonization for colonized patients, with death considered a competing event.

Results: A total of 980 patients were analyzed. Sixty-three patients had at least one PSAE-positive rectal swab, and among these, 9 developed a PSAE infection within 30 days of colonization (cumulative incidence 14.3%, 95% confidence interval [CI] 5.19–22.50%). In contrast, among 917 non-colonized patients, 9 developed PSAE infection within 30 days post-transplant (cumulative incidence 0.98%, 95% CI 0.34–1.62%). Characteristics of colonized patients are in Table 1. Reduced intensity conditioning with Thiotepa-Fludarabine-Melphalan was more frequent among colonized patients who developed infection (66.7% vs. 27.8%, p=0.017). Overall mortality was low and comparable between groups (11.1% vs. 9.3%). Multiple-site colonization was more common in infected patients compared with non-infected patients (66.7% vs. 31.5%, p=0.046). Antimicrobial susceptibility patterns of rectal isolates are shown in Figure 1: susceptibility to carbapenems increased over time, likely reflecting antimicrobial stewardship interventions, whereas resistance to ceftazidime/avibactam and ceftolozane/tazobactam increased.

Variable	Not infected n=54	PSAE infection n=9
Male	30 (55.6%)	4 (44.4%)
Charlson Comorbidity Index, Median (IQR)	3 (2-4)	2 (2-3)
Disease		
Acute Leukemia	28 (51.9%)	3 (33.3%)
Chronic Leukemia	2 (3.7%)	2 (22.2%)
Myelodispastic Syndrome/Myelofibrosis	6 (11.2%)	0 (0%)
Lymphoma	12 (22.2%)	2 (22.2%)
Multiple Myeloma	6 (11.1%)	2 (22.2%)
Type of Transplant		
Allogenic	38 (70.4%)	8 (88.9%)
Autologous	16 (29.6%)	1 (11.1%)
Absolute Neutrophil Count at the Colonization date, Median (IQR)	0.69 (0.045-2.05)	0.61 (0.11-2.91)
Site of P. Aeruginosa Colonization		
Rectal	41 (73.2%)	9 (100%)
Pharyngeal	12 (26.8%)	0 (0%)
Multiple site of colonization	17 (31.5%)	6 (66.7%)
90 day pre-transplant antimicrobial exposure	28 (51.9%)	3 (33.3%)
Mucositis	37 (68.5%)	5 (55.6%)



Conclusions: Patients colonized with PSAE exhibited a markedly higher 30-day cumulative incidence of invasive infection compared with non-colonized patients (14.3% vs 0.98%). Rectal colonization with PSAE is strongly predict subsequent invasive infection in HCT recipients, underscoring the importance of systematic surveillance and targeted preventive strategies.

Disclosure: Nothing to declare

B106

INTRODUCING MIPI-RADS, MOLD-ASSOCIATED INVASIVE PULMONARY INFECTION - REPORTING AND DATA SYSTEM, FOR UNIFORM ASSESSMENT AND REPORTING OF CHEST CT-IMAGING OF PULMONARY INVASIVE MOULD INFECTIONS

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Background: In haemato-oncology patients, ambiguous radiological reports are a common reason for starting antifungal therapy inappropriately. Current EORTC/MSGERC2020 imaging features have low sensitivity in the detection of pulmonary invasive mould infections (pIMI). These features are time-dependent and can be missed or misinterpreted by radiologists and clinicians in the presence of coinciding pulmonary pathology. In this study we developed a standardised reporting system for pIMI: MIPI-RADS, to be used in the assessment of unenhanced chest CT imaging in the haemato-oncology population at risk. We describe its performance and interobserver agreement.

Methods: MIPI-RADS was developed using current EORTC/MSGERC 2020 imaging features for pIMI and appraisal of 53 chest CT scans of haemato-oncology patients with EORTC/MSGERC probable or proven pIMI.
The MIPI-RADS was subsequently retrospectively evaluated on 110 chest CT scans (38 probable/proven pIMI) performed for suspicion of pIMI in two multicentre randomised controlled trials. A total of 8 observers were included with varying experience (range 1-24 years). In the reference standard, positives were defined as those with probable or proven pIMI only. Fleiss kappa value was calculated, and performance of the median scores of the observers were compared with the reference standard.

Results: MIPI-RADS is structured similar to other imaging reporting and data systems and grades the suspicion for pIMI in haemato-oncology patients with neutropenia on a scale from 1 (low) to 4 (high). The sensitivity, specificity, positive and negative predictive value for the median score of observers compared to the reference standard was 82%, 46%, 44% and 83%, respectively. The Fleiss kappa agreement between observers was 0.61 (p-value <0.001), indicating substantial agreement.

Table 1 MIPI-RADS

Mold associated Invasive Pulmonary Infection-Reporting And Data System

Grade	Summary	Imaging findings	Level of suspicion for pIMI
0	Not readable	Not readable	Not readable
1	no abnormalities	Normal CT imaging	No suspicion
2	aspecific findings or features not compatible with pIMI	• tree-in-bud • consolidation with or without air-bronchogram (and no other associated findings) • clustered bronchocentric solid or nonsolid nodules • diffuse ground glass or diffuse groundglass and (geographic) consolidations • Nodules <5 mm • Typical PFNs**	Low suspicion
3	Features not entirely compatible with pIMI and/or compatible with other etiologies	• Single solid nodule 5-10 mm • Single solid nodule >10 mm without halo • Multiple solid nodules in 1 lobe without halo • Multiple solid nodules in multiple lobes <10 mm without halo • tree-in-bud / airway thickening with surrounding groundglass	Indeterminate suspicion
4	Features compatible with pIMI	• Single solid nodule >10 mm with halo • Multiple solid nodules in 1 lobe at least one with halo • Multiple solid nodules in more than 1 lobe • Cavitating nodules • One or multiple consolidations + associated finding (bronchus cut-off or perifocal thickened interlobular septa or rim of ground glass) • Reversed halo	High suspicion

* pIMI =pulmonary invasive mold infection.**PFN=perifissural nodule

Radboudumc

	Value by indicated test	95% Confidence interval
Sensitivity	0,82	0,64-0,92
Specificity	0,46	0,35-0,57
Positive predictive value	0,44	0,33-0,56
Negative predictive value	0,83	0,69-0,92
Fleiss kappa	0,61	0,58-0,64

Table 2

Diagnostic performance of MIPI-RADS* and interobserver agreement
*MIPI-RADS was divided in low versus high suspicion for pulmonary invasive mold infection.

Conclusions: MIPI-RADS performs moderately well in categorizing pIMI in hemato-oncology patients. Adopting MIPI-RADS will enable concise and discrete communication of imaging results between radiologists and clinicians. Importantly, it will facilitate consistent data collection and outcome monitoring in research and daily practice.

Disclosure: E. de Kort has received a research grant from Gilead sciences which was paid to institution.

B107

HUMAN HERPES VIRUS 6 INFECTION IN ALLOGENEIC STEM CELL TRANSPLANTATION RECEIVING POST-TRASPLANT CYCLOPHOSPHAMIDE

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Background: HHV-6 viremia is frequent after allogeneic hematopoietic cell transplantation (allo-HCT), but there is great difficulty in knowing its pathogenic capacity. The HHV-6B subtype is the main pathogen that causes sudden exanthema in childhood and remains latent in T lymphocytes and monocytes. Among allo-HCT recipients, encephalitis represents the most recognized clinical manifestation of HHV6 infection (incidence 1%), and has also been associated with delayed hematopoietic engraftment. In contrast, involvement of other organs is rarely reported, such as hepatitis, or underrecognized, particularly in the gastrointestinal tract, partly due to the inherent difficulties in establishing a definitive diagnosis.
Considering that changes in transplant strategies, including the widespread use of post-transplant cyclophosphamide (PTCy) and the introduction of letermovir for CMV prophylaxis, may have contributed to an increased incidence of HHV-6 infection, this study describes the incidence and clinical spectrum of HHV-6 infection in allo-HCT recipients at our institution.

Methods: All patients undergoing allo-HCT from 2015 to 2025 (June) at our institution were included. According to major modifications in transplant strategies, patients were classified into three sequential periods: Period 1: 2015-2019, when PTCy was used only in haploidentical and mismatched unrelated donor transplantation (MMUD); Period 2: 2020 and Sept-2021, when PTCy use was progressively extended to matched related and unrelated donors; Period 3: Oct-2021 and June-2025, when PTCy use was universalized, and letermovir was implemented for CMV prophylaxis.
Cases of HHV-6 infection were retrospectively analyzed. HHV-6 PCR in blood was performed in the presence of fever, rash and cytopenias; in blood and cerebrospinal fluid in cases with neurological symptoms; and HHV-6 PCR in tissue, in presence of symptoms in other organs (hepatitis or gastrointestinal), after having ruled out other causes (CMV, GvHD).

Results: A total of 514 adult patients were included, and their baseline characteristics are reported in Table 1.
A total of 80 patients had HHV6 reactivation or infection, in a median of 28,5 days (range 4-340 days) after allo-HCT, with a cumulative incidence function (CIF) of 16%. Cumulative incidence for HHV6 infection was 5% in first period (PTCy in Haplo and MMUD); 28% in the second period (PTCy for all types of allo-HCT) and 26% in the third period (PTCy for all types of transplants and Letermovir for CMV prophlylaxis). Viremia was detected in 14% of cases; Encephalitis was diagnosed in 2% of patients and Gastrointestinal (GI) infection was detected in 84% of patients. GI infection was diagnosed in symptomatic patients and confirmed in endoscopic biopsy by PCR-RT detection. Median viral load in tissue was 17,100 copies/ml (range 2,580-71,731,500) or 140 copies/100.000 cel (range 25-7,032).
Approximately, 60% of patients with HHV6 infection received and responded to antiviral treatment, the median duration of antiviral treatment was 7 days for viremia and 21 days for GI infection.

Table 1. Baseline characteristics and main results

	Period 1 (n=262)	Period 2(n=78)	Period 3 (n= 174)	p value
Median Age	53 (18-70)	53 (18-70)	54 (18-75)	0.721
Sex (% Male/Female)	53/47	68/32	59/41	0.694
Baseline Diagnosis (%) AML/MDS/ALL NHL/CLL CML/MPN Others	 70 14.5 9 6.5	 78 10 8 4	 74 11 6 9	0.005
Conditioning Intensity (%) MAC RIC	 42 58	 54 46	 46 54	0.175
Donor Type (%) Haplo MMUD MUD MRD	 15 25 36 24	 9 24 41 26	 18 19 33 30	0.337
GvHD Prophylaxis (%) PTCy	62	95	93	0.001
Stem cell Source (%) Peripheral Blood	96	96	98	0.563
Letermovir Prophylaxis (%)	0	0	85	<0.001
Relapse Rate (%)	31	32	27	0.458
Rates of mortality (%)	43	36	25	<0.001
Viral Infection	Period 1 (n=262)	Period 2 (n=78)	Period 3 (n=174)	

Table 1. Baseline characteristics and main results

CMV infection (%)	56	45	9	<0.001
CMV Disease (%)	9	10	2	0.004
HHV-6 Infection/Disease (%)	5	28	26	<0.001

AML: Acute myeloid Leukemia, MDS: Myelodisplasic syndrome, ALL: Acute lymphoblastica leukemia, NHL: NonHodgkin Lymphoma; CLL; Chronic lymphocitic leukemia; CML: Chronic myeloid leukemia, MPN: Myeloproliferative neoplasms; MAC: myeloablative conditioning, RIC: Reduced intensity conditioning

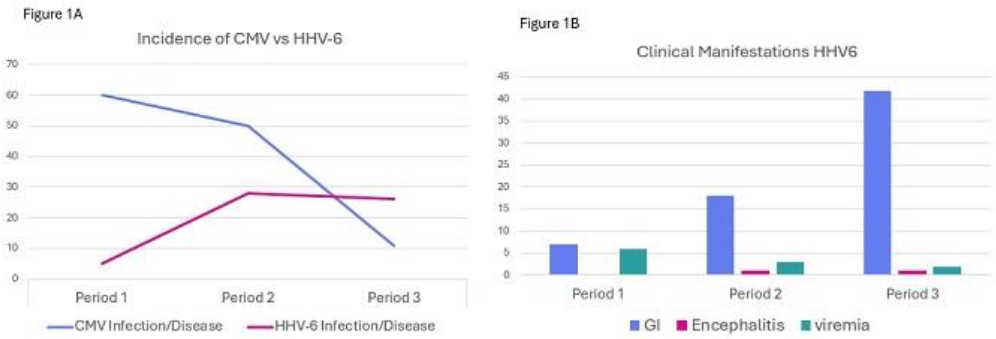

Figure 1. Incidence (%) of HHV-6 infection (Figure 1A) and incidence (%) of clinical manifestations of HHV6 (Figure 1B) according to the three study periods: Period 1, PTCy for haplo and MMUD; Period 2, PTCY for all types of allo-HCT, Period 3: PTCy for all Allo-HCT and Letermovir for CMV prophylaxis

Conclusions: Epidemiology of HHV6 infection is changing in allo-HCT due to the new approaches in GvHD prophylaxis (PTCy regimen) and Letermovir prophylaxis for CMV infection (excellent control on CMV infection). Gastrointestinal infection is the most frequent organ presentation with a good response to antiviral treatment.

Clinical Trial Registry: Not Applicable.

Disclosure: Nothing to declare.

B108

IMPACT OF DONOR CMV-SPECIFIC HUMORAL AND CELL-MEDIATED IMMUNITY ON CMV-IMMUNE RECONSTITUTION AND INFECTION AFTER ALLOGENEIC HEMATOPOIETIC STEM-CELL TRANSPLANTATION

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Background: Cytomegalovirus (CMV) infection is a common complication after allogeneic hematopoietic stem-cell transplantation (allo-HSCT) whose risk largely depends on donor/recipient serostatus. We investigated the combined effect of donor CMV serology and CMV-specific cell-mediated immunity (CMV-CMI) on the kinetics of post-transplant immune reconstitution and the incidence of clinically significant CMV (csCMV) infection.

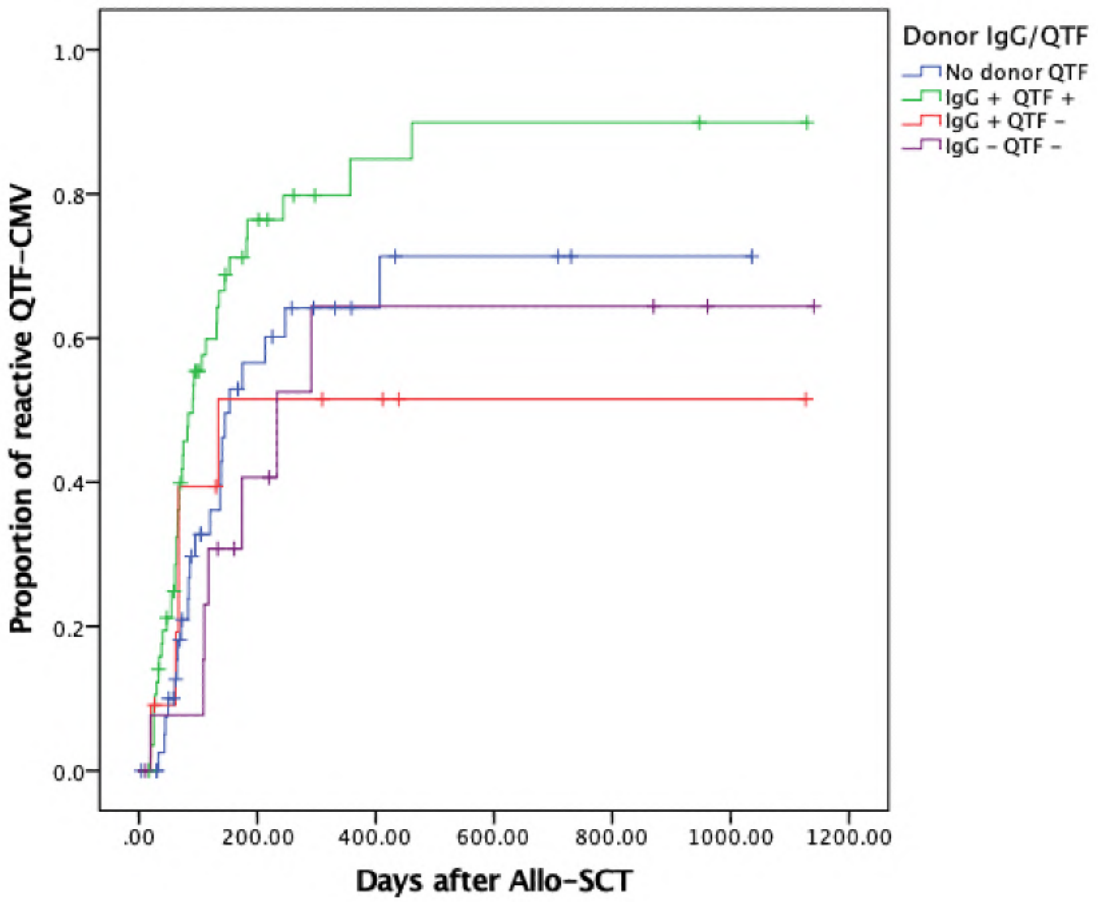
Methods: We conducted a prospective observational cohort study including 127 consecutive allo-HSCT recipients (94 [74.0%] CMV IgG+) at our center between January 2022 and July 2025. CMV-IgG serology was determined in all donors and recipients prior to transplantation. CMV-CMI was evaluated by means of an interferon (IFN)-γ release assay (QuantiFERON® [QTF-CMV]) in related donors before transplantation, as well as at monthly intervals in recipients through month +6. csCMV infection was defined as CMV DNAemia requiring pre-emptive therapy and/or CMV disease.

Results: Patient characteristics were summarized in table 1. Most patients received PTCy-based GVHD prophylaxis (94%) and 53% received primary CMV-prophylaxis with letermovir (Recipients who were CMV IgG + and who deemed at high risk of CMV reactivation as per Spanish reimbursement policy). Global incidence of CMV reactivation was 63%. Letermovir prophylaxis significantly reduced the incidence of csCMV infection. (18% vs 25%, p< 0,05), although it did not have a significant impact in NRM or OS in our population.
The cumulative incidence of reactive QTF-CMV (QTF-CMV_R) increased over time: 19.6% (20/102) at month +1, 42.8% (30/70) at month +3 and 52.5% (21/40) at month +6. Recipients from CMV IgG+ donors had significantly higher median IFN-γ levels in the QTF-CMV assay at months +3 (0.17 vs. 0.00 IU/mL; *P* = 0.025) and +6 (0.54 vs. 0.01 IU/mL; *P* = 0.003) compared to CMV IgG- donors. QTF-CMV was determined prior to transplantation in 84 related donors (70 [83.0%] CMV IgG+ and 16 [17.0%] CMV IgG-). Among the CMV IgG+ donors, 84.3% (59/70) had a reactive QTF-CMV assay (QTF-CMV_R). There were no significant differences in letermovir use between groups (55,7% in IgG+ QTF-CMV_R, 54% in IgG+ QTF-CMV_{NR} and 64% in IgG- donors). All recipients of IgG+ QTF-CMV $_{NR}$ donors were CMV IgG +, while 91.4% of recipients of IgG+ QTF-CMV_R donors were IgG+ (p= 0.5).
Recipients from QTF-CMV_R donors exhibited higher IFN-γ production at months +1 (0.01 vs. 0.00 IU/mL; *P* = 0.057), +3 (0.15 vs. 0.00 IU/mL; *P* = 0.086) and +6 (1.48 vs. 0.02 IU/mL; *P* = 0.038) as compared to non-reactive (QTF-CMV_{NR}) donors. The incidence of csCMV at

months +3 (37.7% vs. 63.3%; *P* = 0.107) and +6 (41.5% vs. 72.7%; *P* = 0.059) was lower in recipients from CMV IgG+ QTF-CMV_R donors as compared with QTF-CMV_{NR} donors. We also noted a higher proportion of reactive QTF during follow-up in the IgG +/QTF-CMV_R than in the IgG + / QTF-CMV_{NR} group (78% vs 45%). There were no significant differences in overall mortality or GVHD between QTF-CMV_{NR} and QTF-CMV_R donors.

Table 1: Patient Characteristics			
Gender	**n (%)**	**Conditioning type**	**n (%)**
Female	59 (46.5%)	RIC	87 (68,5)
Age at transplant	**Median (range)**	MAC	34 (26,8)
	50 (17-69)	Sequential	6 (4,7)
Disease	**n (%)**	**HLA status**	**n (%)**
AML	56 (46.5)	Haploidentical	48 (37,8%)
ALL	15 (11,8)	MRD	41 (32,3%)
MDS	14 (11)	MURD	23 (18,1%)
TCL (Includes CTCL)	10 (7,9)		
HL	8 (6,3)		
OTHER	21 (16,5)		
Donor CMV status (In patients with known donor QTF) n (%)		**CMV viremia and disease n (%)**	
IgG + QTF +	59 (46,5)	CMV reactivation	81 (63,8)
IgG- QTF -	14 (11)	Clinically significant Infection	55 (26,6)
IgG + QTF -	11 (8,7)	CMV disease	7 (3,7)
GVHD prophylaxis		**CMV prophylaxis**	**n (%)**
PTCY + CNI + MMF	119 (93,7)	Recieves Letermovir	68 (53,5)
MTX + CNI	3 (2,4)	Median duration of letermovir treatment: 175 days.	
Other (ATG based)	5 (3,9)		

Figure 1: Evolution of CMV QTF reactivity by donor CMV inmune status



Conclusions: Donor CMV-specific humoral and cellular immunity contribute to earlier CMV-CMI reconstitution after allo-HSCT, consequently reducing the risk of csCMV infection. This could have implications in graft viability and donor selection.

Disclosure: Nothing to declare.

B109

INCIDENCE OF EBV DNAEMIA AND POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD) AMONG HCT WITH POSTTRANSPLANT CYCLOPHOSPHAMIDE (PTCY). A SINGLE CENTER EXPERIENCE

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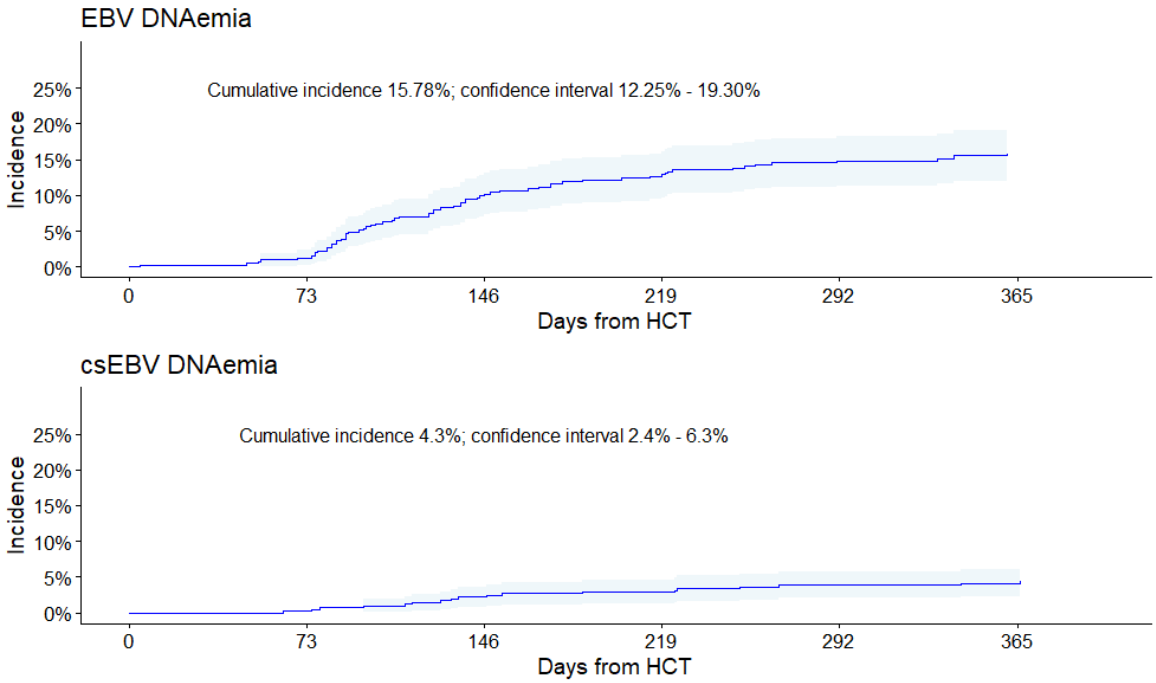
Background: The incidence of EBV-DNAemia and posttransplant lymphoproliferative disorder (PTLD) post HCT ranges from 0.1–63% (median 30%) and 1-11% (median 3%) respectively depending on transplant type and EBV monitoring. We examined the incidence of EBV-DNAemia and PTLD at Day 365 (D +365) post HCT in PTCy recipients routinely monitored by EBV qPCR in plasma at a single center.

Methods: Retrospective, observational study of adult PTCy recipients transplanted between January 2017 to June 2024 at MSK and followed through D +365. Patients received bone marrow or peripheral blood stem cell (PBSC) graft on Day (D) 0; PTCy (50 mg/kg/day) was given on D +3 and +4, and tacrolimus (or sirolimus) plus mycophenolate mofetil (or investigational itacitinib) starting on D +5. ECIL-2 definitions were used: 1) EBV DNAemia was defined as detection of EBV DNA in plasma >500 IU/mL; 2) Clinically significant EBV DNAemia (cs-EBV DNAemia) was asymptomatic EBV DNAemia treated with Rituximab. 3) EBV-PTLD was EBV DNAemia and clinical symptoms and compatible PET scan findings (Probable) and/or biopsy confirmed (Definite) respectively. Univariate logistic regression analysis was used to identify predictors of EBV DNAemia.

Results: Of 412 patients analyzed (median age 64.5 years), 69% had mismatched or haploidentical donors, 2.9% received anti-Thymocyte Globulin (ATG) and 27.4% received myeloablative conditioning. Sixty-five (15.8%) and 18 (4.3%) patients developed EBV DNAemia and cs-EBV DNAemia respectively (**Figure**). Probable and definite PTLD occurred in 10 (2.4%) and 0 (0%) patients respectively. Of 18 patients treated with Rituximab, 17 (94.4%) cleared EBV DNAemia and 1 patient died with EBV DNAemia from GVHD. By D +365, 86 patients had died, including 79 of 394 (20%) without cs-EBV DNAemia and 7 of 18 (38.9%) with cs EBV DNAemia. Death occurred at a median of 79 days (IQR 43-112) from diagnosis of cs-EBV DNAemia.
HCT from mismatched/haploidentical donor was associated with EBV-DNAemia; [odds ratio (95% confidence interval): 4.44 (2.09-10.9); $p < 0.01$]. ATG was associated with cs-EBV DNAemia and PTLD with an odds ratio of 8.56 (1.77, 32.2) and 18.7 (3.61, 80.7) respectively ($p < 0.01$) **(Table)**.

Figure: Incidence of EBV DNAemia and cs-EBVDNAemia in PTCy recipients.



Footnote: The cumulative incidence function was used. Death was a competing risk.

Table: Univariate analyses of risk factors for EBV DNAemia and cs-EBVDNAemia

Variable		EBV DNAemia			cs-EBV DNAemia		
		OR	**95% CI**	**P-value**	**OR**	**95% CI**	**P-value**
Age	Increments of 1 year	0.99	(0.97, 1.01)	0.17	0.98	(0.95,1.02)	0.26
Underlying Disease	Leukemia	**Reference**			**Reference**		
	Lymphoma	1.11	(0.52, 2.27)	0.79	2.08	(0.56,7.67)	0.26
	MDS/MPN	0.98	(0.50, 1.86)	0.94	1.25	(0.34,4.57)	0.73
	Multiple Myeloma	1.99	(0.42, 7.22)	0.33	0		>0.99
	NM-HD/Aplastic Anemia	3.97	(1.24, 12.1)	0.016	8.1	(1.52,37.4)	0.008
Source	Marrow	**Reference**			**Reference**		

	Peripheral blood	0.37	(0.20, 0.70)	0.002	0.64	(0.22,2.32)	0.45
Intensity	Ablative	**Reference**			**Reference**		
	Non-ablative	2.1	(1.06, 4.27)	0.035	2.11	(0.70,7.08)	0.19
	Reduced Intensity	0.8	(0.40, 1.60)	0.52	0.45	(0.11,1.72)	0.24
Donor Match	Matched	**Reference**			**Reference**		
	Mismatched/Haploidentical	4.44	(2.09, 10.9)	<0.001	3.76	(1.05,24.0)	0.08
ATG	None	**Reference**			**Reference**		
	ATG	4.05	(1.17, 13.1)	0.02	8.56	(1.77,32.2)	0.003

Footnote: MDS: myelodysplastic syndrome; MPN: myeloproliferative disorder; NM-HD non-malignant hematologic disorder, CI: confidence interval: ATG: anti-thymocyte globulin

Conclusions: 1) The cumulative incidence of EBV viremia and cs-EBV DNAemia at D +365 among PTCy recipients was 15.8% and 4.3% respectively. 2) Probable PTLD developed in 10 (2.4%) patients. 3) ATG was associated with cs-EBV DNAemia and probable PTLD. 4) No death was directly attributed to EBV. Further studies are needed to define high risk PTCy groups for targeted routine EBV monitoring post HCT.

Disclosure: (Genovefa, Papanicolaou) reports being an investigator for Symbio and AiCuris, received research funding paid to her institution from MSD and AiCuris and consulting/other fees from Symbio, MSD, Takeda, Scynexis and Pulmocide.
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(Miguel-Angel, Perales) reports honoraria from Allogene, Celgene, Bristol-Myers Squibb, Exevir, ImmPACT Bio, Incyte, Kite/Gilead, Merck, Miltenyi Biotec, Nektar Therapeutics, Novartis, Omeros, OrcaBio, Pierre Fabre, Sanofi, Syncopation, Takeda, VectivBio AG, and Vor Biopharma. He serves on DSMBs for Cidara Therapeutics and Sellas Life Sciences. He has ownership interests in Omeros and OrcaBio. He has received institutional research support for clinical trials from Allogene, Genmab, Incyte, Kite/Gilead, Miltenyi Biotec, Novartis, and Tr1x.

B110

MONITORING MATTERS - SUPRATHERAPEUTIC LEVEL OF TACROLIMUS IS A PREDICTOR OF BK VIRUS REACTIVATION IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: BK virus (BKV)–associated hemorrhagic cystitis (HC) causes significant morbidity following allogeneic hematopoietic stem cell transplantation (HSCT) in children. The reported incidence varies between 8% and 25%, depending upon conditioning regimens and graft characteristics. Calcineurin inhibitor (CNI) exposure, particularly tacrolimus, is implicated in BKV nephropathy. There is emerging evidence that fluctuating or elevated levels of CNI may predispose to BKV reactivation post-HSCT.

Methods: The objective was to characterize the clinical and virologic profile of BKV infection in pediatric HSCT recipients and to evaluate the association between tacrolimus trough concentrations and BKV reactivation.
We performed a retrospective cross-sectional analysis that included pediatric patients (≤18 years) who underwent HSCT at a tertiary care centre between January 2014 and December 2023 with documented BKV viruria, confirmed via quantitative polymerase chain reaction in urine. We reviewed patient records for demographic variables, transplant-related parameters, timing and symptomatology of BKV reactivation, and immunosuppressive drug monitoring data. We specifically collected data on tacrolimus levels within the two-week window preceding or immediately following BKV detection and labelled trough levels of over 15 ng/ml as supratherapeutic range. Statistical significance was determined using chi-square testing, with a p-value <0.05 considered significant.

Results: Among 1062 pediatric HSCT recipients over the 10-year study period, 62 patients (5.8%) developed BKV viruria. Of these, 41 patients (66.1%) exhibited tacrolimus trough levels above the institutional upper limit of therapeutic range during the critical window surrounding viral detection. This association reached statistical significance (p = 0.04), supporting a role for supratherapeutic tacrolimus exposure in BKV reactivation.
We documented urogenital symptoms like fever 8/62 (13%), hematuria 40/62 (64%), dysuria 52/62 (83%) and flank pain 14/62 (22%). A majority of the children 37/62 (59%) exhibited external genital discomfort with peculiar pain and swelling of the clitoris in female patients and balanitis in male children. The ultrasound findings include bladder wall thickening, blood clots in the bladder and hydroureteronephrosis in two cases due to obstructive uropathy. The treatment varied from symptomatic relief and hydration to severe cases needing bladder irrigation with a Foley catheter and intravenous cidofovir for up to four doses. Three children developed acute kidney injury requiring dialysis, and two needed percutaneous nephrostomy to relieve the obstructive uropathy caused by blood clots in the bladder. This varied spectrum of clinical manifestations and severity reinforces the importance of prompt evaluation of urinary symptoms.

Conclusions: Our study highlights the clinical relevance of stringent pharmacokinetic monitoring of CNIs, particularly tacrolimus, in children undergoing HSCT as elevated trough levels strongly predict subsequent BKV viruria. Vigilance for genitourinary symptoms should prompt early diagnostic screening mitigates progression to hemorrhagic cystitis and renal dysfunction. Monitoring CNI level is a simple and effective modifiable risk factor to prevent BK virus reactivation available to all transplant centres.

Disclosure: No disclosures.

B111

ERAVACYCLINE IN ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS: A REAL-WORLD STUDY OF DRUG-DRUG INTERACTIONS WITH CYCLOSPORINE/TACROLIMUS AND ANTI-INFECTIVE EFFICACY

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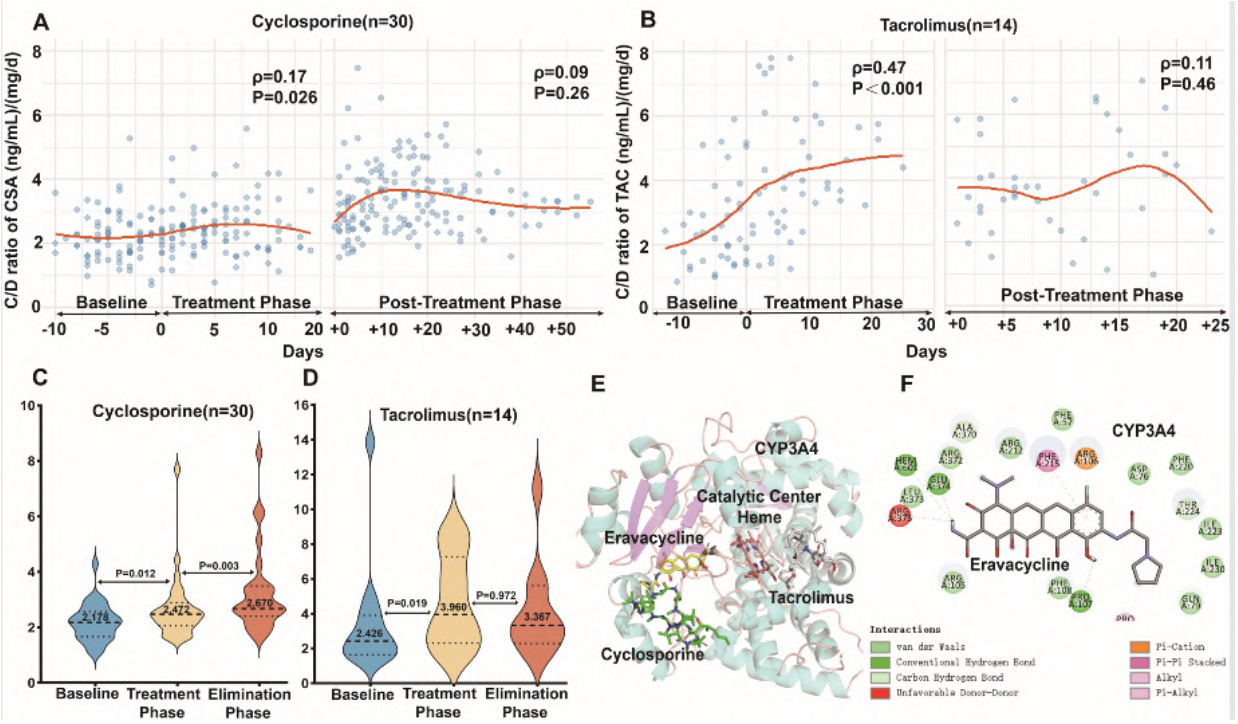
Background: Calcineurin inhibitors (CNIs) are standard prophylaxis for aGVHD after allo-HSCT. Given their narrow therapeutic window, rigorous therapeutic drug monitoring is mandatory. Eravacycline, a novel synthetic tetracycline, shares the CYP3A4 metabolic pathway with CNIs, yet comprehensive data on their potential pharmacokinetic interactions are scarce. This study aimed to evaluate the drug-drug interactions between eravacycline and CNIs.

Methods: This single-center, retrospective study was conducted at the Hematology & Blood Diseases Hospital from August 2023 to July 2025, enrolling allo-HSCT recipients who received CNIs and eravacycline (50 mg q12h). CNI concentration-to-dose (C/D) ratios were monitored at a median interval of every 3 days before, during, and after eravacycline administration, with mean C/D ratios calculated for each phase.

Results: A total of 44 patients were included, with 30 receiving cyclosporine and 14 receiving tacrolimus. 72.7% (32/44) received eravacycline prior to neutrophil engraftment, while 6.8% (3/44) were treated during aGVHD. 36.4% (16/44) once experienced infections during the conditioning phase, with a median treatment duration of 11 days (IQR: 7-15). Primary infection sites were pulmonary (36.4%, 16/44) and bloodstream (27.3%, 12/44), with *Stenotrophomonas maltophilia* (38.6%, 17/44) as predominant pathogens.
In the cyclosporine group (n=30), C/D ratios increased gradually by 13.5% during eravacycline co-administration (P=0.012), necessitating a mean dose reduction of 11.1% to maintain therapeutic levels. Correlation analysis and Lowess regression demonstrated a weak but statistically significant association between eravacycline exposure and C/D ratio elevation (ρ=0.17, P=0.026). Following eravacycline discontinuation, C/D ratios further increased by 8.0% within five half-lives (approximately 5 days) compared with the on-treatment period (P=0.003), requiring an additional 6.0% dose reduction. Thereafter, C/D ratios gradually declined approximately 10 days after eravacycline withdrawal (figure A, C).

In the tacrolimus group (n=14), C/D ratios progressively increased by 62.2% during eravacycline administration (P=0.019). A moderate positive correlation was observed between eravacycline exposure time and C/D elevation (ρ=0.47, P<0.001). After drug discontinuation, C/D ratios decreased compared with the on-treatment period but remained fluctuating and higher than baseline(figure B, D).
These trends persisted in patients with normal liver and kidney function. Subgroup analysis revealed that when co-administered azoles and letermovir, no significant changes in C/D ratio were observed between pre-treatment and during treatment both in cyclosporine group (n=18) and tacrolimus group (n=7). Molecular docking analysis indicated that eravacycline exhibited a higher affinity for CYP3A4 (binding energy: -9.125 kcal/mol) than CNIs, interacting via hydrogen bonds with the heme in the active site(figure E, F).
The infection-related mortality rate was 4.5% (2/44), with a clinical remission rate of 84.1% (37/44). During anti-infective treatment, hepatic and renal toxicities occurred in 13.6% (6/44) and 20.5% (9/44) , respectively. The cumulative incidence of aGVHD within 100 days post-eravacycline treatment was 34.1% (95% CI: 20.0%-48.8%).



Conclusions: This study provides the first clinical evidence of pharmacokinetic interaction between eravacycline with CNIs in allo-HSCT, characterized by increased CNI exposure during eravacycline administration and delayed post-cessation exposure elevation, with this effect waning within around 2 weeks. Despite its modest magnitude, Intensified CNI monitoring and stepwise dose adjustments are recommended throughout and after eravacycline therapy, particularly for tacrolimus during eravacycline administration.

Disclosure: Nothing to declare.

B112

GASTROINTESTINAL MUCOSITIS AS CONTRIBUTOR TO FEVER IN AUTOLOGOUS STEM CELL TRANSPLANT RECIPIENTS CONDITIONED WITH HIGH-DOSE MELPHALAN

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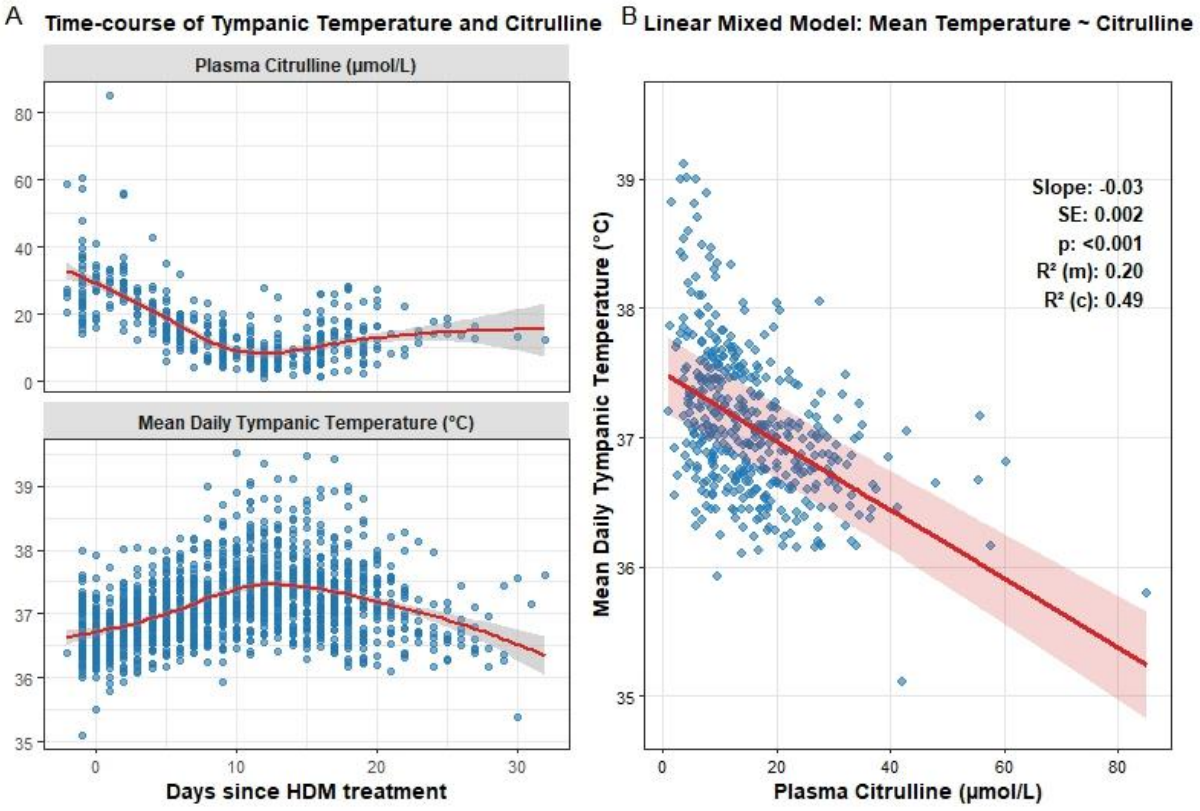
Background: Aetiology of fever without confirmed infectious cause is often unclear in patients receiving intensive therapy for haematological malignancy. Gastrointestinal mucositis (GIM) may contribute via systemic inflammation. We analysed the relation of GIM to tympanic temperature (TT) and fever in autologous hematopoietic stem cell transplantation (auto-HCT)-recipients conditioned with high-dose melphalan (HDM).

Methods: We retrospectively studied auto-HCT-recipients conditioned with HDM (200 mg/m^2) at Radboudumc and UMC Groningen (2015–2025) who had ≥4 plasma citrulline measurements during admission as marker of GIM and were not on immune-dampening regimens. Data on demographics, treatments, blood cultures, TT (four times daily), and neutrophil counts were extracted from hospital records. Bloodstream infections (BSIs) were classified per CDC guidelines. Severe GIM was defined as citrulline ≤10 µmol/L; values >10 µmol/L indicated no to moderate GIM. Profound neutropenia was defined as ANC <0.5 × 10^9/L. Associations between GIM, mean and maximal daily TT, and fever status (TT≥38.5°C) on days of citrulline measurements were analysed including and excluding patients who experienced BSI during admission, using linear mixed-effects models, adjusting for relevant covariates.

Results: A total of 52 patients with 438 citrulline measurements were included. Plasma citrulline declined rapidly after HDM to a mean nadir of 9.4 ± 3.1 µmol/L on 13.5 ± 2.0 days post-HDM, and recovered thereafter. Severe GIM occurred in 63.9% of patients. Mean and maximal daily TT increased in parallel with declining citrulline, with citrulline accounting for 20.4% and 22.5% of variation, respectively (β = -0.03, p < 0.001; β = -0.04, p < 0.001). This remained significant after adjustment for sex, age, HDM-dose (mg/kg), days since HDM, and neutropenia (β = -0.02, p < 0.001; β = -0.02, p = 0.001), with citrulline and days since HDM as the only independent predictors.
Fever risk was significantly higher at lower citrulline concentrations (OR = 0.79, p < 0.001), as well as during severe GIM compared to days with no to moderate GIM (42/154 [27.3%] vs. 8/284 [2.82%], OR = 12, p < 0.001). After adjustment for covariates, fever risk remained associated with lower citrulline concentrations (OR = 0.83, p < 0.001) without other significant contributors, and with severe GIM (OR = 6.06, p < 0.001), with days since HDM and neutropenia also contributing significantly.
In analyses excluding 14 patients with BSI, citrulline levels also showed independent associations with mean and maximal daily TT (β = -0.02, p < 0.001; β = -0.02, p < 0.001), and with fever risk (OR = 0.86, p = 0.013). Severe GIM was also independently significantly associated with likelihood of fever compared to days with no to moderate GIM (OR = 5.56, p

= 0.006).



	Fever			Fever without BSI		
Predictors	*Odds Ratios*	*CI*	*p*	*Odds Ratios*	*CI*	*p*
- (Intercept)	0.00	0.00 - 0.09	0.008	0.00	0.00 - 1.61	0.063
- Severe GIM (≤10 µmol/L)	6.06	2.48 - 14.86	<0.001	5.56	1.64 - 18.91	0.006
- Sex (Male)	1.67	0.76 - 3.68	0.200	2.49	0.71 - 8.68	0.153
- Age (Years)	0.91	0.64 - 1.31	0.616	0.86	0.50 - 1.48	0.577

	Fever			Fever without BSI		
- HDM-dose (mg/kg)	1.95	0.58 - 6.59	0.282	1.61	0.28 - 9.17	0.591
- Time since HDM (Days)	1.08	1.00 - 1.17	0.041	1.06	0.96 - 1.18	0.247
- Neutropenic (Yes vs No)	2.98	1.16 - 7.64	0.023	5.09	1.16 - 22.33	0.031
Marginal R2 / Conditional R2	0.354 / 0.518			0.363 / 0.574		

Conclusions: GIM is strongly associated with higher TT and fever risk in auto-HCT-recipients conditioned with HDM, even in absence of BSI. This suggests that fever in this setting may frequently reflect GIM-driven systemic inflammation (febrile mucositis). Recognition of GIM as contributor to fever could refine diagnostic algorithms and improve supportive care. Future studies should validate citrulline-guided risk stratification to guide antibiotic stewardship and explore interventions to mitigate GIM-related systemic effects.

Disclosure: Nothing to declare.

B113

CMV AND EBV REACTIVATION AFTER HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION IN ELDERLY PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Background: Elderly patients undergoing haploidentical hematopoietic cell transplantation (haplo-HCT) exhibit an increased risk of cytomegalovirus (CMV) and Epstein-Barr virus (EBV) reactivation following immunosuppressive regimens. However, data regarding viral management and its prognostic impact specifically in elderly recipients remains limited. This study aimed to investigate the reactivation patterns of CMV and EBV, identify early risk predictors, and evaluate their impact on transplant outcomes in this population.

Methods: This multicenter retrospective study included patients aged≥60 years with hematologic malignancies undergoing their first haplo-HCT. The primary endpoint was overall survival (OS). Secondary endpoints included the incidence of CMV/EBV reactivation, graft-versus-host disease (GVHD), progression-free survival (PFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM).

Results: A total of 74 patients were included in the analysis. The median age was 63 years (range, 60-75). Main diagnoses included acute myeloid leukemia (AML) in 58.1% (n=43) of patients and myelodysplastic syndromes (MDS) in 26.0% (n=20). Prior to HCT, 70.3% (n=52) of patients were in complete remission (CR), and 33.8% (n=25) had achieved measurable residual disease (MRD) negativity. Regarding GVHD prophylaxis, anti-thymocyte globulin (ATG) was used in 83.8% (n=62) of patients, and post-transplant cyclophosphamide (PTCy) was used in 17.6% (n=13). For pre-transplant antiviral prophylaxis, ganciclovir was administered to 89.2% (n=66) of patients and foscarnet to 21.6% (n=16). Letermovir was used for post-transplant CMV prophylaxis in 18.9% (n=14) of patients. The median time to CMV and EBV reactivation post-transplant was 1.7 months and 2.7 months, respectively. CMV reactivation occurred rapidly, peaking within 3 months post-transplantation (Figure 1A). Cumulative incidence of CMV was 45.9% (95% CI, 34.2%-56.9%) at 3 months and 52.8% (95% CI, 40.7%-63.5%) at 6 months (Figure 1B). In contrast, EBV reactivation exhibited a delayed onset, with 3- and 6-month cumulative incidences of 15.0% (95% CI, 7.9%-24.0%) and 21.7% (95% CI, 13.1%-31.8%), respectively. CMV-EBV co-reactivation occurred in 10.8% (95% CI, 5.0%-19.1%) by 3 months and 12.2% (95% CI, 6.0%-20.8%) by 6 months. In multivariate analysis, letermovir prophylaxis was identified as an independent protective factor for CMV reactivation (HR 0.37, P=0.039) but an independent risk factor for EBV reactivation (HR 3.14, P=0.015). CMV reactivation within 100 days had no significant impact on OS (HR 1.18, P=0.641), PFS (HR 1.31, P=0.422), or NRM (HR 0.81, P=0.614), although it was significantly associated with an increased risk of CIR (HR 5.50, P=0.031). In contrast, EBV reactivation within 180 days was associated with inferior OS (HR 3.51, P=0.006) and PFS (HR 2.60, P=0.033), but no significant differences were observed in CIR (HR 2.15, P=0.248) or NRM (HR 2.05, P=0.159).

Conclusions: In elderly haplo-HCT recipients, EBV reactivation correlates with inferior survival, whereas early CMV reactivation predicts disease relapse without compromising survival. Letermovir prophylaxis effectively mitigates CMV risk but is independently associated with increased EBV reactivation, presenting a clinical trade-off. These findings highlight the distinct prognostic implications of viral kinetics and underscore the necessity for balanced prophylactic strategies and vigilant monitoring in this vulnerable population.

Disclosure: Nothing to declare.

B114

EARLY DISCONTINUATION OF EMPIRIC ANTIBIOTIC THERAPY IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Early discontinuation of empirical antibacterial therapy (EABT) for febrile neutropenia (FN) before neutrophil recovery to > 0.5 × 10^9/L is recommended in hematological patients in the absence of documented infection. However, the safety of this approach in recipients of allogeneic hematopoietic stem cell transplantation (allo-HCT) is insufficiently studied. Published data are limited to a few studies in mixed patient populations.

Methods: A study was conducted in 58 adult allo-HCT recipients between January 2022 and December 2024, who underwent early discontinuation of EABT before neutrophil recovery above 0.5 x 10^9/L and in the absence of documented infection. The study aimed to assess the safety of the early discontinuation approach in allo-HCT recipients, evaluating the following endpoints within 30 days of EABT discontinuation: FN recurrence, bloodstream infection, sepsis, transfer to the ICU, and mortality. Patient characteristics are presented in Table 1. The median follow-up was 409 days (15–1073).

	Study group (n = 58)
Age, median (range)	41 (19 - 65)
Sex Male Female	 27 (46.6%) 31 (53.4%)
Diagnosis AML ALL AA CML MDS nHL	 32 (55.2%) 7 (12.1%) 6 (10.3%) 6 (10.3%) 4 (6.9%) 3 (5.2%)
Indications for allo-HCT Standard Salvage	 45 (77.6%) 13 (22.4%)

Number of allo-HCT First allo-HCT Second allo-HCT	 57 (98.3%) 1 (1.7%)
Donor type MUD Haploidentical MMUD MRD	 18 (31.0%) 17 (29.3%) 12 (20.7%) 11 (19.0%)
Stem cell source PBSC BM	 51 (87.9%) 7 (12.1%)
Conditioning regimen RIC MAC	 40 (69.0%) 18 (31.0%)
Post-transplant cyclophosphamide GVHD prophylaxis	51 (87.9%)

Results: The median time to FN onset after allo-HCT was 2 days (-7 to 15). The median neutrophil count at FN onset was 0.39 x 10^9/L (0–2.88). As first-line EABT, carbapenem-containing regimens were used in 36 patients (62%), while 22 patients (38%) received regimens with inhibitor-protected cephalosporins. At the onset of FN, 35 patients (60.3%) were colonized with extended-spectrum beta-lactamase-producing strains. The median duration of EABT was 8 days (3–22). The median neutrophil count at the time of EABT discontinuation was 0.05 x 10^9/L (0–0.48). *Staphylococcus epidermidis* was identified in blood cultures of 12 patients (20.7%), but it did not meet the criteria for bloodstream infection diagnosis and did not affect the decision to discontinue EABT. FN recurrence was observed in 26 patients (44.8%). The median time to FN recurrence after EABT discontinuation was 3 days (0–15). The median neutrophil count at FN recurrence was 0 x 10^9/L (0–2.12). Carbapenem-containing EABT was resumed in 21 cases (80.7%), and therapy with protected cephalosporins was resumed in 5 cases (19.3%). Five patients (8.6%) were diagnosed with Gram-negative bloodstream infections (BSI) caused by Klebsiella *pneumoniae* (2/5, 40%), *Escherichia coli* (2/5, 40%), and *Pseudomonas aeruginosa* (1/5, 10%). The median time to BSI development from allo-HCT was 11 days (11–13), and from EABT discontinuation was 4 days (3 – 7). All of the BSIs were diagnosed after FN recurrence with a median time of 2 days (0 – 3). Two episodes (2/5, 40%) of sepsis in patients with BSI were recorded within 30 days after early EABT discontinuation, leading to subsequent transfer to the ICU (2/3, 66.6%). Additionally, 1 more patient (1/3, 33.4%) was transferred to the ICU due to cardiac arrhythmia. The overall 30-day survival from the time of early EABT discontinuation was 98.3% (95% CI 88.4–99.8). During the 30-day observation period, 1 allo-HCT recipient, who underwent transplantation as salvage therapy, died from sepsis with multiple organ failure.

Conclusions: The results of this retrospective study demonstrate the safety of early discontinuation of empirical antibacterial therapy in recipients of allo-HCT. However, this approach should be used with caution when performing allo-HCT as salvage therapy.

Disclosure: Nothing to declare.

B116

THE ROLE OF PCR DETECTION OF CARBAPENEMASE GENES IN NATIVE SPECIMENS FOR ROUTINE COLONIZATION SCREENING IN THE EARLY POST–ALLO-HCT PERIOD

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Background: The rising rates of multidrug-resistant pathogens and the limited timeliness of culture and susceptibility testing (CST/AST) complicate early selection of empirical antimicrobial therapy (EAT) based on colonization in allogeneic hematopoietic cell transplantation (allo-HCT) recipients. Polymerase chain reaction (PCR) detection of carbapenemase genes directly from rectal swabs may support colonization-guided febrile neutropenia (FN) protocols, but its place in routine screening and FN algorithms has not yet been clearly defined.

Methods: A total of 116 patients undergoing a first allo-HCT between 2022 and 2024 at the R.M. Gorbacheva Research Institute were prospectively enrolled in a study evaluating serial PCR-based detection of carbapenemase genes during the peri-transplant period. The median age was 40 years (range, 18–71); 46.5% were male (n=54). The underlying disease was predominantly acute leukemia – 73% (n=85). Patients and HCT characteristics are presented in Table 1. Colonization screening comprised standard CST/AST, rectal swabs plated on CHROMagar™ KPC plates, and PCR-based detection of carbapenemase genes directly from native rectal swab specimens from day −7 to day +35 of the allo-HCT period. EAT was administered according to the local colonization-guided protocol. We design the analysis in order to clarify should the PCR guide the upfront EAT strategy.

Results: Febrile neutropenia (FN) developed in 90% (n=104) of the cohort, with a median onset at day +10 (range, 1–18). On the day of FN onset, carbapenem-resistant organisms (CRO) colonization was detected in 11% (n=13) by CST/AST, 24% (n=28) by CHROMagar™ KPC, and 43% (n=50) by PCR: VIM 14% (n=16), IMP 2.5% (n=3), NDM 11% (n=13), OXA-48 1,5% (n=2), KPC 1% (n=1), OXA-48+KPC 2.5% (n=3), VIM+NDM 1% (n=1), NDM+KPC 6% (n=7), NDM+OXA-48 1,5% (n=2), NDM+OXA-48+KPC 1% (n=1), and VIM+NDM+OXA-48+KPC 1% (n=1). Concordance between CHROMagar™ KPC and PCR was 44%, between CST/AST and CHROMagar™ KPC - 77% and between PCR and CST/AST - 84%. Among patients with PCR-detected carbapenemase genes, FN occurred in 88% (n=44). An escalation strategy within EAT was used in 54.5% (n=24), with a treatment response

achieved in 50% (n=12); de-escalation was applied in 45.5% (n=20), with a response in 50% (n=10). In the PCR-positive colonized subgroup, Gram-negative bloodstream infection (GN-BSI) occurred in 20% (n=10): *Klebsiella pneumoniae* -50% (n=5), *Escherichia coli* 30% (n=3), *Klebsiella pneumoniae* + *Escherichia coli* + *Raoultella ornithinolytica* - 10% (n=1), and *Klebsiella pneumoniae* + *Pseudomonas aeruginosa* -10% (n=1). With an escalation strategy, BSI occurred in 16% (n=4), whereas with a de-escalation strategy - 30% (n=6), p=0,694. In 62,5% (n=5/8) of patients who developed GN-BSI, the carbapenemase genes detected during colonization screening matched the gene identified in the isolate causing the BSI (Figure 2). The 60-day overall survival in patients with PCR-detected carbapenemase-gene colonization was 95.9%, with one sepsis-attributable death.

Table 1. Patients' characteristics

Characteristics	Study group n=116
Period of HCT	01.2022-12.2024
Age, years, median (range)	40 (18-71)
Gender, male, n (%)	54 (46,5)
Diagnosis, n (%) AML ALL MPN MDS Other	 65 (56) 20 (17) 10 (8,5) 10 (8,5) 11 (10)
Transplantation type (donor) MRD MUD MMUD Haplo	 14 (12) 29 (25) 36 (31) 37 (32)
Graft source BM PBSC	 6 (5) 110 (95)
Relapse/active disease, n (%)	32 (28)
Myeloablative conditioning regimen, n (%)	54 (46,5)

HCT - hematopoietic cell transplantation, AML - acute myeloid leukemia, ALL - acute lymphoblastic leukemia, MPN - myeloproliferative neoplasms, MDS - myelodysplastic

Table 1. Patients' characteristics

syndromes, MRD - matched related donor, MUD - matched unrelated donor, MMUD - mismatched unrelated donor, haplo - haploidentical donor, BM - bone marrow, PBSC - peripheral blood stem cells

Figure 2.

N	CST/AST *BSI*	CST/AST *BSI*	Carbapenemase genes *GN-BSI*	Carbapenemase genes *rectal swab*	CHROMagar™ KPC *rectal swab*	CST/AST *rectal swab*	Therapy
1	*Klebsiella pneumonia*	R- Carb, AG, CAZ/AVI S - CMS, ATM	NDM	NDM	Detected	Not detected	CAZ/AVI, ATM, CMS
2	*Klebsiella pneumonia*	R - Carb, CAZ/AVI, ATM S - CMS	-	NDM, KPC	Detected	Klebsiella pneumonia CRE	CAZ/AVI, ATM, CMS
3	*Klebsiella pneumonia*	R - Carb, CAZ/AVI, ATM S - CMS	-	NDM, KPC	Detected	Klebsiella pneumonia CRE	CAZ/AVI, ATM, CMS
4	*Klebsiella pneumonia*	R – Carb, ATM S – CAZ/AVI	OXA-48	KPC	Not detected	Klebsiella pneumonia CRE	CAZ/AVI, ATM, CMS
5	*Klebsiella pneumonia*	R – Carb, CAZ/AVI, ATM S - CMS	NDM, KPC	NDM, OXA-48	Not detected	Not detected	CAZ/AVI, ATM, CMS
6	*Escherichia coli*	S – Carb, CAZ/AVI, ATM	Not detected	VIM	Not detected	Not detected	Carb, AG
7	*Escherichia coli*	S - Carb, AG, CAZ/AVI R - ATM	NDM, KPC	VIM	Not detected	Not detected	CAZ/AVI, ATM, CMS
8	*Escherichia coli*	S - Carb, AG, CAZ/AVI R - ATM	Not detected	NDM, KPC	Detected	Klebsiella pneumonia CRE	Carb, AG
9	*Klebsiella pneumonia,* *Pseudomonas monteilii*	R - Carb, ATM S - CMS, CAZ/AVI R - Carb, ATM S – AG, CMS	KPC, OXA-48 – *Kl. pneumonia* VIM, KPC, OXA-48 – *Pseudomonas aeruginosa*	NDM, KPC	Detected	Not detected	CAZ/AVI, ATM, CMS
10	*Klebsiella pneumonia, Escherichia coli, Raoultella ornithinolytica*	R - Carb, ATM S - CMS, CAZ/AVI	NDM, KPC	NDM, KPC	Detected	Not detected	CAZ/AVI, ATM, CMS

GN-BSI - Gram-negative bloodstream infection, CST/AST-culture and susceptibility testing, Carb - carbapenem(s), AG - aminoglycosides, CMS - colistin, CAZ/AVI - ceftazidime/avibactam , ATM - aztreonam, CRE - carbapenem-resistant *Enterobacterales*

Conclusions: Rectal-swab PCR detected carbapenemase genes in 43% of allo-HCT recipients at FN onset, potentially prompting overuse of antibiotics in upfront EAT. However, 27% (n=12/44) of PCR-positive cases responded on an escalation strategy, supporting that PCR positivity alone should have limited impact on upfront EAT strategy at FN. Larger prospective studies are needed to define its role in FN algorithms.

Disclosure: Nothing to declare.

B117

CURRENT TRENDS IN THE MANAGEMENT OF CYTOMEGALOVIRUS IN CELL THERAPIES RECIPIENTS IN SPAIN: RESULTS OF THE 2025 GETH-TC SURVEY

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Background: Cytomegalovirus (CMV) remains one of the most significant infectious complications after allogeneic hematopoietic stem cell transplantation (allo-HSCT). The arrival of novel antivirals is transforming approaches to prophylaxis, monitoring, and treatment. To capture current nationwide practice, the Spanish Group for Cell Therapy and Hematopoietic Transplantation (GETH-TC) conducted a survey on CMV management in allo-HSCT recipients and in patients receiving new cellular therapies.

Methods: A structured online survey addressing 5 domains—use of letermovir (LMV), use of maribavir (MBV), advanced diagnostic tools, management of CAR-T/BITE recipients, and implementation of ECIL-10 recommendations—was distributed in May 2025 to adult and paediatric hematologists within the GETH-TC.

Results: Twenty-six HSCT units (22 adult, 3 paediatric, 1 mixed), representing 65% of Spanish transplant centers, completed the survey. All reported using LMV as primary prophylaxis, mainly restricted to high-risk CMV-positive recipients according to the Spanish Ministry of Health criteria (54%), while 23% administered LMV to all CMV-positive patients. Among recipients receiving post-transplant cyclophosphamide, 50% prescribed LMV only in

the presence of additional risk factors. Extended prophylaxis beyond day +100 is used by 81% of centers, particularly in cases of graft-versus-host disease (GVHD) or delayed immune reconstitution. LMV is used as secondary prophylaxis in 84% of units, usually in selected situations (65%).
MBV has been incorporated into routine management for refractory or resistant CMV, or when conventional antivirals are not tolerated, by 84% of centers. Four centers—three paediatric—do not use MBV.
All units have established monitoring protocols for CMV reactivation. More than half (54%) modify pre-emptive therapy thresholds when LMV prophylaxis is in place. Resistance testing is available in 65% of centers, while CMV-specific immune monitoring is performed in 19%. No center measures LMV plasma levels.
Systematic CMV monitoring in all CMV-positive individuals is performed by 60% of centers in CAR-T recipients and 8% in patients receiving BITE therapy. Pre-emptive therapy in cases of reactivation is systematically used in 88% and 74% of these patients, respectively. Use of LMV or MBV in these settings remains anecdotal.
Regarding the adoption of ECIL-10 CMV guidelines, 85% of centers plan to implement selected recommendations, particularly dual-time-point serology (65%), baseline CMV PCR testing (69%), and updated serostatus nomenclature (69%).

Conclusions: The 2025 GETH-TC survey demonstrates widespread adoption of modern CMV prevention and treatment strategies in Spain, including universal LMV use for primary prophylaxis and broad extension beyond day +100. MBV is increasingly integrated into the management of refractory or resistant CMV. Diagnostic practices are also evolving, with expanded use of resistance testing and immune reconstitution assessment. Nonetheless, heterogeneity persists in prophylaxis criteria, pre-emptive thresholds, and management of CAR-T and BITE recipients.

Disclosure: Nothing to declare

B118

RISK OF BACTEREMIA IN LEVOFLOXACIN-RESISTANT EXTENDED-SPECTRUM B-LACTAMASE-PRODUCING ENTEROBACTERALES COLONIZED RECIPIENTS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT

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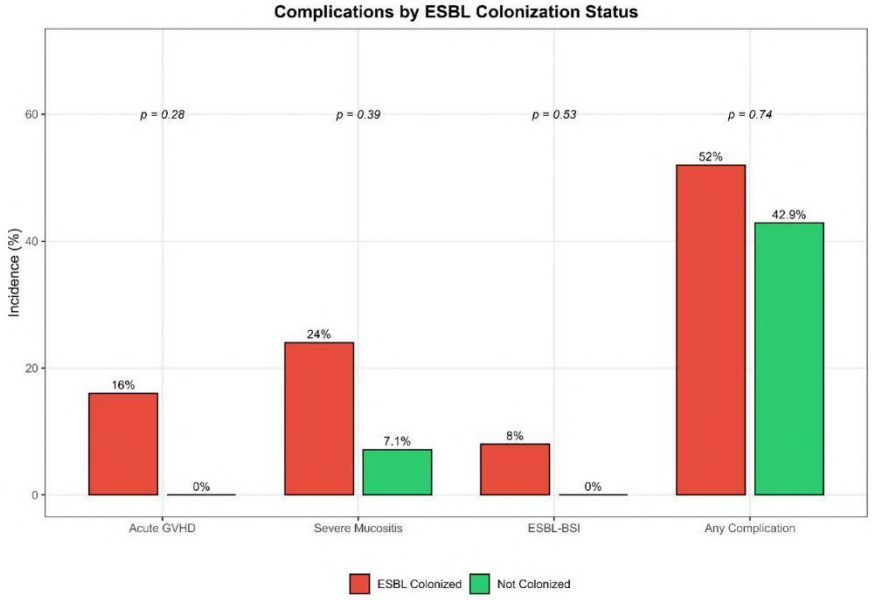
Background: Extended-spectrum beta-lactamase-producing Enterobacterales (ESBL-E) bloodstream infections (BSI) affect up to one-third of allogeneic hematopoietic stem cell

transplant (allo-HSCT) recipients with rectal colonization at the time of transplant. Patients with gastrointestinal ESBL-E colonization who receive levofloxacin prophylaxis may be at increased risk for ESBL-E BSI, particularly in settings with high ESBL prevalence and fluoroquinolone resistance.

Methods: We retrospectively analyzed 39 adult allo-HSCT recipients at our center in Treviso, Italy (January 2024–September 2025) in a region endemic for CTX-M ESBL Enterbacterales. No patients received levofloxacin prophylaxis. Weekly perianal swabs were cultured and tested by PCR for β-lactamase genes (CTX-M) and susceptibility testing. ESBL-colonized patients with neutropenic fever received empirical meropenem.

Results: Of the 39 patients transplanted patients, 25 (64%) were ESBL-colonized—9 detected by PCR only, 16 by culture. CTX-M was detected in 87.5% of swabs, and 94% of culture isolates were fluoroquinolone-resistant. Among colonized patients, 24/25 (96%) developed fever requiring empiric meropenem, with microbiological confirmation of pathogens in 13/24 cases. However, ESBL-E BSI accounted for only 2/24 (8%) of infections. Overall ESBL-E BSI incidence was low 2/39 (5%), and peaked at neutropenia nadir (10 days post-transplant), with an incidence density of 1.37 per 1,000 patient-days (95% CI: 0.00–3.43). No patients without prior ESBL-E colonization developed ESBL-E BSI. Both patients with ESBL-E BSI responded to empiric meropenem and survived without complications. ESBL-colonized patients had higher 90-day cumulative rates of acute GVHD (16% vs 0%) and severe mucositis (24% vs 7.1%) compared to non-colonized patients, irrespective if they developed BSI.



Conclusions: Despite high rectal colonization rates (64%) with CTX-M ESBL and fluoroquinolone-resistant Enterobacterales, ESBL-E BSI incidence was low (5%) after allogeneic HSCT in patients who did not receive fluoroquinolone prophylaxis. Acute GVHD and mucositis, beyond colonization alone, probably contributes to dysbiosis and ESBL-E BSI risk.

Disclosure: Nothing to declare

B120

DETERMINANTS OF EARLY AND LATE INFECTIONS AFTER CAR-T IN SECOND- AND THIRD-LINE LBCL

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Background: CD19-directed CAR T-cell therapy has moved into second-line (2L) treatment for relapsed/refractory large B-cell lymphoma (LBCL), whereas most historical data derive from more heavily pretreated third-line (3L) cohorts. The impact of line of therapy on immune reconstitution and infectious risk, including COVID-19, is not fully defined.

Methods: We retrospectively analyzed 53 adults with LBCL receiving commercial CAR T cells in 2L or 3L. Humoral and cellular immunity (IgG, IgA, IgM, $CD3^+CD4^+$ T-cells, $CD19^+$ B-cells) was evaluated at lymphodepletion (LD) and at 1, 3, 6, 9, and 12 months after infusion. Infections were recorded through 12 months, categorized as early (<30 days) or late (>30 days). No IgG replacement was given. Continuous variables were summarized as median and compared using with non-parametric tests; categorical variables were compared using Fisher's exact test; two-sided $p<0.05$ was considered.

Results: Fifty-three patients were included, 15 treated in 2L and 38 in 3L. At LD, 3L patients showed a more profound humoral immunodeficiency. Baseline IgG levels were significantly lower in 3L (4.69 g/L, IQR 3.90–5.99) than in 2L (6.63 g/L, IQR 5.94–9.36; p=0.0007), as were IgA (0.55 vs 1.15 g/L; p=0.018) and IgM (0.20 vs 0.48 g/L; p=0.0003). $CD3^+CD4^+$ T-cell counts at LD tended to be lower in 3L, while $CD19^+$ B cells were virtually absent in both groups.
Overall, 12/15 2L patients and 34/38 3L patients experienced at least one infectious episode, with a significantly higher overall infection rate in 3L (p=0.0009). Early infections occurred in 6.7% of 2L versus 18.4% of 3L patients (p=ns), whereas late infections were observed in 20.0% of 2L versus 71.1% of 3L patients (p=0.0015). In 2L, early infection was limited to a single fungal event, and late infections were uncommon (bacterial 13.3%, COVID 6.7%). In 3L, early infections were mainly bacterial or non-COVID viral (each 10.5%), while late infections were predominantly bacterial (28.9%) and viral, (COVID 39.5%, non-COVID 15.8%), with few fungal events (5.3%).
ICANS duration (r=0.48, p=0.021), use of corticosteroids for either ICANS (r=0.40, p = 0.010) or ICANS+CRS (r=0.40, p=0.015) were associated with increased risk of early infections. In multivariable analysis, ICANS duration and steroid use for management remained significantly associated with early infectious risk (AUC 0.85, p=0.00003). Beyond day 30, no CRS/ICANS-related predictors were associated with infections.
In 3L patients, IgG levels remained systematically lower at each time point (all $p\leq0.04$),

whereas $CD3^+CD4^+$ T-cell reconstitution from 3 to 12 months was comparable between 2L and 3L.
The overall 1-year cumulative incidence of first infection was 65.3% (26.7% in 2L vs 80.9% in 3L; log-rank p=0.00078). One-year overall mortality was 20.8%, including 15.1% lymphoma-related and 5.7% infection-related deaths.

Conclusions: 3L CAR T-cell therapy, compared to 2L, showed deeper and prolonged hypogammaglobulinaemia, with similar $CD3^+CD4^+$ T-cell recovery, resulting in a significantly higher overall and late infection burden in 3L, primarily due to bacterial and viral infections, especially late COVID. These data supporting intensified anti-infective strategies in heavily pretreated 3L patients.

Clinical Trial Registry: None.

Disclosure: No COI.

B121

MANAGEMENT OF PEDIATRIC HCV-INFECTED PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: A MULTICENTER RETROSPECTIVE ITALIAN STUDY

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Background: Hepatitis C virus (HCV) infection is rarely diagnosed in children born in Italy but it can be observed in children from low-income countries referred to Italian centers for hematopoietic stem cell transplantation (HCT). HCV increases the risk of HCT- and immunosuppression-related complications. While direct-acting antivirals (DAAs) have improved the results of HCV treatment, published data in pediatric HCT patients remains limited and transplant urgency may preclude their use.
We report the outcomes of a series of pediatric HCT patients with active HCV infection who received DAAs before or after transplant.

Methods: This retrospective multicenter study was conducted by the Infectious Diseases Working Group of the Italian Association of Pediatric Hematology and Oncology (IDWG-AIEOP). Pediatric HCV patients undergoing HCT between 2002 and 2023 were included. Demographic, clinical, transplant, and virological data (HCV genotype, viral load at transplant, and HCV treatment) were collected by an anonymized paper case report form. Study follow-up was as 30 November 2025. Descriptive statistics were used; a p value <0.05 was considered statistically significant.

Results: Seventeen HCV patients (9 M, 8F) from five AIEOP were eligible. The patients were from Kyrgyzstan (3), Venezuela (9), Albania (3), Ukraine (2), and Libya (1). Underlying diagnoses were acute lymphoblastic leukemia (n=13), severe aplastic anemia (n=2), Diamond–Blackfan anemia (n=1), and Langerhans cell histiocytosis (n=1). Median age at transplant was 9.8 years (2.1–19.9).
Donors were HLA-matched related (n=1), matched unrelated (n=9) and mismatched related (n=7). All patients received myeloablative conditioning, including total body irradiation–based regimens (n=13) or busulfan/treosulfan-based regimens (n=3); one patient received thiotepa, fludarabine, and cyclophosphamide. Cyclosporine, ATG, and ATLG were administered in 9, 4, and 6 patients, respectively; ex vivo and in vivo T-cell depletion was performed in 6 and 1 patients.
HCV genotypes were 1 (n=7) and 2 (n=8). Five patients received pre-HCT treatment with lamivudine (n=2), ledipasvir/sofosbuvir(n=2), and ribavirin (n=1), while 9 patients were treated after HCT with sofosbuvir (n=2), ledipasvir/sofosbuvir (n=3), glecaprevir/pibrentasvir (n=3), and sofosbuvir/velpatasvir (n=1); three were never treated.
Median time to neutrophil and platelet engraftment was 19 (11–35) and 18 days (11–52), respectively. Acute grade II–IV GVHD occurred in 8 patients, chronic GVHD in 2, veno-occlusive disease in 1, untreated for HCV pre-HCT, and transplant-associated thrombotic microangiopathy in 1. All patients except one, who died from hemorrhage on day +8, were alive at a median follow-up of 3 years, (1.0 – 19.4)
Neither pre-HCT HCV viral load nor DAA treatment was associated with engraftment, aGVHD, TA-TMA, or VOD. An association was observed between higher pre-HCT viral load and cGVHD, but driven by a very limited number of events (point-biserial correlation r = 0.58, p = 0.037).

Nationality	Sex	Age	Diag.	Donor	ATG y/n	TBI y/n	Ex vivo Graft manipulation	GvHD Prophylaxis	HCV Genotype	HCVUI/ml x10⁶ (preHCT)	HCV Treatment (pre)	HCV Treatment (post)	Status @ Last Follow-up (Years)
Kyrgyzstan	F	3.7	ALL	SIB	n	y	no	CSA/TAC /MTX	1b	12.1	Lamivudine		NA
	F	3.4	ALL	MUD	n	y	no	PTCY/CSA MTX MMF	1b	22.1		Glecaprevir/ pibrentasvir	NA
	F	1.7	ALL	MUD	y	y	no	CSA/MTX	1b	NA	Ledispasvi/ Sofosbuvir		Alive (2.79)
Venezuela	M	16.1	ALL	HAPLO	n	y	T reg/T cons	none	2	6.54		Sofosbuvir	Alive (3)
	M	7.9	ALL	HAPLO	n	y	T reg/T cons	none	2	3.51		Sofosbuvir	Alive (4.2)
	M	9.8	ALL	HAPLO	n	y	T reg/T cons	none	2a/2c	NA	none	none	NA
	M	5.8	ALL	HAPLO	n	n	no	none	2b	1.25		Ledispasvir/ Sofosbuvir	Alive (19.4)
	F	6.8	ALL	MUD	y	y	no	CSA/MMF	2b	1.69		Glecaprevir/ pibrentasvir	NA
	M	12.7	ALL	MUD	y	y	no	CSA/MMF	2b	1.10		Glecaprevir/ pibrentasvir	Alive (8.3)
	F	8.3	ALL	MUD	y	y	no	CSA/MMF	2b	0.72		Sofosbuvir/ velpatasavir	Alive (8.5)
	M	8.5	SAA	HAPLO	y	n	CD19- Tα/β depletion	none	2a	NA	Ribavirin		NA
	F	12.6	LLA	MUD	y	y	no	CSA/MTX	1a	2.8		Ledispasvir/ Sofosbuvir	Alive (4.3)
Ucraina	M	5.0	ALL	MUD	y	y	no	CSA/MTX	UK	NA	Lamivudine		Alive 2
	M	14	SAA	MUD	y	y	no	CSA/MTX	1a	1.68	none	none	Alive (2.6)
Albania	F	10.4	ALL	HAPLO	y	y	no	no	1b	0.5		Ledispasvir/ Sofosbuvir	Alive 2.5)
	M	2.1	Langh erans	MUD	y	n	T-depletion	CSA/MPD	UK	NA	none	none	Alive (1)
Libia	UK	16.3	BDA.	HAPLO	y	n	CD19- Tα/β depletion	no	1a	NA	Ledispasvi/ Sofosbuvir		Dead (day +8)

Conclusions: Our data suggest that HCT can be safely performed in pediatric patients with active HCV infection, even in the setting of intensive immunosuppression including in vivo

and ex vivo T-cell depletion. Pre-transplant HCV viral load and DAAs exposure did not negatively impact engraftment or early transplant-related complications. DAAs were well tolerated when administered before or after HCT, supporting timely transplantation without delay.

Disclosure: NO COI

B122

SURGICAL TREATMENT OF PULMONARY INVASIVE FUNGAL DISEASE IN PATIENTS AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: The effectiveness and safety of surgical treatment for pulmonary invasive fungal disease (pIFD) after allogeneic hematopoietic cell transplantation (allo-HCT) remain undetermined, with only isolated cases of surgical intervention reported in the literature. This study presents the largest experience with surgical treatment of pIFD following allo-HCT to our knowledge.

Methods: A retrospective analysis was conducted on the outcomes of surgical treatment for pIFD in allo-HCT recipients from 2013 to 2025. The study included 12 patients who underwent 13 surgical interventions for probable and proven pIFD: children (n=2) and adults (n=10) with the median age 26 years (range 10-64), males (n=11), with diagnoses including chronic myeloproliferative disorders (5, 41.7%), acute leukemia (3, 25%), aplastic anemia (3, 25%), and lymphoma (1, 8.3%). Patient characteristics, allo-HCT, pIFD, and surgical interventions are detailed in Table 1.

Table 1. Characteristics of allo-HCT recipients with pIFD undergoing surgery n=12

Donor Type: MUD / MMUD / MRD / Haplo	2 (16,7) / 5 (41,7) / 1 (8,3) / 4 (33,3)
Conditioning Regimen: MAC / RIC	4 (33,3) / 8 (66,7)
Pulmonary invasive fungal disease: IA / MM / MM + IA	5 (41,7) / 4 (33,3) / 3 (25)
Bilateral lung involvement	6 (50%)

Median day of IM onset post-allo-HCT, days	96 (21-510)
Therapy with Voriconazole	5 (41,7)
Therapy with Amphotericin B ± voriconazole, posaconazole, isavuconazole	7 (58,3)
Median days of therapy pre-surgery, days	61 (13-526)
Median days from allo-HCT to surgery, days: IA / MM / IA+MM	182 (41-547) / 296 (133-547) / 138 (41-348)
Surgical Volume: Pneumonectomy / Lobectomy / Wedge resection / Atypical wedge resection / Chest wall resection	4 / 6 / 3/ 1 / 1
Surgical Approach: Thoracotomy / Endoscopic video-assisted thoracoscopy	11 / 2

Results: Surgical treatment for pIFD post-allo-HCT achieved a complete response (radical surgery) in 91.7% (n=11); one patient with mucormycosis underwent successful repeat surgery in 250 days after the first to remove a second lesion. pIFD recurrence post-surgery occurred in one patient (8.3%) with invasive aspergillosis 1.5 years later. At surgery, 2 patients (15.4%) had grade 3-4 neutropenia and 8 (61.5%) patients had grade 4 thrombocytopenia. Intraoperatively, a mean blood loss was 600 mL (0-2,600 mL). The duration of operation ranged from 60 to 290 min (median, 175 min). Minor complications were reported in two patients: hydropneumothorax and air leak syndrome n=1, 7.7%; pleural empyema n=1, 7.7%. One death in early period was registered (7.7%). Overall survival after first surgery at 30 days, 12 weeks, and 12 months was 83.3%, 83.3%, and 58.3%, respectively; five patients died within 1 year, 4 (80%) from underlying disease progression. Postoperative histology and mycology confirmed diagnoses in seven patients and increased pathogen species identification and antifungal susceptibility testing from 33.3% (4/12) to 66.7% (8/12), improving overall diagnostic precision to 91.7%.

Conclusions: Surgical treatment is effective and safe option in management of pulmonary invasive fungal disease among patients with hematological diseases after allo-HCT.

Disclosure: Authors have nothing to disclosure.

B123

NOT ALL AUTOLOGOUS TRANSPLANTS ARE LOW RISK: DELAYED PLATELET ENGRAFTMENT SIGNALS THE NEED FOR CMV MONITORING

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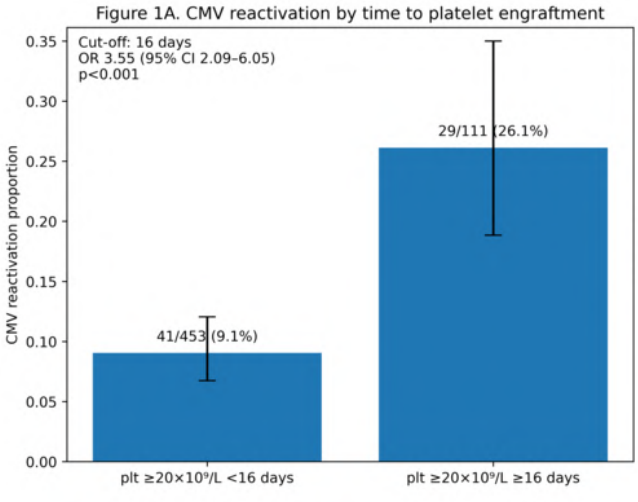
Background: Although CMV PCR monitoring is standard after allogeneic transplantation, it is not routinely recommended following autologous stem cell transplantation due to a perceived low risk. However, real-world data indicate that CMV risk after ASCT is heterogeneous, and the absence of simple clinical markers has hindered risk-adapted surveillance strategies.

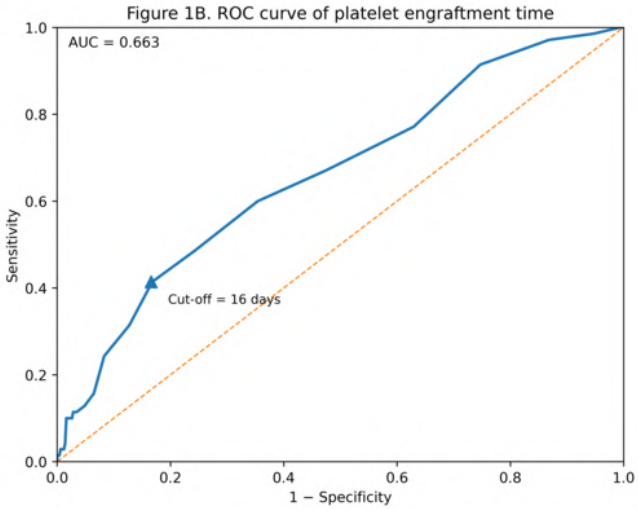
Methods: We conducted a retrospective multicenter cohort study including adult patients who underwent ASCT. CMV reactivation was defined as PCR-detected CMV DNAemia following transplantation. Baseline demographic, clinical, laboratory, and transplant-related variables were collected. Univariate analyses were performed to identify factors associated with CMV reactivation. Continuous variables were compared using the Mann–Whitney U test, and categorical variables using the chi-square or Fisher's exact test, as appropriate. Variables with $p<0.10$ in univariate analyses were further evaluated using receiver operating characteristic (ROC) curve analysis to determine optimal cut-off values based on the Youden index. A multivariable logistic regression model incorporating these variables was constructed to identify independent predictors of CMV reactivation. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs).

Results: A total of 614 adult patients undergoing ASCT were analyzed, of whom 77 (12.5%) developed CMV reactivation. The median age was 56 years, and 58.1% were male, with no significant differences in age or sex distribution between CMV-positive and CMV-negative groups. Baseline laboratory parameters, including neutrophil count, lactate dehydrogenase, beta-2 microglobulin levels, and infused $CD34^+$ cell dose, were comparable between groups. In contrast, hematopoietic recovery kinetics differed markedly. Patients with CMV reactivation exhibited significantly delayed platelet engraftment, defined as achievement of a platelet count $\geq 20\times10^9$/L, compared with CMV-negative patients (median 14 days [IQR 12–17] vs. 12 days [IQR 10–14]; $p<0.001$). Neutrophil engraftment was also modestly delayed in the CMV-positive group (12 vs. 11 days; $p=0.017$). Baseline lymphocyte counts were numerically lower among patients with CMV reactivation (1.17 vs. 1.30 $\times10^9$/L), although this difference did not reach statistical significance ($p=0.058$).
Among categorical variables, advanced disease stage ($p=0.012$), prior rituximab exposure ($p=0.008$), and the presence of comorbidities ($p=0.027$) were more frequent in CMV-positive patients, whereas conditioning intensity, radiotherapy exposure, and CMV serostatus were not associated with CMV risk.

ROC analysis identified time to platelet engraftment as the strongest discriminator of CMV reactivation. Using a Youden index–derived cut-off of approximately 16 days, delayed platelet

engraftment was associated with a substantially increased risk of CMV reactivation (Figure 1).





In multivariable logistic regression analysis adjusting for neutrophil engraftment time and baseline lymphocyte count, delayed platelet engraftment remained the only independent predictor of CMV reactivation (adjusted OR 2.4, 95% CI 1.5–3.9; p<0.001), whereas other variables lost statistical significance (Table 1).

Table 1. Univariate and multivariable analyses of factors associated with CMV reactivation after autologous stem cell transplantation

Variable	CMV+ (n = 77)	CMV− (n = 537)	Univariate p value	Multivariable OR (95% CI)	Multivariable p
Delayed platelet engraftment (≥16 days to plt ≥20×10⁹/L)	14 (12–17)	12 (10–14)	<0.001	2.4 (1.5–3.9)	<0.001
Neutrophil engraftment (days)	12 (11–13)	11 (10.8–12)	0.017	1.6 (1.0–2.6)	0.041
Baseline lymphocyte count (×10⁹/L)	1.17 (0.72–1.65)	1.30 (0.99–1.70)	0.058	1.4 (0.9–2.2)	0.11

Table 1. Univariate and multivariable analyses of factors associated with CMV reactivation after autologous stem cell transplantation

Rituximab exposure (%)	24.7	12.7	0.005	1.57 (0.77–3.20)	0.215
Stage 3 vs Stage 1 (%)	28.4	41.6	0.012	0.43 (0.20–0.92)	0.029

Univariate and multivariable analyses of factors associated with CMV reactivation after autologous stem cell transplantation. Delayed platelet engraftment was defined as ≥16 days to achieve a platelet count ≥20×10⁹/L, based on receiver operating characteristic analysis using the Youden index. Continuous variables are presented as median (interquartile range), and categorical variables as percentages. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were obtained from a multivariable logistic regression model including variables with p<0.10 in univariate analysis.

Conclusions: Although ASCT is generally considered low risk for CMV reactivation, our findings show that CMV risk is heterogeneous. Delayed platelet engraftment emerged as the strongest independent predictor of CMV reactivation, supporting a risk-adapted approach in which targeted CMV PCR monitoring may be warranted in patients with delayed platelet recovery. Incorporating platelet engraftment kinetics into post-transplant surveillance could facilitate earlier CMV detection and optimize patient management.

Disclosure: Nothing to declare.

B124

RESPIRATORY VIRAL INFECTIONS AND NONINFECTIOUS PULMONARY COMPLICATIONS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Allogeneic haematopoietic stem cell transplantation is a therapeutic alternative for many malignant and non-malignant blood disorders. Acute or chronic GVHD is a common complication with a prognostic impact. Post-allograft non-infectious pulmonary complications (NIPC) involves numerous entities, the most common of which is bronchiolitis obliterans syndrome (BOS), but also interstitial lung disease. NIPC occurring after allogeneic hematopoietic stem cell transplantation are a major cause of morbidity and mortality. Respiratory viral infections could play a triggering role in their occurrence.
The objective of our study was to evaluate the association between respiratory viral infection and the risk of NIPC, as well as to identify the viruses most commonly involved and compare them during the infectious episode.

Methods: We conducted a retrospective monocenter study at Caen University Hospital, including all patients who underwent allogeneic haematopoietic stem cell transplantation between 1st January 2014 and 31st December 2022, and collected data on transplant conditions, viral respiratory episodes and the occurrence of aCGHVD, cGVHD and NIPC.

Results: Among the 341 patients included, 147 had a first respiratory viral infection, and 19 developed NIPC, mainly of the bronchiolitis obliterans type.
The most prevalent community respiratory viruses in all infectious episodes were HRV/ENT (18%), SARS-CoV-2 (10%), coronaviruses (8%), parainfluenzas (7%), RSV and hMPV (6%) and influenza (6%).
After adjustment, the occurrence of acute GVHD (OR 3.3 [95% CI 1.08-10.27]), *Influenzavirus* infection (OR 4.7 [95% CI 1.29-17.19]), *Coronavirus* infection (OR 5.9 [95% CI 1.71-20.38]), *Rhinovirus* (OR 5.2 [95% CI 1.79-15.20]) or *Pseudomonas aeruginosa* superinfection (OR 10.5 [95% CI 1.20-92.56]) were significantly associated with the development of NIPC.
One hundred and eighty patients died, and nearly one-third of these deaths were respiratory in origin. Among the 19 patients with NIPC, 10 died, with NIPC which is not associated with an increased risk of death from any cause, but there is a significant link with death from respiratory causes (OR: 6.3 [95% CI: 1.56–25.36]).
The viruses associated with an increased, albeit non-significant, risk of death compared to HRV/ENT were parainfluenza (OR: 1.9 [95% CI: 0.6–6.0]), influenza (OR: 1.3 [95% CI: 0.4–4.3]) and 'other' viruses (OR: 1.6 [95% CI: 0.3–7.5]). Regarding deaths from respiratory causes, all viruses appear to offer protection against HRV/ENT.

Conclusions: In conclusion, our study once again confirms the link between respiratory viruses and the development of NIPC. It also highlights the impact of viral infection on the prognosis of NIPC and emphasises the seriousness of this diagnosis for patient survival. All respiratory viruses appear to be a trigger for NIPC, even if the acute episode is not very symptomatic and, from the first infection onwards, it is necessary to be vigilant about the need to document each viral infection in order to personalise respiratory function monitoring to track NIPC induced by this respiratory virus. The role of Pseudomonas aeruginosa co-infection as a potential factor in NIPC is an important new element to consider.

Clinical Trial Registry: This non-interventional study was approved by the Observational Research Protocol Evaluation Committee (Comité d'Evaluation des Protocoles de Recherche Observationnels, CEPRO) and the Institutional Review Board of the French Society of Respiratory Medicine (Société de Pneumologie de Langue Française, SPLF). Reference: CEPRO 2020-012.

Disclosure: Non conflict of interest

B125

HHV6 MONITORING AND DONOR ASSESSMENT IN PAEDIATRIC HAEMATOPOIETIC STEM CELL TRANSPLANT – A SINGLE CENTRE PROSPECTIVE STUDY

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Background: Human herpesvirus 6 (HHV-6) reactivation is a frequent complication after allogeneic haematopoietic stem cell transplantation (HSCT), but its clinical impact and need for PCR monitoring and treatment remain unclear. Cost-feasibility according to the clinical significance of HHV6 monitoring has not been studied in the paediatric setting.

Methods: We prospectively analysed paediatric patients who underwent transplantation at Great Ormond Street Hospital between June 2024 and May 2025. All donors were screened for HHV6 viremia and/or viral integration, while recipients were screened before HSCT and weekly until 6 months post-transplant. Variables included age at transplant, donor type (MUD/MSD/MFD/MMUD/haploidentical), stem cell source (BM vs PBSC), immune reconstitution (CD3 and CD4 counts at 3 and 6 months), and occurrence of post-transplant cytopenia, pneumonia, rash, or encephalitis. HHV6 reactivation was considered when persistent for at least 2 consecutive weeks, and viral load was measured as the number of PCR cycles required for detection (CT). Continuous variables were compared with Mann–Whitney tests, and categorical variables with Fisher's tests.

Results: We collected data from 51 patients with a minimum follow-up of 6-months. Sixteen patients reactivated HHV6 with a median CT of 35.19 (IQR 33.6–36.8) and a range from 29.03 to 38.87. Age at HSCT was higher in the Reactivated group (median 5.05 vs 1.79 years; p=0.065). Pre-transplant HHV6 positivity was strongly associated with subsequent HHV-6 reactivation (6/16 vs 2/35; OR 9.90, 95% CI 1.72–56.96; p=0.008). Donor type distribution and stem cell source were comparable between groups (p=0.513 and p=1.000, respectively; OR 0.96, 95% CI 0.29–3.18). There was no difference in CD3 and CD4 counts at 3 and 6 months between the groups (CD3 at 3 months: 310 vs 160 cells/μL, p=0.103; CD4 at 3 months: 163 vs 70 cells/μL, p=0.410). No differences were found in the timing of engraftment for neutrophils and platelets in both groups.
No viral DNA integration was found in the positive donors. Cytopenia was more frequent in reactivated patients (7/16 vs 4/33; OR 5.64, 95% CI 1.34–23.76; p=0.025), while other transplant-related variables were similar between groups. However, cytopenia was not clinically significant, and only 3/16 required treatment with G-CSF for more than a month, and all self-resolved with no treatment. No significant differences were found in bacterial infections, sepsis, or PICU admissions. Non-relapse mortality and overall survival were both

better in the reactivated group. No encephalitis or rash related to HHV6 occurred in both study groups.

Variable	Reactivated	Not Reactivated	p-value
Age at BMT (years)	n=16; median 5.05 (IQR 2.08–11.0)	n=33; median 1.79 (IQR 0.92–5.30)	0.065
CD3 at 3 months (cells/µL)	n=18; median 310 (IQR 75–607.5)	n=29; median 160 (IQR 70–320)	0.103
CD4 at 3 months (cells/µL)	n=18; median 163 (IQR 53–210)	n=29; median 70 (IQR 40–210)	0.41
CD3 at 6 months (cells/µL)	n=13; median 545 (IQR 340–1100)	n=21; median 350 (IQR 190–770)	0.489
CD4 at 6 months (cells/µL)	n=13; median 190 (IQR 140–350)	n=21; median 190 (IQR 80–530)	0.79
Donor type (Haplo/MFD/MMUD/MSD/MUD)	MUD 7 (44%) MSD 6 (38%) MFD 1 (6%) MMUD 2 (12%)	MUD 20 (60%) MSD 6 (19%) MMUD 2 (6%) Haplo 5 (15%)	ND
Stem cell source (BM vs PBSC)	BM=9, PBSC=7	BM=20, PBSC=15	1
HHV6 pre-BMT positive	6/16 (37%)	2/35 (6%)	0.008
Cytopenia	7/16 (43%)	4/33 12%)	0.025
Non-Relapse Mortality	0/16 (0%)	7/33 (21%)	0.08
Overall Survival	16/16 (100%)	25/33 (75%)	0.041

Conclusions: In this cohort, HHV-6 reactivation was not associated with donor type, stem cell source, or clear differences in early T-cell reconstitution, but showed strong associations with pre-transplant HHV-6 positivity and a higher incidence of post-transplant cytopenia. These findings suggest that pre-BMT HHV-6 status may help identify patients at increased risk of reactivation and cytopenias. Also, the low clinical impact of HHV6 in our cohort, with

no clinical events associated and no differences in bacterial infections, sepsis, and PICU admissions in the reactivated patients, does not justify regular HHV6 PCR monitoring in patients with no HHV6 positivity before transplant.

Disclosure: No disclosure

B126

CHANGES IN ANTIBODY TITERS AND PREDICTIVE FACTORS FOR SEROCONVERSION FOLLOWING LIVE VACCINATION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION RECIPIENTS

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Background: Hematopoietic stem cell transplant (HSCT) recipients often experience a reduction or loss of pre-existing immunity. Although revaccination after immune reconstitution is recommended, the optimal conditions for achieving effective seroconversion remain unclear. This study retrospectively evaluated changes in antibody titers before and after live attenuated vaccine (LAV) administration and identified factors associated with seroconversion.

Methods: We retrospectively analyzed data from 67 patients (28 for varicella, 27 for rubella, 34 for measles, and 47 for mumps) who underwent allogeneic HSCT at Kyoto University Hospital between August 2018 and July 2025, received at least one LAV, and had antibody titers measured before and after vaccination. Seropositivity was defined as an IgG antibody titer of 4 or greater for each virus, as determined by the Enzyme Immunoassay (EIA) for measuring various viral IgG antibody titers, following the vaccination guidelines established by the Japan Society for Transplantation and Cellular Therapy. Logistic regression was used to identify factors associated with seroconversion. Optimal cutoff values for the IgG levels and lymphocyte counts were determined using receiver operating characteristic curve analysis.

Results: The median age of the subjects was 47 years, with 39 males and 28 females. Donor sources included 4 cases of related bone marrow transplantation (BMT), 9 cases of related peripheral blood stem cell transplantation (PBSCT), 20 cases of unrelated BMT, and 34 cases of umbilical cord blood transplantation (UCBT). The seroconversion rates for each vaccine were: varicella 32.1%, rubella 96.3%, measles 91.2%, and mumps 25.5%. For the mumps vaccine, preserved IgG levels (≥1000 mg/dL) were associated with seroconversion in both univariate (odds ratio [OR], 4.7; P=0.067) and multivariate analyses (OR, 8.9; P=0.039). Conversely, lower total lymphocyte counts (<1950/μL) were associated with reduced seroconversion (OR, 0.09; P=0.003). Detailed lymphocyte subset analyses could not be performed due to insufficient available data.

Conclusions: Seroconversion rates after LAV administration in allogeneic HSCT recipients varied depending on the vaccine type. Markers of immune reconstitution, particularly preserved IgG levels, were strongly associated with improved seroconversion following mumps vaccination. These findings suggest that successful revaccination in HSCT survivors depends primarily on the recovery of antibody-mediated immunity, underscoring the importance of individualized assessment based on immune status rather than timing alone.

Disclosure: Nothing to declare

B127

MANAGEMENT OF CMV INFECTION WITH MARIBAVIR IN PATIENTS TREATED WITH CAR-T THERAPY

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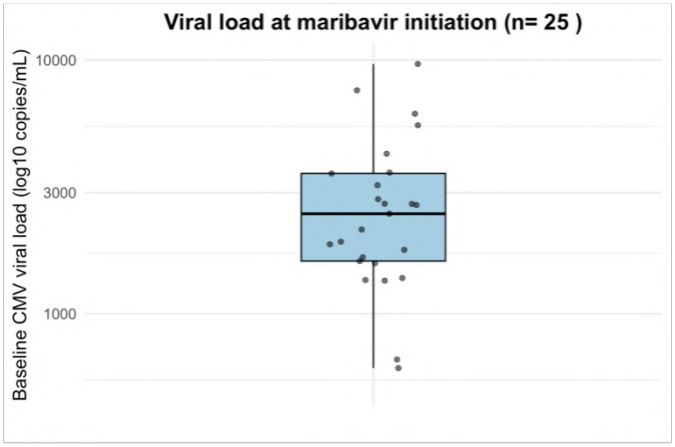
Background: Clinically significant cytomegalovirus (CMV) reactivation in patients undergoing CAR-T therapy represents a therapeutic challenge due to the combined toxicities of both the cellular product and conventional antivirals. Our objective was to evaluate the effectiveness and toxicity of maribavir in this patient population.

Methods: We conducted a single-center retrospective study including patients treated with CAR-T therapy who developed CMV reactivation and received pre-emptive maribavir between September 2020 and September 2025. CMV viral load was monitored twice weekly during the first month after infusion. Maribavir was initiated in cases with DNAemia ≥1,500 copies/mL (measured in plasma by qPCR) and a viral doubling time ≤2 days. Viral clearance was defined as at least one undetectable viral load measurement.

Results:

Table 1: **BASELINE CHARACTERISTICS (N=25) AND RESULTS**		
	n(%)	Median (IQR)
Sex, Female	15 (60)	
Age (years)		68 (64-73)
Underlying disease		

Diffuse Large B-cell Lymphoma		19 (76)
Multiple myeloma		6 (24)
CRS ≥ 2	11 (44)	
ICANS ≥ 2	8 (32)	
Tocilizumab use and cumulative dose (mg)	18 (72)	1200 (600 – 1,600)
Corticosteroid use and cumulative dose (mg)	23 (92)	180 (70-360)
Other CRS/ICANS treatments	14 (58)	
Days from CAR-T infusion to first CMV reactivation		16 (5-23)
Days from first reactivation to initiation of maribavir		7 (2-11)
Viral load at first post–CAR-T reactivation (UI/mL)		1,499 (1,045-2,477)
Viral load prior to maribavir initiation		2,477 (1,613-3,573)
Days on maribavir treatment		14 (11-18)
Days to viral clearance		7 (28)
Death	7 (28)	
Median follow-up (days)		220 (97-335)



We analyzed 25 patients, including 19 with B-cell non-Hodgkin lymphoma and 6 with multiple myeloma. The most frequently infused CAR-T product was axicabtagene ciloleucel (80%), and the median number of prior treatment lines was 2 (IQR, 1–2). Grade ≥2 CRS and ICANS occurred in 44% and 32% of patients, respectively, with frequent use of corticosteroids (92%), tocilizumab (72%), and other immunomodulators (58%), such as siltuximab and anakinra. *Table 1.*

Following CAR-T infusion, CMV reactivation occurred at a median of 16 days (IQR, 5–23), with a median viral load of 1,499 copies/mL (IQR, 1,045–2,477). Maribavir was used as first-line antiviral therapy in 84% of patients. *Figure 1* shows the distribution of CMV viral load at the time of maribavir initiation (median 2,477 copies/mL; IQR, 1,613–3,573). In 80% of cases, the indication for maribavir was grade 3–4 cytopenias, followed by toxicity (12%) and refractoriness (8%) to other antivirals.

Viral clearance was achieved in 100% of patients after a median of 8 days of treatment (IQR, 6–15). Median treatment duration was 14 days (IQR, 11–18). Only 12% of patients experienced a subsequent CMV reactivation after achieving initial viral clearance, and no cases of primary treatment failure with maribavir were observed. No maribavir-related toxicities were reported, and no CMV-related hospital admissions, CMV disease, or CMV-related deaths occurred.

Median progression-free survival (PFS) and overall survival (OS) were not reached due to the short follow-up period. A total of 7 patients (28%) died during follow-up, mainly due to progression of the underlying disease (16%), with additional deaths attributed to non-CMV infections (4%) and other causes (8%).

Conclusions: In this small cohort, maribavir demonstrated rapid and effective viral control with minimal toxicity. These findings suggest that maribavir may represent a safe and effective option for the management of CMV reactivation in severely immunocompromised CAR-T recipients, who frequently experience concomitant treatment-related toxicities.

Disclosure: Nothing to declare.

B128

NORMAL IGG DOES NOT EQUATE TO IMMUNE COMPETENCE AFTER HSCT IN PEDIATRIC SICKLE CELL DISEASE

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Background: Invasive pneumococcal disease (IPD) is a persistent threat after allogeneic hematopoietic stem cell transplantation (HSCT). Clinical practice commonly assumes that normal serum IgG levels reflect adequate humoral immunity, yet this has never been validated in pediatric sickle cell disease (SCD), a population characterized by functional asplenia, dysregulated antibody quality, and pre-transplant hypergammaglobulinemia. Emerging institutional observations and published reports suggest that normal IgG levels may mask profound vaccine-specific vulnerability. We evaluated the relationship between total serum IgG and pneumococcal serotype-specific protection after matched sibling donor HSCT in pediatric SCD.

Methods: We conducted a retrospective cohort study of 57 pediatric SCD HSCT recipients with available post-vaccination pneumococcal titers (2005–2024). Data included IgG levels at days 30–365, pneumococcal titers at ~1 year, vaccination type, immune reconstitution (CD3, CD4, CD8, CD19 counts), splenectomy status, and days between vaccination and titer assessment. Protective immunity was defined per standardized serotype threshold. Analyses included correlation testing, diagnostic performance of IgG thresholds, and penalized multivariable logistic regression incorporating clinical and immunologic covariates.

Results: Normal or elevated IgG levels did not reliably predict protective pneumococcal titers.

Primary objective:

- Correlation between IgG and percentage of protective serotypes was weak across all timepoints (r = 0.15–0.35; day-365 r ≈ 0.25).
- Diagnostic performance of IgG was poor:
    - At commonly used thresholds (400–600 mg/dL), the specificity was 0%, despite high sensitivity (0.96).
    - Even at 1000–1200 mg/dL, specificity remained limited (0.50–0.79), with no clinically actionable cut-point.
        - IgA and IgM levels were not associated with protection (|r| < 0.12).

Secondary immune predictors:

- Day-180 lymphocyte reconstitution was more informative than immunoglobulins:
    - CD19 mean: 798 vs. 623 cells/μL (protective vs. non-protective)
    - CD3: 1220 vs. 885 cells/μL
    - CD4: 496 vs. 373 cells/μL
    - CD8: 631 vs. 452 cells/μL

- Splenectomy was associated with 0% protective immunity (n=4) versus ~59% in non-splenectomized patients.

Multivariable modeling (N=54):

A penalized logistic model incorporating IgG, immune reconstitution, timing of titer assessment, vaccine type, splenectomy, and genotype achieved AUC = 0.76, outperforming IgG alone (AUC = 0.63). Strongest predictors included:

- Splenectomy (OR ~0.33, reduced protection)
- IgG 365d (OR ~1.61)
- CD3 recovery (OR ~1.28)
- Days from vaccination to titer (OR ~1.44)

Conclusions: In pediatric SCD, normal total IgG levels do not equate to pneumococcal protection after HSCT. Vaccine-specific immunity correlates more strongly with cellular immune reconstitution and spleen function than with bulk immunoglobulin levels. Reliance on IgG as a surrogate marker results in substantial misclassification and may delay recognition of vulnerable patients. These findings support transitioning from IgG-based monitoring to routine serotype-specific antibody assessment and risk-adapted revaccination strategies, particularly for patients with poor lymphocyte recovery or splenectomy. Prospective multicenter evaluation is warranted to establish evidence-based guidelines for post-HSCT pneumococcal immunity in SCD.

Disclosure: Alexander Ngwube: Vertex Therapeutics (paid consultant one-time, ended November 2025) and Beam Therapeutics (paid consultant one-time, ended December 2025).

B129

PHYSICIAN SURVEY OF REAL-WORLD MARIBAVIR USE AND TREATMENT DECISION MAKING IN REFRACTORY CYTOMEGALOVIRUS INFECTION AFTER TRANSPLANTATION

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Background: Cytomegalovirus (CMV) infection increases morbidity and mortality in transplant recipients. Refractory or resistant (RR) CMV infection, or intolerance to anti-CMV agents, complicates disease management. Guidelines and protocols for treatment vary across countries and institutions and can be difficult to apply in real-world practice. The anti-

CMV agent maribavir has shown higher clearance rates and lower incidence of myelosuppression compared with ganciclovir/valganciclovir in transplant recipients with RR CMV infection in a randomized clinical trial (NCT02931539). The ARISE study aims to describe the real-world use, effectiveness and safety of maribavir in transplant recipients with RR CMV infection, and to explore factors influencing CMV management decisions, including potential gaps between guidelines and clinical practice.

Methods: ARISE is a multinational, non-interventional, retrospective cohort study across Europe that includes a cross-sectional survey of physicians from 43 participating sites. The survey was issued during the study conduct and the database was extracted in September 2025. Data were validated for consistencies through edit checks and queries. Descriptive statistics were used for analysis. Statistical analyses were performed using SAS Enterprise Guide 8.2 and SAS 9.4 for Windows.

Results: Thirty-nine physicians from 10 European countries participated in the survey. Most specialized in hematology or nephrology (both n=13, 33.3%), followed by infectious disease (n=8, 20.5%); median (Q1–Q3) experience in management of CMV infection was 15.0 (10.0–20.0) years. Most physicians followed international guidelines (n=30, 76.9%), with 15 (38.5%) and 14 (35.9%) following hospital protocols and/or national guidelines, respectively. Half of physicians (n=20, 51.3%) did not perceive a gap between the guideline/literature definition of refractory patients and clinical practice, whilst 8 (20.5%) did, and 11 (28.2%) were unsure. The availability of new treatment options was confirmed to influence the treatment approach to refractory CMV in terms of switching before 2 weeks if current treatment seemed ineffective (n=28, 71.8%), using regimens with lower toxicity risk (n=28, 71.8%), and/or switching at initial signs of toxicity (n=22, 56.4%). Characteristics considered most important for guiding treatment management were dynamic change in CMV viral load (n=12, 31.6%), followed by absolute viral load level, and donor/receiver CMV serostatus (both n=6, 15.8%). Most physicians (n=27, 71.1%) reported factors/barriers to decision making, most frequently patient-specific clinical factors not related to CMV (n=21, 77.8%). Regarding maribavir treatment, the most common reason for discontinuing maribavir was undetectable or sub-quantifiable viral load (n=26, 66.7%; Table). The most common reason to prolong maribavir treatment after clearance was to avoid recurrent CMV infection (n=25, 65.8%; Table), and the most common reason to prolong maribavir treatment past 8 weeks was persistent viral load (n=28, 73.7%; Table).

Question	Answer	Physicians (N=39)[a]
Main clinical reasons to discontinue treatment with maribavir in refractory patients	CMV viral load that is undetectable or under the lower limit of quantification	26 (66.7%)
	Detection of resistance	6 (15.4%)
	Achieved CMV-viremia control (sustained	5 (12.8%)

with or without resistance	reduction of CMV viral load)	
	Adverse events and treatment toxicities	2 (5.1%)
Main clinical reasons to prolong treatment with maribavir after confirmation of CMV viremia clearance	Avoid recurrent CMV infection	25 (65.8%)
	CMV-specific immune reconstitution status	6 (15.8%)
	None	6 (15.8%)
	Other	1 (2.6%)
	Missing	1
Main clinical reasons to prolong treatment with maribavir in refractory patients with or without resistance beyond 8 weeks	Persistent CMV viral load (clearance not achieved)	28 (73.7%)
	Maintain CMV-viremia control	14 (36.8%)
	Avoid recurrent CMV infection	13 (34.2%)
	CMV-specific immune reconstitution status	3 (7.9%)
	None	1 (2.6%)
	Other	2 (5.3%)
	Missing	1

[a]Physicians were able to select more than one answer.
CMV, cytomegalovirus

Conclusions: Survey findings indicate variability and perceived gaps between guidelines and clinical practice in the management of RR CMV infection following transplantation. Following the introduction of new treatment options, physicians reported a tendency to switch earlier to maribavir if the current agent was ineffective or to avoid toxicity. These results highlight the need for treatment options that achieve CMV clearance with fewer treatment-related toxicities, and for practical guidance on optimizing maribavir use in real-world practice.

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B130

COMPARATIVE ANALYSIS OF CYTOMEGALOVIRUS REACTIVATION AFTER HAPLOIDENTICAL VS MATCHED SIBLING DONOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Cytomegalovirus (CMV) reactivation remains one of the most frequent infectious complications after allogeneic hematopoietic stem cell transplantation (HSCT), particularly in settings of delayed immune recovery. The increasing use of haploidentical donors with post-transplant cyclophosphamide (PTCy) has broadened access to HSCT but is commonly associated with slower myeloid and platelet engraftment, impaired early T-cell reconstitution, and consequently higher rates of viral reactivation. Comparatively, matched sibling donor (MSD) transplants typically show faster engraftment and more robust immune recovery, potentially leading to lower CMV-related morbidity. This study compares the incidence, timing, and outcomes of CMV reactivation after haploidentical versus matched sibling donor HSCT, aiming to clarify clinically relevant differences that may guide surveillance and preemptive management.

Methods: We conducted a retrospective, comparative study including all allogeneic HSCTs performed at a national referral center in Mexico between January 2018 and December 2024. Conditioning regimens included myeloablative (BuCy2, BuFlu) and reduced-intensity

approaches (BuCy, MelFlu, CYATG). GVHD prophylaxis consisted of cyclosporine plus methotrexate for MSD transplants, and post-transplant cyclophosphamide on days +3/+4 followed by cyclosporine and mycophenolate for haploidentical HSCT. Peripheral blood stem cells were used as the sole graft source. CMV surveillance followed a preemptive strategy with weekly qPCR monitoring, and reactivation was defined as >1,000 copies/mL. No patient received letermovir prophylaxis, as it only became available in Mexico after 2025. Outcomes analyzed included overall survival (OS), disease-free survival (DFS), and non-relapse mortality (NRM). Statistical analyses were performed using SPSS v25.

Results: A total of 182 transplanted patients were analyzed. The median age was 34 years (range, 17–67), and 58% were male. Acute lymphoblastic leukemia was the most frequent indication for transplantation, followed by acute myeloid leukemia in both donor groups. Overall, 106 patients (58%) received a matched related donor transplant and 76 patients (42%) underwent haploidentical transplantation.
CMV reactivation was significantly more frequent in the haploidentical donor group compared with the matched related donor group (53% vs. 19%, p <0.01). The median time to CMV reactivation was similar between groups (41 vs. 40 days, respectively). Most cases were detected as asymptomatic viremia, while a minority developed CMV-related end-organ disease, mainly pneumonia and gastrointestinal involvement. Peak CMV viral load varied widely, with no significant differences in median viral load or duration of antiviral therapy between groups.
Five-year overall survival was comparable between donor types (59% in matched related vs. 53% in haploidentical transplants). Relapse of the underlying hematologic malignancy was the leading cause of death (49%), followed by infections (23%). In contrast, five-year overall survival was significantly lower in patients with CMV reactivation compared with those without reactivation (50% vs. 60%, p = 0.01).

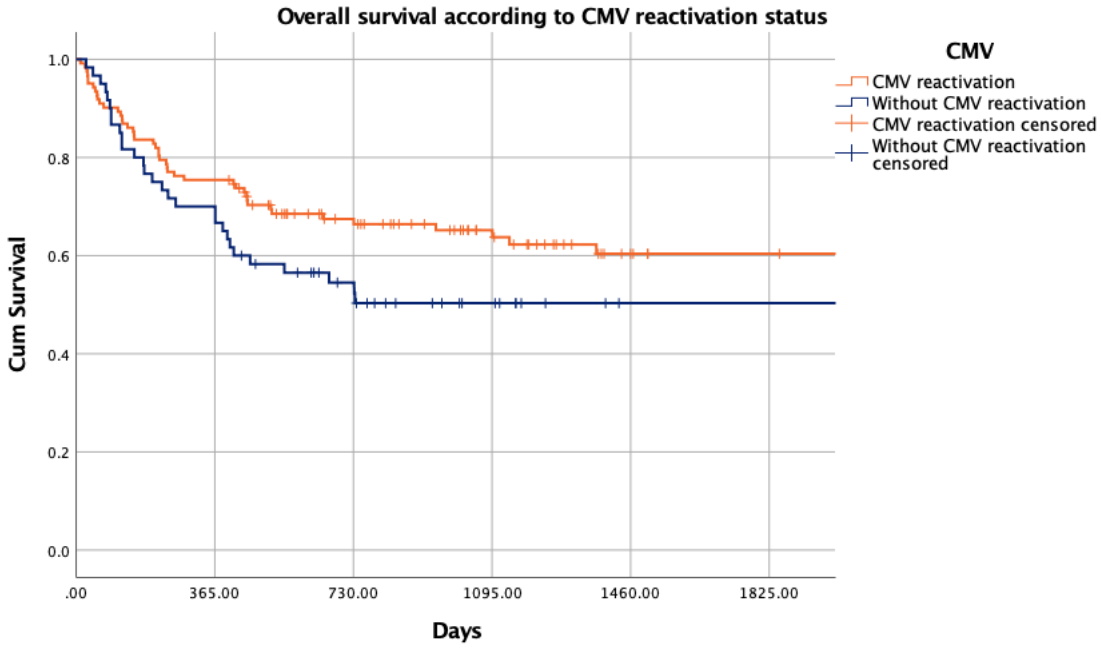

Table 1. Baseline epidemiological and CMV-related characteristics of the population			
Variable	Matched related donor	Haploidentical donor	Significance (p)
	106 (58%)	76 (42%)	
Age (years)	34 (17-64)	32 (17-66)	>0.05
Sex (male)	61 (58%)	46 (60%)	>0.05
Diagnosis			
ALL	54 (50%)	45 (58%)	>0.05
AML	21 (20%)	13 (17%)	>0.05
MDS	12 (11%)	2 (3%)	0.001
AA	8 (8%)	0	NA
CML	8 (8%)	14 (19%)	0.001
Myelofibrosis	3 (3%)	2 (3%)	>0.05
$CD34^+$ cell dose ($\times 10^6$/kg)	5.6 (2.0-17.5)	6.1(2.1-15.4)	>0.05
Day of engraftment	12 (9-29)	16 (13-25)	0.003
CMV reactivation	20 (19%)	40 (53%)	0.001
Peak CMV viral load (copies/mL)	9943 (1210-183,000)	8239 (1406-419,000)	>0.05
Day of CMV Diagnosis	41 (11-124)	40 (25-307)	>0.05
Time to CMV remission (days)	20 (5-43)	23 (7-44)	>0.05

Conclusions: CMV reactivation was significantly more frequent after haploidentical transplantation, although the timing of reactivation and CMV-related clinical presentation were similar across donor types. Overall survival did not differ according to donor type; however, CMV reactivation was associated with inferior long-term survival. These findings suggest that CMV reactivation represents a clinically relevant event influencing outcomes after allogeneic hematopoietic stem cell transplantation, beyond donor type alone

Disclosure: Nothing to declare

B131

HOSPITAL EXEMPTION USE OF VIRUS-SPECIFIC T-LYMPHOCYTES IN CHILDREN: EARLY EXPERIENCE WITHIN THE ALLOVISTA FRAMEWORK

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Background: Adoptive transfer of virus-specific T lymphocytes (VST) is an emerging strategy for refractory viral infections in immunocompromised individuals and is being prospectively evaluated in the ALLOVISTA trial. Here we describe our experience with hospital-exemption advanced therapy medicinal product (ATMP-HE) VST in six pediatric transplant recipients.

Methods: Six children and adolescents (median age 4.5 years, range 2.5–17.5; HLH n=2, SAA, GCD, HL, AML n=1 each) treated in two Polish centers received VST for refractory viremia: adenovirus (ADV) in three cases, EBV-driven disease (EBV/PTLD or HL relapse with EBV reactivation) in three, including one patient with concomitant CMV/EBV/ADV infection. All had failed conventional antiviral and/or immunochemotherapy (cidofovir, rituximab, chemotherapy). VST_RCKiK were generated from HSCT or related donors using automated CliniMACS Prodigy Cytokine Capture System (IFN-γ CCS, Miltenyi Biotec) following antigenic stimulation with viral peptide pools and released as ATMP-HE according to the ALLOVISTA protocol. A single intravenous infusion of 1.01×10^5–1.85×10^6 VST (median 2.5×10^5) was administered. Virological response was assessed by quantitative PCR up to 4 weeks post-infusion, acute GVHD (aGVHD) and survival were recorded.

Results: Virological outcomes were evaluable in five patients. A virological response defined as ≥1-log viral load reduction was achived in four patients (80%). Complete viral clearance by week 4 occurred in two cases (33% of all, 40% of evaluable; one EBV and one ADV). Two additional patients had marked but incomplete or transient viral load reductions, one patient showed minimal virological change. Despite biological activity, four children died: from progressive EBV disease (n=1), ADV infection (n=1), relapse of HL (n=1) and multi-organ failure with invasive fungal disease in a child with multi-viral infection (n=1). Two patients with complete virological responses are alive with sustained remission of viremia at last follow-up. No new-onset or worsening aGVHD was documented after VST infusion.

Conclusions: VST administered as an ATMP-HE are feasible in routine clinical practice and demonstrate rapid antiviral activity in heavily pretreated pediatric patients. However, advanced viral disease and competing complications limit overall survival, underscoring the need for earlier intervention and advocate for treatment within the ongoing ALLOVISTA trial.

Clinical Trial Registry: EUCT number: 2024-517696-21-01

Disclosure: Nothing to declare.

B132

IMPACT OF LETERMOVIR PROPHYLAXIS ON CYTOMEGALOVIRUS EVENTS AND RELAPSE AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR AML AND MDS

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Background: Early cytomegalovirus reactivation (ECMVR) has been inversely associated with relapse after allogeneic hematopoietic stem cell transplantation (allo-HSCT), but whether this association persists in the letermovir era remains uncertain.

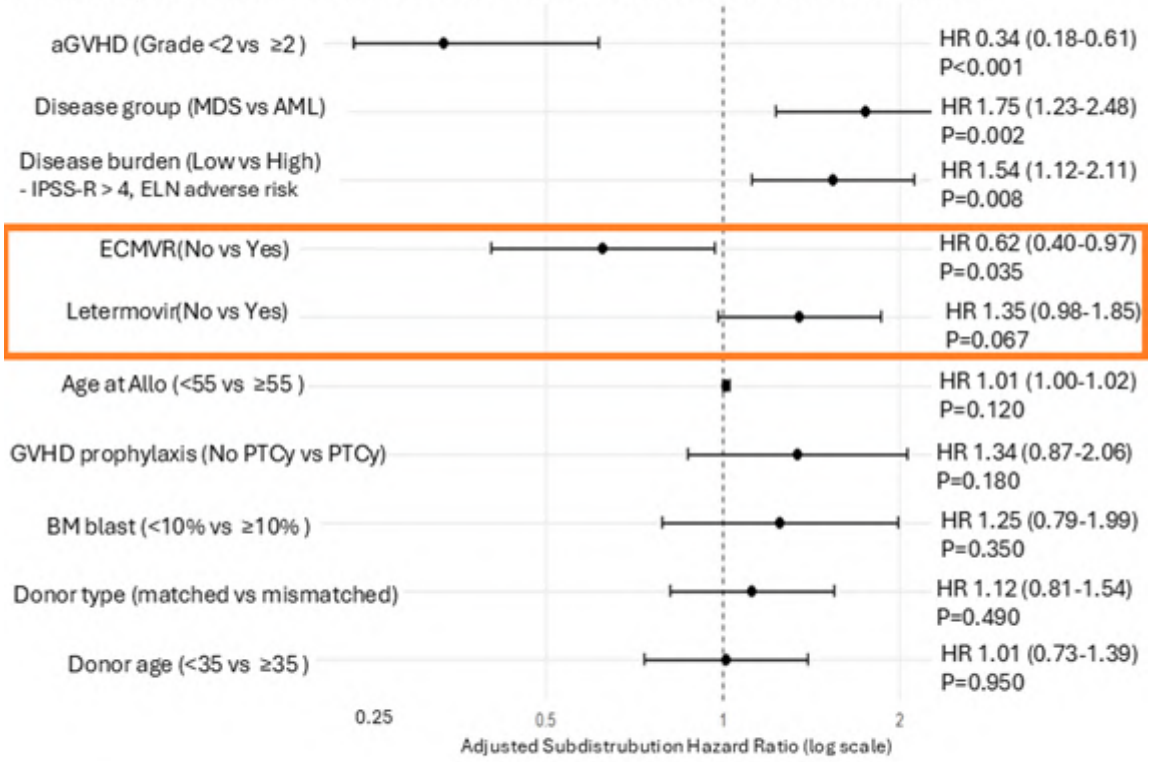
Methods: We conducted a single-center retrospective study of adult patients with acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) who underwent first allo-HSCT with uniform fludarabine/busulfan-based conditioning between January 2016 and September 2024. Letermovir prophylaxis from day +7 to +100 was administered to CMV-seropositive recipients with undetectable CMV DNA at transplantation (letermovir group, LG), while patients transplanted before its introduction comprised the non-letermovir group (NLG). CMV reactivation and disease were prospectively monitored using quantitative PCR or antigenemia assays. ECMVR was defined as CMV reactivation before day +100. A day +100 landmark analysis was performed among patients alive and relapse-free at day +100. Competing-risk regression and multivariable Cox models were used to assess relapse, non-relapse mortality (NRM), and overall survival (OS), adjusting for clinically relevant covariates.

Results: A total of 397 patients were included, of whom 171 (43.1%) received letermovir prophylaxis. The median follow-up was 49.0 months (95% CI, 44.2–56.3). Baseline characteristics were largely balanced, although the LG more frequently received contemporary transplant approaches, including haploidentical donors and PTCy. For the overall cohort, 3-year and 5-year OS were 56.8% and 53.4%, respectively. One-year NRM was 16.0% (95% CI, 12.5–19.7), and 1-year cumulative incidence of relapse was 27.8% (95% CI, 23.5–32.3).
Letermovir prophylaxis significantly reduced CMV events. The cumulative incidence of CMV reactivation by day +100 was markedly lower in the LG compared with the NLG (6.4% vs. 40.0%, P<0.001), and CMV disease was also reduced (1.16% vs. 8.44% at day +100, P=0.013).
Despite comparable 2-year OS between the LG and NLG (56.2% vs. 57.1%, P=0.99), the 2-year cumulative incidence of relapse was higher in the LG (40.0% vs. 29.7%, P=0.034), whereas NRM did not differ significantly. The 100-day cumulative incidence of grade ≥2 acute GVHD was significantly lower in the LG (19.4% vs. 28.3%, P=0.028).
The inverse association between ECMVR and relapse was evident in the NLG, but not in the LG, in which ECMVR events were markedly reduced, limiting the ability to detect an ECMVR–

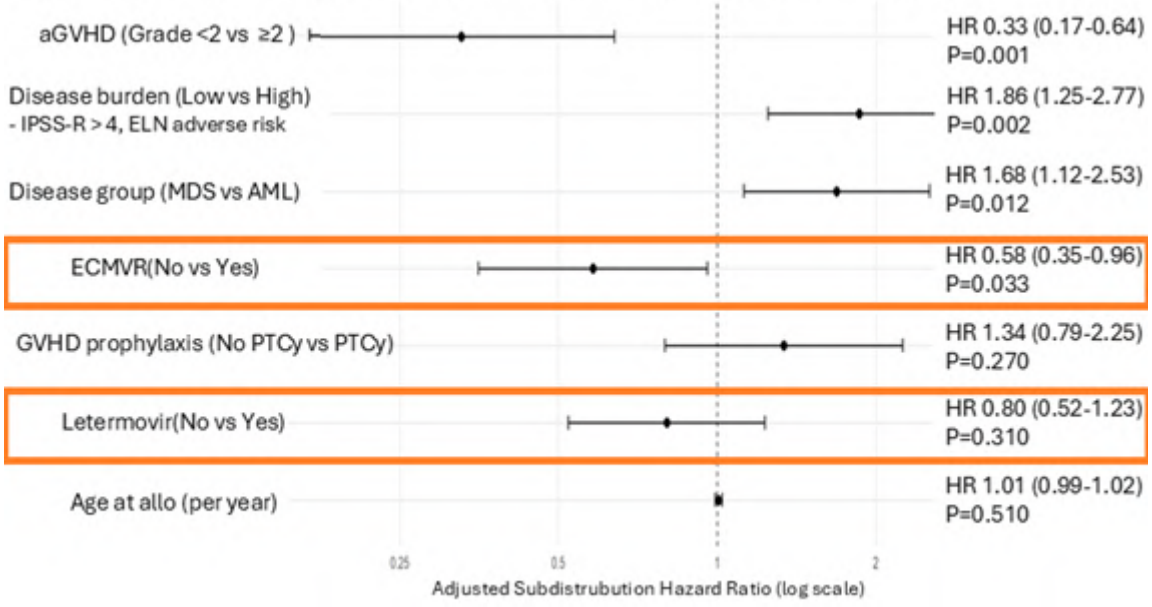
relapse association. In univariable analyses, letermovir prophylaxis appeared to be associated with a higher relapse incidence; however, in multivariable models adjusting for ECMVR, GVHD, disease risk, and transplantation-related factors, letermovir prophylaxis was no longer independently associated with relapse. In contrast, ECMVR remained independently associated with a reduced risk of relapse (Figure).

Figure

a) Fine-Gray univariate cox analysis of association between relapse and clinical characteristics



b) Fine-Gray multivariate cox analysis of association between relapse and clinical characteristics



Conclusions: Letermovir prophylaxis fundamentally reshapes the post-transplant CMV landscape, uncoupling ECMVR from routine clinical observation. Although letermovir use was associated with higher unadjusted relapse incidence, this association disappeared after accounting for ECMVR and transplant-related covariates, while ECMVR itself remained independently protective against relapse. These data suggest that letermovir does not promote relapse but rather may obscure a CMV-associated immune signal linked to graft-versus-leukemia effects.

Disclosure: Nothing to declare.

B133

ADDITION OF ANTITHYMOCYTE GLOBULIN TO CYCLOSPORIN AND MYCOPHENOLATE IN UNMANIPULATED HAPLO-TRANSPLANT WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE IN CHILDREN AND TEENAGERS. RESULTS OF A SERIE OF 40 PATIENTS

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Background: The addition of anti-thymocyte globulin (ATG) to classic platform of cyclosporine, mycophenolate and post-transplant cyclophosphamide (PTCy) in the setting of haplo transplantation has shown good results in adults, however, it has not been well described in children. We present here the long-term results with this combination in a pediatric population.

Methods: From March 2017 to May 2025, forty patients between 1 and 15 years underwent Haplo-PTCy. Written informed consent from parents or legal guardians was obtained previous to the procedure and before the data collection. Twenty-four had acute lymphoblastic leukemia and sixteen had acute myeloid leukemia. Cellular source was peripheral blood stem cell (PBSC) in older than 10 years old and/or patients with ABO group incompatibility while it was bone marrow (BM) in the others. Patients received melphalan 140 mg/m2 day −7, fludarabine 160 mg/m2 in 4 days and TBI 200 cGy day -2, children aged 3 years or less received thiotepa instead of TBI. The GVHD prophylaxis consisted of PTCy 50 mg/kg days +3+4, cyclosporine days 0 to +180, mycophenolate days +1 to +60 and ATG 2 mg/kg/day on days -8-7. Since June 2023, methotrexate at 7.5 mg/m2/d days +1+5+8+11 was added. Regarding the donor, it was a parent in 85% of the cases and a sibling in 15%. The cellular source was BM in 18 and PBSC in 22.

Results: Neutrophil recovery day +30 was 100%, median 15 days (range 11-26), and 97% for platelets, median 19 days (range 13-27). Chimerism at D+100 was available in 30/34 patients alive. It was performed in 13 patients by cytogenetics and in 14 by short tandem repeat; all had 100% donor hematopoiesis. In the remaining, a blood red cell group change

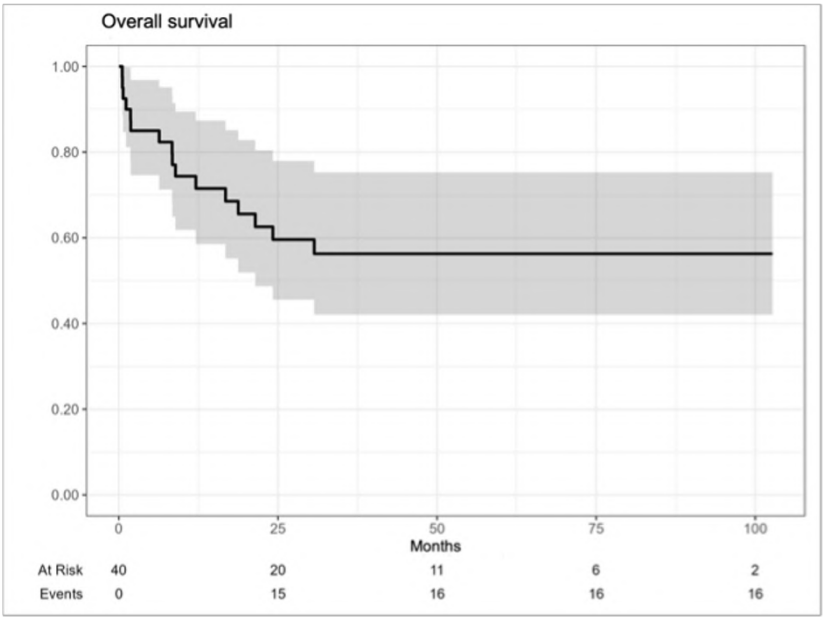
was documented. Infections are described in table 1; the pathogens were bacteria (62%), virus (41%), fungus (7%). Infection was the cause of death in 4 patients (10%).

Cause	Number (%)
Bacteria	25 (62%)
Bacteremia	20 (50%)
Urinary tract infection	2 (5%)
Clostridioides	3 (7%)
Fungus	3 (7%)
Pulmonary aspergillosis	2 (5%)
Candidemia	1 (2%)
Virus	17 (41%)
BK virus	1 (2%)
Adenovirus	2 (5%)
Respiratory syncytial virus	2 (5%)
Human metapneumovirus	3 (7%)
Parainfluenza	4 (10%)
Rhinovirus	4 (10%)
Epstein Barr virus associated post trasplant lymphoproliferative disease	1 (2%)
Citomegalovirus reactivation	24 (60%)
Citomegalovirus colitis	3 (7%)
Related infection deaths	4 (10%)

1. E. coli - Stenotrophomonas maltophilia: Multiple organ dysfunction syndrome
2. Serratia marcescens and rhinovirus: Pulmonary sepsis
3. Klebsiella pneumoniae group, KPC NDM Ceftazidime avibactam resistant sepsis. Rhinovirus/Enterovirus, parainfluenza virus pneumonia. Proven pulmonary aspergillosis

4.	Urinary tract infection/sepsis resistant S. aureus. Adenovirus, rhinovirus, CMV pneumonia

The median follow-up for the whole group was 34 months (range 1-103) and for surviving patients was 48 months (range 1-103). The incidence of aGVHD II-IV and III-IV for the whole group was 60% and 12%; and the cumulative incidence of moderate-severe cGVHD at 2 years was 27%. The incidence of relapses was 25% and the mortality related to transplant was 17%. The overall and event-free survival (Kaplan-Meier) at 36 months was 56% and 54% respectively (Figure 1).



Conclusions: The addition of ATG to the standard PTCy platform in haplo transplant in a pediatric population could decrease the incidence of severe aGVHD, however, it was not observed a protective effect against the less severe cases. The relapse rate was not higher than expected, but the incidence of viral infections is a concern. It is necessary to explore new alternatives.

Disclosure: No conflicts of interest.

B134

OUTCOMES OF HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS REQUIRING INTENSIVE CARE: A RETROSPECTIVE COHORT STUDY

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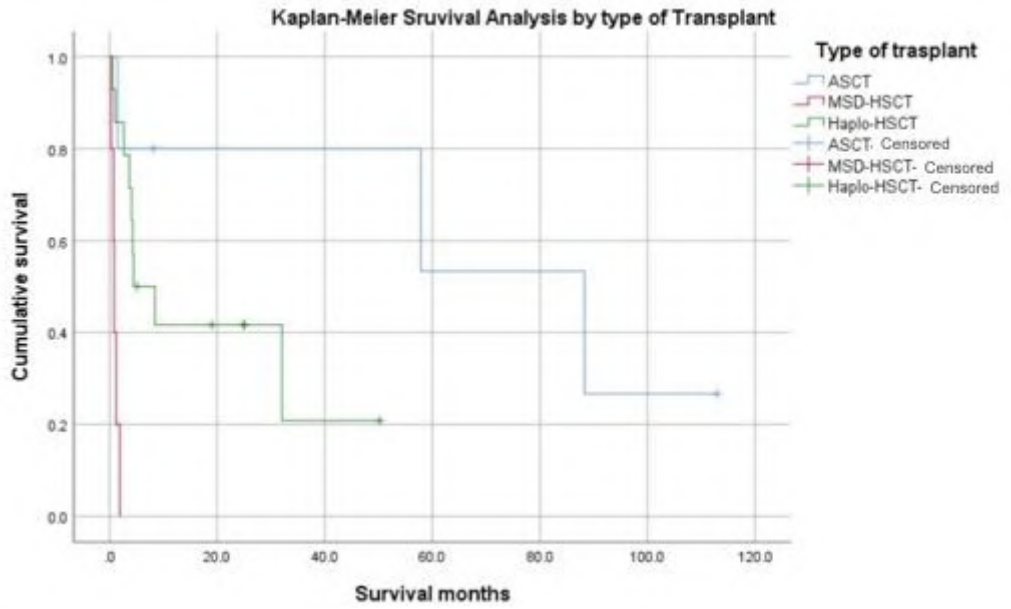
Background: Hematopoietic stem cell transplantation (HSCT) is a potentially curative therapy for a wide range of hematologic malignancies and non-malignant disorders. Despite improvements in supportive care, HSCT is associated with profound but transient immunosuppression, which predisposes patients to severe infections and other life-threatening complications. Admission to the intensive care unit (ICU) after HSCT is uncommon but represents a critical clinical event associated with high morbidity and mortality. Data describing the clinical characteristics and outcomes of HSCT recipients requiring ICU admission in Latin American transplant centers are limited.

Methods: We conducted a retrospective observational cohort study including all hematopoietic stem cell transplant (HSCT) recipients admitted to the intensive care unit (ICU) at the Instituto Nacional de Cancerología, Mexico, between January 2009 and December 2025. Demographic data, underlying diagnosis, transplant characteristics, conditioning intensity, graft-versus-host disease, timing and indication for ICU admission, infectious complications, organ support requirements, and outcomes were collected from electronic medical records. During the study period, 1,178 HSCTs were performed, including 600 autologous and 578 allogeneic transplants. Conditioning regimens were classified as myeloablative or reduced-intensity, and transplant modality was categorized as ASCT, MRD-HSCT, or Haplo-HSCT.

Results: Twenty-four patients required ICU admission, representing a small proportion of the total transplanted population. Thirteen patients (54%) were male, and the median age was 33.5 years. Acute leukemia was the most frequent underlying diagnosis, present in 16 patients (67%). Other indications for HSCT included Hodgkin lymphoma, multiple myeloma, and myelodysplastic syndrome (each 8%), as well as non-Hodgkin lymphoma and T-cell lymphoma (each 4%).
Regarding transplant modality, five patients (21%) underwent ASCT, five (21%) MRD-HSCT, and fourteen (58%) Haplo-HSCT. MAC was used in 22 patients (92%), while RIC was administered in two patients (8%). Acute GVHD (aGVHD) occurred in 11 patients (46%), with severe disease (grade III–IV) in seven cases. Gastrointestinal involvement was the most common manifestation. Thirteen patients (54%) were admitted to the ICU within the first 100 days after transplantation.
All patients had suspected infection at the time of ICU admission. The main indications for ICU admission were respiratory failure (42%), multiorgan failure (29%), septic shock (21%), and sepsis or metabolic disturbances (8%). Seventeen patients (71%) required invasive mechanical ventilation, and 19 patients (79%) required vasopressor support.
The most frequent infectious syndromes were pneumonia (62%) and bloodstream infection

(42%). Invasive fungal infection and cytomegalovirus infection were each documented in 29% of patients, while colitis occurred in 25%. Overall ICU mortality was 70%. Bivariate analysis comparing survivors and non-survivors is presented in Table 1. Survival analysis according to transplant modality (ASCT, MRD-HSCT, and Haplo-HSCT) showed no statistically significant differences (Figure 1).

Variable	Alive (n = 7) n (%)	Dead (n = 17) n (%)	*p* value
Severe pre-transplant infection	2 (28.6)	9 (52.9)	0.386
Conditioning intensity (MAC)	5 (71.4)	17 (100)	0.076
Transplant type			0.461
ASCT	2 (28.6)	3 (17.6)	
MRD-HSCT	0 (0)	5 (29.4)	
Haplo-HSCT	5 (71.4)	9 (52.9)	
ICU admission < 100 days post-HSCT	2 (28.6)	11 (64.7)	0.182
SOFA score ≥ 8 at ICU admission	4 (57.0)	10 (59.0)	1.000
Acute GVHD (any grade)	3 (60.0)	8 (57.0)	1.000
Acute GVHD grade III–IV	5 (83.3)	4 (30.8)	1.000
Mechanical ventilation	3 (42.9)	4 (23.5)	0.374
Vasopressor support	2 (28.6)	3 (17.6)	0.608
Pneumonia	5 (71.4)	10 (58.8)	0.669
Invasive fungal infection	2 (28.6)	5 (29.4)	1.000
Bloodstream infection	3 (42.9)	7 (41.2)	1.000
CMV infection	0 (0)	7 (41.2)	0.065



Conclusions: Admission to the ICU after hematopoietic stem cell transplantation (HSCT) is a rare but high-risk event. Infections were the leading cause of admission, and mortality remained extremely high. Recipients of haplo HSCT and patients transplanted for acute leukemia predominated. These findings underscore the need to improve infection prevention, early detection of clinical deterioration, and optimize intensive care strategies to improve outcomes in this vulnerable population within contemporary transplant programs worldwide.

Disclosure: The authors have no conflicts of interest to declare.

B135

LONG TERM COVID-19 VACCINE EFFECTIVENESS AND ANTY-SARS-COV-2 IGG DYNAMICS IN CHILDREN AND YOUNG ADULTS AFTER ALLOGENEIC HSCT

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Background: Children and young adults after allogeneic haematopoietic stem cell transplantation (allo-HSCT) are at increased risk of severe COVID-19, but long-term data on vaccine effectiveness in this population are limited. We aimed to assess clinical effectiveness and 36-month humoral responses to COVID-19 vaccination, and to examine their relationship with immune reconstitution in allo-HSCT recipients.

Methods: We conducted a single-centre, retrospective observational study including 425 allo-HSCT recipients below the age of 30 who were monitored throughout the COVID-19 pandemic. COVID-19 vaccination status (CovVac+ vs CovVac−), anti–SARS-CoV-2 IgG concentrations (CovAb, BAU/mL), and SARS-CoV-2 infections (CovInf+ vs CovInf−) were recorded over 36 months. Primary endpoints were the incidence of confirmed SARS-CoV-2 infection and CovAb geometric mean concentrations (GMCs) at 6, 12, 18, 24, 30 and 36 months. Secondary endpoints included COVID-19 severity, complications and associations between CovAb levels and immune reconstitution.

Results: Overall, 187/425 patients (44%) were vaccinated (CovVac+), and 202/425 (48%) had at least one confirmed SARS-CoV-2 infection. Infection occurred in 35/187 CovVac+ versus 120/238 CovVac− patients (18.7% vs. 50.4%, p = 0.03). Vaccination was associated with a markedly lower risk of documented SARS-CoV-2 infection (OR 0.23, 95% CI 0.14–0.35). Six patients (1.4%) died from COVID-19, and four developed serious non-fatal complications. Across all timepoints, CovVac+ patients demonstrated substantially higher CovAb GMCs than CovVac− patients. A three-dose primary series yielded significantly higher GMCs at 18, 24, 30 and 36 months compared with one/two doses. In vaccinated patients, higher long-term CovAb levels were associated with older age at vaccination, a longer interval since allo-HSCT, higher baseline CD4+ and B-cell counts, and absence of regular immunoglobulin replacement therapy (in 6,24,30,36 months p=0.01, p=0.05, p=0.02, p=0.004 respectively; test Wilcoxon Rank Sum).

Conclusions: COVID-19 vaccination, particularly a three-dose primary schedule, is associated with a lower incidence of SARS-CoV-2 infection and with durable anti–SARS-CoV-2 IgG responses over 36 months. These findings support the concept of risk-adapted prevention strategies in allo-HSCT recipients.

Disclosure: Nothing to declare.

B136

RISK OF INFECTIONS AFTER CAR-T CELLS IS HIGH AND DIFFICULT-TO-PREDICT

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Background: Although CAR-T cell has emerged as a potent treatment for relapsed or refractory (R/R) haematological malignancies, infection is increasingly recognized as a significant cause of morbidity and mortality after the procedure.

Methods: In this retrospective multicenter study we aim to describe the characteristics of infections in patients with R/R DLBCL and MM after antiCD19 or antiBCMA CAR-T cells. We also aim to analyze possible risk factors associated with infections.

Results: We included 94 patients who received CAR-T cells from august-22 to September-25 in two CAR-T centres of Spain (H. Marqués de Valdecilla and H. Donostia). Median age at infusion was 66-yo (range 36-81) and 48% were females. Sixty-two patients had lymphomas (66%) [56 DLBCL and 6 other B cell lymphomas] and 32 MM (34%). Prior autologous HSCT was performed in 31 (33%). Median number of lines prior CAR-T was 2 (range 1-5). Eleven patients (12%) were in complete remission (CR) at infusion, 42 (45%) in partial response (PR) an 41 (43%) were in (R/R).
Fifty-three patients (56%) developed 164 episodes of infections after CAR-T. Median number of episodes per patient was 2 (0-11) for lymphoma, and 5 (0-14) for MM patients. Majority of patients had respiratory tract infections [92 episodes (56%)], urine [21 (13%)], bloodstream [19(12%)] or GI infections [17(10%].
Microbiological documentation was detected in 114 (69%) of the episodes [64 (39%) bacterial, 44 (29%) viral, 5 (3%) fungal and 1 (1%) parasite]. In lymphoma patients, bacterial was the main cause (46 episodes [53%]) and unknown origin in MM (33 [43%]). Taken isolations into account, viral origin was the main cause in the MM (22 [29%]). Most common bacterial isolations were: *E. coli* 12 (18%), *K. pneumoniae* 10 (15%) and *P. aeruginosa* 8 (12%). In the viral group, *Rhinovirus* 10 (22%), *COVID-19* 9 (20%) and *Influenza A* 7(15%). Fungi isolations mainly were oral *C. glabratra* (2 patients). Cumulative incidence of bacterial, viral and fungal infections are shown in TABLE 1.
With a median follow up of 12 months (IQR 2-21) 1-year non-relapsed-mortality (NRM) in the lymphoma and MM group was: 10% (CI95% 4-19) and 3% (CI95% 1-17). At last follow-up 21 patients (22%) died: 12 due to disease (13% of all patients) and 9 due to NRM. Among those nine, infections were attributed as main cause of NRM with 6 patients (7%) and 3 (3%) due to other causes. The 100-day infection-related mortality (IRM) was 7% (95% CI 3–15%), 8% for lymphomas and 3% for myelomas. A total of 6 patients died due to infections, causes of death were: septic shock in 4 patients (3 with gram –negative pneumonia and 1 with polymicrobial bloodstream infection from abdominal focus) and global respiratory insufficiency in 2 patients. Univariate analysis of potential risk factors did not show statistically significant differences (FIGURE 1).

TABLE 1	TOTAL			LYMPHOMA			MYELOMA		
	D30 % (CI95%)	D30-90 % (CI95%)	D>90 % (CI95%)	D30 % (CI95%)	D30-90 % (CI95%)	D>90 % (CI95%)	D30 % (CI95%)	D30-90 % (CI95%)	D>9 % (CI9
CI bacterial infections	22 (14-31)	28 (20-38)	32 (23-43)	26 (16-39)	30 (21-44)	32 (22-46)	13 (5-30)	21 (10-42)	36 (64)

CI fungal infections	1 (0.2-8)	4 (1-12)	9 (4-19)	2 (0.3-12)	2 (0.3-12)	6 (2-18)	4 (1-25)	9 (2-33)	16 (
CI viral infections	7 (4-15)	21 (14-32)	33 (24-45)	6 (2-16)	15 (8-27)	25 (15-38)	9 (3-26)	36 (20-58)	57 (80)
CI global infections	27 (18-36)	44 (34-55)	61 (50-72)	29 (19-42)	39 (28-52)	55 (42-68)	27 (14-47)	50 (49-78)	86 (98)

FIGURE 1. Univariate analysis of potential risk factors for infections

Variable	HR (95% CI)	p-value
Age <65 vs >65	1.5 (0.9-2.7)	0.1
Myeloma vs lymphoma	1.6 (0.9-2.9)	0.1
Response prior to CART	0.8 (0.5-11.1)	0.1
Prior lines	0.9 (0.6-1.2)	0.4
Basal EASIX	0.8 (0.4-1.7)	0.7
Basal mEASIX	1 (0.7-1.5)	0.7
D1 EASIX	1.5 (0.7-3)	0.3
D1 mEASIX	1.2 (0.6-2.3)	0.6
Basal Hipogamma <400	0.6 (0.3-1.3)	0.2
Neutropenia <500 D7	1.6 (0.8-3.1)	0.2
Lymphocyte count D10	1 (0.9-1.1)	0.8
Grade 3-4 CRS	0.8 (0.2-3.2)	0.8
Grade 3-4 ICANS	1.1 (0.5-2.3)	0.8

Values are hazard ratio (HR) with 95% confidence interval (CI).
Abbreviations: CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; CAR-T, chimeric antigen receptor T-cell therapy.

Conclusions: In our study, infections were the most frequent cause of NRM, observing an infection-related mortality (IRM) of 7% (95% CI 3–15%). No significant risk factors or association with CAR-T toxicities (CRS/ICANS) were identified, suggesting a multifactorial and difficult-to-predict infection risk.

Disclosure: Nothing to declare.

B137

METAGENOMIC NEXT-GENERATION SEQUENCING AS A DIAGNOSTIC TOOL TO DETECT PATHOGENS IN IMMUNOCOMPROMISED PATIENTS WITH PULMONARY INFECTIONS - A SINGLE CENTER PROSPECTIVE STUDY

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Background: Immunocompromised patients with hematologic malignancies, particularly recipients of allogeneic hematopoietic stem cell transplantation (allo-HSCT), are at high risk for severe pulmonary infections that significantly contribute to morbidity and mortality. Broad-spectrum anti-infective therapy is frequently initiated early, but conventional standard-of-care (SOC) microbiological diagnostics from bronchoalveolar lavage (BAL) and blood often remain negative or inconclusive, especially under ongoing prophylactic or empiric treatment. Metagenomic next-generation sequencing (mNGS) has emerged as a culture-independent diagnostic approach that may increase pathogen detection and may help differentiate between inflammation or (clinically relevant) infection in this high-risk population. The aim of this single-centre prospective study is to evaluate the additional diagnostic yield and potential clinical impact of mNGS from BAL and blood on top of comprehensive SOC diagnostics in hematologic patients with suspected pulmonary infection, with a particular focus on those after cellular therapy such as allo-HSCT.

Methods: Adult patients with hematologic malignancies, with or without prior allo-HSCT, who underwent clinically indicated BAL for suspected pulmonary infection were prospectively enrolled. SOC diagnostics from BAL comprised microscopy, culture including fungi, galactomannan, *Pneumocystis jirovecii* PCR, respiratory virus multiplex PCR and targeted mycobacterial/bacterial PCRs as well as cytology and immunophenotyping of leukocytes. SOC blood diagnostics included blood cultures (including fungi), galactomannan, beta-D-glucan and basic laboratory parameters such as procalcitonin and interleukin-6. In parallel, mNGS (DISQVER, Noscendo) was performed on BAL and blood samples to detect DNA-based bacterial, fungal and viral pathogens. Clinically relevant pathogens were adjudicated by experienced clinicians integrating clinical, radiological and laboratory findings, with careful distinction between infection and colonization.

Results: So far, BAL episodes from 20 patients (median age 54 years; 50% after allo-HSCT; 60% neutropenic; 40% treated at ICU; 100% on systemic antibiotics; 30-day mortality after BAL was 25%) were analysed. Clinically relevant pathogens were identified in 10/20 episodes. Comparing episode-based diagnostic yield, SOC negative/mNGS negative occurred in 10 cases, SOC negative/mNGS positive in 1, SOC positive/mNGS positive in 7, and SOC positive/mNGS negative in 2 episodes, indicating a modest increase in diagnostic yield through mNGS. Across BAL and blood, mNGS and SOC showed comparable detection rates for bacteria and fungi, whereas RNA viruses could only be detected by multiplex PCR, as the mNGS assay is able to detect DNA only. In 1 of 8 patients with mNGS-detected pathogens, mNGS lead to modification of anti-infective therapy (escalation to meropenem and linezolid

after detection of *Nocardia elegans* in BAL and blood), concordant with later SOC culture findings in pleural fluid.

Conclusions: In this prospective single-centre cohort of high-risk hematologic patients mNGS findings influenced anti-infective management in selected cases, underlining its potential therapeutic relevance. Careful clinical adjudication remains essential, and larger controlled studies are needed to learn more about and define the role of BAL- and blood-based mNGS-diagnostic tools in immunocompromised hosts. mNGS from BAL and blood provided plausible results with a small but clinically meaningful additive diagnostic yield.

Disclosure: JF received honoraria from medac. The other authors do not declare any conflicts of interest.

B139

TRANSPLANTING THROUGH UNCERTAINTY: SINGLE CENTER EXPERIENCE OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH SEVERE APLASTIC ANEMIA AND POSSIBLE PULMONARY INVASIVE FUNGAL INFECTION

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Background: Invasive fungal infection (IFI) represents a serious cause of morbidity and even mortality in pediatric patients undergoing hematopoietic stem cell transplantation (HSCT), particularly those with severe aplastic anemia (SAA). The presence of pulmonary infiltrates suspicious for IFI prior to HSCT poses a significant clinical dilemma. While delaying transplantation may worsen outcomes related to prolonged marrow failure and infections, proceeding with HSCT under intense immunosuppression may increase the risk of fungal progression. This challenge is further complicated in children, where invasive diagnostic procedures such as bronchoalveolar lavage or lung biopsy are often not feasible resulting in many cases being classified as "possible" IFI. Evidence guiding transplant decisions in this context remains challenging.

Methods: This is a retrospective descriptive review of medical files of children with SAA who underwent allogenic HSCT with radiologic findings suggestive of possible pulmonary IFI, at the Bone Marrow and Stem Cell Transplantation Center, Istishari Hospital, Jordan, between June 2016 and June 2025.

Results: Four patients, with a median age of 6 (1–16) years were included, one was male. All patients had persistent fever unresponsive to broad-spectrum antibiotics and suspicious pulmonary infiltrates on chest CT scan, including nodular lesions, ground-glass opacities, halo or reverse-halo signs, and subpleural consolidations. Bronchoalveolar lavage or tissue biopsy was not performed in any case due to clinical instability. Following comprehensive evaluation, all patients were initiated on dual antifungal therapy with an echinocandin and

azole according to institutional protocol. Immediately after achieving clinical stabilization and radiological response/non-progression, antifungal therapy was de-escalated to single-agent treatment, and patients proceeded to HSCT . Two patients received matched sibling donor HSCT conditioned with Cyclophosphamide (200 mg/kg) and rATG (7.5 mg/kg), while the other two underwent T-replete haploidentical HSCT with post-infusion Cyclophosphamide (100 mg/kg) and conditioning with rATG (5 mg/kg), Fludarabine (150 mg/kg), Cyclophosphamide (29 mg/kg) and 300 cGy single fraction total body irradiation. Three patients received bone marrow as stem cells source. The median CD34 cell dose was 4.9 (2.2-10.2) $\times 10^6$/kg .
Neutrophil engraftment was documented in all patients between 11 and 18 days post-HSCT. All patients showed significant clinical response after neutrophil engraftment, and none required ICU admission. All patients demonstrated complete radiological resolution of pulmonary findings, the earliest was 30 days post-HSCT. All patients received at least 3 months of therapeutic antifungal treatment post-HSCT and continued on proper secondary fungal prophylaxis. At a median follow-up of 52 (12-68) months all patients are alive, doing well and transfusion independent.

Conclusions: Our findings suggests that proceeding with HSCT in carefully selected pediatric patients with SAA and radiological evidence of possible pulmonary IFI is feasible and associated with favorable outcomes. Customized HSCT and antifungal strategies appear to be key factors in mitigating infection-related risks. Larger multicenter pediatric studies are needed to better define risk stratification and optimize management strategies in this high-risk population.

Disclosure: Nothing to declare.

B140

ACCURATE CMV IGG DETECTION USING BUCCAL SWABS IN STEM CELL DONOR SCREENING

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Background: Cytomegalovirus (CMV) serostatus assessment is a key component of donor evaluation for hematopoietic stem cell transplantation, as CMV mismatch increases the risk of viral reactivation and survival. Standard CMV IgG determination requires serum obtained by venipuncture, which may limit its use in rapid triage, early donor registration and selection, or large-scale screening. Buccal swab–based serology has emerged as a promising alternative for these situations; however, comparative data with validated serum assays remain limited. This study assessed the diagnostic performance, concordance and

reproducibility of buccal swab CMV IgG testing relative to serum-based serology, considered the reference standard.

Methods: Matched samples were obtained from volunteer donors, consisting of paired buccal swabs and serum specimens collected simultaneously. Buccal swab CMV IgG testing was performed using the DRG ELISA CMV IgG Buccal Swab (DRG Instruments GmbH, Marburg, Germany) and serum CMV IgG was determined using the Elecsys CMV IgG assay (Roche Diagnostics International AG, Rotkreuz, Switzerland). Buccal swabs were collected during planned mobile blood donation campaigns (BST), and after a standardized drying protocol were placed in paper envelopes to ensure safe transport. Samples were traceable and accompanied by donor's signed informed consent. Samples were processed within 24-72h (Hospital Clínic Barcelona) and serum fractions was stored at -20°C and buccal swabs at 4°C.
Diagnostic accuracy metrics included sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy. Agreement between methods was assessed using Cohen's Kappa coefficient. When discordant results were observed, new samples were obtained for confirmation. Reproducibility was evaluated by testing duplicated buccal swabs one and three months after initial collection. The study received approval from the CEIM: HCB/2025/0627.

Results: A total of 222 volunteer donors were included. Among paired samples, 115 had positive results in both serum and buccal swab (51.8%), and 91 were negative by both methods (41.0%). Five samples (2.3%) were positive in serum but negative in swab, considered potential false negatives. Eleven samples (5.0%) were positive in swab but negative in serum; seven corresponded to grey zone values and four were clearly positive. New samples (swabs and serum) were obtained in seven of the eleven discordant cases. Two discrepancies were resolved upon retesting, while five maintained their initial results.
The diagnostic performance metrics for CMV IgG detection using buccal swabs after repeating discordant results were as follows: sensitivity 96.8%, specificity 90.1%, PPV 92.1%, NPV 95.8%, and overall accuracy 93.7%. Cohen's Kappa was 0.873, indicating almost perfect agreement between the two methodologies.
Reproducibility analysis showed consistent results in 50/54 buccal swabs (92.6%) at one month and in 28/28 samples (100%) at three months after sample's collection.

Conclusions: Buccal swab CMV IgG detection demonstrated excellent concordance with serum-based serology with high sensitivity, specificity, and reproducibility. These findings support the use of buccal swabs as a reliable, minimally invasive alternative for CMV serostatus determination, particularly in stem cell donor screening scenarios requiring rapid or simplified logistics.

Disclosure: nothing to declare

B141

LATE CYTOMEGALOVIRUS REACTIVATION AFTER ALLOGENEIC HSCT PERSISTS IN THE ERA OF LETERMOVIR PROPHYLAXIS – A SINGLE-CENTRE REAL WORLD STUDY

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Background: Patients undergoing allogeneic haematopoetic stem cell transplantation (allo-HSCT) have impaired virus-specific immunity. Cytomegalovirus (CMV) reactivation, if untreated, can lead to clinically significant manifestations including colitis, pneumonitis and retinitis. Letermovir, a CMV-specific viral terminase complex inhibitor, is indicated as prophylaxis against CMV reactivation in adult CMV seropositive recipients (R+) of an allo-HSCT, and has been funded for the first 100 days post allo-HSCT by the UK National Institute for Health and Care Excellence (NICE) since 31st July 2019.

Methods: We performed a retrospective analysis of all patients who underwent allo-HSCT at a single UK centre between 1st Jan 2016 – 31st Dec 2024 and aimed to observe the relationship between letermovir administration and the occurrence of clinically significant CMV reactivation (csCMV). csCMV was defined as two consecutive positive PCR results >3log(10) in patients with a negative PCR at baseline.

Results: During the study period 480 patients underwent allo-HSCT, 192/480 (40%) pre-, and 288/480 (60%) post-letermovir introduction. The most common indications for allo-HSCT were AML (182/480; 37.9%), MDS (83/480; 17.3%) and non-Hodgkin lymphoma (59/480; 12.2%). Median age was 55 (range 18-75) and 293/480 (61%) were male. 413/480 (86%) received reduced intensity conditioning regimens, and 397/480 were T-cell deplete (Campath 226/480; 47.1%, ATG 93/480; 19.4%, PTCy 79/480; 16.5%). In the pre-letermovir cohort, 98/192 (51.0%) of patients were R+ and 37/98 (37.8%) developed csCMV. In the post-letermovir cohort, 140/288 (48.6%) patients were R+, all received letermovir prophylaxis, and 27/140 (19.3%) developed csCMV. In letermovir-ineligible CMV negative recipients (R-) receiving a CMV positive graft, 4/36 (11.1%) reactivated.
In a multivariate competing risk model to test whether T-cell depletion increased the risk of CMV reactivation (treating death without reactivation as a competing event), T depletion increased the risk of csCMV (HR 2.64, 95%CI 1.05-6.6, *p=0.03*). This remained significant after adjusting for age, sex, diagnosis and treatment era.
The median time to first reactivation pre-letermovir was 40 days (range 13-525). Post-letermovir, the median time to first reactivation was 155 days (range 26-778). Pre-letermovir, 37/98 (37.8%) at-risk patients reactivated by D100 post-allograft, compared to 2/140 (1.4%) post-letermovir (*p<0.01*). The median peak viral load did not significantly differ between groups.

33/37 (89.2%) of the pre-letermovir reactivators required treatment with an anti-viral agent, most commonly Valganciclovir; 4 patients required admission for treatment with foscarnet (2 having been pre-treated with valganciclovir). Clinically significant colitis occurred in 2 patients. 20/27 (74.1%) of the post-letermovir reactivators required treatment with an additional anti-viral agent (*p=0.52*); 3 required admission for treatment with foscarnet (2 having been pre-treated with valganciclovir). Clinically significant colitis occurred in 1 patient. No patients had clinical pneumonitis or retinitis in either group. The median duration of treatment with valganciclovir was 26 days (range 7-186) in the pre-letermovir cohort, and 30 days (range 12-54) in the post-letermovir cohort (*p=0.21*). Patients with csCMV frequently had concurrent GvHD (18/37; 48.6% in pre-letermovir cohort; 15/27; 55.6% in post-letermovir cohort) and associated immunosuppression.

Conclusions: CMV reactivation remains a frequent issue post-allo-HSCT. Letermovir defers the median onset of csCMV to post-D100, but does not reduce the need for further anti-viral treatment.

Disclosure: Nothing to declare.

B142

IMPACT OF HUMAN PARVOVIRUS B19 INFECTION ON THE OUTCOME OF PEDIATRIC HCT FOR HEMOGLOBINOPATHIES AND OTHER HEREDITARY ANEMIAS

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Background: Hematopoietic cell transplantation (HCT) exposes the recipient to a high risk of viral reactivations especially during the first weeks after transplant. Human Parvovirus B19 (B19V) is a common DNA virus with tropism forerythroid progenitors, but also for megakaryocytes and endothelium. Infection in immunocompetent individuals is mostly asymptomatic, but in immunocompromised hosts it may cause hematological disorders including anemia and aplastic crisis. B19V disease is a rare complication after HCT, however, the virus has been described to persist after primary infection, raising questions on its clinical impact on the outcome of HCT. Therefore, we evaluated B19V infection before and longitudinally after allogeneic pediatric HCT for hemoglobinopathies and other congenital anemias.

Methods: Thirty-nine pediatric subjects given HCT from a matched family donor (MFD, 18%), a matched unrelated donor (MUD, 77%) or a partially matched family donor (PMFD, 5%) for hereditary anemias between 2019 and 2025 were evaluated for B19V serology, the presence of viral DNA on bone marrow precursors before transplantation, and on peripheral blood samples collected in the first year after HCT. Donor serology was also evaluated.

Results: Seropositivity for B19V was observed in 13 of 39 patients (33%) and in 28 of 39 donors (72%), respectively. We identified 7 out of 39 patients (18%) with B19V DNA in the bone marrow before transplantation, and 17 of 39 (43%) recipients were found to be positive for blood B19V DNA in the first year post transplantation. B19V infection/reactivation onset was generally observed within the first 3 months after transplantation. The peak viral load was a median of 315 cp/mL (range 1– 46362 cp/mL). Viral loads >100 cp/mL were observed in 11 patients (28%), with a median value of 630 cp/mL. Transmission from the donor was not a common event, as only in 4/17 cases seronegative recipients with negative viral load on pretransplant BM received HSCs from B19V-positive donors. The occurrence of B19V infection, considered as a categorical variable, did not affect transplant outcome, in particular neutrophil and platelet engraftment, acute and chronic GvHD, rejection, OS, EFS and TRM. However, two patients with high posttransplant load (7353 and 26389 cp/ml) developed B19V-related complications, such as severe anemia and rejection, respectively.

Conclusions: We observed an increased incidence of B19V infection in our pediatric population, that may be due to both longitudinal post-HCT monitoring and the recent B19V outbreak in the years 2023-2024. However, this occurrence did not result in an increased incidence of virus-related disease, and symptomatic B19V infection following HCT remains a rare, though potentially challenging, complication. Based on the results obtained, B19V infection/reactivation does not seem to have an impact on HCT outcomes. Therefore, routine viral monitoring may not give added benefit in the pediatric HCT setting. However, in selected populations, such as hereditary anemia patients transplanted with an alternative donor, early monitoring may identify HCT recipients at risk of B19V-related disease, that may benefit from IVIG therapy.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

B143

COMPARATIVE STUDY OF RESPIRATORY SYNCYTIAL VIRUS BURDEN AND TREATMENT POLICIES IN HAEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Respiratory syncytial virus (RSV) is a significant cause of morbidity in haematopoietic cell transplant (HCT) recipients, yet comparative data from diverse international settings remain scarce. We evaluated RSV incidence, clinical characteristics, management practices, and outcomes across three HCT centres in South Africa and the Netherlands.

Methods: This retrospective multicentre cohort included adults (≥18 years) with PCR-confirmed RSV infection following HCT between January 2015 and December 2024. Incidence was calculated as a proportion of all transplants and per 100 person-years. Demographic and clinical characteristics, treatment strategies, and outcomes were assessed. Centre roles were considered: Erasmus MC and Wits Donald Gordon Medical Centre (WDG) function as full transplant centres, whereas Spaarne Gasthuis serves as a referral centre for early post-HCT follow-up.

Results: Among 1,189 transplants, 82 RSV infections were identified (65 Erasmus MC; 9 Spaarne; 8 WDG). Centre-level rates ranged from 4.2–7.7%, corresponding to 1.2–1.5 cases per 100 person-years; these reflect overall centre populations rather than true transplant-type specific incidence. Most infections (65%) occurred within 15 months post-HCT, peaking between 0–9 months. Co-infections were documented in 16–33%. Treatment practices varied, with ribavirin ± IVIG used exclusively at Erasmus MC (51% of cases). Hospitalisation occurred in 25–56% of patients, ICU admission in 3–22%, and in-hospital mortality remained low (3–13%) across all centres.

Conclusions: RSV infection was infrequent and associated with relatively low morbidity and mortality across geographically and economically diverse HCT centres. Universal pre-transplant RSV prophylaxis appears unnecessary; however, targeted preventive strategies may benefit patients at highest risk. These findings provide a contemporary benchmark for developing harmonised RSV management pathways in HCT recipients.

Disclosure: no conflicts of interest and received no funding for this project

B144

HOW DO DEFINITIONS FOR NOSOCOMIAL INVASIVE ASPERGILLOSIS PERFORM IN HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS?

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Background: Invasive aspergillosis (IA) is the most common invasive fungal infection in hematopoietic cell transplant (HCT) recipients. However, there are no standardized definitions for nosocomial invasive aspergillosis (nIA) to guide when to conduct comprehensive infection prevention (IP) investigations in this population, which may include costly engineering assessments and mitigation measures.

Methods: We conducted a retrospective review of HCT recipients diagnosed with IA at our center between 3/2021-6/2025. IA cases were defined using consensus guidelines; galactomannan (GM) enzyme immunoassays were considered positive if confirmed levels were ≥0.5. We collected demographic and clinical data including oncologic and transplant history, fungal diagnostics, and mortality outcomes at 30 and 90 days. Incident IA was defined by the date of first positive mycologic test for *Aspergillus* spp. For primary analyses,

we applied a conservative, admission-based definition of nIA, defined as IA diagnosed > 14 days after hospital admission. Cases diagnosed ≤14 days after admission were classified as community-acquired IA (cIA). This definition was used to compare baseline characteristics, clinical outcomes and GM values between groups. For secondary analyses we applied additional proposed definitions, including the Centers for Disease Control and Prevention (CDC) definition for possible nIA (>7 days post-admission) and another expanded definition classifying probable nIA if diagnosed >14 days after admission or if discharged from the hospital within 14 days prior to the current admission. These alternative definitions were used to estimate the proportion of IA cases that would meet criteria for IP investigation.

Results: A total of 40 HCT recipients with IA were included; 22 (55%) were diagnosed ≤14 days after hospital admission and 18 (45%) were diagnosed >14 days post-admission. Baseline characteristics were similar between nIA and cIA cases, except for the median time from HCT to IA diagnosis for cIA cases was longer (255 days; IQR [interquartile range]: 53-879) compared with nIA cases (20 days; IQR: 14-39; p<0.001; Table 1). The median time from admission to diagnosis was 27 days (IQR: 20-34) in the nIA group. While there were no significant differences in serum GM between the 2 groups (p = 0.11), bronchoalveolar lavage fluid (BALf) GM values were significantly higher in the nIA group (p = 0.024; Figure 2A). All-cause mortality at day 30 was 32% for cIA and 28% for nIA cases, and mortality at day 90 was 36% and 44%, respectively. When applying the expanded 14-day plus recent hospitalization definition, 28 cases (70%) were classified as probable nIA whereas the CDC definition classified 21 (53%) as possible nIA(Figure 2B).

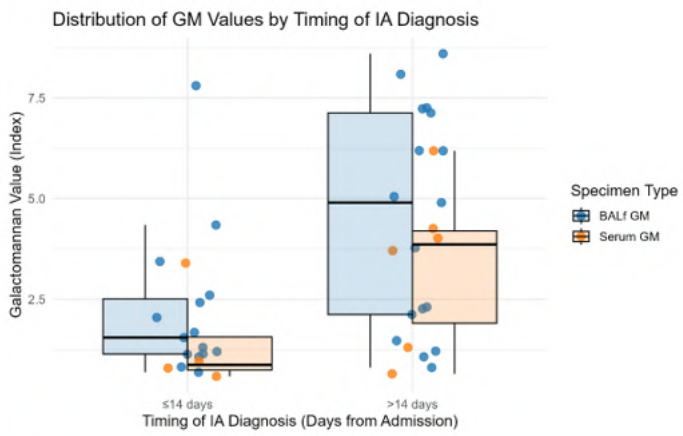
Table 1. Baseline Characteristics by timing of IA diagnosis

Characteristic	**≤14 days** N = 22[1]	**>14 days** N = 18[1]	**p-value**[2]
Age (years)			
Median [Q1, Q3]	57 [50, 67]	58 [45, 66]	
Time from hospital admission to IA (days)			<0.001
Median [Q1, Q3]	4 [1, 6]	27 [20, 34]	
Time from HSCT to IA (days)			<0.001
Median [Q1, Q3]	255 [53, 879]	20 [14, 39]	
History of GVHD	12 (55%)	5 (28%)	
Steroid receipt in prior 90 days	8 (38%)	5 (28%)	
Neutropenia at diagnosis	13 (59%)	11 (61%)	
Neutropenia duration (days)			0.804

Characteristic	**≤14 days** N = 22[1]	**>14 days** N = 18[1]	**p-value**[2]
Median [Q1, Q3]	31 [5, 49]	22 [15, 40]	
Antifungal prophylaxis	18 (82%)	18 (100%)	
Fluconazole	10 (45%)	10 (56%)	
Posaconazole	3 (14%)	4 (22%)	
Isavuconazole	4 (18%)	1 (5.6%)	
Voriconazole	1 (4.5%)	3 (17%)	
Antifungal ppx duration (days)			0.476
Median [Q1, Q3]	32 [15, 61]	24 [19, 30]	

[1]n (%) [2]Wilcoxon rank sum test

Figure 1A.



1B.

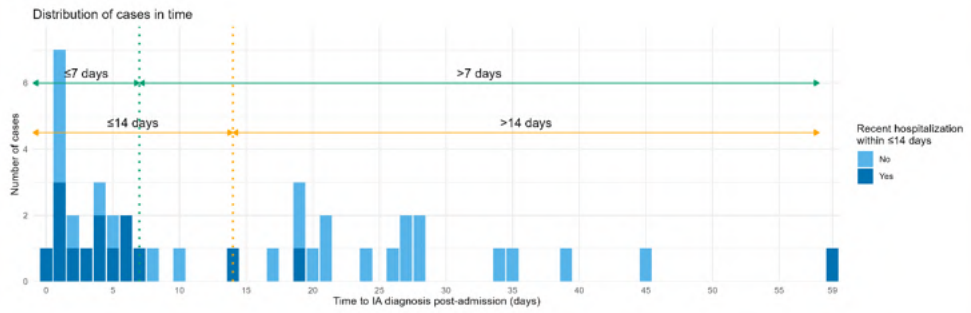


Figure 1A. Shows BAL and serum GM values by diagnosis ≤14 vs >14 days after admission. Figure 1B shows time to IA diagnosis, with markers indicating 7- and 14-day thresholds and recent hospitalization status.

Conclusions: In this HCT cohort, the application of proposed nIA definitions classified 50-70% of IA cases as nosocomial. Cases classified as nIA (>14 days after admission) were diagnosed earlier post-transplant and had higher BALf GM at diagnosis when compared to cIA cases. Given the prolonged and complex hospital courses of HCT recipients, current guidelines for costly and often unrevealing IP investigations may be overly sensitive in this population. Clinically-based nIA definitions that incorporate host risk factors and degree of immunosuppression are needed.

Disclosure: DJM – research funding from Pfizer and Shinogi unrelated to this work. (unrelated to this work)
CL – research support SNIPR Biome (unrelated to this work)
SAP – participates in clinical trials with F2G, Mundipharma and Symbio (unrelated to this work)

B145

CANADIAN SURVEY ON ANTIBACTERIAL PROPHYLAXIS AND FEBRILE NEUTROPENIA MANAGEMENT IN ADULT ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: Bacterial infections during neutropenia remain a major cause of morbidity in allogeneic hematopoietic cell transplantation (allo-HCT) recipients. Several international guidelines address antibacterial prophylaxis in this setting; however, most recommendations are conditional, intended for selected high-risk patients, and supported by low-quality evidence, particularly regarding survival outcomes. Evidence demonstrating a reduction in mortality is lacking, and thus routine prophylaxis remains controversial in the context of rising antibiotics resistance and microbiota disturbance associated risks. Thus, management strategies for antibacterial prophylaxis and first-line treatment of febrile neutropenia (FN) vary considerably between centers. To better understand current Canadian practice, we conducted a pan-Canadian survey of adult allo-HCT programs.

Methods: A cross-sectional electronic survey was distributed to Canadian allo-HCT centers in October 2025. The questionnaire consisted of eleven items and assessed center characteristics and province, transplant volume, use of routine antibacterial prophylaxis, antimicrobial selection, duration, and first-line empirical therapy for FN, as well as monitoring of resistant bacteria colonization. Data were analyzed descriptively.

Results: The eleven Canadian centers performing adult alloHCT responded. Provincial distribution included British Columbia (n=1), Alberta (n=1), Saskatchewan (n=1), Manitoba (n=1), Ontario (n=3), Quebec (n=3), and Nova Scotia (n=1). Most were adult-only programs (n=10); one treated both adults and pediatric patients. Annual alloHCT volume was 20–50 procedures in four centers, 51–100 in two, and >100 in five.
Routine prophylaxis was reported by six centers (54.5%), while five centers (45.5%) reported no prophylaxis. Among centers using prophylaxis, three administered it to all patients, one restricted it to non-myeloablative outpatient procedures, one exclusively to cord blood transplant recipients, and one to patients with sickle-cell hemoglobinopathy.

Fluoroquinolones were the most used prophylactic agents (n=5), followed by cephalosporins (n=1), with duration typically maintained until neutrophil engraftment. No center modified prophylaxis based on conditioning regimen or haploidentical transplant. Overall, 72.7% (8/11) of centers reported no routine antibacterial prophylaxis for most patients. Piperacillin–tazobactam was the most frequently used empirical therapy across centers (n=10); while one center used cefepime. Initial antimicrobial regimens were not stratified according to conditioning intensity (myeloablative vs. non-myeloablative) or donor type (including haploidentical transplants).
Routine multidrug-resistant organism surveillance cultures were performed in six centers; one center obtained them only at admission to the transplant unit, while four centers reported no routine surveillance.

Conclusions: Considerable heterogeneity exists in antibacterial prophylaxis strategies across Canadian allo-HCT programs, with the majority opting against routine universal prophylaxis. Empirical management of FN was largely uniform, with piperacillin–tazobactam as the preferred agent. Importantly, while antibacterial prophylaxis may reduce early infectious complications, potential harms—including antimicrobial resistance, *Clostridioides difficile* infection, and disruption of the gut microbiome—must be weighed against uncertain benefits on survival outcomes. These findings support the need for evidence-informed, standardized guidance to optimize risk-adapted infection prevention strategies in allo-HCT recipients.

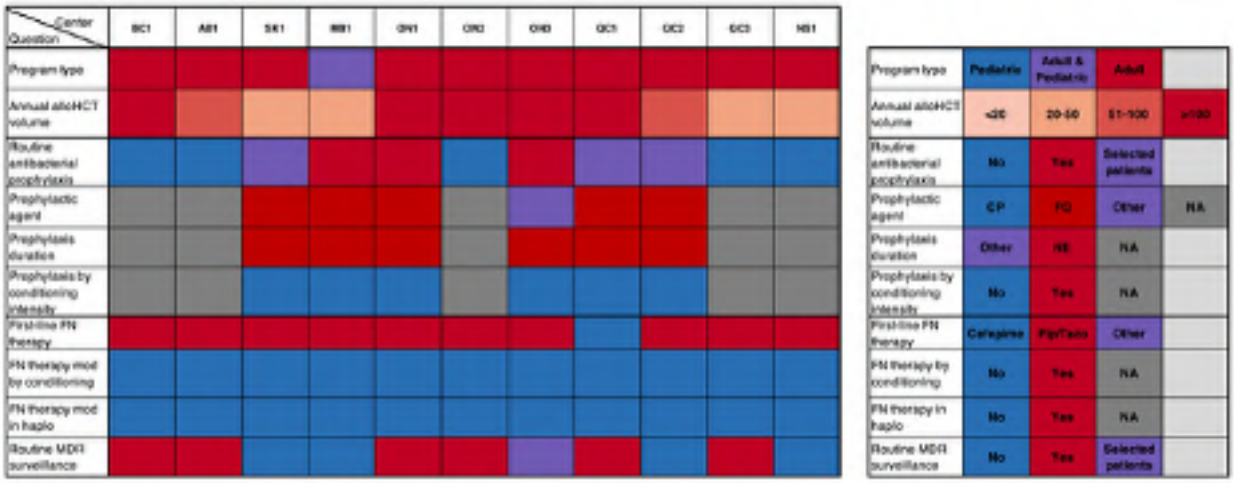

Figure 1. Heatmap of Canadian Survey Results.
BC: British Columbia; AB: Alberta; SK: Saskatchewan: MB: Manitoba; ON: Ontario; QC: Quebec;
NS: Nova Scotia CP: Cephalosporins; FQ: Fluoroquinolones.

Disclosure: The authors declare no conflict of interest

B146

MANAGEMENT OF PROTRACTED CLOSTRIDIOIDES DIFFICILE INFECTION IN CHILDREN WITH GI-GVHD AFTER ALLOGENEIC HSCT: A SINGLE-CENTER PEDIATRIC EXPERIENCE

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Background: Clostridioides difficile infection (CDI) occurs in approximately 8–15% of children after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Major risk factors include gastrointestinal graft-versus-host disease (GI-GvHD), mucosal injury, immunosuppression, and broad-spectrum antibiotic exposure. CDI is often severe in this population, with recurrence rates of 15–20%. According to ECIL-10 recommendations, bezlotoxumab and fecal microbiota transplantation (FMT) may be considered in recurrent CDI after vancomycin or fidaxomicin therapy in high-risk patients.

Methods: We report three immunosuppressed pediatric patients after allo-HSCT with severe GI-GvHD and transplant-associated thrombotic microangiopathy (TA-TMA), illustrating a complex, individualized management of protracted and severe CDI. Therapeutic strategies included antibiotic therapy, bezlotoxumab, FMT, and support of intestinal mucosal regeneration with teduglutide.

Results: **Case 1:** An 18-year-old boy after matched sibling donor HSCT for Ph+ B-ALL developed grade IV acute GI-GvHD from day +37. Persistent CDI was documented from day +55 despite intensive immunosuppression (cyclosporine A, corticosteroids, ruxolitinib, mesenchymal stromal cells, extracorporeal photopheresis, vedolizumab). Fidaxomicin was ineffective, with recurrent pseudomembranous colitis. Long-term oral vancomycin and two doses of bezlotoxumab were administered. Three FMTs via enema and four additional FMTs via PEJ were performed. TA-TMA was confirmed and treated with ravulizumab. CDI resolved after repeated FMTs; however, long-term gastrointestinal dysfunction persisted, with progression to moderate chronic GI-GvHD.
Case 2: A 2-year-old boy with alphamannosidosis after mismatched unrelated donor HSCT developed grade IV acute GI-GvHD and TA-TMA. CDI persisted despite fidaxomicin, vancomycin, metronidazole, and two doses of bezlotoxumab, with recurrent pseudomembranous colitis and paralytic ileus. The course was complicated by *Pseudomonas aeruginosa* sepsis and prolonged intestinal failure. Teduglutide enabled enteral nutrition. Four FMTs via enema resulted in rapid CDI eradication after the first FMT, with sustained remission.
Case 3: A 17-year-old boy with CML after mismatched unrelated donor HSCT (PBSC, HLA 9/10) developed grade IV acute GI-GvHD. Severe CDI occurred on day +32 and was treated with fidaxomicin and intravenous metronidazole. Two FMTs led to CDI eradication. A single relapse occurred during concomitant Escherichia coli sepsis and was successfully treated with oral vancomycin. Bezlotoxumab was administered, with no further CDI recurrence.

Conclusions: Management of CDI after allo-HSCT requires a comprehensive and highly individualized approach, as CDI frequently coexists with GI-GvHD and TA-TMA. CDI may exacerbate GI-GvHD, while immunosuppression increases infection severity. Protracted CDI can lead to long-lasting intestinal dysfunction requiring supportive interventions, including teduglutide. Careful antibiotic selection is essential: microbiota-sparing agents should be preferred for CDI whenever possible, while broad-spectrum antibiotics are often unavoidable in sepsis. FMT represents a promising option even in HSCT recipients (reported success rates 78–86%) but carries a risk of severe complications, including sepsis (up to 9%). Bezlotoxumab appears safe; however, according to ECIL-10 recommendations, its efficacy in pediatric patients remains limited.

Disclosure: Nothing to declare

B147

MICAFUNGIN AS ANTIFUNGAL PROPHYLAXIS DURING THE PRE-ENGRAFTMENT PERIOD OF ALLO-HSCT. ANALYSIS OF A 450-PATIENT COHORT

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Background: Allogeneic hematopoietic stem cell transplant (allo-HSCT) recipients are at high risk of invasive fungal infections (IFI) during the pre-engraftment period. Although azoles are widely used, hepatotoxicity and drug-drug interactions may limit their applicability. Micafungin, a once-daily echinocandin with excellent tolerability, has demonstrated efficacy comparable to azoles; however, real-world evidence in large cohorts remains limited.

Methods: We conducted a single-center, retrospective study including all adult allo-HSCT recipients between January 2010 and June 2025 who received systematic primary antifungal prophylaxis with micafungin from day 0 (50 mg/day) throughout the pre-engraftment period until neutrophil recovery. Baseline characteristics (*Table 1*), duration of prophylaxis, breakthrough IFI, toxicity, and need for antifungal escalation were recorded. Primary endpoints were proven IFI incidence, IFI-free survival, and IFI-related mortality. Descriptive analyses were performed with SPSS® v16.0.

Results: **Table 1: *"Baseline characteristics of patients undergoing allo-HSCT receiving micafungin prophylaxis"*; n = 450**

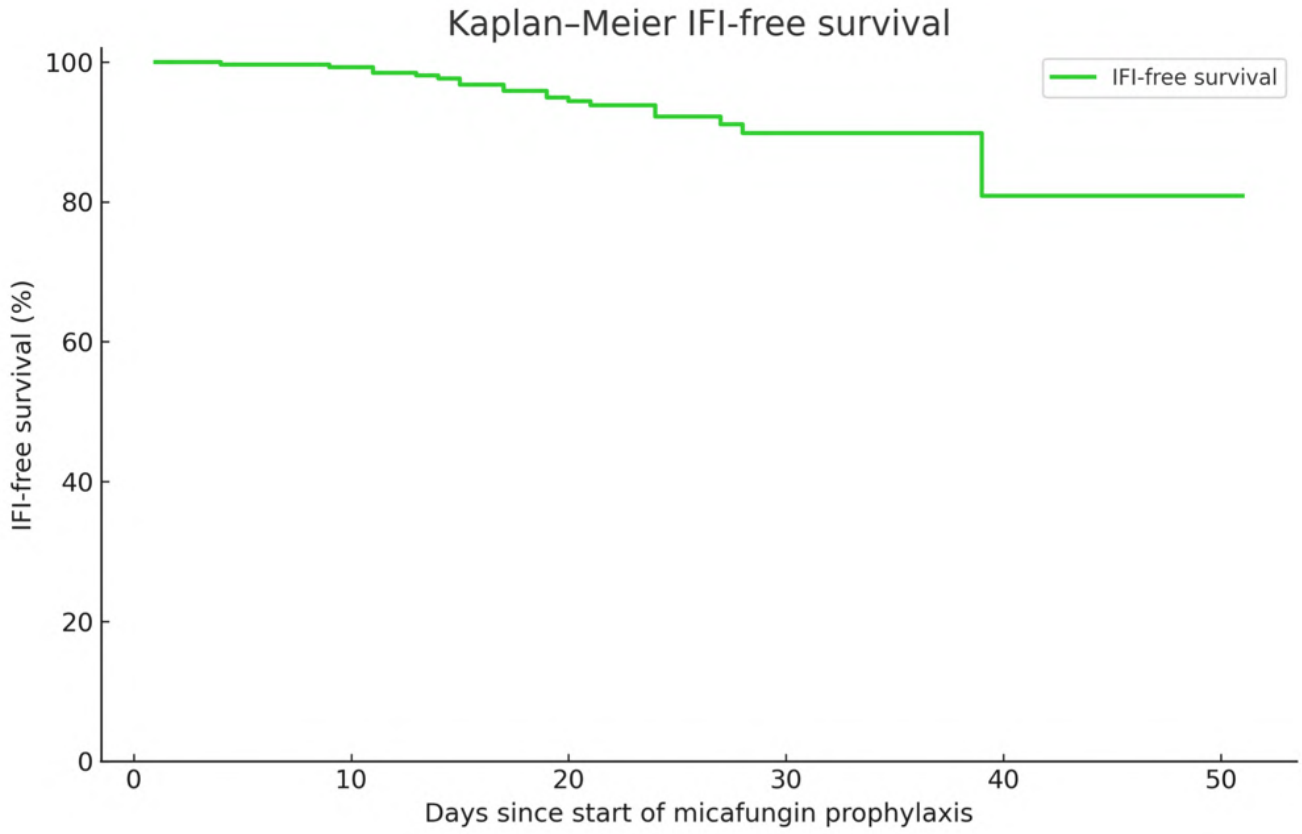
Sex (M/F)	245 (54.4%) / 205 (45.6%)

Median age at HSCT	50 years (range 19 – 73)
Underlying disease	AML 44.9%; ALL 10.9%; MDS 20.2%; Lymphomas 11.6%; aplastic anemia 3.3%; others 9.1%
Donor type	Unrelated 50.7%; Related 47.1%; Haploidentical 2%
Stem cell source	Peripheral blood: 96.9%; Bone marrow: 3.1%
Conditioning regimen	MAC 32.9%; RIC 66.2%; Sequential 0.9%
GVHD prophylaxis	Cs+MTX 45.69%; Cs/MF/CF post 19.2%; Cs/CF post 16.5%; Cs alone 7.2%; ATG: 1.3% Others 10.11%

HSCT: Hematopoietic stem cell transplantation; AML: Acute myeloid leukemia; ALL: Acute lymphoblastic leukemia; MDS: Myelodysplastic síndrome; GVHD: Graft-versus-host disease; MAC: Myeloablative conditioning; RIC: Reduced-intensity conditioning; Cs: Cyclosporine; MTX: Methotrexate; MF: Mycophenolate mofetil; CF post: Post-transplant cyclophosphamide; ATG: Antithymocyte globulin.

A total of 450 patients were included. Median duration of micafungin prophylaxis was 21 days (range 1–51). Micafungin was maintained throughout the pre-engraftment period in 75.2% of patients; 24.8% required a switch, mainly due to proven or possible IFI (16.1%) or liver function abnormalities (8.7%).
The incidence of proven IFI was 4.2% (19/450). Most infections were caused by yeasts (84.2%), predominantly *Candida spp* (73.7%). Among the 14 patients with *Candida* isolation, 8 (57.1%) had positive cultures from central venous catheter blood samples; all were receiving parenteral nutrition and required intensive care support at diagnosis. Two azole-resistant and one anidulafungin-resistant *Candida* isolates were detected. Filamentous fungi accounted for 15.8% of cases: *Aspergillus spp* (2/19) and multiresistant *Acremonium sclerotigenum* (1/19), isolated from bronchoaspirate (BAS) or central line blood cultures; all showed positive galactomannan (AGA) screening. Additionally, 12 patients (2.7%) were managed as possible IFI due to positive AGA results without microbiological confirmation. Empirical antifungal escalation was required in 43 patients (9.6%) due to pulmonary infiltrates or clinical deterioration with negative AGA tests. Among patients with proven or possible IFI (n=34), 26.5% had received corticosteroids during the pre-engraftment period. Antifungal treatments were heterogeneous: liposomal amphotericin B (37.9%), isavuconazole (24.1%), and double-agent combinations (24.1%), mainly in critically ill patients with severe pneumonia or intensive care needs.
IFI was the primary cause of death in 3 of 19 patients (15.8%). IFI-free survival at day +21 was 93.8% *(Figure 1).*

Figure 1*: "Invasive fungal infection–free survival"*



Conclusions: In this large real-world cohort, micafungin prophylaxis during the pre-engraftment period of allo-HSCT was associated with a low incidence of proven IFI, IFI-free survival above 90% during the first post-transplant month, and a highly favorable safety profile. Proven *Candida* infections were closely linked to critical illness, severe mucositis and parenteral nutrition. Overall, in our experience, micafungin is an effective and safe antifungal prophylactic strategy in allo-HSCT recipients.

Disclosure: Nothing to declare.

B148

SEROPREVALENCE OF HBV IN UNRELATED DONORS AT CONFIRMATORY TYPING STAGE AND ITS IMPACT ON THE CHOICE OF HEMATOPOIETIC CELL DONOR – DATA OF DKMS POLAND

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Background: Hepatitis B virus (HBV) infection has a significant impact on hematopoietic cell (HPC) donation safety, and therefore post-exposure serological status may influence donor choice due to the risk of occult hepatitis B infection.

Methods: We retrospectively analyzed 26542 unrelated HPC donors within DKMS Poland Donor Center at confirmatory typing (CT) stage between 2020 and 2024. Donor blood samples were tested for anti-HBc antibodies and HBs antigen (HBsAg). Donors were stratified by age groups to assess the frequency of positive anti-HBc and positive HBsAg in Polish unrelated donors (UD) requested for CT. In addition, the number of donors with positive anti-HBc antibodies at Work-Up stage was analysed to check whether the presence of these antibodies affects the probability of positive selection of this group for HPC donation. Transplant centres always received CT infectious disease markers, with a proactive communication in case of serological signs of past HBV infection.

Results:

Age group	AntiHBc (-)	AntiHBc (+)	Prevalence	HBSAg (+)	Total
18-25	10482	39	0,37%	5	10521
26-30	5970	62	1,03%	7	6033
31-35	4145	96	2,26%	5	4242
36-40	2957	100	3,27%	4	3057
41-60	2553	136	5,06%	6	2689
Total	26107	433	1,63%	27	26542

Among 26542 donors analyzed, 433 (1,63%) were positive for anti-HBc, indicating past HBV exposure. Positive HBsAg with accompanying anti-HBc indicating active, acute or chronic, HBV infection was positive in 27 donors (0,10%). As for the seroprevalence of anti-HBc, the older the age group, the higher was the percentage of anti-HBc-positive donors, with statistically significant differences ($p < 0,05$). The age group between 18-25 years old had the lowest (0,37%), while the 41-60 y.o. donors had the highest (5,06%) anti-HBc prevalence. Proportion of HBsAg-positive blood samples seemed to be similar in all age groups and no statistical correlation was found ($p > 0,05$). A comparison of the proportion of anti-HBc–seropositive donors at the CT and Work-Up stages demonstrated a statistically significant difference ($p < 0.05$), with rates of 1.40% and 1.07%, respectively. Overall 98 donors were selected for HPC collection, despite the seropositivity (anti-HBc (+), HBsAg (-)),

with negative HBV NAT at physical examination. None of the transplant centers informed DKMS Poland of possible HBV transmission.

Conclusions:

- Presence of anti-HBc suggesting past HBV exposure is important for donor selection and recipient safety due to the risk of chronic occult hepatitis B and donor-recipient viral transmission. This may influence donor choice.
- In Poland, universal HBV vaccination was introduced in 1996, which influences seroprevalence patterns among donors of different age groups. Our findings confirm that past HBV infection markers are more prevalent among older donors, which probably reflects pre-vaccination era exposure.
- In all age groups there was similar proportion of HBs-Ag positive donors. These results underscore the importance of comprehensive HBV screening during CT to ensure transplant safety and inform donor selection policies.
- The results show that donors with past HBV infection, albeit somewhat less frequently, are selected for HPC donation with no reported cases of transmitted HBV infection among patients who received HPC form the analyzed group of donors.
- WMDA Donor Suitability recommendations regarding past HBV infection state that anti-HBc(+), HBsAg(-) donors can be accepted at the discretion of transplant centers, with the recommended anti-HBs level ≥100 IU/l.

Disclosure: Nothing to declare.

B149

EPIDEMIOLOGY OF CATHETER-RELATED BLOODSTREAM INFECTIONS IN STEM CELL TRANSPLANTATION

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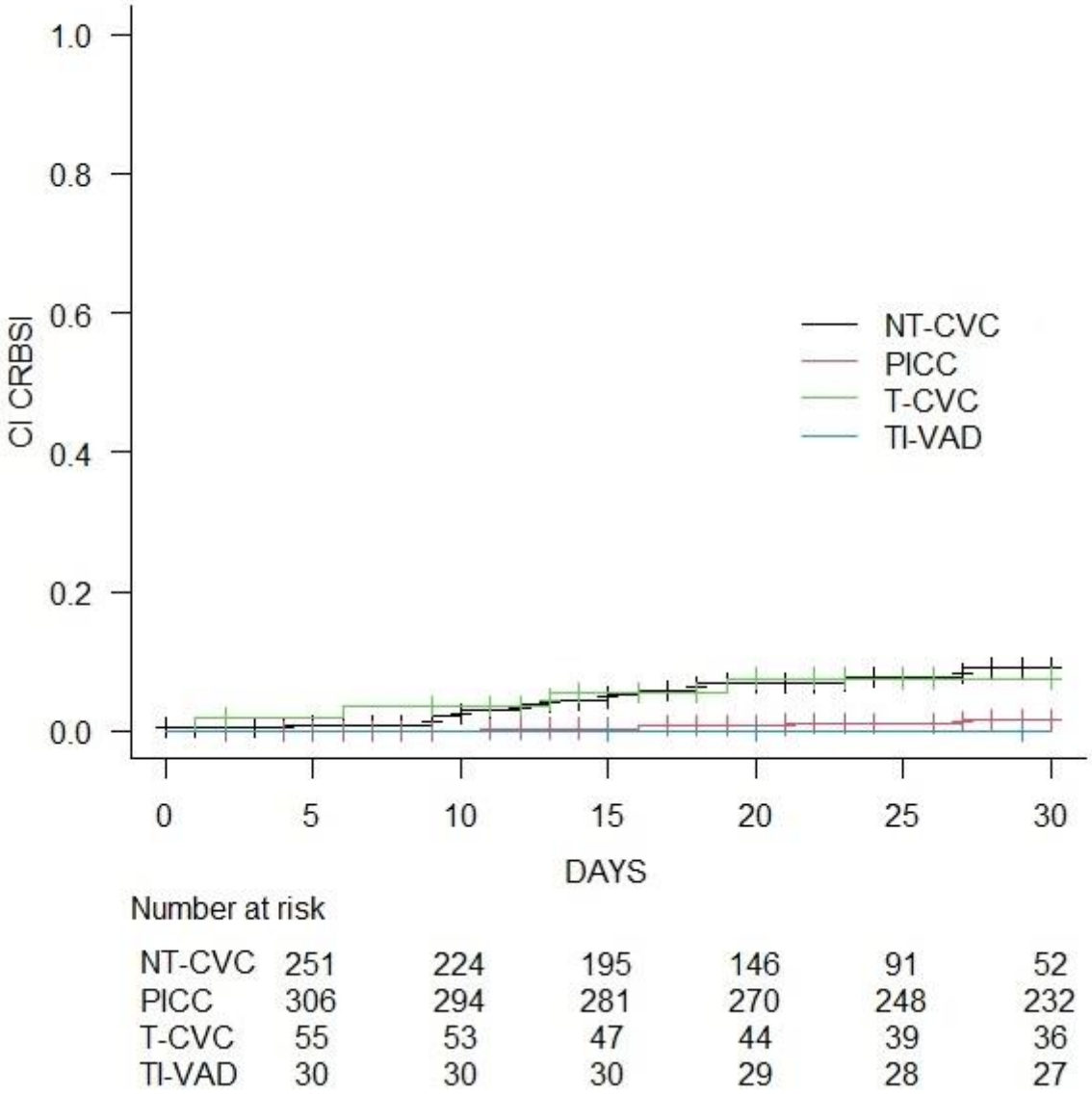
Background: The use of a central venous catheter (CVC) is essential for patients undergoing an allogeneic hematopoietic stem cell transplant (SCT) but it comes with a higher risk for catheter-related bloodstream infections (CRBSI). Updated data is limited in this context.
The aim of this study was to identify the incidence of CRBSI, the causative agents, and describe risk factors for its development in SCT.

Methods: This was a single-center, retrospective, observational study on all SCT consecutively performed in our center between 2015 and 2024. Type (PICC: peripherally inserted central catheter, NT-CVC: non-tunneled central venous catheter, T-CVC: tunneled central venous catheter and TI-VAD: totally implanted venous access device) and number of catheters were collected both at the time of transplantation and afterwards. CRBSI was

defined as definite CRBSI according to the EBMT Infectious Diseases Working Party and PHG Committee criteria (EBMT, *Clin Microbiol Infect*. 2025), which adopt the microbiological definitions of the IDSA 2009 guidelines. Only definite CRBSI episodes were included in the analysis.

Results: We included 432 patients. The median age was 56 years (2-82) and 62.3% were male. The most frequent underlying diseases were AML (37%), MDS (13%) and ALL (12%) and HCT-CI was ≥3 in 48% of patients. Myeloablative conditioning was used in 51.6% patients, the most common donor was HLA matched unrelated 10/10 (53%) and the main stem source was the peripheral blood (59%). Most common GVHD prophylaxis was CNI+MTX/MMF in 43% of patients and PTCy+CNI+MMF in 33% of them.
A total of 694 catheters were collected. PICC was the leading option (45%) followed by jugular CVC (27%), subclavian CVC (8%), T-CVC (8%), TI-VAD (6%) and femoral CVC (4%). The main reasons for withdrawal were end of treatment (62%) and persistent fever (10%).
We identified a total of 47 definite CRBSI. The most frequent agents were Gram-positive cocci (61%), Gram-negative bacilli (33%) and others (6%). Twenty-six (55%) were caused by *Staphylococcus coagulase-negative*, 3 by *Enterobacter spp* (6%), 3 were caused by *E. coli* (6%), 1 by *S. aureus* (2%), and 1 by *P. aeruginosa* (2%). One patient died due to CRBSI.
The cumulative incidence of CRBSI at 7, 15 and 30 days since catheter insertion were 1% (95% CI 0-2), 2.4% (95% CI 1-5) and 4.7% (95% CI 3-7). CI at days 7, 15, and 30 for PICC was 0 / 0.3% / 1.5%, for NT-CVC 0.8% / 4.3% / 8.9%, for T-CVC 3.5% / 5.4% / 7.5%, and no CRBSI was observed at day 30 for TI-VAD ($p<0.01$). (Figure 1).
Among the different risk factors for CRBSI, age > 65 years HR 1.4 (1.1-1.9) $p=0.04$ and type of catheter HR 1.2 (1.1-1.4) $p<0.01$ showed statistical significance in the multivariable

analysis.



Conclusions: CRBSI remains a significant complication in SCT. PICC and TI-VAD appear to be the safest options, and its choice should be considered above other types of intravascular devices.

Disclosure: Nothing to declare.

B150

REAL-WORLD UTILIZATION AND EFFICACY OF BIOEQUIVALENT GENERIC LETERMOVIR PROPHYLAXIS IN ALLOGENEIC HSCT RECIPIENTS: PEDIATRIC SUBGROUP ANALYSIS FROM DEFENDER STUDY

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Background: Prior to introduction of Letermovir prophylaxis, Cytomegalovirus (CMV) reactivation was a major cause of morbidity and mortality among paediatric allogeneic hematopoietic stem cell transplantation (allo-HSCT) recipients. Letermovir access was an issue in India. Hence, real world data of letermovir prophylaxis in Indian paediatric patients was limited. With launch of Bioequivalent Generic Letermovir, this study is to evaluate, its real-world utilization and efficacy in Paediatric Population of DEFENDER study group.

Methods: This multicenter retrospective observational study evaluated Generic letermovir tablets (Anvimo) utilization patterns and outcomes in 101 pediatric patients who underwent allo-HSCT across 10 centers in India between Januvary 2025 and December 2025. For optimal pediatric dose, Letermovir 240 mg and 480 tablets were cut. Outcomes assessed included CMV reactivation incidence, clinically significant CMV reactivation, adverse events, and 100-day survival using Kaplan-Meier analysis.

Results: Mean age of study participants was 7.49±4 years, and mean weight was 22±10.77 kg. Primary indications included thalassemia (54.46%), sickle cell disease (14.85%), and acute leukemias (18.81%). Most patients (66.34%) were high CMV risk, with 67.33% being D+/R+ serostatus. Haploidentical transplants constituted 60.39% (32.67% T-cell depleted, 27.72% T-cell replete), while 29.70% received HLA-matched related transplants. Myeloablative conditioning was used in 82.18% of patients, and 83.17% received anti-thymocyte globulin. Letermovir was administered primarily as primary prophylaxis (95.05%) with weight-based dosing: 120 mg (55.45%), 240 mg (32.67%), and 480 mg (6.93%) (Table 1).

Dose of Letermovir in Paediatric patients	Frequency	Percentage
480 mg	7	6.93%

240 mg	33	32.67%
120 mg	56	55.45%
80 mg	1	0.99%
60 mg	4	3.96%
Total	101	100%

Median prophylaxis duration was 70 days (IQR 59-95), with 69.31% receiving planned 100-day prophylaxis. Dose modification occurred in 58.42% of cases. CMV reactivation post-transplant occurred in 23 patients (22.77%), experiencing reactivation while on letermovir prophylaxis, in 8 patients, lower CMV viral copies (Letermovir Blip) subsided in 1-2 weeks. While progression to clinically significant CMV reactivation was observed in 15 patients (14.85%). Kaplan-Meier analysis for time to CMV reactivation demonstrated a mean event-free survival of 164.5±8.0 days (95% CI: 148.9-180.2), with 85.15% of patients remaining CMV reactivation-free. Post-transplant acute GVHD occurred in 19 patients (18.81%), with one case of Grade 1. Most patients (77.23%) completed their planned prophylaxis duration. Discontinuation reasons included clinically significant CMV reactivation (4.95%), death (10.89%), physician decision (4.95%), and patient withdrawal (0.99%). Adverse events were minimal, with nausea reported in only 3 patients (2.97%). Pre-emptive therapy was required in 13 patients (12.87%), primarily ganciclovir (10.89%) and cidofovir (1.98%).

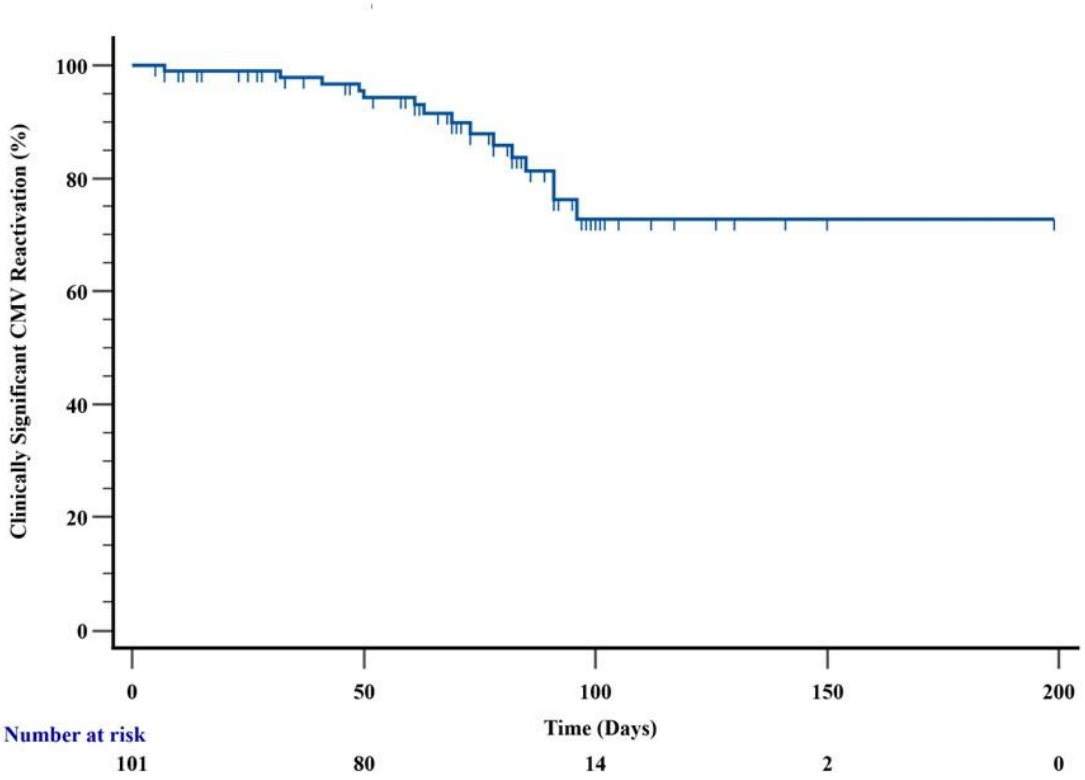

Figure 1: CMV-infection-free survival with CMV Letermovir (bioequivalent generic) prophylaxis in Paediatric Allo-HSCT patients

Conclusions: Letermovir prophylaxis demonstrated acceptable efficacy and excellent tolerability in pediatric allo-HSCT recipients, with low adverse event rates and high completion rates. Real-world data support letermovir use in pediatric transplant populations and highlight the need for individualized dosing strategies.

Disclosure: Nothing to declare.

B151

LETERMOVIR CYTOMEGALOVIRUS PROPHYLAXIS IN ALLOGENIC HEMATOPOIETIC-CELL TRANSPLANTATION: REAL-WORLD EVIDENCE FROM HIGH-ENDEMIC REGION

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Background: Cytomegalovirus (CMV) reactivation is a significant infectious complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT), contributing substantially to morbidity, graft-versus-host disease (GVHD), prolonged hospitalisation, and transplant-related mortality (TRM). Letermovir, a novel CMV terminase inhibitor, has shown remarkable efficacy as primary CMV prophylaxis in CMV-seropositive recipients; however, real-world comparative data from mixed-donor, resource-limited transplant programs are limited. Our centre introduced routine Letermovir prophylaxis in 2024. This retrospective study compares CMV outcomes, GVHD, survival, and TRM between allo-HSCT recipients who received Letermovir prophylaxis and those who did not.

Methods: We conducted a retrospective review of all CMV-seropositive allo-HSCT recipients transplanted between 2019 and 2025 at Apollo Hospital International Limited, Gujarat, India. Patients were divided into two cohorts: the Letermovir prophylaxis group (n = 17) and the non-Letermovir group, also known as the control group (n = 58). Data extracted included demographics, diagnosis, donor type, graft source, conditioning intensity, engraftment kinetics, CMV viremia episodes, clinically significant CMV infection (csCMVi), CMV recurrence, steroid-treated GVHD, overall survival (OS), and TRM. Categorical variables were compared using Fisher's exact test or Chi-square test, and continuous variables using Mann–Whitney U test. Statistical significance was defined as $p<0.05$.

Results: The groups were comparable at baseline. Letermovir prophylaxis significantly reduced early CMV events. csCMVi by week 12 was 35% vs 75.9% (p=0.004), and CMV recurrence was 12% vs 38.4% (p=0.03). Total CMV viremia episodes were markedly lower (9 vs 73). No patient on Letermovir developed CMV disease. Steroid-treated GVHD was lower (17.6% vs 34.4%). Overall survival was significantly higher with Letermovir (94% vs 62%; p=0.01), and TRM was reduced from 9% to 0%.

Conclusions: In this real-world cohort from a high CMV endemic region, letermovir prophylaxis substantially lowered the incidence of clinically significant CMV infection in high-risk allo-HCT recipients. Patients receiving letermovir showed reduced CMV infection rates at both Week 12 and Week 24, reduced CMV viremia burden, and absence of CMV disease. These findings reinforce Letermovir's role as an effective and valuable addition to antiviral prophylaxis strategies for high-risk post-transplant patients.

Disclosure: Nothing to declare.

P150

HHV-6 REPLICATION AS A RISK FACTOR FOR GRAFT LOSS IN ALLO-HSCT: A COHORT STUDY AT A REFERENCE CENTER

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Background: Reactivation of human herpesvirus type 6 (HHV-6) is a common complication in patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT). This reactivation has been linked to an increased risk of graft loss and delayed hematological recovery. Likewise, a higher incidence of graft-versus-host disease (GVHD) has been documented, suggesting a possible immunomodulatory effect of HHV-6 in the post-transplant setting.

Methods: Retrospective cohort study including all patients receiving allo-HSCT at our center in 2024, dividing them into two groups: patients with clinical suspicion of graft loss due to HHV-6 reactivation (intervention group) and patients without clinical suspicion who underwent viral load determination by the microbiology service in frozen samples obtained between days +14 and +35 post-allo-HSCT (control/blind group), therefore without clinical intervention by our HSC Transplant Unit.
The frequencies of graft loss, acute and chronic GVHD in both groups and their association with HHV-6 VL were analyzed.

Results: Forty-four patients were included, 84% with myelodysplastic syndromes (MDS)/acute leukemias (AL) and 16% with lymphoproliferative syndromes (LS), mainly males (66%) with a mean age of 53 years (range 20–71). In 23% (10/44) an HLA-identical (HLA-i) donor was used, in 27% (12/44) an unrelated donor (URD) and in 50% (22/44) a haploidentical donor.
The descriptive analysis of results according to VL +/- is shown in Table 1. Forty per cent (18 patients) had a positive HHV-6 VL in at least one determination, with a mean VL of 4709 (R 250–25267). Of these patients, 2/18 (11%) with VL+ presented primary graft failure as a complication, compared to 0/26. In the bivariate analysis, categorically defining HHV-6 VL replication, an association was found with the presence of cGVHD (OR=8) p 0.006 and a trend, although not significant, with aGVHD. No association was found with VOD, IFI or hemorrhagic cystitis.
The descriptive analysis of results by group (suspicion/control) is described in Table 1. Thirteen patients were included in the suspicion group and 31 in the control/blind group. Replication for HHV-6 was confirmed in 38.4% of the intervention group vs. 41.9% in the control/blind group. The mean HHV-6 VL in the intervention group was 2061.6 (SD = 3661.935) and 5812.67 (R 250 -25267) in the control group, with no significant differences. The specificity and PPV of the HHV-6 VL were 62% and 11% for graft loss. If we add the clinical suspicion condition and HHV-6 VL, the E and PPV rise to 72% and 40%, respectively.

Table 1. Analysis.

Analysis by viral load		
	VL +	VL -
Total	18 (40%)	26 (60%)

Average VL HHV-6	4709 (R 250-25267)	0
% Graft failure	2 (11%)	0
Days to graft	18.33 (13-26)	17.92 (14-30)
Analysis by groups		
	VL+ in supected group	VL + in control/blind group
Total	5/13	13/31
Mean VL HHV-6	2061 (R 268-8603)	5812.67 (R250-25267)
% Graft failure	2/5	0/13
Days until grafting	18 (16-22)	17.38 (13-26)
aGVHD	2/5	3/13
cGVHD	0/5	9/13
NPV VL HHV-6	100	
PPV VL HHV-6	11	
NPV VL HHV-6 and clinical suspicion	100	
PPV VL HHV-6 and clinical suspicion	40	

Conclusions: HHV-6 replication was as frequent in the group with suspected graft loss as in the control group, without being able to identify a mean HHV-6 viral load value that would indicate the risk of graft loss. In a cohort with a high prevalence of VHH-6-positive VL, the highest specificity and PPV are obtained by combining the presence of HHV-6 replication with clinical suspicion.

Disclosure: No conflict of interest.

P151

VIRUS-SPECIFIC LYMPHOCYTE THERAPY FOR PHARMACOLOGICALLY REFRACTORY VIRAL REACTIVATIONS IN PEDIATRIC IMMUNOCOMPROMISED PATIENTS: A 13-YEAR SINGLE-CENTER EXPERIENCE

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Background: Viral reactivations are a potentially life-threatening complication in pediatric immunocompromised patients, particularly following hematopoietic cell transplantation (HCT). Adoptive transfer of virus-specific lymphocytes (VSLs) has emerged as a promising therapeutic approach.

Methods: We retrospectively analyzed pediatric patients treated at the Giannina Gaslini Institute (Genoa, Italy) between 2012 and 2025 who received parental- or third-party–derived VSLs for viral reactivations due to cytomegalovirus (CMV), Epstein–Barr virus (EBV), adenovirus (ADV), or JC polyomavirus (JCV). Patients were included regardless of whether they had undergone HCT or were immunocompromised due to other conditions.
All patients had previously received at least one line of antiviral pharmacologic therapy without achieving adequate virological response. Clinical data, treatment characteristics, and outcomes were collected.

Results: Eighteen patients received VSL infusions for a total of nineteen viral reactivations. Underlying conditions included malignant disorders (n=8), severe combined immunodeficiency (SCID, n=3), congenital bone-marrow failure syndromes (n=5), acquired aplastic anemia (n=1), and mucopolysaccharidosis type I (n=1). Seventeen patients had undergone allogeneic HCT; three required a second transplant for graft failure. One patient with SCID received VSLs without prior HCT. Among patients undergoing more than one transplant, all but one developed viral reactivation after the second procedure. One patient developed viral reactivation after the first transplant, and the viremia persisted after the second, with VSL infusion administered following the latter procedure.
Documented infections included adenovirus (ADV, n=10), cytomegalovirus (CMV, n=4), Epstein–Barr virus (EBV, n=2), JC polyomavirus (JCV, n=1), and one ADV/CMV co-infection (n=1). Eleven patients received a single infusion, one received two separate infusions—one anti-ADV and one anti-CMV—and three patients received two infusions each; three additional patients received four infusions each. In total, 31 VSL infusions were administered. Thirteen products were third-party–derived and eighteen were family-donor-derived; twenty-five were manufactured in Pavia and six in Genoa.
The median time from first documented viremia to the initial VSL infusion was 27 days (mean 52.2 days). The median first-dose infusion was 2×10^5 cells/kg (mean 5.1×10^5 cells/kg).
At last follow-up, nine patients were alive and nine had died. Five deaths were attributable to

adenovirus. The remaining four deaths were unrelated to viral replication: among these, three patients had achieved complete viral clearance following VSL infusion, whereas one remained CMV-positive and died of bacterial sepsis (Table 1).
Among patients treated for adenovirus infection, those who achieved viral clearance (6/11) received their first VSL infusion after a mean of 13 days (range: 8–15), whereas the five

patients who died received VSLs later, with a mean interval of 42 days (range: 14–122).

	Sex	TCE	2°TCE	Virus	Time from dection of viremia to VSL infusion (days)	>1 infusion of VSL	Viral clearance	Cause of death, where applicable
Pt 1	F	Haplo αβ/CD19 -depl		ADV	122		NO	ADV
Pt 2	M	Haplo αβ/CD19 -depl	YES MUD	ADV	30		NO	ADV
Pt 3	M	MUD		ADV	15		YES	
Pt 4	F	UCB		ADV	30		NO	ADV; HHV6
Pt 5	M	MUD		ADV	18		YES	
Pt 6	F	Haplo PTCy		ADV	10		YES	
Pt 7	M	-	-	ADV	14		NO	ADV
Pt 8	F	Haplo PTCy		ADV	14		YES	
Pt 9	M	Haplo αβ/CD19 -depl		ADV	14	YES	NO	ADV
Pt 10	F	Haplo αβ/CD19 -depl		ADV	14	YES	YES	
Pt 11	M	MUD		ADV	8		YES	Sepsis
				CMV	90		NO	
Pt 12	F	MUD		CMV	30	YES	YES	
Pt 13	F	Haplo PTCy		CMV	165	YES	YES	Relapse of LMA
Pt 14	M	MUD		CMV	24		YES	
Pt 15	M	MUD	YES Haplo αβ/CD 19	CMV	13		YES	Pulmonary insufficiency due to DC
Pt 16	F	UCB	YES Haplo PTCy	EBV	15		YES	Graft failure
Pt 17	M	MUD		EBV	220	YES	YES	
Pt 18	M	Haplo αβ/CD19 -depl		JC	46	YES	YES	

Conclusions: VSL infusion showed encouraging effectiveness, achieving complete viral clearance in 13 of 19 cases (68.4%) of refractory viral reactivations. Adenovirus infection was associated with the highest mortality (5/18, 27.8%), particularly among patients who received VSLs later. These findings underscore the importance of early availability and timely administration of VSLs in patients who fail to respond to conventional therapies.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

P152

PREDICTIVE BIOMARKERS OF SARS-COV-2 VACCINE SEROCONVERSION IN PATIENTS WITH HAEMATOLOGICAL MALIGNANCIES

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Background: SARS-CoV-2 vaccination is crucial in protecting against severe COVID-19 disease, however, patients with haematological malignancies (HM) respond poorly to vaccination due to immunosuppression driven by chemotherapy, targeted cell depletion and immune dysregulation. We sought to define novel biomarkers that predict for effective vaccination in patients with HM.

Methods: HM patients and healthy controls received SARS-CoV-2 vaccines and were followed for six months post vaccination. Virus-specific humoral and cellular immune response were analysed in serum and whole blood pre-and post-vaccination and serum proteomics analysed pre-vaccination to identify potential biomarkers for vaccine response. 24 participants were included who had any haematological malignancy and have received treatment with a range of therapies including B-cell targeted therapy and both autologous and allogeneic haematopoietic stem cell transplantation.

Results: HM patients displayed delayed antibody seroconversion and 37.5% failed to seroconvert. Baseline proteomic and cellular immune profiles revealed T cell associated chemokines CXCL13 and CRTAM were differentially expressed, with increased levels seen in vaccine responders. Vaccine response was also associated with a reduced frequency of circulating monocytes, greater numbers of B cells and a trend toward greater numbers of CD4+ helper cell phenotypes including T peripheral helper cells pre-vaccination. *In vitro* generation of COVID--specific T cells from a subset of participants showed increased cytotoxic CD4+ and CD8+ T cell activity in seroconverters and dysfunctional COVID specific T cell responses in non-seroconverters.

Conclusions: These results demonstrate that in addition to expected decreased humoral immune responses to vaccination, a proportion of HM patients have impaired T cell immunity, and circulating serum CXCL13 and CRTAM may predict for successful seroconversion, permitting identification of a group of at-risk patients who would benefit from alternative COVID prophylaxis strategies.

Clinical Trial Registry: ACTRN12621000538842

Disclosure: ASH has previously received honoraria from Astra-Zeneca.

P153

EARLY INFECTIOUS COMPLICATIONS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: MICROBIOLOGICAL PROFILE AND ANTIMICROBIAL RESISTANCE PATTERNS

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Background: Early infectious complications remain a major source of morbidity after hematopoietic stem cell transplantation (HSCT), with antimicrobial resistance posing an increasing challenge in the early post-transplant period.

Methods: This single institution study retrospectively analyzed early infectious complications during the index post-transplant hospitalization focusing on microbiological isolates, antimicrobial resistance patterns, and catheter-associated infections.

Results:

A total of (n = 112) patients were included in the analysis. Neutropenic fever occurred in (n=96, 85.7%) of patients, of which 74 (77.08%) underwent auto-HSCT, whereas 22 (22.92%) received an allogeneic transplant. In this cohort (n = 96), multiple myeloma was the most frequent diagnosis, accounting for 40 cases (41.67%). This was followed by mantle cell lymphoma with 11 cases (11.46%), acute myeloid leukemia with 9 cases (9.38%), and acute lymphoblastic leukemia, including precursor B-cell and other variants, with 8 cases (8.33%).

Microbiological documentation was obtained in 16 (16.67%) patients. Among documented isolates, Gram-negative bacteria predominated, accounting for approximately 60% of positive cultures, followed by Gram-positive bacteria (6.8%). The most frequently isolated pathogens were Escherichia coli (3.9%), Pseudomonas aeruginosa (1.9%), and Staphylococcus epidermidis (4,82%). Carbapenemase-producing organisms were identified in approximately 2–3% of isolates.

Among 22 infectious episodes with sufficient clinical information to assign an infection source, a focus was identified in 45.5%, most frequently catheter-related infections (27.3%) and gastrointestinal infections (18.2%), while primary bacteremia without an identifiable focus accounted for 45.5% of cases. The remaining episodes corresponded to other or unspecified infection sources. The median time from onset of fever to initiation of antibiotic therapy was 20 minutes (IQR 15–30), reflecting early antimicrobial treatment in most episodes. Kaplan–Meier analysis showed a median time to neutropenic fever of 14.9 days (SD=4.88).

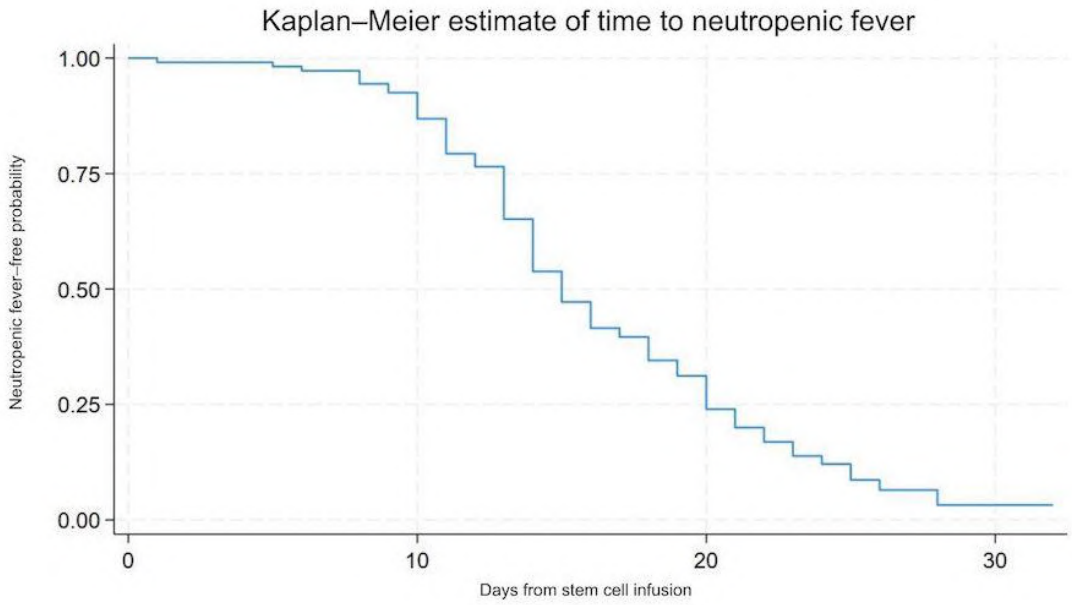

Table 1. Microbiological findings and infectious foci in early post-transplant infections

Category	Variable	Frequency / %
Microbiological documentation	n	16 (23.3%)
	Escherichia coli	4 (3.9%)
	Pseudomonas aeruginosa	2 (1.9%)
	Staphylococcus epidermidis	5 (4.8%)
	Staphylococcus hominis	1 (0,9%)
	Klebsiella pneumoniae	1 (0,9%)
	Serratia marcescens	1 (0,9%)
	Enterobacter cloacae	1 (0,9%)

Table 1. Microbiological findings and infectious foci in early post-transplant infections

Combined infections	Escherichia coli + Pseudomonas aeruginosa	1 (0,9%)
	Klebsiella pneumoniae + Streptococcus agalactiae	1 (0,9%)
Resistant microorganisms	Escherichia coli IRT	1 (0,9%)
	Multiresistant KPC + Staphylococcus epidermidis	1 (0,9%)
	Multiresistant KPC	1 (0,9%)
Infectious focus	n	22
	Catheter-associated infection	6 (27.3%)
	Gastrointestinal infection	4 (18.2%)
	Primary bacteremia (no identifiable focus)	10 (45.5%)
	Other / unspecified source	2 (9.1%)

Conclusions: Early post-transplant infections were frequent in this real-world cohort, with a high incidence of neutropenic fever occurring early after transplantation. Microbiological documentation was obtained in a minority of cases, predominantly involving Gram-negative pathogens, with a low but relevant proportion of carbapenemase-producing organisms. Catheter-associated infections and primary bacteremia without an identifiable focus accounted for most documented infectious episodes, highlighting the heterogeneity of early infectious complications following hematopoietic stem cell transplantation.

Disclosure: Beatriz Wills: Consultancy with Johnson, Pfizer, Astrazeneca and Roche, grants with BMS, speaker for Abvie.

P154

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN PATIENTS WITH HIGH-RISK ACUTE LEUKEMIAS AND HIV INFECTION

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) serves as a curative therapy for acute leukemias and holds potential for curing HIV infection. Five patients achieved HIV cure through allo-HCT from donors with homozygous CCR5 gene mutation. In 2024-2025, two cases of HIV cure resulted from allo-HCT from donors without homozygous mutation (Sáez-Cirión, A., et al. 2024; Gaebler, C., et al. 2025), that's raising questions about cure mechanisms while risking unwarranted optimism. Experience with allo-HCT in HIV patients remains limited to case reports and series; this study presents the largest to our knowledge single-center experience in patients with HIV and acute leukemias.

Methods: From 2010 to 2025 at the RM Gorbacheva Research Institute 14 allo-HCTs were performed in 10 adult HIV-infected patients (median age of 36 years (25-59)) with high-risk acute leukemia. Indications included acute myeloid leukemia (AML) in 6 (60%), including 2 secondary AML, acute lymphoblastic leukemia (ALL) in 3 (30%), including one T-ALL and mixed-phenotype acute leukemia in 1 (10%). Three patients (30%) lacked remission at allo-HCT; hepatitis C co-infection occurred in 5 (50%). Median follow-up was 5 months (1-191), and 79 months (7-191) for survivors. Allo-HCT characteristics appear in Table 1. The study reports key allo-HCT outcomes, including one antiretroviral therapy (ART) discontinuation case.

Table 1. Characteristics of Allo-HCT in patients with high-risk acute leukemias and HIV

First allo-HCT	n=10
Donor type: MUD / MMUD / MRD / haploidentical	4 / 3 / 2 / 1
Donor CCR5 mutation status: Wild type / wt	4
Donor CCR5 mutation status: CCR5 heterozygote	3
Donor CCR5 mutation status: Unknown	3
Conditioning regimen: FluBu10 / FluBu8 / FluMel140	6 / 3 / 1
GVHD prophylaxis with ATG-based + CsA + MMF ± Maraviroc	2
GVHD prophylaxis with PTCy-based + Tacro + MMF ± Maraviroc/Ruxo	6
GVHD prophylaxis with No ATG/PTCy + CsA + Mtx/Tacro + MMF	2
Second allo-HCT	3

Third allo-HCT	1

Results: Median HIV-infection duration at allo-HCT was 89 (25-59) months. Nine patients received ART with suppressed viral load; median CD4 count was 281 cells/µl (77-1178). Graft failure occurred in 2 patients (20%) after first allo-HCT but succeeded engraftment after second. Acute GVHD affected 2 patients (20%, grades 2-3: skin, GI); localized chronic GVHD occurred in 1 (10%). One-year non-relapse mortality was 30% (95% CI 7.1-57.8%). Five patients either relapsed or showed disease progression (50%). Overall 10-year survival reached 50% (95% CI 18.4-75.3%). One patient post-allo-HCT from heterozygous CCR5 donor and Maraviroc GVHD prophylaxis discontinued ART after 8 years and HIV antibody loss (immunoblot); HIV rebound registered in 2 months and leukemia relapse in 6 months. Second remission was achieved and second allo-HCT (also from heterozygous CCR5 donor) have been performed, but patient died after anti-CD123 CAR-T and third allo-HCT without remission.

Conclusions: Allo-HCT outcomes in high-risk acute leukemias with HIV comparable with general patient cohorts. ART discontinuation, even post-allo-HCT from heterozygous CCR5 donors associated with risks of HIV rebound and leukemia relapse.

Disclosure: All authors are nothing to disclosure.

P156

REAL-WORLD UTILIZATION, CMV REACTIVATION OUTCOMES AND SURVIVAL ANALYSIS OF BIOEQUIVALENT GENERIC LETERMOVIR PROPHYLAXIS IN INDIAN ALLOGENEIC HSCT RECIPIENTS: DEFENDER STUDY

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Background: CMV reactivation is a major cause of morbidity and mortality following allogeneic hematopoietic stem-cell transplantation (allo-HSCT). While Letermovir prophylaxis has significantly reduced CMV incidence, real-world outcomes in generic bioequivalent formulations remain under-reported, especially from resource limited settings. This multicenter study evaluated utilization patterns and CMV outcomes following generic Letermovir prophylaxis in India.

Methods: A retrospective multicenter cohort consisting of 156 allo-HSCT recipients receiving Letermovir prophylaxis was evaluated. Primary endpoints were incidence and timing of CMV reactivation and patterns of Letermovir utilization. Secondary endpoints included safety and discontinuation by Day+100. Statistical analysis included Kaplan–Meier survival for time to CMV reactivation and subgroup analyses by HSCT donor type and CMV risk in HSCT patients.

Results: The study analysed 156 patients who received Bioequivalent Generic Letermovir Prophylaxis post-hematopoietic stem cell transplantation (HSCT) of which 101 were pediatric patients and 55 were adult patients. Hemoglobinopathies (Transfusion dependent thalassemia and sickle cell disease) (54.5%) were the most common indication in Pediatric patients and AML (49.1%) was the most common Indication in adults. Most patients received primary prophylaxis (96.15%), with doses predominantly 240 mg (37.18%) and 120 mg (35.90%) in pediatric cohort. Sixty-one (39.1%) patients received cut or crushed tablets as only available SKU of Generic Letermovir is 240 and 480 mg tablets. A majority were high-risk for CMV (58.97%) as per established criteria.

Demographic Parameters: (n=156)	Adult Patients (n=55)	Paediatric Patients (n=101)
Age (Years) (Mean ± SD)	39.40 ± 15.7	7.49 ± 4
Weight (Kgs) (Mean ± SD)	64.83 ± 11.73	22 ± 10.77
HLA compatibility	Frequency	Percentage (%)
Haploidentical TCR	53	33.97%
HLA-matched Related	49	31.41%
Haploidentical TCD	39	25%
HLA-matched Unrelated	15	9.61%
Risk of CMV: High Risk	92	58.97
Risk of CMV: Low Risk	64	41.03%

Table 1: Demography and Clinical Parameters

Median duration of Letermovir use was 73 days (IQR 54.25–99), and incidence of CMV reactivation was 15.38%. None of the patients developed CMV disease. As on 06-12-2025, Kaplan–Meier analysis showed a mean CMV-infection-free survival of 173.2 days (95% CI: 160.2–186.1), with no statistically significant differences between CMV risk categories or donor types (Figure 1). Adverse events were rare (nausea 1.92%, vomiting 1.92%), and Letermovir discontinuation due to toxicity was infrequent (1.28%). Most patients discontinued prophylaxis after completion of the planned 100 days duration (76.28%).

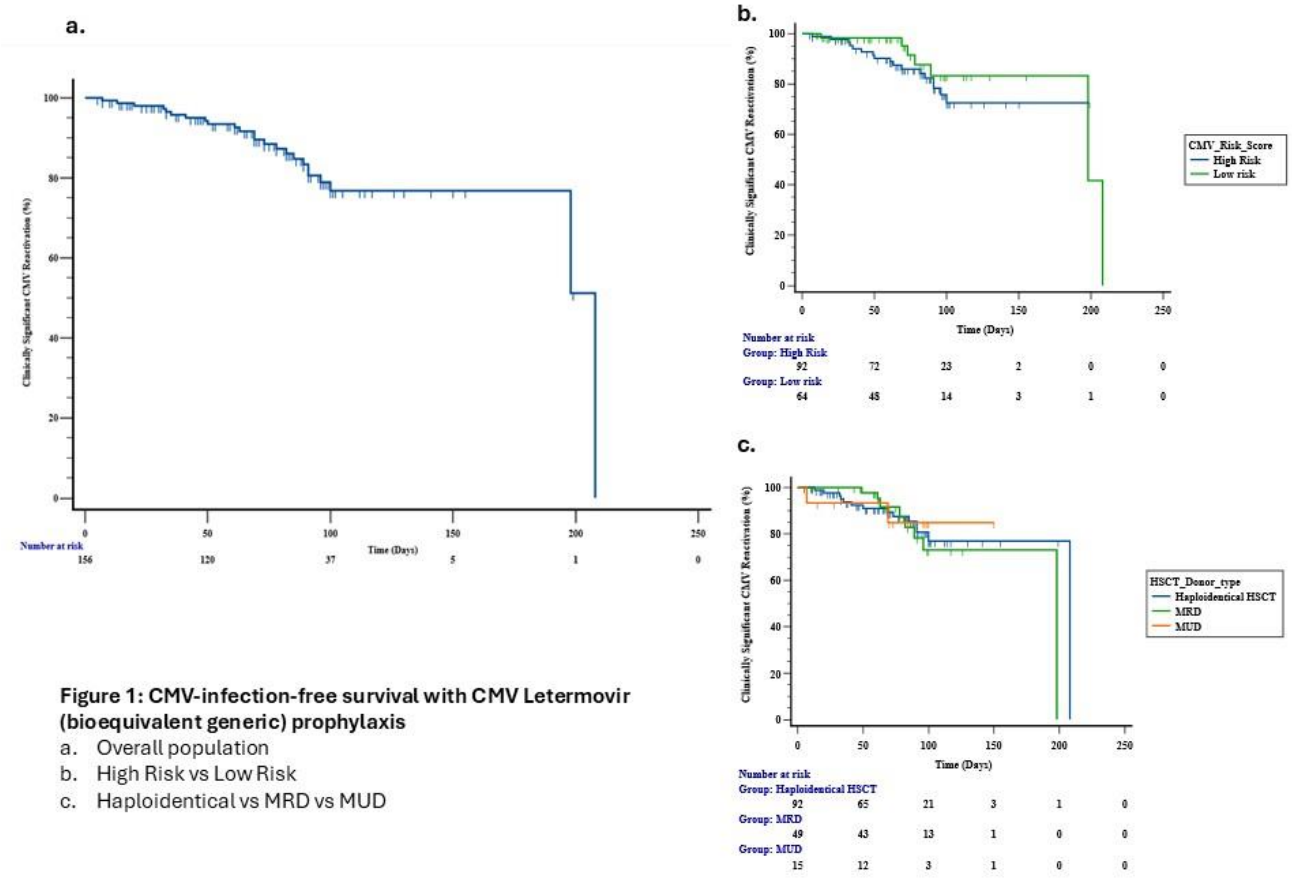

Figure 1: CMV-infection-free survival with CMV Letermovir (bioequivalent generic) prophylaxis

a. Overall population
b. High Risk vs Low Risk
c. Haploidentical vs MRD vs MUD

Conclusions: Real-world use of bioequivalent generic Letermovir demonstrates high tolerability, favourable CMV-infection-free survival, low breakthrough infection rates, and excellent adherence across varied transplant settings in India. These findings support its continued integration into routine CMV prophylaxis strategies for allo-HSCT recipients.

Disclosure: Nothing to declare.

P157

DECOLONIZATION OF MULTIDRUG-RESISTANT BACTERIA BY FECAL MICROBIOTA TRANSPLANTATION IN A PATIENT BEFORE ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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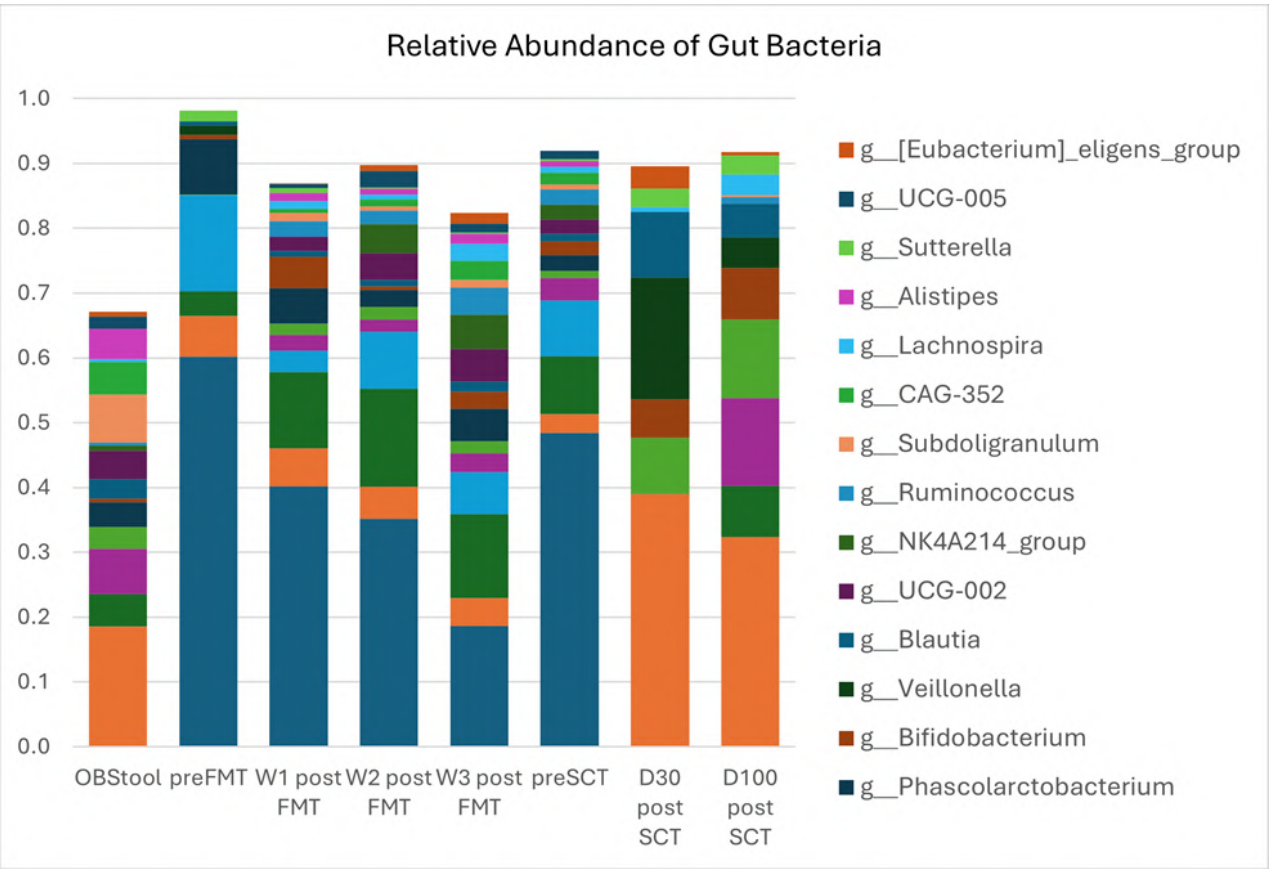
Background: The gut microbiome is adversely affected by chemotherapy and antibiotics in patients undergoing hematopoietic stem cell transplantation (HSCT). Due to limited antibiotic options, multidrug-resistant organism (MDRO) infections are associated with high non-relapse mortality after HSCT. A few small cohort studies have reported successful fecal microbiota transplantation (FMT) to decolonize MDROs in immunosuppressed patients.

Methods: We describe a case report of a 63-year-old Indian male with acute myelogenous leukemia who developed infection with MDR *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* post-consolidation chemotherapy. FMT was performed pre-HCT with the intent to decolonize the gut from these MDROs. This single patient study was approved by the institutional (City of Hope) IRB. Stool was tested for blaNDM and blaOXA-48 resistance genes using a commercial assay. Stool bacterial biodiversity was analyzed using 16s ribosomal DNA sequencing. Both testing was performed once prior to FMT, weekly after FMT until HSCT, and on day 30 and day 100 post-HSCT.

Results: The patient came to our center for treatment of AML, after undergoing induction chemotherapy in India. His course was complicated by Klebsiella pneumoniae carbapenemase (KPC)-producing *Klebsiella pneumoniae* bacteremia that was effectively treated with colistin. After receiving consolidation chemotherapy at our institution, he developed KPC-producing *Klebsiella pneumoniae* bacteremia and New Delhi metallo-beta-lactamase (NDM) and carbapenemase producing *Pseudomonas aeruginosa* bacteremia complicated by right thigh myositis, fasciitis, femoral osteomyelitis and abscess. He was successfully treated with cefiderocol and high-dose extended infusion of meropenem in conjunction with debridement of right femoral osteomyelitis/abscess. He completed 6-weeks of antibacterial therapy from surgical debridement. Upon clinical improvement and allowing for a 10-day washout period from stopping antibacterials, the patient underwent FMT on compassionate grounds. The stool product from OpenBiome stool bank was delivered via colonoscopy. Six weeks post-FMT, he underwent matched unrelated donor allogeneic HSCT using total marrow and lymphoid irradiation and cyclophosphamide conditioning and tacrolimus for graft-versus-host-disease (GvHD) prophylaxis. Cefiderocol and high-dose extended infusion of meropenem were given for neutropenic fever.
FMT was well-tolerated with mild self-resolving diarrhea soon after the procedure. No delayed adverse events were observed. Pre-FMT stool detected blaNDM and blaOXA-48 genes. Post-FMT stool pre-HSCT showed persistence of both resistance genes. On post-HSCT stool analysis, blaNDM gene on day 30 and day 100 and blaOXA-48 gene on day 100 were no longer identified consistent with eradication of MDROs. 16s ribosomal DNA sequencing of

stool showed decrease in *Prevotella* and an increase in *Faecalibacterium* and *Lachnospiraceae* between post-FMT and pre-HSCT time period. Improved stool alpha diversity was noted at day 30 and day 100 post-HSCT with an increased density of *Bacteroides*, *Veillonella*, *Blautia*, and *Bifidobacterium* species, comparable to donor stool. There was no delay in engraftment, no infectious complications post-HSCT, and no acute or chronic GvHD. The patient is doing well for 5 years post-HSCT.



Conclusions: FMT for MDRO-decolonization pre-HSCT was successful, safe, and effective in this patient with one of the longest follow-up periods reported. Given limited therapeutic options to combat MDRO infections, safety and efficacy of gut microbial restoration with FMT in patients undergoing HSCT needs to be actively explored.

Disclosure: Nothing to declare.

P158

ANTIBACTERIAL PROPHYLAXIS IN AUTOLOGOUS STEM CELL TRANSPLANTATION: CEFPODOXIME VERSUS FLUOROQUINOLONES

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Background: Patients undergoing autologous stem cell transplantation (ASCT) are at high risk for infectious complications due to profound neutropenia. Fluoroquinolones are commonly used for antibacterial prophylaxis; however, concerns regarding toxicity, drug–drug interactions, and antimicrobial resistance have increased interest in alternative agents. Oral third-generation cephalosporins such as cefpodoxime may offer a safer option. We aimed to compare cefpodoxime with fluoroquinolone-based prophylaxis in ASCT recipients using a non-inferiority design.

Methods: This retrospective, single-center cohort study included adult patients who underwent ASCT for hematologic malignancies between January 2022 and November 2025. Patients received oral cefpodoxime or fluoroquinolone-based prophylaxis (levofloxacin or moxifloxacin) according to institutional practice. Primary outcomes were duration of hospitalization and time to first febrile episode. Secondary outcomes included rates of bacteremia, site-specific infections, neutrophil and platelet engraftment times, duration of systemic antibiotic therapy, and all-cause mortality. Non-inferiority was assessed using bootstrapped mean differences (MD) adjusted for age and sex. Predefined non-inferiority margins were 1.0 days for time-dependent outcomes and 10% for infectious complications.

Results: A total of 149 ASCT recipients were included (99 cefpodoxime, 50 fluoroquinolone). Median age was 53 years, and 52% were female, with no significant baseline differences between groups. Median hospitalization duration was 21.0 days in the cefpodoxime group and 22.0 days in the fluoroquinolone group; the age- and sex-adjusted MD was −0.47 days (95% CI −1.86 to 0.92), establishing non-inferiority. Median time to first febrile episode was 3.0 versus 4.5 days, respectively, with an adjusted MD of 0.54 days (95% CI −1.73 to 0.65). Adjusted MDs for neutrophil and platelet engraftment were −0.29 days (95% CI −0.77 to 0.18) and −0.75 days (95% CI −2.25 to 0.75), respectively, meeting non-inferiority criteria. Rates of bacteremia, urinary tract, respiratory tract, and Clostridioides difficile infections were similar between two groups, with non-inferiority demonstrated for all except urinary tract infections. All cause mortality did not differ. Non-inferiority was not conclusively established for total antibiotic duration.

Conclusions: Cefpodoxime was non-inferior to fluoroquinolone-based prophylaxis for key clinical outcomes in ASCT recipients. Given increasing safety and resistance concerns related to fluoroquinolones, cefpodoxime represents a reasonable alternative in selected patients. Prospective randomized studies are warranted to confirm these findings.

Disclosure: Nothing to declare.

P159

DIAGNOSTIC VALUE OF CMV PCR ON GASTROINTESTINAL BIOPSIES IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) gastrointestinal (GI) disease remains a significant complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Diagnosis is traditionally based on histopathology and plasma CMV PCR, but the sensitivity of these approaches may be limited.
The present study aimed to evaluate the additional diagnostic value of CMV PCR performed directly on GI biopsy specimens in detecting CMV GI disease post-allo-HSCT.

Methods: A retrospective descriptive study included allo-HSCT recipients from HLA-matched sibling or haploidentical donors (January 2021 - May 2025) who underwent GI biopsy for suspected CMV GI disease. All donors and recipients were screened for CMV serology prior allo-HSCT. Monitoring CMV was assessed for all patients by quantitative RT-PCR (qPCR) in plasma (Cobas AmpliPrep/COBAS TaqMan), from engraftment until 100 days after allo-HSCT, with 61 copies/mL as the limit of detection.
Patients with suspected CMV GI disease underwent simultaneous GI biopsy sampling for both histopathological assessment and quantitative CMV PCR testing performed on the same specimen using real-time PCR (Geneproof) with limit of detection around 123 UI/ml. Concurrent plasma CMV PCR was also performed in this setting.
The histological diagnosis of CMV GI disease was based on the existence of intranuclear and/or cytoplasmic viral inclusions. Preemptive treatment was initiated when plasma qPCR ≥150 copies/mL and curative antiviral therapy was initiated upon confirmation of CMV GI disease.

Results: Thirty-nine GI biopsy were performed in 25 patients, with a median age of 30 years (range, 7 – 50 y) and sex ratio of 2.6. Undelaying diseases included AML (n=8), ALL (n=9) and others (n=8). Before transplant, 35% of patients were in CR1 and 84% had positive CMV serostatus. A total of 20% of patients received TBI-based conditioning regimen. Stem cell source was bone marrow in 84% of patients. A GVHD was observed in 92% of patients and occurred before CMV infections (reactivation/suspected CMV GI disease) in 22 cases (88%).
Histological CMV GI disease was observed in 4/39 biopsies. Tissue CMV PCR was positive in 2/4 cases (both with negative CMV viremia). Among the 35 patients without histologic CMV GI disease, tissue CMV PCR was positive in 12 cases: 11 cases showed graft-versus-host disease (GVHD; 5 with low CMV plasma viral load <150 copies), and 1 case had chemical gastritis (negative CMV viremia). Tissue CMV PCR was negative in 23 cases, including 18 with GVHD (2 with low CMV plasma viral load), 2 with gastritis/colitis, and 3 non-contributive samples (all negative CMV viremia). These results demonstrate that tissue CMV PCR can detect viral presence even in biopsies without histologic confirmation of CMV.

Conclusions: CMV PCR on GI biopsy specimens provides complementary diagnostic information beyond histopathology and plasma PCR. Incorporating tissue PCR into the diagnostic workflow may enhance detection of CMV GI infection and guide timely antiviral therapy in allo-HSCT recipients.

Disclosure: Nothing to declare.

P160

ACICLOVIR-RESISTANT HERPES SIMPLEX VIRUS IN PEDIATRIC PATIENTS UNDERGOING ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANT: A CASE SERIES

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Background: Herpes simplex virus (HSV) reactivation is a significant risk in haematopoietic stem cell transplant (HSCT) recipients and anti-viral resistance poses many clinical challenges.

Methods: We present a case series of nine pediatric patients with aciclovir-resistant HSV infection post allogeneic HSCT.

Results: Indications for HSCT included primary immunodeficiency, sickle cell disease, myelodysplastic syndrome (MDS) and relapsed/refractory leukaemia. T cell depletion was used in 5 patients (55%). Graft versus host disease occurred concomitantly in four patients (44%). All patients received aciclovir prophylaxis and were on immunosuppression at the time of HSV infection. TK mutations were the most common resistance mechanism (n= 7, 77%). Infections manifested as mucocutaneous disease, pneumonitis, keratitis, enterocolitis, and viraemia. Secondary complications included transplant-associated thrombotic microangiopathy (n=3, 33%), idiopathic pulmonary syndrome (n=3, 33%) and graft failure (n=2, 22%). All patients were treated with second-line antivirals (foscarnet and/or cidofovir), and three patients were treated with third-line antivirals (pritelivir). Treatment was complicated by nephrotoxicity (n=4, 44%). Adjunct treatments used included intravenous immunoglobulin (n=3, 33%) and donor lymphocyte infusion (n=1, 11%). Poor outcomes were seen across the cohort including death related to HSV infection and its complications (n=4, 44%).

Conclusions: Aciclovir-resistant HSV infection in pediatric HSCT recipients is associated with high morbidity and mortality, limited therapeutic options, and significant treatment-related toxicity. Early recognition, resistance testing, timely initiation of second-line therapy and weaning of immunosuppression are critical for disease control. Emerging therapies, such as helicase-primase inhibitors and adoptive T-cell therapy, hold promise but remain limited by access and pediatric data.

Clinical Trial Registry: n/a

Disclosure: Nothing to declare

P161

A BUNDLED INTERVENTION TO REDUCE RISK OF CATHETER CENTRAL LINE ASSOCIATED BLOODSTREAM INFECTIONS (CLABSIS) FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Catheter central line-associated bloodstream infections (CLABSIs) represent a major complication in allogeneic hematopoietic stem cell transplantation (allo-HSCT), with reported cumulative incidence rates varying widely from 9% to 66%. However, standardized care bundles have reported 60-70% reductions in CRBSI rates across multiple intervention studies, demonstrating that these infections are largely preventable.

Methods: We conducted a retrospective analysis CLABSIs of adult patients undergoing allogeneic HSCT between January 2024 and September 2025 at our newly established allo-HSCT program in Treviso, Italy. CLABSIs were classified according to EBMT ID Working party criteria. All patients received triple-lumen CVCs with a comprehensive CRBSI prevention bundle incorporating standard elements (hand hygiene, maximal sterile barriers, skin antisepsis, prompt catheter removal criteria). Intravenous infusions were administered through a 5-way RAMP manifold system (Fig 1a). This manifold, connected to the CVC via a 2-meter extension line and replaced every 72 hours, allowed centralized infusion management with dedicated lumens for Tacrolimus and Mycophenolate Mofetil (MMF), while the third lumen delivered all other therapies through the manifold system positioned distant from the insertion site of the patient.

Results: A total of 39 patients were included in the analysis. The median follow-up was 6 months. The median patient age was 60 years (range, 19–73). Donors were matched related (12.8%), matched unrelated (33.4%), mismatched unrelated (12.8%) or haploidentical (41%). Conditioning regimens were myeloablative, reduced intensity, or non-myeloablative in 43,5%, 36%, and 20,5% of patients, respectively. GvHD prophylaxis consisted of post-transplant cyclophosphamide, Tacrolimus, and MMF in 79.4% of patients.
Fluoroquinolone prophylaxis was not administered during the aplastic phase, as the policy of the centre. 77% of patients were colonized with antibiotic-resistant bacteria, as determined by rectal swab screening, at the time of admission.
During the hospitalisation, 84.6% of patients experienced one or more febrile episodes, where in 38.5% of these cases a microbiologically documented infection was identified.

Among these, one definite case of CLASBSI caused by *Staphylococcus epidermidis* and two probable CLABSI caused by *Staphylococcus aureus* BSI were identified. The incidence density of definite or probable CLABSI was 2.11 per 1000 patient days (95% CI 0.44-6.18). This incidence density is low relatively to previous literature reports (Fig 1 b).The median time to engraftment was 22 days, and the median length of hospitalization was 33 days. 1-year overall survival (OS) was 73.9% (95% CI: 58.6-93.2%) and 1-year non-relapse mortality (NRM) was 12.8%.

Figure 1) a. 5-way RAMP manifold system, b. CLABSI Incidence Rate (per 1000 catheter-days).

a.

Conclusions: Our newly established allogeneic HSCT program achieved a low incidence of CLABSIs through implementation of a comprehensive prevention bundle combined with a 5-way RAMP manifold system positioned distant from the CVC insertion site and changed every 72 hours. These results demonstrate that new transplant programs can achieve benchmark CLABSI prevention outcomes from inception through rigorous implementation of evidence-based strategies and innovative catheter management approaches.

Disclosure: Nothing to declare

P163

THE RELEVANCE OF PREVIOUSLY KNOWN BACTERIAL COLONIZATION IN DETERMINING THE ETIOLOGY OF BLOODSTREAM INFECTION IN HEMATO-ONCOLOGY PATIENTS: A TIMEFRAME ANALYSIS

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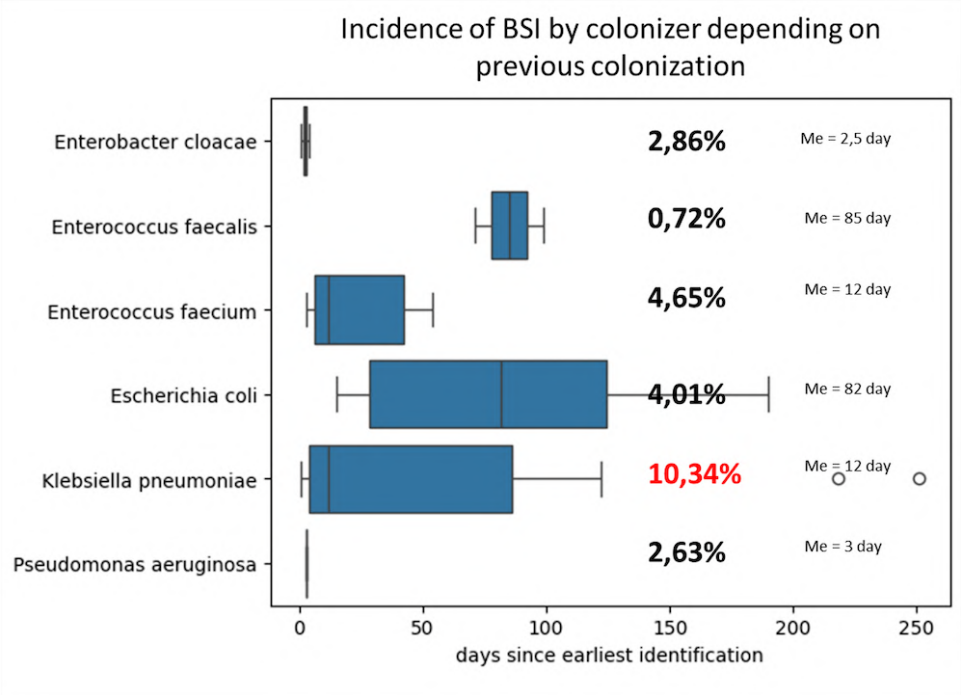
Background: Systematic microbial surveillance is currently recognized as a standard approach to guide treatment in high-risk hemato-oncology patients. Its clinical efficacy, however, is hampered by a lack of empirically defined protocols regarding monitoring frequency, optimal anatomical sampling sites, and the actionable significance of pre-existing colonization. This study aimed to delineate the timeframe of persistent colonization relevant for progression to bloodstream infection (BSI).

Methods: A retrospective analysis was performed using electronic health record (EHR) data from 373 patients of a high risk group defined by prolonged periods of Grade 4 neutropenia (>10 days) admitted to a hemato-oncology unit at a multi-specialty tertiary hospital between 01.01.2025 and 01.12.2025. During hospitalization, each patient underwent twice-weekly surveillance sampling from four non-sterile loci: rectal, buccal, and pharyngeal swabs, and a urine sample. In the event of a febrile episode, blood cultures were also obtained. The total number of bacteriological tests performed was 12,817 (urine - 3,143, buccal / pharyngeal swabs - 2,753, rectal swab - 2,582). All available microbiological data were analyzed to identify the most frequently detected bacterial species across the sampled non-sterile sites. For each confirmed bloodstream infection (BSI) episode, the first detection of the causative organism in any non-sterile site within the preceding 365 days was defined as the reference point for colonization.

Results: During the monitoring, Ac. baumannii was detected in 3.75% of patients (n=14), E. coli in 86.86% (n=324), Kl. pneumoniae in 46.65% (n=174), Enterobacter spp. in 18.77% (n=70), Enterococcus faecalis in 73.99% (n=276), Enterococcus faecium in 46.11% (n=172), Ps. aeruginosa in 10.19% (n=38), Stenotrophamonas maltophilia in 5.36% (n=20). Microorganisms of the Enterobacterales genus, as well as Enterococcus faecalis and faecium were significantly more often detected in rectal swab cultures, while Ac. baumannii and Stenotrophamonas maltophilia were more frequently detected in buccal / pharyngeal swabs, while the detection rate of Ps. aeruginosa was approximately the same for all of the loci (Table 1). A total of 41 cases of bloodstream infection were recorded during the observation period (including 3 cases of polymicrobial BSI). In patients with verified BSI, an identical pathogen was detected during the previous 2.5 to 85 days during microbiological monitoring (pathogen-specific parameters are presented in Fig). The most prominent causal inference between colonization and a BSI event appears to be observed for Kl. Pneumoniae, which may be associated with the spread of hypervirulent strains.

	Buccal swab	Rectal swab	Urine
Acinetobacter baumannii	57,14%	14,29%	21,43%
Enterobacter spp.	24,29%	68,57%	12,86%
Enterococcus faecalis	12,68%	85,14%	58,33%
Enterococcus faecium	20,35%	91,28%	30,81%
Escherichia coli	5,86%	97,53%	40,43%
Klebsiella pneumoniae	28,18%	86,21%	45,98%
Pseudomonas aeruginosa	42,11%	47,37%	31,58%
Stenotrophomonas maltophilia	45,00%	35,00%	15,00%



Conclusions: Microbiological examination of the rectal swab is the most informative method for detecting Enterobacterales. However, it should be noted that the reduction in the number

of analyzed infection loci may be due to the possibility of "missing" NGBN, which necessitates the continued need for microbiological examination of other loci. The data obtained suggest that prior colonization within the previous 2.5 to 85 days may be clinically significant, particularly in cases of Kl. pneumoniae detection (Me = 12 days), which has the highest rate of bloodstream infection detection. Further work should be aimed at determining the optimal frequency of microbiological monitoring, characterizing the virulence of identified microbial pathogens, and further improving approaches to antimicrobial therapy.

Disclosure: The authors have no potential conflict of interest to disclose.

P164

CLINICAL IMPACT OF HERPES ZOSTER INFECTION IN PATIENTS WITH PLASMA CELL DISORDERS: A RETROSPECTIVE STUDY

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Background: Multiple myeloma (MM) is a malignant plasma cell disorder that leads to bone destruction and bone marrow failure. It most commonly affects individuals between 65 and 74 years of age, with a median age at diagnosis of 69 years. Suppression of normal immunoglobulin production by the abnormal plasma cell clone results in impaired humoral immunity. The underlying immune dysfunction in plasma cell disorders predisposes patients to opportunistic infections such as herpes zoster (HZ). Approximately 10–60% of MM patients develop HZ infection, particularly after treatment with proteasome inhibitors or monoclonal antibodies if antiviral prophylaxis is not administered.

Methods: Between January 2008 and February 2025, a total of 353 patients diagnosed with multiple myeloma, amyloidosis, Waldenström macroglobulinemia, or solitary plasmacytoma in our clinic were screened. Among them, 34 patients who developed herpes zoster (HZ) infection were included in the study. The institutional database was reviewed in May 2025 to identify eligible cases for analysis.

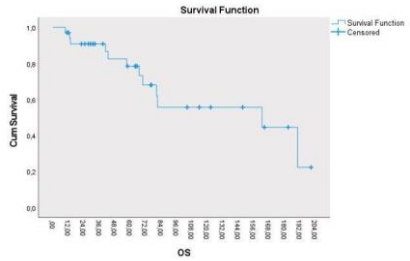
Results:

Among the patients, 76.4% had MM alone, 14.7% had amyloidosis, one had plasma cell leukemia, one had solitary plasmacytoma, and one had Waldenström macroglobulinemia (WM). The baseline characteristics of the study population are summarized in Table 1. The median age at the time of HZ infection was 60 years. Overall, 55.8% of patients had IgG-type MM and 11.7% had IgA-type MM. Regarding comorbidities, two patients had a history of solid malignancy prior to diagnosis, and two developed acute myeloid leukemia (AML) during follow-up. At the time of HZ infection, 12.9% of cases had hypogammaglobulinemia (< 4 g/L). No HZ-related mortality was observed.Two patients who were receiving primary antiviral prophylaxis developed HZ within the first four months of prophylaxis initiation. Among patients on prophylaxis, 79% received acyclovir and 21% received valacyclovir. At the last follow-up, only 26.3% of patients were still receiving antiviral prophylaxis. Acyclovir

doses ranged from 200 mg (in patients with renal impairment) to 400–800 mg, while valacyclovir was administered in varying daily doses between 500 mg and 4000 mg.Postherpetic neuralgia (PHN) developed in 54.8% of patients. Hospitalization due to HZ infection occurred in only two cases. The median time between HZ infection and initiation of prophylactic antiviral therapy was 2.5 months. The median interval between disease diagnosis and the onset of HZ infection was 9.98 months, whereas in patients who developed HZ after autologous stem cell transplantation (ASCT), the median interval was 13.08 months. Overall, 35.3% of the patients died during follow-up, with a median overall survival of 129 months. The survival curve of the study cohort is shown in Figure 1.

Characteristic	**Total (n=34)**
Median age	59 (40-89)
Age ≥60	18 (52.9%)
Sex (female)	22 (64.7%)
R-ISS stage Ⅰ Ⅱ Ⅲ Missing data	 6 (24%) 14 (56%) 5 (20%) 9
Heavy chain type IgG IgA	 19 (55.8%) 4 (11.7%)
Light chain type Kappa Lambda	 5 3
Amyloidosis IgG lambda MM + amyloidosis Lambda light chain + amyloidosis	 3 2
Comorbidities Diabetes mellitus Hypertension Secondary malignancy Pulmonary disease	 6 (17.6%) 12 (35.2%) 4 (11.7%) 3(<1%)
Corticosteroid use Additional immunosuppressive therapy	22 (64.7%) 2 (<1%)
Laboratory data at the time of HZ IgG level (g/L) Lymphocyte count (×10⁹/L) Lymphocyte/monocyte ratio Neutrophil count (×10⁹/L)	 10.51±5.53 1.99±1.04 3.31±2.69 3.97±1.96

Creatinine level (mg/dL)	1.02±0.58
CRP (mg/L)	4.76±6.42
Stem cell transplantation	26 (76.4%)
Antineoplastic exposure at the time of HZ	
Bortezomib	15 (44.1%)
Cyclophosphamide	6 (17.6%)
Doxorubicin	1
Lenalidomide	7 (20.5%)
Daratumumab	2
Ixazomib	1
Carfilzomib	3
Teclistamab	1
Observation only (no active therapy)	9 (26.5%)
Prior antineoplastic exposure (before HZ)	
Bortezomib	32 (94.1%)
Cyclophosphamide	17 (50%)
Lenalidomide	5 (14.7%)
Doxorubicin	15 (44.1%)
Daratumumab	1
Ixazomib	1
Pomalidomide	1
Chlorambucil	1
Corticosteroids	33 (97%)
No therapy	1
Site of HZ involvement	
Thoracic	10 (31.2%)
Cervical	8 (25%)
Lumbosacral	12 (37.5%)
Cranial	2
Disseminated	1
Missing data	2
Clinical severity	
Mild	2
Severe	30 (93.7%)
Missing data	2
Postherpetic neuralgia	17 (54.8%)
Missing data	3
Secondary prophylaxis	17 (50%)
Primary prophylaxis	2
No prophylaxis	15



Conclusions: The interplay between immune deficiency, recurrent infections, drug resistance, and disease progression underscores the need to further investigate prophylactic and immunotherapeutic strategies in MM. As MM requires long-term management, minimizing toxicity and improving quality of life should remain the main goals. The retrospective, single-center design caused missing data. Although HZ vaccines show high efficacy and safety, limited national access prevented vaccine data inclusion. Future prospective studies comparing prophylactic and vaccination approaches will help reduce morbidity and improve outcomes in MM patients.

Disclosure: Nothing to declare

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ACYCLOVIR PROPHYLAXIS FOR VARICELLA ZOSTER VIRUS REACTIVATION IN HEMATOPOIETIC CELL TRANSPLANTATION RECIPIENTS: WHAT IS THE TRULY EFFECTIVE LOW DOSE?

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Background: Autologous hematopoietic stem cell transplantation (auto-HCT) continues to have an impact on the treatment of patients with lymphoma and myeloma. *Varicella zoster* virus (VZV) reactivation is a known complication after auto-HCT. Currently, while guidelines strongly recommend the vaccination, it is an open question which acyclovir dose is beneficial. In this study, we evaluate the incidence of VZV reactivation with different doses of acyclovir prophylaxis in autograft recipients.

Methods: We retrospectively reviewed the clinical charts of 100 consecutive patients who underwent their first auto-HSCT at our institution from September 2021 and May 2025. Adult patients (>18 years) with follow-up for at least 6 months after transplantation were included in this study. SPSS 21 (Chicago, IL, USA) program was used for statistical analyses.

Results: The median age of the patients was 56.4 (19 -74). Forty-six were women, and 54 were men. Fifty-seven patients had MM, 25 had NHL, 16 had HL, 1 had AML, and 1 had APL. The median post-transplant neutrophil engraftment day was 14.5 days(min 10 – max 28).

The median follow-up period after auto-HCT was 23.6 (6-53) months. Four different doses of acyclovir were used for prophylaxis: 800 mg BID two days a week in three patients, 800 mg daily in 11 patients, 800 mg/day two days a week in 83 patients, and 200 mg three times daily in three patients. All patients who received prophylaxis for more than three months after auto-HCT were given acyclovir 800 mg/day twice a week. VZV reactivation developed in four patients whose characteristics are summarized in Table 1. Four patients had a history of shingles before auto-HCT, and none showed reactivation after transplantation. Thirty-six patients continued acyclovir prophylaxis without interruption. All of these patients were diagnosed with multiple myeloma and were receiving proteasome inhibitor therapy. Prophylaxis was discontinued in 64 patients; the median post-transplant prophylaxis duration was four months (min 3 months – max 12 months), and VZV reactivation was observed in only one of them.

Conclusions: The efficacy and safety of acyclovir/valacyclovir prophylaxis for VZV after transplantation are well established, although there is poor consensus on the dose and duration of prophylaxis. Current guidelines recommend acyclovir prophylaxis without a definite dosage. The meta-analysis of six studies with 3420 patients published by Seo et al. in 2017, the overall incidence of herpes zoster in the prophylaxis group is 7.8%. In the subgroup analysis of this study, the incidence was 15.44% in those who received prophylaxis for less than 1 year, while it was 2.1% in those who received it for at least 1 year. Another study in 2015, Kawamura et al., showed that the cumulative incidence of VZV disease after auto-HCT was 14.8% at 1 year, and after the cessation of acyclovir was 19.2%. In our study, the cumulative incidence of VZV reactivation was 4%, and the reactivation rate under prophylaxis was 8.3%, which is similar to the literature. Given the uncertain information in the literature regarding prophylactic dosage, our results are noteworthy, with similar reactivation rates and a tolerable, yet effective, lower dose.

Table 1: The characteristics of patients with VZV reactivation

Case	Age / Sex	Disease	Conditioning regimen	Neutrophil engraftment day	VZV reactivation after auto-HCT (months)	Acyclovir dose
1	58 / F	HL	BEAM	12	4	800 mg/day two days a week
2	66/ F	MM	Melphalan	16	10	800 mg/day two days a week
3	53/ F	NHL	Treosulphan-Fludarabine	11	5 (two months after cessation of	600mg/day everyday

					acyclovir prophylaxis)	
4	46/ F	MM	Melphalan	28	10	800 mg/day two days a week

Disclosure: Conflict of interest and funding: Nothing to declare.

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PERSISTING FEVER AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A CASE REPORT OF A RARE INFECTION WITH LOMENTOSPORA PROLIFICANS

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Background: Primary antifungal prophylaxis substantially reduces the overall incidence of invasive fungal infections in immunocompromised patients but is increasingly associated with breakthrough infections caused by rare, intrinsically resistant molds, such as Lomentospora prolificans. Management of invasive Lomentospora infections remains challenging due to delayed diagnosis and limited therapeutic options, resulting in mortality rates approaching 90%.

Methods: This case report describes a fatal Lomentospora prolificans infection following allogeneic hematopoietic cell transplantation (allo-HSCT) and provides a critical appraisal of the clinical measures taken and omitted, with the aim of informing future management.

Results: A 70-year-old patient proceeded to allo-HSCT due to high risk chronic myelomonocytic leukemia (CMML), characterized by ASXL1, NRAS, RUNX1, SETBP1, and SRSF2 variants, leukocytosis above 13,000/µl and more than 5% bone marrow blasts (CPSS-Mol score = 5). Cytoreductive therapy with hydroxyurea was initiated immediately after diagnosis, with no other prior antineoplastic treatment administered. Conditioning with fludarabine, thiotepa, and melphalan was started 7 months after the initial diagnosis. No neutropenic episodes were reported before transplantation. The patient received an HLA-identical unrelated male donor peripheral blood stem cell graft, with graft-versus-host disease prophylaxis comprising cyclosporine, mycophenolate mofetil, and anti-thymocyte globulin (ATG). Pre-transplant routine chest CT showed no pulmonary infiltrates or signs of fungal infection. Antifungal prophylaxis with fluconazole was started at hospital admission. On day −3, the patient developed febrile neutropenia and broad-spectrum antibiotic treatment (piperacillin/tazobactam) was initiated. Recurrent fever on day +1 led to escalation to meropenem and a switch from fluconazole to posaconazole; blood cultures

remained negative.
Under these measures, the fever persisted. On day +10, the clinical condition worsened with development of tachyarrhythmia absoluta. On day +11, increasing somnolence, pathological breathing pattern, and new oxygen requirement prompted sampling of peripheral and central blood cultures and empiric addition of linezolid and tigecycline. Repeated CT revealed new pulmonary infiltrates and the patient was transferred to the intensive care unit (ICU). As the CT suggested an invasive mold infection, Isavuconazole was started immediately.
Septic shock and progressive respiratory failure led to death on day +13. Post-mortem microbiological examination confirmed Lomentospora prolificans in blood cultures obtained on day +11. Neutrophil engraftment was not achieved prior to the patient's death.

Conclusions: Only a small number of Lomentospora prolificans cases have been reported. In this case, we describe a patient with disseminated infection, most likely originating from a pulmonary focus. The diagnosis was established post mortem, highlighting the diagnostic challenges due to the need for fungal isolation, absence of specific biomarkers and the aggressive disease course. Earlier chest imaging and consideration of bronchoalveolar lavage (BAL) might have allowed earlier detection and intervention. However, BAL is not established as routine procedure in neutropenic patients after allo-HSCT at our institution. Given the organism's intrinsic resistance to most standard antifungals, current recommendations include combination therapy with voriconazole and terbinafine as first-line treatment, combined with surgical debridement and correction of neutropenia whenever feasible. Therefore, in transplant recipients with persistent fever despite adequate prophylaxis and empiric therapy, breakthrough infection with resistant molds such as Lomentospora prolificans should be actively considered.

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All other authors declare no conflicts of interest.

P167

PULMONARY COMPLICATION AFTER ALLO-HCT WITH EBV DETECTION IN BALF – A STUDY ON BEHALF OF THE PALG

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Background: Detection of cytomegalovirus (CMV) DNA in bronchoalveolar lavage fluid (BALf) in patients with lower respiratory tract infection (LRTI) may be associated with probable CMV disease. The available literature is very inconclusive on the clinical significance and management of Ebstein-Barr virus (EBV) identification in BALf. There is increasing data

on the association between viral LRTI and further development of lung graft-versus-host disease (GVHD) with bronchiolitis obliterans syndrome (BOS) phenotype. However, *shedding of Herpesviridae* of unknown significance is often observed in LRT across various conditions.

Methods: We surveyed transplant centers affiliated with the Polish Adult Leukemia Group (PALG) to identify centers that test for EBV in BALf in patients with pulmonary complications after allogeneic hematopoietic cell transplantation (allo-HCT). The data were then retrospectively collected from 3 transplant centers.

Results: In 16 patients diagnosed with LRTI or unexplained deterioration on pulmonary function tests, EBV DNA was detected. Most patients underwent allo-HCT for acute leukemia using myeloablative conditioning regimens (12/16; 75%), and 13/16 received a T-cell-depleting component (anti-thymocyte globulin or post-transplant cyclophosphamide) as part of their immunosuppression protocol. Haploidentical donors were used in 4/16 (25%). Median EBV load in BALf was 2593 IU/mL (138-151 000) and in 4/16 (25%) patients, EBV-DNA was simultaneously present in serum with a median load of 5438 IU/mL (133-25523). Eleven patients (69%) received rituximab at a dose of 375mg/m2 weekly with a median of 3 doses (1-4). In 11/16 (69%) patients, other co-pathogens were identified in BALf, including at least two co-pathogens in 4/11 (36%).
During the post-EBV detection period, 8/16 (50%) patients developed or experienced progression of chronic GVHD (a moderate/severe form), including 4/16 (25%) with non-infectious pulmonary complication: lung GVHD in two patients (bronchiolitis obliterans syndrome; BOS) and non-BOS restrictive pulmonary pathology in the other two. Seven (43.8%) patients died, and only one death was directly related to EBV (EBV-HLH), while two deaths were caused by pulmonary infectious complications during other LRTI episodes. Patients were divided into two groups: a sole EBV and a mixed EBV group if other clinically significant co-pathogens were identified in BALf. The detailed characteristics of the groups are presented in Table 1. In the sole EBV group, a viral load >10,000 was more common: 3/5 (60%) versus 4/11 (36%) in the mixed group. The outcomes of the groups were similar regarding pulmonary complications, including lung-GVHD. Deaths related to infections were only reported in the mixed group.

Table 1. Patient characteristics in the sole EBL group versus the mixed group (with clinically-relevant co-pathogens identified in BALf)

	Patients with only EBV detected in BALf (n=5)	**Patients with co-pathogens detected in BALf (n=11)**
median age (range)	49 (19-66) years	46 (27-66) years
Sex Female/Male	1 / 4	8 / 3
Underlying disease AML/ALL MPN/MDS	 3 (60%) 0	 9 (82%) 1 (9%)

MM/HL/NHL/CLL AA	1 (20%) 1 (20%)	1(9%) 0
Anti-EBV serostatus Donor (+) Recipient (+) Donor (-) Recipient (+)	 4 (80%) 1 (20%)	 9 (82%) 2 (18%)
Conditioning regimen MAC/RTC RIC NMA	 2 (40%) 2 (40%) 1 (20%)	 10 (91%) 1 (9%) 0
Donor type MSD MUD/mMUD HAPLO **Female donors for Males** **Median age of a donor**	 2 (40%) 1 (20%) 2 (40%) 1 39 (22-56)	 3 (27%) 6 (55%) 2 (18%) 1 25 (19-56)
Source of transplant PB / BM	4 / 1	11 / 0
T-cell depleting therapy no ATG ATG PTCy	 1 2 (40%) 2 (40%)	 2 6 (55%) 3 (27%)
CMV Letermovir prophylaxis CMV reactivation Max CMV viral load	 1 (20%) 1 2700	 4 (36%) 5 596 (226-13700)
EBV **EBV reactivation in serum** EBV viral load (copies or IU/ml) **EBV in serum at the time of BAL**	 2 (40%) 1280 1 (20%)	 3 (36%) 846 (346-785406) 3 (27%)
BALf results		
EBV IU/ml **median (range)** <1000 1000-10000 >10000	 1839 (138-151000) 2 (40%) 0 3 (60%)	 2593 (146-53454) 4 (36%) 3 (27%) 4 (36%)
Other pathogens detected Bacteria Viruses	 	 5(45%) 7(64%)

Fungi More than 1 co-pathogen		4 (36%) 4(36%)
Rituximab administration Dose Number of cycles; median (range)	3 (60%) 375/m2 weekly 2 (1-4)	8 (73%) 375 375/m2 weekly 3 (2-4)
Infections after BALf EBV+ Only bacterial Only viral Bacterial and viral Fungal and viral Bacterial and fungal	3 (60%) 0 1 1 0 1	6 (73%) 2 1 3 1 0
GvHD A history of acute GVHD Chronic GVHD moderate-severe **Lung GvHD-BOS** grade **Non-BOS pulmonary complications** Other infections after BOS diagnosis	 0 3 (60%) 1 3 1 Yes Bacterial + Viral	 5 6 (55%) 1 3 1 Yes Bacterial +Viral + Fungal
Deaths cause of death • **infection** • **AML** • kidney failure	1 (20%) 1	6 (73%) 4 2

Abbreviations:
AA, aplastic anemia; ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; ATG, anti-thymocyte globulin; BAL, bronchoalveolar lavage; BALf, BAL fluid; BOS, bronchiolitis obliterans syndrome; CLL, chronic lymphocytic leukemia; CMV, cytomegalovirus; EBV, Ebstein Barr virus; GVHD, graft-versus-host disease; Haplo, haploidentical donor; HL, Hodgkin lymphoma; NHL, non-Hodgkin lymphoma; MAC, myeloablative conditioning; MDS, myelodysplastic neoplasm; MM, multiple myeloma; MPN, myeloproliferative neoplasm; MSD, matched sibling donor; MUD, matched unrelated donor; mMUD, mis-matched unrelated donor; NMA, non-myeloablative conditioning; PTCy, post-transplant cyclophosphamide; RIC, reduced intensity conditioning; RTC, reduced toxicity conditioning

Conclusions: Clinical practice regarding the management of EBV DNA detection in BALf varies among PALG transplant centers. However, in most patients with EBV DNA detected, rituximab was prescribed despite a lack of recommendations.
In patients with a multifactorial etiology of LRTI, EBV DNA detection may reflect viral shedding. However, some patients with isolated EBV DNA in BALf developed immune-mediated sequelae leading to pulmonary complications.
Therefore, well-designed prospective studies are needed to determine a potential link of EBV with pulmonary post-transplant complications and the role of rituximab in management.

Clinical Trial Registry: -

Disclosure: Nothing to declare.

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VERY EARLY-ONSET PULMONARY TUBERCULOSIS FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE REPORT

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Background: Post-transplant infections are common after allogeneic hematopoietic stem cell transplantation (HSCT), but tuberculosis (TB) is a rare opportunistic pathogen in this setting. Most reported cases of post-HSCT TB occur several months after transplant, typically 2–6 months, when prolonged immunosuppression and graft-vs-host disease (GVHD) prophylaxis heighten susceptibility. TB presenting within the first few weeks post-transplant is exceedingly rare and diagnostically challenging. This case is noteworthy for an exceptionally early onset of pulmonary TB (Day +15 post-HSCT), underscoring the need for clinicians to maintain a high index of suspicion for TB even during the immediate post-transplant aplastic phase.

Methods: Ethics committee approval (E-10840098-202.3.02-7688) was obtained from the Istanbul Medipol University Ethics Committee. Patient information was obtained from the electronic system and patient files.

Results: A 23-year-old male with T-acute lymphoblastic leukemia (T-ALL) underwent allogeneic HSCT from an HLA-matched sibling donor. Pre-transplant screening for latent TB with an interferon-gamma release assay (QuantiFERON) was negative. On post-transplant Day +8, during bone marrow aplasia, he developed high-grade febrile neutropenia unresponsive to broad-spectrum antibiotics and later antifungal therapy. By Day +14, he exhibited progressive dyspnea and imaging revealed new patchy right upper lobe infiltrates on chest CT, raising suspicion of an atypical or opportunistic pneumonia (Figure 1).

On Day +15, bronchoalveolar lavage (BAL) was performed. Conventional microbiology was unrevealing: the acid-fast bacilli smear was negative and mycobacterial cultures later showed no growth. However, a rapid PCR-based assay on the BAL fluid detected Mycobacterium tuberculosis, confirming the diagnosis of pulmonary TB. Standard four-drug anti-TB therapy (isoniazid, rifampicin, pyrazinamide, ethambutol) was initiated immediately. The patient's fever defervesced by Day +17 with marked clinical improvement and concurrent neutrophil/platelet engraftment. His course was complicated by Grade III acute cutaneous GVHD, which emerged during TB treatment and required corticosteroids, ruxolitinib and extracorporeal photopheresis for control. Notably, rifampicin's cytochrome P450 induction necessitated close monitoring and adjustment of his calcineurin inhibitor

(cyclosporine) doses to maintain adequate immunosuppression. The patient completed a full course of anti-TB therapy without significant toxicity and achieved durable resolution of TB. At last follow-up, he completed TB therapy without relapse of tuberculosis, GVHD flare, or underlying malignancy.

Conclusions: In conclusion, we report a rare very early-onset pulmonary TB occurring on Day +15 after an allogeneic HSCT for T-ALL. This case demonstrates that tuberculosis, though uncommon, can emerge even in the immediate post-transplant period. Clinicians should not dismiss TB as a cause of fever and pulmonary infiltrates during the aplastic phase, especially in patients from TB-endemic areas. Early diagnostic intervention (including bronchoscopy and molecular testing) facilitated prompt anti-TB treatment in our patient, resulting in defervescence and favorable outcomes despite concurrent GVHD. This experience reinforces the need for heightened awareness of TB in post-transplant patients and rapid diagnostic strategies to improve patient outcomes.

Disclosure: Nothing to declare.

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REAL-WORLD UTILIZATION AND EFFICACY OF LETERMOVIR PROPHYLAXIS IN ADULT ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS: SUBGROUP ANALYSIS DEFENDER STUDY

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Background: Cytomegalovirus (CMV) reactivation remains a significant cause of morbidity and mortality in adult allogeneic haematopoietic stem cell transplantation (allo-HSCT) recipients, with limited real-world data on generic bioequivalent letermovir formulations in routine clinical practice.

Methods: This retrospective observational study evaluated bioequivalent generic Letermovir (Anvimo) utilization patterns and outcomes in 55 adult allo-HSCT recipients who received letermovir for CMV prophylaxis. Data were extracted from electronic medical records of patients who received letermovir for CMV prophylaxis between January 2025 and December 2025. Primary outcomes included CMV reactivation rates and utilization patterns. Secondary outcomes assessed adverse events, drug interactions, discontinuation rates, and mortality. Statistical analysis included descriptive statistics, Chi-square tests for categorical variables, and Kaplan-Meier analysis for time to CMV reactivation.

Results: The mean age of study participants was 39.40±15.7 years and the mean weight was 64.83±11.73 kg. Median duration of letermovir therapy was 91 days (range 45-100). Patients underwent transplantation for various haematological malignancies (AML 34.55%, ALL 20.00%, MDS 14.55%, others 30.90%) with diverse HLA compatibility (haploidentical TCR 45.45%, HLA matched related 34.55%, haploidentical TCD 10.91%, matched unrelated 9.09%). Conditioning regimens included myeloablative (52.73%), reduced intensity (45.45%), and non-myeloablative (1.82%). CMV serostatus distribution was D+/R+ (58.18%), D-/R- (40.00%), and D-/R+ (1.82%), with 45.45% classified as high-risk. Letermovir was administered at 240 mg (45.45%) or 480 mg (54.55%) doses, primarily as primary prophylaxis (98.18%). GVHD prophylaxis included post-transplant cyclophosphamide (63.64%), tacrolimus (45.45%), cyclosporine (41.82%), and mycophenolate mofetil (38.18%). CMV reactivation occurred in 14 patients (25.45%), with 9 (16.36%) progressing to clinically significant reactivation while on Letermovir prophylaxis, rest had reactivation post planned primary prophylaxis with Letermovir. Kaplan-Meier analysis showed mean time to clinically significant CMV reactivation of 177.8 days (95% CI: 158.6-197.0) and median of 198 days (95% CI: 198.0-208.0), with CMV-free survival of 82.5% at day 100. Dose modification was required in 41.82%. Pre-emptive therapy was given to 25.45%: ganciclovir (14.55%), valganciclovir (7.27%), cidofovir (3.64%). Early discontinuation occurred in

25.45% due to CMV reactivation (14.55%), death (5.45%), adverse events (3.64%), or physician decision (1.82%); 74.55% completed planned duration. Adverse events were minimal (vomiting 5.45%). At day 100, 48 patients (87.27%) were alive, 1 (1.82%) alive with relapse, and 6 (10.91%) deceased. Acute GVHD developed in 32.73% (grade 1: 5.45%, grade 2: 12.73%, grade 4: 3.64%, grade unspecified: 10.91%).

Conclusions: Bioequivalent Generic Letermovir (Anvimo) prophylaxis in adult allo-HSCT recipients demonstrated favourable real-world effectiveness with low rates of CMV reactivation and clinically significant reactivation. The 100-day survival rate and low adverse event profile support the safety and tolerability of letermovir in routine clinical practice.

Disclosure: Nothing to declare

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POSTINFLAMMATORY HYPERPIGMENTATION AND ATROPHIC SCARS AFTER HERPES ZOSTER IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENT: CLINICAL CASE REPORT AND COSMETOLOGY TREATMENT OPTIONS

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Background: Infectious complications in patients after allogeneic hematopoietic stem cell transplantation (allo-HSCT) are the most frequent life-threatening issues that cause organ damage, pancytopenia, adverse outcomes and reduced quality of life.
Despite antiviral prophylaxis herpes zoster (HZ) is a common complication after allo-HSCT resulting from the reactivation of varicella-zoster virus from its latent state. Some patients suffer from post-infectious skin complications such as postinflammatory hyperpigmentation (PIH), scars and postherpetic neuralgia.
We report a clinical case of late-onset PIH and atrophic scars after HZ in patient after allo-HSCT and its treatment with cosmetology techniques that interrupted due to leukemia relapse.

Methods: 32-years old patient diagnosed with B-cell acute lymphoblastic leukemia (B-ALL) and treated with allo-HCST from haploidentical donor in 2024 in National Medical Research Center for hematology in Russia. On +180 day after allo-HSCT she developed painful localized rash (vesicles) and deep blisters affecting the thoracic dermatome and the lower third of the face. She diagnosed with HZ and treated with antiviral agents. Recovery completed within 4 weeks. Deep blisters healed with atrophic scars. The area of the skin eruption of herpes zoster became discolored.
On +1 year after allo-HSCT patient started treatment in aesthetic medicine clinic with hematologists and dermatologists. The patient was in complete remission after allo-HSCT and there were no clinical features of chronic graft-versus-host disease. Physical examination revealed PIH on the skin of the right side of the neck, right ear and the lower third of the face. In the area of the previous blisters of the HZ infection presented depigmented atrophic

scars with prominent arborizing vessels.
In scar and PIH treatment protocols we included 3 procedures of radiofrequency microneedling treatment within 3 months. Then to target hyperpigmentation and to improve the texture of the damaged skin we performed 2 procedures of broadband light therapy and 2 procedures of 1927 nm laser within 2 months. On +1.5 year after allo-HSCT we interrupted the treatment in cosmetology due to patients' leukemia relapse.

Results:

Table 1. Global Aesthetic Improvement Scale (GAIS)

Score	Description
1	Very much improved
2	Much improved
3	Improved
4	No change
5	Worse
6	Much worse

Follow-up of 5 months revealed visible improvements of PIH area like brightening of the dark spots, reducing the appearance of the arborized vessels on dermoscopy and improving scar appearance. The preliminary results of unfinished treatment are presented on the image 1 and include before/after and 3D skin imaging system photos. To evaluate the results, we utilized the Global Aesthetic Improvement Scale (GAIS) and the patients score was 3 point (improved: marked improvement in appearance from the initial condition but not completely optimal).

Conclusions: PIH and skin eruptions like scarring after HZ are not associated with the life-threatening conditions but significantly reduce the quality of patients' life. The management of PIH and scars in immunocompromised patients after allo-HSCT has no specific unified protocols but early inclusion of cosmetology treatment options should be considered more. To continue the unfinished treatment plans like collagen and hyaluronic acid filler injections, laser resurfacing of the scars the patient should firstly be treated for relapsed B-ALL.

Disclosure: Nothing to declare.

P171

HRCT LUNG FINDINGS OF HUMAN METAPNEUMOVIRUS (HMPV) IN PATIENTS WITH HAEMATOLOGICAL MALGNANCIES POST BMT: THE GREAT MIMICKER

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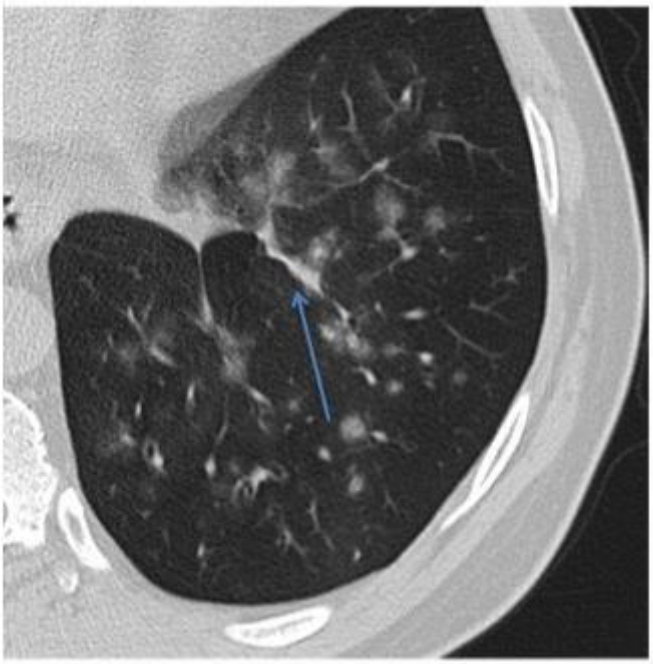
Background: Human metapneumovirus usually involves upper respiratory tract, however there are increasing cases of lower respiratory tract infection being reported, particularly in patients post BMT. Through this exhibit we aim to showcase our experience with different presentations of HMPV and its differentials.

1. To illustrate the different presentations of HMPV in lung parenchyma on CT.
2. Patterned approach to imaging clues for differential diagnosis.

Methods: We analyzed electronic medical records for microbiologically confirmed HMPV cases in patients with haematological malignancies post BMT. Inclusion criteria required a good quality HRCT scan performed within one week of confirmation. Nine patients meeting the criteria were retrospectively identified. Patient demographics, underlying malignancies, and specific HRCT patterns were recorded and analyzed by an expert radiologist.

Results: The cohort consisted of 9 patients (mean age 44.2 years, range 25–61 years), with a female predominance (67%). Radiological abnormalities were present in 7 out of 9 patients (78%). The most frequent radiological pattern was Nodules with Ground-Glass Opacities (GGOs), seen in 4 cases (44%). Other patterns included Centrilobular Nodules (2 cases), Consolidation with GGOs (2 cases), Interstitial Thickening (1 case), Bronchiolitis (1 case), and Pleural Effusion (1 case). Importantly, none of the patients demonstrated cavitation, the

halo sign, or lymphadenopathy. Two patients (22%) had no significant imaging findings.



Conclusions: HMPV infection in patients with hematological malignancies post transplant often manifests on HRCT as nodular GGOs, centrilobular nodules, or consolidation, mimicking other viral, bacterial, and opportunistic fungal infections. The absence of features like cavitation can provide subtle clues, but HMPV remains a "great mimicker" and should be included in the differential diagnosis of pneumonitis in this high-risk population.

Clinical Trial Registry: NA

Disclosure: Nothing to declare

P172

ASTROVIRUS ENCEPHALITIS STATUS POST STEM CELL TRANSPLANT

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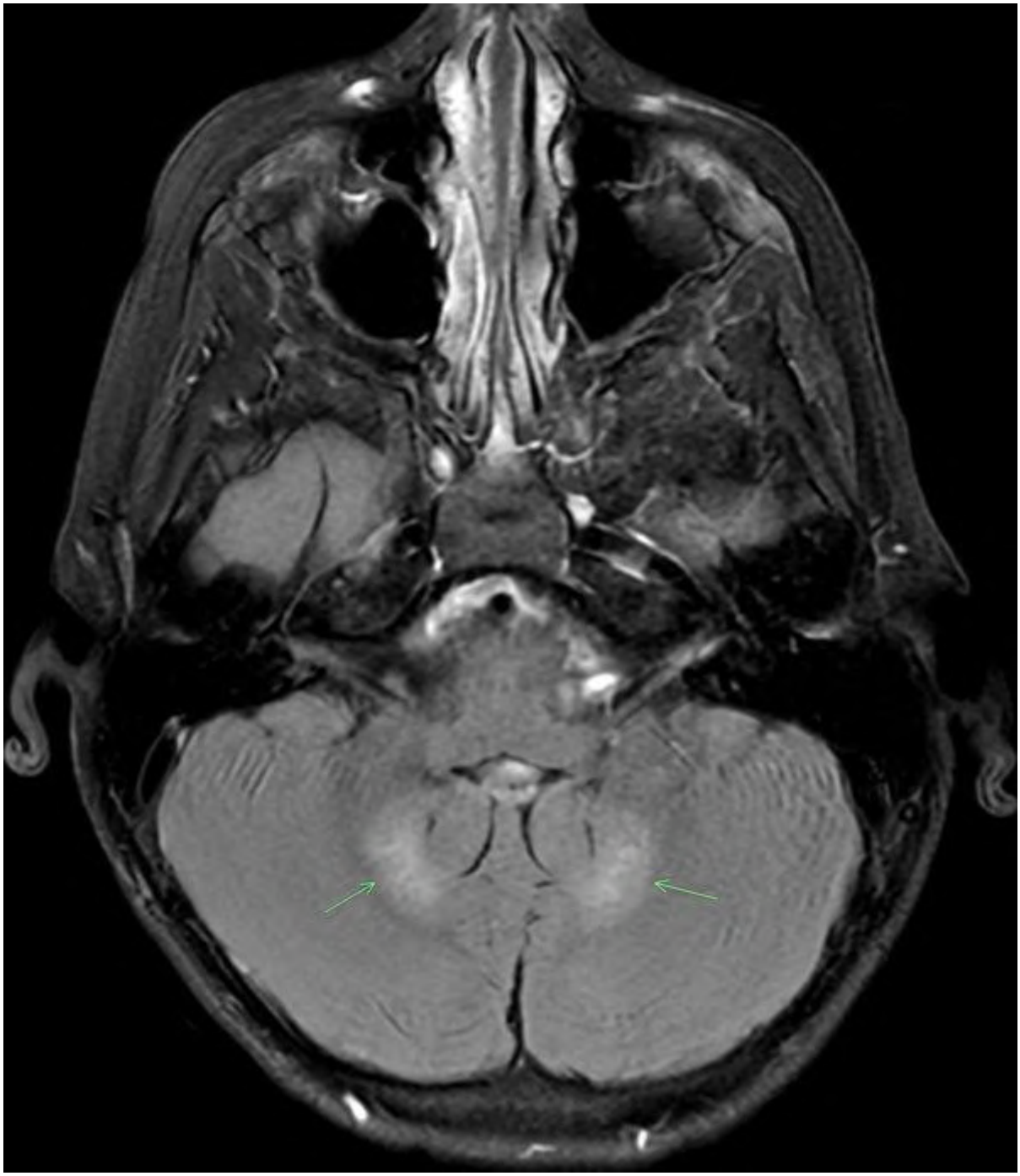
Background: Human astrovirus is classically an enteric pathogen but has emerged as a cause of severe central nervous system (CNS) disease in immunocompromised patients. Neurovirulent strains such as HAstV-VA1 are typically undetectable by standard CSF assays, contributing to diagnostic delay. Since 2010, metagenomic next-generation sequencing (mNGS) has been critical in diagnosing astrovirus encephalitis, although no standard treatment exists and reported mortality is high. We describe a child with relapsed Infantile B-

cell acute lymphoblastic leukemia (B-ALL) who developed progressive encephalopathy following haploidentical peripheral blood stem cell transplant (PBSCT) and was ultimately diagnosed with astrovirus encephalitis using mNGS.

Methods: We describe a 4-year-old boy with relapsed KMT2A-rearranged B-ALL who underwent haploidentical A/B T-cell–depleted PBSCT after bridging chemotherapy. Preparative regimen was TBI (1200 cGY), cyclophosphamide, thiotepa, and distal rabbit ATG without GVHD prophylaxis. Post-transplant complications included cytokine release syndrome, and CMV-, BK-, and adeno-viremia without GVHD.
Around day +90 post-PBSCT, the patient had increased somnolence and behavioral changes without focal deficits and was hospitalized for acute altered mental status on day +91. A complete metabolic and infectious workup and MRI/MRA were non-diagnostic. EEG showed non-specific diffuse cerebral dysfunction. After transient clinical improvement, he experienced progressive decline and was readmitted on day +102 with severe encephalopathy, mutism, bowel incontinence, decreased mobility, and upper-extremity abnormal movements.
Repeat CSF studies included cell count, protein/glucose, bacterial culture, meningoencephalitis panel, HSV PCR, adenovirus PCR, BK virus, autoimmune encephalitis panel, and mNGS. MRI with contrast was repeated. Therapies included empiric cidofovir for adenovirus viremia, and therapeutic plasma exchange (TPE) for a possible immune-mediated process.

Results:



Conventional CSF studies, PCR-based viral assays, and autoimmune testing were negative. Repeat MRI demonstrated enhancement of bilateral oculomotor, trigeminal, and facial–vestibulocochlear nerve complexes, as well as T2 hyperintensity of the dentate nuclei (Image 1) and right thalamus, consistent with infectious or inflammatory meningoencephalitis.

mNGS of CSF subsequently identified human astrovirus VA1, establishing the diagnosis. Antiviral treatments included: administrations of high-dose IVIG, ribavirin, nitazoxanide and remdesivir. Following this multi-treatment approach, neurologic deterioration stabilized and autonomic instability improved. Follow-up CSF mNGS was negative; however, clearance is difficult to interpret due to low sensitivity. The patient remains hospitalized at day+146 undergoing supportive care and continued antiviral therapy including multivirus specific T cells.

Conclusions: Astrovirus encephalitis is a rare but important cause of neurologic decline after HSCT, particularly in patients with T-cell dysfunction. Diagnosis often requires mNGS, as routine CSF testing may be negative. Early consideration of atypical neurotropic viruses is essential when evaluating unexplained encephalopathy in post-transplant patients due to the high morbidity and mortality. Combination antiviral may stabilize disease, although optimal treatment remains undefined. This case underscores the critical role of mNGS in timely diagnosis and highlights the ongoing need for evidence-based therapeutic strategies for astrovirus CNS infection in PBSCT recipients.

Disclosure: Nothing to declare

P173

NOCARDIOSIS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: DIAGNOSTIC PITFALLS, THERAPEUTIC CHALLENGES, AND DIVERGENT CLINICAL OUTCOMES—A DECADE-LONG CASE SERIES

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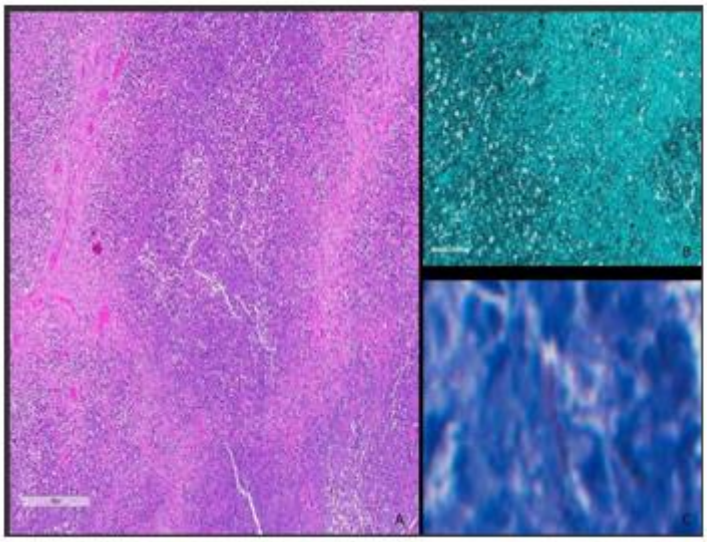
Background: Nocardiosis is a known but rare infection in stem cell transplant patients, caused by multiple Nocardia species. It has been estimated to occur in 0.3-1.7% of allogeneic hematopoietic stem cell transplant (HSCT) recipients. It is considered an opportunistic infection, and a significant risk factor is being immunocompromised. This report describes a heterogeneous group of three cases of nocardiosis over 10 years, one pediatric and two adult cases, with divergent clinical presentations, distinct Nocardia species, and contrasting treatment outcomes.

Methods: A retrospective observational study was conducted at the department of Pediatric and Adult Bone Marrow Transplant Unit between 2015 and 2024. Here we describe a case series describing three patients who developed nocardiosis post-hematopoietic stem cell transplantation: an adult male with disseminated pulmonary disease, a middle-aged woman with isolated CNS involvement, and a pediatric patient with multisystem dissemination.

Results: The patients, ranging from age 7 to 53 years of age, post stem cell transplant, in pediatric and adult stem cell transplant units, encountered Nocardiosis infection post SCT in BMT units.
-Patient 1: An adult with a T cell background, unfortunately, had graft failure, had very low counts, leading to severe Nocardiosis and PICU admission, followed by respiratory failure and death.
-Patient 2: A 44-year-old woman with refractory myeloma had an autologous stem cell transplant and later on an allogeneic stem cell transplant with myeloablative conditioning chemotherapy. The pt. had complicated CNS Nocardiosis post second SCT, confirmed with brain biopsy, successfully treated with almost one year of antibiotic therapy.
-Patient 3: A 7-year-old girl with Familial Haemophagocytic lymphohistiocytosis (HLH). She went through for the second SCT due to graft failure post-first SCT. She was later complicated with disseminated nocardiosis involving the lungs, brain, and skin, successfully cured with 18 months of antibiotic therapy.



Histological findings of brain lesion biopsy. There are multiple foci of suppurative inflammation and micro-abscess formation (A, H&E stain, 10X). GMS stain highlights numerous branching filamentous micro-organisms (B, GMS stain, 40X). Fite stain highlights filamentous rod of *Nocardia* (C, Fite stain, 60X).

Clinical details of three Nocardiosis cases after hematopoietic stem cell transplant.

	Case 1	Case 2	Case 3
Age/gender	53 years male	44 years old female	7 years
Primary diagnosis	T cell acute lymphoblastic leukemia/lymphoma	Refractory multiple myeloma	Familial Hemophagocytic Lymphohistiocytosis.
immune status	Allogenic HSCT with graft failure	Autologous and allogenic HSCT	Allogenic SCT two times

Nocardia species	Nocardia cyriacigeorgica	Nocardia Farcinica	Nocardia cyriacigeorgica
site of infection	Pulmonary (Disseminated).	CNS	Disseminated (CNS, lungs, skin)
Diagnostic methods	Blood cultures	Imagings+biospy	Imagings+biospy
anti-microbial therapy	Imipenem, amikacin, trimethoprim-sulfamethoxazole	Imipenem, moxifloxacin and trimethoprim-sulfamethoxazole	Ceftriaxone, amikacin, moxifloxacin and trimethoprim-sulfamethoxazole
Duration of therapy	10 days	12 months	18 months
Outcome	Died	survived	survived

Conclusions: This case series contributes to the growing body of evidence surrounding nocardiosis in HSCT recipients. Given the high mortality associated with it, clinicians should maintain a high index of suspicion in severe immunocompromised or heavily chemotherapy-treated patients presenting with unexplained pulmonary, skin, or neurological symptoms. Early recognition, appropriate diagnostic strategies, a multidisciplinary approach, and prompt initiation of antibiotic therapy are essential for optimizing outcomes and improving survival in high-risk populations.

Clinical Trial Registry: NA

Disclosure: Nothing to declare.

P174

LATE CYTOMEGALOVIRUS INFECTION IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS AFTER COMPLETING LETERMOVIR PRIMARY PROPHYLAXIS – A SINGLE-CENTER PRELIMINARY ANALYSIS

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Background: Cytomegalovirus (CMV) remains the most important viral pathogen in patients after allogeneic hematopoietic cell transplantation (allo-HCT). Letermovir (LTV) prophylaxis against CMV infection during the first 100 days after allo-HCT is a standard of care in

seropositive recipients. The published data regarding late CMV infection after completing LTV prophylaxis are non-exhaustive and inconclusive.

Methods: We evaluated frequency and main risk factors of any late CMV infection (CMV DNAemia and clinically significant infection-csCMVi) in 81 consecutive allo-HCT conducted in Department of Hematology, Transplantation and Internal Medicine of Medical University of Warsaw between October 2022 and March 2025 in 76 seropositive recipients who received letermovir prophylaxis until the day +100 (5 patients underwent the second allo-HCT, 4 due to relapse of underlying disease).

Results: We identified 35 (43%) CMV late infections in our cohort of transplants but the most cases demonstrated low viral load and were self-limiting. Only 6 (6/35-17%; 6/81–7%) infections were csCMVi and required antiviral therapy. Most recipients underwent allo-HCT due to acute leukaemia (AML–50, ALL–9) with use of myeloablative conditioning regimens in 59 (72%) procedures and in 73/81 (90%) transplants T-cell-depleting component (anti-thymocyte globulin or post-transplant cyclophosphamide) was applied. The median recipient age was 53 (18-72) and median donor age was 29 (18-59). Used donors were matched sibling (MSD) in 12 procedures, matched unrelated (MUD) in 56, mismatched unrelated (mMUD) in 7 and haploidentical in 6, respectively. 29 donors were CMV seronegative – in 15 patients with seronegative donor CMV late infection was diagnosed and 4 was csCMVi. CMV "blips" were diagnosed in 10 patients during LTV prophylaxis and in 5 of these patients any CMV late infection occurred but only in 1 recipient csCMVi. Median immunoglobulin G (IgG) concentration in patients with CMV late infection was 637 mg/dL (117-1829 mg/dL; normal value-700-1600 mg/dL) in comparison to 754 mg/dL (361-1587 mg/dL) in those without late infection. During follow-up, 11 recipients developed acute GvHD and 17 chronic GVHD requiring additional immunosuppressive treatment, 13 patients received ruxolitinib as a second line therapy of GvHD. In 10 of 13 (77%) patients on ruxolitinib therapy any CMV late infection was diagnosed but only in 1 was csCMVi. In 17/35 (47%) recipients with any CMV infection other viral co-pathogens were detected: EBV in 12, BKV in 3, HHV-6 in 1 and AdV in 1, respectively. Relapse of underlying disease was diagnosed in 15/76 (20%) recipients after allo-HCT and in 8 (53%) of them CMV DNA was detected.13/76 (17%) patients died and no one death was directly related to CMV late infection, but 6 (46%) recipients who died presented any CMV late infection during observation.

Conclusions: Primary anti-CMV prophylaxis with LTV substantially reduced occurrence of csCMVi within the first 100 days after allo-HCT. However, any late CMV infection after completing LTV prophylaxis (beyond day +100) is diagnosed in a significant group of recipients (43% in our cohort). Selected risk factors for this complication could be characterized but further studies are needed to determine if and in whom extending the duration of primary LTV prophylaxis is beneficial.

Disclosure: Nothing to declare.

P176

TRIAL IN PROGRESS: A PHASE 2, SINGLE-ARM, MULTICENTER STUDY OF MARIBAVIR FOR CYTOMEGALOVIRUS INFECTION IN PATIENTS WITH LYMPHOID MALIGNANCIES UNDERGOING BISPECIFIC ANTIBODIES (MALMBA)

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Background: Maribavir is an oral, highly selective antiviral agent that inhibits the CMV UL97 kinase, thereby interfering with viral DNA maturation and nuclear egress. Unlike conventional CMV agents such as ganciclovir, cidofovir, and foscarnet—often restricted by myelosuppression or renal toxicity—maribavir provides robust antiviral activity without hematologic toxicity, supporting its use in immunocompromised populations.
Bispecific antibodies (BsAbs) have emerged as an important therapeutic class in multiple myeloma (MM) and B-cell lymphomas, but their use is associated with increased infectious risk due to immunoglobulin suppression, B-cell depletion, cytopenias, and impaired cellular immunity. In MM, clinically significant CMV reactivation or infection has been reported in up to 33% of BsAb recipients, with susceptibility potentially amplified in regions with high CMV seroprevalence. In B-cell lymphomas, CMV is often mentioned as one of the etiologies of fatal infection.

Methods: This is an open-label, single arm, multicenter study conducted in Korea and registered on clinicaltrials.gov as NCT07014319.
Eligible participants are adults with lymphoid malignancies who are receiving approved or investigational BsAbs and develop clinically significant CMV infection, defined as CMV end-organ disease or plasma CMV DNA ≥500 IU/mL in two consecutive assessments accompanied by investigator determination that treatment is indicated. Patients must have adequate organ function and be able to undergo weekly virologic monitoring. Individuals with severe renal or hepatic dysfunction, uncontrolled active viral infections (HIV, replicative HBV, or HCV), pregnancy, or conditions that prevent maribavir administration will be excluded.
All participants will receive maribavir 400 mg orally twice daily from Week 1 until CMV DNA becomes unquantifiable or <500 IU/mL in the absence of CMV end-organ disease. CMV viral loads will be assessed weekly using quantitative plasma CMV DNA PCR, with additional diagnostic evaluation performed as clinically indicated for suspected CMV disease.
Primary endpoints comprise both efficacy and safety measures, including the proportion of patients achieving CMV DNA <500 IU/mL, time to reaching this threshold, and the characterization of maribavir safety based on the type, frequency, severity of adverse events and their relationship to maribavir. Secondary endpoints include the time to a >1 log10 reduction in CMV DNA from baseline, the proportion achieving such decline, and the rate of breakthrough CMV disease. CMV-specific cellular immune responses (CMV-CMI) to IE-1 and pp65 will be assessed as exploratory endpoints at screening and at end of treatment (EOT)

using a T-SPOT.CMV ELISpot assay, with interferon-γ–producing CD4+ and CD8+ T-cell spot counts quantified per 250,000 PBMCs.

Results: No data are available at this stage as the trial is ongoing.

Conclusions: No data are available at this stage as the trial is ongoing.

Clinical Trial Registry: NCT07014319

Disclosure: Nothing to declare

P177

OUTCOMES OF USING GENERIC LETERMOVIR FOR CMV PROPHYLAXIS IN HSCT: RETROSPECTIVE ANALYSIS

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Background: CMV infection remains a major cause of morbidity and mortality following allogeneic hematopoietic stem cell transplant (allo- HSCT). Antiviral prophylaxis with Ganciclovir or Valganciclovir is limited by myelosuppression. Letermovir is an effective alternative with minimal side effect profile.
We aimed to study the outcome of using generic Letermovir in allo-HSCT recipients as primary prophylaxis. Outcome was assessed based on the cumulative incidence of CMV reactivation in our study population at D+100 after HSCT.

Methods: This is a retrospective study of patients undergoing allogeneic HSCT (n=27) between March and November 2025 at Sindhu Hospitals, Hyderabad. All patients were initiated on Letermovir prophylaxis from Day+1 of transplantation and continued till D+100. Patients who died prior to engraftment were excluded. CMV viral load monitoring was done by quantitative PCR. Data was collected from electronic medical record. Statistical analyses were performed using SPSS software.

Results: Total 27 patients were enrolled in the study, including both children and adults. 14(51.8%) were children<18yrs and 13(48.1%) were adults>18yrs. There was a male predominance (M:F=18:9). Ages ranged from 10 months to 49 years. Both donor and recipient were 100% CMV IgG seropositive and CMV IgM negative. Varied spectrum of cases including Acute Leukemia (9), CML(2), Relapsed ALCL (1), Thalassemia major-Class III (6), Sickle Beta thalassemia (1), Sickle cell anaemia (1), IBMFS (2), Enzyme deficiency (1), Osteopetrosis (1), CGD (1), MPS (1) and SAA (1) were part of the study. Haploidentical HSCT predominated(n=22). Graft sources were bone marrow (3), peripheral blood stem cells (22), and combined (2). In small children, the drug was given crushed via nasogastric tube(n=5). Letermovir was dosed as per standard guidelines. CMV reactivation occurred in 8 patients(29 %). CMV copy numbers ranged from 687 to 31,00,000copies/mL, observed between days+12 and+68 post- transplant. Upon reactivation, patients were treated with anitivirals

as per guidelines. Only one mortality was noted, unrelated to CMV. There was no CMV disease or CMV related deaths in the study.

Conclusions: Cumulative incidence of CMV reactivation was marginally higher in our study compared to Western data. All patients responded well to first line Pre-emptive therapy. Time of onset of CMV reactivation was early.

Disclosure: Nothing to declare.

P178

MYCOBACTERIUM ABSCESSUS AS A COMPLICATION OF IMMUNOSUPPRESSION AFTER ALLOGENEIC STEM CELL TRANSPLANTATION FOR CONGENITAL NEUTROPENIA

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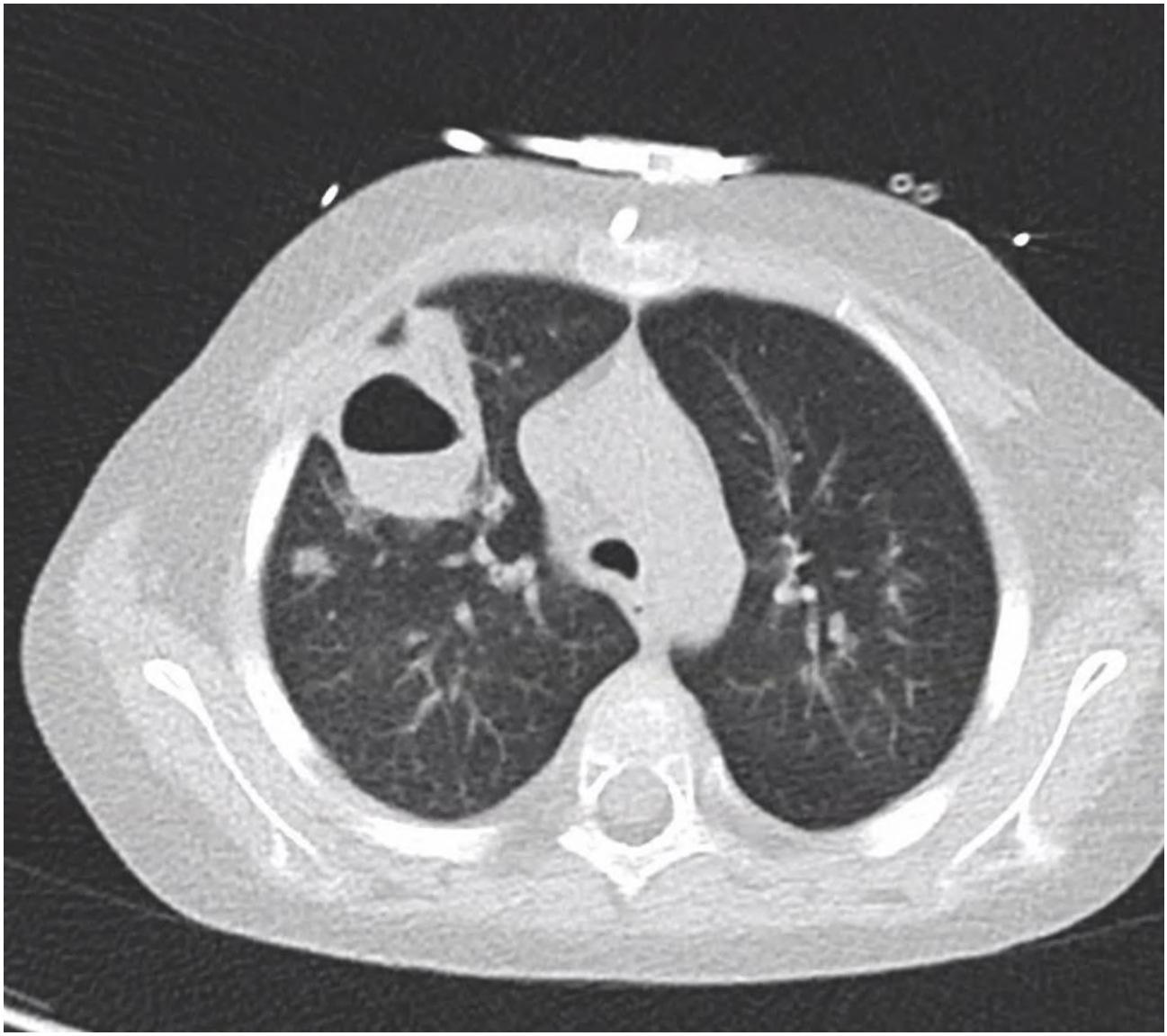
Background: *Mycobacterium abscessus* (Mabs) is a rapidly growing nontuberculous mycobacterium (NTM), commonly found in soil and water. It has an intrinsic resistance to numerous antimicrobial classes. Furthermore, it can form biofilms and survive within macrophages and thus is one of the most difficult NTMs to eradicate. These biological defenses severely limit therapeutic options and complicate standardized treatment, especially in pediatric patients.
Pulmonary disease is the most common presentation. Disseminated infection, while rare, is associated with high morbidity and mortality, particularly in patients with impaired innate and adaptive immunity. It often requires prolonged multidrug therapy and careful monitoring for drug toxicity.
Among the most vulnerable groups are patients undergoing allogeneic stem cell transplantation (allo-SCT). Prolonged neutropenia, delayed T-cell reconstitution, intensive immunosuppression, impaired mucosal barriers and frequent exposure to broad-spectrum antimicrobials create an optimal environment for opportunistic pathogens such as MAbs. Post-transplant complications, such as GvHD, viral reactivation, and fungal infection, further obscure early diagnosis, as their symptoms commonly overlap with those of NTM disease.

Methods: Here we describe a patient case of a 3-year-old boy with congenital neutropenia, due to a homozygous *CSF3R* mutation, who underwent allo-SCT with a 10/10 MUD. Diagnostic evaluation included review of microbiologic data, bronchoalveolar lavage (BAL) studies, radiographic imaging, and serial blood cultures. Clinical decision-making was undertaken by an antibiotic stewardship team to establish the diagnosis of invasive Mabs infection and to guide therapeutic management.

Results: Following early post-transplant complications, including pneumonia, CMV reactivation, and cutaneous GvHD, the patient developed progressive respiratory symptoms by day +78. These were initially attributed to pulmonary GvHD or bronchiolitis obliterans. Despite treatment with systemic corticosteroids, ruxolitinib, ibrutinib, antiviral agents, and antifungal therapy for a probable invasive pulmonary aspergillosis infection, respiratory status continued to decline.

By day +190, the patient presented with septic shock, for which invasive mechanical ventilation (IMV), fluid expansion and vasopressor therapy were required. After shock reversal and weaning off IMV he was eventually discharged home. Worsening oxygenation prompted repeat CT imaging on day +210, revealing a new 30-mm cavitary lung lesion (see figure). BAL and blood cultures were positive for *M. abscessus massiliense*, confirming invasive pulmonary disease with bacteremia.

Treatment consisted of intravenous amikacin, tigecycline, imipenem, and TDM guided azithromycin and clofazimine, in addition to ongoing antifungal therapy. Subsequently the patient showed gradual clinical improvement, with resolution of oxygen dependence and decreasing inflammatory markers. Intravenous therapy was stopped after 3 months, clofazimine and azithromycin are being continued, with a planned treatment duration of one year. During treatment he developed a severe drug-induced hepatitis. Immunosuppression was cautiously tapered, though ruxolitinib was later re-introduced for bronchiolitis obliterans. Follow-up BAL and blood cultures remained negative for Mabs.



Conclusions: This case illustrates how Mabs can emerge insidiously in pediatric alloSCT recipients, mimicking more common post-transplant complications and progressing rapidly to severe invasive infection. The patient's gradual recovery underscores the importance of early recognition, aggressive multidrug therapy, and careful reassessment of immunosuppression and toxicity. More broadly, this case highlights the urgent need for consensus-driven guidelines for managing NTM infections in immunocompromised children.

Disclosure: Nothing to declare.

P179

GRAFT REJECTION AND POOR GRAFT FUNCTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRICS: BEWARE OF PARVOVIRUS INFECTIONS

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Background: Human parvovirus B19 (Parvo) is a DNA virus. The infection has a very wide clinical presentation varying from asymptomatic, fever, erythema, arthralgia, erythroid aplasia) to severe manifestations as myocarditis, glomerulonephritis, hepatitis, vasculitis, myositis and nervous system involvement. Parvo has been detected after allogeneic hematopoietic stem cell transplantation (HCT) in association with engraftment failure and pure red cell aplasia.

Methods: We have recently included marrow Parvo PCR in the work up of poor graft function or delayed engraftment and were surprised by positive results in four patients that are rescribed in this paper.

Results: Case 1. A 4-year-old patient who underwent HLA-identical related HCT for sickle cell anemia conditioned with ATG, busulfan, and cyclophosphamide. Due to delayed engraftment,, a PCR for parvovirus was performed in the bone marrow sample and it was positive.. The patient received immunoglobulin 0.4g/kg for 5 days (IVIG) and engrafted soon thereafter.
Case 2. A 3-year-old patient who underwent unrelated HCT with HLA-B allelic mismatch for B-cell acute lymphoblastic leukemia (ALL) in second remission, conditioned with TBI 1,200cGy and etoposide 60mg/kg. Six months after the HCT, the patient presented with pancytopenia and the marrow aspirate tested positive for Parvo and improved after IVIG. Seven months post HCT, the patient had bloody diarrhea neutropenia and anemia. He tested positive for Parvo again, was retreated with IVIG and resolved all symptoms.
Case 3. A 14-year-old patient underwent Haploidentical HCT for ALL with TBI and etoposide. He had primary graft failure. The D+30 marrow was negative for minimal residual disease, had 53% donor chimerism and tested positive for Parvo PCR. Despite IVIG He remained pancytopenic and underwent a second haploidentical HCT with fludarabine, cyclophosphamide and TBI 200Gy but developed sinusoidal obstructive syndrome and died of pulmonary hemorrhage.
Case 4. A 16-year-old patient had haploidentical HCT for Ph+ ALL conditioned with TBI and Etoposide. Despite neutrophilic engraftment he remained platelet transfusion dependent,had several infections and thrombotic microangiopathy. Five months post-HCT, ParvoPCR was detected in the bone marrow. He received IVIG but has notfully recovered yet.

Conclusions: Parvo infections may have a role in poor graft function and graft failure and sis currently being prospectively studied in our patients.

Disclosure: Nothing to declare.

Non-infectious Early Complications

OS04-01

RAVULIZUMAB PLUS BEST SUPPORTIVE CARE IN PEDIATRIC PATIENTS WITH HEMATOPOIETIC STEM CELL TRANSPLANTATION–ASSOCIATED THROMBOTIC MICROANGIOPATHY: 52-WEEK RESULTS FROM A PHASE 3 TRIAL

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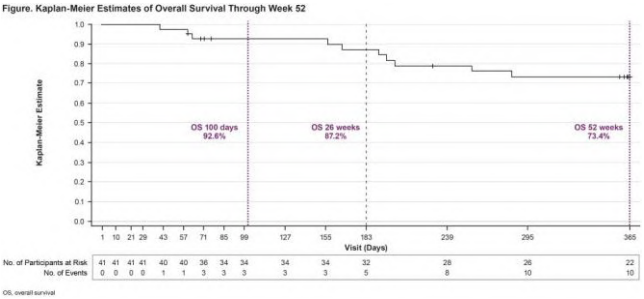
Background: Ravulizumab, a complement C5 monoclonal antibody, demonstrated efficacy and safety over a 26-week treatment period in pediatric hematopoietic stem cell transplantation–associated thrombotic microangiopathy (HSCT-TMA). Here, data up to 52 weeks are reported.

Methods: ALXN1210-TMA-314 (NCT04557735) is a phase 3, open-label, single-arm, multicenter study. Eligible patients were aged 28 days to <18 years, weighed ≥5 kg, received HSCT within the prior 12 months, and had HSCT-TMA persisting for ≥72 hours despite trigger management. Protocol inclusion criteria included proteinuria of ≥1 mg/mg. Patients received body weight–based ravulizumab plus best supportive care for 26 weeks, followed by a 26-week follow-up period with only best supportive care. The primary endpoint was protocol-defined complete TMA response (≥50% reduction in urine protein/creatinine ratio [UPCR], ≥50% improvement in platelets, and lactate dehydrogenase [LDH]

normalization with absence of schistocytes) during the 26-week treatment period. Key secondary endpoints included individual TMA response components, overall survival (OS; at day 100, week 26, and week 52), and safety (incidence of treatment-emergent adverse events [TEAEs] and serious TEAEs). Quality of life, measured by Pediatric Quality of Life Inventory (PedsQL), was assessed.

Results: Of 41 enrolled patients (mean age, 7.6 years; 51% female; 54% White), 28 (68.3%) completed the 26-week treatment period, and 24 (45.5%) completed the 52-week study. At week 26, protocol-defined TMA response occurred in 29 (70.7%) patients meeting ≥1 criterion, of which 7 (17.1%) met protocol-defined complete TMA response, and 22 (53.7%) met protocol-defined partial TMA response. Mean UPCR improved from 5.5 mg/mg at baseline (n=41) to 0.93 mg/mg at week 26 (n=21) and 0.27 mg/mg at week 52 (n=21). Mean platelets were 46,976/mm^3 at baseline (n=41; reference range lower limit of normal = 163,000/mm^3), increased to 169,000/mm^3 at week 26 (n=25), and progressively improved to 216,000/mm^3 at week 52 (n=18). Age-normalized LDH decreased from 1.6 x upper limit of normal (ULN) at baseline (n=37) to <1.0 x ULN at week 26 (n=28), which was maintained through week 52 (n=24). At week 52, 79% of patients had normal LDH. Estimated OS was 92.6% at day 100, 87.2% at week 26, and 73.4% at week 52 (**Figure**). During the 26-week treatment period, all patients experienced ≥1 TEAE (n=860), 30/41 (73.2%) reported 94 serious TEAEs, and 3 (7.3%) had serious TEAEs assessed as related to ravulizumab. During the 26-week follow-up period, 24/29 (82.8%) patients experienced ≥1 TEAE (n=178), 15/29 (51.7%) reported 27 serious TEAEs, and 2 (6.9%) had serious TEAEs assessed as related to ravulizumab. No meningococcal infections were reported, and no unexpected or new safety signals were identified. Respective [VA1] mean (SD) patient-reported and parent-reported PedsQL total score increased from 52.6 (19.2) and 50.4 (20.6) at baseline (n=32 and n=31) to 60.3 (21.3) and 57.7 (21.5) at week 26 (n=25 and n=26) and 72.2 (18.5) and 67.9 (21.4) at week 52 (n=20 and n=18).

Figure. Kaplan-Meier Estimates of Overall Survival Through Week 52



Conclusions: In this global phase 3 trial in pediatric patients with HSCT-TMA, ravulizumab treatment resulted in clinically meaningful OS of 73.4% at 52 weeks and normalization of early laboratory markers of TMA beyond 26 weeks.

Clinical Trial Registry: NCT04557735, https://clinicaltrials.gov/

Disclosure: **David Bueno-Sánchez** has served as a consultant for Alexion, AstraZeneca Rare Disease and MSD, and has received honoraria from Jazz Pharmaceuticals. **Michelle Schoettler** reports consulting and honorarium from Omeros and Alexion, AstraZeneca Rare Disease.

Christopher Dvorak has served as a consultant for Alexion, AstraZeneca Rare Disease.
Aviva Krauss has served as a consultant for Alexion, AstraZeneca Rare Disease.
Sonali Chaudhury reports consulting and honorarium from AbbVie, Alexion, AstraZeneca Rare Disease, Genetix, and Vertex Pharmaceuticals.
Tauseefullah Akhund, **Min Qin**, **Jude Fry**, and **Cory Williams** are employees of Alexion, AstraZeneca Rare Disease.
Yoshiyuki Takahashi has no conflicts of interest relevant to this study to disclose.
Sarah Lawson has served on an advisory board for Alexion, AstraZeneca Rare Disease.
Franco Locatelli has no conflicts of interest relevant to this study to disclose.

OS04-02

UPDATED INTERIM ANALYSIS-POEM MULTI-CENTER STUDY: TOWARDS A SEQUENTIAL TIME ADJUSTED RISK MODEL FOR PREDICTION OF ENDOTHELIOPATHIES POST-HCT

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Background: Pediatric patients undergoing hematopoietic cell transplantation (HCT) are at disproportionately higher risk of developing endotheliopathies including sinusoidal obstructive syndrome (SOS), transplant-associated thrombotic microangiopathy (TMA), capillary leak syndrome (CLS) and diffuse alveolar hemorrhage (DAH), with the potential for progression to pediatric multi-organ dysfunction syndrome (p-MODS) and need for critical care support (CC).

Methods: POEM (NCT05090345) is a multi-center prospective registry/biorepository. Subjects are enrolled prior to HCT and followed to evaluate the proportion who develop endotheliopathies and/or p-MODS within 100 days of HCT. Plasma is collected at baseline, day 0, and weekly for four weeks and at the time of a qualifying event (endotheliopathy/p-MODS) within 100 days of HCT; samples are interrogated to determine the proportion who develop abnormal levels of circulating angiogenic factors.

The risk of p-MODS was assessed within 7 days of HCT and weekly for 4 weeks, to dynamically evaluate organ function across 8 systems: respiratory, cardiovascular, renal, hepatic, hematologic, neurologic, immune, and gastrointestinal. Each system was graded on a 0–5 scale based on clinical and laboratory parameters, with total pMODS calculated using the worst score per organ.

Results: At the time of interim analysis, 264 subjects have enrolled across 12 centers. This report includes outcomes of 239 subjects that are $\geq$ 100 days post-HCT. Overall incidence of endotheliopathies was 13.4%.
All subjects had similar baseline p-MODS scores. Subjects who developed endotheliopathies and/or required critical care support within 30 days of HCT, had a significantly different progressive rise (with median change by 2 points) in p-MODS score starting at week 1 compared to subjects who did not (Figure 1). The median time to diagnosis of endotheliopathies was 12 (range: 2 to 94) days post-HCT and median time to critical care admission was 13 (range: -7 to 94 days).
Comparison of circulating angiogenic factors identified several factors that were significantly lower at baseline in patients who developed SOS compared to controls: CD31 ($p< .0001$), VEGF-D ($p<.0005$), EMMPRIN ($p<.005$), and Lyve-1 ($p<.005$). In contrast, at the point of SOS diagnosis, only two factors were lower in patients with SOS, BMP-9 ($p < 0.005$) and VEGF-D ($p <0.05$), while HGF ($p<0.05$) was higher in patients with SOS, at the time of diagnosis compared to controls.

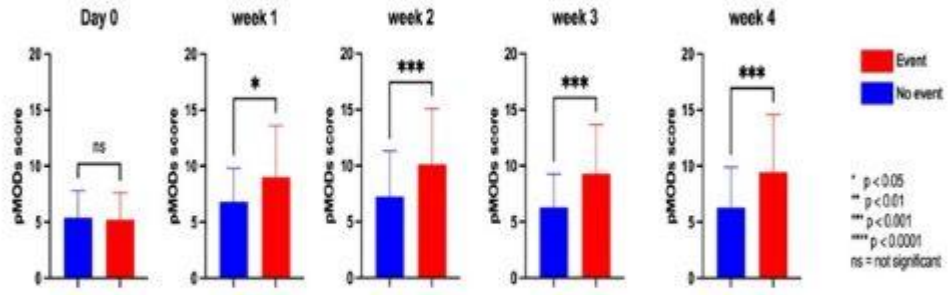

Figure 1A: Progressive rise in p-MODS scores from baseline to Week 4

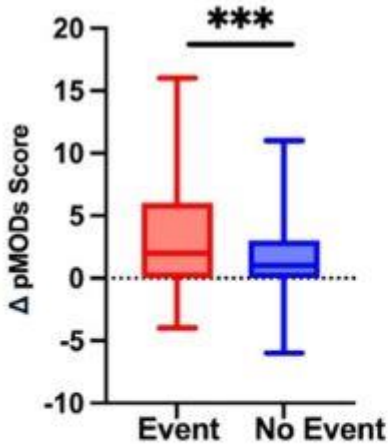

Figure 1B: Significant change in p-MODS score from baseline to Week 1 comparing subjects with events versus no events in the first 30 days post-HCT

Conclusions: Patients who develop SOS may have different circulating angiogenic factors at baseline. Angiogenic signatures may identify patients at highest risk for SOS prior to initiation of preparative regimen. A progressive rise in p-MODS score starting at week 1 post-HCT may further identify subjects at risk for endotheliopathies and clinical deterioration. Future work will validate these findings in a larger number of patients (total planned enrollment, n = 500) and will assess the predictive power of measuring CD31, VEGF-D, EMMPRIN, and Lyve-1 together at baseline in patients preparing for HCT. Characterization of circulating angiogenic factors in subjects with other endotheliopathies is planned. Sequential sample analysis and p-MODS score assessment may enhance sequential time adjusted risk propensity for endotheliopathy and critical care support.

Clinical Trial Registry: NCT05090345.

Disclosure: None.

OS04-03

ORAL IPTACOPAN DEMONSTRATES EFFICACY AS SALVAGE THERAPY FOR HIGH-RISK TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY: FIRST REAL-WORLD EXPERIENCE

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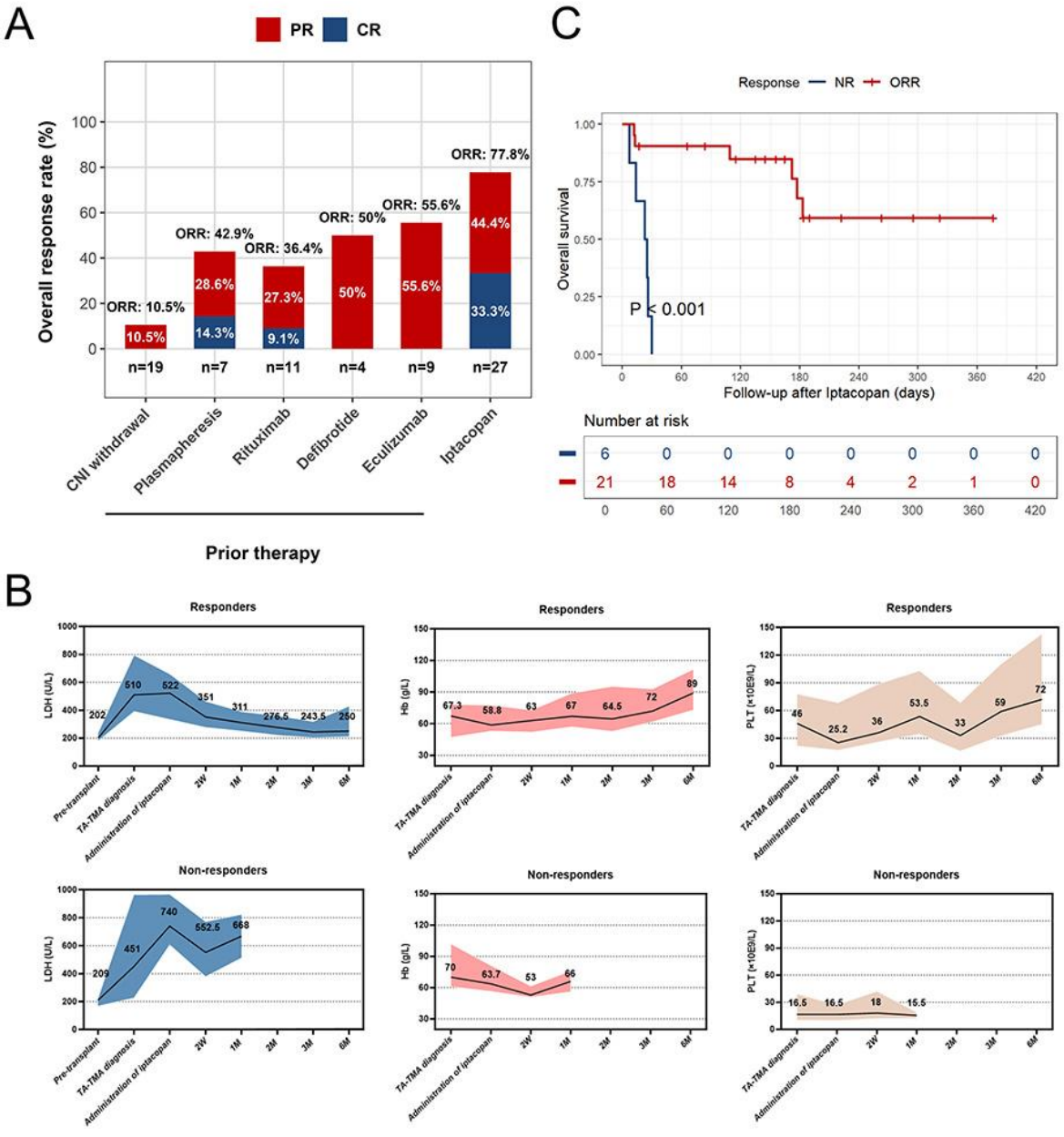
Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is a lethal complication after hematopoietic stem cell transplantation (HSCT). Recent advances in complement inhibition have demonstrated promising therapeutic potential, as evidenced by eculizumab. Activated complement factor B product is significantly elevated in the early period of TA-TMA, thereby supporting the predominant pathogenic role of the alternative pathway. Iptacopan, an oral small-molecule complement factor B inhibitor, can efficiently block the formation of C3 convertase, inhibit C5 convertase, decrease the membrane attack complex formation, and reduce damage to the endothelial system.

Methods: TA-TMA diagnosis and treatment response were assessed according to Jodele et al. High-risk disease was defined by ≥ 1 of the following: concomitant infection, peak LDH ≥ 2 ULN, aGVHD, end-organ dysfunction, rUPCR ≥ 1 mg/mg, and sC5b-9 plasma levels ≥ 250 ng/mL. Iptacopan was to be administered orally at 200 mg twice daily, with discontinuation considered upon resolution of hematologic TA-TMA and stabilization or improvement of MODS, or at the treating physician's discretion. All patients received antibacterial prophylaxis against Neisseria meningitidis and antifungal prophylaxis during iptacopan treatment.

Results: In this retrospective study, a total of 27 TA-TMA patients from 7 Chinese institutions received iptacopan therapy between July 2024 and May 2025. TA-TMA was diagnosed at a median of 81 days (IQR 25–227) post-HSCT. Organ involvement included intestine (n=12), kidney (n=6), and CNS (n=5). Elevated urinary protein excretion and elevated sC5b-9 level were both present in 14 patients, respectively. The median LDH level was 2.2 times the ULN (IQR 1.5–3.1). Specifically, 14 patients (51.9%) had grade II–IV

acute GVHD. Infections were documented in 22 patients (81.5%). Prior salvage therapies were extensive, including calcineurin inhibitor withdrawal (n=19), rituximab (n=11), and eculizumab (n=9), plasma exchange (n=7), and defibrotide (n=4). (Figure 1A) Most had refractory disease (48.1%) or a prior response followed by TMA progression/flare (29.6%). The median time to initial response was 12 days, and the median duration of iptacopan treatment was 27 days. Iptacopan yielded an overall response rate (ORR) of 77.8% (9 complete, 12 partial). Iptacopan resulted in marked reduction of LDH from baseline at 1 month (median 561 IU/L vs 353 IU/L, $p<0.001$). Responders achieved independence from red blood cell transfusion at a median of 47 (IQR 30–84) and from platelet transfusion at 63 (IQR 14–97) days. (Figure 1B) Notably, ORR did not differ significantly between eculizumab-pretreated (66.7%) and treatment-naïve (83.3%) patients ($p=0.36$). The most frequent adverse events were infectious complications (n=11). Contributing causes of death were TMA/MODS (n=5), GVHD (n=2), viral pneumonia (n=2), fungal pneumonia (n=2), and intracerebral hemorrhage (n=1). No relapse of underlying diseases was observed after iptacopan. At the last follow-up, the 6-month OS after TMA diagnosis was 62.7%, with 72.4% of responders (15/21) remaining alive. Survival was significantly higher in responders (67.9%) than non-responders (0%) at 6 months post-iptacopan ($p<0.001$). (Figure 1C)



Conclusions: In conclusion, the oral complement inhibitor iptacopan demonstrated significant clinical efficacy as salvage therapy in high-risk TA-TMA patients, irrespective of prior eculizumab exposure.

Disclosure: Nothing to declare.

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OS04-05

BASELINE LIVER ELASTOGRAPHY PREDICTS THE RISK OF SOS/VOD IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Sinusoidal obstruction syndrome/veno-occlusive disease (SOS/VOD) is a potentially severe complication of allogeneic hematopoietic stem cell transplantation (alloHCT). Liver stiffness measurement techniques, such as transient elastography (TE), are non-invasive tools potentially useful for the diagnosis of SOS/VOD. Early identification of patients at risk is critical due to the high morbidity and mortality associated with SOS/VOD.

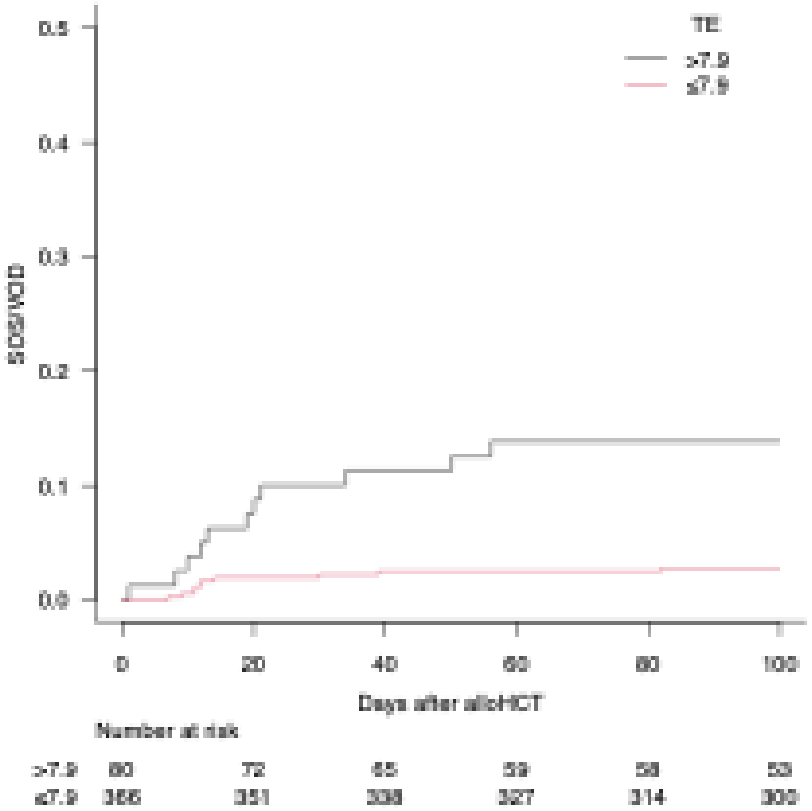
Methods: We conducted a retrospective observational cohort study using prospectively collected data. Between June 2018 and October 2025, 643 adult patients underwent alloHCT at our Center. Of these, 446 patients had at least one evaluable pre-transplant TE assessment and were included in the analysis. TE was routinely performed for all transplant candidates using FibroScan (Echosens, Paris, France) after a minimum of 4 hours of fasting, obtaining at least 10 valid measurements and an interquartile range/median ratio ≤30%. SOS/VOD was diagnosed and graded according to the latest EBMT criteria. Primary endpoint of the study was the incidence of SOS/VOD, while secondary endpoint was non-relapse mortality (NRM).

Results: Patients and transplant characteristics are displayed in *Table 1*. Median follow-up for survivors was 23 months (range, 1-86). The cumulative incidence of SOS/VOD at 100 days was 4.7% (95%CI, 3%-7%) and that of NRM at 1 year was 14.4% (95%CI, 11.3%-18%). Twenty-one patients developed SOS/VOD (5 moderate, 14 severe, 2 very-severe) after a median time of 13 days (range, 1-82) from alloHCT; 28% were late-onset cases. Seven of these patients (of 10 exposed overall) had received inotuzumab ozogamicin before alloHCT, and 8 patients died from transplant-related complications (6 SOS/VOD, 1 fungal and 1 bacterial infection). Defibrotide was administered in 16 SOS/VOD cases.

	TE ≤7.9 kPa (*N*=366)	**TE >7.9 kPa (*N*=80)**	***P***
Age at alloHCT, median year	52 ±15	55 ±14	0.02
Female sex, number (%)	160 (56%)	17 (22%)	<0.001
Previous HCT, number (%)	41 (12%)	12 (15%)	0.5
Disease type, number (%) MDS/MPN	78 (21%)	26 (32%)	0.1

	TE ≤7.9 kPa (*N*=366)	TE >7.9 kPa (*N*=80)	*P*
Lymphoid disorders Acute leukemias Non-malignant diseases	49 (14%) 227 (62%) 12 (3%)	11 (14%) 42 (53%) 1 (1%)	
Disease risk index, number (%) Low/Intermediate High/Very high	 267 (75%) 87 (25%)	 46 (60%) 31 (40%)	<0.01
HCT-CI score, number (%) 0 1-2 ≥3	 135 (37%) 125 (34%) 106 (29%)	 22 (28%) 29 (36%) 29 (36%)	0.2
Donor type, number (%) MRD MUD CBU Haploidentical	 43 (12%) 208 (57%) 22 (6%) 93 (25%)	 9 (11%) 50 (63%) 3 (4%) 18 (22%)	0.9
TCI, number (%) Low Intermediate High	 47 (13%) 201 (55%) 118 (32%)	 20 (25%) 44 (55%) 16 (20%)	<0.01
Prior inotuzumab, number (%)	4 (1%)	6 (7%)	<0.01
GvHD prophylaxis, number (%) PTCy-based ATG-based Other	 333 (91%) 11 (3%) 22 (6%)	 74 (92%) 3 (4%) 3 (4%)	0.5

Patients who developed SOS/VOD had significantly higher baseline TE values compared with those who did not (10.3 ±7.4 kPa versus 6.2 ±4.3kPa; p<0.001). A time-to-event ROC curve for baseline TE identified 7.9 kPa as the optimal threshold (sensitivity 0.53, specificity 0.83; AUC 0.691), consistent with established cutoffs for differentiating a fibrotic liver from a normal one. Using this threshold, patients with elevated baseline TE had a significantly higher cumulative incidence of SOS/VOD (13.8% versus 2.8% at 100 days; p<0.001; *Figure 1*) and NRM (19.8% versus 13.3% at 1 year, p=0.04). Conditioning intensity, disease-risk index, HCT-CI, number of previous transplants, and donor type showed no significant association with SOS/VOD incidence. A linear regression confirmed that baseline TE was a significant positive predictor of SOS/VOD (β=0.8%, 95%CI 0.4%-1.2%; t=3.86, p<0.001).



Conclusions: Baseline TE measurement may serve as a non-invasive tool to identify alloHCT recipients at increased risk of SOS/VOD. Patients with elevated TE, especially those previously exposed to hepatotoxic agents such as inotuzumab ozogamicin, may benefit from targeted preventive strategies to mitigate NRM.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

OS04-07

POOR GRAFT FUNCTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IS ASSOCIATED WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE USE AND DELAYED B AND T-CELL IMMUNE RECOVERY

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Background: Poor graft function (PGF) is a serious early complication of HSCT, characterized by persistent cytopenias despite achieving full-donor chimerism. Its study has long been limited by heterogeneous diagnostic criteria, leading to variable incidence and outcomes. In 2024, an internationally harmonized definition was introduced to standardize classification and enhance comparability across studies.

Methods: This study aims to assess the incidence, risk factors, and clinical outcomes of PGF defined by the 2024 harmonizing criteria, in a cohort of patients undergoing HSCT at our Center between 2015–2025. PGF incidence was calculated using cumulative incidence functions treating death as a competing risk. Predictors of PGF were evaluated using logistic regression. The impact of PGF as a time-dependent variable on NRM was assessed with Simon–Makuch curves and the Fine–Gray model.

Results: We identified 655 adult patients who underwent HSCT. Of these, 46 patients (7%) met the harmonizing criteria for PGF. The median time to diagnosis was 86 days post-transplant. One-third of patients showed pancytopenia, and two-thirds bone marrow hypocellularity. Baseline characteristics are summarized in Table 1.

Characteristics	**All, N=655**	**PGF, N=46**	**Non-PGF, N=609**
Age at HSCT, median (range)	54 (17-72)	58 (19-69)	53 (17-72)
Female	267 (40.8%)	19 (41.3%)	248 (40.7%)
Male	388 (59.2%)	27 (58.7%)	361 (59.3%)
Indication for HSCT			
AML	301 (46%)	8 (17.4%)	293 (48.1%)
ALL	108 (16.5%)	9 (19.6%)	99 (16.3%)
Myelofibrosis	76 (11.6%)	12 (26.1%)	64 (10.5%)

MDS	70 (10.7%)	9 (19.6%)	61 (10%)
Lymphoma	54 (8.2%)	3 (6.5%)	51 (8.4%)
Other	46 (7%)	5 (10,9%)	41 (6,8%)
ABO Compatible	287 (44.3%)	18 (39.1%)	269 (44.7%)
ABO Major incompatible	194 (29.9%)	20 (43.5%)	174 (28.9%)
ABO Minor incompatible	167 (25.8%)	8 (17.4%)	159 (26.4%)
Graft: <5x10^6 CD34+ cells/kg	291 (50.8%)	28 (70.0%)	263 (49.3%)
PTCy	138 (21.1%)	15 (32.6%)	123 (20.2%)
ATG/ATLG	422 (64.4%)	29 (63%)	393 (64.5%)

Table 1: Baseline characteristics

In the multivariable analysis, myelofibrosis (OR 7.25, 95%CI: 2.86–19.01, p <.0001), myelodysplasia (OR 4.91, 95%CI: 1.72–13.82, p= 0.0024), major ABO-incompatibility (OR 2.32, 95%CI: 1.15–4.71, p=0.0187), CD34+ cell dose $<5\times10^6$ cells/kg (OR 2.34, 95%CI: 1.16–5.00, p=0.0222) and post-transplant cyclophosphamide (PTCy) (OR 2.39, 95%CI: 1.11–4.99, p=0.0221) were independently associated with PGF.
PGF patients showed significantly higher 5-year NRM rate (25% vs 15% non-PGF, p=0.0401), with infections accounting for 67% of the NRM vs 27% in non-PGF. This paralleled a marked delay in immune reconstitution: PGF patients showed reduced CD3+, CD4+, CD8+ and CD16+ cell counts during the first year post-transplant (Fig. 1A-D), irrespective of PTCy or anti-thymocyte globulin (ATG) exposure. ROC analysis identified CD3+ count <178/µL at day +30 as the optimal early predictor for developing PGF. B-cell recovery was also impaired, with higher rates of hypogammaglobulinaemia (OR 2.41, 95%CI: 1.07–5.69, p=0.0362), and lower CD19+ counts throughout the first year after transplantation (Fig 1E).

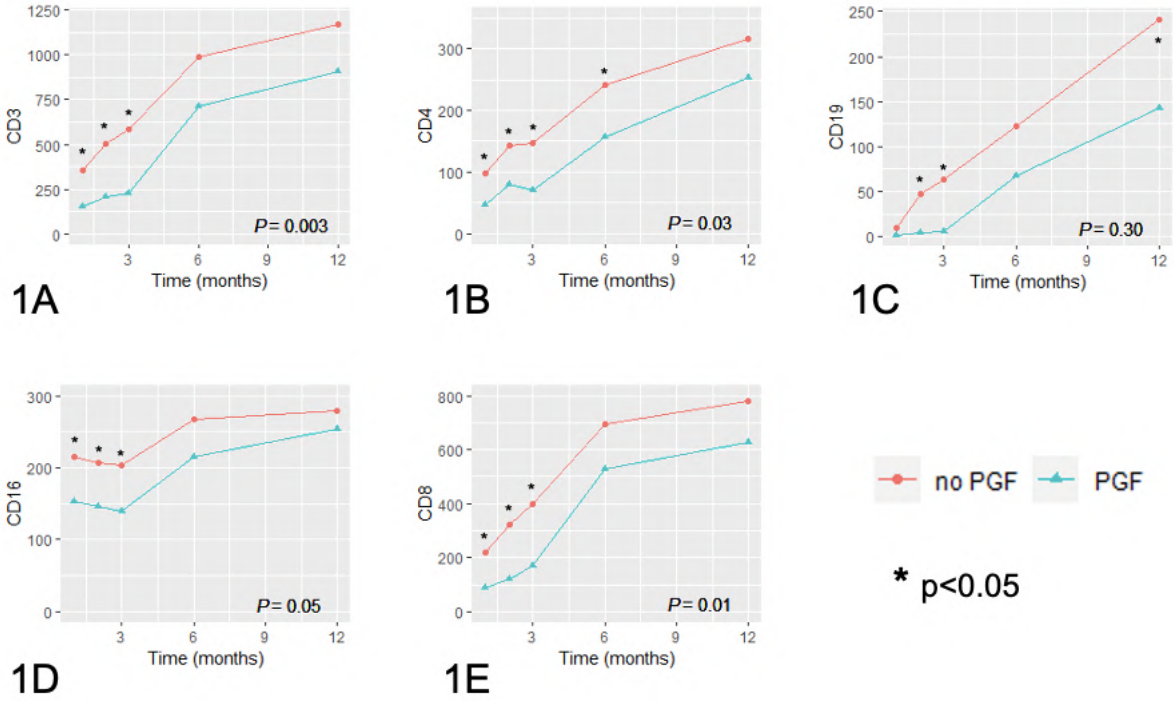

Figure 1: Immune reconstitution during the first year after HSCT in patients with and without PGF.

Among PGF patients, 23 received Eltrombopag, which resulted in platelet, erythroid and neutrophil response rates of 65%, 58% and 50%, respectively. The drug was well tolerated, with only 6 cases of transient transaminitis up to grade 3 CTCAE v5 and no thrombotic events. Moreover, 7 patients received a stem-cell boost (2 cases with CD34+ selection), resulting in the resolution of PGF in 71% of cases. Finally, acute GvHD (up to overall grade 4) occurred in 2 patients after unmanipulated boost infusion.

Conclusions: This single-center retrospective study, one of the first applying the 2024 harmonizing definition, shows that PGF is associated with higher NRM and delayed T- and B-cell immune recovery, with infections as the main cause of NRM. In high-risk diseases, such as myelofibrosis or myelodysplasia, additional risk factors (major ABO incompatibility, low CD34+ dose, PTCy) warrant careful evaluation. Both Eltrombopag and stem cell boosts were effective for managing PGF.

Disclosure: Nothing to declare.

OS04-08

RISK FACTORS FOR HEPATIC VENO-OCCLUSIVE DISEASE AFTER ALLO-HSCT IN ACUTE LEUKEMIA PATIENTS TREATED WITH ANTIBODY-DRUG CONJUGATES

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Background: Hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), remains a severe early complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) associated with high mortality. An elevated risk of VOD has been observed in patients previously treated with targeted agents, particularly antibody-drug conjugates (ADCs). This study aimed to identify clinical and therapeutic factors associated with an increased risk of VOD in patients with acute leukemia undergoing allo-HSCT after prior ADC therapy.

Methods: We retrospectively analyzed 121 patients (median age: 19 years; range: 1-56 years; 57 pediatric patients <18 years) with acute leukemia who underwent allo-HSCT at CIC725 between 2017 and 2025 following ADC-based therapy. ADC exposure included gemtuzumab ozogamicin in acute myeloid leukemia (n=36., median doses: 3; range: 1-3) and inotuzumab ozogamicin in acute lymphoblastic leukemia (n=85, median doses: 3; range: 1-11), Patients transplanted outside first or second complete clinical and hematological remission comprised 60% (advanced disease). In the study group 30 patients had EASIX score>3. Transplant characteristics are summarized in Table 1.

Table 1. Characteristics of allo-HSCT

Characteristic	n(%)
Conditioning regimen	
Myeloablative (MAC)	66 (54,55%)
-based on busulfan 10-14 mg/kg -based on total body irradiation -based on treosulfan 42 mg/m^2	58 (47,93%) 1 (0,83%) 7 (5,79%)
Reduced-intensity (RIC)	55 (45,45%)
-based on melphalan 140 mg/m^2 -based on busulfan 8 mg/kg -based on treosulfan 36 mg/m^2 -other	45 (37,19%) 6 (4,96%) 2 (1,65%) 2 (1,65%)
Graft-versus-host disease (GVHD) prophylaxis	

Post-transplant cyclophosphamide	111 (91,74%)
Calcineurin inhibitors (tacrolimus)	72 (59,5%)
Other	10 (8,26%)
Donor type	
Matched related	13 (10,74%)
Unrelated	21 (17,36%)
Haploidentical	87 (71,9%)
Graft source	
Bone marrow	63 (52,07%)
Peripheral blood stem cells	58 (47,93%)
Number of allo-HSCT	
First allo-HSCT	101 (83,47%)
Second or subsequent allo-HSCT	20 (16,53%)

Results: VOD was diagnosed by EBMT criteria in 36 of 121 patients (30%). Median time to onset was 14 days post-transplant (range: 4–76 days). VOD severity: mild (n = 2, 1,65%), moderate (n = 13, 10,74%), severe (n = 6, 4,96%), and very severe (n = 15, 12,4%). Day-100 non-relapse mortality was significantly higher in the VOD group (42% vs. 5%; p < 0.001). Univariate analysis identified the following significant risk factors for VOD: advanced disease (38.4% vs. 17.5%, p = 0.02), use of calcineurin inhibitors vs calcineurin-free regimens (39% vs. 16.3% , p = 0.008), busulfan-based conditioning: in the pediatric subgroup (60% vs. 21.2%, p = 0.018); with no significant difference in adults (33% vs. 11%, p = 0.22), pretransplant EASIX(>3): 47.2% vs. 26.5% (p = 0.03).
Multivariate logistic regression was performed for the three significant univariate predictors: advanced disease, use of calcineurin inhibitors, and busulfan-based conditioning. In the multivariate model, only transplantation in advanced disease remained a statistically significant independent predictor of VOD (OR 3.14, 95% CI 1.29–8.35; p = 0.02), while calcineurin-containing regimens only showed a trend towards significance (OR 2.54, 95% CI 0.91–7.61; p = 0.08).

Conclusions: In patients with acute leukemia treated with ADCs prior to allo-HSCT, VOD occurred in 30% and was linked to high non-relapse mortality. Transplantation in advanced disease was the only independent risk factor. The study indentified a possible improvement with calcineurin-free regimens, but this should be confirmed by future studies.

Disclosure: Nothing to declare

OS07-07

EXTERNAL VALIDATION OF THE ORIGINAL AND REFINED CARE-BMT SCORES FOR THE PREDICTION OF CARDIAC EVENTS AFTER ALLOGENEIC TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA

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Background: Cardiac events (CE) after allogeneic hematopoietic cell transplantation (allo-HCT) in patients with acute myeloid leukemia (AML) are potentially life-threatening complications. However, identifying patients at higher risk of CE remains challenging due to the heterogeneity of events and the limited availability of validated predictive models in allo-HCT settings.
The CARE-BMT (Vasbinder et al. 2023) score was developed to predict cardiotoxicity after HCT using clinical variables and laboratory biomarkers. Subsequently, given the growing use of post-transplant cyclophosphamide (PTCy) and its association with early CE, a refined CARE-BMT score incorporating the variable PTCy use (50 mg/kg/day for 2 days) was proposed (Torrent-Rodríguez et al. 2025).
This multicenter retrospective study aimed to externally validate the predictive performance of the CARE-BMT and modified CARE-BMT scores in a large AML cohort undergoing allo-HCT.

Methods: 809 adults with AML who underwent their first allo-HCT at the 11 participating transplant centers of the Spanish Hematopoietic Cell Transplant and Cell Therapy Group (GETH-TC) were included. CE incidence was the primary endpoint and was estimated considering relapse and death as competing risks. CE were defined and graded according to CTCAE criteria. Baseline demographics were retrospectively collected. Patients were stratified using both CARE-BMT versions and categorized into risk groups according to the respective definitions (**Figure 1).**

Results: Overall, the median age was 52 (range:17-75) years, 434 (53.6%) were males and 622 (76.9%) were previously treated with high-dose of antracycline-based therapies (dose>250mg/m^2), and 407 (49.7%) patients were transplanted using standard doses of PTCY for GVHD prevention.

Sixty (7.4%) patients had CE, yielding a cumulative incidence of 6.9% (95% CI 5.2–8.8). CE were heterogeneous with arrythmia and heart failure being the most prevalent ones. Patients with CE were older and more frequently had dyslipidemia (26.6% vs 11.1%) and previous CV disease (41.6% vs 7.3%). Moreover, occurrence of CE independently increased NRM risk (HR 3.20, P<0.001).

Using the original CARE-BMT score, 246 (30.4%) and 563 (69.6%) patients were classified into moderate and high-risk groups, respectively, with cumulative incidence of CE of 3.0% and 8.6% (P=0.004), respectively (HR 2.89, p=0.005) **(Figure 1)**. One-year OS was significantly higher in the intermediate-risk group compared with the high-risk group (73.2% vs. 62.2%; P=0.001), while NRM was significantly increased in the high-risk group (18.0% vs. 10.2%; P=0.009), with comparable relapse incidences between groups.

Subsequently, the refined CARE-BMT score with the variable PTCY-use, stratified patients into low (n=85), intermediate (n=558), and high-risk groups (n=166) with CE incidences of 2.4%, 6.1%, and 11.8%, respectively (p=0.011) **(Figure 1)**. High-risk patients had a >5-fold increased hazard of CE than low-risk patients (HR 5.37; p=0.024). Post-transplant outcomes showed that, one-year OS declined across risk categories (72.9%, 66.6%, and 58.4%), while NRM increased (10.5%, 15.7%, and 18.3%), with similar relapse incidence.

Figure 1. A. The CARE-BMT score and the modified score; B. Cumulative incidence of cardiac events according to CARE-BMT groups; C. Cumulative incidence of cardiac events according to modified score groups.

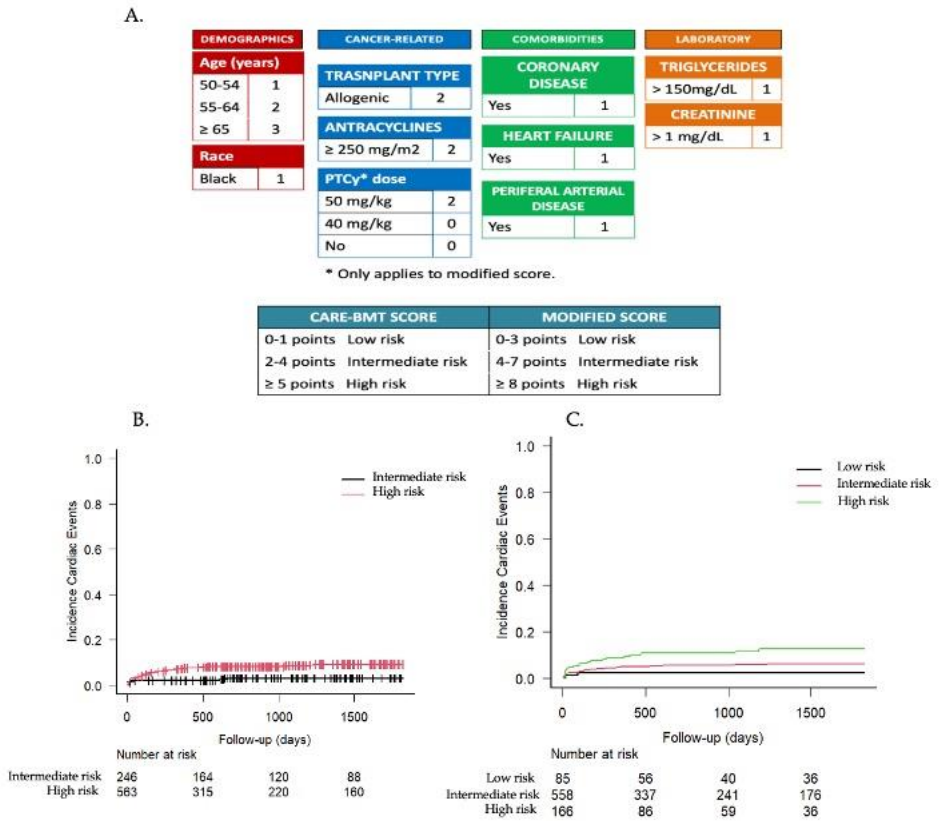

Table 1. Characteristics of the study population according to the CARE-BMT score and modified score.

Groups according to CARE-BMT score	Intermediate risk (N=246)	High risk (n=563)	P value	
Age distribution, n patients (%) <50 years 50-54 years 55-64 ≥ 65	 214 (87.0) 12 (4.9) 20 (8.1) 0 (0.0)	 94 (16.7) 82 (14.6) 255 (45.3) 132 (23.4)	0.002 - - - -	
Black race, n patients (%)	1 (0.4)	1 (0.2)	0.832	
HCT-CI>3, n patients	24 (9.8)	105 (18.7)	0.001	
Creatinine > 1 mg/dL, n patients (%)	3 (1.2)	78 (13.9)	<0.001	
Cardiac event post-HCT, n patients (%) Early cardiac event (0-100 days) Late cardiac event (>100 days)	8 (3.2) 5 (2.0) 3 (4.7)	52 (9.2) 26 (4.6) 26 (4.6)	0.052 - -	
Cardiac event grade (CTCAE), n patients (%) Grade I Grade II Grade III Grade IV Grade V	 3 (1.2) 3 (1.2) 1 (0.4) 1 (0.4) 0 (0.0)	 19 (3.4) 19 (3.4) 7 (1.2) 6 (1.1) 1 (0.2)	0.018 - - - - -	
Cardiac events, n patients (%) Arrythmia Pericardial condition HF Stroke/Ischemia Acute pulmonary edema Hypertensive crisis	 2 (0.8) 2 (0.8) 3 (1.2) 1 (0.4) 0 (0.0) 0 (0.0)	 18 (3.2) 8 (1.4) 14 (2.5) 7 (1.2) 1 (0.2) 3 (0.6)	0.032 - - - - - -	
Days to cardiac event, median (range)	21 (5-2158)	111 (1-2058)	0.001	

Table 1. Characteristics of the study population according to the CARE-BMT score and modified score.

Groups according to the modified score	Low risk (n=85)	Intermediate risk (n=558)	High risk (n=166)	P value
Age distribution, n patients (%) <50 years 50-54 years 55-64 ≥ 65	 70 (82.4) 15 (17.6) 0 (0.0) 0 (0.0)	 234 (41.9) 69 (12.4) 197 (35.3) 58 (10.4)	 4 (2.4) 10 (6.0) 78 (47.0) 74 (44.6)	<0.001 - - - -
Black race, n patients (%)	0 (0.0)	1 (0.2)	1 (0.6)	0.559
HCT-CI>3, n patients	8 (9.4)	82 (14.7)	39 (23.5)	0.006
Creatinine > 1 mg/dL, n patients (%)	1 (1.2)	39 (7.0)	41 (24.7)	<0.001
Cardiac event post-HCT, n patients (%) Early cardiac event (0-100 days) Late cardiac event (>100 days)	2 (2.4) 2 (2.4) 0 (0.0)	38 (6.8) 18 (3.2) 20 (3.6)	20 (12.0) 11 (6.6) 9 (5.4)	0.013 - -
Cardiac event grade (CTCAE), n patients (%) Grade I Grade II Grade III Grade IV Grade V	 2 (2.4) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	 13 (2.3) 14 (2.4) 6 (1.1) 3 (0.5) 0 (0.0)	 7 (4.2) 8 (4.8) 2 (1.2) 4 (2.4) 1 (0.6)	0.035 - - - - -
Cardiac events, n patients (%) Arrythmia Pericardial condition HF Stroke/Ischemia Acute pulmonary edema Hypertensive crisis	 2 (2.4) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	 13 (2.3) 6 (1.1) 12 (2.2) 6 (1.1) 0 (0.0) 1 (0.2)	 5 (3.0) 4 (2.4) 5 (3.0) 2 (1.2) 1 (0.6) 2 (1.2)	0.881 - - - - - -
Days to cardiac event, median (range)	53 (16-89)	125 (1-2158)	98 (9-1185)	0.043

Conclusions: CE occurred in 7% of patients and were strongly associated with increased NRM risk. Both CARE-BMT scores effectively identified patients at higher CE risk, with the

refined version providing superior discrimination. This easy-applicable tool may support tailored cardio-oncology evaluation, monitoring, and preventive strategies in AML patients undergoing allo-HCT.

Disclosure: Nothing to declare.

OS07-08

SYSTEMATIC LIVER STIFFNESS MEASUREMENT FOR DIAGNOSIS OF HEPATIC VENO-OCCLUSIVE DISEASE IN ADULT PATIENTS UNDERGOING ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION: A PROSPECTIVE REAL-WORLD SINGLE-CENTRE EXPERIENCE

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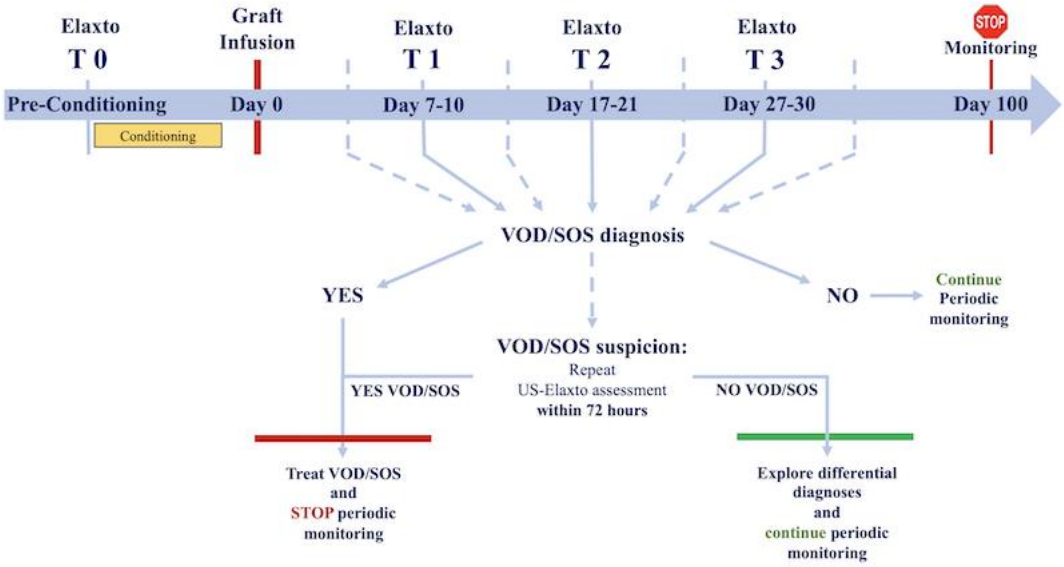
Background: Hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a severe post-HSCT complication with a high risk of mortality, that can exceed 80%. Early diagnosis and treatment of severe cases are decisive for patient outcome. The recent ELASTOVOD study showed that liver stiffness measurement (LSM) is a reliable, non-invasive diagnostic tool for VOD/SOS.

Methods:



LSM by point-shear-wave elastography (pSWE) and two-dimensional-shear-wave elastography (2D-SWE) were performed before conditioning (T0) and post-HSCT at regular intervals (Figure) in consecutive patients undergoing allo-HSCT at Fondazione Policlinico Tor Vergata (Rome, Italy) from August 2023 to October 2025. Revised 2023 EBMT criteria were applied for diagnosis and grading of VOD/SOS. According to ELASTOVOD study, LSMs were interpreted with diagnostic thresholds: ≤6 kPa to rule out VOD/SOS and ≥25 kPa to rule it in. The "grey zone" (>6 kPa and <25 kPa) was evaluated through the ELASTOVOD's stepwise diagnostic algorithm.

Results: A population of 94 patients (median age 59, range 20-74) underwent systematic LSM by pSWE and 2D-SWE (Table). Six patients were diagnosed with VOD/SOS (overall incidence: 6.7% [95%CI 2.5–14.1%]). The median time at diagnosis was 15.5 days (range 7-20), with all cases identified as "classical" VOD/SOS. Four of 6 patients (66%) were classified as "severe", 1 as "very severe", and 1 as "mild". The median number of VOD/SOS risk factors at HSCT was 4.5 (IQR 3-6) for patients who developed VOD/SOS, not significantly different from others (5, IQR 4-6, p=0.5967). No differences were observed in basal (T0) LSM between VOD/SOS patients and others (p=0.2685 by pSWE; p=0.3949 by 2D-SWE). The only patient who experienced "mild" VOD/SOS fully recovered with supportive measures alone. All other cases received defibrotide and showed a therapeutic response, but the "very severe" patient died of multi-organ-failure associated with septic shock. Liver stiffness–based diagnostic performance was comparable across techniques. Using predefined ELASTOVOD cut-offs, pSWE achieved a sensitivity of 83.3% (95%CI 35.9–99.6) and specificity of 97.6% (95%CI 91.6–99.7), with a positive predictive value (PPV) of 71.4% (95%CI 29–96.3), negative predictive value (NPV) of 98.8% (95%CI 93.2–100), and an AUROC of 0.900 (95% CI 0.740–1.00). For 2D-SWE, sensitivity was 66.7% (95% CI 22.3–95.7), specificity 100% (95% CI 95.7–100), PPV 100% (95% CI 39.8–100), NPV 97.6% (95% CI 91.8–99.7), and AUROC 0.830 (95% CI 0.630–1.00). Additionally, both pSWE and

2D-SWE demonstrated significant differences between LSMs of patients who experienced hepatic AE≥G3 and those with VOD/SOS (p=0.035 and p=0.019, respectively).

Descriptive characteristics of the overall population (n=94)

Gender	n (%)
Male	52 (55.3)
Disease	n (%)
AML ALL MDS MPN Lymphomas	42 (44.7) 12 (12.7) 22 (23.4) 8 (8.6) 10 (10.6)
Disease status at HSCT	n (%)
Early Advanced	33 (35) 61 (65)
Conditioning regimen intensity	n (%)
Myeloablative Reduced-intensity	24 (25.6) 70 (74.4)
Conditioning regimen type	n (%)
TBI FLU-TREO TBF	3 (3.2) 20 (21.3) 71 (75.5)
Donor type	n (%)
HLA-Id Haplo UD	8 (8.5) 32 (34) 54 (57.5)
HCT-CI Score	n (%)

Descriptive characteristics of the overall population (n=94)

0 1-2 ≥3	26 (27.6) 42 (44.8) 26 (27.6)
Stem cell source	n (%)
BM PBSC	33 (35) 61 (65)

Abbreviations:
AML - acute myeloid leukemia; ALL - acute lymphoblastic leukemia; BM - bone marrow; FLU-TREO - treosulfan/fludarabine; Haplo - haploidentical related donor; HCT-CI - haematopoietic cell transplantation specific comorbidity index; HLA-Id - HLA identical sibling donor; HSCT - haematopoietic stem cell transplantation; MDS - myelodysplastic syndrome; MPN - myeloproliferative neoplasms; PBSC - peripheral blood stem cells; TBF - thiotepa/busulphan/fludarabine; TBI - total body irradiation; UD - unrelated donor.

Conclusions: In our single-centre experience, the ELASTOVOD cutoff for diagnosis (>25kPa) and exclusion (<6kPa) of VOD/SOS, together with the "stepwise algorithm" to assess LSM in the “grey zone”, were effective with excellent sensitivity and specificity for both pSWE and 2D-SWE. In addition, both pSWE and 2D-SWE values confirmed the ability of discriminating between VOD/SOS and non–VOD/SOS post-HSCT severe hepatopathies. Despite the limited number of VOD/SOS cases, our work confirms LSM as bedside non-invasive diagnostic tool and represents the first validation of the ELASTOVOD study.

Disclosure: Nothing to declare.

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OS13-08

HEPATOTOXICITY AFTER CAR-T CELL THERAPY IN LYMPHOMA: A MULTICENTER REAL-WORLD STUDY OF OVER 1,000 PATIENTS

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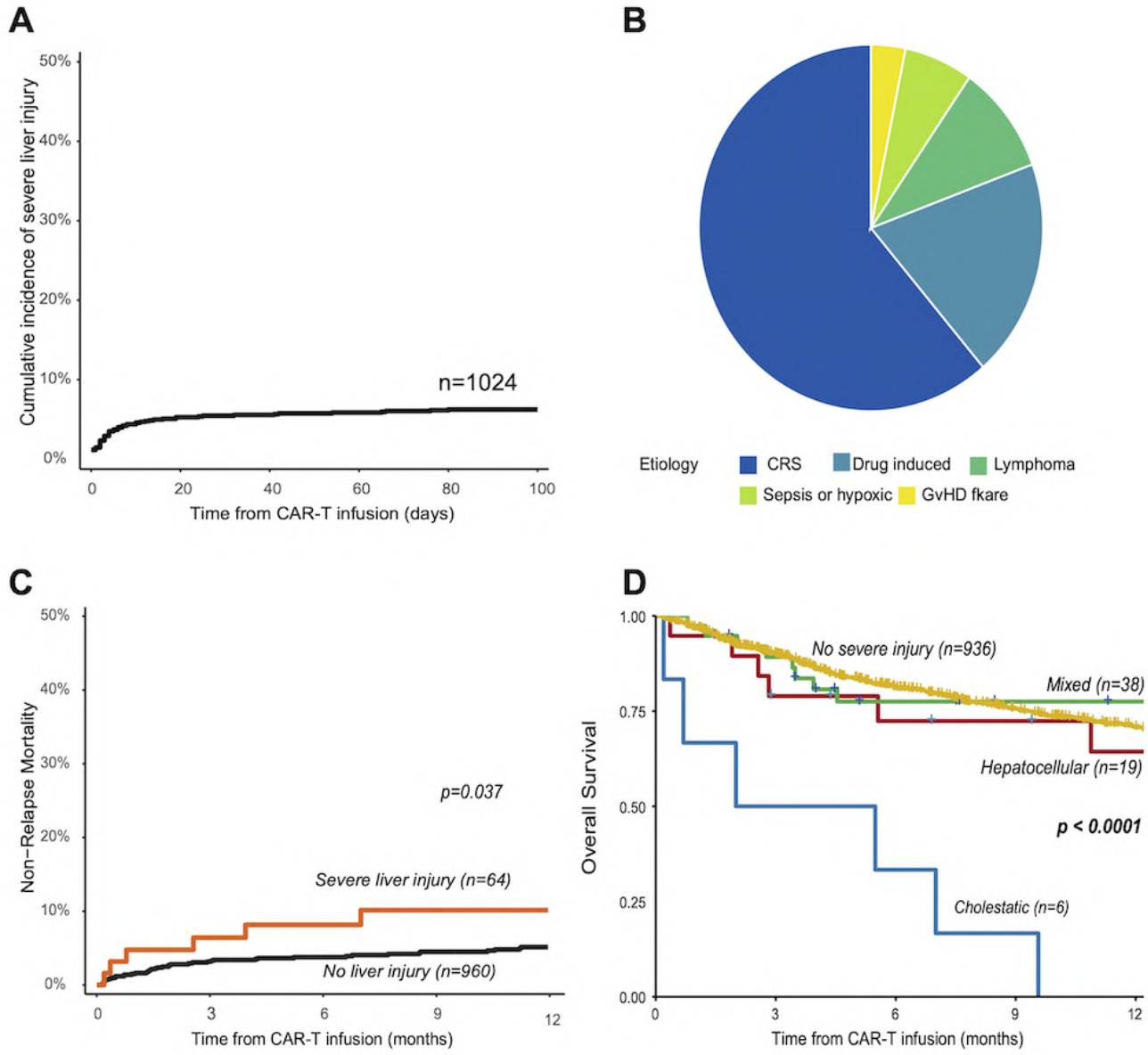
Background: CAR-T cell therapy is associated with a distinct toxicity profile, in which cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), and cytopenias represent the most recognized complications. In contrast, hepatotoxicity remains poorly characterized, with limited data on its incidence, risk factors, and clinical implications. Our aim was to delineate severe liver injury phenotypes after CAR-T therapy and evaluate their clinical relevance.

Methods: We conducted a retrospective multicenter cohort study including adults with non-Hodgkin lymphoma treated with commercial CD-19 directed CAR-T products between 2016 and 2025 across five international centers (United States, Germany and Israel). Longitudinal liver laboratory data were extracted and analyzed through day 100 after infusion, relapse, or death. Severe liver injury was classified as hepatocellular (ALT or AST ≥5×ULN with R-ratio ≥5), cholestatic (ALP ≥5×ULN with R-ratio ≤2), or mixed (ALT/AST ≥3×ULN with 2<R<5). Patients meeting severe liver injury criteria at baseline were excluded. U.S. cases underwent adjudication, with ambiguous episodes reviewed jointly with senior hepatologists. Predictors of severe hepatotoxicity were assessed using uni- and multivariable logistic regression, and time-to-event outcomes were analyzed using standard survival methods.

Results:



Characteristic	Severe liver injury (n=64)	No severe liver injury (n=960)	P-value
Age in years, median (IQR)	63 (49-70)	66 (57-73)	0.019
Diagnosis, n (%)			

Large B-cell lymphoma	42 (66)	639 (67)	
Other lymphoma	22 (34)	321 (33)	
Prior allo-HCT, n (%)	7 (11)	21 (2)	0.001
Prior hepatic disease at baseline, n (%)	4 (7)	72 (9)	0.8
CAR-T product			<0.001
Axi-cel, n (%)	43 (67)	451 (47)	
Liso-cel/Tisa-cel/Brexu-cel, n/n/n (%)	8/5/8 (33)	239/205/65 (53)	

A total of 1,026 adults with non-Hodgkin lymphoma were included. Overall, 22,567 patient-days of longitudinal liver function testing were analyzed within the first 100 days. In the overall cohort, AST and ALT showed modest early fluctuations, whereas ALP remained relatively stable.

The cumulative incidence of severe liver injury was 6.3% during the first 100 days (Fig 1A). Injury patterns were mixed in 61%, hepatocellular in 30%, and cholestatic in 9%. Median time from infusion to onset and peak of liver injury was 4 days (IQR 2–12) and 7 days (IQR 4–21), respectively. CRS occurred in 94% of patients with liver injury vs in 79% of those without (p=0.005).

In adjudicated hepatology review (n=31), CRS-related inflammatory liver injury was the most likely primary etiology (61%), followed by idiosyncratic drug-induced injury (19%), hepatic lymphoma involvement (10%), infection-related or ischemic injury (7%), and hepatic GvHD flare (3%). Contributing mechanisms were frequently observed, and notably all adjudicated cholestatic injury cases (n=3) were attributed to lymphoma involvement of the liver (Fig 1B).

In a multivariable logistic regression, only CAR-T product and baseline LDH were independently associated with severe liver injury; liso-cel (vs. axi-cel) was protective (OR 0.35, 95% CI 0.15–0.72), while elevated pre-LD LDH increased risk (OR 2.25, 95% CI 1.11–4.66).

While overall survival (OS) was comparable between patients with and without severe liver injury (65% vs 71%, p=0.57), non-relapse mortality (NRM) was increased in the former (10% vs 5%, p=0.037, Fig 1C). Finally, within the liver injury patterns, cholestatic abnormalities, although uncommon, were strongly linked to inferior OS (p<0.0001), (Fig. 1D).

Conclusions: In this first comprehensive multicenter real-world study encompassing over 1,000 patients, approximately 6% of CD19 CAR-T recipients experienced severe liver injury. Importantly, NRM was doubled in this population, with particularly low OS in patients with

cholestatic injury. These findings emphasize that hepatic toxicity after CAR-T therapy is clinically meaningful and warrants focused evaluation and management.

Clinical Trial Registry: N/A

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A379

DEFINING AND VALIDATING THE CD34+ CELL DOSE THRESHOLD REQUIRED FOR STEM CELL BOOST IN CHILDREN WITH POOR GRAFT FUNCTION. A REPORT FROM THE GETH-TC

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Background: Poor graft function (PGF) is a life-threatening complication following haematopoietic stem cell transplantation (HSCT). The use of CD34+ selected stem cell boost

(SCB) from the original donor is increasing with promising results, but experience is still limited, particularly in children. In addition, data on the required CD34+ cell dose for complete haematological recovery after SCB infusion, as well as other risk factors associated with response and survival, are scarce. In a previous multicentre retrospective study, we found that only the infused CD34+ cell dose emerged as a significant factor for complete response (CR) (*Communication O149, EBMT 2025*). Since CD34+ cellularity appears to be one of the most important prognostic factors for achieving a CR, this study aims to determine the required CD34+ cell dose for this outcome.

Methods: For this national multicentre retrospective study, we included paediatric patients who had received a SCB for PGF following allogeneic HSCT. PGF was defined according to *Sureda A. et al. Bone Marrow Transplant 2024.*
Nine centres participated in two independent cohorts: the training cohort and the validation cohort.
CR in terms of trilineage hematopoietic recovery was studied in the training cohort, using competing risk approach with Fine & Gray model. Multivariable model was the result of a backward-forward stepwise procedure using Akaike's Information Criterion (AIC). The optimal CD34+ cell dose cut-off was determined in the training cohort using maximally selected rank statistics for time to CR. This threshold was subsequently applied to the validation cohort. Differences in outcomes were analysed using the Fine & Gray model for competing risks.

Results: The characteristics of the training and validation cohort are shown in table 1. The training cohort included 42 patients with a median age of 11.2 years, with malignant (n=23; 54.8%) or non-malignant (n=19; 45.2%) diseases. The validation cohort included 14 patients with a median age of 11.9 years, with malignant (n=9, 64.3%) or non-malignant disease (n=5, 35.7%). No statistically significant differences were found between the two patient cohorts.

Table 1. Characteristics of patients included in the training and validation cohorts

Variable	Training cohort (n=42)	Validation cohort (n=14)	p-value
INCLUSION PERIOD	2013 - 2023	2022 - 2025	___
PATIENT CHARACTERISTICS			
Age at HSCT in years, median (range)	11.2 (0.2 - 19.1)	11.9 (2.4 - 17.2)	0.1105
Sex, n (%) - Male - Female	 26 (61.9) 16 (38.1)	 11 (78.6) 3 (21.4)	0.3377

Underlying disease, n (%) - Malignant - Non-malignant	24 (57.1) 18 (42.9)	9 (64.3) 5 (35.7)	0.7552
Donor type, n (%) - Matched family donor - Unrelated donor - Haploidentical donor	5 (11.9) 19 (45.2) 18 (42.9)	2 (14.3) 5 (35.7) 7 (50)	0.8357
Stem cell source, n (%) - Bone marrow - Peripheral blood	19 (45.2) 23 (54.8)	5 (35.7) 9 (64.3)	0.7552
PGF diagnosis, lines affected, n (%) - Bilineal - Trilineal	5 (12) 37 (88)	4 (28.6) 10 (71.4)	0.2058
CD34+ SCB INFUSION			
Time from HSCT to SCB infusion in days, median (IQR)	149 (105 - 308)	165 (115 - 247)	0.7051
CD34+ cell dose infused (x10^6/kg), median (IQR), range	7.3 (4.6 - 9.2) 1.03 - 20.09	4.72 (4.01 - 7.01) 1.20 - 15.0	0.0636
Time to response in days, median (IQR)	13 (6 - 20)	17 (10 - 34)	0.267
Time to complete response, median (IQR)	43 (26 - 98)	41 (23- 76)	0.6841

In the training cohort, both in the univariable and multivariable analyses CD34+ was significantly associated to complete response (HR 1.14, CI 95%: 1.02 – 1.26, P = 0.019). No other variable was significant in the univariable analysis or selected in the best multivariable model according to AIC.
Using maximally selected rank statistics, we explored best cut-off in the training cohort obtaining 4.65 x 10^6/kg as the best cutoff (Figure 1a, 1b). We furtherly validated this result using a second cohort in which cellularity greater than this value were more likely to respond

(p = 0.013) (Figure 1c).

Figure 1. Establishing and validating the optimal CD34+ cell dose threshold for effective SCB in children with PGF

Figure 1a. Maximally selected rank statistic in training cohort

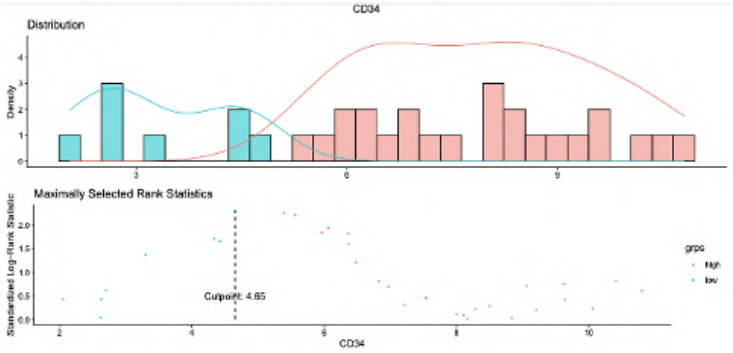


Figure 1b. Probability of CR in the training cohort

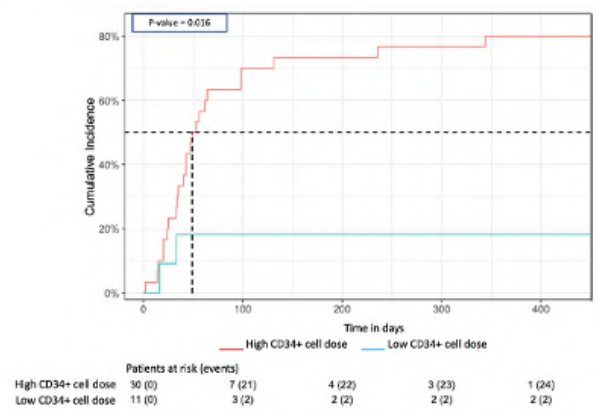
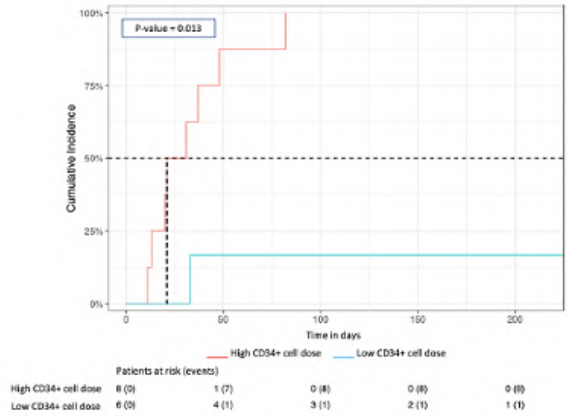


Figure 1c. Probability of CR in the validation cohort



Conclusions: PGF is a severe complication after HSCT and in paediatric HSCT recipients with PGF, SCB can provide durable trilineage engraftment. In this study, we determined the CD34+ cell cut-off point necessary for a CR following a SCB. We also demonstrated that patients with a CD34+ cellularity greater than 4.65 x 10^6/kg are more likely to respond. However, these results need be validated in larger cohort of patients.

Disclosure: Nothing to declare.

A380

ENGRAFTMENT SYNDROME IN PEDIATRIC ALLOGENEIC HSCT: RISK FACTORS AND OUTCOMES

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Background: In this cohort study, we evaluated the outcomes of engraftment syndrome (ES) and identified risk factors for the development of ES in pediatric allogeneic hematopoietic stem cell transplantation (HSCT) recipients.

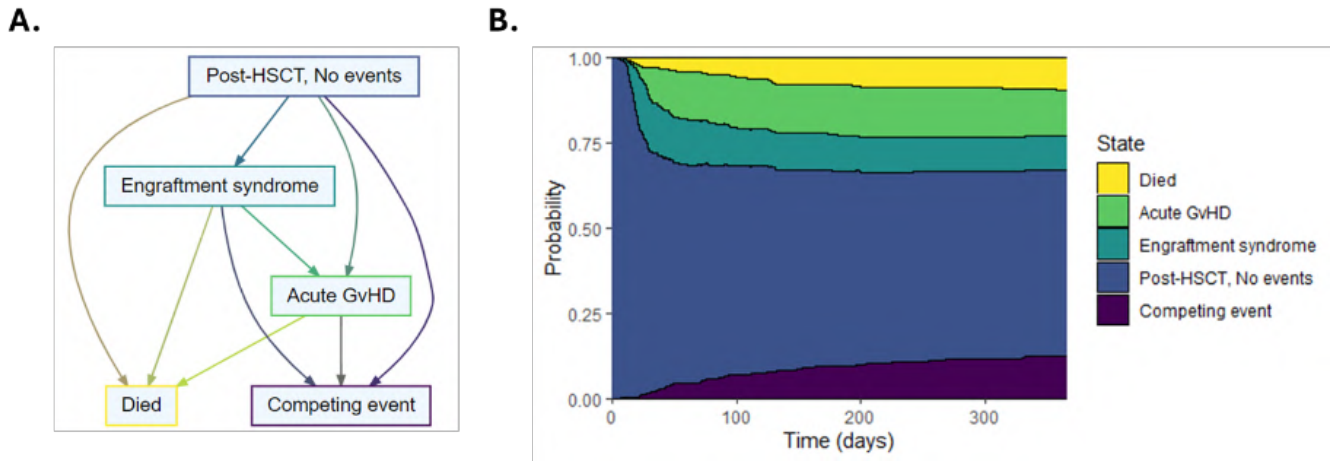
Methods: We included 384 pediatric HSCT recipients who were consecutively transplanted between 2010 and 2022 at our center. Clinical and laboratory data were collected retrospectively from electronic health records. ES was diagnosed using the Spitzer criteria. Twenty-eight inflammatory serum proteins were measured before HSCT using a Luminex immunoassay. Associations between ES and acute GvHD, non-relapse mortality (NRM) and overall survival (OS) were modeled using a Cox model with ES as a time-dependent covariate. Risk factors for ES and unfavorable outcome after ES were identified using a multi-state model, which allows the estimation of hazard ratios (HR) for different events after HSCT (Figure 1A). Multiple testing correction was performed on the Luminex data using the Benjamini-Hochberg procedure.

Results: Patient- and transplant characteristics are displayed in Table 1. The cumulative incidence of ES was 20% at day 50 post-HSCT (N = 75). The most common major criterium of ES was fever without infection (72/75, 96%), followed by rash (52/75, 69%) and pulmonary edema (37/75, 49%). Occurrence of ES was significantly associated with acute GvHD (HR 3.05, 95% CI 1.86-5.01, p <0.001) and OS (HR 1.98, 95% CI 1.14-3.44, p 0.016). We evaluated which of the individual major criteria of ES contributed most to an increased risk of acute GvHD and mortality. All criteria were significantly associated with acute GvHD, skin rash being the most important (HR 3.19, 95% CI 1.93-5.27, p <0.001). Only pulmonary edema was associated with NRM and OS (respectively HR 3.74, 1.88-7.44, p < 0.001 and HR 3.13, 1.80-5.43, p <0.001). CXCL16 serum levels at HSCT correlated most strongly with the development of ES out of all measured inflammatory serum proteins, however, these results were insignificant after multiple testing correction (HR 2.79, corrected p >0.05). Recipients of transplants from unrelated donors had an increased risk of developing ES, as compared to related donors (HR 2.37, 95% CI 1.36-4.12, p 0.002). Furthermore, patients transplanted for malignant diseases (HR 1.91, 95% CI 1.11-3.29, p 0.02) and inborn errors of immunity (HR 2.39, 95% CI 1.36-4.21, p 0.003) had an increased risk of developing ES, as compared to non-malignant hematological diseases.

Table 1. Patient and transplant characteristics	**N = 384**
Age (median, IQR)	8.2 (3.0-13.1)
Patient sex	
Male	235 (61%)
Female	149 (39%)

Table 1. Patient and transplant characteristics	N = 384
Diagnosis	
Hematologic malignancy	115 (30%)
Hemoglobinopathy and other non-malignant hematologic diseases	185 (48%)
Inborn error of immunity	81 (21%)
Other	3 (0.8%)
Donor type	
Matched unrelated	129 (34%)
Mismatched unrelated	112 (29%)
Matched related	105 (27%)
Mismatched related	38 (9.9)
Graft type	
Bone marrow	295 (77%)
Umbilical cord blood	50 (13%)
Peripheral blood stem cells	39 (10%)

Figure 1: Diagram of possible transitions within multistate model (A) and a graphical overview of proportions of patients in each state within the first year after HSCT (B).



Conclusions: These findings highlight the clinical burden of ES through its association with adverse outcomes after HSCT. Careful monitoring of these patients is warranted to recognize patients at risk for further complications, especially in patients suffering from pulmonary edema. Prospective studies are needed to optimize treatment strategies for ES, ultimately improving patient outcomes after HSCT.

Disclosure: Nothing to declare.

A381

INCIDENCE OF VOD AND LONGITUDINAL DYNAMICS OF EASIX AND ENDOTHELIAL BIOMARKERS AFTER ALLO-HCT WITH PTCY

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Background: Veno-occlusive disease (VOD) is a severe complication after allo-HCT, linked to endothelial and hepatocyte injury. Post-transplant cyclophosphamide (PTCy) is widely used for GVHD prophylaxis, but its effect on VOD remains unclear. Emerging evidence suggests that biomarkers of endothelial stress and inflammation may improve early identification and

diagnosis of VOD, while providing mechanistic insights into endothelial dysfunction. Hence, integrating these biomarkers with clinical risk assessment in allo-HCT with PTCy could enhance VOD prevention, early intervention strategies, and optimize patient outcomes. This study characterizes the incidence and outcomes of VOD in adults undergoing allo-HCT with PTCy and evaluates the dynamics and predictive value of endothelial biomarkers.

Methods: The 374 consecutive adults who underwent allo-HCT with PTCy-based prophylaxis between 2014 and January 2025 were included. VOD was diagnosed according to modified Seattle, Baltimore, or EBMT criteria, depending on the timing. Clinical characteristics and outcomes of VOD patients were analyzed. Longitudinal EASIX scores were calculated for all patients during the first six months post-transplant. Complementary, in a subset of 109 patients transplanted between 2022 and January 2025, analyses of endothelial injury biomarkers (VWF, TM, VCAM-1, TNFRI) were performed using plasma samples longitudinally collected at HCT admission, day 0, +7, +14, and +21. Samples were cryopreserved and analyzed in October 2025.

Results: Baseline characteristics of patients are reported in **Table 1.** Overall, the median age was 53 years, 59.9% were male, and 5.3% were diagnosed with myeloproliferative neoplasms (MPN). All patients received PTCy, and donor types are detailed in **Table 1.** VOD occurred in 12 (3.2%) patients at a median of 12 days post-transplant, with a day +100 cumulative incidence of 2.7%. Patients with MPN were overrepresented among VOD cases (41.7% vs. 4.1% in non-VOD; P<0.001). All 8 (66.7%) moderate and severe cases received defibrotide, and one (8.3%) underwent TIPS placement. Complete response was achieved in 11 (91.7%) patients, while one (8.3%) died from unresponsive VOD. However, the two-year overall survival and non-relapse mortality in VOD patients were 33.3% and 31.2%, respectively, compared with 71.8% and 12.6% in non-VOD patients.
As illustrated in **Figure 1,** median EASIX scores were significantly higher in patients who developed VOD both pre-transplant (median EASIX-PRE 3.2 vs. 1.1, P<0.01) and during the early post-transplant period. Additionally, elevated pre-transplant log2-EASIX-PRE and independently predicted VOD in univariate analyses (HR 4.6; P=0.003).
Complementary biomarker analyses were conducted on samples from 109 patients, of whom 4 (3.7%) had VOD. Baseline characteristics are summarized in **Table 1.** At HCT admission, patients with VOD showed higher EASIX scores and elevated levels of endothelial activation markers (VCAM-1 and TNFRI). Furthermore, patients with VOD had increased levels of all endothelial activation biomarkers even before clinical diagnosis and during the early post-transplant period **(Figure 1).**

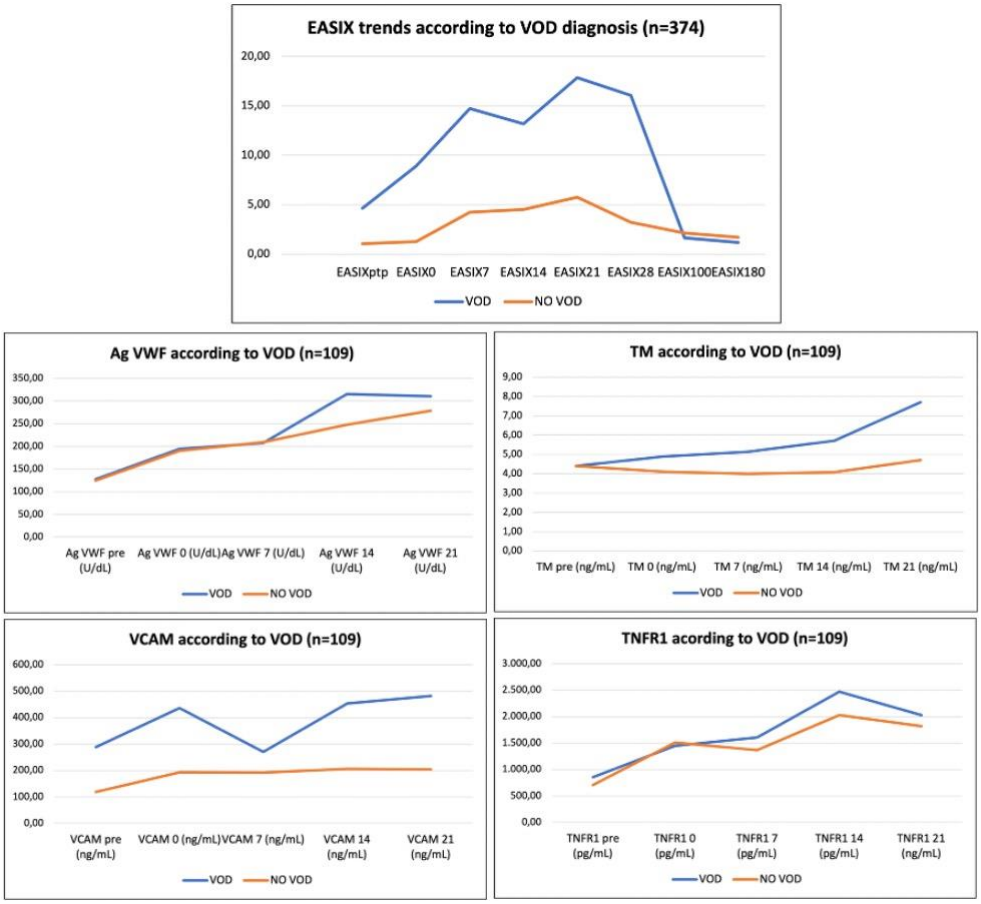
Table 1. Baseline characteristics of patients

ENTIRE COHORT	**All Patients N = 374**	**VOD Diagnosis N = 12**	**No VOD N = 362**	**p value**
Age Continuous (range)	53.52 (18-75)	57.61 (19-66)	53.47 (18-75)	0.375

Sex Male Female	 224 (59.9) 150 (40.1)	 9 (75.0) 3 (25.0)	 215 (59.4) 147 (40.6)	0.278
Diagnosis Acute Myeloid Leukemia Myelodysplastic Syndrome / CMML Myeloproliferative Disorder Acute Lymphoblastic Leukemia Non-Hodgkin Lymphoma Others	 138 (36.9) 66 (17.6) 20 (5.3) 68 (18.2) 47 (12.6) 35 (9.3)	 1 (8.3) 2 (16.7) 5 (41.7) 2 (16.7) 1 (8.3) 1 (8.3)	 137 (37.8) 64 (17.7) 15 (4.1) 66 (18.2) 46 (12.7) 34 (9.4)	<0.001
HCT-CI > 3 **KPS < 90 %**	82 (22.0) 86 (23.0)	3 (25.0) 3 (25.0)	79 (21.8) 83 (22.9)	0.731 1
Conditioning regimen MAC RIC	 163 (43.6) 211 (56.4)	 5 (41.7) 7 (5.3)	 158 (43.6) 204 (56.4)	0.892
GVHD Prophylaxis PTCY-TK PTCY-SIR+/-MMF PTCY-TK-MMF	 285 (76.2) 8 (2.1) 81 (21.6)	 9 (75) 0 3 (25)	 276 (76.2) 8 (2.2) 78 (21.5)	-
Donor type MSD 10/10 MUD 9/10 MUD Haploidentical	 60 (16) 79 (21.1) 131 (35.0) 104 (27.8)	 3 (25.0) 5 (41.7) 1 (8.3) 3 (25.0)	 57 (15.7) 126 (34.8) 103 (28.5) 76 (21.0)	0.465
EXPERIMENTAL COHORT (BIOMARKERS)	**N = 109**	**N = 4**	**N = 105**	
Age Continuous (range)	59 (18-74)	39 (19-60)	57 (18-74)	<0.001

Sex Male Female	 59 (54.1) 50 (45.9)	 2 (50.0) 2 (50.0)	 57 (54.3) 48 (45.7)	0.855
Diagnosis Acute Myeloid Leukemia Myelodysplastic Syndrome /CMML Myeloproliferative Disorder Acute Lymphoblastic Leukemia Non-Hodgkin Lymphoma Others	 44 (40.4) 15 (13.8) 5 (4.6) 21 (19.3) 12 (11.0) 12 (11.0)	 0 0 2 (50.0) 1 (25.0) 1 (25.0) 0	 44 (41.9) 15 (14.3) 3 (2.9) 20 (19.0) 11 (10.5) 12 (11.4)	<0.001
HCT > 3 **KPS < 90 %**	22 (20.2) 22 (20.2)	0 1 (25.0)	22 (21.0) 21 (20.0)	0.581 0.791
Conditioning regimen MAC RIC	 52 (47.7) 57 (52.3)	 3 (75.0) 1 (25.0)	 49 (46.7) 56 (53.3)	0.259
Donor type MSD 10/10 MUD 9/10 MUD Haploidentical	 32 (29.4) 32 (29.4) 26 (23.9) 19 (17.0)	 2 (50.0) 2 (50.0) 0 0	 30 (28.6) 30 (28.6) 26 (24.8) 19 (18.0)	0.409

Figure 1. Median biomarker values according to VOD diagnosis



Conclusions: VOD remains a clinically significant complication after allo-HCT with PTCy, associated with relevant morbidity, organ dysfunction, and reduced survival. Complementary, findings support the central role of endothelial dysfunction in VOD pathophysiology and that biomarker monitoring may enable earlier patient risk stratification.

Disclosure: The research group has received partial financial support from JAZZ Pharmaceuticals to conduct the study. Otherwise, the authors declare that they have no relevant conflicts of interest.

A382

SECOND ALLOGENEIC STEM CELL TRANSPLANTATION TO TREAT PRIMARY AND SECONDARY GRAFT FAILURE: A SINGLE CENTRE EXPERIENCE

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Background: Graft failure (GF) is an unusual but threatening complication after allo-HSCT, associated with several factors, including use of mismatched donors. Second allo-HSCT has been proposed as a safe and effective strategy to rescue these patients.
The objective of this study was to analyse characteristics and outcomes of patients treated with a second allo-HSCT to treat GF.

Methods: We retrospectively analyzed all patients who received a second allo-HSCT to treat GF in a single centre between 2014 and 2024.
Primary GF was defined as the absence of neutrophil engraftment by day +28 with mixed chimerism (MC) and secondary GF as initial engraftment and later development of severe cytopenia and MC. Complete chimerism (CC) was defined as the presence of a percentage of recipient cells below 1% in peripheral blood (PB) and 5% in T lymphocytes (TL). Relapse was ruled out in all cases with GF suspicion.

Results: A second allo-HSCT was used as salvage therapy following GF in 18 patients: 7 (39%) for primary GF and 11 (61%) secondary GF. Five patients were female (28%), median age was 33 (range 18-69) and the most common diagnosis were AML/MDS (n=7, 39%) and ALL (n=6, 33%). Donors used in the first procedure were: MRD (n=2,11%), MUD (n=1,5%), haploidentical (n=12,67%) and UCB (n=3,17%). Eleven patients (61%) had received a reduced intensity conditioning (RIC) regimen. At the time of GF diagnosis, median percentage of recipients' cells were 47% (range 5-100%) and 94% (range 25-100%) in PB and TL, respectively.
Main characteristics of second allo-HSCT are shown in Table 1. Second allo-HSCT was performed at a median of 42 days (range 34-68) and 94 days (range 54-191) after first transplant in patients with primary GF and secondary GF, respectively. An haploidentical donor was used in 13 patients (72%). Seventeen patients (94%) received a RIC regimen and anti-thymocyte globulin (ATG) was part of conditioning regimen in 15 patients (83%), combined with thiotepa and fludarabine in 12 (67%). Neutrophil engraftment was achieved in 15 patients (83%) at a median time of 16 days (range 12-130) after transplant. Platelet engraftment was achieved in 12 patients (67%) at a median time of 29 days (range 13-90) after transplant. Complete chimerism was achieved in 16 patients (88%) at a median time of 19 days (range 8-100) after transplant. The most common complication after salvage therapy were infections. Most patients (n=14,77%) developed at least 1 documented

infection after transplant: 13 patients had at least 1 viral infection, 11 bacterial and 5 fungal infections. 100-day overall survival (OS) and 1-year OS were 67 and 44%, respectively, with infections being the first cause of death in this cohort (n=8, 44%).

Table 1.

	Primary graft failure (n=7)	Secondary graft failure (n=11)
Donor		
Haplo-HSCT	6 (85.7%)	7 (63.6%)
MRD	0	2 (18.2%)
MUD	0	1 (9.1%)
MMUD	1 (14.3%)	1 (9.1%)
Conditioning		
RIC	6 (85.7%)	11 (100%)
MAC	1 (14.3%)	0
Engraftment and chimerism		
Complete chimerism	7 (100%)	9 (81.8%)
Neutrophil engraftment	7 (100%)	9 (81.8%)
Platelet engraftment	5 (71.4%)	8 (72.7%)
Survival		
100 day-OS	4 (57.1%)	8 (72.7%)
1 year-OS	2 (28.6%)	6 (54.5%)

Haplo-HSCT: Haploidentical Hematopoietic Steam Cell Transplantation; MMUD: Mismatched Unrelated Donor; MRD: Matched Related Donor; MUD: Matched Unrelated Donor; RIC: Reduced-Intensity Conditioning; MAC: Myeloablative Conditioning

Conclusions: In our experience, timely and individualized second allo-HSCT may improve outcome after primary or secondary GF. A vast majority of patients achieved engraftment and full donor chimerism, which resulted in a high 100-day survival.

Disclosure: Nothing to declare.

A383

REDUCED EARLY POST-TRANSPLANT GLUTAMINE LEVELS ARE ASSOCIATED WITH SYSTEMIC INFLAMMATION AND SEVERE AGVHD

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Background: Severe acute graft-versus-host disease (aGvHD) remains a major cause of transplant-related morbidity and mortality. Conditioning-induced gastrointestinal mucosal injury may initiate local cytokine release, which can drive systemic inflammation and ultimately promote alloreactivity.
Glutamine, the most abundant free amino acid, is important for maintaining gut integrity as the primary metabolic fuel for enterocytes, and it sustains cellular antioxidant capacity through its role in glutathione synthesis. Glutamine availability also influences systemic immune homeostasis by regulating leukocyte metabolism, activation, and proliferation including regulatory functions.
Thus, we hypothesized that an early post-transplant decrease in plasma glutamine may be associated with cytotoxicity-associated systemic inflammation and aGvHD development.

Methods: A total of 75 children (1–18 years) undergoing myeloablative, matched-donor HSCT in Denmark between 2015 and 2020 were included. Underlying diagnoses comprised malignant (n=47) and benign (n=28) diseases. Donors were either HLA-matched siblings (n=26) or unrelated donors (n=49) (Table 1). aGvHD was diagnosed and graded according to the MAGIC criteria. Plasma glutamine levels were quantified using mass-spectrometry at five time points: before conditioning and days 0, +7, +14, and +21. Statistical analyses included mixed model repeated measures analyses for time-course comparisons, logistic regression analysis and Spearman's rank-order correlation.

Table 1:

Characteristic	Value
Number of patients, no. (%) Males	75 (100) 41 (55)
Median age at transplantation, years (range)	9.7 (1.2-17.3)
Diagnosis, no. (%) Acute leukemia Other malignancies Benign diseases	 33 (44) 14 (19) 28 (37)

Donor type, no. (%) Matched sibling donor HLA-Matched unrelated donor (9/10 or 10/10)	 49 (65) 26 (35)
Stem cell source, no. (%) Bone marrow Peripheral blood	 71 (95) 4 (5)
Conditioning regimen, no. (%) TBI 12 GY + CY/VP16 BU-CY-MEL FLU + THIO/TREO Other regimens	 14 (19) 21 (28) 28 (37) 12 (16)

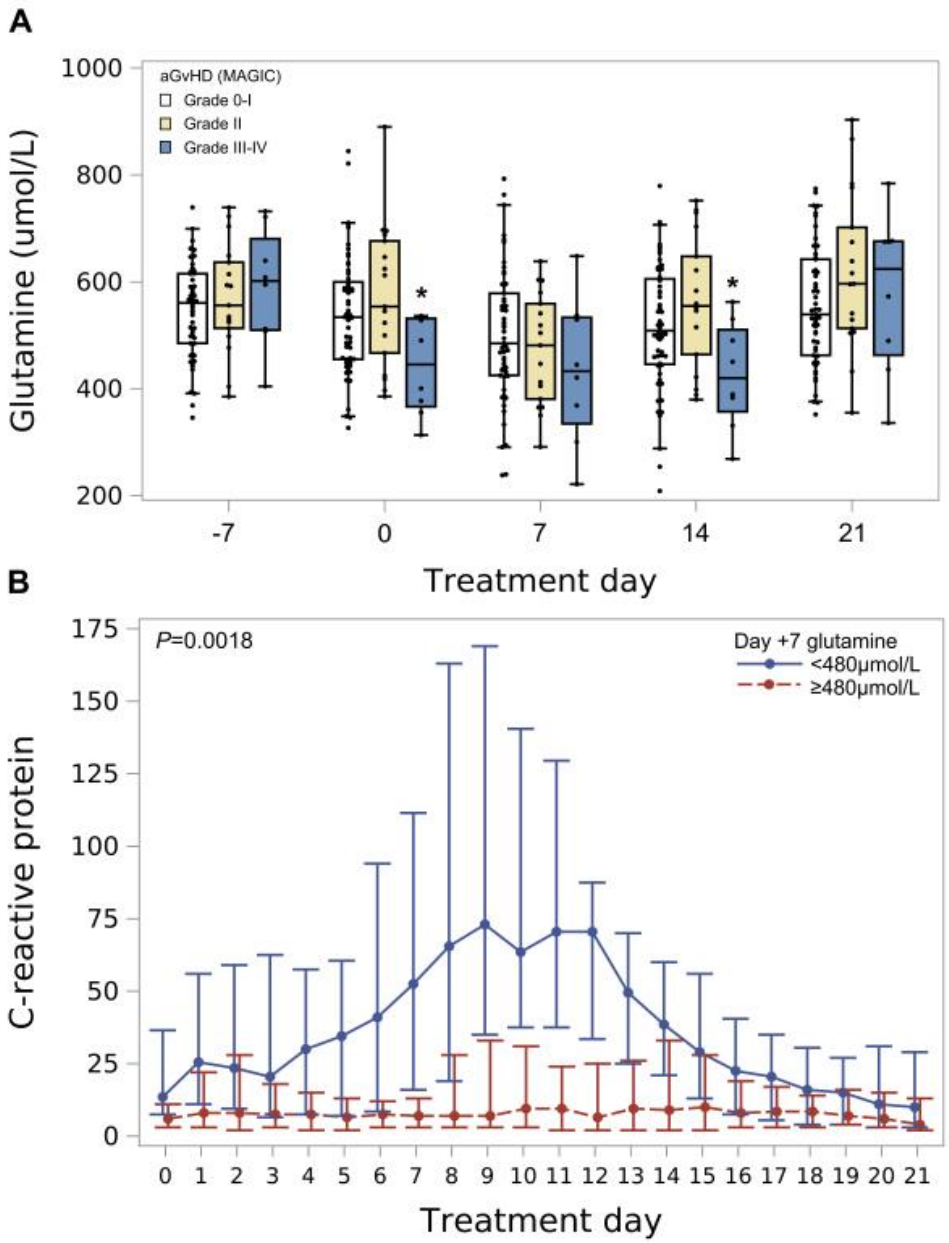
Results: A total of 25 patients (33%) developed grade II–IV aGvHD at median day +14 (range: 5–34), including eight cases with grade III–IV. Lower GI involvement occurred in five patients.

Plasma glutamine levels declined from a median pre-conditioning value of 558 µmol/L (369–1117) to a nadir of 478 µmol/L (222–793) on day +7 (P<0.0001), followed by gradual recovery.

In multivariable analyses adjusted for sex, age, diagnosis, and donor type, patients who developed grade III–IV aGvHD had significantly lower glutamine levels across days 0–14 compared with those with grade 0–I and grade II (Figure 1A). Each 50 µmol/L decrease in glutamine at day 0 was associated with an increased risk of severe aGvHD (OR=1.56; 1.01–2.42; P=0.046). No significant differences were observed between patients with lower GI aGvHD and those with extraintestinal aGvHD.

On day +7, glutamine levels were inversely correlated with C-reactive protein (CRP) (r_s=–0.69, P<0.0001). Patients with below-median glutamine at day +7 displayed a markedly higher inflammatory burden, reflected by persistently elevated CRP, most pronounced during the second week after HSCT (Figure 1B).

Figure 1:



Conclusions: This study demonstrates a significant decline in plasma glutamine levels during the early post-HSCT period, potentially due to a high metabolic demand as well as low dietary intake and impaired endogenous synthesis. Reduced glutamine levels were associated with the development of severe aGvHD and increased systemic inflammation. These findings support the role of glutamine as an important modulator of intestinal integrity and early inflammatory responses after transplantation. Further studies are warranted to determine whether maintaining adequate glutamine availability could mitigate early inflammatory complications and reduce the risk of severe aGvHD.

Clinical Trial Registry: N/A

Disclosure: The authors declare no conflict of interest.

A384

COMPARISON OF THE INFECTIOUS AND IMMUNOLOGICAL SAFETY OF A LOW-BACTERIAL AND MODIFIED DIET IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ADULTS

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Background: Malnutrition is an aggravating factor in hematopoietic stem cell transplantation (HSCT). The absorption of nutrients, among other factors, is closely related to the functional activity of the intestinal microbiota. Due to the need for the intestinal microbiome protection, which is a key element in homeostasis and is under complex negative effects in HSCT, a theory aimed at liberalizing dietary restrictions is being developed, which creates the basis for improving the patient's self-feeding and leads to a number of positive outcomes. The aim of the study was to evaluate the infectious and immunological safety of a modified diet (MD) in comparison with traditional low-bacterial diet (LBD).

Methods: From 2022 to 2023 at the RM Gorbacheva Research Institute 406 allogeneic HSCT recipients with acute leukemia over 18 years old, who followed a LBD (n=177) or MD (n=229) were enrolled to the randomized crossover trial. The concept of LBD included generally accepted anti-infective restrictions in HSCT, the absence of gluten, lactose, and yeast-containing products. Under MD, only the principles of anti-infective measures were preserved in the preparation, storage, transportation and dishes consumption, and the prohibition of a sharply limited list of foods that are difficult to digest and capable of mechanically injuring the oropharynx and gastrointestinal tract mucous membrane.

Results: The patient groups were homogeneous in diagnosis, graft source, HLA-compatibility between the recipient and the donor, conditioning regimen intensity and graft-versus-host disease (GvHD) prophylaxis, except for the age: MD group – 42.3 years, LBD group – 38.4 years, p=0.009. The one-year overall survival was similar in both groups: 72% for MD and 75% for LBD, p=0.6. Relapse-free one-year mortality was comparable between the groups: 8.7% for MD versus 9.1% for LBD, p=0.9. Graft engraftment at D+30 did not differ: 83% and 92%, respectively, p=0.2. The incidence of GvHD grade 3-4 was 3.4% in the MD group and 6.8% in the LBD group, respectively, p=0.14. The incidence of bloodstream infections at D+30 was lower in the MD group (14.4%) compared with the LBD group (45.2%), respectively, p<0.001.

Conclusions: Using the example of the presented cohort of patients who underwent allogeneic HSCT, the use of MD has potential advantages over LBD in the form of a tendency to decrease bloodstream infections and the severe GvHD incidence. Further studies with a large number of participants are needed to confirm these findings.

Disclosure: Nothing to declare

A385

NON-INFECTIOUS NON CARDIOGENIC INTERSTITIAL LUNG DISEASE–RELATED ACUTE RESPIRATORY FAILURE AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: THE FRENCH MULTICENTER EXPERIENCE

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Background: Post-allogeneic hematopoietic cell transplantation (HCT) respiratory failure is associated with high mortality, especially in patients requiring mechanical ventilation. Non-infectious, non-cardiogenic interstitial lung disease (ILD) is a rare condition with many differential diagnoses and no standardized treatment strategy. Toxic and immunologic causes are suspected based on scarce pathophysiological data. The aim of this study was to describe the clinical presentation, diagnostic work-up, treatment and outcome of such non-infectious, non-cardiogenic rapidly progressive ILD requiring intensive care unit (ICU) admission in allogeneic HCT recipients.

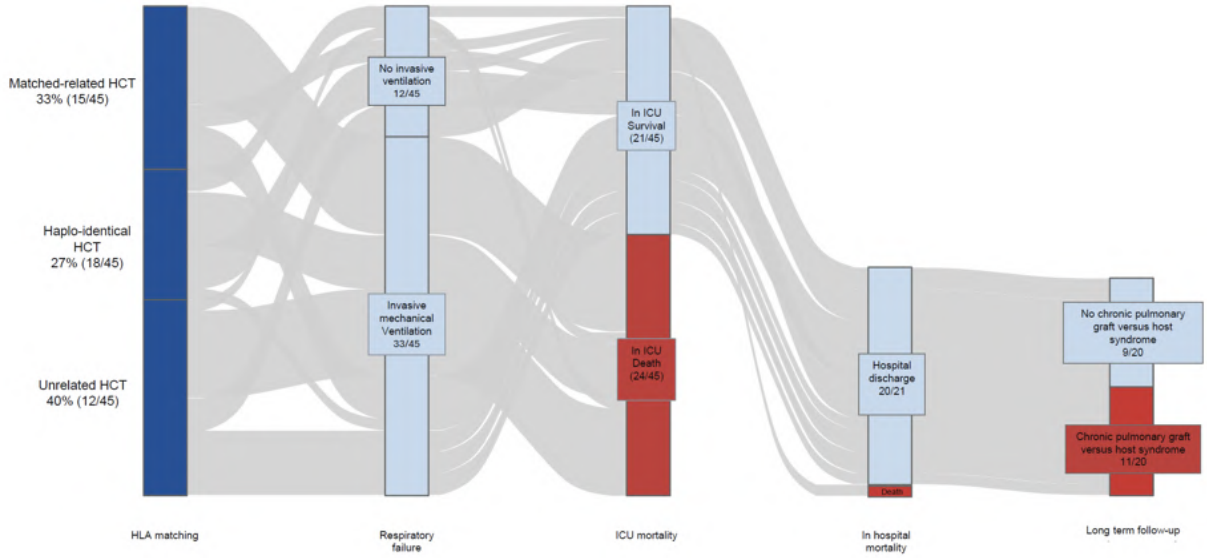
Methods: This French retrospective multicentre cohort study used Grrr-OH network and EBMT registry to identify cases from 01/01/2013 to 31/01/2024. Inclusion criteria were ≥18 years allogeneic HCT recipients hospitalized in ICU for inaugural ILD (evolving since <1 month) with interstitial pattern on chest tomodensitometry and requiring ≥6L oxygen. Exclusion criteria were ILD >1 month before ICU admission, infectious documentation or cardiogenic related respiratory failure.

Results: Forty-five patients were included. The characteristics of the patients are summarized in table 1.
Thirty of the 45 patients had a history of acute GVHD, among them 4/30 (11%) had refractory acute GVHD requiring JAK2 inhibitors, and 6/45 had a history of non-pulmonary chronic GVHD.
At the time of ICU admission, 13/45 (29%) still received systemic steroids and 25/45 (56%) an immunosuppressive treatment. Among them 6/45 (20%) patients still had an active grade ≥2 acute GVHD. The median dose of prednisone at ICU admission was 10 mg per day (IQR, 5–60 mg).
Respiratory symptoms developed at a median of 143 days (IQR 44–309) after allogeneic HCT. ICU admission occurred at a median of 8 days (IQR 5-16) after the onset of respiratory symptoms.
In-hospital mortality (figure 1) occurred mostly during the ICU stay (24/25), with most patients dying of acute respiratory failure at a median of 24 days (IQR 11-30) after ICU admission. Mortality was higher in patients who require invasive mechanical ventilation (22/33 (66%) vs 3/12 (25%), p=0.02).
Most patients received systemic steroids for ILD treatment (40/40 patients with available data). There was no difference in the time to initiation of specific treatment between ICU survivors and non-survivors (median of 2 days in both arms, p=0.42). Among the 13 patients who received a second-line immunosuppressive therapy (cyclosporin (n=4), ruxolitinib (n=3), anti-TNFα (n=3), MMF (n=1), missing data (n=2)) in the ICU, 5/13 (38%) survived the hospital stay. Among 20 survivors, 10/20 (50%) later developed to chronic pulmonary GVHD in the form of bronchiolitis obliterans syndrome requiring long term inhaled bronchodilators (n= 6/10) and/or immunosuppressive agents (n=4/10) (3 patients with systemic steroids alone, 1 with steroids, anti-TNFα and a Jak2 inhibitor).

Age (median, IQR) (45/45)*	60 [40-66]
Female Sex (45/45)*	14 (31%)
HCT-CI (34/45)* ≤2	27 (79%)
Previous respiratory disorder (44/45)* - Obstructive ventilatory disorder - Restrictive ventilatory disorder	6 (14%) - 5 (11%) - 1 (2%)
Underlying disease (45/45)* - Acute leukemia or myelodysplastic syndrom - Lymphoproliferative disease - Others	 37 (84%) 3 (7%) 3 (7%)
Stem cell source (45/45)* : Peripheral blood stem cells	43 (96%)

Donor type (45/45)* - Matched related donor - Haplo-identical - Unrelated donor	15 (33%) 12 (27%) 18 (40%)
Myelo-ablative conditioning (43/45)*	23 (53%)
Total body irradiation (45/45)*	11 (24%)
Previous acute GVHD (45/45)*	30 (67%)
Previous chronic GVHD (45/45)*	6 (13%)

- *The numbers in brackets indicate the number of patients with available data



Conclusions: ILD with inaugural respiratory failure is a rare but severe complication after allogeneic HCT with a high in-hospital mortality rate. Long term follow-up shows a high overall burden of the disease with more than half of patients dying and half of survivors developing chronic pulmonary GVHD.

Disclosure: Nothing to declare

A386

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INCIDENCE AND RISK FACTORS OF NON-INFECTIOUS PULMONARY COMPLICATIONS FOLLOWING LOW-DOSE-RATE TOTAL BODY IRRADIATION

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Background: Non-infectious pulmonary complications (NIPCs) are potentially life-threatening complications following hematopoietic stem cell transplantation (HSCT). Historically, total body irradiation (TBI) at our institution was performed at a high dose rate (17–21 cGy/min). Since high-dose-rate TBI is a known risk factor for NIPCs, we recently reduced the dose rate to <10 cGy/min. This study aimed to evaluate the cumulative incidence and risk factors of NIPCs in patients receiving low-dose-rate TBI.

Methods: We prospectively enrolled patients undergoing allo-HSCT with a conditioning regimen containing TBI at a dose rate of 7–8 cGy/min. NIPCs were defined by the presence of at least one of the following criteria in the absence of infectious etiology (confirmed via blood culture or bronchoalveolar lavage): (1) two or more refractory respiratory symptoms, (2) pulmonary consolidation on chest radiography, or (3) respiratory dysfunction/hypoxia.

Results: A total of 56 patients were included (30 males, 26 females). The mean age was 46.5 years (range: 17–69). The 1-year cumulative incidence of NIPCs was 15.2% (95% CI: 7.0–26.2%). Although a higher incidence was observed in older patients (>50 years) compared to younger patients (21.7% vs. 10.3%), the difference was not statistically significant (P = 0.191). No significant difference was observed between total TBI doses of 4 Gy (14.9%) and 12 Gy (15.9%; P = 0.946), and smoking history was not associated with NIPC incidence (P = 0.722). Notably, none of the five patients who received anti-thymocyte globulin (ATG) for GVHD prophylaxis developed NIPCs, suggesting that T-cell immunity may play a pivotal role in the pathogenesis of NIPCs. The 1-year overall survival was 60% in patients with NIPCs compared to 87% in those without.

Conclusions: Despite the implementation of low-dose-rate TBI, NIPCs remain a significant complication with a cumulative incidence of 15.2%, showing a trend toward higher incidence in older patients. The complete absence of NIPCs in the ATG group underscores the potential involvement of T-cell alloreactivity. Further comparative studies between low- and high-dose-rate TBI cohorts are warranted to establish the optimal irradiation strategy.

Disclosure: Nothing to declare.

A387

A PHASE III, RANDOMIZED, DOUBLE-BLIND, PLACEBO CONTROLLED STUDY OF CURCUMIN TO REDUCE MUCOSITIS IN AUTOLOGOUS TRANSPLANT SETTING

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Background: Mucositis is a significant complication of autologous hematopoietic stem cell transplant, with severe mucositis reported to occur in up to 70% patients receiving melphalan based chemotherapy. In a previous pilot study, we had reported that curcumin reduced incidence of severe mucositis in a cohort of patients receiving melphalan based conditioning. We conducted this randomized, placebo-controlled, double-blind study to definitively evaluate role of curcumin in this setting.

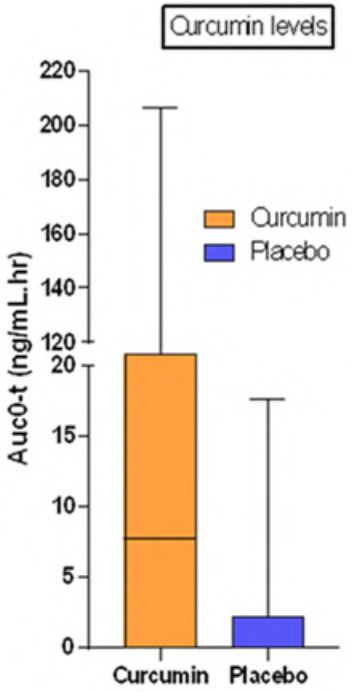
Methods: Patients aged ≥18 years undergoing autologous HSCT with either melphalan 200 mg/m^2 or BEAM or Bu-Mel were randomized centrally in 1:1 ratio (with help of computer-generated random sequence, stratified according to conditioning regimen) to receive curcumin (4 lozenges BD each containing 100 mg of curcumin, starting two days prior to conditioning chemotherapy) or matching placebo. All patients provided written informed consent, had ECOG PS 0-2, and had adequate organ function. Those receiving anti-oxidants, NSAIDs, aspirin or systemic steroids for past 3 months with last dose taken within a week prior to enrolment were excluded. Patients were assessed daily from start of lozenges till day +28 of transplant. The primary endpoint was incidence of grade III/IV mucositis. Secondary endpoints included incidence of grade III/IV nausea, vomiting, diarrhoea, the duration of these toxicities as well as requirement of opioids and total parenteral nutrition. Oral mucositis was graded according to WHO severity scale; nausea, vomiting and diarrhoea as per CTCAE v4.0. Exploratory endpoints included pharmacokinetics of curcumin and evaluation of serum and salivary cytokines. Serum and salivary cytokines were assessed prior to the 1st dose of study drug, on day 0 and then thrice a week till day +14. Pharmacokinetic analysis was done through 4 serum samples on day 7 of start of intervention. Based on information from pilot study, we hypothesized 20% reduction in grade III/IV mucositis with curcumin. A sample size of 95 in each group (total 190) was required to detect a 20% difference with 80% power. A two-sided alpha of 5% was assumed. Two interim analyses were planned, one after 75 patients completed assessment for primary endpoint and another after 125 patients. At interim analysis, it was planned to calculate conditional power and to stop enrolment for futility if conditional power was 0.2 or less.

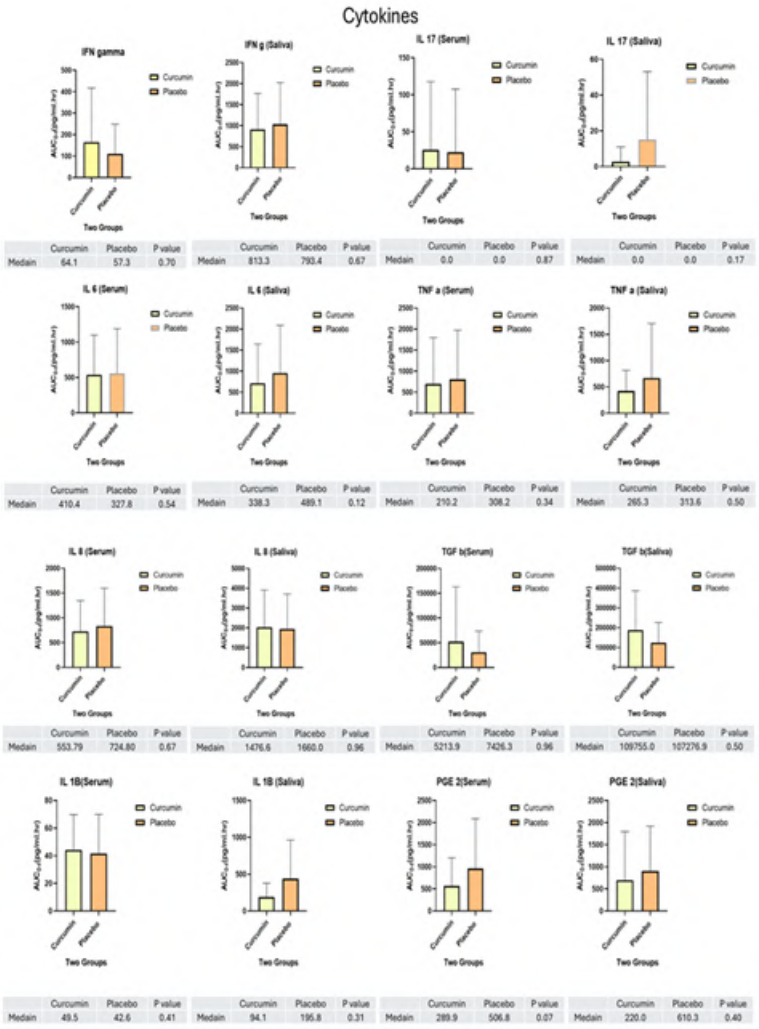
Results: Between December 2018 to April 2025, 77 patients (median age 45 years, 56 males) were enrolled. The baseline characteristics are shown in table. The incidence of grade III/IV oral mucositis was 36.8% in the curcumin group vs 25.6% in the placebo group (p=0.29). There was no difference in any of the secondary endpoints (Table). The study was terminated after the first interim analysis due to futility (Conditional power = 0.13).

Pharmacokinetic analysis confirmed a statistically significant difference in the median curcumin AUC_{0-t} between the intervention and control group (7.7 vs 0 ng•hr/ml), p=0.0003 (Figure, left part). There was no difference in any salivary or serum cytokine between two groups (Figure, right part).

	Curcumin (n=38)	Placebo (n=39)	p value
Baseline characteristics			
Age (median, range)	44 (18-63)	45 (18-63)	0.61
Gender Males Females	 29 (76.32%) 9 (23.68%)	 27 (69.24%) 12 (30.76)	0.61
Diagnosis Multiple myeloma Hodgkin lymphoma NHL Others	 28 (73.68%) 6 (15.79%) 3 (7.89%) 1 (2.64%)	 30 (76.92%) 3 (7.69%) 5 (12.82%) 1 (2.57%)	0.67
Conditioning regimen Melphalan 200 mg/m2 BEAM Bu-Mel	 28 (73.68%) 9 (23.68%) 1 (2.64%)	 30 (76.92%) 9 (23.08%) 0	0.89
Outcomes			
Mucositis grade III / IV Incidence Duration	 14 (36.8%) 4 days	 10 (25.6%) 5.5 days	 0.29 0.66
Diarrhoea grade III / IV Incidence Duration	 15 (39.4%) 3 days	 18 (46.2%) 2 days	 0.55 0.56
Nausea grade III / IV Incidence Duration	 2 (5.2%) 2 days	 5 (12.8%) 5 days	 0.25 0.12

Vomiting grade III / IV Incidence Duration	0 --	1 (2.6%) 3 days	0.32 --
Total parenteral nutrition Requirement Duration of use	19 (50%) 8 days	18 (46.1%) 7.5 days	0.73 0.88
Opioids use Requirement Duration of use	20 (50.6%) 7 days	15 (38.4%) 7 days	0.14 0.96





Conclusions: This double-blinded, placebo-controlled, phase III RCT failed to demonstrate benefit of curcumin in reducing incidence of grade III/IV mucositis associated with high-dose melphalan.

Clinical Trial Registry: Clinical Trial Registry of India (CTRI), website - ctri.nic.in, Registration number - CTRI/2018/09/015846
ClinicalTrials.gov, Registration number NCT04896164

Disclosure: Nothing to declare

A388

COMPREHENSIVE PAIN MANAGEMENT IN PAEDIATRIC ALLOGENIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): RETROSPECTIVE AUDIT OF SPECIALIST PAIN TEAM REFERRALS AND DEVELOPMENT OF A PILOT PAIN-MANAGEMENT PATHWAY

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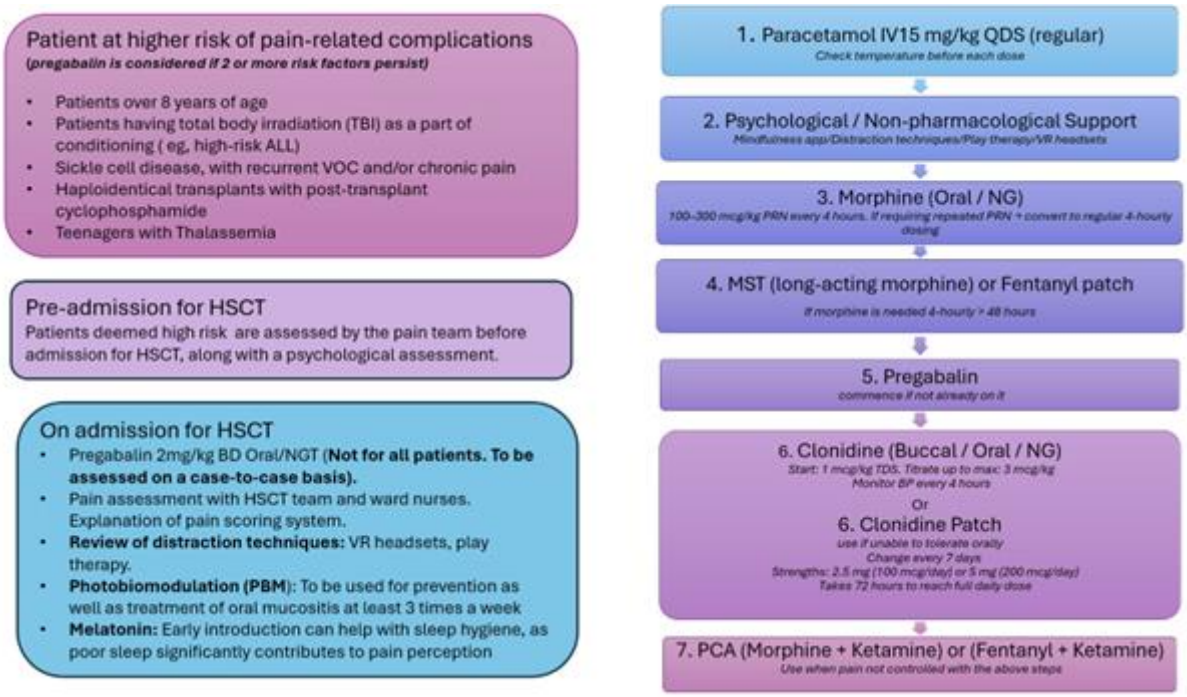
Background: Children undergoing Hematopoietic Stem Cell Transplantation (HSCT) frequently experience significant and prolonged pain, from both physical complications—such as mucositis, graft versus host disease (GVHD), infections, and organ toxicity, as well as psychological distress. Current pain management practices are inadequate, leaving children vulnerable to suffering. There is an urgent need to develop evidence-based supportive care guidelines tailored to paediatric HSCT.

Methods: We conducted a retrospective audit of paediatric patients undergoing allogeneic HSCT who were referred to a specialist pain management service. Following the audit, certain high-risk groups and risk factors were identified, and a pilot pain management pathway was established (Figure 1). Multiple novel interventions are being undertaken via this pain pathway, including pre-HSCT assessment from the specialist pain nurses for patients identified as high risk, use of pregabalin in patients with chronic pain, especially with underlying sickle cell disease, nonpharmacological measures like use of play therapy, distraction techniques including virtual reality(VR) sets, photobiomodulation (PBM), focus on sleep hygiene and a stepwise escalating analgesia plan incorporating regular paracetamol at an early stage.



Results: From 1st January 2023 to 31st December 2024, 29.8% (14/47) of patients were referred and reviewed by the specialist pain team, with 27.6% (13/47) requiring patient- or nurse-controlled analgesia (PCA/NCA). Table 1 describes patient characteristics. Sex and intensity of conditioning do not impact PCA/NCA use. The odds of requiring specialist input were higher among patients older than 8 years (odds ratio 3.84, p = 0.05). Similarly, increased referrals were seen in patients undergoing HSCT for osteopetrosis, HSCT with haploidentical donors, TBI-based conditioning for ALL, and teenagers undergoing HSCT for haemoglobinopathies. The mean duration of PCA use was 16.8 days (range, 6 to 33 days), and 70% of patients required a PCA/NCA within 7 days of stem cell infusion. 53.8% (7/13) of patients required PCA for unexpected complications like perianal abscess(n=2), haemorrhagic cystitis (n=2) and severe hepatic Veno-occlusive disease (VOD) (n=1).
Since the implementation of the pathway, five patients were deemed high risk, reviewed pre HSCT by the pain team and initiated on pregabalin. Patients undergoing HSCT for non-malignant conditions did not require a PCA/NCA, and no adverse events have been reported with the regular use of paracetamol and pregabalin. Three (3/12, 25%) patients have needed PCA/NCA. All three patients were high-risk HSCT for relapsed/refractory acute leukaemia (and developed severe acute complications in the immediate post-HSCT period (grade IV GVHD, grade III VOD with GI bleeding post defibrotide and fatal grade IV VOD).

Table 1: Characteristics of patients referred to pain services

Characteristics	Referred to pain services	Not referred to pain services

Male Female	26.9% (7/26) 33.3% (7/21)	73.1% (19/26) 66.7% (14/21)
Age groups • 0-2 years • 2-5 years • 5-8 years • 8-12 years • 12-16 years	 30% (3/10) 0 14.3% (1/7) 36.4% (4/11) 50% (6/12)	 70% (7/10) 100% (7/7) 85/7% (6/7) 63.7% (7/11) 50% (6/12)
Common Transplant Indications • Acute lymphoblastic leukaemia (ALL) • Acute myeloid leukaemia (AML) • Aplastic anaemia • Osteopetrosis • Inborn errors of metabolism • Sickle cell disease • Thalassemia	 42.8% (3/7) 0 14.3% (1/7) 50% (2/4) 14.3% (1/7) 42.8% (3/7) 50% (3/6)	 57.2% (4/7) 100% (3/3) 85.7% (6/7) 50% (2/4) 85.7% (6/7) 57.2% (4/7) 50% (3/6)
Conditioning • Myeloablative • Nonmyeloablative	 29.3% (12/41) 33.3% (2/6)	 70.7% (29/41) 66.7% (4/6)
HLA matching • Fully matched • Mismatched (including mismatched cords, ≤2 HLA mismatches) ** • Haploidentical	 32.4% (11/34) 10% (1/10) 66.7% (2/3) *	 67.6% (23/34) 90% (9/10) 33.3% (1/3)
Stem cell source • Bone marrow • Cord • Peripheral blood	 34.4 % (11/32) 16.7% (2/12) 33.3% (1/3)	 65.6% (21/32) 83.3% (10/12) 66.7% (2/3)

*Both patients received post-transplant cyclophosphamide (PTCy)
**mismatched cord HSCT for high-risk paediatric AML

Conclusions: Better, more focused management of pain, using novel pharmacological and non-pharmacological measures, can improve the HSCT experience for children, and specialist pain management services and dedicated guidance are vital. Regular paracetamol can be safely used as an analgesic without masking sepsis. Use of Pregabalin is safe in the immediate post-transplant setting, with no adverse toxicities, interactions, or negative impact on engraftment. This pilot is currently underway, with real-time data analysis.

Disclosure: Nothing to declare

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EARLY ACUTE KIDNEY INJURY IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: A 634-RECIPIENT COHORT STUDY

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Background: Acute kidney injury (AKI) is a frequent complication after allogeneic hematopoietic cell transplantation (HCT). Its etiology is multifactorial, including pre-renal causes such as dehydration from gastrointestinal toxicity, intrinsic injury from sepsis, transplant-associated thrombotic microangiopathy and nephrotoxic drugs, and post-renal obstruction. Calcineurin inhibitors (CNIs), namely cyclosporine (CSA) and tacrolimus (TAC), contribute to nephrotoxicity but represent only part of this complex scenario. Early AKI is particularly relevant because it too occurs during the initial and most vulnerable post-transplant phase, when patients remain hospitalized and exposed to intense metabolic and inflammatory stress, and may require CNI reduction or interruption with implications for GVHD prophylaxis. We aimed to characterize the incidence and severity of early AKI and to explore its temporal association with CSA and TAC plasma levels in a large single-center cohort of allogeneic HCT recipients.

Methods: This retrospective single-center cohort included allogeneic HCT recipients transplanted from 2002 to 2023, excluding umbilical cord blood grafts. Clinical, laboratory and transplant-related variables were extracted from electronic medical records. AKI was

defined and staged according to KDIGO 2012 serum creatinine criteria (Stage 1: ≥1.5 to 1.9 × baseline or ≥0.3 mg/dL increase; Stage 2: 2.0 to 2.9 × baseline; Stage 3: ≥3.0 × baseline or ≥4.0 mg/dL). Baseline creatinine was the last stable value prior to CNI initiation, maintained for ≥5 days. Early AKI was assessed during the D1 to D21 window after CNI initiation. CSA and TAC were administered intravenously with therapeutic drug monitoring. Descriptive statistics included absolute and relative frequencies or medians with interquartile ranges. Temporal patterns of CSA and TAC concentrations were examined using LOESS smoothing according to AKI status. The study was approved by the institutional ethics committee in accordance with the Declaration of Helsinki.

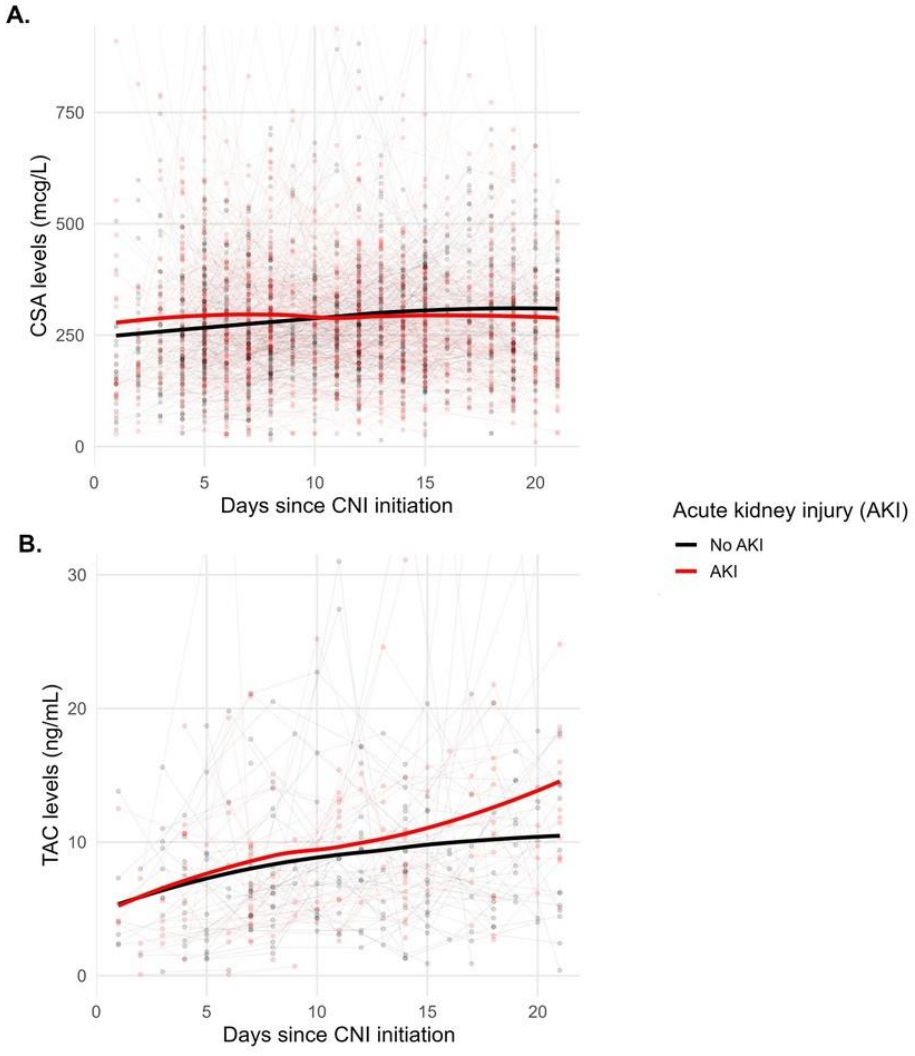
Results: A total of 634 allogeneic HCT recipients were included. The median age was 28.6 years, 67.7% were adults and 84.7% had malignant diseases. CSA was used in 563 patients (88.8%) and TAC in 71 (11.2%). Bone marrow was the predominant graft source (70.2%) and 65.3% underwent myeloablative conditioning. Early AKI occurred in 297 recipients (46.8%), while 337 (53.2%) had no AKI (Table 1). According to KDIGO staging, Stage 1 occurred in 16.4%, Stage 2 in 21.9% and Stage 3 in 8.5%. Moderate-to-severe AKI (Stages 2 and 3) was more frequent among CSA recipients (31.3%) compared with TAC (23.9%). LOESS analyses revealed distinct CNI exposure-response patterns. In the CSA group, mean levels were similar between AKI and non-AKI patients, with slightly higher early concentrations among AKI cases in the first 10 days, followed by reversal (Figure 1A). In contrast, TAC-treated patients showed a progressive widening separation between AKI and non-AKI curves, with higher TAC levels among AKI cases mainly from the second week onward (Figure 1B)**.**

Table1. Incidence and severity of acute kidney injury (AKI) in allogeneic HCT recipients

Category	Subgroup	n (%)
Overall AKI incidence	No AKI	337 (53.2)
	AKI	297 (46.8)
AKI stage (KDIGO)	No AKI	337 (53.2)
	Stage 1	104 (16.4)
	Stage 2	139 (21.9)
	Stage 3	54 (8.5)
AKI severity by CNI	CSA – No / Stage 1	387 (68.7)
	CSA – Stage 2–3	176 (31.3)

	TAC – No / Stage 1	54 (76.1)
	TAC – Stage 2–3	17 (23.9)

Abbreviations: AKI, acute kidney injury; CNI, calcineurin inhibitor; CSA, cyclosporine; TAC, tacrolimus.



Conclusions: Early AKI was frequent, with a considerable proportion of moderate-to-severe cases. CSA and TAC showed distinct temporal exposure patterns, suggesting different windows of nephrotoxic vulnerability during the early post-transplant period. These findings support individualized CNI monitoring and early risk-stratification strategies to mitigate renal toxicity in allogeneic HCT recipients.

Clinical Trial Registry: Not applicable. This study is not a clinical trial.

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A PHASE 1 DOSE-ESCALATION STUDY OF UMBILICAL CORD BLOOD MONONUCLEAR CELL INFUSION FOR SECONDARY POOR GRAFT FUNCTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Secondary poor graft function (sPGF) is a life-threatening complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT), characterized by persistent cytopenias despite complete donor chimerism. Currently, no standardized treatment is available for sPGF.
Umbilical cord blood mononuclear cells (UCB-MNCs) are heterogeneous, comprising hematopoietic stem cells, immune regulatory cells, and other functional subsets. These cells have been shown to secrete hematopoietic growth factors, promote tissue repair, and modulate the immune microenvironment, suggesting potential for restoring sPGF hematopoiesis. However, the safety and optimal dosing of UCB-MNCs remain unclear, requiring prospective clinical evaluation.

Methods: We conducted an open-label, phase 1 clinical trial (ClinicalTrials.gov, NCT06792682) using a standard 3+3 dose-escalation design to assess the safety and preliminary efficacy.
Eligible patients were ≥18 years of age, met the diagnostic criteria for sPGF and had an Eastern Cooperative Oncology Group (ECOG) performance status ≤2.
In the dose-escalation phase, patients were sequentially enrolled into three cohorts receiving UCB-MNCs at doses of 2.0×10^6, 3.5×10^6, and 5.0×10^6 cells/kg per infusion. All patients received four consecutive weekly intravenous infusions with standard supportive care. Dose-expansion phase will enroll an additional six patients at the recommended dose level, using the same administration schedule.
The primary endpoint was safety, assessed by the incidence and severity of adverse events (AEs), graded according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. Secondary exploratory efficacy endpoints included time to neutrophil and platelet recovery.

Results: As of December 8, 2025, six patients (three each in the 2.0×10^6 cells/kg and 3.5×10^6 cells/kg cohorts) had completed the four-week UCB-MNCs infusion protocol and a minimum follow-up of seven weeks. Enrollment in the 5.0×10^6 cells/kg cohort and the dose-expansion phase is ongoing.
During treatment and follow-up, two patients experienced adverse events, including one case

of grade 2 cytomegalovirus (CMV), one case of grade 1 pulmonary infection, and one case of grade 2 chronic graft-versus-host disease (cGVHD). All adverse events were managed successfully with standard clinical interventions and resolved without long-term sequelae. None of the reported AEs were considered related to UCB-MNCs infusion.
No dose-limiting toxicities (DLTs) were observed in either cohort. Importantly, no acute infusion-related adverse events—such as fever, chills, hypotension, or allergic reactions—occurred during or within 24 hours after UCB-MNCs administration. All patients maintained stable vital signs and organ function throughout the study period, and all remained alive at the time of last follow-up.
The best post-treatment platelet counts in the low- and medium-dose cohorts were 46 (9-65) $\times 10^9$/L and 63 (15-110) $\times 10^9$/L, respectively, increasing from the baseline values of 19 (13-22) $\times 10^9$/L and 14 (5-26) $\times 10^9$/L; corresponding neutrophil counts were 1.07 (0.87-1.24) $\times 10^9$/L and 2.94 (2.46-7.33) $\times 10^9$/L, rising from the baseline of 0.73 (0.73-1.03) $\times 10^9$/L and 0.76 (0.07-1.51) $\times 10^9$/L.

Conclusions: This phase 1 dose-escalation study indicate that repeated intravenous infusion of UCB-MNCs at doses of 2.0×10^6 and 3.5×10^6 cells/kg is well tolerated in sPGF patients. Ongoing dose-escalation and expansion phases will determine the recommended dose, further characterize long-term safety, and evaluate the hematopoietic efficacy of UCB-MNCs in this high-risk population.

Clinical Trial Registry: ClinicalTrials.gov, NCT06792682 ; Study Details | NCT06792682 | The Safety and Efficacy of Umbilical Cord Blood Mononuclear Cells in Patients With Secondary Poor Graft Function After Hematopoietic Stem Cell Transplantation | ClinicalTrials.gov

Disclosure: Nothing to declare.

A391

THE ROLE OF DEFIBROTIDE AS PROPHYLAXIS FOR VENOCCLUSIVE DISEASE IN PEDIATRIC THALASSEMIA STEM CELL TRANSPLANTATION USING IV BUSULFAN CONDITIONING. A RETROSPECTIVE SINGLE-CENTER 10-YEAR EXPERIENCE

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Background: Venocclusive disease (VOD) remains a significant post-transplant complication in pediatric hematopoietic stem cell transplantation (HSCT), particularly in high-risk patients, i.e., Thalassemia. Defibrotide is approved for the treatment of severe hepatic VOD/SOS after HCT in patients older than 1 month of age in the European Union. Several studies have found that defibrotide prophylaxis can reduce the incidence of VOD/SOS in high-risk patients; however, the latest literature shows no significant difference in VOD incidence with

defibrotide prophylaxis. This study evaluates our center's retrospective experience with defibrotide as prophylaxis to prevent VOD in pediatric thalassemia patients undergoing stem cell transplantation with IV busulfan-based conditioning.

Methods: We retrospectively evaluated 43 pediatric thalassemia patients (age < 14 years) who underwent HSCT with IV busulfan-based conditioning, with a targeted level dose adjusted above 60mg/h/L, at our institution from 2015 to 2024. VOD was diagnosed and graded following the latest EBMT criteria. Statistical analysis was performed using SPSS version 28.0 with descriptive statistics, Chi-square tests, Fisher's exact tests, and independent t-tests ($p < 0.05$ considered significant).

Results: 43 patients (mean age 6.7 ± 3.8 years; 60.5% male), 38 (88.4%) received defibrotide prophylaxis, predominantly from day −7 to +21 (42.1%). VOD developed in 17 patients (39.5%), with mild-to-moderate severity predominating (82.4%). Most VOD cases presented early (52.9% within 0−14 days post-transplant), with a primary clinical diagnosis (64.7%). Management included strict input/output balance, diuretics, and continued defibrotide. Notably, all 17 VOD patients achieved complete resolution, with zero PICU admissions, zero VOD-related morbidity, and zero VOD-related mortality. All patients survived (100%), with one patient had idiopathic secondary graft failure with aplastic anemia (2.2%), rescued by a second unrelated stem cell transplant. Almost five (11.6%) of 43 patients did not receive defibrotide prophylaxis; interestingly, two of those patients developed VOD (40%). No statistically significant associations were found between VOD development and gender ($p = 0.415$), age ($p = 0.539$), pre-transplant risk factors ($p = 0.446$), conditioning type ($p = 0.735$), or defibrotide prophylaxis ($p = 1.000$). The duration of hospitalization was shortened, possibly after the switch to the TBF (Thiotepa, Busulfan, and Fludarabine) regimen.

Table: Patient characteristics and outcome

		Presence of VOD No # (%)	***Presence of VOD Yes # (%)***	***Sig. Values***
Gender	*Female*	*9 (52.9%)*	*8 (47.1%)*	*0.415[a]*
	Male	*17 (65.4%)*	*9 (34.6%)*	
Age (Years)	*Mean (Sd)*	*6.43 (4.0)*	*7.16 (3.4)*	*0.539 [c]*
Pre-Transplant Risk Factors	*No*	*6 (75.0%)*	*2 (25.0%)*	*0.446 [b]*
	Yes	*20 (57.1%)*	*15 (42.9%)*	
Conditioning Type	*RT-MAC*	*21 (58.6%)*	*13 (38.2%)*	*0.735 [a]*
	MAC	*5 (55.6%)*	*4 (44.4%)*	
	Class 1	*12 (60.0%)*	*8 (40.0%)*	*0.946 [b]*

		Presence of VOD No # (%)	***Presence of VOD Yes # (%)***	***Sig. Values***
Pissarro Classification	*Class 2*	*13 (41.9%)*	*8 (38.1%)*	
	Class 3	*1 (50.0%)*	*1 (50.0%)*	
Defibrotide Prophylaxis	*No*	*3 (60.0%)*	*2 (40.0%)*	*1.000* [b]
	Yes	*23 (60.5%)*	*15 (39.5%)*	
PICU Admission	*No*	*25 (59.5%)*	*17 (40.5%)*	*-*
	Yes	*0 (0.0%)*	*0 (0.0%)*	
GVHD Prophylaxis	*CSA/MTX*	*23 (59.0%)*	*16 (41.0%)*	*0.761* [b]
	CSA/Prednisolone	*1 (50.0%)*	*1 (50.0%)*	
	CSA/MMF	*2 (100.0%)*	*0 (0.0%)*	
Deaths	*No*	*25 (59.5%)*	*17 (40.5%)*	*1.000* [b]
	Yes	*0 (0.0%)*	*0 (0.0%)*	

(a) Chi-Square Test, (b) Fisher's Exact Test, (c) Independent T Test
Reduced toxicity-Myeloablative chemotherapy (RT-MAC), Myeloablative chemotherapy (MAC)

Conclusions: Despite a high incidence of around 39.5% patients having VOD in our pediatric thalassemia cohort, fortunately, none of the patients had severe VOD leading to any morbidity or mortality. All patients were managed at the pediatric BMT unit without any significant complications. We acknowledge the limited sample size, the retrospective nature of the study, and the limited control group. These observations suggest that the routine use of defibrotide prophylaxis in patients undergoing HCT for B-thalassemia major may not reduce the incidence of VOD post-SCT as described in the latest literature. However, we will seek a larger control group at our institute for future studies to verify our results.

Disclosure: Nothing to declare.

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IMPACT OF ANTIBIOTIC USE IN EARLY FEVER AFTER HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE

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Background: Early fever is a frequent complication after haploidentical hematopoietic stem cell transplantation (haplo-HSCT) with post-transplant cyclophosphamide (PTCY), most often related to cytokine release syndrome (CRS), although infectious causes must always be excluded. The impact of broad-spectrum antibiotic (BSA) use in this context remains unclear. This study evaluates the incidence of early fever after haplo-HSCT, associated infectious events, and transplant outcomes.

Methods: We conducted a single-center, retrospective study including 144 consecutive adult patients who underwent haplo-HSCT with PTCY between January 2019 and March 2024. All patients received PTCY 50 mg/kg on days +3 and +4, followed by tacrolimus and mycophenolate mofetil as graft-versus-host disease (GVHD) prophylaxis. Early fever was defined as temperature ≥37.8°C between stem cell infusion (day 0) and day +4. Twenty-three patients with fever or antibiotics before infusion were excluded.

Results: Median age was 53 years, 60.3% were male. AML wast the most frequent diagnosis (38.8%). Most had intermediate disease risk (65.3%) and high age-adjusted HCT-CI (76%). Peripheral blood was the graft source in 99% of cases, and donors were most commonly children (48.8%). The incidence of early fever was 85% (103/121), with no significant differences by conditioning regimen. Fever commonly started on day +1 (range 0–4). Median peak temperature was 38.5 °C; median C-reactive protein (CRP) was 142.8 mg/L. Fever duration was a median of 4 days (IQR 3–5). Early fever met criteria for CRS in 92.2% of cases (95/103), mostly grade 1 (86/95,90.5%). Eleven patients received tocilizumab for CRS grade ≥2. Levofloxacin prophylaxis was used in 72.8%, and empirical BSA in 82.5% (85/103), mainly piperacillin/tazobactam(67%).
A microbiological isolate was the primary cause of fever in 8 (7.8%), all catheter-related: three catheter-related bloodstream infections (S. haemolyticus, S. epidermidis, S. oralis) and five catheter colonizations (coagulase-negative Staphylococcus, methicillin-resistant, Bacilllus spp, S. epidermidis, S. maltophiilia). In three additional cases with positive isolates, fever was attributed to CRS: low-level CMV reactivation, CRS grade ≥2 with C. jejuni stool culture, and asymptomatic bacteriuria with K. pneumoniae. No differences were observed in fever onset, peak, duration, or CRP between CRS and microbiological documented cases. Antibiotic therapy was adjusted when a pahogen was identified.
Subsequently, 86.4% (89/103) developed significant infections and 15.5% (16/103) new colonizations, all due to multidrug-resistant organisms. Two patients developed infections

caused by previously identified colonizing organisms (one catheter colonization, and one catheter-related bloodstream infection). No other patient develop infections with these microorganisms.
With a median follow-up of 22 months (IQR 11.2–47.4), 12-month overall survival (OS) and event-free survival (EFS) were 73.5% (95%CI,64.7–80.5) and 61.1% (95%CI,51.9–69.2) respectively. There were no significant differences in OS (p=0.082) or EFS (p=0.487) between patients with or without early fever. Early fever was not significantly associated with neutrophil/platelet engraftment, or acute/chronic GVHD.

	Summary N=121 (100%)
Age, years, median (range)	53 (18-71)
Sex recipient (male), N (%)	73 (60,3)
Diagnosis, N (%) - AML - MDS - ALL - NHL/CLL - HL - SMPC - Other	 47 (38.8) 11 (9.1) 18 (14.9) 23 (19) 7 (5.8) 8 (6,6) 7 (5,8)
Disease Risk Index (DRI), N (%) - Low - Intermediate - High/Very high - Not applicable	 9 (7.4) 79 (65.3) 29 (24) 3 (2.5)
HCT-CI (age-adjusted), N (%) - 0 - 1-2 - ≥ 3	 4 (3.3) 25 (20.7) 92 (76)
Stem cell source – peripheral blood, N (%)	120 (99.2)
Infused CD34+ cells (×10⁶/kg), median (range)	6.8 (3.2-12.1)
Donor relationship, N (%) - sibling - father - mother - child - second-degree relative - unrelated	 31 (25.6) 8 (6.6) 4 (3.3) 59 (48.8) 18 (14.9) 1 (0.8)
Donor sex (male), N (%)	68 (56.2)
Donor age, median (range)	35 (15-66)

Conclusions: Early fever after haplo-HSCT with PTCY is common and mostly CRS-related. Only a minority of episodes are infectious. However, most patients received empirical BSA, potentially contributing to pathogen selection and subsequent infectious complications. These findings highlight the need for biomarkers and standardized criteria to guide BSA in this setting.

Disclosure: Nothing to declare

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AUTOIMMUNE-LIKE HEPATITIS OF ALLOGENIC ORIGIN: A RARE BUT DISTINCT ENTITY IN POST-TRANSPLANT LIVER DYSFUNCTION

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Background: Liver disfunction (LD) is common after allogenic hematopoietic stem cell transplant (allo-HSCT). Graft-versus-host disease (GvHD) is a frequent cause of LD, and it typically occurs alongside GVHD-driven injury to other organs. Isolated hepatic GvHD is rare, with reported incidences below 3%. When multiple etiologies are suspected, liver biopsy becomes essential. Beyond conventional hepatic GVHD histopathological patterns, autoimmune-like hepatitis (AILH) constitutes a rare and poorly characterized entity. This study aims to determine the incidence and describe the clinicopathological features of AILH within our post-transplant cohort.

Methods: We conducted a retrospective study of adult patients undergoing allo-HSCT from January 2015 to December 2024. Acute LD was defined as alanine aminotransferase (ALT) or aspartate aminotransferase (AST) ≥2× the upper limit of normal (ULN) or total bilirubin (Br) ≥1.5× the ULN. Primary objective was to estimate the cumulative incidence of biopsy-proven AILH of allogeneic origin. Clinical data, transplant characteristics, biochemical parameters at LD onset, histopathological findings, treatment and outcomes were reviewed.

Results: A total of 246 allo-HSCT procedures were performed during the study period, 107 cases were clinically classified as acute GvHD, but only 2 of these presented isolated hepatic involvement (1.8% of all cases of acute GvHD, 0.8% of all allo-HSCT). In addition, 4 patients (Table 1) exhibited late isolated hepatic disease at a median of 274 days post-allo-HSCT (range, 241–292) with biopsy features consistent with AILH, accounting for 1.6% of all allo-HSCT. Histopathological evaluation (Figure 1) demonstrated a plasma-cell–rich inflammatory infiltrate involving both lobules and portal tracts, causing multifocal hepatocellular necrosis and variable cholestasis without duct loss. This histopathological pattern differs from the usual hepatic GvHD, defined by bile-duct damage (apoptotic lymphocytic cholangiolitis) with lobular hepatitis of mild degree. All four patients received glucocorticoids and calcineurin inhibitors, achieving early complete response. Nevertheless, as with AILH outside the allo-HSCT setting, they required prolonged low-dose immunosuppression due to biochemical relapses upon discontinuation of corticosteroids. All four remain on active treatment with a median of 1175 days after diagnosis (range, 372-3531).

Table 1: Clinical and transplant characteristics of the patients diagnosed with AILH.

	Patient and Transplant characteristics									Laboratory da diagnosis	
Case	Age (years)	Sex	Underlying disease	Donor type	Cell source	HLA disparity	Conditioning regimen	GvHD prophylaxis	Day of onset of LD	ALT (U/L)	AS (U/
1	39	F	HL	RD	PB	Matched	RIC	MTX + Tac	241	2042	162
2	36	M	AML	RD	PB	Matched	MAC	MTX + Tac	266	405	296
3	68	F	MM	RD	PB	Matched	RIC	MTX + Tac	282	1026	120
4	65	M	AML/MDS	RD	PB	Mismatched	RIC	PTCy + Tac + MMF	292	574	501

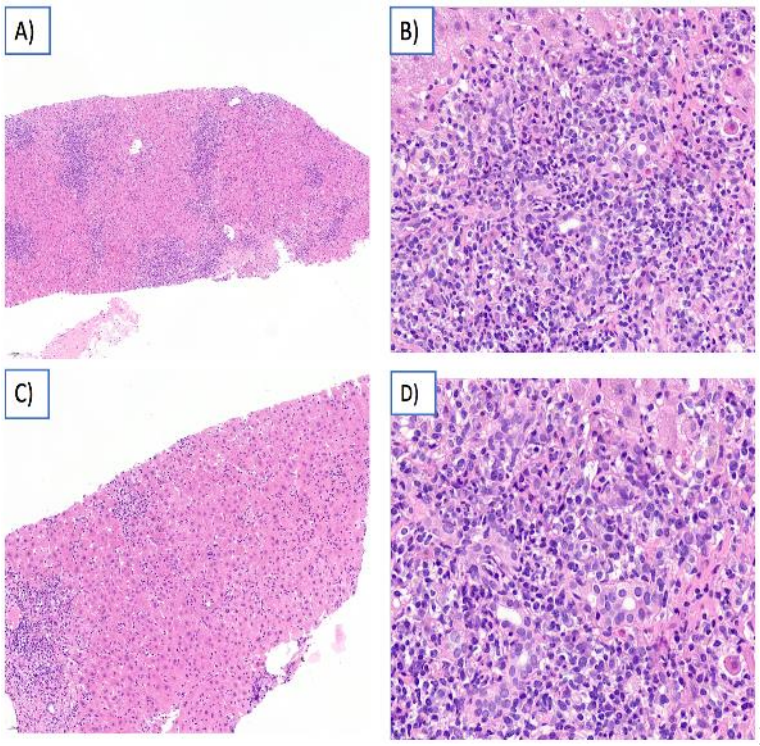

Image 1: Pathology of AILH. A): Hepatic parenchyma showing a dense inflammatory infiltrate at the portal and lobular levels (100X). B) The inflammatory infiltrate is predominantly composed of plasma cells, accompanied by lymphocytes and occasional eosinophils. Hepatocellular apoptosis is identified (400X[DP1] [DP2]). C) Lobular involvement by the inflammatory infiltrate (400X). D) Evidence of bile duct injury characterized by intraepithelial lymphocytes, cytoplasmic eosinophilia of ductal epithelium, and vacuolization (400X).

Conclusions: AILH constitutes an uncommon yet distinctive form of late alloimmune hepatic injury with autoimmune features after allo-HSCT. Its characteristic biopsy pattern allows differentiation from classical hepatic GvHD. In addition, their clinical behavior does not follow the induction of tolerance common to alloresponses in GVHD, and despite achieving rapid complete responses, they continue to require sustained long term inmunosupression.

Disclosure: No conlict of interest declared.

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TRANSPLANTATION-ASSOCIATED THROMBOTIC MICROANGIOPATHY: INCIDENCE AND MANAGEMENT IN SETTINGS WITH LIMITED BIOMARKERS AND NO ACCESS TO TARGETED THERAPIES

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Background: Thrombotic microangiopathy (TMA) is one the most serious complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT) and associated with high morbidity and mortality. The objective of the study was to evaluate the cumulative incidence (CI) of transplantation-associated TMA (TA-TMA), clinical features, and management in patients transplanted with hematological disorder**.**

Methods: A retrospective descriptive study, included all consecutive patients with hematological disorder, who underwent allo-HSCT from HLA-matched sibling or haplo-identical donors, between January 2016 and December 2023. Conditioning regimens were TBI or Busulfan iv-based. Graft versus host disease (GVHD) prophylaxis consisted on cyclosporine and short course of methotrexate +/- ATG. Stem cell source was bone marrow or peripheral blood stem cells (PBSCs). The EASIX score was assessed at day 0, day +30, day +100 and at last follow-up. The diagnosis of TMA was established according to Jodele criteria with the unavailability of plasma sC5b-9 measurements. The consensus defines TA-TMA response by combining hematologic/biologic improvement with organ-specific recovery.

Results: This study included 243 patients with a median age of 27 years (range, 4 - 55y) and a sex ratio of 1.8. Underlying diseases were aplastic anemia (31.7%), ALL (30.5%), AML (22.2%), others (15.6%).
Twelve patients (5%) developed TA-TMA after a median time of 67 days (range, 15 days – 12 months). Early TA-TMA (<100 days) was observed in 83% of cases. EASIX score was significantly higher in patients with TA-TMA compared to patients without TA-TMA, at day 30, day 100 and at last follow-up ($p<10-3$,$<10-3$ and 0.022, respectively).
In multivariate analysis, acute GVHD and microbiologically documented fever were significantly associated with TA-TMA ($p= 0.048$ and 0.032, respectively).
Cyclosporine was discontinued in all cases of TA-TMA and switched to mycophenolate mofetil. Blood transfusion was required in 10 patients (83%) with a median transfusion of red blood cell 5 (range, 3-39) and platelet concentrates 7 (range, 3-78). None patient received plasma

exchange and one patient received iv N-acetylcysteine. Partial response was observed after a median time of 30 days (range, 15–110d) and complete response after a median of 90 days (range, 14–8 months).
After a median follow-up of 36 months (range, 5 day –110 months), 3-year overall survival (OS) was 42% in patients with TA-TMA vs 82% in patients without TA-TMA (p=<10-3). The CI of non-relapse mortality (NRM) was 61% and 13%, respectively (p < 0.0001). The causes of death in patients with TA-TMA were: acute respiratory distress (n=3), multiorgan failure (n=3), and septic shock (n=1). The attributable mortality of TA-TMA was 22%. The CI of relapse was 17% and 13%, respectively (p=0.74).

Conclusions: In our experience, the TA-TMA was associated with a high NRM. Early monitoring using plasma sC5b-9 levels and access to targeted therapies are essential.

Disclosure: Nothing to declare.

A395

NARSOPLIMAB IN CRITICALLY ILL PATIENTS WITH TA-TMA REQUIRING INTENSIVE CARE: A SINGLE CENTER STUDY

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Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is a severe endothelial injury syndrome following allogeneic hematopoietic stem cell transplantation (allo-HSCT), frequently leading to multiorgan dysfunction and high mortality. Outcomes are particularly poor for patients requiring intensive care, and therapeutic options remain limited. Targeted inhibition of the lectin complement pathway with narsoplimab (anti–MASP-2) has emerged as a promising strategy in high-risk TA-TMA, but evidence in critically ill patients remains scarce. We describe our single-centre real-world experience with narsoplimab in allo-HSCT recipients with TA-TMA requiring ICU support.

Methods: This retrospective single-centre observational study included all adult allo-HSCT recipients diagnosed with TA-TMA who required ICU admission and received narsoplimab. Narsoplimab was provided via an Expanded Access Program (EAP) (https://www.omeros.com).

Results: Seven patients were included (Table 1). Median time from allo-HCT to TA-TMA diagnosis was 26 days (range −1 to 769); the outlier corresponds to a patient who developed TA-TMA two years after allo-HSCT in the context of lung transplantation for pulmonary GVHD (#3). Median time from TA-TMA diagnosis to ICU admission was 5 days (range −27 to 137). All patients fulfilled diagnostic and high-risk TA-TMA criteria according to the 2023 Harmonized Consensus.
ICU admission was prompted by acute kidney injury, respiratory failure, or shock. At ICU admission, median APACHE II score was 15 (range 10–26), 6/7 patients (85.7%) required

renal replacement therapy, 6/7 mechanical ventilation (one patient invasive mechanical ventilation), and 3/7 patients (42.8%) required vasopressors. Four patients had concomitant infections, and two had active GVHD. Median ICU stay was 14 days (range 4–36). Narsoplimab was initiated at a median of 3 days after TA-TMA diagnosis (range 1–144), with a median of 13 doses per patient (range 12–26), one patient remains on therapy to date. It was used as first-line therapy in all but one patient (#2), who was refractory to prior treatment with the C3 inhibitor pegcetacoplan. According to ASTCT/EBMT consensus criteria, an overall response was observed in 5/7 (71.4%) patients, complete in 1/7 and partial in 4/7 (57.1%), and 2 were nonresponders (28.6%). No infusion-related reactions were observed. Severe infections during treatment occurred in 4/7 patients (57.1%), all while in the ICU. All cases survived at day 30 from the start of treatment with narsoplimab. Five out of seven (71.4%), were discharged from ICU and remained alive at day 90 of treatment initiation, while two patients died from TA-TMA at a median of 41 days (34 and 48 days;#1 and #7, respectively). One additional patient died months after TA-TMA resolution from an unrelated post-transplant lymphoproliferative disease (#5). Five of these very high-risk critically ill TA-TMA cohort (57.1%) were alive at 1 year since the start of narsoplimab therapy.

Table 1. Baseline characteristics of patients.

Patient	Sex	Age	Hematological disease	Donor	Conditioning	Indications for ICU admission	APACHE score	Response
#1	M	22	ALL	MUD	MA	ARF	10	NR
#2	F	63	NHL	MSD	SM	ARF, AKI	10	PR
#3	M	22	ALL	Haplo	MA	PC	15	CR
#4	F	20	AML	Haplo	MA	HC	15	PR
#5	M	27	ALL	CB	MA	ARF	17	PR
#6	M	46	ALL	CB	MA	ARF, AKI	12	PR
#7	F	23	AA	MUD	SM	ARF	26	NR

M= Male; F= Female; ALL= Acute Lymphoblastic Leukemia; NHL= Non Hodgkin Lymphoma; AML= Acute Myeloblastic Leukemia; AA= Aplastic Anemia; MUD: Matched Unrelated Donor; MSD: Matched Sibling Donor; Haplo: Haploidentical donor; CB: Cord Blood; MA: Myeloablative; SM: Sub-myeloablative; ARF: Acute Respiratory Failure; AKI: Acute Kidney Injury; PC: Postoperative Care; HC: Hemorrhagic Complications; CR: Complete Response; PR: Partial Response; NR: No Response.

Conclusions: In this real-world cohort of critically ill allo-HSCT recipients, narsoplimab was feasible, well tolerated and associated with clinical responses despite the severity of illness. Although limited by small sample size, these findings support narsoplimab as a potentially effective therapeutic option for severe TA-TMA requiring intensive care. Larger multicentre studies are warranted.

Disclosure: Nothing to declare.

A396

RESELECT1&2: INTERVENTIONAL STUDIES FOR THE TREATMENT OF POOR GRAFT FUNCTION POST ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Poor Graft Function (PGF), defined by the presence of multilineage cytopenia despite complete donor chimerism, is a significant complication of allogeneic stem cell transplant (alloSCT). PGF is associated with a high burden of non-relapse mortality and lacks an established standard of care, calling for the development of novel therapeutic strategies.

Methods: RESELECT 1&2 are sequential investigator-initiated single-arm clinical trials repurposing established therapeutics to target bone marrow microenvironment (BMME) dysfunction in PGF. Both studies have the same inclusion criteria; PGF defined as complete donor chimerism and 2-3 lineage cytopenias. The primary efficacy endpoint for both studies is restoration of neutrophil and platelet count at the end of the 12-week treatment period. Prior publications identified reactive oxygen species (ROS) and endothelial cell (EC) dysfunction as features of the BMME in PGF. RESELECT1 (ACTRN12620001339943) evaluated atorvastatin as EC directed therapy and the ROS scavenger N-acetyl cysteine (NAC) in combination as treatment for patients with PGF. Correlative studies using flow cytometry and single-cell RNA sequencing were performed on peripheral blood and bone marrow mononuclear cells collected during RESELECT1. These analyses informed the design of RESELECT 2 (NCT06607367), a currently recruiting Phase II study evaluating the safety and efficacy of combination eltrombopag and ruxolitinib in the treatment of PGF.

Results: A total of ten out of twenty planned patients were recruited to RESELECT1 (Table1). Nine of the ten completed the 12-week treatment period. One patient experienced early disease relapse and discontinued study participation. Only one participant achieved a complete response, and recruitment was discontinued prematurely for futility after a prespecified interim look on ten completed patients.
Correlative analyses from RESELECT1 identified atypical monocyte and T-cell populations in patients with PGF, with transcriptomic analysis implicating IFN-γ and JAK-STAT signalling as central mediators of the dysregulated immunity in the BMME of PGF patients. This informed the decision to combine ruxolitinib, a JAK inhibitor that suppresses cytokine production in T and NK cells, and eltrombopag, a TPO mimetic with pre-clinical evidence of mitigating the suppressive effect of IFN-γ on haematopoietic function and an established role in aplastic anaemia.
A total of 20 patients will be recruited into RESELECT2 across two sites in Australia, and outcomes will be compared with a historic patient cohort. Five patients with PGF have been recruited to RESELECT2, of whom three have completed three months of therapy and have

12-week efficacy data available for evaluation (Table1). All three evaluable patients have achieved response defined by independence from growth factor and transfusion support. One patient developed clinically relevant minor bleeding in the context of persistent thrombocytopenia and ceased ruxolitinib therapy on trial day 28. Ruxolitinib associated cytopenias have not been observed in other participants to date.

Table 1: Demographic and transplant data at trial enrolment of RESELECT 1&2

Trial	RESELECT1 (Participants N=10)	RESELECT2 (Participants N=5)
Age in years at enrolment: Median (Range)	54 (46 – 74)	62 (53 – 66)
Sex, n (%)	Female 7 (70%)	Female 3 (60%)
Primary Diagnosis, n (%)	AML 5 (50%) MF 2 (20%) NHL, MDS, B-ALL 3 (30%)	MDS 2 (40%) AML, MF, MCL 1 (20%)
Donor Type, n (%)	MSD 4 (40%) MUD 3 (30%) Haplo, MMUD 3 (30%)	MSD 2 (40%) MUD 2 (40%) Haplo 1 (20%)
Conditioning Intensity, n (%)	RIC 8 (80%) MAC 2 (20%)	RIC 3 (60%) MAC 1 (20%) Unconditioned* 1 (20%)
Graft Type, n (%)	PBSC (90%)	PBSC (100%)
Days post transplant D0, Median (Range)	134 (48 – 253)	112 (49 – 434)
Screening CD3+ chimerism (%), Median (Range)	100 (85 – 100)	100 (43 – 100)
Screening $CD3^-$ chimerism (%), Median (Range)	100 (97 – 100)	100 (100 – 100)

*Unconditioned second transplant following graft failure.

AML = acute myeloid leukaemia, MF = myelofibrosis, NHL = non-Hodgkin lymphoma, MDS = myelodysplastic syndrome, B-ALL = B cell acute lymphoblastic leukaemia, MCL = mantle cell lymphoma, MSD = matched sibling donor, MUD = matched unrelated donor, MMUD = mismatched unrelated donor, haplo = Haploidentical donor, RIC = reduced intensity conditioning, MAC = myeloablative conditioning, PBSC = peripheral blood stem cell

Conclusions: Correlative analyses from the RESELECT1 trial identify immune dysregulation in the BMME as targetable mediators of PGF. Early data from the ongoing RESELECT2 trial suggests that the combination of ruxolitinib and eltrombopag holds promise as a potentially safe and efficacious intervention for PGF. Further studies are required to improve the outcomes of patients suffering from this under recognised clinical entity.

Clinical Trial Registry: RESELECT1: anzctr.org.au ACTRN12620001339943
RESELECT2: clinicaltrials.gov NCT06607367

Disclosure: This trial was funded by a project grant from Maddie Riewoldt's Vision. Trial medications for RESELECT2 were supplied by Novartis.

A397

HEPATIC VENOUS PRESSURE GRADIENT TO DIAGNOSE VENO-OCCLUSIVE DISEASE AFTER HEMATOPOIETIC BONE MARROW TRANSPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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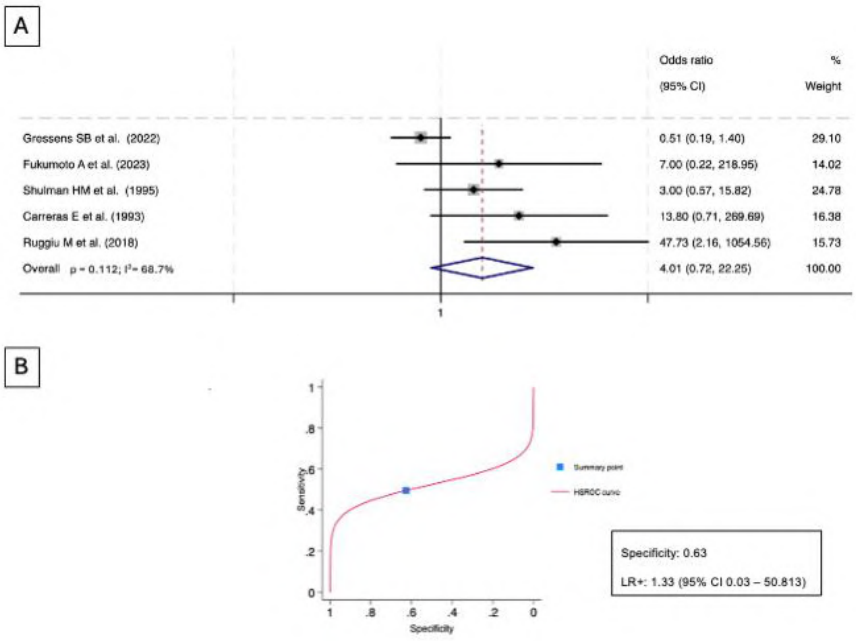
Background: Veno-occlusive disease (VOD) is a severe and potentially fatal complication after hematopoietic stem cell transplantation (HSCT). Although portal hypertension is a key pathophysiological feature of VOD, the diagnostic value of hepatic venous pressure gradient (HVPG) measurement, historically considered the gold standard, recent evidence has questioned its accuracy. Moreover, it is an invasive technique, only available in few tertiary centers, limiting its applicability. Given these methodological limitations, non-invasive techniques such as liver stiffness measurement (LSM), commonly used in hepatology as an alternative to HVPG, have also been proposed in the HSCT setting for the diagnosis of VOD. Therefore, in this systematic review, we aimed to re-evaluate HVPG diagnostic accuracy in patients with suspected VOD after undergoing HSCT.

Methods: MEDLINE and Scopus were systematically searched up to July 17, 2025 for studies evaluating HVPG in patients with suspected VOD after HSCT. Eligible studies included patients undergoing HVPG measurement with available data on VOD diagnosis based on histology. A random-effects meta-analysis was performed to assess the association between HVPG ≥10 mmHg and VOD. Diagnostic accuracy was evaluated using a bivariate random-effects and hierarchical summary receiver operating characteristic (HSROC) model, estimating pooled sensitivity, specificity and likelihood ratios (LR).

Results: Six studies met the inclusion criteria, comprising 214 patients who underwent HVPG measurement; VOD was diagnosed in 81 patients, while 133 had alternative diagnoses. Mean HVPG values were higher in patients with VOD than in those without (13.5 vs 8.5 mmHg). HVPG ≥10 mmHg was associated with increased odds of VOD (pooled odds ratio (OR) 4.01), but this did not reach statistical significance (95% confidence interval (CI) 0.72 – 22.25; p = 0.112), with moderate between-study heterogeneity (I^2: 68.7%). (Figure 1A) Regarding the diagnostic accuracy, the pooled sensitivity was 0.50 (95% CI 0.25 – 0.75) and pooled specificity was 0.63 (95% CI 0.01 – 1.00). Positive likelihood ratios was 1.33

(95% CI 0.03 – 50.813), while the negative likelihood ratio 0.81 (95% CI 0.077 – 8.467). (Figure 1B)



Conclusions: HVPG ≥10 mmHg shows limited and imprecise diagnostic accuracy for VOD after HSCT. In fact, although higher HVPG values are more frequent in VOD, this systematic review and meta-analysis shows that HVPG values ≥10 mmHg show both a low sensitivity and specificity. Therefore, HVPG is not reliable in confirming or excluding VOD diagnosis. These findings support current guideline recommendations that HVPG should not be used as a standalone diagnostic tool and highlight the need for integrated diagnostic strategies, both with invasive (e.g. liver biopsy) and non-invasive methods (e.g. liver elastography).

Disclosure: Nothing to declare.

A400

PLASMINOGEN ACTIVATOR INHIBITOR-1 (PAI-1) IS AN EARLY BIOMARKER OF SEVERE SINUSOIDAL OBSTRUCTION SYNDROME AFTER PEDIATRIC HSCT

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Background: Sinusoidal obstruction syndrome (SOS) remains a potentially life-threatening complication after allogenic HSCT. Early diagnosis and treatment can limit disease severity but are challenged due to the lack of specific diagnostic criteria. The pathogenesis of SOS is initiated by damage to sinusoidal endothelial cells, by toxic metabolites of the conditioning regimen with subsequent coagulation. Therefore, biomarkers reflecting endothelial damage and coagulation may facilitate early and more accurate diagnosis. Plasminogen activator inhibitor-1 (PAI-1) is released from activated platelets and synthesized by endothelial cells in response to inflammatory stress. We investigated PAI-1 as a biomarker for SOS and other endothelial toxicity syndromes after pediatric allogenic HSCT.

Methods: We prospectively included 114 children (median age: 8.8 years) undergoing standard HSCT at Rigshospitalet, Denmark (2010-2019) for malignant or benign diseases and 200 healthy controls (Table 1). SOS was diagnosed according to the paediatric EBMT criteria.
Plasma levels of PAI-1 were measured by Luminex before conditioning and on days 0, +7, +14, +21, +30, +90, and +180 post-HSCT. Due to PAI-1´s association with platelets, PAI-1 levels were normalized with concurrent platelet count (PLT).

Results: PAI-1/PLT ratio increased from pre-conditioning, peaked on day +14 (111 vs. 267 ng/10^9 platelets, p<0.0001) and then gradually declined. High PAI-I/PLT ratio at pre-conditioning and throughout day +180 was associated with higher patient age (all p< 0.05). Further, higher PAI-1/PLT was associated with malignant diagnosis (day +0: 175 vs. 123 ng/10^9 platelets (p=0.001); day +30: 200 vs. 97 ng/10^9 platelets (p=0.0073)), and with busulfan-based conditioning (day +21: 668 vs. 179 ng/10^9 platelets (p=0.03); day +30:266 vs. 100 ng/10^9 platelets (p= 0.0007)). PAI-I/PLT was not associated with recipient sex, donor type, graft type, ATG or aGvHD prophylaxis (p≥0.05).
Fifty-one patients were diagnosed with SOS at median day +7 (range: +2 to +58). PAI-1/PLT was significantly higher in patients diagnosed with SOS grade II-IV (n=47) than in patients with grade 0-I (n=67) from day 0 to +90 (figure A). Four patients, who were started on defibrotide for severe SOS had significantly increased PAI-1/PLT ratio (figure B).
In a multivariable analysis, a doubling in PAI-1/PLT on day 0 was independently associated with increased risk of SOS after adjusting for busulfan, malignant diagnosis and age (PAI-1/PLT: OR=1.47, 95%CI=1.03-2.17, p=0.042; busulfan: OR= 7.12, 95%CI=2.89-20.89, p=<0.0001; malignant diagnosis: OR=1.41, 95%CI=0.54-3.70, p=0.48; age above median: OR=1.42, 95%CI=0.56-3.65, p=0.46).
PAI-1/PLT was significantly higher on day 0 in patients with capillary leak syndrome (CLS) (n=15) compared to those without CLS (260 vs 140 ng/10^9 platelets, p=0.0018). No associations were observed between PAI-1/PLT and aGvHD (grade 0-I vs. II-IV) (n=52) or with engraftment syndrome (n=13).

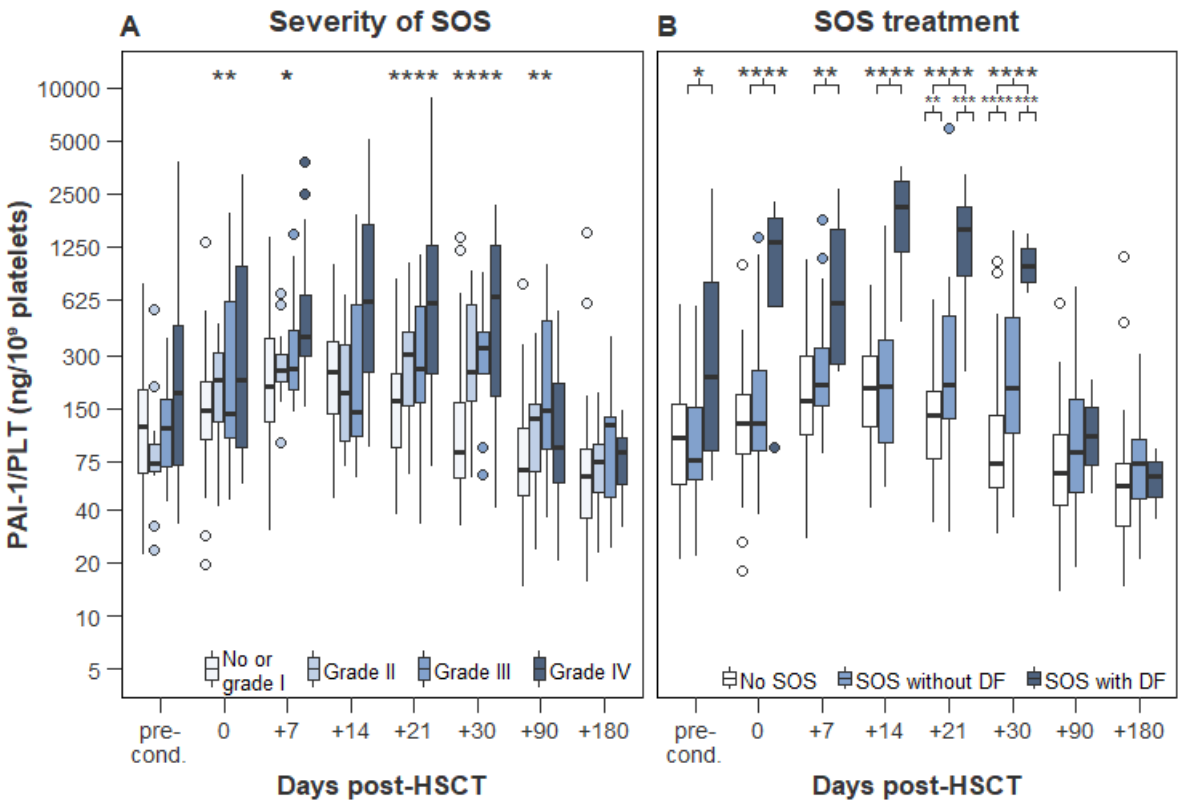

Table 1: Characteristics of study population	Patients (n=114)	Controls (n=200)
Sex, male, *n* (%)	67 (58.8%)	97 (48.5%)
Age *(years)*, median *(range)*	8.8 (1.1-17.6)	11.7 (6.0-18.8)
Diagnosis, *n (%)*		
ALL	29 (25.4%)	
AML	17 (14.9%)	
Other malignancies	23 (20.2%)	
PID	17 (14.9%)	
SAA	10 (8.8%)	
Other non-malignant diseases	18 (15.8%)	
Donor type, *n (%)*		
Matched unrelated donor (9/10 and 10/10)	81 (71.1%)	
Matched sibling donor	33 (28.9%)	

Stem cell source, *n (%)*		
Bone marrow	109 (95.6%)	
Peripheral blood	5 (4.4%)	
Conditioning regime, *n (%)*		
TBI 12 Gy + CY/VP16	23 (20.2%)	
BU-based	50 (29.9%)	
TREO-based	26 (0.9%)	
Other	15 (13.2%)	
ATG as part of GvHD-prophylaxis, *n (%)*	86 (75.4%)	
Prophylactic Defibrotide, *n (%)*	7 (6.1%)	

Conclusions: PAI-1/PLT appeared to be an early, independent biomarker for the prediction of severe SOS. In patients requiring treatment with defibrotide, this difference was significant already before the start of conditioning. These results suggest that PAI-1/PLT may serve as a prognostic biomarker for severe SOS after pediatric HSCT.

Disclosure: Nothing to declare.

A401

DEFIBROTIDE RESCUE FOR PEDIATRIC VENO-OCCLUSIVE DISEASE/SINUSOIDAL OBSTRUCTION SYNDROME; A SINGLE-CENTER 10-YEAR EXPERIENCE

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Background: Veno-occlusive Disease (VOD, aka sinusoidal obstruction syndrome) is a highly morbid and potentially fatal endothelial hepatotoxicity in the post-HSCT setting. The development of VOD has been linked to multiple risk factors relating to patient, disease, or transplant characteristics. Outcome of VOD has tremendously improved since the approval of defibrotide (DF) as a rescue agent. The EBMT criteria for diagnosing and grading VOD in pediatrics have been adopted worldwide since their publication in 2018, thus unifying clinical practice and adding to the conformity across literature. We report our 10-year single-center experience with post-HSCT VOD for pediatric patients treated with DF rescue.

Methods: We conducted a retrospective chart review. Patients included were those who received DF rescue for post-HSCT VOD in the pediatric department at King Hussein Cancer Center between 1/1/2014 and 31/12/2024. Diagnosis of VOD was made via Baltimore and EBMT criteria before and after 2018, but both criteria were retrospectively applied to the whole cohort.
The primary outcomes were DF treatment response, VOD resolution by day 100, 100-day and 1-year mortality. Secondary outcomes included overall survival (OS) estimates at 12

months, as well as analysis of risk factors for survival and VOD resolution.
Descriptive statistics were used to summarize cohort characteristics. Survival probabilities were estimated using Kaplan-Meier methodology. Cox proportional hazards regression models were used to evaluate risk factors for overall survival. Variables considered included age, VOD severity, conditioning intensity, and DF response. Analyses were performed using R (version 4.5.1).

Results: Thirty-four patients met criteria for inclusion, representing 4% of the total transplanted patients in the study period. Median age was 5.8 years (range; 0.5, 23) with 18% below 1 year and 6% above 18 years. Male:female ratio was 1.3.
Eighty-eight percent of patients underwent allogeneic HSCT, mostly for non-malignant disease (76%). Twenty-five patients (73.5%) had more than one risk factor for VOD before HSCT, the commonest risk factors being myeloablative conditioning (79%), haplo-identical donor (53%), and high pre-transplant ferritin (41%).
While all patients fulfilled diagnosis per EBMT criteria, only 53% fulfilled it per Baltimore criteria. Seven cases were late-onset VOD. DF rescue was started at median of 12 days post-HSCT (range, 4-172), for a median duration of 18 days, mostly for severe VOD (16 patients). Rate of VOD resolution by day 100 was 88.2%. Four patients died of very severe VOD and multi-organ failure at a median duration of 58 days from VOD diagnosis (range; 5,133). All-cause mortality at 100 days and 1 year was 8.8% and 18%, respectively. Overall mortality rate was 20.6%. Estimated Overall survival at 12 months was 80.4%. DF response was the only statistically significant factor found to be related to survival on Cox regression (HR 0.04, 95% CI 0.01–0.33, p=0.002). Earlier diagnosis of VOD (median 11 vs. 31 days post-HCT, p=0.023) was associated with higher likelihood of resolution.

Conclusions: DF rescue offers an effective treatment for VOD. Early recognition of VOD and response to DF are major determinants of survival. The EBMT criteria offer a reliable tool for early recognition and treatment of VOD.

Disclosure: Nothing to Declare.

A402

ASSESSMENT OF CARDIOVASCULAR RISK BURDEN AND ITS IMPACT ON OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Cardiovascular events (CVE) represent an emerging long-term complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Traditional cardiovascular risk factors (CVRF) are prevalent in the general population, but their specific burden and clinical consequences in allo-HSCT recipients, considering post-transplant cardiovascular outcome, overall survival (OS) and transplant-related mortality (TRM) remains insufficiently described.

Methods: We performed a retrospective, single-centre analysis including adult patients who underwent allo-HSCT for malignant or non-malignant high-risk hematologic diseases between 2013 and 2023. Patients were stratified into two groups based on the presence or absence of CVRF at the time of transplantation, including arterial hypertension, dyslipidaemia, diabetes, obesity, active or past smoking and family history of cardiovascular disease. We evaluated the association of baseline CVRF and the occurrence of CVE during post allo-HSCT long-term follow-up, as well as their impact on transplant outcomes, including OS and TRM. CVE included new onset moderate-to-severe heart failure, arrhythmias, valvular heart disease, myocardial infarction, deep vein thrombosis, pulmonary embolism, and cerebrovascular events.

Results: A total of 710 patients were included in the study, among them, 292 (41%) had no CVRF, while 418 (59%) had at least one CVRF at the time of allo-HSCT. The median follow-up of the population was 548 days (95% CI, 461-690 days). Patients and transplantations´ characteristics are listed in **Table 1**. Of note, in both cohorts more than 80% of patients had an EBMT risk-score of 3 or higher. Two-hundred and three patients out of 418 (49%) had 1 CVRF, 123 (29%) presented 2 CVRF and 92 (22%) had 3 or more CVRF. The most frequently observed CVRF was obesity (n=219, 52%), followed by arterial hypertension (n=192, 46%) and smoking (n=174, 42%). Patients presenting CVRF at the time of allo-HSCT had an increased incidence of CVE during the follow-up (27% in the CVRF-cohort versus 16.7% in the non CVRF-cohort, p=0.0011). We did not observed statistically significant differences in 1-year OS between the two groups (60% in the non CVRF-cohort versus 56% in the CVRF-cohort, p=0.47). Considering the TRM, no differences were detected considering day +100 early mortality (12% vs 11%, p=0,1097), however TRM at 1-year post-transplant was significantly higher among patients with CVRF compared with those without (57.7% vs. 46.2%, p = 0.0372) and increased proportionally with the number of cardiovascular risk factors (p = 0.0292).

Number		710	292	418	
Age at transplant	median (years), range	57 (18-75)	54 (18-75)	59 (18-75)	**p<0.001**
Sex	male, n (%)	432 (61%)	158 (54.1%)	274(65.5%)	**0.0023**
	female, n (%)	278 (39%)	134 (45.9%)	144 (34.5%)	
Diagnosis	AML, n (%)	313 (44,1%)	134(46%)	179(44%)	**0.0008**
	MDS, n (%)	114 (16,1%)	31 (10.6%)	83 (20%)	
	MPN, n (%)	93 (13%)	33 (11.3%)	60 (14%)	
	ALL, n (%)	60 (8.5%)	34 (11.6%)	26 (6%)	
	NHL, n (%)	68 (9.6%)	33 (11.3%)	35 (8%)	
	MM, n (%)	20 (2.8%)	11 (3.8%)	9 (2%)	
	SAA, n (%)	13 (1.8%)	8 (2.7%)	5 (1%)	
	others, n (%)	29 (4,1%)	8 (2.7%)	21 (5%)	
Anthracycline Treatment	yes, n (%)	419 (59%)	185 (63.4%)	234 (56%)	0.0528
	no, n (%)	291 (41%)	107 (36.6%)	184 (44%)	
Disease status at transplant	upfront + CR, n (%)	421 (59%)	173 (59.3%)	248 (59%)	0.0352
	PR, n (%)	74 (10.5%)	40 (13.7%)	34 (8.5%)	
	REL/REF, n (%)	215 (30.5%)	79 (27%)	136 (32.5%)	
Donor type	SIB, n (%)	129 (18.1%)	62 (21.2%)	67 (16%)	0.3221
	MUD, n (%)	410 (57.7%)	164 (56.2%)	246 (59%)	
	MMUD, n (%)	148 (20.8%)	56 (19.2%)	92 (22%)	
	Haplo, n (%)	23 (32,4%)	10 (3.4%)	13 (3%)	
Conditioning regimen	MAC, n (%)	325 (45.7%)	155 (53%)	170 (41%)	**0.0011**
	RIC, n (%)	385 (54.3%)	137 (47%)	248 (59%)	
GvHD Prophylaxis	ATG + CNI +/- MMF, n (%)	565(79.6%)	227 (77.6%)	338 (81%)	0.563
	PT-Cy + CNI + MMF, n (%)	56 (8%)	25 (8.4%)	31 (7%)	
	others, n (%)	89 (12.4%)	41 (14%)	48 (12%)	
Donor source	PBSC, n (%)	693 (97.6%)	284 (97.3%)	409 (98%)	0.626
	BM, n (%)	17 (2.4%)	8 (2.7%)	9 (2%)	
EBMT-risk score	0-2, n (%)	90 (12.8%)	52 (17.8%)	38 (9%)	**p<0.001**
	3-4, n (%)	344 (48.4%)	136 (46.6%)	208 (50%)	
	≧5, n (%)	276 (38.8%)	104 (35.6%)	172 (41%)	

Table 1: Patients and transplantations´ characteristics. AML:Acute myeloid leukemia, MDS:Myelodysplastic syndrome, MPN:Myeloproliferative neoplasms, ALL:Acute lymphoblastic leukemia, NHL:Non-Hodgkin lymphoma, MM:Multiple myeloma, SAA:Severe aplastic anemia, CR:Complete remission,PR:Partial remission,REL/REF:Relapsed / Refractory disease, SIB:HLA-identical sibling donor, MUD:Matched unrelated donor, MMUD:Mismatched unrelated donor, Haplo:Haploidentical donor, MAC: Myeloablative conditioning, RIC:Reduced-intensity conditioning,GvHD:Graft-versus-host disease, ATG:Anti-thymocyte globulin, CNI: Calcineurin inhibitor, MMF: Mycophenolate mofetil, PT-Cy:Post-Transplant cyclophosphamide, PBSC:Peripheral blood stem cells, BM:Bone marrow, EBMT risk score: European Society for Blood and Marrow Transplantation Risk Score

Conclusions: Our data suggest that patients with CVRF have a higher risk to develop CVE during the post-transplant long-term follow-up. Furthermore, despite baseline differences, OS and early TRM were comparable between groups, with 1-year TRM being higher in patients with CVRF and increasing with the number of CVRF. These results underscore the importance of integrating cardiovascular risk assessment and management into transplant care to reduce transplant-related toxicity and improve patient outcomes.

Disclosure: Nothing to declare.

A403

TRANSPLANT ASSOCIATED THROMBOTIC MICROANGIOPATHY CLINICAL CHARACTERISTIC, RISK FACTORS, THERAPEUTIC MANAGEMENT AND OUTCOME: A SINGLE CENTER RETROSPECTIVE COHORT STUDY

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Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is a serious and potentially life-threatening complication of hematopoietic stem cell transplantation (HSCT), caused by endothelial injury leading to microangiopathic hemolytic anemia, thrombocytopenia, and multi-organ dysfunction. Its true incidence remains underestimated due to heterogeneous diagnostic criteria and overlap with other post-transplant complications such as graft-versus-host disease and viral infections. This study evaluated the clinical characteristics, management, and outcomes of TA-TMA HSCT population.

Methods: A retrospective cohort study was conducted including patients who underwent HSCT between 01 September 2013 and 01 April 2025. TA-TMA was diagnosed using criteria aligned with established international consensus definitions, mainly the Jodele et al Criteria. diagnostic framework. Data were extracted from medical records and transplant databases that included demographics, underlying diagnoses, transplant and donor characteristics, conditioning regimens, engraftment kinetics, post-transplant complications, CNI exposure, therapeutic interventions, and survival outcomes. Descriptive statistics were used to summarize clinical features, and survival analyses were performed to evaluate outcomes at day +100, day +180, and median overall survival.

Results: During the study period, 36 patients developed TA-TMA following HSCT. The median age at transplantation was 24.5 years (range: 1.0–59.0), with a male predominance (53%). Underlying diagnoses were malignant in 58% and non-malignant in 42%, most commonly leukemias (44%) and sickle cell disease (31%). All TA-TMA cases occurred after allogeneic HSCT, with matched related donors accounting for 50%, haploidentical donors 31%, and matched unrelated donors 19%. Reduced-intensity conditioning was used in 69% of cases. TA-TMA developed following a first HSCT in 67% and after a second transplant in 33%. The median time to TA-TMA diagnosis was 61.5 days post-HSCT (range: 2–381). All patients demonstrated laboratory evidence of microangiopathic hemolytic anemia, including schistocytes, elevated LDH (median 891.5 U/L), and thrombocytopenia, fulfilling Jodele diagnostic criteria. Hypertension was present in 89%, and renal involvement in 72%. Acute GVHD was observed prior to or concurrent with diagnosis in 55%, while viral reactivation occurred in 72%, mainly CMV and EBV. At diagnosis, majority of patients were receiving tacrolimus or cyclosporine, and CNI withdrawal was implemented in all cases. A-TMA–directed therapy included supportive care alone in 25% (Defibrotide, plasma Exchange), CNI withdrawal alone in 6%, and complement-targeted therapy in 69%. Eculizumab and

Ravulizumab were used in 31% and 39% of patients, respectively. Hematologic response was achieved in 56%. Overall survival was 83% at day +100 and 72% at day +180, with a median overall survival of 312 days. TA-TMA–attributable mortality occurred in 17% of patients. Lower survival rates were observed in patients with Concurrent GVHD at 34.7% (P=0.907).

Conclusions: Transplant-associated thrombotic microangiopathy (TA-TMA) remains a serious early complication following allogeneic HSCT, frequently associated with infection, GVHD, and viral reactivation. A higher incidence was observed in matched-related donor transplants compared with haplo-identical and matched-unrelated donors, likely reflecting the center's higher utilization of matched-related donors. Early diagnosis using Jodele criteria, prompt calcineurin inhibitor withdrawal, and complement-targeted therapy were associated with improved short-term survival. Nonetheless, TA-TMA-related mortality remained substantial, underscoring the need for standardized diagnosis, early risk-adapted intervention, and prospective studies to improve long-term outcome.

Clinical Trial Registry: None.

Disclosure: No Conflict of interest.

A404

REAL-WORLD EFFICACY AND SAFETY OF DEFIBROTIDE FOR SINUSOIDAL OBSTRUCTION SYNDROME - NATIONWIDE SURVEY

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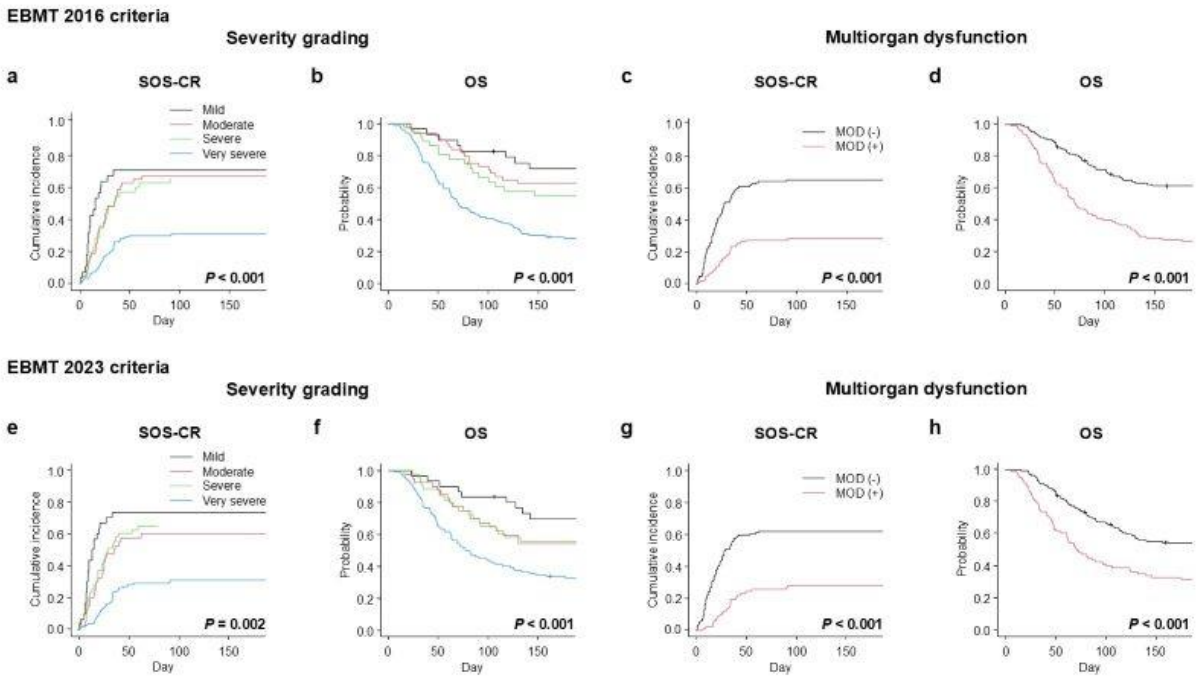
Background: Hepatic sinusoidal obstruction syndrome (SOS) is a severe and life-threatening complication after allogeneic hematopoietic stem cell transplantation (HSCT). Defibrotide (DF) has been demonstrated the efficacy for the treatment of SOS.

Methods: We conducted a nationwide survey to evaluate the efficacy and safety of DF for SOS. We collected data of patients who developed SOS after HSCT and were treated with DF between 2019 and 2021 from the Transplant Registry Unified Management Program. The

detailed background of SOS and treatment outcomes were obtained by additional questionnaires.

Results: A total of 221 patients with the median age of 51 years were analyzed. The median interval from HSCT to SOS diagnosis was 18 days (range, 0 - 365 days). The Modified Seattle criteria were met in 125 patients, the EBMT 2016 classical criteria were met in 66 patients, the EBMT 2016 late-onset criteria were met in 87 patients, and only the EBMT 2023 probable criteria were met in 6 patients, respectively. The EBMT 2016/2023 severity grading were mild in 29/30 patients, moderate in 49/40 patients, severe in 36/43 patients, and very severe in 106/107 patients, and multiorgan dysfunction were observed in 96/83 patients. The median interval from diagnosis to start of DF was 0 day (range, -1 - 46 days), with a median duration of DF treatment of 18 days (range 1 - 93 days). With a median follow-up of 1190 days from the diagnosis of SOS in survivors, the cumulative incidence of complete remission of SOS (SOS-CR) was 48.9% and the probability of overall survival (OS) at 100 days and 1-year after HSCT were 57.3 and 34.6%, respectively. Achievement of SOS-CR significantly predicted better OS (CR: 64.7% vs. non-CR: 6.2%, $P < 0.001$). Both the EBMT 2016 and 2023 severity grading and multiorgan dysfunction significantly associated with SOS-CR and OS (Figure 1). Multivariate analysis showed that higher age (HR, 1.574; 95% CI, 1.037 – 2.389; $P = 0.033$), male of sex (HR, 1.648; 95% CI, 1.112 – 2.442; $P = 0.013$), and prior HSCT (HR, 1.859; 95% CI, 1.205 – 2.869; $P = 0.005$) were significantly associated with SOS-CR, and higher age (HR, 1.833; 95% CI, 1.313 – 2.559; $P < 0.001$), prior HSCT (HR, 1.920; 95% CI, 1.327 – 2.779; $P < 0.001$), and higher performance status (HR, 1.559; 95% CI, 1.028 – 2.364; $P = 0.037$) were significantly associated with OS. Grade 3 or higher adverse events were observed in 85 (38.5%) patients, including 27 patients (12.2%) of bleeding-related events.

Figure. 1



Conclusions: Our study showed the efficacy and safety of DF for the treatment of SOS comparable to previous studies. Both the EBMT 2016 and 2023 severity grading showed significant predictive ability for the prognosis of SOS treated with DF.

Disclosure: This study was conducted with research funding from NIPPON SHINYAKU. SS reports research funding from NIPPON SHINYAKU, KY, HI, JK, and TT reports payment from NIPPON SHINYAKU, and KY reports payment from JAZZ pharmaceuticals.

A405

EASIX SCORE AS A PREDICTOR FOR TRANSPLANTATION-ASSOCIATED THROMBOTIC MICROANGIOPATHY IN PAEDIATRIC PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The Endothelial Activation and Stress Index (EASIX) score [(creatinine × LDH) ÷ platelets]) has emerged as a marker of endothelial damage and predictor of endothelial complications and non-relapse mortality (NRM) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Transplantation-associated thrombotic microangiopathy (TA-TMA) is a major complication of HSCT associated with high morbidity and mortality, and initiating targeted therapy at an early stage of the disease may significantly improve outcomes. We explore the EASIX score as a predictive tool for TA-TMA.

Methods: We conducted a retrospective study at a single centre. All consecutive patients undergoing allo-HSCT between 2019 and 2023 were included. The EASIX score was calculated before conditioning (pre-EASIX), on the day of transplantation (EASIX-0) and subsequently on days 7, 14, 21 and 30. The score was log2-transformed according to the literature. TA-TMA was diagnosed according to the Jodele criteria. We analysed the correlation between the EASIX score and the occurrence of TA-TMA. Variables associated with the occurrence of TA-TMA were evaluated using univariate and multivariate analyses with a Cox proportional hazards model.

Results: A total of 143 patients were included, with malignant (n=63;44.1%) and non-malignant (n=80;55.9%) diseases. Median age at transplantation was 7.69 years (IQR 3.04-12.77) and 87 patients were male (60.8%). Most patients received an unrelated donor transplant (n=73,51%), followed by matched related donor (n=39,27.3%) and a mismatched donor transplant (n=31,21.7%). The most common stem cell source was bone marrow, and most patients received a myeloablative or reduced toxicity conditioning regimen (n=114,79.7%).
Globally, 14 patients (9.5%) were diagnosed with TA-TMA, with a cumulative incidence of

8.96% (95%CI 5.19-15.24) 1 year after HSCT.

Table 1 shows the characteristics of patients with or without TA-TMA.

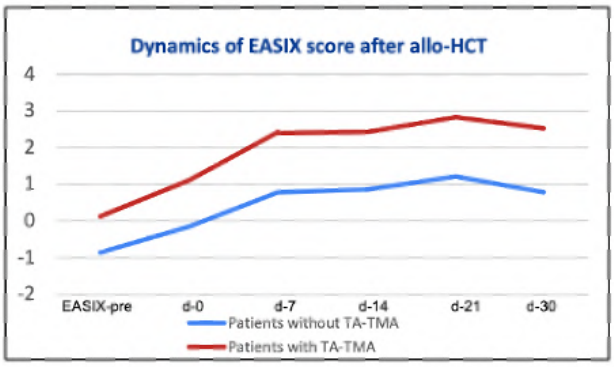
Variable	Patients without TA-TMA (n=129)	Patients with TA-TMA (n=14)	All patients (n=143)	p-value
Age at HSCT, median (range)	7.00 (2.61; 11.30)	14.99 (9.74; 17.28)	7.69 (3.04; 12.77)	**0.0001**
Sex, n (%) Male Female	 79 (61.2%) 50 (38.8%)	 8 (57.1%) 6 (42.9%)	 87 (60.8%) 56 (39.2%)	0.7655
Underlying disease, n (%) Non-malignant Malignant	 73 (56.6%) 56 (43.4%)	 7 (50%) 7 (50%)	 80 (55.9%) 63 (44.1%)	0.6372
Donor, n (%) Matched family donor Unrelated donor Haploidentical donor	 39 (30.2%) 62 (48.1%) 28 (21.7%)	 0 (0%) 11 (78.6%) 3 (21.4%)	 39 (27.3%) 73 (51%) 31 (21.7%)	**0.0171**
Stem cell source, n (%) Bone marrow Peripheral blood Cord blood	 90 (69.8%) 29 (22.5%) 10 (7.8%)	 9 (64.3%) 5 (35.7%) 0 (0%)	 99 (69.2%) 34 (23.8%) 10 (7%)	0.5007
Conditioning regimen, n (%) MAC / RTC RIC	 105 (81.4%) 24 (18.6%)	 9 (64.3%) 5 (35.7%)	 114 (79.7%) 29 (20.3%)	0.1599
Serotherapy, n (%) No Yes	 25 (19.4%) 104 (80.6%)	 1 (7.1%) 13 (92.9%)	 26 (18.2%) 117 (81.8%)	0.4659
***Ex vivo* T cell depletion** No Yes	 121 (93.8%) 8 (6.2%)	 12 (85.7%) 2 (14.3%)	 133 (93%) 10 (7%)	0.2540

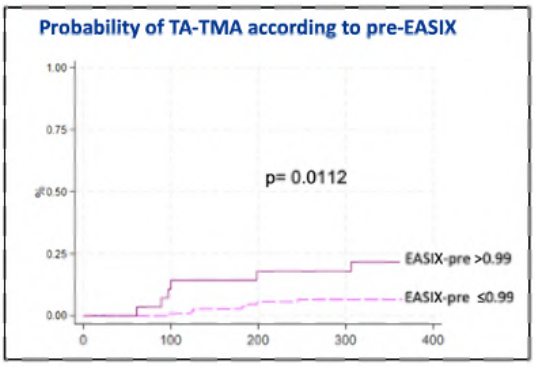
Pre-EASIX, median (IQR)	-0.87 (-1.90; 0.22)	0.99 (-0.45; 2.44)	-0.68 (-1.87; 0.44)	**0.0009**
EASIX-0, median (IQR)	-0.16 (-1.53; 0.87)	1.28 (0.11; 2.65)	0.03 (-1.42; 1.13)	**0.0024**
EASIX-7, median (IQR)	0.78 (-0.08; 1.86)	1.63 (1.14; 2.26)	0.89 (-0.04; 1.94)	0.0988
EASIX-14, median (IQR)	0.86 (0.03; 1.85)	1.56 (1.40; 2.37)	1.02 (0.04; 1.88)	**0.0071**
EASIX-21, median (IQR)	1.22 (0.55; 1.91)	1.61 (0.90; 2.18)	1.26 (0.60; 1.99)	0.0947
EASIX-30, median (IQR)	0.78 (0.05; 1.78)	1.75 (1.19; 3.09)	1.11 (0.18; 1.94)	**0.0117**

EASIX score was superior from admission to day +30 in patients diagnosed with TA-TMA [(pre-EASIX 0.99 vs. -0.87 (p=0.0009), EASIX-0 1.28 vs. -0.16 (p=0.0024), EASIX-14 1.56 vs. 0.86 (p=0.0071), EASIX-30 1.75 vs. 0.78 (p=0.0117)]. In the univariate analysis, the pre-EASIX, EASIX-d0, and EASIX-d14 were statistically associated with the occurrence of TA-TMA: HR 1.52, 95%CI 1.14-2.02, (p=0.0048); HR 1.30, 95%CI 1.05-1.60, (p=0.0153); and HR 1.53, 95%CI 1.06-2.20 (p=0.0236). The other variable significantly predictive of TA-TMA in the univariate analysis was the age at HSCT (HR 1.23, 95%CI 1.09-1.38; p=0.0006).
In the multivariable analysis, both the age (HR 1.17, CI 95% 1.04-1.32 (p=0.0080) and the pre-EASIX strongly predicted the risk of TA-TMA (HR 1.44, 95%CI 1.01-2.04 (p=0.0412). A significant association was also found between the temporal evolution of EASIX and the development of TMA (p=0.0070)
One-year NRM was 9.58% (95% CI 5.67-15.93), with significantly higher EASIX-d21, 2.21 vs. 1.22 (p=0.0488). However, in the multivariate analysis we did not find an association

with the EASIX score and the NRM.

Figure 1. EASIX in patients with or without TA-TMA





Conclusions: Endothelial complications after allo-HSCT are associated with high morbidity and mortality. Our study suggests that the EASIX score could be a useful tool for predicting the development of TA-TMA in paediatric patients undergoing allo-HSCT, and it could guide diagnostic and clinical interventions in patients at risk. However, these results need to be validated in larger cohort of patients.

Disclosure: Nothing to declare

A406

POSITIVE OUTCOMES AMONG PEDIATRIC HCT PATIENTS TREATED WITH DARATUMUMAB FOR AUTO-IMMUNE HEMOLYTIC ANEMIA

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Background: Autoimmune hemolytic anemia (AIHA) is a rare complication following hematopoietic cell transplant (HCT), with an incidence between 4-6%. There are no defined therapies and prospective clinical trials addressing the best approach to treatment. Approach to treatment in the United States have included corticosteroids, rituximab and intravenous immunoglobulin (IVIG) as usually approved by payors for initial management. Yet this post-HCT complication is severe and usually refractory to these treatments. AIHA is considered to be mediated by donor/host derived antibodies and B cell dysregulation. Daratumumab is an anti-CD38 MoAb that potentially targets CD38 expressing nonmalignant autoantibody-producing plasma cells and may be effective for patients with post-HCT AIHA. This study aims to characterize the safety and efficacy of daratumumab for the treatment of post-transplant refractory autoimmune hemolytic anemia.

Methods: Retrospective study among all patients transplanted at our institution between January 2018-December 2025. Demographic and clinical variables were extracted from the electronic medical record, including clinical course and treatment history for patients with a diagnosis of AIHA. Descriptive statistics were used to summarize findings.

Results: The incidence of AIHA during the study period was 0.05%. Patients with AIHA were transplanted at a median age of 20.5 (6-162) months of age and the majority (70%) were transplanted for non-malignant indications (inborn errors of metabolism (50%), primary immune deficiencies (30%). All patients received a myeloablative preparative regimen and 90% received an unrelated cord blood HCT (1 patient received an alpha-beta T cell depleted related haploidentical HCT). The median time from HCT to diagnosis of AIHA was 185 (111-361) days.
Among patients that developed AIHA, 70% were refractory to initial therapy with corticosteroids and rituximab. All patients with refractory AIHA were treated with daratumumab (16 mg/kg/dose, starting weekly) with a median of 13 infusions until resolution. Premedication for daratumumab infusion included diphenhydramine, solumedrol, acetaminophen and famotidine. Daratumumab infusions were well tolerated without reported toxicity. Treatment course for patients with refractory AIHA who received daratumumab are summarized in Table 1.

Subject	HCT Indication	Age at HCT (months)	Preparative Regimen	Donor	Time Post-HCT to AIHA (days)	Prior Treatment for AIHA	Number of Infusions of Daratumumab to resolution of AIHA	A B
1	Hurler Syndrome	4	Bu/Cy/ATG	UCB	344	Corticosteroids, Rituximab, IVIG	7	N
2	Wiskott-Aldrich Syndrome	28	Bu/Cy/ATG	UCB	361	Corticosteroids, Rituximab, IVIG	13	N
3	HLH	6	Bu/Flu/Cy		257	Corticosteroids, Rituximab, IVIG	4	N
4	Hurler	4	Bu/Cy/ATG	UCB	111	Corticosteroids, Rituximab, IVIG	21	N
5	VODI	13	rATG Flu/Treo /TBI 400cGy	Alpha-beta depleted r-Haplo	190	Corticosteroids, Rituximab, IVIG	31	N
6	AML	90	Bu/Flu/Mel	UCB	132	Corticosteroids, Rituximab, IVIG	4	N

7	Hurler	4	Bu/Cy/ATG	UCB	180	Corticosteroids, Rituximab, IVIG	38

Table 1: Treatment course for patients with refractory AIHA who received daratumumab

Conclusions: The majority of patients with AIHA post-HCT were refractory to initial treatment with corticosteroids and rituximab. Daratumumab was well tolerated in this patient cohort. All patients with refractory AIHA treated with daratumumab achieved resolution. Prospective trials are needed to optimize the approach to initial management of patients with AIHA and those with refractory disease.

Clinical Trial Registry: n/a

Disclosure: Vinod Prasad is an employee of Genetix Biotherapeutics

A408

DAY 0 EASIX SCORE PREDICTS NON-RELAPSE MORTALITY, BUT NOT GRAFT-VERSUS HOST DISEASE OR RELAPSE FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER REAL-WORLD ANALYSIS

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Background: The Endothelial Activation and Stress Index (EASIX) is emerging as a surrogate marker of endothelial dysfunction after allogeneic stem cell transplant (allo-SCT) and, while it has been linked to transplant outcomes, its relationship with non-relapse mortality (NRM), graft-versus-host disease (GVHD), and relapse remains incompletely defined in real-world settings.

Methods: We conducted a retrospective unicenter analysis in patients recieving allo-SCT at the Regional Oncology Institute from Iași, Romania. The EASIX score was calculated as follows: LDH (U/L) xCreatinine (mg/dl) /platelet count (10^9/L). Day 0 EASIX (log2-transformed) was evaluated in relation to NRM, acute GVHD (aGVHD), chronic GVHD (cGVHD), relapse, and overall survival (OS). Competing-risk endpoints were analyzed using cumulative incidence functions with Gray's test, and Fine–Gray regression was applied for univariate and multivariable analyses. OS was estimated using the Kaplan–Meier method. All statistical analyses were performed using SPSS v.26 and R v4.5.2.

Results: A number of 98 patients were included in this study, in whom 101 allo-SCT procedures were peformed. Day 0 EASIX was available in 84 patients. A higher log-2 EASIX was strongly associated with increased NRM. The cumulative incidence of NRM differed significantly between patients with high versus low EASIX, as defined by median split and across EASIX quartiles (Gray's test $p < 0.001$). Furthermore, NRM risk augmented progressively across increasing EASIX quartiles. In Fine–Gray regression, increasing EASIX

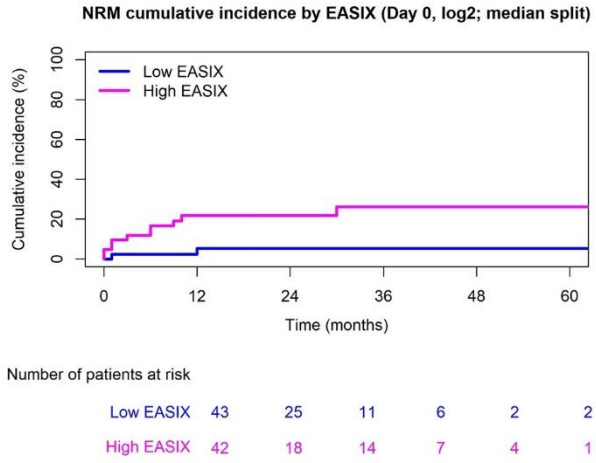
was associated with a significantly higher sub-distribution hazard for NRM, with a significant trend across quartiles (p = 0.0049).In contrast, day 0 EASIX was not associated with the incidence of relapse. Similarly, associations between EASIX and aGVHD or cGVHD were weak and inconsistent, with no clear separation of cumulative incidence curves. Patients with high EASIX experienced inferior OS compared with those with low EASIX, an effect driven primarily by excess NRM rather than relapse.

Table 1. Baseline Patient Characteristics.

Baseline Characteristics	n (%) (n=98)*
Age (years), median	41
Female sex	46 (46.9%)
Underlying disease AML ALL Other	 55 (54.5%) 22 (21.8%) 24 (23.7%)
Allo-SCT-related Characteristics	n (%) (n=101)*
HCT-CI > 2	11 (10.9%)
1st Transplant	98 (97%)
2nd Transplant	3 (3%)
Conditioning regimen Myeloablative Reduced intensity	 55 (54.5%) 46 (45.5%)
Donor type Sibling donor Matched unrelated donor Haploidentical donor	 40 (39.6%) 46 (45.5%) 15 (14.9)
GVHD Prophylaxis Tacrolimus+MMF CsA+MTX PTCy ATG	 93 (92.1%) 8 (7.9%) 73 (72.3%) 4 (4%)
Acute GVHD	24 (23.8%)
Chronic GVHD	14 (13.9%)

Table 1. Baseline Patient Characteristics.

ALL= Acute Lymphoblastic Leukemia, AML= Acute Myeloid Leukemia, ATG= Anti-Thymocyte Globulin, CsA= Cyclosporin A, GVHD= Graft-Versus Host Disease, MMF= Mycophenolate Mofetil, MTX= Methotrexate, PTCy= Post-Transplant Cyclophosphamide, SCT= Stem Cell Transplant
*Percentages are calculated per patient (n=98) or per transplant event (n=101), as indicated.



Conclusions: In our real-world allo-SCT cohort, day 0 EASIX was a strong predictor of non-relapse mortality but did not predict relapse or GVHD. These findings suggest that EASIX primarily reflects baseline endothelial vulnerability predisposing patients to transplant-related toxicity. EASIX may therefore represent a practical and easily applicable tool for early risk stratification and for guiding individualized supportive and preventive strategies aimed at reducing non-GVHD transplant-related mortality after allo-SCT.

Disclosure: Nothing to declare.

A409

ANAKINRA AS TREATMENT FOR SECONDARY HAEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS FOLLOWING ALLOGENIC STEM CELL TRANSPLANT: A RETROSPECTIVE ANALYSIS IN A UNIVERSITY HOSPITAL TRANSPLANT CENTRE

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Background: Secondary Haemophagocytic Lymphohistiocytosis (sHLH) is a rare but recognised life-threatening complication following allogeneic haematopoetic stem cell transplantation (allo-HSCT). Anakinra is an approved treatment for sHLH, but few studies have evaluated its use in the post-allograft setting.
The aim of this review was to evaluate the efficacy of anakinra in post-allograft sHLH. The primary end point was the 30-day mortality incidence following anakinra initiation. Secondary endpoints included: the 100-day mortality incidence, the Intensive Care Unit (ICU) admission incidence and median length of stay, the median length of treatment, and response to treatment measured by serum ferritin levels.

Methods: Between March 1st 2022 to March 1st 2025, a retrospective case-series analysis of anakinra-treated post-allograft sHLH cases in a University Hospital transplant centre was performed. Patients that met the sHLH criteria based on: HLH-2004 protocol, Hscore >169, modified Hscore >132, ferritin >10 000 mcg/L, or confirmed tissue diagnosis, that received at least one dose of anakinra were included in the analysis. Data was extracted from electronic patient records.

Results: During this period, 12 patients met the inclusion criteria. The median age at diagnosis was 56 years old (range 34 to 69), 7/12 were male (58%), 11 had matched unrelated donor transplants and 1 had a haplo-identical transplant. The median pre-treatment ferritin level was 6419 mcg/L (range 1014 to 91141). Transplant indications are summarised in Table 1. One patient had two separate occasions of sHLH, making a total 13 cases of sHLH. 12 (92.3%) occurred within one year of allo-HSCT and one case 2.5 years post-HSCT, following a donor lymphocyte infusion. 158 patients received an allo-HSCT at this centre during this period, making the sHLH incidence 7.59%.
The 30-day mortality post anakinra initiation was 23% (n=3/13) and the 100-day mortality was 38.5% (n=5/13). 30.7% (n=4/13) required an ICU admission with a 9-day median length of stay (range 4-13). All those admitted to ICU were alive at day 30, with one subsequently deceased by day 100. The median length of anakinra treatment was 54 days (range 10 to 127). Comparing the baseline ferritin to end of treatment levels, the median change was -53.2% (range -93.9 to +63.5%) in those who survived (n=8), vs -5.5% (range -35.7% to +200%) in those who died (n=5).
Median ferritin levels at baseline were higher in the 30-day mortality cohort compared to the 30-day survival cohort (8812 vs 3007 mcg/L). A similar pattern was seen in the Day 100 mortality vs survival cohort (4720 vs 2057 mcg/L). The mortality rate at Day 30 was higher in those on concurrent immunosuppression. The median age was similar across all groups. Subject numbers were too small to comment on concurrent viral infections and other HLH treatments.

Table 1: **Post allograft sHLH: demographics and**	**Total cases (n= 13)**	**Day 30 survival cohort (n= 10)**	**Day 30 mortality cohort (n= 3)**	**Day 100 survival cohort (n= 8)**	**Day 100 mortality cohort (n= 5)**

outcomes with anakinra use					
Median age (range)	56 (34-69)	52 (34-69)	56 (56-58)	52 (34-68)	56 (42-69)
Gender: male (%)	7 (53.8%)	6 (60%)	1 (33.3%)	4 (50%)	3 (60%)
Transplant indication (%): AML B-ALL Lymphoma MDS MPN Non-malignant	3 (23.1%) 1 (7.7%) 1 (7.7%) 4 (30.8%) 2 (15.3%) 2 (15.3%)	3 (30%) 1 (10%) 1 (10%) 2 (20%) 1 (10%) 2 (20%)	0 (0%) 0 (0%) 0 (0%) 2 (66.7%) 1 (33.3%) 0 (0%)	2 (25%) 1 (12.5%) 1 (12.5%) 2 (25%) 0 (0%) 2 (25%)	1 (20%) 0 (0%) 0 (0%) 2 (40%) 2 (40%) 0 (0%)
Transplant conditioning (%): Myeloablative Reduced intensity	3 (23.1%) 10 (76.9%)	3 (30%) 7 (70%)	0 (0%) 3 (100%)	2 (25%) 6 (75%)	1 (20%) 4 (80%)
Median onset of sHLH – day since transplant (range)	101 (37-983)	136 (37-239)	51 (51-983)	93 (37-239)	206 (51-983)
Median ferritin mcg/L pre-anakinra treatment (range)	5594 (1014 - 91141)	3897 (1014 - 91141)	11038 (7337-12532)	3158 (1014-91141)	7337 (4145-12532)
Median ferritin mcg/L end of anakinra treatment (range)	4530 (724 - 16548)	3007 (724-12214)	8812 (4720-16548)	2057 (724-12214)	4720 (3916-16548)
ICU admission (%)	4 (30.8%)	4 (40%)	0 (0%)	3 (37.5%)	1 (20%)
Concurrent GVHD requiring systemic treatment (%)	8 (61.5%)	6 (60%)	2 (66.7%)	4 (50%)	4 (80%)

Concurrent infection EBV (%)	3 (23.1%)	2 (20%)	1 (33.3%)	2 (25%)	1 (20%)
Concurrent infection CMV (%)	1 (7.7%)	1 (10%)	0 (0%)	1 (12.5%)	0 (0%)
On concurrent immunosuppression (ciclosporin/MMF/sirolimus) (%)	7 (53.8%)	4 (40%)	3 (100%)	4 (50%)	3 (60%)
Other HLH treatment (%): IVIG alone methylprednisolone alone IVIG + methylprednisolone	5 (38.5%) 6 (46.2%) 2 (15.4%)	4 (40%) 4 (40%) 2 (20%)	1 (33.3%) 2 (66.7%) 0 (0%)	4 (50%) 3 (37.5%) 1 (12.5%)	1 (20%) 3 (60%) 1 (20%)

Conclusions: From our data, sHLH remains an uncommon complication following allogeneic HSCT. Anakinra appears to be effective in post-allograft sHLH with over 60% of patients alive at day 100 in a condition typically associated with a high mortality rate. Elevated baseline ferritin levels may be predictive of severity, including mortality, despite anakinra use. This could be evaluated with further studies.

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A410

EARLY POST-TRANSPLANT ELECTROLYTE DISTURBANCES IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS: INCIDENCE AND SEVERITY

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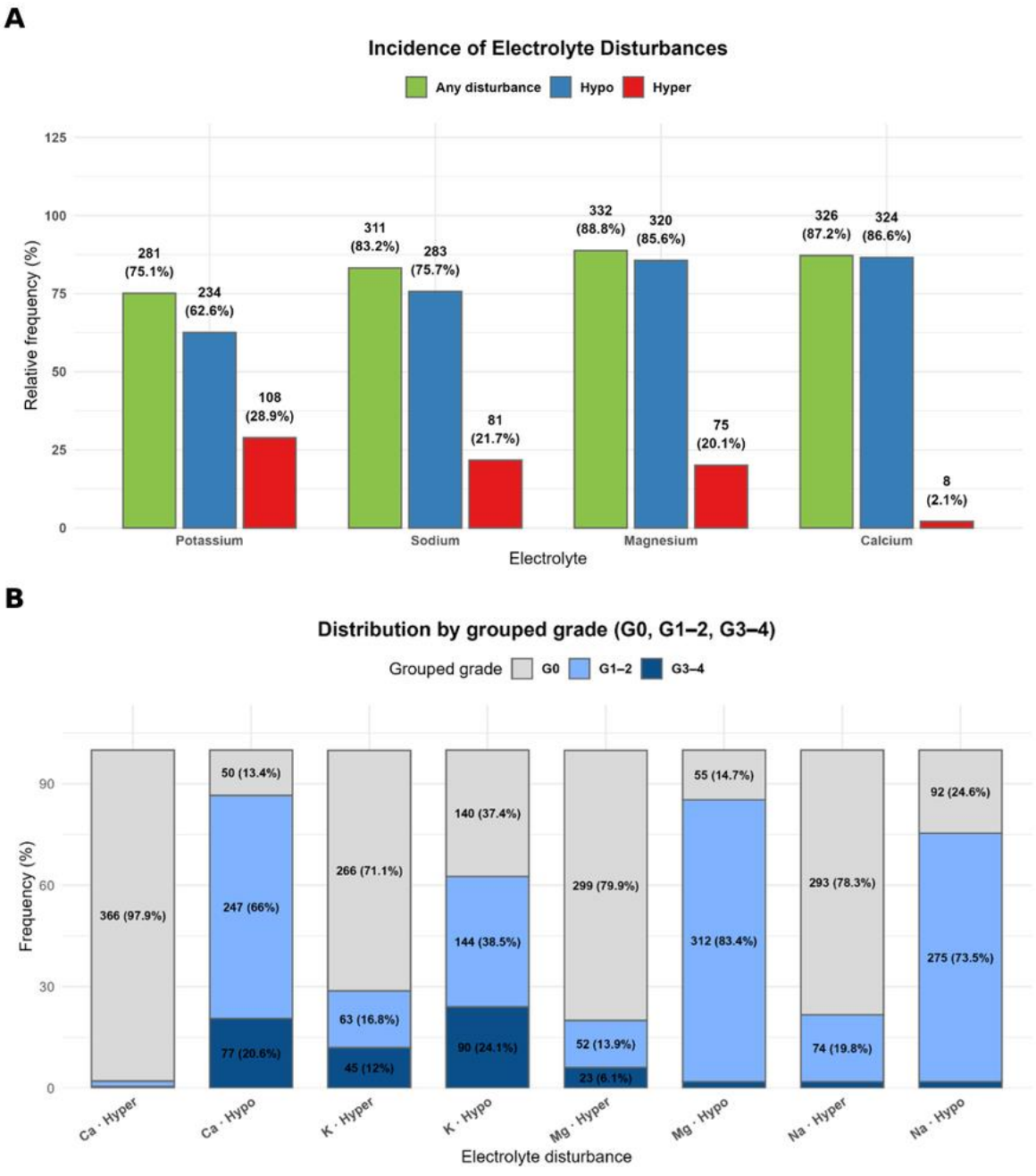
Background: Electrolyte disturbances are common and clinically significant in the early post–allogeneic HCT period. Abnormalities involving sodium, potassium, magnesium, and calcium may precipitate hemodynamic instability and arrhythmia, and potassium disturbances represent a well-recognized cause of cardiac arrest. During the first 21 days after infusion, patients face metabolic, inflammatory, gastrointestinal, and renal stressors that increase susceptibility to electrolyte imbalance. However, the true incidence and severity of these early disturbances remain poorly described. This study evaluated the frequency and clinical severity of electrolyte disturbances within the first 21 days after allo-HCT.

Methods: This was a retrospective, single-center study including all patients who underwent allogeneic HCT between January 2010 and December 2023 and had laboratory data available for sodium, potassium, magnesium, and calcium during the first 21 days post-transplant. Patients receiving umbilical cord blood grafts were excluded. Data was extracted from electronic medical records. Electrolyte disturbances were classified according to CTCAE v5.0 as deficiency (hypo-) or excess (hyper-) and graded from 1 to 4; grades 1–2 were considered mild or moderate, and grades 3–4 were severe. Clinical and transplant variables were summarized as absolute and relative frequencies or as medians and standard deviations. The study was approved by the institutional ethics committee and conducted in accordance with the Declaration of Helsinki.

Results: A total of 374 allogeneic HCT recipients were included, with a mean age of 28.2 ± 18.4 years; 67.1% were adults and 58.8% were male. Most patients had malignant diseases, mainly acute lymphoblastic leukemia (32.1%) and acute myeloid leukemia (25.1%). Bone marrow was the predominant graft source (70.1%). Donors were related (44.9%), unrelated (33.7%), or haploidentical (21.4%). Myeloablative conditioning was used in 55.6% of cases and cyclosporine-based prophylaxis in 63.9%. Electrolyte disturbances were highly prevalent in the first 21 days after transplant, with deficiencies markedly more frequent than excesses. Potassium abnormalities occurred in a large proportion of patients. Hypokalemia was observed in 62.6%, including 38.5% with grade 1–2 and 24.1% with grade 3–4. Hyperkalemia occurred in 28.9%, with 12% classified as severe. Sodium disturbances were also common. Hyponatremia affected 75.7% of patients, predominantly grade 1–2; severe hyponatremia occurred in approximately 2.2%. Hypernatremia was documented in 21.7%. Magnesium disturbances showed one of the highest incidences. Hypomagnesemia affected 85.6% of the cohort, mostly grade 1–2, with 2.2% reaching grades 3–4. Hypermagnesemia occurred in 20.1%, including 6.1% severe. Calcium abnormalities were the most frequent overall. Hypocalcemia was present in 86.6% of patients, including 66% with grade 1–2 and 20.6% with grade 3–4. Hypercalcemia was rare at 2.1%. The overall pattern demonstrated a predominance of hypomagnesemia, hypocalcemia, and hyponatremia, with clinically meaningful proportions of severe hypokalemia, hypocalcemia, and hyperkalemia.



Conclusions: While most abnormalities were mild or moderate, a relevant proportion of patients developed severe disturbances, particularly hypokalemia, hyperkalemia, and hypocalcemia, which may contribute to hemodynamic instability and arrhythmias during this high-risk period. Incidence and severity were comparable between cyclosporine and tacrolimus. These findings emphasize the need for systematic electrolyte monitoring and timely correction strategies to reduce preventable early post-transplant morbidity.

Clinical Trial Registry: Not applicable. This study is not a clinical trial.

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A411

HEMOSTATIC ALTERATIONS AND HISTOPATHOLOGICAL FINDINGS OF SINUSOIDAL OBSTRUCTION SYNDROME AFTER ALLOGENEIC HSCT FROM A REFERENCE CENTER IN LATIN AMERICA

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Background: Sinusoidal obstruction syndrome (SOS/VOD) remains a life-threatening complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT), despite advances in conditioning strategies, prophylaxis, and treatment, identification of early hemostatic markers may help timely diagnosis and succesful treatment. We aimed to analyze hemostatic alterations and describe histopathological findings in patients who developed SOS/VOD after allo-HSCT.

Methods: We conducted a retrospective observational study including patients diagnosed with SOS/VOD based on clinical and/or histological criteria according to McDonald et al. Clinical diagnosis required jaundice, hepatomegaly with right upper quadrant pain, and ascites and/or unexplained weight gain. Histological confirmation was based on liver biopsy or autopsy findings, after exclusion of other causes of liver injury. Clinical characteristics, transplant-related variables, and hemostatic parameters—fibrinogen, factor VII activity (FVII), plasminogen activator inhibitor-1 (PAI-1), and protein C activity were analyzed from the start of conditioning until day +28 post-transplant. Statistical analysis included univariate analysis, Student's t-test, chi-square testing, and linear correlation analysis.

Results:

Twenty-six patients treated at a reference center in Mexico (UMAE No. 25, IMSS, Monterrey) who developed SOS/VOD after allo-HSCT between 2001 and 2016 were included. Median age was 28 years (14–42). Diagnoses included acute lymphoblastic leukemia (n = 15), acute myeloid leukemia (n = 5), and other hematologic disorders (n = 6). Most transplants were HLA-matched (6/6, n = 23); two were 5/6 matched and one haploidentical. Conditioning was busulfan/cyclophosphamide-based in 25 patients and busulfan/fludarabine-based in one. GVHD prophylaxis consisted of cyclosporine plus methotrexate (n = 25) or post-transplant cyclophosphamide with tacrolimus and mycophenolate (n = 1). Grafts were not T-cell depleted. All patients received SOS/VOD prophylaxis with heparin and ursodeoxycholic acid.

SOS/VOD severity (Seattle criteria) was mild (n = 5), moderate (n = 12), or severe (n = 9), with onset between days +6 and +15 post-transplant (92.3%). Hemostatic changes preceded SOS/VOD, including increased fibrinogen and PAI-1, and decreased FVII and protein C activity. Significant correlations were observed among these parameters (Table 1). Histology was available in 17 patients, confirming SOS/VOD in 10, with findings ranging from subintimal edema and sinusoidal fibrosis to extensive necrosis and hemorrhage; hepatic hemosiderosis was observed in six cases (Figure 1).

Table 1. Hemostatic alterations preceding the onset of sinusoidal o

PATIENTS	FIBRINOGEN	FVIIc
*Mean time (days) to onset and mean levels of hemostatic parameter abnormalities.	Days/Level	Days/Level
SOS/EVO-H	3.9/539	3.03/43.7
Period I (0-5 days) Period II (6-10 days) Period III (11-15 days)	2.8/565 3.1/627.7 2.0/603.7	2.6/45 2.5/40 1.8/27.1

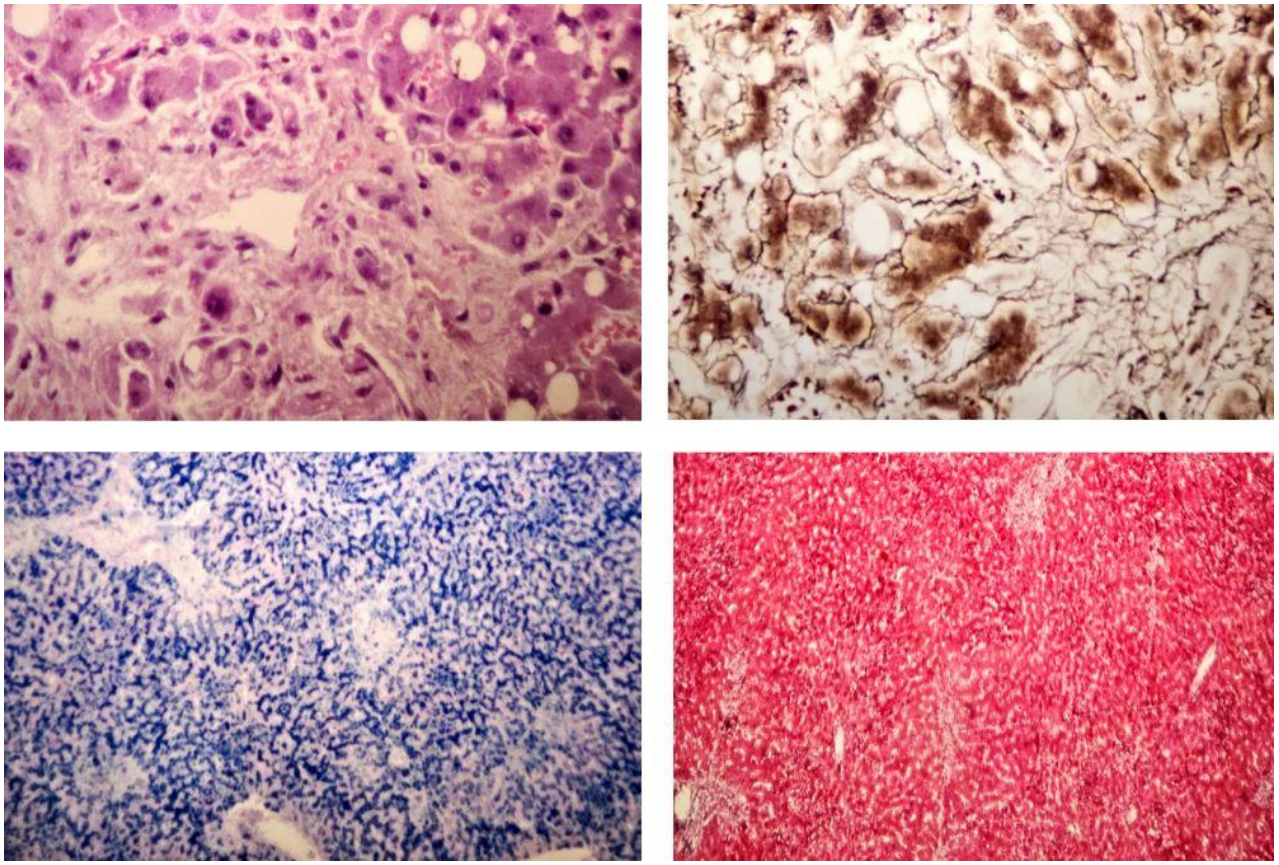

Figure 1. Representative liver histopathology. Hematoxylin–eosin staining shows hepatocyte necrosis (upper right). Silver staining shows focal sinusoidal fibrosis and partial occlusion of a central venule with subendothelial edema (upper left). Perl's Prussian blue (lower right) and Masson's trichrome stains (lower left) reveal marked hepatic hemosiderosis, centrilobular loss, and mild portal fibrosis.

Conclusions: Early hemostatic alterations related to SOS/VOD included hypofibrinolysis, elevated fibrinogen and PAI-1, and reduced FVII and protein C activity. These findings support a key role of endothelial injury and thrombin generation in SOS/VOD pathogenesis and suggest that hemostatic markers may aid in early diagnosis and risk stratification.

Disclosure:

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A412

THE CLINICAL SIGNIFICANCE AND SAFETY OF BRONCHOSCOPY AFTER ALLO-HSCT

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Background: Pulmonary complications are occasionally observed after allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, bronchoscopy is often avoided due to concerns regarding coagulopathy, leaving the etiology unclear.

Methods: We conducted a retrospective cohort study of all patients who underwent their first bronchoscopy for pulmonary complications after allo-HSCT at Kyoto University between 2005 and 2025 to evaluate its clinical significance and safety. We also assessed whether corticosteroids were administered for pulmonary complications and evaluated treatment responses using CT scans (CR/PR/SD/PD). Furthermore, we analyzed multiple parameters potentially associated with corticosteroid treatment decisions and responsiveness.

Results: A total of 72 patients were included, with a median age of 49 years (range, 18-70). At bronchoscopy, 40 patients (56%) required no supplemental oxygen, 25 (35%) were on low-flow oxygen devices with a median flow rate of 2 L/min (range, 1-6), and 7 (10%) were intubated. Median platelet count at examination was 110,000/μL (range, 10,000-481,000); 18 (25%) received platelet transfusion on the examination day. Transbronchial lung biopsy (TBLB) was performed in 24 (33%), and bronchoalveolar lavage fluid (BALF) cytology in all. Diagnoses included cryptogenic organizing pneumonia (24; 33%), fungal pneumonia (10; 14%), diffuse alveolar hemorrhage (7; 10%), Pneumocystis jirovecii pneumonia (5; 7%), idiopathic pneumonia syndrome (5; 7%), diffuse alveolar damage (3; 4%), pulmonary alveolar proteinosis (2; 3%), and bronchiolitis obliterans (1; 1%). Eight cases (11%) were histologically diagnosed by TBLB. Ten cases (14%) were diagnosed based on cytology, culture, PCR, or galactomannan antigen testing. Seven cases (10%) were diagnosed grossly, and 47 (65%) were diagnosed clinically. Corticosteroids were administered in 43 patients (60%), and 39 of them (91%) responded to treatment (CR: 16; PR: 23). Because almost all corticosteroid-treated cases were responsive, we focused on identifying factors associated with the decision to initiate corticosteroids rather than treatment response. Logistic regression analyses identified BALF lymphocytes > 20% and LDH > 263.5 U/L (ROC curve analysis showed the appropriate cutoff of LDH levels to be 263.5; AUC=0.75) as factors associated with corticosteroid treatment even after adjustment for potential confounders (odds ratio (OR), 7.29; 95% confidence interval (CI), 1.79-38.7; p=0.0094 for BALF lymphocyte >20%, OR, 5.31; 95% CI, 1.28-28.9; p=0.031 for LDH > 263.5). Other factors including CRP > 1.35 mg/dL (AUC=0.62) and cumulative TBI ≥ 8 Gy were not significantly associated with corticosteroid treatments (OR, 2.09; 95% CI, 0.51-8.91; p=0.30 for CRP > 1.35, OR, 2.52; 95% CI, 0.65-10.6; p=0.19 for cumulative TBI ≥ 8 Gy), though they were significant in univariate analyses. Procedural complications occurred in only 5 patients (7%),

including 3 following TBLB, all of which were manageable with supportive care alone. There were no procedure-related severe adverse events or mortality.

Conclusions: Bronchoscopy after allo-HSCT is a safe and clinically informative procedure that frequently provides actionable diagnostic information. BALF lymphocyte proportion and LDH levels may help guide corticosteroid treatment decisions. Even in the post-allo-HSCT setting, bronchoscopy is valuable for addressing pulmonary complications with minimal risk.

Disclosure: Nothing to declare

A413

COLD AGGLUTININ SYNDROME FOLLOWING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The diagnosis and treatment of autoimmune and alloimmune hemolysis in the post-transplant setting is challenging due to the lack of standardized diagnostic criteria and interference in blood samples caused by factors such as ABO incompatibility, as well as chronic mild hemolysis secondary to medications and microangiopathy. The following case presentation illustrates the challenges in accurate diagnosis and classification of AIHA.

Methods: A 36-year-old female underwent myeloablative allogeneic transplantation with a peripheral blood stem cell graft from a male, ABO-matched, 10/10 HLA-matched unrelated donor. GVHD prophylaxis included Thymoglobulin©, Fresenius, 4 mg/kg, cyclosporin, and methotrexate. The early post-transplant course was largely uneventful, except for mild acute graft-versus-host disease of the skin.
At three months post-transplant, donor chimerism remained at 99% for myelod cells and 85% for T cells. There were no cytopenias, and no CMV- og EBV-reactivation. The immune reconstitution showed CD3 counts of 839 x 10^6/L, CD4 counts 223 x 10^6/L, CD8 counts 600 x 10^6/L and CD19 223 x 10^6/L and there were normal levels of IgG and IgM.

Results: From day +120, the patient was treated on an outpatient basis with a five-day course of nirmatrelvir/ritonavir for SARS-CoV-2 infection, and admitted at day +142 with anemia, suppressed haptoglobin, elevated LDH and bilirubin, with normal free hemoglobin and no hemoglobinuria (Table 1). The blood smear revealed spherocytes, no red cell agglutination, and no schistocytes. The direct antiglobulin test (DAT) was strongly positive for C3d, while the cold agglutination titer was 1:16. Antibody screening (IAT), a test which reveals the presence of antibodies in the patient serum targeting potential donor red blood cells, showed agglutination in all tested cells at room temperature, which resolved with strict handling of the sample at 37°C.
The patient was transfused using a blood warmer, and treatment with prednisolone (1 mg/kg) was initiated. Due to no increase in hemoglobin levels (Figure 1), daily therapeutic plasma exchange (TPE) was started. After three days of TPE, with no improvement in hemolysis, treatment with the C5 inhibitor eculizumab was initiated at day+146. Within a

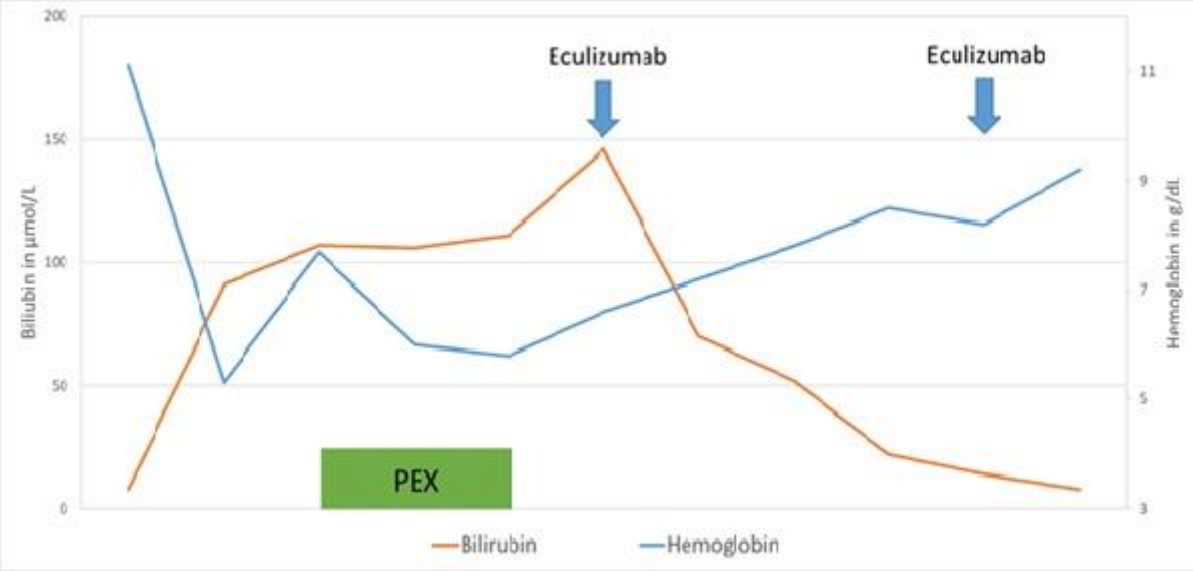
few days, hemoglobin increased and the bilirubin dropped to normal range (Figure 1). By six days, the LDH, reticulocytes and haptoglobin were within normal range. A second dose of eculizumab was administered on day +152. Hemoglobin levels gradually normalized, and no further hemolytic episodes have occurred.
Deep frozen serum harvested prior to commencing TPE was analyzed at a reference laboratory to specify the type of AIHA. The IAT was again positive against all tested cells at room temperature, and anti-I panel was negative. Cold antibody-screening was negative.

Table 1

Day post HSCT	Day AIHA	Hemoglobin (g/dL)	Reticulocytes (x10^9/L)	Leukocytes (x10^9/L)	LDH (U/L)	Bilirubin (micromol/L)	Haptoglobin (g/L)	CRP (mg/L)	C3 (g/L)	C4 (g/L)
+120	-23	11,1		4,5	154	8		< 5		
+128	-15	11,1		3,5	152	8		< 5		
+142	1	5,3	33	9,5	281	91		6	0,85	0,17
+143	2	7,7		11,5	350	107		8		
+144	3	6,0		17,9	225	106		< 5		
+145	4	5,8	169	13,5	211	111		< 5	0,34	0,06
+146	5	6,6	212	7,0	189	146		< 5		
+147	6	7,2	191	5,1	226	70	< 0,1	6	0,66	0,12
+148	7	7,8	201	4,9	242	52	< 0,1	< 5		
+149	8	8,5	162		249	22	< 0,1	< 5	1,01	0,21
+152	11	8,2	89	3,0	204	14	0,6	< 5	1,01	0,27

+159	18	9,2	86	3,2	154	8	0,7	< 5	0,82	0,21
+166	25	10,2	56	4,2	130	7	0,8	< 5	0,89	0,20

Figure 1



Conclusions: This case highlights the challenges of accurately classifying AIHA, particularly after transplantation, where interfering antibodies may obscure serological findings and complicate therapeutic decision-making. Laboratory findings of pan-agglutination at room temperature resolving with heating, together with C3d deposition on red blood cells, supported cold agglutinin syndrome. The rapid response to C5 inhibition suggests that complement-targeted therapy may be a viable option in selected treatment-refractory patients.

Disclosure: Nothing to declare.

P180

IMPACT OF NUTRITIONAL STATUS IN THE POPULATION OF PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION ON TREATMENT OUTCOMES – VALIDATION OF NUTRITIONAL ASSESSMENT TOOLS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a key therapeutic modality for patients with hematologic malignancies. Although numerous studies suggest that malnutrition adversely affects post-transplant outcomes, no validated nutritional assessment tool reliably predicts prognosis in allo-HSCT recipients. This study aimed to evaluate the impact of nutritional status on clinical outcomes in hemato-oncology patients undergoing allo-HSCT using traditional body mass index (BMI) assessment as well as the Nutritional Risk Index (NRI) and the Prognostic Nutritional Index (PNI).

Methods: A retrospective analysis was conducted in 166 adult patients who underwent allo-HSCT at the Bone Marrow Transplant Unit, Department of Hematology, Jagiellonian University Medical College, between 2015 and 2018. Nutritional status was assessed using BMI, NRI, PNI, and serum albumin levels at three time points: admission, day +30, and day +60–90 post-transplantation. Clinical outcomes were evaluated during a 2-year follow-up period. Patients were stratified into subgroups with better or worse nutritional status according to each indicator. Changes in nutritional parameters were analyzed using Student's t-test and the Wilcoxon signed-rank test. The impact of nutritional status on outcomes was assessed using Cox proportional hazards regression and the Cox-Mantel test, and overall survival (OS) and disease-free survival (DFS) were evaluated using Kaplan-Meier analysis.

Results: Nutritional status deteriorated significantly following allo-HSCT across all assessed parameters. Median BMI declined from 25.3 kg/m² at admission to 23.8 kg/m² at day +30 and 23.0 kg/m² at day +60-90. Median NRI decreased from 114.8 at admission to 105.8 at day +30 and 103.9 at day +60-90, with a growing proportion of patients crossing the clinically relevant cutoff of 97.5. Median PNI dropped markedly from 49.7 to 43.6 by day +30 and remained low thereafter, while serum albumin declined from 4.4 g/dL at admission to 4.0 g/dL post-transplant, accompanied by a significant increase in hypoalbuminemia. Hypoalbuminemia at admission independently predicted inferior overall survival (OS; HR = 4.24, p = 0.01) and disease-free survival (DFS; HR = 3.44, p = 0.02). Albumin remained prognostically significant at day +30 and day +60-90 (HR ≈ 2.0, p = 0.04). Two-year OS was 70.5% in patients with albumin ≥3.5 g/dL versus 44.4% in hypoalbuminemic patients (p = 0.04). NRI <97.5 and PNI below ROC-derived cutoffs were associated with significantly worse OS and DFS at later time points (p = 0.05), with early divergence of survival curves. In contrast, BMI showed no association with OS or DFS at any time point. 2-year OS was approximately 65-70%, and DFS 55-60%.

Conclusions: Allo-HSCT is associated with a significant decline in nutritional status, regardless of the assessment method used. Serum albumin concentration is a strong and consistent predictor of both OS and DFS. The demonstrated prognostic value of NRI and PNI supports their clinical use as complementary nutritional assessment tools in allo-HSCT. The most striking finding of this analysis is that albumin may serve as a simple, widely accessible prognostic marker for transplant outcomes. In contrast, BMI assessed at any time point did not correlate with survival and appears unsuitable for risk stratification in allo-HSCT recipients.

Disclosure: Nothing to declare.

P181

MELPHALAN-INDUCED INTESTINAL MUCOSITIS IN HEMATOPOIETIC STEM CELL TRANSPLANT: RAPID RESPONSE TO SHORT-COURSE ORAL BUDESONIDE

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Background: High-dose melphalan (HDM) is widely used as conditioning for autologous hematopoietic stem cell transplant (ASCT), particularly in multiple myeloma, but it frequently causes severe gastrointestinal mucositis. Approximately 30–40% of patients develop grade III–IV diarrhea, which usually resolves after neutrophil engraftment. However, persistent diarrhea beyond 24 hours post-engraftment leads to significant morbidity, electrolyte imbalances, and prolonged hospitalization. Currently, there is no established therapy once supportive measures fail.

Methods: We retrospectively analyzed patients undergoing ASCT with melphalan-based conditioning who developed grade III–IV diarrhea persisting > 24 hours after engraftment. Infectious etiologies were excluded by stool cultures and PCR testing. Patients received oral budesonide (3–9 mg/day) in addition to standard supportive measures. Clinical outcomes included time to diarrhea improvement, budesonide duration, hospital discharge timing, and adverse events.

Results: Twenty patients met inclusion criteria (median age 66 years, range 44–74). Diagnoses included multiple myeloma (n = 14), lymphoma (n = 5), and T-cell Acute Lymphoblastic Leukemia (n = 1). Melphalan doses were 200 mg/m² (n = 11) or 140 mg/m² (n = 9). Budesonide was started a median of 2 days after engraftment (range 0 to +11); six patients began 1–4 days earlier. Diarrhea improved in 19 of 20 patients (95%)—typically within 1 day (range 1–7)—with a median treatment duration of 2 days. Median time to hospital discharge after starting budesonide was 2 days (range 1–7). No adverse effects, delayed engraftment, or infections were observed.

Table 1. Clinical characteristics and outcomes of patients treated with oral budesonide for persistent melphalan-induced diarrhea

Variable	Findings
Patients (n)	20

Median age, years (range)	66 (44–74)
Sex (M/F)	10 / 10
Underlying diagnosis	MM (n=14); Lymphoma (n=5); T-ALL (n=1)
Melphalan dose	200 mg/m² (n=11); 140 mg/m² (n=9)
Median day of neutrophil engraftment (range)	+12 (9–18)
Timing of budesonide initiation	Median +2 days post-engraftment (–4 to +11)
Budesonide dose	6–9 mg/day (3 mg BID–TID)
Median duration of therapy (range)	2 days (1–13)
Clinical response	19/20 (95%) improved; median 1 day (1–7) to resolution
Median time to discharge post-budesonide (range)	2 days (1–7)

Conclusions: Short-course oral budesonide resulted in rapid and sustained resolution of severe melphalan-induced diarrhea, with excellent tolerability and no infectious or hematologic complications. By exerting a potent local anti-inflammatory effect with minimal systemic exposure, budesonide represents a safe, practical intervention that may reduce morbidity, hospitalization duration, and healthcare cost in transplant recipients. Prospective trials are warranted to validate its role in managing chemotherapy-related gastrointestinal toxicity.

Disclosure: All Authors have **nothing to declare**. The study received **no external funding or industry support**. All data were collected as part of routine clinical care.

P182

IMPACT OF THERAPEUTIC PLASMA EXCHANGE ON IMPROVEMENT OF ERYTHROID ENGRAFMENT IN MAJOR INCOMPATIBLE AB0-GROUP AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER ANALYSIS

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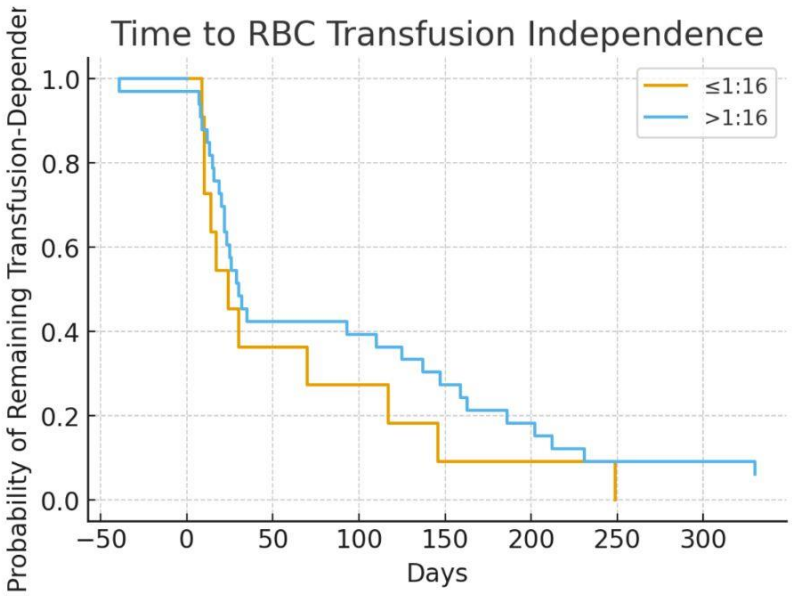
Background: ABO-incompatible allogeneic hematopoietic stem cell transplantation (allo-HSCT) is increasingly performed, but hemolytic complications, delayed erythroid engraftment

and prolonged red blood cell (RBC) transfusion dependence remain major concerns. Therapeutic plasma exchange (TPE) is widely used to reduce anti-A and anti-B isoagglutinins before graft infusion, but the relationship between post-transplant isoagglutinin titers, anemia duration, transfusion burden and overall survival (OS) is poorly defined.

Methods: We retrospectively analyzed 44 consecutive patients undergoing major ABO-incompatible allo-HSCT at our center (CTMO – RC, Italy) between January 2020 and June 2025, allo of whom received pre-transplant TPE (1–3 procedures). Anti-A1 and anti-B isoagglutinin titers were measured before and after TPE. OS was calculated from transplant to death or last follow-up. Anemia duration was defined as the time from transplant to first documented hemoglobin (Hb) >8 g/dL. RBC transfusion dependence was defined as the interval between the first and last RBC transfusion occurring on or after the day of transplant. Kaplan–Meier curves were generated for OS, time to Hb >8 g/dL and time to transfusion independence, and patients were compared according to post-TPE anti-A/B isoagglutinin titers, focusing on (I) IgM/IgG ≤1:16 vs >1:16 and (II) IgM ≥1:128 vs <1:128. All TPE procedures were well tolerated, and no side effects were reported.

Results: Median age at transplant was 56,5 years, and the majority of patients had acute mieloid leukemia (43,2%), acute lymphoblastic leukemia (18,2%) and myelodysplastic syndrome (11,4%). With a median follow-up of approximately 1.8 years for survivors, estimated OS was 75% at 1 year and 68% at 2 years. Post-transplant anemia (Hb <8 g/dL) was common; median anemia duration was 20 days (IQR 13–39), with a minority experiencing prolonged anemia ≥90 days. Overall, 93% of patients required at least one post-transplant RBC transfusion, with a median transfusion period of 24 days (IQR 10–135) (figure 1). Patients achieving low post-TPE anti-A/B IgM/IgG titers (≤1:16) showed a shorter median duration of anemia (14 days) compared with those with residual titers >1:16 (approximately 3–4 weeks). A similar trend was observed for time to RBC transfusion independence, with shorter transfusion periods in patients with lower post-TPE titers. When stratified by a higher cut-off (post-TPE IgM ≥1:128 vs <1:128), both anemia duration and transfusion exposure tended to be longer in the high-titer group, although differences did not reach statistical significance in this limited cohort. In our population, more effective antibody reduction (lower post-TPE titers) was associated with faster hematologic recovery and a reduced RBC transfusion burden. OS did not differ significantly across titer strata. No infectious complications due to TPE have been documented.



Conclusions: In this small single-center cohort, pre-transplant TPE for major ABO incompatibility was associated with a shorter duration of post-transplant anemia and earlier RBC transfusion independence. The advantage of using TPE in the setting of ABO incompatibility lies in the absence of infectious complications, which may occur with other procedures used for the same purpose (e.g Rituximab). TPE therefore represents a safe and effective strategy for managing ABO incompatibility, minimizing infectious risk while preserving transplant feasibility.

Disclosure: Nothing to declare.

P183

EARLY POST-TRANSPLANT EOSINOPHILIC GASTROENTERITIS IN TWO ALLOGENIC HSCT RECIPIENTS

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Background: Eosinophilic gastroenteritis (EGE) is an uncommon inflammatory disorder characterized by gastrointestinal symptoms and marked eosinophilic infiltration of the gut (≥20 eosinophils per high-power field, HPF). Gastrointestinal (GI) complications are frequent after allogeneic hematopoietic stem cell transplantation (allo-HSCT), but EGE seems exceptionally rare, with only a few histologically confirmed cases reported to date.

Methods: We retrospectively reviewed two cases of EGE in allo-HSCT recipients, identified as part of a prospective protocol in our center that systematically performs upper and lower gastrointestinal tract biopsies in all allo-HSCT recipients with GI symptoms and potential GVHD. Clinical, laboratory, endoscopic, histopathological data and therapeutic management and outcomes are summarized descriptively.

Results: Case 1: A 58-year-old woman on day +54 after an HLA-matched related donor (MRD) allo-HSCT for AML was admitted with a 10-day history of nausea, vomiting, and diarrhea associated with pronounced eosinophilia (31.3×10^3/μL). Gastroscopy and rectosigmoidoscopy revealed dense eosinophilic infiltrate in the esophageal, gastric, and duodenal lamina propia and submucosa biopsies (up to 26 eos/HPF), findings consistent with EGE (Image 1A-1B), but without features typical of GVHD. Rectal biopsies showed eosinophilic infiltration damaging colonic crypts (Image 1C). A lactose-free diet was initiated and continues to this day, leading to clinical improvement and complete resolution of eosinophilia and GI symptoms within 2 weeks. Serum IgE levels were within the normal range (157 KU/L), and an allergy work-up showed negative results.
Case 2: A 62-year-old man on day +50 after a MRD allo-HSCT for TP53-mutated AML presented with nausea, vomiting, and diarrhea associated with marked eosinophilia in peripheral blood (9.6×10^3/μL). Gastroscopy and rectosigmoidoscopy showed only macroscopic signs of diffuse gastritis but systematic biopsies of the gastrointestinal tract revealed not only eosinophilic gastritis and duodenitis but also a diffuse eosinophilic infiltrate involving the colorectal mucosa and submucosa, with no evidence of GvHD. Microbiological studies were negative. The patient's symptoms resolved along with the peripheral eosinophilia in less than 2 weeks with the avoidance of dairy products and the administration of omeprazole (20 mg/day) without corticosteroid therapy. Eight months lather the patient remains asymptomatic maintaining a lactose-free diet.

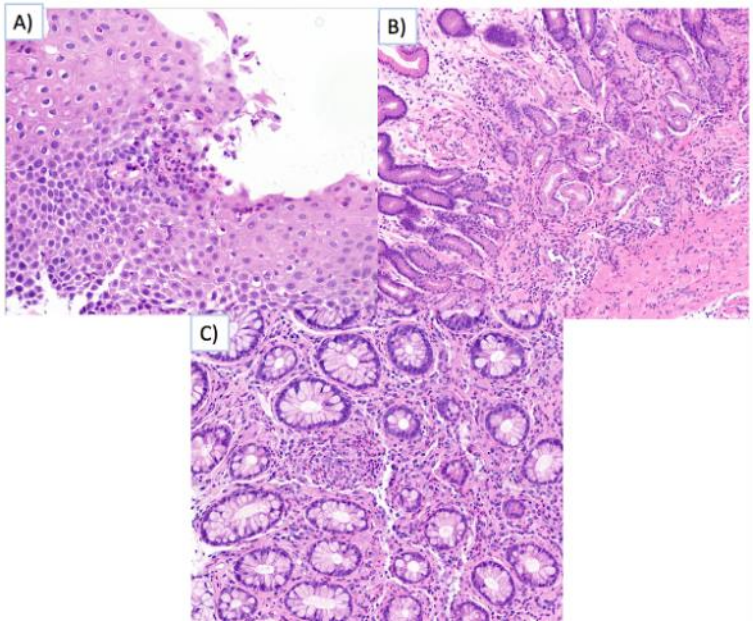

Image 1: A) Esophageal mucosa showing squamous epithelium with the presence of

eosinophils forming microabscesses, along with epithelial spongiosis and desquamation (400X). B) Gastric mucosa demonstrating a diffuse eosinophilic infiltrate within the lamina propia, occasionally permeating the glandular epithelium (400X). C) Colorectal mucosa with abundant eosinophils in the lamina propia permeating and disrupting the colonic crypts (400X).

Conclusions: EGE is a rare GI complication after allo-HSCT that may mimic other transplant complications such as infectious colitis and GvHD. Systematic endoscopic and histologic evaluation was critical to establishing the diagnosis and avoiding unnecessary immunosuppression. Both patients showed excellent response with a lactose-free diet, behaving as if they had developed lactose intolerance. Immune-mediated complications can be transferred from the donor to the allo-HSCT recipient. Histopathological findings in this clinical setting may also support a predominantly allergic etiology, although the physiopathology behind this entity remains poorly understood, highlighting the need for further studies to clarify its mechanisms and guide optimal management.

Disclosure: No conflict of interest declared.

P184

OPTIMIZED TREATMENT OF HEMORRHAGIC CYSTITIS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH ALLOGENEIC PLATELET-RICH PLASMA

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Background: Hemorrhagic cystitis (HC) is a common complication after allogeneic hematopoietic stem cell transplantation (alloHSCT). Severe cases of HC can persist and not improve due to worsening acute graft-versus-host disease (GvHD) or various viral infections. Platelet-rich plasma contains many growth factors and cytokines that influence inflammation and tissue regeneration.

Methods: We present 4 cases of late-onset HC treated with addition of allogeneic platelet-rich plasma (alloPRP) to the treatment of HC. The patients received alloHSCT from matched unrelated donors (n=3) and from sibling (n=1) with myeloablative conditioning regimen (BuCy). Two patients developed acute GvHD. All patients received conservative treatment of HC: hyperhydration, alkalization, analgesics, platelet transfusions, bladder irrigation by urinary catheter (with normal saline, repeated syringe aspiration, aminocaproic acid) and still had frequent and painful urination, haematuria with blood clots, proteinuria. Visual analog scale was used for pain assessment, urine analysis and ultrasound examinations of the bladder were done.

Results: Patient 1: 42 y.o. female with chronic myeloid leukemia developed HC at day +40 after alloHSCT. She received conservative treatment of HC with partial effect and had recurrent episode of HC at day +80. AlloPRP was added to the treatment: 8 intravesical instillations (every 48 hours) with an exposure time of 30 min. After alloPRP treatment she showed a decrease in the bladder wall thickness (from 7 mm to 4 mm) and proteinuria (from 2.18 to 1.85 g/L).
Patient 2: 42 y.o. male with acute myeloblastic leukemia (AML) presented with HC at day +32 after HSCT. He received 5 intravesical instillations of alloPRP (every 72 hours) along with conservative treatment of HC. After alloPRP treatment the thickness of the bladder wall has reduced from 8.4 mm to 5.8 mm, proteinuria decreased from 2.8 to 0.36 g/L.
Patient 3: 47 y.o. female with AML developed HC at day +46 after HSCT. She received 7 intravesical instillations of alloPRP (3 instillations every 24 hours, then 4 – every 72 hours). A reduction in the thickness of the bladder wall (from 10 mm to 6 mm) and proteinuria (from 3.69 to 1.04 g/L) was achieved after alloPRP treatment.
Patient 4: 30 y.o. female with post-essential thrombocythemia myelofibrosis experienced HC at day +59 after HSCT. She received 3 intravesical instillations of alloPRP (every 24 hours). After alloPRP treatment we detected a decrease in the thickness of the bladder wall from 6.5 mm to 5.3 mm and in proteinuria (from 5.89 to 0.3 g/L).
All patients experienced a decrease in pain intensity (the mean is by 27.5 mm), in urination frequency and disappearance of the blood clots in urine. The degree of haematuria didn't change after alloPRP instillations and remained at the level of 200 Rbc/ul. Subsequently, we obtained positive PCR test results for BK polyomavirus in the blood and urine of all patients.

Conclusions: Intravesical alloPRP instillations reduce the bladder wall thickness, pain intensity and have positive effects on the other clinical manifestations of HC. The effectiveness of post-HSCT HC therapy can be improved by adding alloPRP to the treatment strategy.

Disclosure: Nothing to declare

P185

POST-TRANSPLANT PURE RED CELL APLASIA: A SINGLE CENTER EXPERIENCE WITH PLASMA EXCHANGE AND HIGH DOSE ERYTHROPOIETIN

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Background: Post-Transplant Pure Red Cell Aplasia (PT-PRCA) is a rare complication of ABO incompatible allogeneic hematopoietic stem cell transplants (HSCT). It is believed to be mediated by residual recipient isohemagglutinins (IHA), which hinder donor erythroid precursor development, inducing hyporegenerative anemia. Prolonged PT-PRCA is associated to heavy transfusion requirements and iron overload. Differential diagnoses include infections, hematologic disease relapse, graft failure, autoimmune hemolytic anemia, and thrombotic microangiopathy. Given the possibility of spontaneous recovery, PT-PRCA criteria

for treatment and standard of care have yet to be established. Therapeutic approaches include immunosuppression/immunomodulation (steroids, cyclosporine A, anti-B cell strategies as Rituximab, and anti-plasma cell treatments as Bortezomib and Daratumumab); erythropoiesis enhancement (recombinant human erythropoietin [rhEPO], thrombopoietin mimetics); and eradication of residual IHA (immunoglobulins, plasma exchange [PEX]). We report our experience with 6 PT-PRCA patients who underwent treatment with PEX and high dose rhEPO.

Methods: Single center retrospective observational study at the Hematology and Cell Therapy Unit of the Mazzoni Hospital in Ascoli Piceno. All patients signed an informed consent form. PT-PRCA was defined as persistence of anemia and reticulocytopenia, and isolated erythroid hypoplasia/aplasia in an otherwise normal bone marrow. Threshold for IHA titer was set at 1:64. PT-PRCA treatment regimen comprised 8 biweekly PEX sessions and high dose rhEPO (80.000 IU) administration 3 days after each PEX procedure.

Results: We report the data from 6 patients who received HSCT from July 2020 to March 2023. The patients, transplant and PT-PRCA characteristics are reported in Table 1. 5/6 patients were diagnosed with acute myeloid leukemia, 1/6 had myelodysplastic syndrome. All patients received myeloablative conditioning and underwent ABO mismatched HSCT. All patients developed transfusion-dependent PT-PRCA and underwent specific treatment with PEX and high dose rhEPO. 2/6 patients also received Rituximab prior to PEX initiation. All patients obtained a complete response, with transfusion independency and normalization of hemoglobin values. Median response time from treatment initiation was 90 days.

Table 1. Patients, Transplant, and PT-PRCA Characteristics.

Sex Male Female	 4/6 2/6
Diagnosis AML MDS	 5/6 1/6
Disease Status at HSCT 1st CR 2nd CR SD	 3/6 2/6 1/6
Median Age at HSCT (IQR)	60.5 years (56.5-65.3)
GvHD Prophylaxis CSA-MTX-ATG CSA-MTX CSA-PTCy-MMF	 4/6 1/6 1/6

Table 1. Patients, Transplant, and PT-PRCA Characteristics.

Donor Type	
MUD	3/6
MMUD	1/6
Haplo	1/6
Sibling	1/6
Incompatibility	
Major	4/6
Bidirectional	2/6
IHA Titer pre-HSCT	
High Titer	2/6
Not tested	4/6
Stem Cell Source	
Peripheral Blood Stem Cell	2/6
Bone Marrow	4/6
Median Time from HSCT to PT-PRCA Diagnosis (IQR)	60.5 days (41.3-81.3)
PT-PRCA Treatment	
PEX+rhEPO	4/6
RTX followed by PEX+rhEPO	2/6
Median Time from PT-PRCA Diagnosis to Treatment (IQR)	129.0 days (64.8-150.5)
IHA Titer pre-Treatment	
High Titer	1/6
Low Titer	3/6
Not Tested	1/6
Median Response Time (IQR)	90.0 days (44.0-120.3)
IHA Titer post-Treatment	
Low Titer	3/6
High Titer	1/6
Not Tested	2/6
Abbreviations: PT-PRCA: Post-Transplant Pure Red Cell Aplasia, AML: Acute Myeloid Leukemia, MDS: Myelodysplastic Syndrome, HSCT: Allogenic Hematopoietic Stem Cell Transplant, IQR: Interquartile Range, GvHD: Graft versus Host Disease, CSA: Cyclosporine A, MTX: Methotrexate, ATG: Anti-Thymocyte Globulin, PTCy: Post-Transplant Cyclophosphamide, MMF: Mycophenolate Mofetil, MUD: Matched Unrelated Donor, MMUD:	

Table 1. Patients, Transplant, and PT-PRCA Characteristics.

Mismatched Unrelated Donor, IHA: Isohemagglutinins, PEX: Plasma Exchange, rhEPO: recombinant human Erythropoietin, RTX: Rituximab.

Conclusions: The pathophysiology of PT-PRCA is yet to be fully uncovered and further studies to determine when and how to treat this complication are needed. Despite the small cohort, we report our positive experience with PEX and high dose EPO for the treatment of persistent PT-PRCA. All of our patients obtained a complete response and no treatment-related complications occurred.

Disclosure: Nothing to declare.

P186

LEVETIRACETAM FOR THE PREVENTION OF BUSULFAN-INDUCED SEIZURES IN HEMATOPOIETIC CELL TRANSPLANTATION

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Background: High dose busulfan (Bu) is widely used in conditioning regimens for patients undergoing hematopoietic stem cell transplantation (HSCT). Since seizure is a major complication of high-dose Bu, antiepileptic prophylaxis, such as phenytoin was given. As various anticonvulsant drugs have been reported, we conducted a retrospective analyze the preventive effects and adverse events with levetiracetam alongside intravenous Bu.

Methods: We retrospectively evaluated the levetiracetam prophylaxis during high dose Bu conditioning between July 2019 and October 2025. Levetiracetam was administered at ad dose of 500 mg twice daily beginning 12 hours to Bu through 24 hours after the last Bu dose. Busulfan-based conditioning regimens included: BuCy, BuFlu, BuFluATG.

Results: A total of 93 patients were enrolled in this study, 56 (60.2%) were male. The median age at HSCT was 52 years (range, 18 to 75). Seventy-two (77.4%) had acute myeloid leukemia/myelodysplastic syndrome, ten (10.8%) had acute lymphoblastic leukemia, four (4/3%) had lymphoma, and seven (7.5%) had myeloproliferative neoplasm. The seizure prevention rate was 100% for levetiracetam and there was no significant drug-related adverse effect.

Conclusions: Levetiracetam is considered useful as a preventative drug against seizure during intravenous Bu infusion because it is easy to administer and there was no drug-related adverse effect.

Disclosure: Nothing to declare.

P187

PATTERNS AND PREDICTORS OF ORAL MUCOSITIS FOLLOWING HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT): A PROSPECTIVE SINGLE-CENTRE EXPERIENCE

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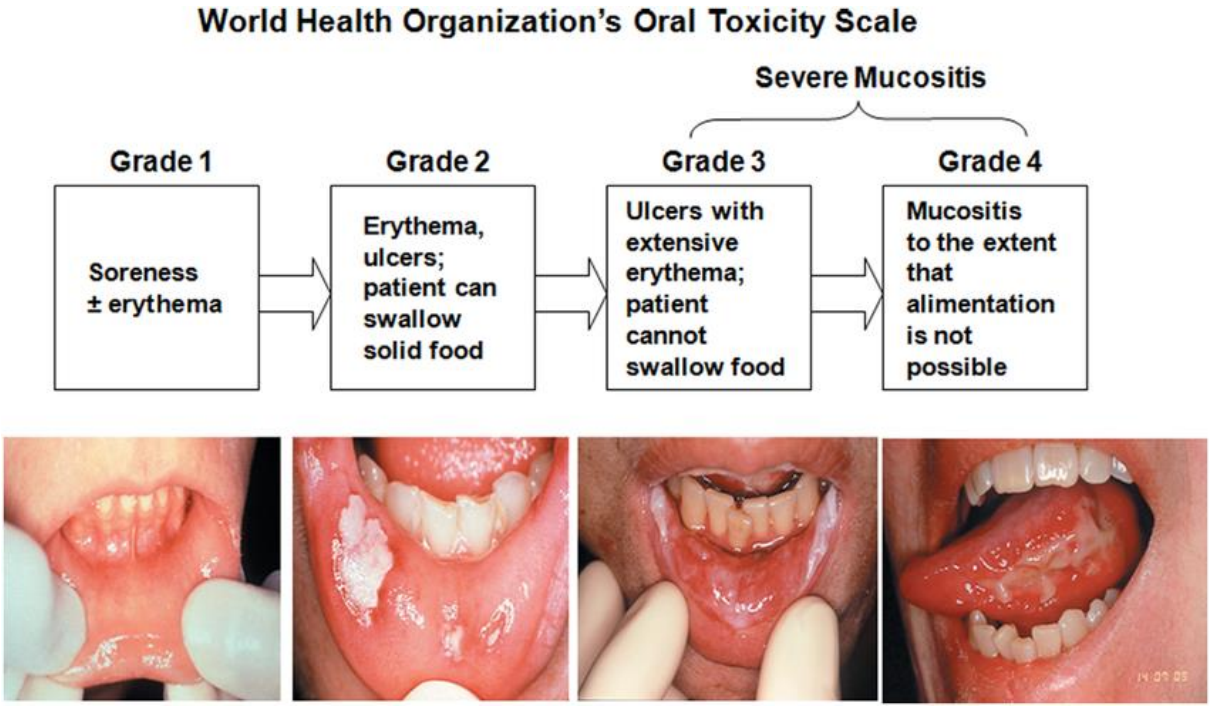
Background: Oral mucositis (OM) is an almost universal and disabling complication of transplant arising from cytotoxic injury of conditioning regimen to the oral mucosa that is particularly susceptible to injury. It contributes to significant pain, nutritional compromise, infectious risk and prolonged hospital stay. As most other acute complications following transplant are life-threatening, oral mucositis is often overlooked as there is no mortality from this seemingly innocuous complication. OM adds abundantly to the morbidity from transplant. Prospective data on this important post HSCT adverse event remain scarce. We aimed to assess the incidence and severity of oral mucositis following HSCT, to compare outcomes across transplant type and conditioning intensity, and to explore the association of supportive and preventive strategies, including oral cooling, with mucositis severity.

Methods: This prospective observational study included adult patients undergoing HSCT between the study period. Oral mucositis was graded using WHO criteria (Figure). Severe mucositis was defined as grade ≥3. Demographic and transplant-related details, conditioning intensity, body mass index (BMI), analgesic requirement, and preventive measures were recorded. Oral cooling was used as a preventive strategy in selected patients. Categorical variables were compared using Fisher's exact test and continuous variables using the Mann–Whitney U test. A p value <0.05 was considered statistically significant.

Parameter	**Comparison / Group**	**Key findings (severe OM) n, (%)**	**P value**
Incidence of severe OM (Grade ≥3)	Overall	12/29 (41.4%)	-
Transplant Type	Auto n = 15 Allo n =14	7/15 (46.7%) 5/14 (35.7%)	0.71
Conditioning intensity (Allo only)	MAC n = 5 RIC n = 9	3/5 (60%) 2/9 (22.2%)	0.27
Onset of OM (median days)	MAC vs RIC Auto vs Allo	5 vs 5 3.5 vs 5	0.75 0.53
Resolution of OM (median days)	MAC vs RIC Auto vs Allo	14 vs 13 12.5 vs 14.5	0.75 0.60

BMI (median kg/m^2)	Grade ≥3 vs < 3 OM	23.37 vs 25.55	0.43
Preventive strategy - Oral cooling	n = 4	3/4 severe OM (75%)	not significant



Results: A total of 29 patients were included in the final analysis. The median age was 49.5 years (range 21–77 years), and 65.5% were male. Fifteen patients underwent autologous HSCT and 14 underwent allogeneic HSCT. Severe oral mucositis (grade ≥3) occurred in 12 patients (41.4%). The incidence of severe mucositis did not differ significantly between autologous and allogeneic transplantation (46.7% vs 35.7%, p = 0.71). Patients receiving myeloablative conditioning showed a higher incidence of severe mucositis compared to those receiving reduced intensity conditioning (60% vs 22.2%), although this difference was not statistically significant (p = 0.27).
The median onset and resolution of mucositis were comparable between myeloablative and reduced intensity conditioning, as well as between autologous and allogeneic transplantation. Opioid analgesic requirement was observed exclusively in patients with severe mucositis, reflecting greater symptom burden, though this association did not reach statistical significance (p = 0.16). Median BMI was lower in patients with severe mucositis compared to those with non-severe mucositis, without statistical significance (p = 0.43). Four patients received oral cooling as a preventive measure, 3 of whom developed severe mucositis, suggesting that oral cooling system did not appear to reduce the incidence of severe oral

mucositis; however, interpretation is limited by very small numbers and potential confounding.

Conclusions: Oral mucositis remains a common complication following HSCT. A substantial proportion of patients develop severe disease requiring opioid analgesia. No statistically significant predictors of severe mucositis were identified in our study. However conditioning intensity and BMI appear to play a role. The hypothesis that oral cooling systems may mitigate OM severity was not supported in our limited data. Larger studies with systematic documentation of preventive strategies are needed to better define risk factors and alleviation strategies for oral mucositis in HSCT.

Disclosure: None to disclose.

P188

ENGRAFTMENT SYNDROME IN AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION: INCIDENCE, ASSOCIATED FACTORS AND CLINICAL IMPACT

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Background: Engraftment syndrome (ES) is an inflammatory complication of autologous haematopoietic stem cell transplantation (ASCT) occurring around neutrophil recovery and characterised by non-infectious fever and capillary leak manifestations.

Methods: We performed a single-centre, retrospective study including 130 consecutive ASCT episodes performed between 2023 and 2025. Collected variables included demographics, underlying disease, disease status, number of prior treatment lines, HCT-CI score, conditioning regimen and graft characteristics (CD34+ $\times 10^6$/kg, infused volume and viability). Pre-ASCT laboratory parameters were C-reactive protein (CRP), lactate dehydrogenase, creatinine and platelet count. Variables related to ES were collected according to the Maiolino criteria and included non-infectious fever (≥38ºC without microbiological documentation or response to antimicrobials within ±24 h of engraftment), weight gain >3%, maculopapular rash, non-infectious diarrhoea and non-infectious pulmonary infiltrates. Additional data included CRP and procalcitonin at fever, time to neutrophil recovery, use or withdrawal of filgrastim, steroid treatment, length of stay, ICU admission and day +100 mortality. Statistical analyses were performed using SPSS. Comparisons between ES and non-ES episodes were performed using chi-square or Fisher's exact test for categorical variables and Mann–Whitney U test for continuous variables.

Results: Median age at ASCT was 61 years (IQR 51–66), and 68% of episodes occurred in male patients. Underlying diseases were multiple myeloma (50%), B-cell non-Hodgkin

lymphoma (21%) and other diagnoses (T-cell non-Hodgkin lymphoma, Hodgkin lymphoma, primary CNS lymphoma, amyloidosis [5 cases], plasma cell leukaemia, solid tumours and non-malignant diseases); amyloidosis showed a significantly higher incidence of ES compared with other diagnoses (p≈0.03). Median HCT-CI was 2 (IQR 0–3). Median CD34+ dose was 3.98 ×10⁶/kg (IQR 3.00–5.27), infused volume 408 mL (IQR 288–532) and graft viability 84% (IQR 76–89). Median length of stay was 16 days (IQR 14–19). Clinical ES was diagnosed in 22/130 episodes (16.9%), while 56/130 (43.1%) fulfilled Maiolino criteria. Compared with non-ES episodes, ES was associated with higher pre-ASCT creatinine (p≈0.01) and a trend towards higher HCT-CI (p≈0.08); CD34+ dose (median 4.40 vs 3.93 ×10⁶/kg; p≈0.64) and infused volume (median 442 vs 404 mL; p≈0.29) were similar between groups. ES typically developed around day +10 and was characterised by non-infectious fever (100%), weight gain >3% (~77%), non-infectious diarrhoea (~60%), rash (~33%) and non-infectious pulmonary infiltrates (~25%). CRP at fever was higher in ES (p≈0.01), whereas procalcitonin was comparable. Length of stay was longer in ES (median ~18 vs 16 days; p≈0.02), with no significant differences in ICU admission or day +100 mortality. Among episodes fulfilling criteria but not clinically labelled as ES (35/130; 26.9% of the cohort), an alternative diagnosis was documented in 68.6% and 11.4% improved after filgrastim withdrawal.

Conclusions: In our single-centre ASCT cohort (2023–2025), engraftment syndrome defined by the Maiolino criteria was a frequent complication associated with increased inflammatory response and longer hospitalisation, without a clear impact on early mortality. Amyloidosis appeared to be associated with a particularly high risk of ES.

Disclosure: Nothing to declare.

P189

PROPHYLAXIS WITH DEFIBROTIDE VERSUS EARLY TREATMENT OF SEVERE VOD IN PEDIATRIC ONCO-HEMATOLOGICAL PATIENTS: A MONOCENTRIC EXPERIENCE

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Background: Severe hepatic veno-occlusive disease/sinusoidal obstruction syndrome (VOD/SOS) is a potentially life-threatening complication of hematopoietic stem cell transplantation (HSCT). New EBMT criteria allow to early identify patients at high risk of developing VOD and to early diagnose and treat this toxic seriuous adverse event. This

monocentric report had focused on the role of prophylaxis versus early treatment with Defibrotide in selected very high risk pediatric and young adult patients who received SCT.

Methods: From 01/2018 to 09/2025, in our Center we performed 49 allogeneic transplants in HR acute leukemia patients: 26 from haploidentical donors, 13 from matched unrelated donors (MUD), 10 from identical siblings; and 14 autologous SCT in patients affected by solid tumors, in particular neuroblastoma and Ewing's sarcoma. Patient median age was 9 years (range 1-24). Four patients received a second allo-SCT for acute leukemia relapse (n=1) or graft-failure (n=3), and 3 a second auto-SCT as consolidation therapy for solid tumors, in most cases high risk neuroblastoma.

Results: We observed a total of 10 cases of severe VOD (16%): 3 after allo-SCT (6%), and 7 after auto-SCT (50%). They were 6 males and 4 females, with a median age of 6.5 years (range: 1-22). VOD diagnosis and staging was done according to new EBMT criteria. Prophylaxis with Defibrotide was administered in 5 procedures, 3 allogenic (1 relapsed acute lymphoblastic leukemia, ALL, who had received Inotuzumab Ozogamicin as salvage therapy, and 2 acute myeloid leukemia, AML), and 2 autologous transplantations (for HR neuroblastoma). Defibrotide was started with conditioning regimen at the dosage of 25 mg/Kg/day and suspended after engraftment, in absence of any sign or symptom of VOD; treatment was continued until VOD sign and/or symptoms diseapperance in case of severe VOD diagnosis. In patients who did not received prophylaxis, in case of post-HSCT VOD diagnosis, defibrotide was given at a median day of +14 from graft infusion (range: 11-42 days), always at the dosage of 25 mg/Kg/die for a median of 21 days (range: 10-54 days). Five out of 10 patients who did received prophylaxis, three developed VOD and 2 did not (60% vs 40%). The remaining 5 patients did not received prophylaxis, even if they were considered at very high risk of VOD, and they all developed severe VOD (100%), but they received treatment very early, at the first VOD sign and/or symptom (in particular, platelet refractoriness). All patients recovered from VOD, only one developed multi-organ failure, MOF, but none died for VOD.

Conclusions: We did not observed a significant difference in patients who received Defibrotide prophylaxis compared to patients who received a very early treatment according to new criteria, but we can confirm a trend in improvement incidence and outcome in patients who received defibrotide as prophylaxis instead treatment. Moreover, we observed a very high incidence of severe VOD in patients affected by HR neuroblastoma and Ewing's sarcoma who received Busulfan in the conditioning regimen. In these selected patients, VOD prophylaxis with defibrotide would represent a good strategy to improve outcome.

Disclosure: Nothing to declare.

P190

POSSIBLE ROLE OF FLUDARABINE IN EARLY POST TRANSPLANT CEREBRAL TOXICITY. A SINGLE CENTRE EXPERIENCE

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Background: Neurological complications in patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT) represent a clinically significant event, frequently associated with substantial decline in overall health status and quality of life, and often culminating in poor outcomes. These manifestations arise from a broad range of etiologies, including but not limited to iatrogenic injury, infectious processes, vascular events, neurodegenerative conditions, and metabolic disturbances. Based on their temporal onset, neurological complications are conventionally categorized as pre-engraftment, early post-engraftment, and late post-engraftment.

Methods: In this single-center retrospective observational study, we evaluated 7 patients who underwent allogeneic hematopoietic stem cell transplantation between July 2023 and September 2025 at our institution and subsequently developed post-transplant neurological complications.
Among the 7 patients (median age, 63 years), 4 had acute myeloid leukemia—including 1 undergoing a second allogeneic transplant—whereas 1 had B-cell acute lymphoblastic leukemia, 1 T-cell non-Hodgkin lymphoma, and 1 plasmacytic leukemia.
All patients received conditioning regimens containing fludarabine: specifically, 3 received treosulfan–fludarabine, 3 reduced-intensity thiotepa–fludarabine–busulfan (RIC TBF), and 1 full-intensity TBF.
In our cohort, donors included 3 HLA-identical related donors, 2 unrelated registry donors, and 2 haploidentical related donors.
For GVHD prophylaxis, 4 patients received cyclosporine (CSA), methotrexate (MTX), and rabbit anti-thymocyte globulin (ATG); 1 received CSA, tacrolimus, and ATG; and 2 received post-transplant cyclophosphamide, mycophenolate mofetil (MMF), and tacrolimus.

Results: The median onset of neurological symptoms was 45 days after transplantation (range, 14–55). All patients underwent brain MRI and cerebrospinal fluid (CSF) evaluation by lumbar puncture after neurologic symptoms. CSF analysis was positive for HHV-6 (15,000 cp/mL) in only 1 case, while the remaining 6 samples were microbiologically negative.
On imaging, 4 cases were reported as therapy-related leukoencephalopathy, 2 showed multifocal T2/FLAIR hyperintensities, and 1 revealed severe chronic multi-infarctional encephalopathy, all of them markedly worsened compared with the pre-transplant MRI.
All patients received high-dose intravenous methylprednisolone as first-line treatment; in 5 of the 7 cases, therapy was combined with intravenous immunoglobulins (IVIG).
Cyclosporine was discontinued in all patients receiving it as part of GVHD prophylaxis.

Conclusions: At present, 4 patients remain in outpatient follow-up, including one with significant persistent neurological motor deficits, who has shown partial improvement after rehabilitation. The remaining 3 patients died because of these complications. Autopsy was performed in all 3 deceased patients and revealed spongiform leukoencephalopathy in each case.
Radiological and histopathological findings suggest a predominant iatrogenic aetiology, most likely related to fludarabine exposure which is also the common background in all the patients.
Given the small sample size, further studies are required to substantiate this hypothesis.

Disclosure: Nothing to declare.

P191

PAIN MANAGEMENT WITH NARCOTIC INFUSION IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Hematopoietic stem cell transplantation (HSCT) offers a potential cure for children with malignant and non-malignant diseases that are otherwise incurable. However, HSCT is associated with multiple comorbidities, and many post-transplant complications are accompanied by significant pain requiring careful assessment and management.

Methods: This retrospective study included pediatric patients who underwent HSCT at the Pediatric HSCT Program at King Hussein Cancer Center (KHCC) between January 2025 and mid-December 2025.

Results:

Side effects	Number of patients
Urinary retention	1
Constipation	1
Pruritus	5
Elevated bilirubin	1
Hallucinations	1

A total of forty-eight patients underwent HSCT during the study period. The majority received allogeneic transplants, with thirty-five patients undergoing allogeneic HSCT.

Thirty-seven patients (77%) required narcotic infusion during their transplant course. The median age was 7 years (range: 1.2–24.1 years). Among these patients, twenty-seven underwent allogeneic HSCT and ten received autologous HSCT.

Malignant diseases were the indication for transplantation in twenty-three patients, including acute lymphoblastic leukemia (n=9), acute myeloid leukemia/myelodysplastic syndrome (n=3), lymphoma (n=4), high-risk neuroblastoma (n=2), and retinoblastoma (n=1). Fourteen patients underwent transplantation for non-malignant conditions, including hemoglobinopathies (n=6), severe aplastic anemia (n=4), and other disorders such as Fanconi anemia, DADA-2 mutation, Wiskott–Aldrich syndrome, and familial hemophagocytic lymphohistiocytosis (n=4).

Pain assessment was conducted using either the Wong–Baker Faces Pain Scale or the Numeric Rating Scale. Oral and anal mucositis was the most common indication for narcotic infusion, occurring in thirty-three patients. Bone pain and cystitis were indications in three patients each.

Narcotic infusions were generally well tolerated. No patients discontinued treatment due to uncontrolled side effects or experienced life-threatening adverse events. Infusion was discontinued in one patient due to tampering with the infusion pump.

Switching from morphine to fentanyl infusion was required in fifteen patients, primarily due to uncontrolled pain (n=9) or pruritus (n=4). Only two patients required the addition of ketamine infusion for refractory pain.

The median time to initiation of narcotic infusion was 5 days post-transplant (range: 2–580 days), and the median duration of infusion was 8 days (range: 3–35 days).

Conclusions: Mucositis was the most prevalent cause of pain during the post-transplant period in pediatric HSCT recipients. Narcotic infusion proved to be a safe and well-tolerated strategy for pain management, with a low incidence of significant adverse effects and no life-threatening complications observed.

Disclosure: I have nothing to declare.

P192

TAKOTSUBO CARDIOMYOPATHY MIMICKING ACUTE CORONARY SYNDROME DURING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Cardiovascular complications during hematopoietic stem cell transplantation (HSCT) are clinically relevant and may be life-threatening, particularly when they mimic acute coronary syndromes. Takotsubo cardiomyopathy (TTC), also known as stress-induced cardiomyopathy, is characterized by transient specific pattern left ventricular systolic dysfunction, electrocardiographic changes, and elevation of cardiac biomarkers in the absence of significant coronary artery disease. Emotional and physical stressors, including oncological treatments and transplantation procedures, are recognized triggers. Early differentiation between acute coronary syndrome and TTC is crucial to guide management and avoid unnecessary invasive procedures.

Methods: A 62-year-old woman was diagnosed with a solitary plasmacytoma of the pubic bone after presenting with right groin pain. Initial treatment followed the VTD regimen (bortezomib, thalidomide, dexamethasone). Due to elevated liver enzymes, thalidomide was discontinued and therapy was adjusted to CYBORDEX (cyclophosphamide, bortezomib, dexamethasone). After five months, the patient was evaluated for autologous HSCT. She had arterial hypertension, no family history of coronary artery disease, and was a non-smoker. Her general condition was good (ECOG-0).
Pre-transplant echocardiography showed preserved left ventricular ejection fraction (LVEF 55%), impaired diastolic relaxation, slightly dilated left atrium, mild valvular insufficiencies, and no pulmonary hypertension. In the absence of contraindications, stem cell mobilization with cyclophosphamide and G-CSF was performed, followed by autologous HSCT with infusion of 3.3×10^6 CD34+ cells/kg.
During transplantation procedure, the patient developed nausea, vomiting, hypotension, and a transient episode of unconsciousness with convulsions. Shortly after the procedure, chest pain occurred. Electrocardiography revealed new diffuse T-wave inversions, and troponin I increased from 0.07 µg/L to 1.89 µg/L (normal <0.04 µg/L). Echocardiography demonstrated reduced LVEF with regional wall motion abnormalities involving the apical and mid-ventricular segments, with preserved basal contraction.

Results: A working diagnosis of non-ST elevation myocardial infarction was made. Due to post-transplant immunosuppression and infection risk, urgent coronary angiography was deferred and conservative medical therapy was initiated (beta-blocker, ACE inhibitor, statin, nitrates, aspirin). Follow-up echocardiography 16 days later showed complete recovery of left

ventricular systolic function (LVEF 59.6%) with resolution of regional wall motion abnormalities.
Coronary angiography performed 20 days after HSCT revealed only a mild (35%) stenosis of the left anterior descending artery. Cardiac magnetic resonance imaging at six weeks demonstrated normal global systolic function (LVEF 64%), absence of myocardial edema or ischemic scar, and mildly increased native T1 values suggestive of diffuse myocardial changes. Based on clinical presentation, imaging findings, reversibility of dysfunction, and lack of significant coronary disease, the final diagnosis of TTC was established.

Conclusions: This case highlights Takotsubo cardiomyopathy as an important and under-recognized differential diagnosis of acute coronary syndrome during autologous HSCT. Transplant-related physical stress and acute procedural complications may act as triggers. Awareness of this condition among transplant teams is essential to ensure appropriate diagnosis, optimize management, and prevent unnecessary invasive interventions. Multidisciplinary collaboration between haematology, cardiology, and nursing staff plays a key role in achieving favourable outcomes.

Disclosure: Nothing to disclose.

P193

A CASE OF CAPILLARY LEAK SYNDROME FOLLOWING HAPLOIDENTICAL ALLOGENEIC STEM CELL TRANSPLANTATION IN A PATIENT WITH ACUTE MYELOID LEUKEMIA

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Background: Capillary leak syndrome (CLS) is a rare and life-threatening complication of hematopoietic stem cell transplantation (HSCT), typically occurring early in the post-HSCT course. It is characterized by generalized endothelial damage leading to vascular hyperpermeability and fluid shifting to the interstitial space.

Methods: This report describes a 61-year-old woman with acute myeloid leukemia who developed CLS following haploidentical allogeneic HSCT.

Results: The patient was diagnosed with AML with poor-risk cytogenetics due to the presence of DEK-NUP214 and FLT3-ITD mutations. She achieved remission with incomplete hematologic recovery after induction therapy with cytarabine and idarubicin, followed by a combination of azacitidine, venetoclax, and gilteritinib. Evaluation and workup prior to allogeneic HSCT identified a haploidentical, related stem cell donor with a minor ABO blood group mismatch and absent donor-specific antibodies. The stem cell recipient underwent reduced-intensity conditioning with thiotepa (5 mg/kg), fludarabine (120 mg/m²), and busulfan (5.5 mg/kg). A total CD34 count of 6.8 million cells/kg was infused.
Immediately post-infusion, she developed mild cytokine release syndrome (CRS), as

evidenced by fever, desaturation, hypertension, and tachycardia. After supportive medications were given, there was temporary resolution of signs and symptoms. Post-transplant cyclophosphamide (40 mg/kg) was given on day +3 for graft-versus-host disease (GVHD) prophylaxis, after which she developed new-onset arrhythmia and hemorrhagic cystitis. With persistently positive fluid balance and generalized edema despite maximizing the use of diuretics, the patient developed severe pulmonary congestion leading to acute respiratory failure and hypotension requiring vasopressor support as early as day +4. A high index of suspicion for CLS was considered, prompting the medical team to start methylprednisolone and implement aggressive supportive treatment. Due to the refractoriness of the patient's CLS and her rapid clinical deterioration, 1 dose of bevacizumab 5 mg/kg was given. However, she did not respond to the treatment, ultimately leading to her demise.

Conclusions: This case highlights the diagnostic and therapeutic challenges in patients who develop fatal CLS post-HSCT. Because its clinical features frequently overlap with other post-HSCT complications, maintaining a high index of suspicion is crucial in the timely recognition and management of this rare syndrome. The lack of standard diagnostic criteria and effective treatment options for CLS despite the recent advances in transplantation medicine necessitates further research.

Disclosure: Nothing to declare.

P194

ALLOGENEIC STEM CELL TRANSPLANT FOR NEAR ETP ACUTE LYMPHOBLASTIC LEUKAEMIA IN A DECEASED-DONOR RENAL TRANSPLANT RECIPIENT: A CASE STUDY AND LITERATURE REVIEW

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Background: Patients with previous end-stage organ failure, who develop haematological disorders, may require allogeneic stem cell transplantation (AlloSCT) for potential cure and/or long-term disease control. Although successful AlloSCT are reported, the risk of solid organ graft failure and rejection in literature are inconsistent. Limited evidence and guidance on optimal immunosuppressive therapies (IST) peri-engraftment makes clinical management and outcome prediction challenging.

Methods: A 36-year-old female presented with near ETP Acute Lymphoblastic Leukaemia (ALL) following a 10-week history of neck swelling. The patient is a deceased-donor renal transplant recipient 15 years ago for IgA nephropathy with mycophenolate mofetil, cyclosporine and prednisone as post renal transplant IST. She achieved complete remission, both morphological and flow minimal residual disease (MRD) negativity, with the ALL06 treatment protocol. Treatment course was complicated by recurrent cytomegalovirus (CMV) reactivation including CMV colitis. Consolidative AlloSCT using an HLA identical sibling donor was subsequently performed with a reduced-intensity conditioning regimen (fludarabine and

8 Gy total body irradiation). Post-transplant cyclophosphamide (PtCy) and cyclosporine were used for graft versus host disease (GvHD) prophylaxis as per our institutional protocol with peripheral blood stem cells as graft source. A second oral immunosuppressive agent was not added given the increased infection risk with prior viral reactivation.
On Day 16 post-transplant there was evidence of neutrophil engraftment but this was accompanied by acute renal injury with rapid clinical deterioration, oliguria, fever and localised pain at the renal graft site. A renal biopsy was undertaken which demonstrated histological evidence of acute vascular rejection and necrosis confirming graft kidney rejection. The patient proceeded to emergency transplant nephrectomy and subsequently maintained on haemodialysis three times per week. Post-transplant progress was further complicated by asymptomatic CMV reactivation and transplant-associated thrombotic microangiopathy with large pericardial effusion requiring pericardiocentesis and anti-C5 therapy (eculizumab). These in conjunction with infection led to significantly delayed recovery and prolonged hospitalisation. Nevertheless, she achieved gradual clinical improvement and was discharged two and a half months later. Her haematological disease remains in complete remission with full donor chimerism and adequate graft function at day 100 post-transplant.

Results: A retrospective literature review was undertaken using PubMed and Google Scholar search for relevant studies assessing peri-stem cell transplant immunosuppression following previous solid organ transplants.[1–4] Key findings are summarised in Table 1. Long term survival is reported post SOT with low rates of solid organ rejection.[4] Higher graft failures were observed in renal transplant recipients compared to liver transplants.[2,3] There were no standardised recommendations for conditioning regimen, donor type or stem cell sources. Variable GvHD/solid organ graft rejection prophylaxis were documented mostly consisting of two different immunosuppressive agents including PtCy and cyclosporine combination which was utilised in our patient without significant impact on outcomes.

Table 1: HSCT post SOT study summary

Studies	Study design and participants	Immunosuppressive therapies	Outcomes
Basak et al. 2015[2]	Retrospective study; n = 28 (kidney 12; liver 13; heart 3); donor types: MRD 12, MUD 5; MMUD 3, haploidentical 5.	CSA/MTX (n=12); CSA/MMF (n=5); Tacro/MMF (n=5); other/unknown (n=6).	SOGF: 33%; OS: 40% overall (kidney 42%, liver 51%) at 60 months post-AlloSCT.
Jang and Hsu. 2024[1]	Case series; n = 3 (liver 1, kidney 1;, heart 1); graft sources: cord blood 1; haploidentical 2.	PtCy/MMF/Tacro (n=2); Tacro/MMF (n=1).	OS from HSCT: 13 months (heart); 27 months (liver); 43 months (kidney).

Shinohara et al. 2019[3]	Retrospective study; n = 22; type of transplant AlloSCT 17 (kidney 9; liver 7); donor types: MRD 12, MUD 5.	Calcineurin inhibitor in all; steroids (n=13); MTX (n=10); MMF (n=8); ATG (n=4).	OS: 41.7% at 5 years post-AlloSCT; renal rejection in 3 patients.

AlloSCT: allogeneic stem cell transplantation; ATG: antithymocyte globulin; CSA: cyclosporine; HSCT: haematopoietic stem cell transplant; MMF: mycophenolate mofetil; MMUD: mismatched unrelated donor; MRD: matched related donor; MUD: matched unrelated donor; MTX: methotrexate; OS: overall survival; PtCy: post-transplant cyclophosphamide; SOGF: solid organ graft failure; Tacro: tacrolimus.

Conclusions: We present our experience of AlloSCT for ALL in a deceased-donor renal transplant recipient. This case highlights the risk of solid organ graft failure and rejection and importance of careful consideration of appropriate IST peri-engraftment. Standardised guidelines in current literature are limited and further studies are required to improve outcomes in this challenging and unique population.

Clinical Trial Registry: Nil

Disclosure: Nothing to declare

Conditioning Regimens and lymphodepletion

OS06-01

PICKING STRONG BRIDGING REGIMENS BEFORE CD19 CAR-T CELL THERAPY OF LARGE B CELL LYMPHOMA – HOW HISTOLOGY AND HIGH LDH IMPACT LONG-TERM OUTCOMES

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Background: Bridging therapy is the treatment after leukapheresis but before CD19-directed chimeric antigen receptor T cell (CAR-T) infusion. If and what bridging is utilized represents the physician's choice and depends on previous treatment, disease characteristics, and drug availability.

Methods: We retrospectively analyzed patients treated between January 2019 and May 2025 across 16 German and Austrian centers. Bridging choices were grouped as No-Bridging, radiotherapy, ancient (Pixantrone, CHOP-variants), intensive (e.g., R-DHAP, R-MATRIX), R-gemcitabine/oxaliplatin (R-GemOx), sequential, R-Polatuzumab (R-Pola), or R-Pola-Bendamustine (Pola-BR). Bridging efficacy was assessed before lymphodepletion by Lugano criteria. The primary endpoint was progression-free survival (PFS). Influence of Ann-Arbor stage, extranodal disease (END) status, ECOG, sex, and LDH-levels at bridging and at lymphodepletion on outcomes were determined by multivariate Cox regression analyses.

Results: 508 patients (384 DLBCL-NOS, 124 trFL) treated with Axi-cel (65.2%), Tisa-cel (25.4%), or Liso-cel (9.4%) were included. Sex distribution, median age, median prior lines of therapy, LDH or ECOG at lymphodepletion and bridging were well-balanced between the two groups. trFL had better 24m-PFS than DLBCL-NOS. Response to bridging predicted PFS after CAR-T in DLBCL-NOS with a 24m-PFS of 62.6% in patients who achieved CR, 44.6% for PR, 42.0% for SD and 21.8% for PD with no-Bridging patients at 50.2%. Patterns in trFL were less clear with similar PFS between SD and PD patients (grouped 24m-PFS of 40%) and no-Bridging/PR (grouped 24m-PFS 63%). LDH-elevation at bridging predicted poorer PFS for trFL and NOS. Because NOS included >3-times more patients, we performed granular subset analyses only for NOS. DLBCL-NOS with always normal LDH performed best (24mPFS 64.2%), whereas elevated LDH at bridging, at lymphodepletion, or both performed similarly poorly (mPFS 32.1%, 37.6%, 30.0%, $p < 0.001$). Neither delta-LDH nor fold-change of LDH grouped patient quartiles in response-reflecting PFS groups. Additionally, LDH-elevation and response were independent risk-factors. Of all bridging types, No-Bridging, radiotherapy, and Pola-BR had better (24mPFS 51.5%, 46.1%, 50.5%) and R-GemOx, sequential, R-Pola, intensive, and ancient worse 24m-PFS (31.4%, 31.0%, 31.3%, 36.3%). Because of their use in similar patients, we then compared the well-balanced R-GemOx with the Pola-BR group (except for relatively more women in R-GemOx (50% vs. 32.5%, $p=0.014$). Pola-BR resulted in improved survival compared with R-GemOx (24m-PFS: 50.5% vs. 31.4%, $p=0.004$). In multivariate analyses including ECOG, LDH, END (all at lymphodepletion) and LDH (before bridging), only bridging-LDH showed significantly worse bridging-dependent CAR-T outcome ($p = 0.005$).

Conclusions: Our dataset is limited by the retrospective nature including a possible bias that worse bridging outcome may prevent patients from CAR-T infusion. We found outcomes were distinct for trFL and DLBCL-NOS. In NOS, responses to bridging as well as any LDH-

elevation strongly and independently influenced outcomes. That any LDH>ULN was independent of LDH-reduction and of tumor response a strong risk factor for poor PFS, highlights disease biology as a driver of CAR-T failure. Though well-balanced, R-Gem/Ox was inferior to Pola-BR suggesting that choice of bridging matters for the outcomes after CAR-T which has previously been underappreciated.

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OS06-02

MYELOABLATIVE IS NOT ALWAYS BETTER: DISMANTLING THE ONE-SIZE-FITS-ALL APPROACH TO HAPLOIDENTICAL CONDITIONING INTENSITY

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Background: In haploidentical hematopoietic cell transplantation, the potent graft-versus-leukemia (GVL) effect challenges the historical superiority of myeloablative conditioning (MAC). While reduced intensity (RIC) and nonmyeloablative (NMA) regimens reduce toxicity, it remains unclear if they provide sufficient disease control across all age group. We aimed to define the optimal intensity across age-stratified disease groups.

Methods: We analyzed 5,143 adult patients using a publicly available CIBMTR dataset with acute myeloid leukemia (AML, n=2698 [52%]), acute lymphoblastic leukemia (ALL, n=1037 [20%]), or myeloproliferative neoplasm/ myelodysplastic syndromes (MPN/MDS, n=1408 [27%]) between 2017-2021. Age was stratified using clinically relevant, data-guided cut-offs tailored to each disease: AML (≤ 55 vs > 55 years), MPN/MDS (≤60 vs > 60 years), and ALL (≤ 40 vs > 40 years). Conditioning regimens were stratified into four groups, with MAC with total body irradiation (TBI) serving as the reference group for all analyses: MAC-no TBI, the most common NMA/RIC platform of fludarabine/ cyclophosphamide/ TBI (Flu/Cy/TBI), and a composite of all other RIC regimens (RIC/other). Our primary endpoint was overall survival (OS); secondary endpoints were relapse and non-relapse mortality (NRM).

Results: Notably, in multivariable analysis, OS was similar across all conditioning intensities and all subgroups, shifting the clinical focus entirely to the distinct trade-offs between relapse and NRM.
In younger patients, the reduction in NRM offered by RIC/NMA regimens was counterbalanced by higher relapse risk. In AML patients (≤55 years), Flu/Cy/TBI was associated with half the NRM risk (HR 0.50, p=0.017) but at the cost of nearly double the relapse risk (HR 1.98, p<0.001). Similarly, in ALL patients (≤40 years), the RIC/NMA platform was associated with reduced NRM (HR 0.22, p=0.046) but more than double the risk of relapse (HR 2.32, p=0.002). MDS/MPN (≤60 years) patients showed a similar trend, where Flu/Cy/TBI was associated with increased relapse (HR 1.90, p=0.057) but reduced NRM (HR 0.59, p=0.054). In young patients, RIC/all regimens showed comparable relapse and NRM rates across all disease, compared to MAC.
In contrast, in older cohorts, the trade-off favored de-escalation. In AML patients (>55 years), MAC-chemo was associated with higher risk of NRM (HR 2.16, p=0.003) without a significant difference in relapse. In ALL patients (>40 years), Flu/Cy/TBI was associated with half the risk NRM (HR 0.50, p=0.034) and comparable relapse rates to MAC. In MDS/MPN patients (>60 years), RIC/Other regimens were associated with reduced relapse (HR 0.31, p=0.002) with no difference in NRM, and Flu/Cy/TBI showed reduced relapse (HR 0.69, p=0.30) and NRM (HR 0.70, p=0.40) rates without statistical significance, compared to MAC.

Conclusions: Since OS is comparable across regimens, choice of conditioning intensity represents a strategic management of competing risks rather than a survival imperative. Our data characterize the specific relapse/NRM profile of each regimen by age and disease. Compared to MAC/TBI, RIC/other showed comparable relapse/NRM profile in younger patients across all diseases. While RIC/NMA was associated with comparable or superior outcomes in older patients across all diseases, challenging the notion that higher intensity equates to better outcomes and warrant a paradigm shift toward risk-adapted regimen selection.

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OS06-03

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH BRIQUILIMAB ANTI-CD117 ANTIBODY-BASED NONMYELOABLATIVE CONDITIONING FOR GATA2 DEFICIENCY

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Background: GATA2 deficiency is associated with a wide spectrum of disease, including immunodeficiency with increased risk of certain infections, bone marrow failure, and myeloid malignancies. Allogeneic hematopoietic cell transplantation (HCT) with myeloablative conditioning can reverse the hematologic manifestations; however, the conditioning carries considerable toxicity. Briquilimab is an anti-c-Kit/CD117 monoclonal antibody that clears host HSCs from the bone marrow niche with minimal toxicity. We report early outcomes of 11 patients transplanted on a Phase II HCT study (NCT05907746) using briquilimab with standard nonmyeloablative conditioning for GATA2 deficiency.

Methods: Patients with GATA2 deficiency and a hypocellular bone marrow without increased blasts and normal or low-risk cytogenetic abnormalities were eligible. All patients received briquilimab 0.6 mg/kg on transplant day (TD)-11 and total body irradiation 200 cGy on TD-1. HLA-matched donor recipients received fludarabine 30 mg/m^2 for three days (TD-4 to -2). Haploidentical related donor recipients received fludarabine 30 mg/m^2 for five days (TD-6 to -2) and cyclophosphamide 12.5 mg/kg for two days (TD-6, -5). Graft-versus-host disease (GVHD) prophylaxis consisted of cyclophosphamide (50 mg/kg on TD +3, +4), tacrolimus, and mycophenolate mofetil.

Results: Eleven patients with median age of 22 (range 13-28) years underwent HCT with follow-up of 3 to 24 months (Table 1). Indications for transplant included myelodysplastic syndrome (n=5), clonal monocytosis (n=1), bone marrow failure (n=2), severe infection (n=2), and was preemptive in 1. Patients received peripheral blood stem cells from matched sibling (n=3), 8/8 HLA-matched unrelated (n=6), and haploidentical related (n=2) donors. One patient had a flare of pre-existing cryptogenic organizing pneumonia (COP), and one patient had progression of *Mycobacterium abscessus* infection during conditioning. Otherwise, conditioning was well tolerated, and there were no infusion toxicities or serious adverse events attributed to briquilimab. Neutrophils and platelets engrafted at a median of 13 (range 12-17) and 17 (range 0-20) days post-HCT, respectively. One patient experienced secondary graft failure at TD+73 and was successfully retransplanted from a different donor with busulfan and fludarabine conditioning. Myeloid chimerism in the remaining 10 patients was 100% donor at all time points (TD+30, +60, +100, +180, +365); T cell donor chimerism increased over time and was 77% to 100% at last follow-up. All engrafted patients had normalization of peripheral blood cell counts, and day 100 and 1 year bone marrow biopsies demonstrated normal trilineage hematopoiesis with resolution of pre-existing abnormalities. There have been no cases of Grade II-IV acute GVHD, chronic GVHD, or viral reactivation. One patient developed asymptomatic COP between 6 and 12 months post-HCT that responded rapidly to steroids. The patient with pre-existing COP had improvement in lung disease post-HCT, and the patient with *M. abscessus* had resolution of infection. Four of five engrafted female patients have had return of menses. All patients are alive and well at last follow-up.

Table 1. Patient characteristics and transplant outcomes

Pt	Age at HCT (y)	GATA2-associated disease manifestations at baseline	Donor	Neutrophil engraftment (D)	Platelet engraftment (D)	Grade II-IV acute or chronic GvHD	Infections post-HCT	Other major post-HCT complications	Outcome
1	19	MDS with trisomy 8, *STAG2*variant	MRD	13	13	N	None	COP	Alive & well at 24 mos

2	13	MDS with severe neutropenia, *STAG2* variant, verrucae	MRD	12	0	N	None	None	Alive & well at 22 mos
3	26	Necrotizing fasciitis, disseminated HSV + HLH, HPV+ vulvar SCC, vulvar abscess	MMRD	14	17	N	Demodex folliculitis	None	Alive & well at 20 mos
4	23	Clonal monocytosis with *ASXL1* & *STAG2* variants, lymphedema	MRD	13	0	N	*E. coli* bacteremia	Self-limited hepatitis	Alive & well at 20 mos
5	24	Severe neutropenia	MUD	15	17	N	*E. faecalis* UTI	None	Alive & well at 18 mos
6	21	Disseminated Mycobacterium abscessus infection, trisomy 8	MUD	13	0	N	None	None	Alive & well at 18 mos
7	21	Severe neutropenia, *ASXL1* & *STAG2* variants, EBV, HSV, disseminated VZV	MUD	17	17	N	*Salmonella* enteritis	Drug-induced neutropenia	Alive & well at 17 mos
8	22	MDS with severe neutropenia, trisomy 8, *ASXL1* & *STAG2*	MUD	13	14	N	None	None	Alive & well at 12 mos

		variants, verrucae							
9	28	MDS with *ASXL1* & *STAG2*variants, extensive verrucae	MMRD	17	20	N	*S. mitis* bacteremia	None	Alive & well at 12 mos
10	24	Hypocellular bone marrow with megakaryocytic atypia	MUD	16	20	N	*E. coli* bacteremia	Secondary graft failure at Day +73	Alive & well 6 mos post-HCT#2
11	21	MDS with severe anemia, trisomy 8, *ASXL1*, *STAG2*, *DNMT3A*, *RUNX1* variants, COP	MUD	13	19	N	None	None	Alive & well at 3 mos

HCT=hematopoietic cell transplantation, GVHD=graft-versus-host disease, MDS=myelodysplastic syndrome, HSV=herpes simplex virus, HLH=hemophagocytic lymphohistiocytosis, HPV=human papillomavirus, EBV=Epstein Barr virus, HSV=herpes simplex virus, VZV=varicella zoster virus, SCC=squamous cell carcinoma, MRD=matched related donor, COP=cryptogenic organizing pneumonia, MMRD=mismatched related donor, MUD=matched unrelated donor, UTI=urinary tract infection

Conclusions: HCT with briquilimab-based nonmyeloablative conditioning resulted in sustained donor engraftment with full donor myeloid chimerism and minimal toxicity in patients with GATA2 deficiency. There may, however, be an increased risk of graft failure than with standard myeloablative conditioning.

Clinical Trial Registry: clinicaltrials.gov NCT05907746

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OS06-04

CAN WE ELIMINATE TBI/BUSULFAN AND GVHD IN FANCONI ANEMIA TRANSPLANTATION? RESULTS FROM A PROSPECTIVE HAPLOIDENTICAL TRANSPLANT APPROACH

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) remains the only curative therapy for progressive bone marrow failure (BMF) in patients with Fanconi Anemia (FA). Given the DNA-repair defects in FA, genotoxic exposures with irradiation or busulfan can lead to substantial short- and long-term toxicity. In addition, a significant proportion of FA patients lack a fully matched sibling donor (MSD) or a suitably matched unrelated donor (MUD), creating an urgent need for expanded donor options.

Methods:

Figure 1: Trial Schematic

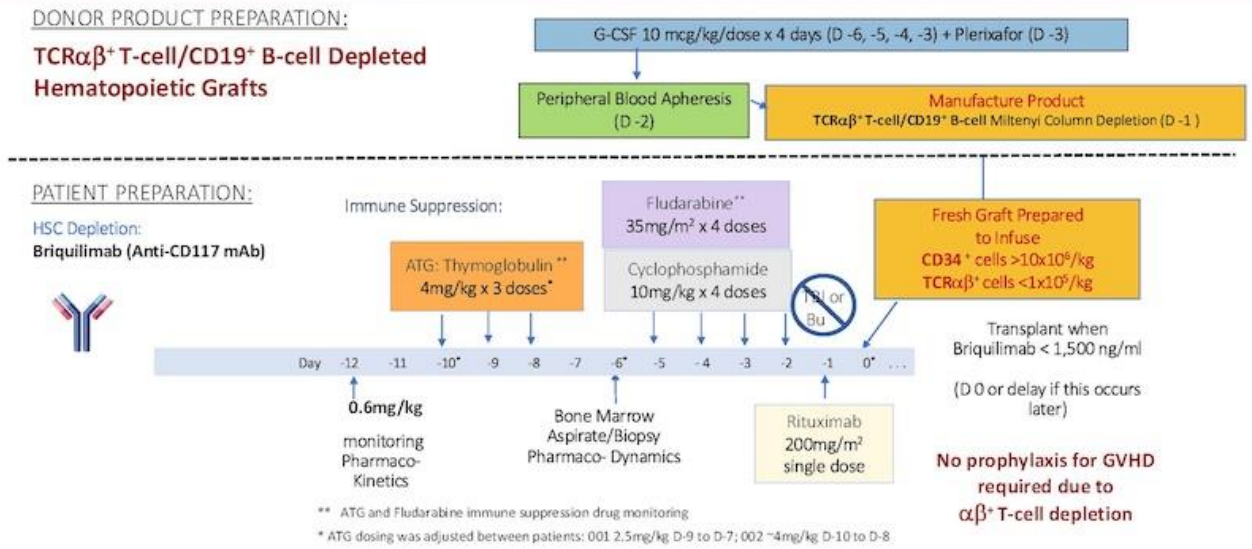

Figure 1: Treatment schema for transplantation of aB depleted-HSC grafts with Briquilimab, rATG, Fludarabine, Cyclophosphamide, and Rituximab immunosuppression and close PK monitoring of each drug.

We applied a prospective haploidentical donor transplant approach for patients with FA without MSDs with the dual goals of reducing genotoxic conditioning and minimizing GVHD

through TCRαβ+ T-cell/CD19+ B-cell depletion. We aimed to compare two conditioning strategies: (1) a regimen incorporating low-dose (200 cGy) total body irradiation (TBI) and (2) a busulfan- and irradiation-free antibody-based regimen that includes briquilimab, a CD117-directed monoclonal antibody that targets host hematopoietic stem cells. Both regimens also include rabbit anti-thymoglobulin (rATG), cyclophosphamide, fludarabine, and rituximab for immunosuppression, followed by transplantation with TCRαβ+ T-cell/CD19+ B-cell depleted grafts.

Methods: Patients with FA with BMF and without MSDs were eligible for allo-HCT with TCRαβ+ T-cell/CD19+ B-cell depleted hematopoietic grafts from MUD or haploidentical family donors with preference given to haploidentical family donors unless. All patient grafts contained ³ 10 x 10^6 CD34+ cells/kg and £ 1 x 10^5 TCRαβ+ cells/kg. Patients were treated on one of two conditioning protocols. In the cohort with TBI (n=9), patients received 200 cGy TBI combined with FA-standard immunosuppression with rATG, cyclophosphamide, fludarabine, and rituximab. In the antibody-based cohort (briquilimab, n=12), patients received briquilimab 0.6 mg/kg and the same immunosuppressive backbone (Figure 1). Kinetics of antibody clearance, engraftment, blood count recovery, and donor chimerism across multiple subsets (CD3, CD15, CD19, CD34, CD56) were assessed. Acute and Chronic GVHD was graded.

Results: A total of 21 patients with FA underwent haploidentical allo-HCT with TCRαβ/CD19-depleted grafts across the two conditioning protocols (9 TBI and 12 briquilimab cohorts) with follow up ranging from 6 months to 7 years. Briquilimab was well tolerated, with no infusion reactions or unexpected toxicities, and demonstrated predictable clearance to below threshold levels in all patients by the time of graft infusion. Engraftment kinetics were comparable between cohorts, with early recovery of full blood counts by Day +16 in engrafted patients. One patient in each cohort experienced primary graft failure. Among patients who engrafted, full and stable donor chimerism was achieved across evaluated subsets (CD3, CD15, CD19, CD34, CD56), with no meaningful differences between cohorts. No patient in either cohort developed grade III–IV acute GVHD. Immune reconstitution and performance status have been comparable in the 2 cohorts.

Conclusions: Haploidentical allo-HCT using TCRαβ/CD19-depleted grafts is feasible, safe, and effective in patients with FA, providing near-universal donor access with low rates of severe acute and cGVHD. Briquilimab-based, genotoxicity-sparing conditioning offers a compelling alternative to TBI- or busulfan-containing regimens, achieving reliable engraftment and outcomes comparable to a similar irradiation-based protocol. These findings support further development of antibody-based conditioning as a next-generation platform for FA and other bone marrow failure disorders.

Clinical Trial Registry: Clinical Trials .gov
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NCT04249830

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OS06-05

EFFICACY OF A LOW-DOSE ATG-CONTAINING CONDITIONING REGIMEN FOR UMBILICAL CORD BLOOD TRANSPLANTATION IN SEVERE APLASTIC ANEMIA: A PROSPECTIVE, SINGLE-ARM CLINICAL TRIAL

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Background: Antithymocyte globulin (ATG) is commonly used to enhance engraftment and prevent graft-versus-host disease (GVHD) in haploidentical hematopoietic stem cell transplantation (haplo-HSCT). However, its role in umbilical cord blood transplantation (UCBT) remains unclear and optimal ATG exposure is not well defined.

Methods: We conducted a single-center prospective clinical trial to evaluate the efficacy of a reduced-intensity conditioning regimen containing low-dose ATG in patients with severe aplastic anemia (SAA) undergoing UCBT (NCT06039436). The conditioning regimen consisted of fludarabine (200 mg/m^2), cyclophosphamide (120mg/kg) and total body irradiation/total bone marrow irradiation (400 cGy). In addition, rabbit ATG (2mg/kg) was administered on the first day of conditioning regimen before transplantation. Active ATG (aATG) concentrations were serially measured to explore the relationship between aATG exposure and clinical outcomes, including engraftment, acute GVHD (aGVHD), and viral infections.

Results: Twenty-four patients with a median age of 18.5 years (range, 2.0-45.0 years) were enrolled. The median follow-up for surviving patients was 376 days (range, 114-685). The baseline characteristics were shown in Table 1. The cumulative incidences of 42-day neutrophil engraftment and 60-day platelet engraftment were 91.7% (95% CI, 76.7%-98.6%) and 86.4% (95% CI, 60.1%-95.9%), respectively. The cumulative incidences of grade II-IV aGVHD, III-IV aGVHD and chronic GVHD (cGVHD) were 22.7% (95% CI, 10.2%-46.3%), 19.1% (95% CI, 7.6%-43.1%) and 12.1% (95%CI, 1.8%-32.8%), respectively. In 20 evaluable patients, pre-transplant aATG area under the curve (pre-UCBT AUC) was the best pharmacokinetic predictor of aGVHD based on receiver-operating characteristic (ROC) analysis (AUC 0.933; 95% CI 0.823-1.000). An optimal pre-UCBT AUC range (7.486-9.928 AU*d/mL) was associated with the lowest incidence of aGVHD without increasing viral infection risk (Figure 1). Patients within the optimal pre-UCBT AUC range (n = 9) had significantly lower cumulative incidence of grade II-IV aGVHD (0% vs. 45.5%, P = 0.024) and grade III-IV aGVHD (0% vs. 40.0%, P =0.039) compared to those outside the range (n = 11), with no significant differences in engraftment time, viral infections, cGVHD, GVHD-free relapse-free survival (GRFS), or overall survival (OS) (Figure 2).

Table 1.Baseline Characteristics of Enrolled Patients

Characteristics		All patients (n=24)	Patients analyzed for optimal AUC (n=20)		
			Optimal AUC group (n = 9)	Non-optimal AUC group (n = 11)	*P*-value
Age (years), median (range)		18.50 [2.00, 45.00]	35.00 [11.00, 45.00]	14.00 [2.00, 38.00]	0.119
Weight (kg), median (range)		55.58 [15.00, 78.80]	58.40 [54.00, 71.10]	52.90 [15.00, 78.80]	0.425
UCBT setting, n (%)	First-line therapy	3 (12.5)	1 (11.1)	2 (18.2)	1.000
	Secondary therapy (post-IST failure)	21 (87.5)	8 (88.9)	9 (81.8)	
Donor to recipient sex, n (%)	Female to male	6 (25.0)	4 (44.4)	2 (18.2)	0.336
	Others	18 (75.0)	5 (55.6)	9 (81.8)	
ABO incompatibility, n (%)	Identical	8 (33.3)	3 (33.3)	4 (36.4)	1.000
	Minor incompatibility	8 (33.3)	3 (33.3)	4 (36.4)	
	Major incompatibility	7 (29.2)	2 (22.2)	3 (27.3)	
	Bidirectional incompatibility	1 (4.2)	1 (11.1)	0 (0.0)	
HLA compatibility (/10), n (%)	9-10	3 (12.5)	2 (22.2)	1 (9.1)	0.770
	7-8	19 (79.2)	6 (66.7)	9 (81.8)	
	5-6	2 (8.3)	1 (11.1)	1 (9.1)	
Infused stem cell dose,	TNCs ($\times 10^7$/kg)	2.79 [1.13, 7.77]	2.74 [1.13, 5.60]	2.84 [1.70, 7.77]	0.271

median (range)	$CD34^+$ ($\times 10^5$/kg)	2.74 [0.95, 13.13]	2.28 [0.95, 7.10]	3.15 [1.08, 13.13]	0.239
	$CD3^+$ ($\times 10^6$/kg)	6.98 [1.47, 62.10]	5.48 [1.47, 33.70]	7.05 [1.72, 62.10]	0.518
	$CD56^+$ ($\times 10^6$/kg)	1.70 [0.05, 9.55]	0.97 [0.05, 5.49]	2.57 [0.98, 9.55]	0.087
Follow-up days, median (range)		376.0 [114.0-685.0]	461.00 [144.00, 685.00]	362.50 [114.00, 641.00]	0.475

Abbreviation: AUC, area under the curve; UCBT, umbilical cord blood transplantation; IST, immunosuppressive therapy.

Figure 1. Incidences of grade II-IV aGVHD and viral infection according to pre-UCBT aATG AUCs
Abbreviation: acute graft-versus-host disease (aGVHD), AUC, area under the curve; UCBT, umbilical cord blood transplantation.
Figure 2. Comparison of transplantation-related outcomes between the optimal pre-UCBT AUC group and non-optimal pre-UCBT AUC group.
Abbreviation: AUC, area under the curve; UCBT, umbilical cord blood transplantation

Figure 1

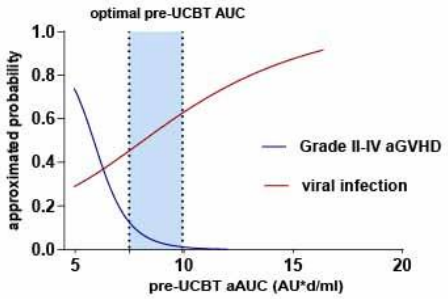
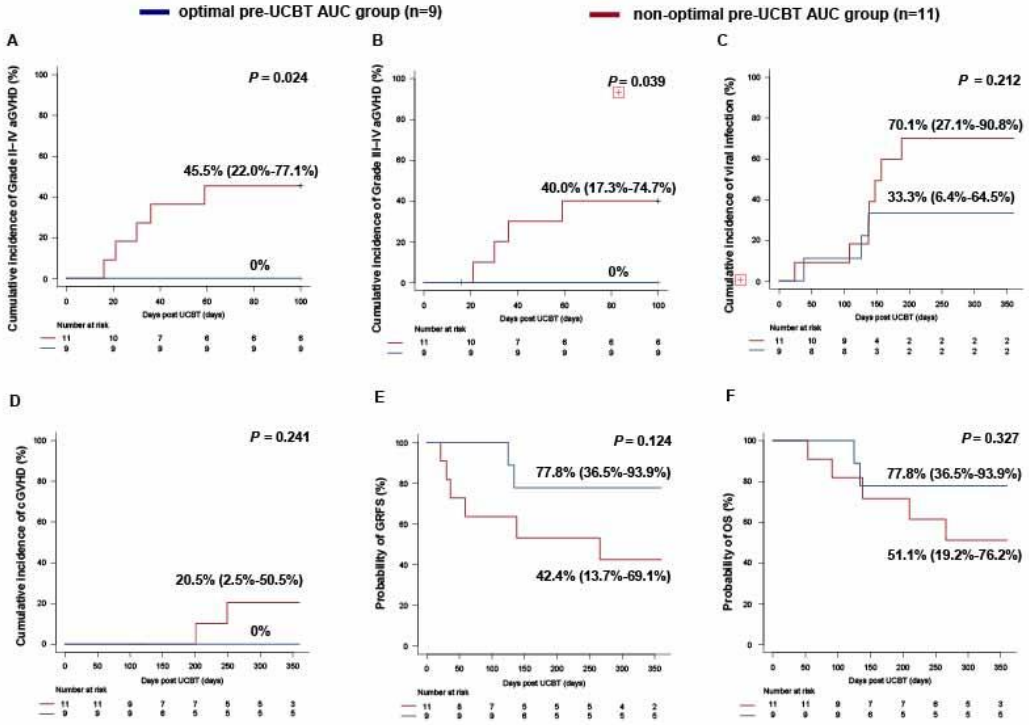


Figure 2



Conclusions: This study demonstrates that a low-dose ATG-containing conditioning regimen is effective and well-tolerated in SAA patients undergoing UCBT. Individualized aATG exposure monitoring may further optimize outcomes by minimizing GVHD without increasing infection risk.

Clinical Trial Registry: Clinical Trial registry number: NCT06039436
Website: https://clinicaltrials.gov/

Disclosure: Nothing to declare.

OS06-06

TREOSULFAN MODEL INFORMED PRECISION DOSING FOR OPTIMIZED CLINICAL OUTCOME IN CHILDREN AT HIGH RISK FOR OVER- OR UNDEREXPOSURE UNDERGOING ALLOGENEIC HSCT FOR NON-MALIGNANT DISEASES

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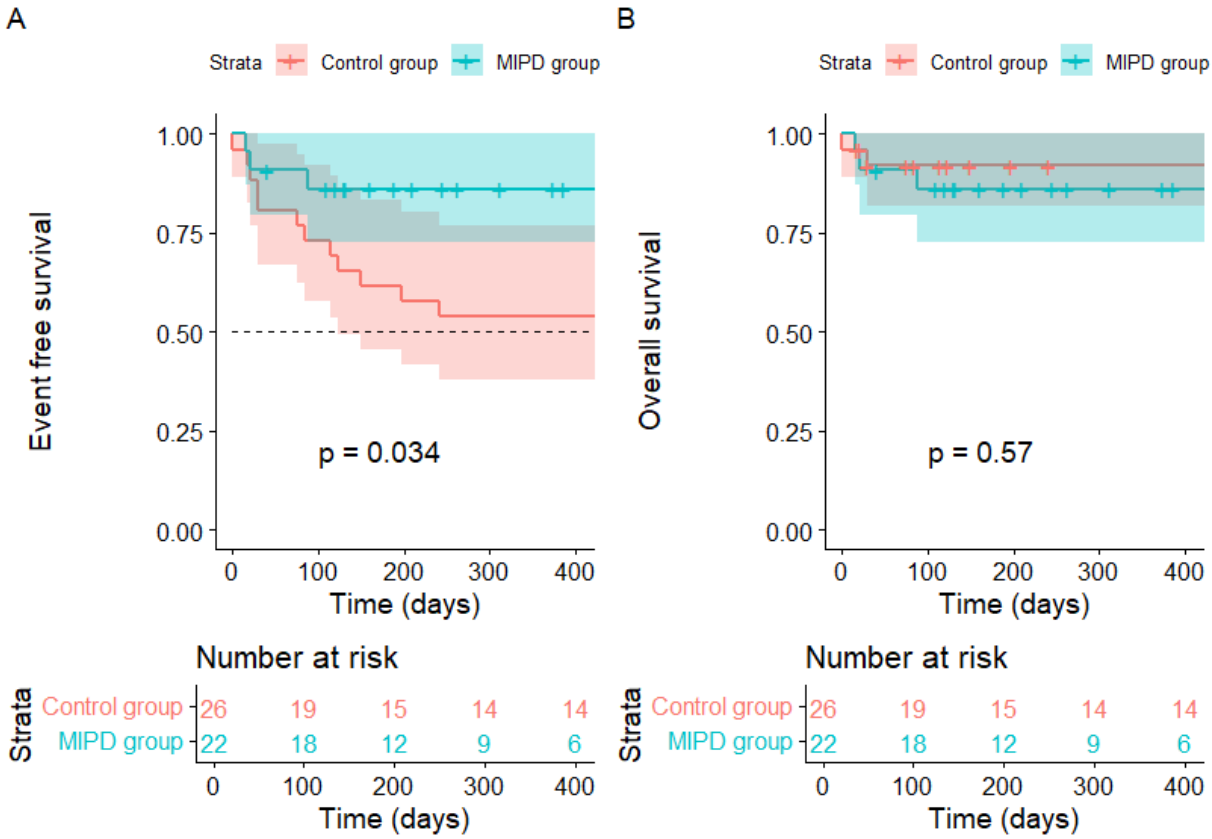
Background: Treosulfan-based conditioning regimens have been shown to provide high efficacy while presenting a favorable toxicity profile in children undergoing allogeneic hematopoietic stem cell transplantation (HSCT) for non-malignant diseases. Standardized treosulfan dosing based on body surface area results in excellent outcome in the overall cohort, but overexposure has been associated with higher mortality and underexposure correlated with an increased risk of graft failure(1). For optimizing exposure and clinical outcome, patients presenting with additional risk factors for higher pharmacokinetic (PK) and pharmacodynamic (PD) variability may benefit from model informed precision dosing (MIPD). However, no outcome data on children undergoing HSCT receiving treosulfan MIPD has been published yet.

Methods: In this pilot study, we included all children at high-risk for treosulfan over- or underexposure due to very young age at transplant (<1 year old), obesity, underweight or severe organ dysfunction undergoing HSCT for non-malignant diseases between 2022 and 2025 in Leiden, The Netherlands. Based on a limited sampling strategy of 3 measured concentrations and our previously developed PK model(2), we assessed the impact of treosulfan MIPD on event free survival (EFS) and overall survival (OS) by comparing the study group with patients selected according to the same high-risk criteria from our historical cohort transplanted in Leiden between 2011 and 2019(3). Log-rank test and cox proportional hazard survival analysis has been performed considering death and graft failure as events. Target cumulative area under the concentration versus time curve ($AUC_{0-\infty}$) was 4950 mg*h/L (+/- 10%).

Results: 22 children with a median age of 0.8 years at the time of HSCT (interquartile range [IQR] 0.4-2.4) have been included in the MIPD study group. The control group consisted of 26 children with a median age of 1.64 years (IQR 0.50-7.92) at transplant. Median $AUC_{0-\infty}$ after the first dose was 1854 mg*h/L (IQR 1604-2130) and 16 out of 22 children (73%) received a dose modification ranging from -55% to +32% to achieve target exposure. All study patients experienced sustained engraftment, no one needed a second HSCT at a median follow-up time of 8 months (IQR 4-15). 3 out of 22 patients (14%) died within the first 100 days post-HSCT due to severe preexisting infections. In the study group, OS and EFS at 100 days and 1 year post HSCT were both 86% (95% CI 73%, 100%). In the control group, EFS at 100 days and 1 year post HSCT was 73% (95% CI 58%, 92%) and 54% (95% CI 38%, 77%), respectively. OS in the control group at both 100 days and 1 year post HSCT was 92% (95% CI 82%, 100%). Survival analysis revealed significant improvement of EFS in the study group compared with the control group (p-value 0.034, Figure 1A). In contrast, no

significant difference between the groups has been found in OS analysis (p-value 0.57, figure 1B).



Conclusions: Our results support the use of treosulfan MIPD in children at high risk for hampered clinical outcome due to high PK/PD variability for optimizing EFS. Further research in larger cohorts is required to confirm these promising preliminary results.

Disclosure: Nothing to declare

OS06-07

ANTIBODY TARGETED RADIOTHERAPY CONDITIONING PRIOR TO ALLOGENEIC STEM CELL TRANSPLANTATION: LONG-TERM FOLLOW-UP OF 40 PATIENTS WHO RECEIVED YTTRIUM-90 ANTI-CD66 IN A PHASE I/II TRIAL

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Background: Survival of patients after allogeneic stem cell transplantation is adversely affected by two main factors, disease relapse and transplant related mortality (TRM). An ideal conditioning regimen would provide maximum disease reduction while causing minimal toxicity to non-haematopoietic tissues. Targeted radiotherapy delivered by a monoclonal antibody that preferentially targets haematopoietic organs has the potential to deliver high doses of radiation selectively to these tissues avoiding therapy related toxicity while maintaining effective disease eradication.

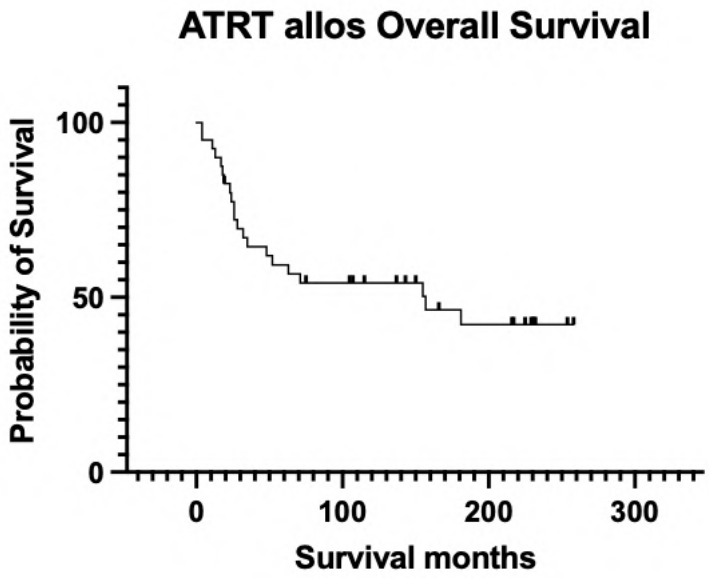
Methods: Forty-two patients due to receive allogeneic stem cell transplants for high risk haematological malignancies were entered into a Phase I/II study using antibody-targeted radiotherapy (ATRT) using an anti-CD66 monoclonal antibody radiolabelled with yttrium-90 (^{90}Y-besilesomab). Disease indications: Myeloma 22, AML/MDS 11, CML 5 and B-ALL 4, ages 20 - 68 years. All patients had initial dosimetry with the anti-CD66 radiolabelled with tracer activity of indium-111 (^{111}In-besilesomab), patient-specific internal dosimetry estimated from gamma-imaging and blood sampling. Whole-body gamma-camera images were taken 1 hour after infusion and 3 additional whole-body and SPECT(-CT) acquisitions between days 2 and 7. If imaging indicated favourable biodistribution patients received ^{90}Y-besilesomab fourteen days before the scheduled infusion of donor stem cells. On D -10 patients were admitted to start standard conditioning (fludarabine 30mg/m^2 D-7 to D-3, CAMPATH IH 10mg D -10 to D-8 (sibling) or D -6 (unrelated donor), melphalan 140mg/m^2 D - 2). Donor cells, sibling 9, unrelated donor 31, all PBSC. Immunosupression with ciclosporin A from D -1. Following transplant patients were managed according to standard procedures for the centres.

Results: There were no infusion related toxicities. Of the 42 patients that received ^{111}In-besilesomab, two had excessive hepatic uptake, excluded from receiving ^{90}Y-besilesomab and received a standard transplant. At the highest infused activity of ^{90}Y-besilesomab (45MBq/kg body weight) the mean BM radiation dose was 35Gy, range 18.1 - 40Gy (table 1). Of the 40 patients receiving ^{90}Y-besilesomab plus FMC all engrafted, median days to neutrophils >0.5 x 10^9/L D+17, plts >20 x 10^9/L D+18. D+30 chimerism >97% donor in all patients. Post-transplant adverse events (AE) and serious adverse events (SAE) were similar to those in patients receiving standard allogeneic transplants, no SAEs causally related to the ATRT. All patients achieved complete disease responses post transplant. Overall 19 patients (47.5%) remain alive with a median follow up of 216 months (range 19 - 258), median survival 155 months; 21 patients died, three transplant related causes (7.5%), four from unrelated causes (Alzheimers 1, trauma 1, secondary cancers 2), 16 patients relapsed (MM 10, AML 3,

ALL 2, CML-BT 1) with 14 relapse related deaths. Incidence of acute GvHD > grade 2 2.5% (n=1), chronic GvHD was seen in 2 patients (5%) and was limited. Three patients developed secondary cancers several years post transplant, one lung, one pancreatic and one with breast cancer who remains in remission. Nineteen patients remain in complete remission without serious long-term complications.

Table 1

^{90}Y-antiCD66 activity level MBq/kg body wt	**Total ^{90}Y-antiCD66 activity infused MBq**	**Organ Dosimetry Gray (Gy)**					
		Bone marrow	**Liver**	**Spleen**	**Kidney**	**Lung**	**Whole Body**
10 (n = 2)	**671 ± 208**	**4.8 ± 0.7**	**1.3 ± 0.4**	**6.7 ± 4.6**	**0.2 ± 0.0**	**0.2 ± 0.0**	**0.3 ± 0.0**
25 (n = 2)	**1468 ± 80**	**14.6 ± 2.0**	**4.2 ± 1.5**	**16.9 ± 13.5**	**0.6 ± 0.1**	**2.2 ± 0.4**	**0.6 ± 0.1**
37.5 (n = 10)	**2098 ± 231**	**25.3 ± 5.3**	**5.9 ± 2.9**	**21.2 ± 8.7**	**1.8 ± 0.7**	**2.0 ± 0.6**	**0.8 ± 0.1**
45 (n = 26)	**2528 ± 480**	**35.2 ± 5.7**	**6.8 ± 3.2**	**25.7 ± 14.0**	**2.4 ± 1.0**	**2.5 ± 1.2**	**1.1 ± 0.2**



Conclusions: The addition of an ^{90}Y-anti-CD66 delivered up to 40Gy of radiation to the BM with no additional early or late toxicities while achieving sustained responses in patients with high risk diseases.

Clinical Trial Registry: NCT01521611; https://clinicaltrials.gov/study/NCT01521611

Disclosure: Kim Orchard: consultancy for Telix Pharmaceuticals; advisory board member for Novartis.
No other authors have any CoI relating to this work.

OS06-08

TOTAL MARROW AND LYMPHOID IRRADIATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE-BASED GVHD PROPHYLAXIS CONFERS FAVORABLE GVHD/RELAPSE-FREE SURVIVAL AND QUALITY-OF-LIFE IN PATIENTS WITH ACUTE MYELOID LEUKEMIA IN REMISSION

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Background: We have found that dose escalation of organ-sparing whole-body radiation using total marrow and lymphoid irradiation (TMLI) with chemotherapy results in favorable outcomes in patients with high-risk acute leukemia. In this study, we have combined TMLI 20 Gy with post-transplant cyclophosphamide (PTCy) and tacrolimus for patients with acute myeloid leukemia (AML) in first or second remission. Herein, we report interim results of this study on graft-versus-host disease/relapse-free survival (GRFS) including participants' quality of life.

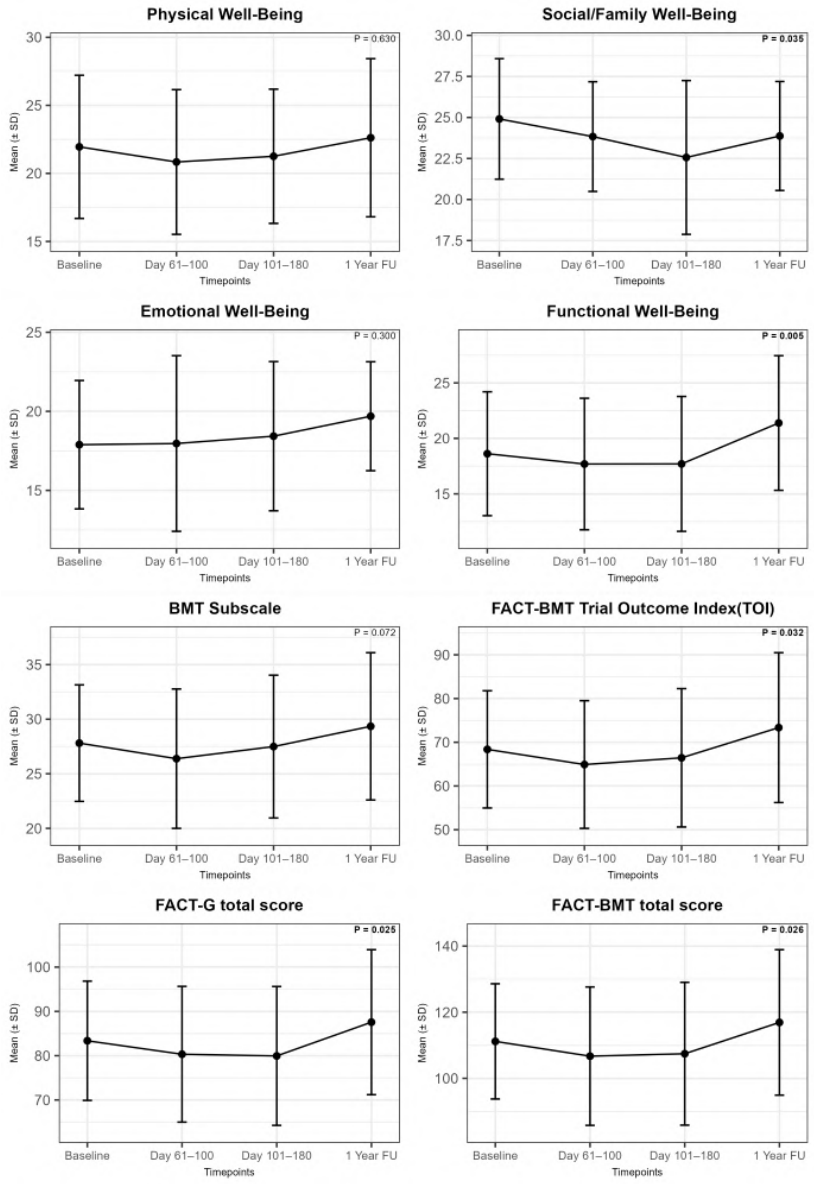
Methods: Between 03/2018 and 09/2024, we enrolled 43 patients with minimal residual disease–negative (by multicolor flow cytometry) AML in this single-center phase 2 trial, with a minimum follow up of 1 year for all patients. English- and Spanish-speaking patients were enrolled in the study and completed the Functional Assessment of Cancer Therapy – Bone Marrow Transplantation (FACT-BMT, Version 4) and the 36-Item Short Form Survey (SF-36) patient-reported outcomes assessments at baseline, day 61-100, day 101-180, and 1 year. A repeated measures ANOVA was used to evaluate the changes of the quality-of-life scores over time. All p values were 2-sided at a significance level of 0.05.

Results: Patient characteristics are reported in the Table. The 1-year GRFS rate was 67% (95%CI: 51-79%), overall survival (OS) 100%, progression-free survival (PFS) 88% (95%CI: 74-95%), relapse 12% (95%CI: 4-23%), and non-relapse mortality (NRM) 0%. The incidence of grade II-IV graft-versus-host disease (GVHD) was 9% (95%CI: 3-20%) and grade III-IV was 2% (95%CI: 0-11%). The incidence of chronic GVHD was 23% (95%CI: 12-37%), and moderate to severe GVHD was 7% (95%CI:2-18%).
Twenty-nine patients (67%) completed all timepoints in the FACT-BMT questionnaire. Social/family well-being improved at 1 year after a nadir at day 101-180 (p=0.035). Functional well-being was also improved at 1 year after a plateau at the previous timepoints (p=.005). Sums of subscales represented by the FACT-BMT Trial Outcome Index, FACT-G Total Score, and FACT-BMT Total Score were all enhanced at one year (see Figure for FACT-BMT outcomes). As assessed by SF-36, role limitations due to physical health (p=0.005) or due to emotional problems exhibited recovery at one year (p=0.025). Social functioning likewise was more favorable at one year (p=0.015).

	Total (N = 43)		Total (N=43)
Age at TMLI, Median (range)	41 (19-56)	HCT-CI	
ELN risk		0	31 (72.1%)
Favorable*	2 (4.7%)	1	8 (18.6%)
Intermediate	26 (60.5%)	≥2	4 (9.3%)
Adverse	15 (34.9%)		
Sex		KPS	

Female	24 (55.8%)	80	4 (9.3%)
Male	19 (44.2%)	90	32 (74.4%)
Disease status		100	7 (16.3%)
1st Remission	38 (88.4%)		
2nd Remission	5 (11.6%)	Donor	
		Related	17 (39.5%)
		Unrelated	26 (60.5%)

Table. Patient characteristics. *The two patients with favorable risk were in second complete remission.



Conclusions: At one-year post-transplantation, this study demonstrates an encouraging GRFS and preserved quality of life. We found that all patients engrafted, with low incidence of GVHD. The NRM rate of 0% highlights the safety of this regimen.

Clinical Trial Registry: clinicaltrials.gov: NCT03467386

Disclosure: Nothing to declare.

OS08-07

TREOSULFAN – BASED CONDITIONING IN ALLOGENEIC HEMATOPOIETIC STEM-CELL TRANSPLANTATION; LONG-TERM FOLLOW-UP

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Background: Treosulfan was approved by the European Medicines Agency (EMA) in 2019 and more recently by the FDA for the use in the conditioning regimen for allogeneic hematopoietic stem-cell transplantation (HSCT). Prior studies have shown that Treosulfan is associated with strong anti-leukemia effect combined with relatively low rates of non-relapse mortality (NRM) and GVHD. However, there is limited data on long-term survival after Treosulfan- based conditioning and on the use of Treosulfan in diseases other than myeloid malignancies.

Methods: We have used the combination of fludarabine and treosulfan as the conditioning regimen for allogeneic HSCT in patients with various hematological malignancies, considered eligible for low to intermediate transplant conditioning intensity, over the last 20 years. Treosulfan dose (10-14gr/m^2 x3) was determined based on patient and disease characteristics. GVHD prophylaxis included cyclosporine and methotrexate or mycophenolate. ATG was added to unrelated donor HSCT.

Results: The study included 562 patients following their first HSCT, median age 57 years (range, 18-76). Diagnosis was AML (n=176), ALL (n=37), various lymphoproliferative diseases (n=185), MDS (n=166), others (n=8). The donor was an HLA-matched sibling (n=236), matched-unrelated (n=270), mismatched unrelated/ haploidentical (n=66). The median follow-up is 7 years (range, 0.4-20). The estimated 2- ,5- ,10- and 20-year overall survival (OS) rate is 54% (95%CI, 50-58), 42% (95%CI, 38-46), 38% (95%CI, 33-42) and 33% (95%CI, 26-39), respectively. The cumulative incidence of NRM is 22% (95%CI, 18-25), 28% (95%CI, 24-32), 30% (95%CI, 26-35) and 35% (95%CI, 29-42), respectively. The cumulative incidence of relapse mortality is 25% (95%CI, 21-28), 30% (95%CI, 26-34), 32% (95%CI, 28-35) and 33% (95%CI, 29-38), respectively. OS was significantly better in the last 10 years than in the previous 10 years, 5-year OS of 49% (95%CI, 31-43) and 34% (95%CI, 28-40), respectively (P=0.0001). This was mostly due to reduction of NRM, 5-year rate 23% (95%CI, 18-29) and 34% (95%CI, 28-40), respectively (P=0.004), while relapse morality was not significantly different, 28% (95%CI, 22-34) and 33% (95%CI, 27-39), respectively (P=0.20). Multivariate analysis identified advanced age (>60 years), HR 1.5 (1.18-1.91, P=0.009), and HSCT in the more recent period, HR 0.65 (0.50-0.82, P=0.009) as prognostic factors for OS. Outcomes were not significantly different across the various diagnoses. The incidence of acute GVHD grade II-IV, grade III-IV and chronic GVHD was 26%, 9% and 26%, respectively.

Conclusions: Treosulfan- based conditioning can allow promising long-term OS in patients with a variety of hematological malignancies. It is associated with potent anti-malignancy effect combined with relatively low NRM and GVHD rates. Long-term outcome analysis (up to

20 years) shows significant cure rate, although late events (beyond 2 years) are significant, underscoring the importance of long-term monitoring in assessing HSCT outcomes. HSCT safety is consistently improving over the last years.

Disclosure: Nothing to declare.

OS14-07

REFINING THE TRANSPLANT CONDITIONING INTENSITY (TCI) INDEX BY INTEGRATING POST-TRANSPLANT CYCLOPHOSPHAMIDE: A RETROSPECTIVE ANALYSIS IN ALLO-HCT

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Background: The Transplant Conditioning Intensity (TCI) index was developed standardize the evaluation of conditioning regimen intensity by classifying patients into low-, intermediate-, and high-intensity groups based on chemotherapy and radiotherapy doses to predict overall survival (OS) (Spyridonidis Et. Al. 2024). However, the TCI was created without considering post-transplant cyclophosphamide (PTCy), now widely used for GVHD prophylaxis at doses that add significant cytotoxic burden (40-50 mg/kg/day for two days). As this aspect may limit the applicability of the TCI in contemporary allo-HCT practice, we evaluated its performance in a large transplant cohort and developed a refined model incorporating PTCy exposure.

Methods: We included 538 patients who underwent allo-HCT at our institution between 2012 and 2024. GVHD prophylaxis evolved over time with the gradual adoption of PTCy, initially restricted to haploidentical transplantation and later extended to all donor types between 2016 and 2019. Since 2021, PTCy dose reduction to 40 mg/kg/day was implemented in 10/10 HLA-matched transplants.
Patients were retrospectively assigned to low-, intermediate-, and high-intensity categories according to TCI original definitions. A modified TCI score (nTCI) was defined by incorporating PTCy exposure, assigning 0.5 points for PTCy 40 mg/kg/day and 1 point for PTCy 50 mg/kg/day, corresponding to the weights used in the original TCI for equivalent doses of cyclophosphamide administered during conditioning. Patients were reclassified into nTCI categories using the same numerical thresholds as the original TCI. Baseline characteristics across TCI groups were compared, and predictive performance was evaluated for OS, non-relapse mortality (NRM), and cumulative incidence of relapse (CIR).

Results: Using the original TCI classification, 70 (13.0%), 422 (78.4%) and 46 (8.6%) patients were assigned to the high-, intermediate-, and low-intensity groups (Table 1).

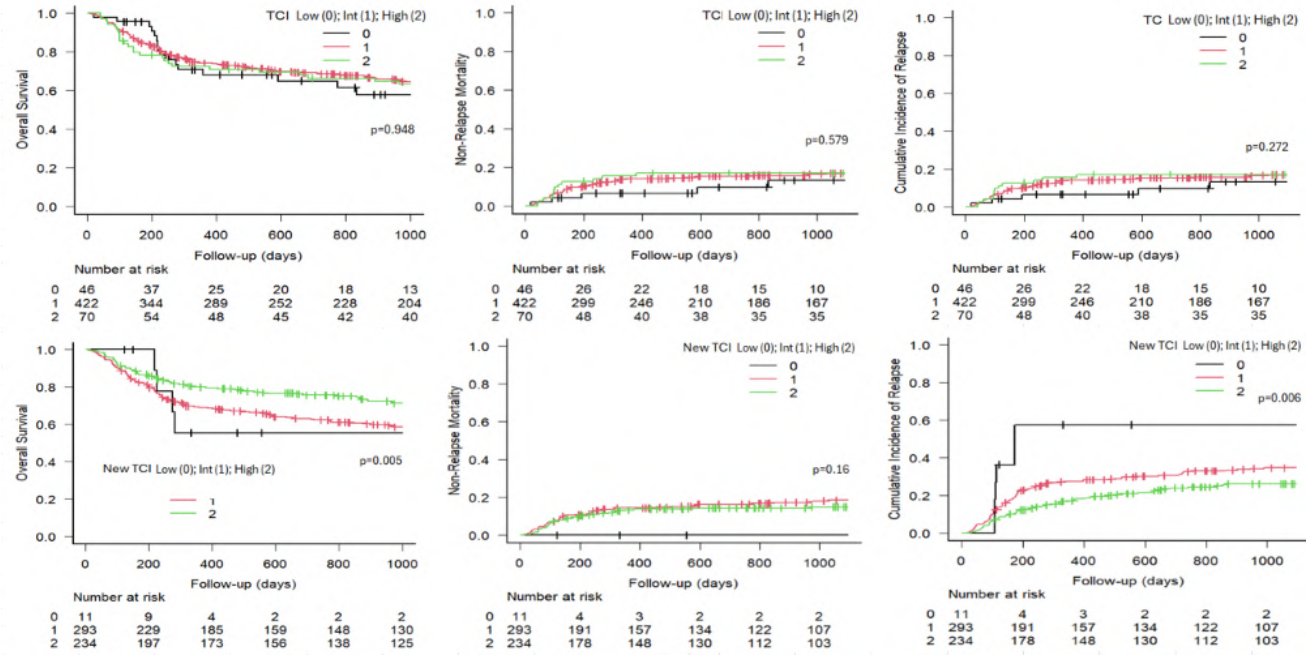
Baseline characteristics differed across TCI categories with older patients more frequently receiving low or intermediate conditioning intensity regimens. As shown in Figure 1, no significant differences in OS (p=0.948), NRM (p=0.579) and CIR (p=0.272) were observed across TCI groups. Specifically, 2-year OS, NRM, and CIR were 81.7%, 17.2%, and 27.5% in the high-; 85.2%, 17.0%, and 31.0% in the intermediate-; and 88.8%, 13.4%, and 44.9 in the low-intensity group.
Subsequently, patients were reclassified according to the nTCI into high- 234 (43.5%), intermediate- 293 (54.5%), and low- (2.0%) intensity groups. Baseline characteristics again differed across categories, reflecting clinical practice in conditioning selection based on age, comorbidities, and disease characteristics. In contrast to the original TCI, the nTCI demonstrated good prognostic discrimination, with differences being observed in OS (p=0.005) and CIR (p=0.006) and no significant differences NRM (p=0.16), across nTCI intensity groups (Figure 1). Specifically, the 2-year OS, NRM, and CIR were 85.2%, 14.9%, and 26.2% for high; 82.1%, 18.6%, and 34.8% for intermediate; and 100%, 0, and 57.6% for low conditioning intensity group.

Table 1. Baseline Characteristics According to TCI and New-TCI

TCI	**All Patients N = 538**	**TCI High N = 70 (13.0%)**	**TCI Int N = 422 (78.4%)**	**TCI Low N = 46 (8.6%)**	**p value**
Age					
Continuous	53.3	44.0	54.1	60.4	<0.001
(Range)	(41.6-61.7)	(35.9-48.7)	(42.8-62.0)	(44.1-67.9)	<0.001
Age ≥65 years	72 (13.4)	1 (1.4)	56 (13.3)	15 (32.6)	
Diagnosis					
Acute Myeloid Leukemia	189 (35.1)	27 (38.6)	147 (34.8)	15 (32.6)	<0.001
Myelodysplastic Syndrome / CMML	87 (16.2)	8 (11.4)	71 (16.8)	8 (17.4)	
Myeloproliferative Disorder	83 (15.4)	12 (17.1)	68 (16.1)	3 (6.5)	
Acute Lymphoblastic Leukemia	95 (17.7)	16 (22.9)	73 (17.4)	6 (13.0)	
Non-Hodgkin Lymphoma	73 (13.6)	6 (8.6)	54 (12.8)	13 (28.3)	
Others	11 (2.0)	1 (1.4)	9 (2.1)	1 (2.2)	
HCT-CI > 3	110 (20.4)	6 (8.6)	92 (21.8)	12 (26.1)	0.260
KPS < 90		13 (18.6)	88 (20.9)		0.748

	113 (21.0)			12 (26.1)	
Conditioning Regimen MAC RIC	240 (44.6) 298 (55.4)	70 (100) 0 (0.0)	170 (40.3) 252 (59.7)	0 46 (100)	<0.001
GVHD Prophylaxis PTCY-based Others	352 (65.4) 186 (34.6)	8 (11.4) 62 (88.6)	303 (70.0) 119 (30.0)	41 (89.1) 5 (10.9)	<0.001
Donor Type MSD 10/10 MUD 9/10 MMUD Haploidentical	151 (28.1) 195 (36.3) 117 (21.7) 75 (13.9)	37 (52.9) 20 (28.6) 5 (7.1) 8 (11.4)	107 (25.4) 162 (38.4) 101 (23.9) 52 (12.3)	7 (15.2) 13 (28.3) 11 (23.9) 15 (32.6)	<0.001
New TCI	**All Patients N = 538**	**TCI High N = 234 (43.5%)**	**TCI Int N= 293 (54.5%)**	**TCI Low N = 11 (2.0%)**	
Age Continuous (Range) Age ≥65 years	53.3 (41.6-61.7) 72 (13.4)	44.0 (32.0-51.8) 7 (3.0)	59.4 (52.8-64.5) 58 (19.8)	67.0 (64.0-70.5) 7 (63.6)	<0.001 <0.001
Diagnosis Acute Myeloid Leukemia Myelodysplastic Syndrome / CMML Myeloproliferative Disorder Acute Lymphoblastic Leukemia	189 (35.1) 87 (16.2) 83 (15.4) 95 (17.7) 73	83 (35.5) 23 (9.8) 31 (13.2) 68 (29.1) 24 (10.3) 5 (2.1)	100 (34.1) 61 (20.8) 52 (17.7) 25 (8.6) 49 (16.8) 6 (2.0)	6 (54.5) 3 (27.3) 0 2 (18.2) 0 0	<0.001

Non-Hodgkin Lymphoma Others	(13.6) 11 (2.0)				
HCT-CI > 3 **KPS < 90**	110 (20.4) 113 (21.0)	35 (14.9) 42 (17.9)	68 (23.2) 66 (22.5)	7 (63.6) 5 (45.5)	0.001 0.066
Conditioning Regimen MAC RIC	240 (44.6) 298 (55.4)	205 (87.6) 29 (12.4)	35 (11.9) 258 (88.1)	0 11 (100)	<0.001
GVHD Prophylaxis PTCY-based Others	352 (65.4) 186 (34.6)	172 (73.5) 62 (26.5)	173 (59.0) 120 (41.0)	7 (63.6) 4 (36.4)	0.002
Donor Type MSD 10/10 MUD 9/10 MMUD Haploidentical	151 (28.1) 195 (36.3) 117 (21.7) 75 (13.9)	61 (26.1) 75 (32.0) 52 (22.2) 46 (19.7)	86 (29.3) 113 (38.6) 65 (22.2) 29 (9.9)	4 (36.4) 7 (63.6) 0 0	0.008



Conclusions: Pending of external validation, the TCI classification appeared insufficient for accurately predicting survival events based on accumulated toxicity specially in patient cohorts that contain transplant platforms with PTCy. Nevertheless, the incorporation of PTCy into the model, suggests improved stratification, risk adjustment, and predictive value.

Disclosure: The authors declare no relevant conflicts of interest, financial or otherwise.

B152

IMPACT OF ONE VERSUS TWO INDUCTIONS TO ATTAIN FIRST COMPLETE REMISSION IN ACUTE MYELOID LEUKEMIA PATIENTS UNDERGOING ALLOGENEIC TRANSPLANTATION WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE: FROM THE ALWP/EBMT

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Background: Allogeneic transplantation (HSCT) is a curative therapeutic option for high-risk AML. Undergoing HSCT while in CR1 is an important prognostic factor. Moreover, HSCT outcomes in patients (pts) receiving conventional GVHD prophylaxis also correlate with the number of induction courses needed to achieve CR1 (Loke J, Cancer 2024). However, whether it holds for HSCT with post-transplant cyclophosphamide (PTCy) is unknown.

Methods: The study aim was to compare transplantation outcomes in AML pts achieving CR1 after one *vs*. two inductions. HSCTs were performed between 2012-2022, and all pts received PTCy as GVHD prophylaxis. Statistical tests included a multivariate analysis (MVA).

Results: 677 pts (de novo-542, secondary-135) were included, 518 (77%) with 1 induction and 159 with 2 inductions. Median follow-up was 2.2 (range, 2-2.6) years, and the median year of transplant was 2020 (interquartile range [IQR], 2017-2021) with no significant difference between the two groups (p=0.14). Median pt age was 56.5 (IQR, 43.4-64.1)

years, and 58.8% were male, comparable between both groups (p=0.08 and p=0.93). The cytogenetic risk was categorized as intermediate (69.1% *vs.* 69.7%), adverse (25.8 % *vs.*27%), and favorable (5.1% *vs. 3.3%)*, in the 1 and 2 induction groups, respectively (p=0.65; data missing for 33 pts). Donors were haploidentical 65.6% *vs.* 69.2%; HLA matched sibling 9.3% *vs.* 11.3%; matched (10/10) unrelated 14.3% *vs.* 10.1%, and mismatched (9/10) unrelated 10.8 *vs.* 9.4%, respectively (p=0.46). PB grafts were the main stem cell source in 74.7 % and 71.7% of the pts, respectively (p=0.45). Myeloablative conditioning (MAC) was used in 46.3% *vs.* 53.5%, respectively (p=0.12). Day 30 ANC $\geq$0.5 x 10^9/L was 90.4% *vs*.91.1 % and day 60 platelet count $\geq$20,000/L was 87.3% *vs.* 86.5% for pts receiving 1 *vs.* 2 inductions, respectively. Day 180 acute (a) GVHD II-IV was 29.7% *vs.* 31.2 % and of III-IV it was 9.1% *vs.* 9.8%, respectively. The 1- y total and extensive chronic (c) GVHD was 29.8% *vs.* 34.2% and 11.3% *vs.* 16.1 %, respectively, with no significant difference between pts receiving 1 *vs.* 2 inductions. These data were confirmed by MVA. The 2-y relapse incidence (RI) was higher in pts receiving 2 inductions compared to those receiving 1 induction, 27% *vs.* 19.3%, HR = 1.75 (95% CI, 1.21-2.53, p=0.003). The 2-y overall survival 69% *vs.* 62.8%, GVHD-free, relapse-free survival 50.4% *vs.* 46,3%, leukemia-free survival 65% *vs.* 61.1% and non-relapse mortality 15.7% *vs.* 11.9% (Figure) did not differ significantly between pts receiving 1 *vs.* 2 inductions. These data were confirmed by MVA. The main cause of death was the original disease, 48.7% *vs.* 70.9% of the deaths, respectively.

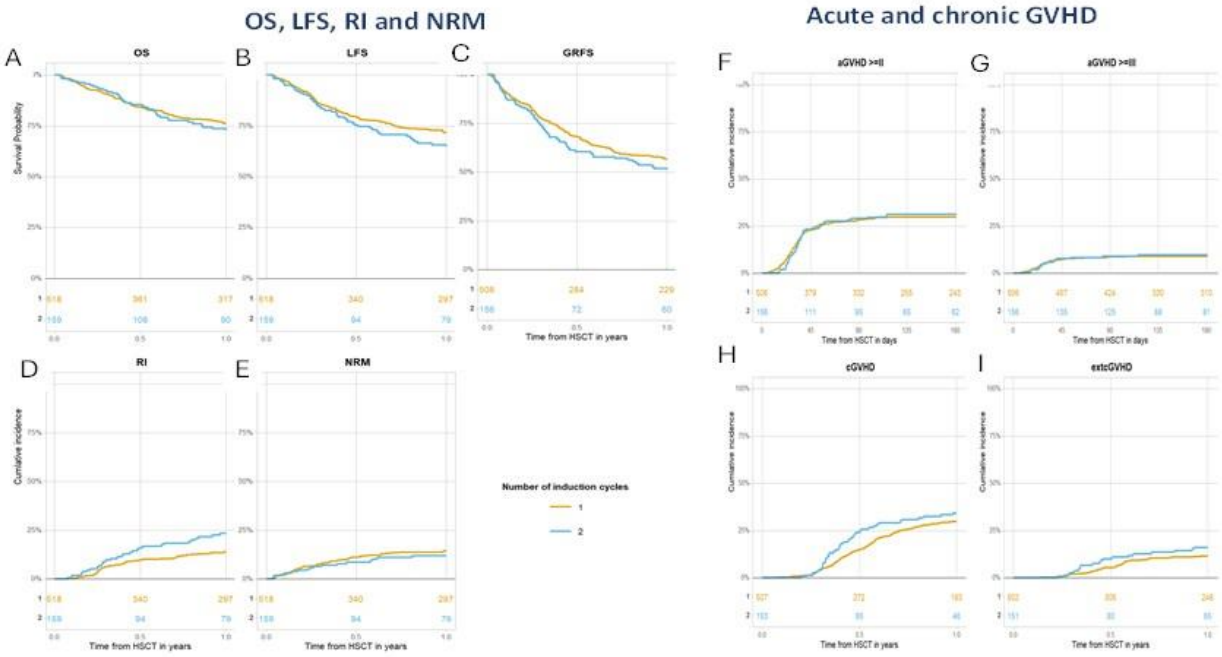

Figure Legend: Outcomes of HSCT with post-transplant cyclophosphamide (PTCy) in patients with AML achieving 1st CR after one versus two inductions: A. overall survival (OS), B. leukemia-free survival (LFS), C. GVHD free relapse free survival (GRFS), D. relapse incidence (RI), E. non-relapse mortality (NRM); F. acute GVHD grade II-IV (>=II) and G. III-IV (>=III); H. chronic GVHD total(cGVHD) and I. extensive (extcGVHD).

Conclusions:
In this registry-based retrospective analysis of HSCT for AML in CR1, achieved after one *vs*. two inductions, we observed similar transplantation outcomes other than for pts with a higher incidence of relapse achieving CR1 after 2 inductions. These data may indicate that in pts receiving PTCy as GVHD prophylaxis, the number of induction courses to attain CR loses its predictive value, which we previously observed in non-PTCy transplants, suggesting the uniqueness of PTCy biology.

Disclosure: Nothing to disclose

B153

POST-TRANSPLANT CYCLOPHOSPHAMIDE COMPARED WITH OTHER GVHD PROPHYLAXIS STRATEGIES IN REDUCED-INTENSITY ALLOGENEIC TRANSPLANTATION FOR AML AND MDS: AN SFGM-TC REGISTRY STUDY

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Background: Optimizing graft-versus-host disease (GVHD) prophylaxis remains a key challenge to improve allo-HCT outcomes. In Europe, anti-thymocyte globulin (ATG) is widely used, while post-transplant cyclophosphamide (PTCy) is increasingly adopted, particularly for mismatched unrelated donors (MMUD). In matched related (MRD) and matched unrelated (MUD) allo-HCT, comparative studies of PTCy versus ATG have yielded conflicting results, preventing clear recommendations. We report a large national registry analysis to complement existing evidence.

Methods: We retrospectively analyzed SFGM-TC registry patients who underwent a first allo-HCT from MRD or MUD for acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS) between 2014 and 2022. We restricted the analysis to reduced intensity conditioning (RIC) with peripheral blood stem cells (PBSC). GVHD prophylaxis consisted in: immunosuppressive agents (IS) alone (group NONE), PTCy with or without (+/-) IS (group PTCy), ATG +/- IS (group ATG), PTCy+ATG +/- IS (group PTCy+ATG). IS regimens included mainly calcineurin inhibitor (CNI) + antimetabolite (methotrexate or mycophenolate mofetil), or CNI alone.

Results: A total of 3702 patients were analyzed: group PTCy n=103, group ATG n=3340, group PTCy+ATG n=46 and group NONE n=213. The groups were comparable in age at allo-HCT, gender, disease type, remission status at transplant and HCT-CI score but differed significantly in transplant year, blood group compatibility, and RIC regimen. In addition, in the PTCy and PTCy+ATG groups, 14% of allo-HCT were performed without additional IS, compared to 0% in the other groups. In the NONE group, 65% of allo-HCT used MRD donors versus 45% in the remaining groups. These variables (except transplant year) were included as adjustment factors in multivariable analysis.
At day 100, all groups experienced similar cumulative incidence (CI) of grade ≥ II or grade III-IV acute GVHD (aGVHD). At 2 years, the CI of extensive chronic GVHD (ext cGVHD) was 9%, 7%, 15% and 2% in PTCy, ATG, NONE and PTCy+ATG groups respectively (p <0.001). In adjusted multivariable analysis, PTCy was associated with a significant reduction in grade III-IV aGVHD compared to ATG (HR 0.49, p=0.040). Regarding ext cGVHD, PTCy and ATG were both significantly superior to NONE. PTCy+ATG was not significantly different from other groups but the statistical power was limited by the small number of patients.
With a median follow-up of 16.6 months for the overall population, the 2-year OS, PFS and extGRFS were 59.8% [58.1 - 61.5], 53.8% [52.1 - 55.6] and 43.9% [42.2 – 45.6] respectively. These outcomes were not significantly influenced by donor type or by GVHD prophylaxis group in multivariable analysis.
The cumulative incidence of relapse (RI) and non-relapse mortality (NRM) at 2 years were similar between groups. An analysis of toxicity patterns and causes of death will be presented.

Conclusions: In this large retrospective cohort of MRD/MUD RIC allo-HCT for AML/MDS, PTCy significantly reduced severe aGVHD compared with ATG, while cGVHD, RI, OS, PFS, and

GRFS did not differ. These findings are consistent with previous reports and now await confirmation from ongoing randomized trials.

Clinical Trial Registry: F20210504143333

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T.C. has received research grant from MEDAC; consulting fees from Sanofi, Pierre Fabre and AbbVie; travel support from Pierre Fabre, Neovi, all via the institution

B154

ARCHIVE CONDITIONING (ALKYLATING AGENTS, CYTARABINE, CLADRIBINE, HYPOMETHYLATING AGENTS, AND VENETOCLAX) FOR UPFRONT ALLOGENEIC STEM CELL TRANSPLANTATION IN NEWLY DIAGNOSED OR RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA

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Background: Allogeneic stem cell transplantation (alloSCT) after remission induction remains the cornerstone for relapsed/refractory (R/R) or newly diagnosed (ND), adverse-risk acute myeloid leukemia (AML). We report the efficacy and safety of an investigational conditioning with alkylating agents, cytarabine, cladribine, hypomethylating agents, and venetoclax (ARCHIVE) in patients with ND adverse-risk, or R/R AML who proceeded to upfront alloSCT without remission induction.

Methods: We performed an observational, prospective, single-center study. Treatment regimens and data collection were approved by the Vilnius University Hospital Santaros Klinikos Hematology Board and the Vilnius Regional Biomedical Research Ethics Committee. The patients were 18 years or older, had AML or MDS/AML with >5% blasts and/or extramedullary disease, and were alloSCT-eligible.
ARCHIVE conditioning regimen (Picture 1) consisted of cytarabine 500 or 1000 mg/m^2, cladribine 5 mg/m^2 on days -8, -7, -6, -5, -4, venetoclax 600 mg/d and decitabine 20 mg/m^2 / azacitidine 75 mg/m^2 on days -8, -7, -6, -5, -4, -3, -2. The backbone alkylating agent was either busulfan (3.2 mg/kg on days -3 and/or -2) or melphalan (100 mg/m2 on day -2 in patients with previous busulfan exposure and/or *TP53*-mutated disease), whereas thiotepa was added to busulfan or melphalan in selected cases. Gilteritinib 120 mg/d was administered with ARCHIVE until day -2 in *FLT3*-mutated AML. Idarubicin or etoposide was

added on days -8 and -7 in selected cases. GVHD prophylaxis consisted of cyclophosphamide 40 mg/kg (days +3, +4), calcineurin inhibitor, and mycophenolate mofetil.
We collected baseline characteristics, CR+CRp rate at day +30, MRD negativity rate (by MFC and PCR), time-to-engraftment, grade 3-5 non-hematological toxicity (CTCAE v5.0), OS, and RFS.

Picture 1. ARCHIVE conditioning regimen

ARCHIVE conditioning and GVHD prophylaxis for upfront allogeneic stem cell transplantation in newly di						
2-day ramp-up	-8	-7	-6	-5	-4	-3
	Venetoclax 600 mg	Venetoclax 600 mg	Venetoclax 600 mg	Venetoclax 600 mg	Venetoclax 600 mg	Venetocla 600 mg
	Decitabine 20 mg/m^2 or Azacitidine 75mg/m^2	Decitabine 20 mg/m^2 or Azacitidine 75mg/m^2	Decitabine 20 mg/m^2 or Azacitidine 75mg/m^2	Decitabine 20 mg/m^2 or Azacitidine 75mg/m^2	Decitabine 20 mg/m^2 or Azacitidine 75mg/m^2	Decitabin 20 mg/m^2 Azacitidin 75mg/m^2
Venetoclax 100 mg + Decitabine 20mg/m^2 or Azacitidine 75mg/m^2 (day 1)	Cytarabine 500-1000 mg/m^2	Cytarabine 500-1000 mg/m^2	Cytarabine 500-1000 mg/m^2	Cytarabine 500-1000 mg/m^2	Cytarabine 500-1000 mg/m^2	ALKYL Bu8/4: Busulfan
Venetoclax 200 mg + Decitabine 20mg/m^2 or Azacitidine 75mg/m^2 (day 2)	Cladribine 5 mg/m^2	Cladribine 5 mg/m^2	Cladribine 5 mg/m^2	Cladribine 5 mg/m^2	Cladribine 5 mg/m^2	TT5+Bu4: Th Busulfa
	G-CSF 5 mcg/kg	G-CSF 5 mcg/kg	G-CSF 5 mcg/kg	G-CSF 5 mcg/kg	G-CSF 5 mcg/kg	TT5/10+Bu8: Th Busulfan 3
	Idarubicin 8 mg/m^2 or Etoposide 100 mg/m^2 (in selected cases)	Idarubicin 8 mg/m^2 or Etoposide 100 mg/m^2 (in selected cases)				MEL100: Mel TT5+MEL100: Melphal

Results: Thirty-two patients were enrolled, with their baseline characteristics summarized in Table 1.
Dose-escalated cytarabine (1000mg/m^2), additional Idarubicin/Etoposide, and Gilteritinib were used in 13% (4/32), 9% (3/32), and 13% (4/32), respectively. Thiotepa was added to busulfan/melphalan in 59% (19/32). Matched sibling, matched unrelated, mismatched unrelated, and haploidentical donors were used in 6% (2/32), 34% (11/32), 13% (4/32), and 47% (15/32), respectively.
The CR+CRp rate at day +30 post-alloSCT was 97% (30/31) with all responders successfully

engrafting. MRD negativity was achieved in 90% (26/29) of MRD-evaluable responders. The median time to neutrophil recovery was 17 (13-30) days after the stem cell infusion and 25 (19-38) days after the start of ARCHIVE.
The most common grade 3-5 toxicities were infectious complications (84%, 27/32) and mucositis (44%, 14/32). Adverse events of special interest were veno-occlusive disease (6%, 2/32), secondary graft failure (3%, 1/32), and grade 3-4 acute GVHD (16%, 5/32). Day 30 mortality rate was 6% (2/32).
At the data cut-off (2025-12-08), 26 patients are alive and in CR, with no confirmed relapses. Six patients died due to infectious complications (4), GVHD (1), and progressive disease (1). After the median follow-up of 6.5 months, the median OS and RFS were not reached, whereas the estimated 12-month OS and RFS were 77% and 85%, respectively.

Table 1. Baseline Characteristics

Characteristics	**Patients (N32)**
Female	59% (19/32)
Age (years), median (min-max)	58 (23-70)
ECOG 0-1	69% (22/32)
ECOG 2	31% (10/32)
AML	81% (26/32)
MDS/AML	19% (6/32)
ELN 2022 adverse risk group	81% (26/32)
*MECOM*r	25% (8/32)
*TP53*m	13% (4/32)
ELN 2022 Adverse karyotype	25% (8/32)
Newly diagnosed disease	16% (5/32)
Relapsed/refractory disease	84% (27/32)

1 prior treatment line	67% (18/27)
>1 prior treatment line	33% (9/27)
Prior Venetoclax	56% (15/27)
Prior *FLT3* inhibitors	7% (2/27)
Prior Revumenib	4% (1/27)
Prior alloSCT	22% (6/27)
Blast count % at baseline, median (min-max)	13 (0-70)

Conclusions: Upfront alloSCT with ARCHIVE conditioning demonstrates high antileukemic efficacy and manageable toxicity in patients with ND adverse-risk or R/R non-CR AML.

Clinical Trial Registry: No: 2019/2-1088-591
https://www.mf.vu.lt/mokslas/vilniaus-regioninis-biomedicininiu-tyrimu-etikos-komitetas

Disclosure: *AbbVie:* Consultancy, Honoraria, Other: travel expenses; *Servier:* Consultancy, Honoraria, Other: travel expenses; *Astellas:* Consultancy, Honoraria; *Takeda:* Other: travel expenses; *Pfizer:* Consultancy; *Novartis:* Consultancy, Honoraria, Other: travel expenses; *Johnson & Johnson:* Consultancy, Honoraria, Other: travel expenses.

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REJECTION PROPHYLAXIS IN AUTOLOGOUS GENE THERAPY PROTOCOLS: CHOOSING AN ALEMTUZUMAB DOSE

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Background: Graft rejection is increasingly described in children with inborn errors of metabolism following haematopoietic stem cell gene therapy (HSCGT), as autologous T-cells reject the transgene protein and modified cells expressing the transgene protein product. There is evidence from primate studies that pre-transplant immune suppression with TBI

prevents such rejection, but TBI is clearly not suitable in clinical practice. We have proposed utilising alemtuzumab in place of TBI to promote recipient tolerance following HSCGT and thereby reduce graft rejection.
Alemtuzumab is an anti-CD52 monoclonal antibody used in transplant conditioning regimens to both prevent graft failure and acute graft-vs-host disease (aGvHD). Current protocols recommend dosage of 0.2mg/kg daily over 3-5 days (cumulative dose of 0.6-1mg/kg, capped at total dose 100mg). However, high exposure due to pharmacokinetic differences between patients is common and leads to delayed immune reconstitution and increased risk of viral reactivation and infection in the peri-transplant period. Locally, we have established a protocol utilising a dosage of 0.1mg/kg x 3 days (cumulative dose of 0.3mg/kg) on days -7 to -5 in matched related donor transplant in children with non-malignant disease to reduce side effects while preserving clinical efficacy. We report our experience utilising this lower dose within this cohort.

Methods: We performed a retrospective analysis of medical records at a single site (Royal Manchester Children's Hospital, UK) for patients aged 0 – 19 years who underwent first transplant for non-malignant indications between 01/01/2018 – 31/12/2024. Patients were included if they underwent matched related donor transplant and received 0.1mg/kg x 3 days alemtuzumab during the conditioning phase. Data collection included baseline characteristics, transplant characteristics and outcomes, presence of significant viral re-activation (positive result with viral copy number ≥1000), and immune reconstitution.

Results: 52 patients were identified during in the study period, who underwent transplant at a median age of 6.6 years (range: 0.2 to 18.7). The overall survival at 5-years was 90.3% (causes of death: pulmonary haemorrhage, n=2; parainfluenza pneumonitis, n=1; respiratory failure, n=1; TA-TMA, n=1).
Viral reactivation was not uncommon but there was no mortality from reactivated infection. Significant adenovirus reactivation occurred in 9/52 (17.3%), Epstein-Barr virus reactivation in 14/52 (26.9%), and cytomegalovirus reactivation in 17/52 (32.7%). There was no mortality in relation to viral reactivation for this cohort.
Immune reconstitution occurred promptly after transplant. The median absolute CD3 count (cells/μL) was 197 (range: 19-1225) at 3 months, 730 (range: 83-946) at 6 months, 1004 (range: 509-2765) at 9 months and 1452 (range: 395-2280) at 12 months. Acute GvHD of any grade was reported in 12/52 (23.1%) with only 1 patient experiencing GvHD of grade III-IV. There was no graft rejection.

Conclusions: Alemtuzumab at a dosage of 0.1mg/kg x 3 days is safe and well tolerated in this cohort. Immune suppression is adequate to prevent graft rejection, and immune reconstitution is sufficiently prompt to prevent virus-related mortality. We present our experience of such immune suppression in an ongoing, first-in-world clinical trial of HSCGT in MPSII, including in boys with demonstrable sensitisation to the transgene protein product.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

B156

VENETOCLAX-ENHANCED REDUCED-INTENSITY CONDITIONING IN ELDERLY PATIENTS WITH HIGH-RISK MYELOID MALIGNANCIES UNDERGOING ALLOGENEIC PERIPHERAL BLOOD STEM CELL TRANSPLANTATION: A PHASE II STUDY

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Background: Reduced-intensity conditioning (RIC) for high-risk acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) is associated with high relapse rates, and it remains unclear whether Venetoclax can enhance the efficacy of RIC in these patients undergoing allogeneic hematopoietic stem cell transplantation.

Methods: A prospective, single-arm, phase 2 trial enrolled patients with high-risk AML or MDS, who were aged ≥55 years and underwent allogeneic peripheral blood stem cell transplantation (allo-PBSCT). High-risk AML was defined as non-remission (NR) prior to transplantation, complete remission (CR) with measurable residual disease (MRD)-positive status, or adverse-risk disease according to the 2022 European LeukemiaNet (ELN) classification. High-risk MDS was defined as intermediate-2 or higher risk according to the International Prognostic Scoring System (IPSS), therapy-related MDS, or the presence of pathogenic mutations in *ASXL1, EZH2, RUNX1, SRSF2, U2AF1, STAG2, NRAS, ZRSR2*, or *TP53.*
All patients received venetoclax-enhanced RIC (VEN-RIC), which consisted of venetoclax, fludarabine, cytarabine, busulfan, and total body irradiation (TBI). Venetoclax was administered in an ascending dose regimen for patients with NR AML or untreated MDS: 100 mg on day -11, 200 mg on day -10, and 400 mg once daily from days -9 to -3. For all other patients, venetoclax was given at a dose of 400 mg daily from days -9 to -3. Fludarabine (30 mg/m²/d) was given from days -6 to -2, cytarabine (1 g/m² /d) from days -6 to -2, intravenous busulfan (3.2 mg/kg/d) on days -6 and -5, and TBI (3 Gy) on day -1.
The primary endpoint was 1-year progression-free survival (PFS), and secondary endpoints included overall survival (OS), graft-versus-host disease/relapse–free survival (GRFS), relapse, non-relapse mortality (NRM), graft versus-host-disease (GVHD), and safety.

Results: Fifty patients (median age 62) were enrolled, including 37 with AML and 13 with MDS. At a median follow-up of 14.9 months, the 1-year PFS was 72.5% (95% CI, 60.8–86.5%), with 1-year OS and GRFS rates of 73.8% (95% CI, 62.1–87.9%) and 56.9% (95% CI, 44.2–73.4%), respectively. The 1-year cumulative incidence of relapse was 16.8% (95% CI, 6.0–27.6%), while non-relapse mortality (NRM) was 10.6% (95% CI, 1.6–19.6%). Acute graft-versus-host disease (aGVHD) occurred in 22.9% (95% CI, 10.9%-34.8%) of patients within 180 days, with 1-year cumulative incidence of cGVHD at 25.8% (95% CI, 10.8%-40.8%). The 1-year cumulative incidence of CMV and EBV reactivation was 12.8% (95% CI, 3.3%-22.8%) and 47.9% (95% CI, 33.2%-61.9%), respectively.
Multivariable analysis showed that TP53 mutation was the strongest predictor of worse OS,

PFS, and GRFS, as well as higher relapse rates. A high Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI ≥3) and aGVHD were significantly associated with higher NRM. In subgroup analyses, patients aged 55–65 years had significantly better GRFS compared to those aged ≥65 year.

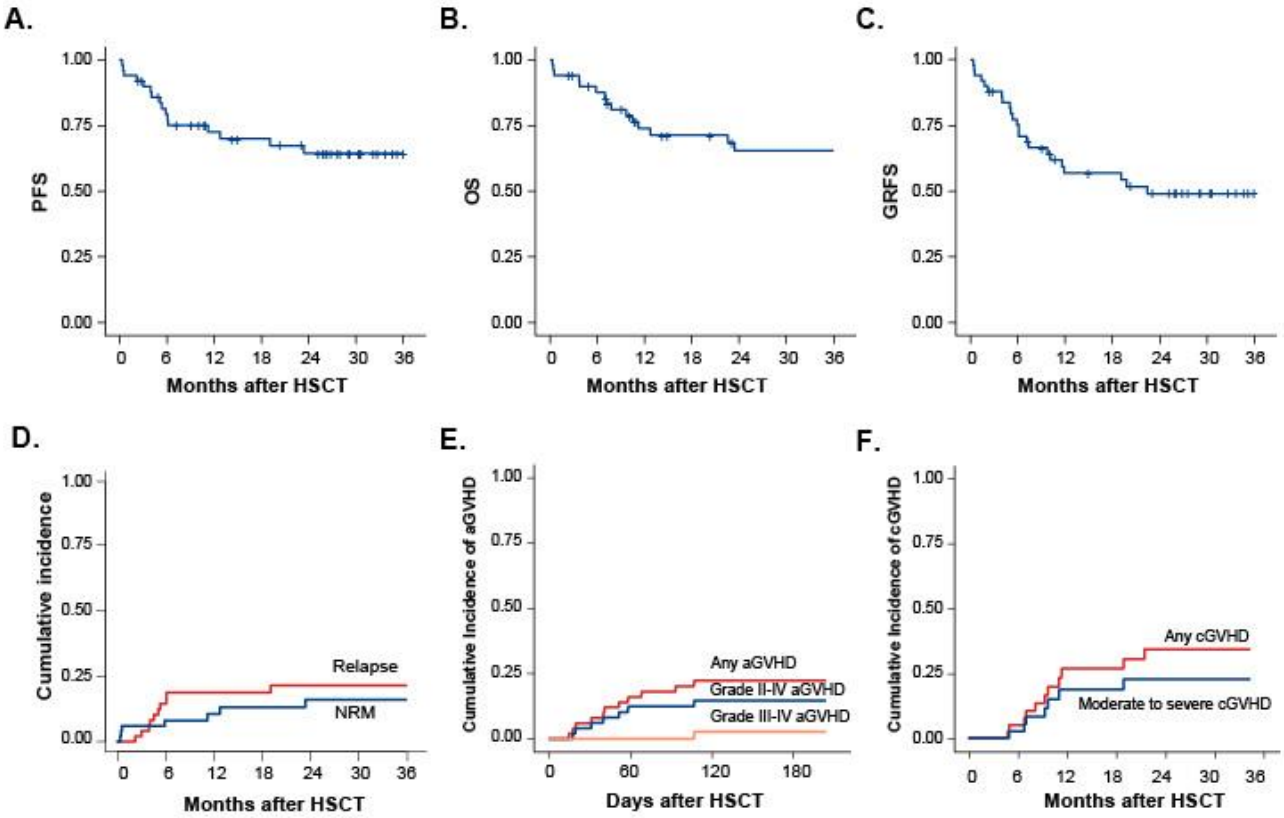

Figure: (A) PFS; (B) OS; (C) GRFS; (D) Relapse (red) and NRM (blue); (E) Acute GVHD by grade; (F) Chronic GVHD by grade.

Characteristics	N (%)
Age, years	
55≤age<65	40 (80.0%)
≥65	10 (20.0%)
Gender	
Male	30 (60.0%)
Female	20 (40.0%)

Disease status before transplantation	
AML-CR with MRD-	12 (24.0%)
AML-CR with MRD+	14 (28.0%)
AML-PR/NR	11 (22.0%)
MDS-CR	5 (10.0%)
MDS-NR	8 (16.0%)
HCT-CI	
0-2	46 (92.0%)
3-4	4 (8.0%)
Donor type	
HLA-matched related	2 (4.0%)
HLA-matched unrelated	3 (6.0%)
Haploidentical	45 (90.0%)

Table: Patient characteristics.

Conclusions: VEN-RIC is feasible, safe, and associated with encouraging survival and acceptable NRM in elderly high-risk AML and MDS, warranting confirmation in randomized studies.

Clinical Trial Registry: NCT05583175
https://clinicaltrials.gov/study/NCT05583175

Disclosure: Nothing to declare.

B160

VENETOCLAX-AUGMENTED CONDITIONING REGIMENS IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MYELOID NEOPLASMS: A SCOPING REVIEW AND EVIDENCE LANDSCAPE

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Background: Relapses remain a leading cause of treatment failure following allogeneic hematopoietic stem cell transplantation (allo-HSCT) for high-risk myeloid neoplasms. Venetoclax, a selective BCL-2 inhibitor with proven activity in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), has emerged as a promising adjunct to conditioning regimens. However, its role in the transplant conditioning setting remains incompletely defined.

Methods: We performed a hybrid scoping review and evidence-mapping analysis in accordance with PRISMA-ScR guidelines to summarize published clinical experience and ongoing trials of venetoclax-augmented conditioning or sequential regimens prior to allo-HSCT. Systematic searches of PubMed/MEDLINE, Embase, Scopus, ClinicalTrials.gov, and major hematology conference proceedings (ASH, EHA) were conducted from inception through October 2025. Eligible studies included adult patients with AML or other myeloid neoplasms receiving venetoclax as part of conditioning. Outcomes of interest included engraftment, graft-versus-host disease (GVHD), relapse, non-relapse mortality (NRM), survival, and toxicity.

Results: Eighteen studies (20 reports) met the inclusion criteria, including nine published cohorts (n = 238 patients) and 11 ongoing registered trials. Published studies primarily enrolled patients with high-risk AML or MDS and incorporated venetoclax into myeloablative, reduced-intensity, or sequential FLAMSA-like conditioning backbones (Table 1). Venetoclax was administered at doses of 200–400 mg/day (occasionally up to 800 mg) for 3–14 days, most commonly in combination with busulfan–fludarabine-based regimens.
Engraftment occurred within expected timeframes, with median neutrophil recovery of 12–16 days and platelet recovery of 13–23 days. Acute GVHD rates ranged from 28–64%, with grade III–IV acute GVHD reported in 3–26%, while chronic GVHD occurred in 7–43%, predominantly mild to moderate. Relapse rates varied from 7–41%, and NRM ranged from 7–37%. One-year overall survival ranged from 63–84% (Figure 1). Venetoclax-associated toxicities were mainly infectious or mucosal; tumor lysis syndrome and veno-occlusive disease were rare.
Ongoing trials (n = 11) are predominantly phase I–II studies exploring venetoclax integration across myeloablative, reduced-intensity, and sequential platforms, with two randomized studies underway.
Table 1. Baseline Characteristics of Published Studies Evaluating Venetoclax-Augmented Conditioning before Allogeneic HSCT

Study ID (Author Year)	Country	Sample size (n)	Age, median (range)	Design / Publication Type
Gracia 2021	USA	22	64 (25–71)	Prospective phase I clinical trial, Full text
Schulz 2024	Germany	61	58 (20–74)	Retrospective, Full text
Popat 2024	USA	49	59 (18–69)	Prospective phase II trial, Abstract
Popat 2021	USA	33	59 (23–69)	Prospective, Abstract
Cao 2023	China	31	25 (3–58)	Retrospective, Full text
Zheng 2023	China	19	53 (50–56.5)	Prospective, Full text
Cui 2024	China	20	47 (16–62)	Prospective, Abstract
Žučenka 2025	Lithuania	2	19 and 32*	Case report, Full text
Murakami 2022	Japan	1	44*	Case report, Full text

*Values marked with an asterisk (*) denote single-patient ages.

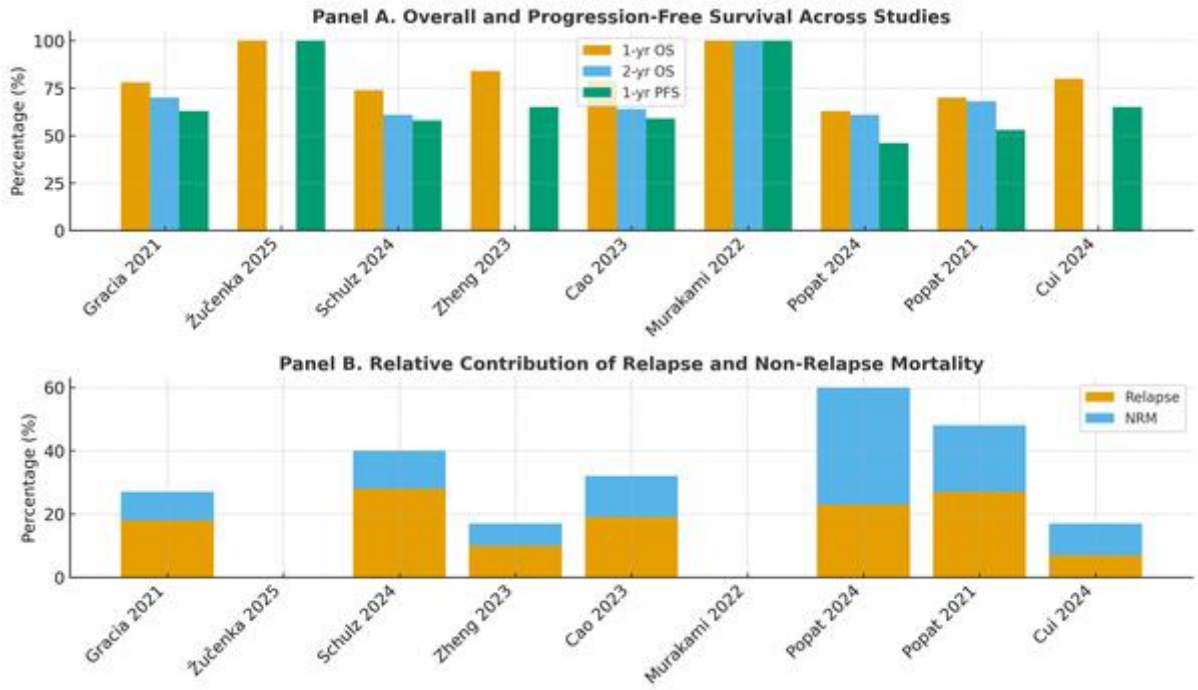

Figure 1. Transplant survival outcomes and mortality composition across included studies

Conclusions: Current evidence suggests that venetoclax-augmented conditioning regimens prior to allo-HSCT are feasible and generally well tolerated, with engraftment, GVHD, and survival outcomes comparable to contemporary transplant benchmarks in high-risk myeloid malignancies. Ongoing prospective and randomized trials will be critical to define optimal dosing, scheduling, and patient selection, and to clarify whether venetoclax-based conditioning improves disease control and post-transplant outcomes.

Disclosure: Nothing to declare.

B161

FLUDARABINE AUC EXPOSURE IS NOT PREDICTIVE OF MORTALITY IN THE CONTEXT OF FLUDARABINE BUSULFAN AND ATG CONDITIONED TRANSPLANTATION

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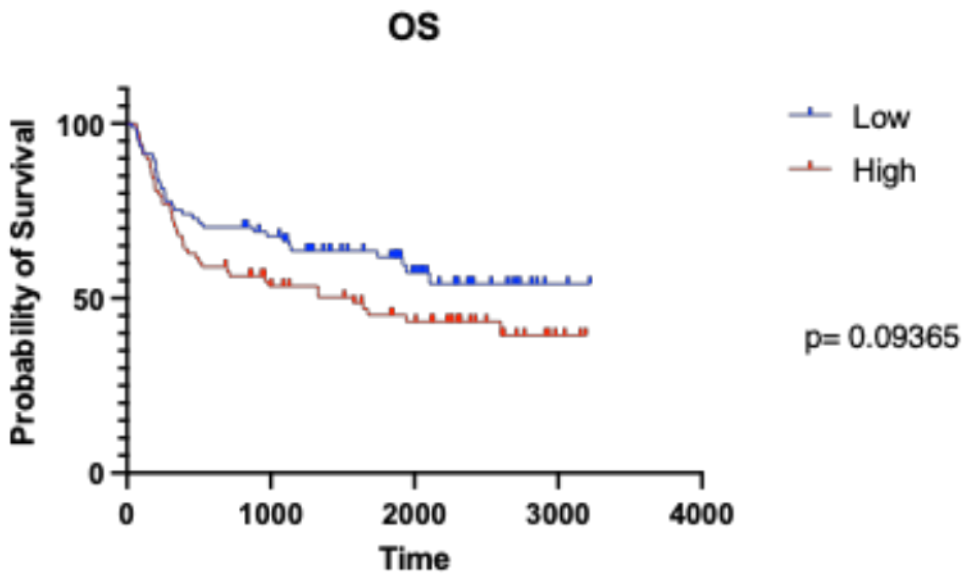
Background: Fludarabine (Flu) is a core component of allogeneic transplantation conditioning, providing lymphodepletion and reducing graft rejection risk. However,

conventional body-surface-area (BSA) dosing results in wide interpatient variability in drug exposure, measured as the area under the plasma concentration–time curve (AUC). Both high and low Flu exposure have been linked to increased non-relapse mortality (NRM), particularly in myeloablative or T-replete settings. We evaluated the association between Flu AUC and outcomes in patients receiving a uniform reduced-intensity conditioning (RIC) regimen of Flu/Busulfan/rabbit anti-thymocyte globulin (Flu/Bu/rATG), using a population pharmacokinetic (popPK) model to assess whether AUC-guided dosing could provide clinical benefit.

Methods: We retrospectively identified all patients with myeloid malignancies who received a Flu/Bu/rATG RIC allogeneic transplant at Nottingham City Hospital between January 2016 and September 2022. Conditioning consisted of Fludarabine 30 mg/m² (Day −9 to −5), Busulfan 3.2 mg/kg (Day −5 to −3), and rATG 2.5 mg/kg (Day −2 to −1). Fludarabine dose was reduced by 20% for patients with creatinine clearance 30–70 mL/min. Graft-versus-host disease (GVHD) prophylaxis included ciclosporin and mycophenolate mofetil. Fludarabine AUC was calculated using a validated population pharmacokinetic (popPK) model: AUC= (cumulative dose)/(((0.782 ×EGFR)+3.24)×((〖BW/70)〗^0.75)) (Langenhorst et al., 2019). The cutoff for fludarabine exposure was determined compared to median exposure. Kaplan-Meier logrank analysis was used to compare survival outcomes between the exposure groups. Multivariable Cox regression analysis was used to calculate the role of fludarabine exposure when adjusting for age, gender, donor type, HCT-CI score and diagnosis. The principal outcome measure was overall survival (OS) with secondary outcomes including progression free survival (PFS) and NRM.

Results: A total of 159 patients were included (median age 61 years; 55% male; median HCT-CI 2). Underlying diagnoses were AML (62%), MDS (18%), MPN (13%), and CML (8%). Matched sibling donors accounted for 20% and unrelated donors for 80%. Median follow-up was 68 months. Median Flu AUC was 31.8 mg·h/L (IQR 27.8–35.7), used as the exposure cutoff.
There was no significant difference in OS between the high- and low-exposure groups (p=0.09); median OS was 51 months in the high-exposure group and was not reached in the low-exposure group. One-year NRM was similar between groups (13.6% high vs 12.0% low). Maximally selected log-rank statistics did not identify an alternative AUC threshold predictive of OS. In multivariable Cox regression, Flu exposure category was not associated with OS. PFS was modestly superior in the low-exposure group (p=0.04), although this was not significant in the regression analysis. Given prior evidence linking high Flu exposure primarily to NRM rather than relapse risk, the clinical relevance of this isolated PFS difference remains uncertain.



Conclusions: In this single-centre cohort treated with homogeneous Flu/Bu/rATG RIC, we did not identify a Flu AUC threshold associated with increased NRM or inferior OS, contrasting with studies in myeloablative, T-replete or haplograft settings. These findings suggest that in RIC regimens incorporating rATG, optimising Flu exposure alone may not substantially influence outcomes. Further validation in external cohorts is needed before adopting AUC-guided Flu dosing in this context.

Clinical Trial Registry: N/A

Disclosure: All authors have no conflict of interest in relation to this abstract.

B162

SUPERIORITY OF TBI-BASED COMPARED TO MELPHALAN-BASED CONDITIONING REGIMEN IN HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION: COMPARISON BETWEEN DIFFERENT APPROACHES OF TWO MAJOR PEDIATRIC TRANSPLANTATION UNITS

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Background: Transplantation of *ex vivo* α/β T- and CD19-depleted stem cell grafts has become an established approach for haploidentical stem cell transplantation (HSCT), particularly in the pediatric setting. Beyond graft manipulation, multiple transplant-related

variables influence clinical outcomes, including the conditioning regimen administered prior to graft infusion. Both chemotherapy-based and total body irradiation (TBI)-based regimens are commonly employed; we therefore aimed to compare their impact between two major transplant centers.

Methods: All consecutive paediatric patients undergoing HSCT for acute lymphoblastic T- or B-cell leukemia (ALL) or acute myeloblastic leukemia (AML) in Tuebingen, Germany and Rome, Italy, over the time span of 10 years (2010-2022) were analyzed.
A propensity scored full matching model including age, status at transplant, number of transplantations and minimal residual disease (MRD) at transplant, was calculated in order to dissect the role of conditioning regimen in determining the outcome of patients.

Results: Patients diagnosed with acute lymphblastic leukemia (ALL) or acute myeloblastic leukemia (AML) at a median age of 10.1 years underwent HSCT in Rome (n=225) or Tuebingen (n=70). Overall, patients treated in Rome presented with a more favorable risk profile, most undergoing first transplantation in complete remission, and received total body irradiation (TBI) as part of the conditioning regimen. In contrast, the majority of patients treated in Tübingen had an unfavorable risk profile, frequently undergoing second or subsequent transplantation for refractory disease, and received melphalan-based conditioning. In details, the majority of patients undergoing HSCT in Rome received the first transplantation (n=195/225, 87%) in complete remission (n=196/225, 87%), whereas in Tuebingen, many patients underwent the second or third transplantation (n=48/70, 69%), and n=26 patients transplanted in non-remission. For patients in first or second CR, 3-year event-free survival (EFS) was 75% (69-81; 95 CI) in Rome vs. 46% (27-76; 95 CI) in Tuebingen ($p<0.001$). The propensity scored matching model calculated was not reliable for AML patients as not enough matching pairs could be identified, while it was well applicable to ALL patients. The model included age, status at transplant, number of transplantations and minimal residual disease (MRD) at transplant, and showed that the type of conditioning regimen used (TBI- vs. Melphalan-based) was a highly predictive prognostic factor for EFS in ALL patients with a HR of 0.24 [0.10-0.57; 95 CI, $p=0.001$].

Conclusions: Matched-pair analysis of patients with comparable risk profiles demonstrated that a TBI-based conditioning regimen significantly improved event-free survival compared with a melphalan-based approach in children with ALL. Despite advances in haploidentical stem cell transplantation, survival outcomes remain suboptimal in ALL or AML patients with an unfavorable risk profile. In this high-risk subgroup, HSCT might be used as a platform for subsequent post-transplant interventions, such as immunotherapy with therapeutic antibodies or cellular therapy.

Disclosure: No conflicts of interest to disclose.

B163

EFFICACY AND SAFETY OF MELPHALAN/TBI-BASED CONDITIONING REGIMENS (MCAC/TCAC) FOR AUTOLOGOUS HSCT IN ADULT ACUTE LYMPHOBLASTIC LEUKEMIA: A MULTICENTER, PROSPECTIVE COHORT STUDY

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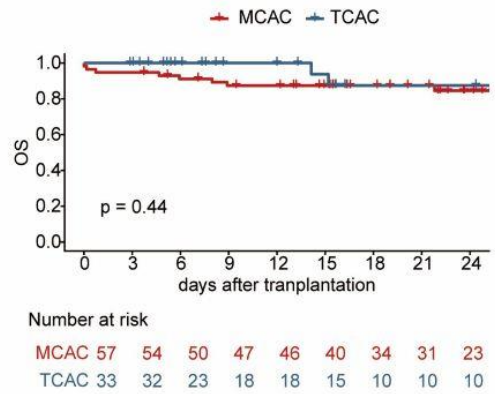
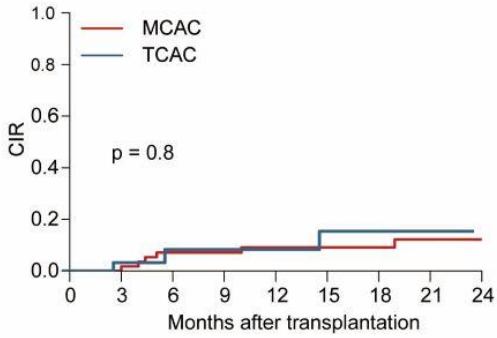
Background: Autologous hematopoietic stem cell transplantation (auto-HSCT) is a primary consolidation option for adult acute lymphoblastic leukemia (ALL) patients with sustained minimal residual disease (MRD) negativity, valued for its safety and donor independence. While traditional TBI-based conditioning is effective, its use is limited by poor accessibility and severe long-term toxicities. Consequently, we initiated a prospective, multicenter trial to evaluate a novel melphalan-based conditioning regimen for adult ALL undergoing auto-HSCT.

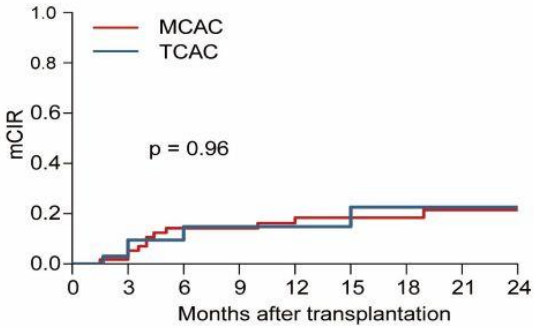
Methods: From Oct 2023 to Apr 2025, 90 B-ALL patients were enrolled, assigned based on TBI availability and patient preference. Eligibility required sustained MRD negativity (and complete molecular response for Ph+ patients) within three chemotherapy cycles. Exclusion criteria included CNS leukemia, extramedullary disease, ETP-ALL, Ph-like ALL, or T-ALL. The MCAC regimen comprised melphalan (70 mg/m², days -8, -7), cyclophosphamide (40 mg/kg, days -6, -5), and cladribine (5 mg/m²) plus cytarabine (2 g/m²) on days -4 to -2. The TCAC regimen used fractionated TBI (10 Gy total) followed by identical chemotherapy.

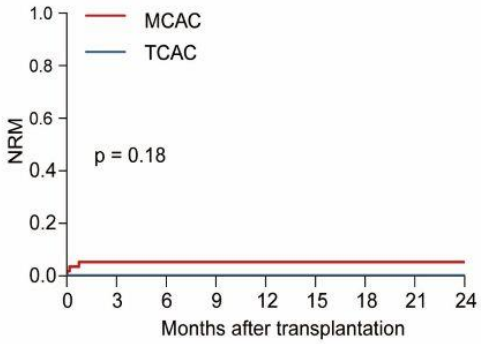
Results: A total of 90 adult ALL patients were enrolled, with 57 in the MCAC group and 33 in the TCAC group. The MCAC and TCAC groups were comparable at baseline, with no significant differences in age, sex, infused cell dose, disease type, or risk stratification. The median follow-up period was 16.5 months. Engraftment kinetics were comparable between the MCAC and TCAC arms, with a median time to neutrophil engraftment of 11 vs 12 days (p=0.3) and platelet engraftment of 17 vs 18 days (p=0.4), respectively.
At 18 months, survival outcomes were comparable between the MCAC and TCAC groups. The OS rate was 87% (95% CI, 79-97%) for MCAC vs 88% (95% CI, 73-100%) for TCAC (p=0.44). The cumulative incidence of relapse (CIR) was also similar at 9% (95% CI, 3-19%) vs 15% (95% CI, 3-36%) (p=0.8), as was molecular CIR at 18% (95% CI, 9-30%) vs 23% (95% CI, 7-44%) (p=0.96). Non-relapse mortality (NRM) was 5% (95% CI, 1-13%) in the MCAC group and 0% in the TCAC group (p=0.18).
In subgroup analysis, Ph+ B-ALL patients appeared to benefit more from the MCAC regimen (18-month mCIR: 19% vs 46%, p=0.24), while Ph- B-ALL patients seemed to favor the TCAC regimen (mCIR: 18% vs 0%, p=0.12); however, neither difference was statistically significant.
The incidence of Grade 3-4 toxicities during conditioning for MCAC versus TCAC group was: diarrhea (8 [14%] vs 0), hepatic dysfunction (2 [3.5%] vs 0), and oral mucositis (2 [3.5%] vs 1 [3%]). Other adverse events in MCAC group, included engraftment syndrome (4 [7%]), cardiac dysfunction (3 [5.3%]), and cerebral hemorrhage (1 [1.8%]). In TCAC group, notable events included engraftment syndrome (3 [9%]) and gastrointestinal bleeding (2

[6%]).









Conclusions: These preliminary findings suggest that the MCAC regimen appears to be a viable and safe alternative to TBI-based conditioning for auto-HSCT in adult ALL patients who achieve and sustain early MRD negativity. However, as enrollment in the TBI-based conditioning arm is not yet complete and the follow-up duration for both groups remains short, long-term efficacy and safety require further investigation.

Clinical Trial Registry: ChiCTR2200063863； https://www.chictr.org.cn/

Disclosure: The authors represent that they have no other conflicts of interest.

B164

COMBINATION OF 7.5 MG/KG ATG WITH BASILIXIMAB AS AN EFFECTIVE REGIMEN FOR PATIENTS WITH SEVERE INFUSIONAL SIDE EFFECTS IN HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The granulocyte colony-stimulating factor (G-CSF)/antithymocyte globulin (ATG)-based protocol is widely employed in haplo-hematopoietic stem cell transplantation (HSCT). However, ATG-associated severe infusional side effects(ISE) necessitates drug discontinuation, which cumulatively increases graft-versus-host disease (GVHD) risk. Accordingly, at our center, any patient that with severe ISE during the ATG course, the ATG dosage was reduced to 7.5 mg/kg and basiliximab was added.

Methods: To evaluate the efficacy and safety of this regimen in patients with ATG associated severe ISE compared to a control group (patients without severe ISE) administered the classical protocol (ATG 10 mg/kg). We conducted a single-center, retrospective, case-pair cohort study included 544 consecutive patients diagnosed with hematological malignancies that underwent haplo-HSCT at the Peking University People's Hospital between January 2023 and December 2024. Among them, 30 patients received 7.5 mg/kg ATG combined with basiliximab. Propensity score matching (PSM) ratio using nearest-neighbor matching was used to minimize the impact of potential confounders, matching 90 patients who underwent haplo-HSCT with ATG 10 mg/kg. Ultimately, 120 patients were included in the study.

Results: Till 18 September 2025, the median follow-up time was 485 days (range: 21–962) post-HSCT. Cumulative incidences of grades I–IV and II–IV acute GVHD were comparable between the two groups (23.3±7.8% vs. 26.7±4.6%; 6.7±4.6% vs. 14.4±3.7%). Similarly, the 1-year cumulative incidences of moderate-to-severe chronic GVHD (13.8±6.6% vs. 8.0±2.9%), did not differ significantly between the two groups.
One patient in the ATG 7.5 mg/kg + CD25 group did not achieve white blood cell (WBC) engraftment, and one patient in the ATG 10 mg/kg group also failed to achieve WBC engraftment. The cumulative incidence of platelet engraftment on day 100 were similar between the two groups (83.3±7.4% vs. 93.3±2.8%), with median engraftment times of 15 and 13 days post-HSCT, respectively. The 1-year cumulative incidences of relapse (6.9±4.9% vs. 14.8±3.8%), The 1-year cumulative incidences of TRM (16.7±6.9% vs. 12.2±3.4%) and the cumulative incidence of Cytomegalovirus and Epstein-Barr virus viremia at 180 days post-HSCT did not differ significantly between the two groups. At 1 year post-HSCT, the probabilities of overall survival and disease-free survival, were 79.7% vs. 80.4% and 76.4% vs. 72.9% for the ATG 7.5 mg/kg+CD25 and ATG 10 mg/kg groups, respectively.

Conclusions: Overall**,** the combination of 7.5 mg/kg ATG with basiliximab represents a feasible and effective protocol for treating patients who develop severe ISE during ATG treatment.

Disclosure: The authors declare no financial or commercial conflict of interest.

B165

FROM PBPK TO BEDSIDE: VIRTUAL TWIN–GUIDED FLUDARABINE DOSING IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Fludarabine is a key lymphodepleting agent in conditioning regimens before hematopoietic stem cell transplantation (HSCT). Yet, its pharmacokinetics show marked interpatient variability in children, contributing to suboptimal exposure–outcome relationships despite body surface area–based dosing. Physiologically based pharmacokinetic (PBPK) virtual twin (VT) approaches allow integration of patient-specific physiology, including renal function and protein binding, and may support model-informed precision dosing (MIPD) in pediatric HSCT.

Methods: A whole-body PBPK model for fludarabine and its main metabolites (fludarabine-hypoxanthine and fludarabine triphosphate) was developed in PK-Sim® using literature-derived physicochemical and pharmacokinetic data, and optimized with a middle-out strategy in adult HSCT cohorts. The model was then scaled to pediatrics by implementing age-dependent physiological changes and validated against published pediatric concentration–time data, including intracellular triphosphate levels. For VT simulations, individual virtual twins were generated for a subset of pediatric HSCT patients receiving intravenous fludarabine, by replacing population PK-Sim® default values with observed values such as renal function (estimated or measured glomerular filtration rate, eGFR/nGFR), hematocrit, and serum protein concentrations via a plasma protein scale factor (PPSF). Model performance was assessed by comparing predicted and observed total and unbound plasma $AUC_{0-->24h}$ using mean and geometric mean fold error (MFE, GMFE), absolute average fold error (AAFE), proportions of predictions within predefined fold-error ranges, Deming regression, and Bland–Altman analyses.

Results: In adults and external pediatric datasets, the PBPK model captured fludarabine and metabolite disposition across dose levels, with most observed concentrations and AUCs falling within the 0.8–1.25 bioequivalence bounds, and urinary excretion consistent with reported renal elimination. In the pediatric VT cohort, the demographics-only model slightly underestimated exposure but already achieved acceptable accuracy, with approximately 90% of $AUC_{0->24h}$ values for total and unbound fludarabine concentrations within a two-fold range of observed data and AAFE below 2.0. Informing the VT model with PPSF improved prediction of total plasma exposure, whereas incorporating measured nGFR better reflected true renal clearance; the combined PPSF and nGFR-informed VT model yielded the lowest bias, and

most favorable MFE (about 0.91 and 0.88 for total and unbound compartments, respectively), with Deming regression slopes closest to unity and minimal Bland–Altman bias. In contrast, models simultaneously informed by PPSF, hematocrit, and GFR did not further enhance accuracy and sometimes increased variability.

Conclusions: This PBPK-based VT framework reliably predicts individual fludarabine exposures in pediatric HSCT patients across age groups, supporting its use in selecting initial doses and refining conditioning regimens. Among the tested configurations, the PPSF and nGFR-informed VT model offers the best balance between accuracy and bias for both total and unbound fludarabine and is therefore the preferred model to retain for VT-guided MIPD in this setting. Implementation of this approach in clinical practice could help target exposure windows associated with improved HSCT and cellular therapy outcomes, ultimately contributing to safer and more effective conditioning in children.

Clinical Trial Registry: ACTRN12612000544875 in the Australian clinical trial registry Website : https://www.anzctr.org.au/TrialSearch.aspx#&&conditionCode=&dateOfRegistrationFrom=&interventionDescription=&interventionCodeOperator=OR&primarySponsorType=&gender=&distance=&postcode=&pageSize=20&ageGroup=&recruitmentCountryOperator=OR&recruitmentRegion=&ethicsReview=&countryOfRecruitment=&registry=&searchTxt=ACTRN12612000544875&studyType=&allocationToIntervention=&dateOfRegistrationTo=&recruitmentStatus=&interventionCode=&healthCondition=&healthyVolunteers=&page=1&conditionCategory=&fundingSource=&trialStartDateTo=&trialStartDateFrom=&phase=

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Khalil Ben Hassine is an employee of AC Immune SA.
Fanny Gonzales is on the advisory board for MSD.
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B166

A SIMULATED PK/PD INVESTIGATION OF RATG, FLUDARABINE, AND THIOTEPA IN HAPLO-IDENTICAL TRANSPLANT FOR SICKLE CELL DISEASE; A VANDERBILT GLOBAL HAPLO-IDENTICAL BMT LEARNING COLLABORATIVE (VGC^2) ANALYSIS

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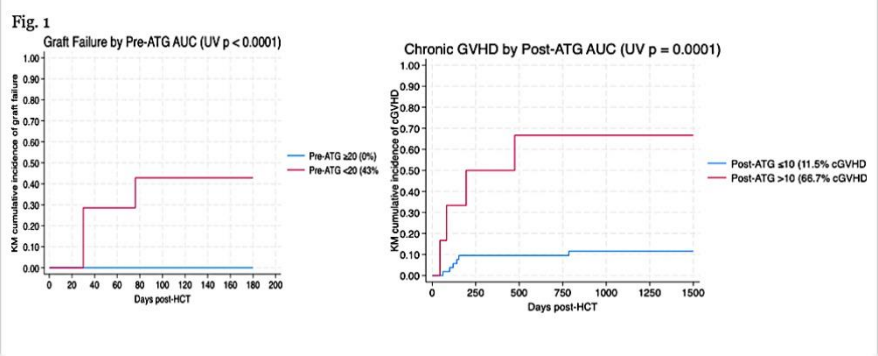
Background: Outcomes of haplo-identical hematopoietic cell transplant (haplo-HCT) for sickle cell disease (SCD) are promising in adults, with no graft failure (GF) and low rates of

chronic graft-versus-host disease (cGvHD) (Blood, 2024). However, outcomes in participants <18 years are markedly worse, with GF occurring in 15–25% and cGvHD in up to 30% of pediatric patients. We hypothesized that variability in conditioning agent exposure (pharmacokinetics, PK) between weight cohorts correlates with these clinical differences.

Methods: SCD patients on the VGC2 haplo-HCT protocol were included. They received the reduced-toxicity conditioning including rabbit anti-thymocyte globulin [rATG], Thiotepa [TT], Fludarabine, and 200cGy TBI. GVHD prophylaxis consisted of post-HCT cyclophosphamide (PTCy), sirolimus, and mycophenolate mofetil. rATG, TT, and Fludarabine exposures were simulated using validated population-PK models on the InsightRx platform. Main outcomes were GF and moderate/severe cGvHD. Based on cohort distributions and published data, we evaluated Pre-HCT rATG exposure) <20 vs ≥20 AU·day/mL and post-HCT rATG exposure ≤10 vs >10 AU·day/mL. Cumulative incidence was estimated using Kaplan–Meier failure curves with univariate log-rank tests.

Results: 59 patients were included (8 participants <18 years); median age was 23 years (range 8–52). Three patients (all<18 years) experienced GF, and 10 total developed moderate/severe cGvHD. Median pre-HCT rATG exposure was 25 AU·day/mL (range 9.94–36.7) while median post-HCT rATG exposure was 5.39 AU·day/mL (range 0.289–16.2). Combined thiotepa + TEPA exposure was median 54.1 mg·h/L (range 36.2–73.2). Median fludarabine exposure was 21.7 mg·h/L (range 18.8–36.3). Patients with pre-HCT rATG exposure of < 20 AU·day/mL had a 180-day GF rate of 43% (3 out of 7), compared to 0% (0 out of 52) with pre-HCT rATG-exposure ≥20 AU·day/mL (p<0.0001) (Fig.1 Right). All GF events occurred in the low-exposure group and were associated with negligible donor CD3 T-cell chimerism (median 0%, range 0–15%). Conversely, patients with pre-HCT rATG exposure ≥20 AU·day/mL, achieved high chimerism (median 100%; range 27%-100%). Patients with post-HCT rATG exposure >10 had a 66.7% (4/6) cGVHD rate, compared to 11.5% (5/53) in those with post-HCT rATG exposure ≤10 (p=0.0001; Fig. 1Left). Although exposures to TT/TEPA and fludarabine were highly variable, in this small cohort of 59, exposures were not related to the outcomes of interest.



Conclusions: This preliminary analysis suggests that pre-HCT rATG underexposure is associated with GF, while post-HCT rATG overexposure is associated with cGVHD. Inadequate recipient immune-ablation, and interference of rATG with alloreactive T-cell depletion by PTCy might be the cause for this. A larger dataset, potentially including patients from the BMT-CTN 1507 trial, is needed to confirm these findings. Model-based dosing of rATG and possibly also

TT and Fludarabine (targeting to optimal exposures), might improve the outcomes and needs to be tested in a prospective trial.

Disclosure: Jaap-Jan Boelens reports consulting and/or advisory board relationships with Merck, Alexion, Rocket Pharmaceuticals, Papillon Bio, Sobi, Sanofi, and the Abu Dhabi Stem Cell Center, and participation on Data Monitoring Committees for Advanced Clinical and CTI.
James A. Connelly reports no conflicts of interest related to this study.
Haley J. Hawkins reports no conflicts of interest.
Adetola A. Kassim reports no conflicts of interest.
Hemalatha G. Rangarajan reports no conflicts of interest.
Janel Long-Boyle reports no conflicts of interest.
Kanayo Nwankwo reports no conflicts of interest.

B167

ASSOCIATION BETWEEN BUSULFAN EXPOSURE AND OVERALL SURVIVAL AND TOXICITY IN HAPLOIDENTICAL HAEMATOPOIETIC STEM CELL TRANSPLANT WITH MYELOABLATIVE CONDITIONING – A PROSPECTIVE, MULTICENTRE ANALYSIS

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Background: Busulfan(Bu) is an alkylating agent used in myeloablative conditioning (MAC) for haematopoietic stem cell transplant (HSCT). Bu has highly variable pharmacokinetics (PK) and there is currently no consensus regarding the optimal target range, particularly in the haploidentical setting (haplo-HSCT). To the best of our knowledge, this is one of the first prospective studies exploring outcomes associated with Bu exposure in adult patients undergoing busulfan-fludarabine MAC prior to haplo-HSCT.

Methods: This prospective subgroup analysis was derived from the phase 2 study of peripheral blood haplo-HSCT (ANZHIT-1 study), conducted between 2015 and 2020.[1] Patients from four centres with Bu PK assessment were included. Standard conditioning comprised intravenous fludarabine and Bu 3.2 mg/kg on days −5 to −2. In a subset of 10 patients, the day -5 was given as 1.6 mg/kg divided over D−5 and −4, with PK monitoring guiding Bu dose adjustment commencing on day−3. Bu area-under-the-concentration–time curves ($AUC_{0-\infty}$), calculated using trapezoidal rule, were available for the first dose in 28 patients and for both first and last doses in 18 patients. Clearance (CL) was calculated as dose/AUC, and cumulative AUC (cAUC) as total Bu dose divided by average CL (first and last day). Paired Wilcoxon test compared CL between days 1 and 4. Kaplan–Meier survival

analysis and multivariate Cox regression assessed the impact of Bu cAUC above versus below the median (79.7 mg/L·h) on outcomes.

Results: 28 patients with haematological malignancies (median age 40 years) were included. At a median follow up of 686 days, (range 76–1522 days), 5 experienced TRM within 1 year due to chronic GvHD(2), acute GvHD, VOD, and graft failure. There were 2 deaths secondary to relapse and 1 death due to multiorgan failure.
Median Bu AUC was 18.9 mg/L.h(IQR:15.9–22.7) on day 1 and 20.4 mg/L.h(IQR:19.1–23.5) on day 4; a significant decrease (median 14%) in CL was observed (p<0.005). Median cAUC was 79.7mg/L.h overall for 18 patients who had AUC measured after the last dose. Dose reductions (median −24%) in 13 patients maintained AUC despite declining CL with no adverse effect on outcomes. Median days to chimerism was 50; median donor cells 100%. cAUC above or below 79 mg/L.h was associated with a median of 46 and 54 days to chimerism respectively. Two graft failure and two (of 3) VOD cases occurred with cAUC >79.7 mg/L·h despite Bu dose reduction on day -2. Mean OS was 3.96 years and longer with Bu cAUC >79.7 mg/L·h (3.96 vs 2.69 years; p = 0.151). Mean DFS was 3.6 years. In multivariate analysis, higher cAUC tended to have a protective effect on OS (HR 0.214, 95% CI 0.04 – 1.2, p =0.078). Graft failure predicted worse OS, TRM and DFS (p< 0.05).

Conclusions: In haplo-HSCT, higher Bu cAUC was associated with a trend to longer mean survival time, however was associated with VOD. Larger studies are required to define the optimal AUC target and clarify the impact of Bu exposure on outcomes in haploidentical HSCT.

Disclosure: Nothing to declare.

B168

LONG-TERM FOLLOW-UP WITH TREOSULFAN BASED CONDITIONING REGIMEN IN HEMATOLOGICAL MALIGNANCIES: A SINGLE CENTER EXPERIENCE

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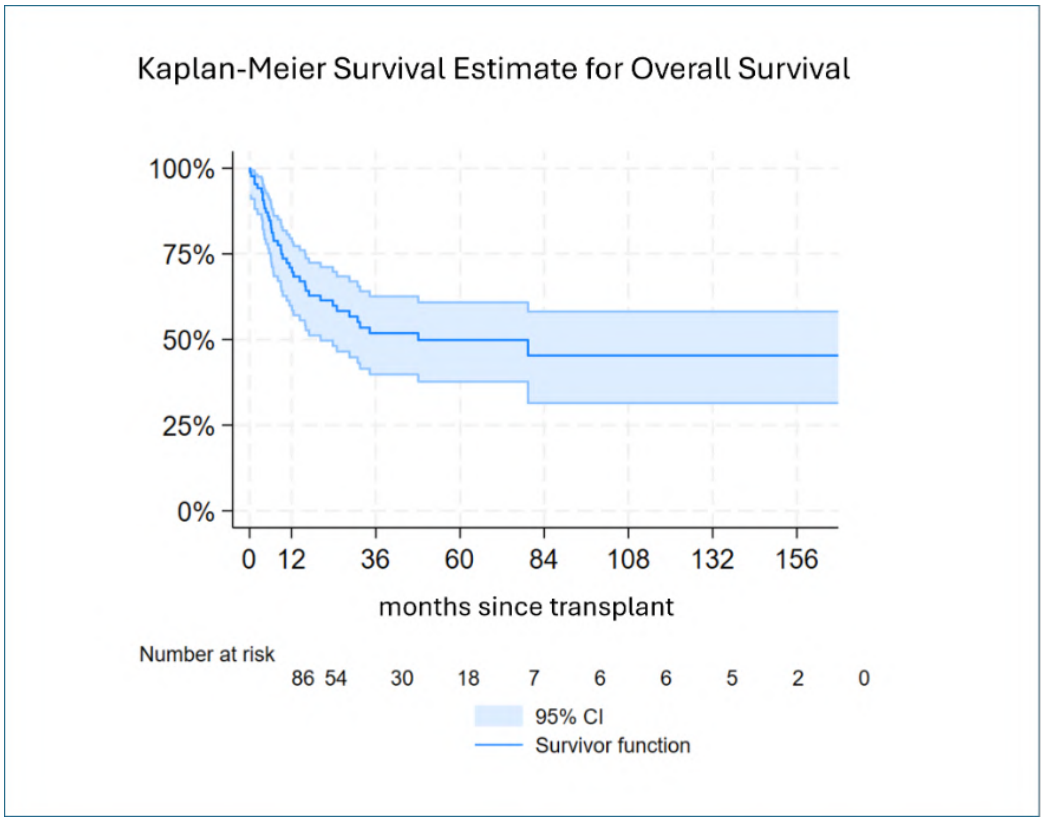
Background: Treosulfan is increasingly used in conditioning regimen for allogeneic hematopoietic stem-cell transplantation (HSCT) due to its myeloablative activity and immunosuppressive effect with low toxicity. Its favorable toxicity profile supports its use for malignant and non-malignant indications, including in older or frail patients. Evidence from real-world clinical practice, especially in adult populations, remains limited and heterogeneous.

Methods: We conducted a monocentric retrospective analysis of adult and pediatric patients who underwent HSCT at our center between 2006 and 2024. All patients received treosulfan-based conditioning (total dose 30–42 g/m²) plus fludarabine. Graft Versus Host Disease

(GvHD) prophylaxis was administered following institutional protocols. Outcome parameters analyzed were engraftment, acute and chronic GvHD, non-relapse mortality (NRM), relapse incidence, overall survival (OS), and disease-free survival (DFS). Statistical analyses were performed using STATA 19.0. OS and DFS were estimated using the Kaplan–Meier method, and NRM with cumulative incidence analysis.

Results: A total of 90 patients (50 males and 40 females) underwent HSCT, with a median age at transplant of 57.5 years (range 4–75). Treosulfan was administered at a total dose of 14 g/m² in 66 patients, 12 g/m² in 18 patients, and 10 g/m² in 6 patients, according to patient-specific characteristics. The analysis included 86 patients who had complete data available. Underlying diseases, patients' stratification according to HCT comorbidity index, stem cell sources and donor type are detailed in Table 1. GvHD prophylaxis was administered considering donor type and institutional protocols, as reported in Table 1. Neutrophils and platelets engraftment occurred at a median of 20 (IQR 18-24 days) and 24 days (IQR 18-33 days), respectively. The cumulative incidence of acute III-IV grade GvHD was 34.9%: grade III-IV aGVHD was observed in 8% of patients. The cumulative incidence of chronic GvHD was 12.8%. Veno-occlusive disease (VOD) occurred in two patients, one of whom had pre-existing portal hypertension due to myelofibrosis. We observed 1-year NRM of 19.8%; the relapse incidence was 10.5%. OS at 1, 3 and 5 years after HSCT was 71%, 51%, and 50% respectively. DFS at 1 year and 5-year post transplant were 58% and 41% respectively.



Charateristics	value n (%)
Diagnosis	
AML	57 (66.2%)
MDS	13 (15.3%)
MPN	14 (16.5%)
Other	2 (2.3 %)
Comorbidities (HCT-CI / Sorror Index)	
Low risk	7 (8.1%)
Intermediate	42 (48.8%)
High risk	22 (25.6%)
Missing	15 (17.5)
Donor type	
Sibling	24 (27.9%)
Matched unrelated donor (MUD)	42 (48.8%)
Haploidentical	16 (18.6%)
Mismatched unrelated donor (MMUD)	3 (3.4%)
Cord blood	1 (1.2%)
Stem cell source	
Peripheral blood (PBSC)	67 (77.9%)
Bone marrow	18 (20.9%)
Cord blood	1 (1.2%)
GvHD prophylaxis	
ATG + CSA + MTX	37 (43 %)
CSA + MTX	28 (32.6%)
PT-Cy + CSA + MMF	18 (20.9%)
Other	3 (3.5%)
GvHD	
Acute GvHD	30 (34.9%)
Grade III-IV aGVHD	7 (8.1%)
Chronic GVHD	11 (12.8%)
Moderate-severe cGvHD	7 (8.1%)

Conclusions: This study is the longer monocentric real-world experience with treosulfan-based conditioning. In this study, we confirm that treosulfan offer a manageable safety profile, characterized by low organ toxicity and favorable engraftment kinetics. This is particularly beneficial for older or frail patients, where reduced toxicity is a priority. One-year OS and DFS rates align with previously reported clinical trial data. These findings reinforce the role of treosulfan as a versatile conditioning agent and highlight the need for further

prospective studies to better define its optimal indications and long-term benefits in real-world clinical practice.

Disclosure: Nothing to declare.

B169

HAPLOIDENTICAL HCT IN ADULTS WITH A NON-TBI CONDITIONING REGIMEN: A 10-YEAR SINGLE-CENTER COHORT

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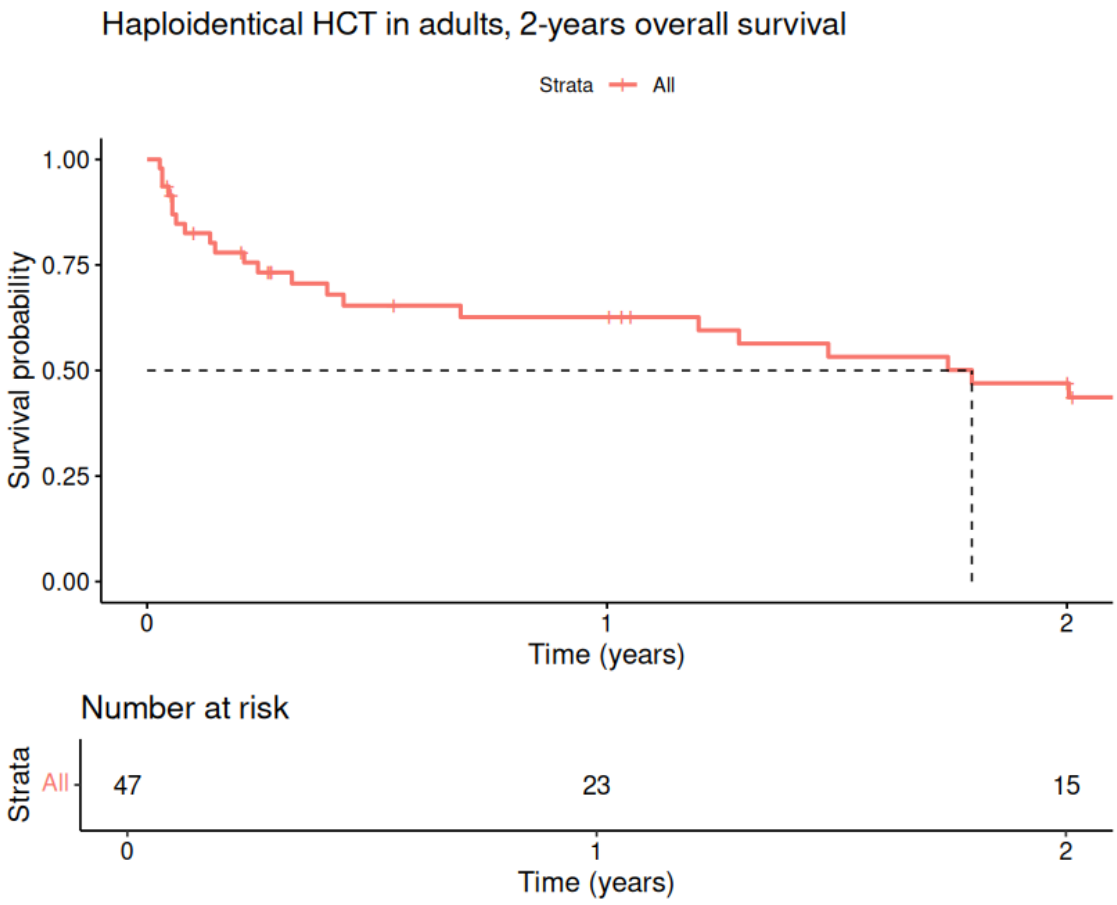
Background: The use of haploidentical donors has enabled hematopoietic cell transplantation (HCT) for a larger number of patients with hematologic malignancies. Total body irradiation (TBI) is widely used in conditioning regimens for this donor type. However, its availability is limited in resource-constrained regions.

Methods: We conducted a descriptive analysis of data regarding haploidentical allogeneic transplants performed in adults aged 18 years or older between 2016 and 2025, indicated for hematologic malignancies, at a university hospital in Northeast Brazil. Survival analysis was performed using the Kaplan-Meier method in R software (version 4.4.2).

Results:

During this period, 47 haploidentical transplants were performed. Acute myeloid leukemia was the most common indication (n = 19), followed by acute lymphoblastic leukemia (n = 16). Peripheral blood was the predominant stem cell source (n = 46). All patients received a conditioning regimen containing busulfan and fludarabine. GVHD prophylaxis consisted of cyclosporine, mycophenolate mofetil, and post-transplantation cyclophosphamide (PTCy). The 1-year and 2-year overall survival (OS) rates for this cohort were 63% and 47%, respectively. Median survival was 1.8 years.

Regarding the older adult subgroup, 14 transplants were performed during this period in patients 50 years or older, with ages ranging from 53 to 66 years. Most received HSC from offspring (n = 12) and siblings (n = 2). Regarding conditioning intensity, 11 transplants utilized reduced-intensity conditioning (RIC). The most frequent severe toxicities (grade 3 or 4) were mucositis (n = 7), hepatic toxicity (n = 2), and vomiting (n = 2). The median time to neutrophil and platelet engraftment was 16 and 21 days, respectively. Two patients developed sinusoidal obstruction syndrome (SOS), progressing to death. Transplant-related mortality (TRM) occurred in 21% of cases (n = 3). Overall survival was 79% at 1 year and 67% at 2 years. Median survival was 2.1 years. Causes of death were relapse (n = 3), SOS (n = 2), infection (n = 1), and secondary malignancy (n = 1).



Conclusions: Haploidentical allogeneic transplantation remains a viable curative option for adults. Non-TBI conditioning regimens may facilitate the procedure in resource-limited regions, in addition to avoiding potential toxicities associated with irradiation.

Disclosure: Nothing to declare.

B171

CLADRIBINE WITH TOTAL BODY IRRADIATION AS A STRATEGY TO OPTIMIZE CONDITIONING REGIMEN IN AML AND MDS: A PROSPECTIVE STUDY OF THE POLISH ADULT LEUKEMIA GROUP

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Background: Allogeneic haematopoietic stem cell transplantation (allo-HCT) is a standard of care for patients with acute myeloid leukemia (AML) and for intermediate or high-risk myelodysplastic syndrome (MDS). Studies from the the Polish Adult Leukemia Group (PALG) have demonstrated that adding cladribine to induction therapy increases the chances of achieving complete remission and improves overall survival. Both cladribine and Ara-C enhance Ara-CTP levels in leukemia blasts; however, only cladribine exhibits direct cytotoxic and hypomethylating effects, which accounts for the observed differences in efficacy.

Methods: The CLARA study is a project funded by the Medical Research Agency. The aim of this study is to analyze the efficacy and safety of a conditioning regimen combining cladribine with total body irradiation (TBI).
The analysis included 40 patients, with a median age of 45 years (range: 21–60). Patients received allo-HCT from either siblings (15 patients) or unrelated donors (25 patients). The conditioning regimen involved cladribine administration from days -8 to -4, followed by TBI (4Gy in once-daily fractions) from days -3 to -1. Immunosuppressive therapy was based on the donor type: CNI + Mtx + ATG for HLA-matched donors, and PTCy + Tak + MMF for HLA-mismatched donors. Peripheral blood was the stem cell source.

Results: The current median follow-up is 22 (1-43) months. The analysis includes only patients who have been followed for at least 1 year. The 12-month probability of progression-free survival (PFS) and overall survival (OS) was 78% (± 7%). Eight patients died, seven of whom the first 6 months after allo-HCT. The causes of death were as follows: relapse (6 patients), infection complications (1 patient), and other complications (1 patient). For 14 patients, the two-year post-transplant follow-up period has not yet been completed. Grade 3 of acute GvHD was observed in 5 patients, and no cases of grade 4 were reported. Severe chronic GvHD was observed in 3 patients.

Conclusions: The myeloablative conditioning regimen consisting of TBI combined with cladribine may contribute to improved outcomes following allo-HCT for patients with AML and MDS.

Clinical Trial Registry: No

Disclosure: None

B172

IMPACT OF TMLI VERSUS TBI CONDITIONING ON TOXICITY, OUTCOMES, AND RELAPSE IN ALLOGENEIC STEM CELL TRANSPLANTATION FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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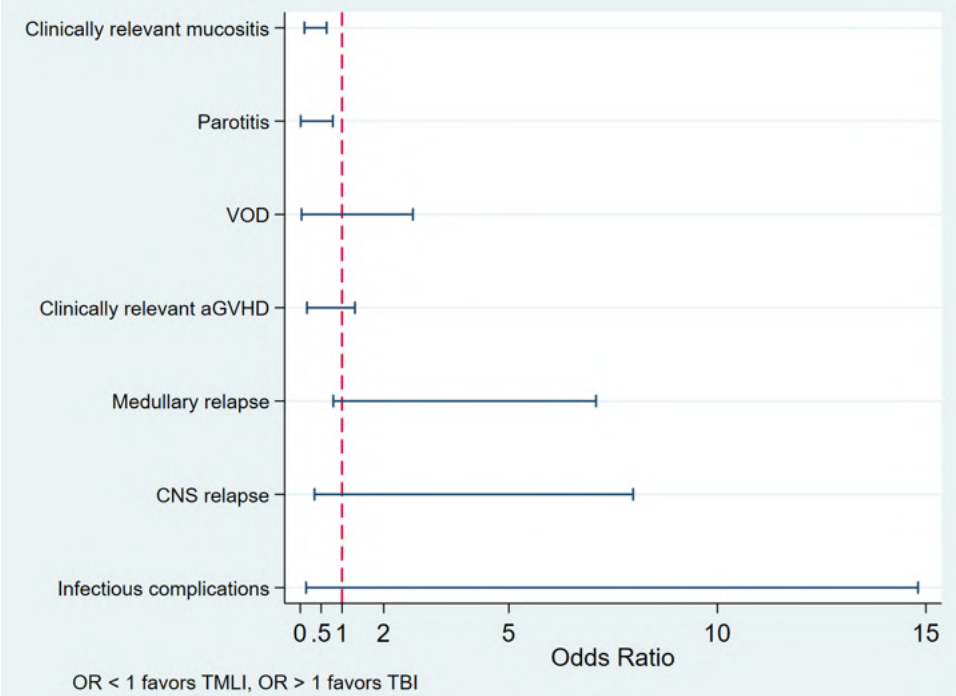
Background: Allogeneic stem cell transplantation (allo-SCT) is the standard consolidation therapy for patients with high-risk B-cell acute lymphoblastic leukemia (B-ALL) in first complete remission (CR1), for standard-risk patients with detectable minimal residual disease (MRD), and for those achieving second or subsequent remissions. Conventional conditioning regimens typically combine fludarabine or cyclophosphamide with total body irradiation (TBI).Total marrow and lymphoid irradiation (TMLI) is an innovative approach that limits toxicity compared to TBI by maximizing the preservation of healthy organs, without compromising antileukemic efficacy. The objectives were to compare the safety and relapse outcomes of TMLI versus TBI at 12 Gy dose as conditioning regimens for allogeneic stem cell transplantation in patients with B-ALL.

Methods: A retrospective study was conducted, including 90 patients with B-ALL who underwent allogenic hematopoietic stem cell transplantation at the Clínica Universidad de Navarra between September 2019 and May 2025. All patients were followed-up for a minimum of 6 months, and relevant clinical and laboratory data were collected. Data analysis was performed using STATA (StataCorp LP).

Results: The median age was 19 years-old (range 5-52) and the cohort included 39 children. 96% of the patients received post-transplant cyclophosphamide as GVHD prophylaxis. Mucositis was observed in 70% and 82% of patients in the TMLI and TBI groups, respectively. Patients receiving TMLI had a significantly lower risk of relevant mucositis (grade≥2) compared to those receiving TBI (OR 0.25, 95% CI 0.10–0.63, p<0.01). TMLI was also associated with a significantly lower risk of parotitis compared with TBI (OR 0.10, 95% CI 0.01–0.78, p=0.03). No cases of radiodermatitis were observed in the TMLI group, in contrast to the TBI group, resulting in a statistically significant difference (p=0.03). No cases of transplant-associated thrombotic microangiopathy (TA-TMA) occurred neither in the TMLI group whereas 4 cases (7%) were observed in the TBI group; however, the difference in incidence between the groups was not statistically significant (p=0.3). Sinusoidal obstruction syndrome (SOS) occurred 3% in TMLI group vs 10% in TBI group without significant association. The incidence of clinically relevant acute graft-versus-host disease (aGVHD) (grade ≥2) was lower in the TMLI group (20% vs 35%) although no association was found (p=0.14). Pulmonary function at 3 months showed no significant differences in overall toxicity (OR 0.93, p=0.88) or diffusion capacity decline (DLCO median: -15.2% TMLI vs -28.4% TBI; p=0.71). Trends toward greater declines in FEV1 (-7.01% vs -2.45%, p=0.11) and FVC (-6.28% vs -1.88%, p=0.07) were observed in TBI, without statistical significance. DLCO impairment was the most frequent pulmonary toxicity in both groups, suggesting early alveolar-capillary compromise, with comparable 3-month pulmonary risk. No association was observed between the use of TMLI and medullary or CNS relapse (OR 2.37, 95% CI 0.79–7.09 and OR 1.66, 95% CI 0.34–7.98 respectively).

	Total (n=90)	TMLI (n=30)	TBI (n=60)	p value
Age (years) (median, range)	19 (5-52)	22 (5-49)	17 (6-52)	0.01

Sex, n (%) Male Female	 59 (66) 31 (34)	 23 (77) 7 (23)	 36 (60) 24 (40)	0.1
Karnofsky-Lansky, n (%) 100 ≤90	 86 (96) 4 (4)	 30 (100) -	 56 (93) 4 (7)	0.3
HCT-CI, n (%) 0-1 ≥2	 64 (71) 26 (29)	 23 (77) 7 (23)	 41 (68) 19 (32)	0.4
Disease status, n (%) CR1 ≥CR2 SD PD	 33 (37) 51 (57) 3 (3) 3 (3)	 13 (43) 16 (53) 1 (3) -	 20 (33) 35 (59) 2 (3) 3 (5)	0.6
Donor type, n (%) MSD MUD MMUD Haploidentical	 3 (3) 16 (18) 16 (18) 55 (61)	 2 (7) 10 (33) 7 (23) 11 (37)	 1 (2) 6 (10) 9 (15) 44 (73)	<0.01
Source, n (%) Peripheral blood Bone marrow	 88 (97) 2 (3)	 30 (100) -	 58 (97) 2 (3)	0.6
EASIX score pre-conditioning, (median, IQR)	0.56 (0.33-0.97)	0.61 (0.42-0.86)	0.52 (0.32-0.97)	0.6



Conclusions: TMLI emerges as a safe radiation modality, with potentially lower rate of complications compared to TBI and no more relapses. However, further studies with larger sample sizes are needed to confirm these findings. Long-term follow-up is essential to better assess the safety profile and efficacy of this new modality.

Disclosure: The authors declare no conflicts of interest.

B173

OUTCOMES OF ALLOGENIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION USING POST-TRANSPLANT CYCLOPHOSPHAMIDE: A 5 YEAR SINGLE CENTRE EXPERIENCE

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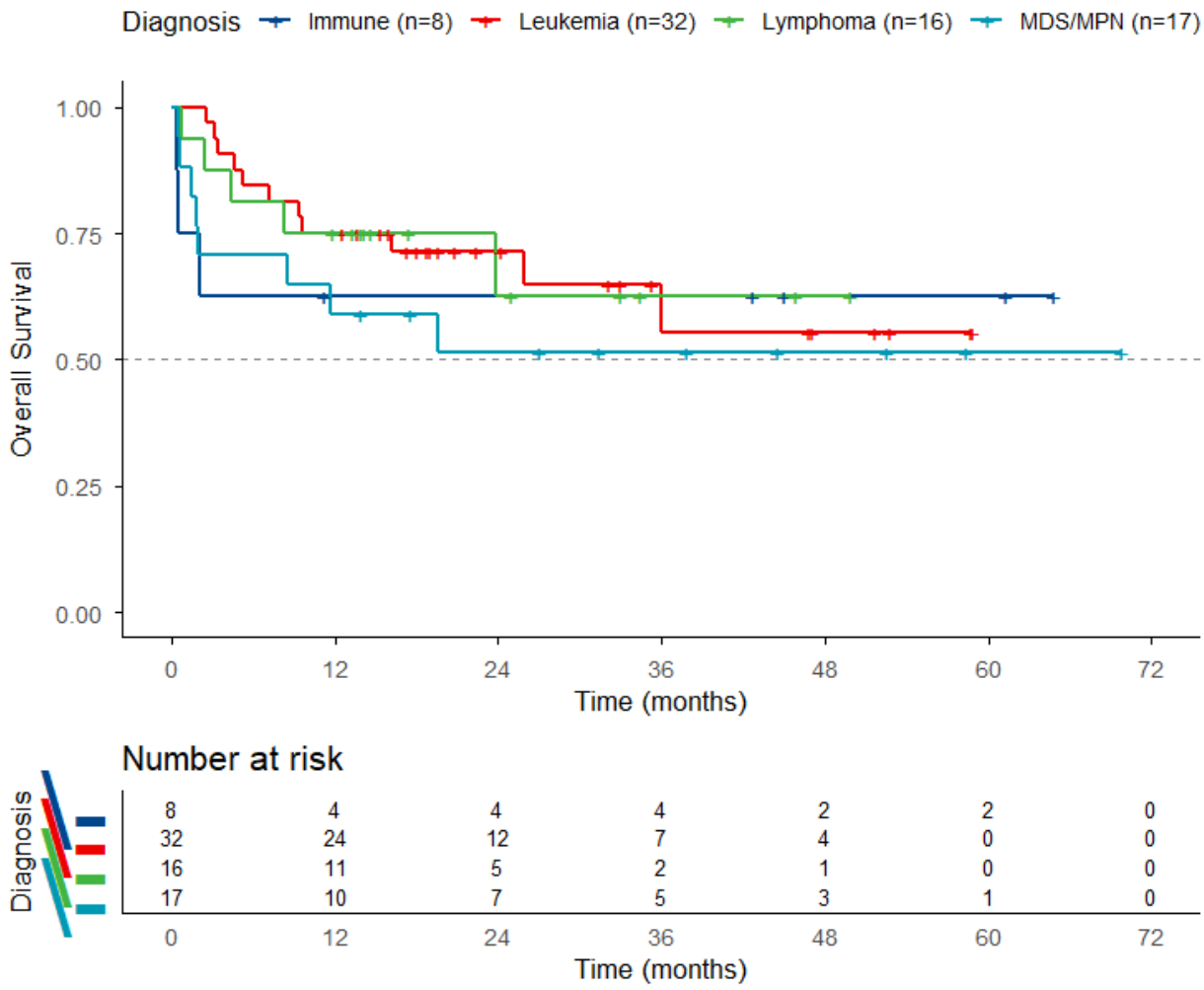
Background: Post-transplant cyclophosphamide (PTCy) has become a widely adopted strategy for T-cell depletion and graft-versus-host disease (GVHD) prophylaxis in both haploidentical and unrelated donor transplant settings. We conducted a retrospective analysis

to evaluate transplant outcomes, toxicities, infectious complications, and GVHD incidence in patients who received PTCy at our institution.

Methods: All patients who underwent allogeneic haematopoietic stem cell transplantation with PTCy between January 2020 and December 2024 were included. Clinical data were reviewed for demographics, underlying disease, transplant characteristics, survival outcomes, relapse, non-relapse mortality (NRM), infectious and non-infectious complications, chimerism, graft failure, and acute and chronic GVHD.

Results: A total of 73 patients were analysed (median age 54 years, 23 female/50 male). Underlying diagnoses included leukaemia (n=32: AML 23, ALL 5, CML 4), lymphoma (n=16), MDS/MPN (n=16), myeloma (n=1), and immune disorders including aplastic anaemia (n=8). 53 patients received haploidentical transplants and 20 received unrelated donor grafts.
All patients developed neutropenic sepsis; 38 (52%) had culture-proven bacterial infections, 2 had fungal chest infections, 33 (45.2%) patients had viral reactivations. Non-infectious complications included haemorrhagic cystitis (n=4), veno-occlusive disease (n=4), and cardiac events (n=5). Median time of neutrophil and platelet engraftment was 18 and 28 days respectively.
Acute GVHD occurred in 29 (39.5%) patients (median onset day 28), predominantly involving the skin (n=28). Cumulative incidence of grade 3 acute GVHD was 12.3% (8 skin, 2 GI, 1 liver). Chronic GVHD developed in 27 (36.9%) patients (13 mild, 9 moderate, 5 severe) with a median onset at day 210. Thirty patients (41%) did not develop any form of GVHD. Of the 48 patients alive at 1 year post HSCT, 8 patients had chronic GVHD and 4 of these were on systemic treatment.
Graft failure occurred in 7 (9.5%) patients. At 3 months, whole blood donor chimerism was >95% in 46 patients and <95% in 16; it was not assessable in 11 due to early mortality. 48 (65.7%) patients were alive 1 year post HSCT. Median total lymphocyte count was 1.47 $x10^9$/L ,CD4 +T cell count was 324 and CD8 +T cell count was 479 at 1 year.
At a median follow-up of 17 months (0–69), 46 (63%) patients were alive and 27(37%) had died. Relapse occurred in 13 patients, and 15 experienced NRM. 12 (16.4%) patients died within day 100 post-transplant due to infective complications. Of these 1 patient each has stage 3 gut GVHD, CMV colitis, HHV6 CNS infection and VOD along with concomitant sepsis. 54.7% patients were GVHD free and relapse free at 1 year.



Conclusions: PTCy-based GVHD prophylaxis in our cohort was associated with acceptable rates of acute GVHD and manageable chronic GVHD. Infectious complications, particularly bacterial sepsis and viral reactivation remained frequent. Overall survival and outcomes were consistent with contemporary PTCy-based transplant data. Further prospective evaluation is warranted to optimize infection prevention and reduce non-relapse mortality.

Disclosure: We have no disclosures.

B174

FLUDARABINE PLUS TREOSULFAN CONDITIONING FOR OLDER AND COMORBID PATIENTS BEFORE ALLOGENEIC HSCT - A RETROSPECTIVE ANALYSIS IN A REAL-WORLD COHORT

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Background: Reduced-intensity conditioning (RIC) regimens, such as fludarabine/treosulfan (Flu/Treo), offer promising outcomes for older or comorbid patients undergoing allogeneic hematopoietic stem cell transplantation (HSCT). This study evaluates the efficacy and safety of Flu/Treo in an AML cohort at the Medical University of Vienna, comparing our findings to those reported in Beelen et al. (Am. J. Hematol. 2022).

Methods: In our retrospective, IRB approved study we included all AML patients who received Flu/Treo-based HSCT between 2020 and 2024 at our institution. Baseline characteristics and outcomes including overall survival (OS), relapse, non-relapse mortality (NRM), and graft-versus-host disease (GvHD) were recorded. Outcomes were assessed by plotting Kaplan-Meyer curves and evaluated against data from Beelen et al.. Moreover, multivariate COX-regression analyses were computed to identify significant predictors of outcomes.

Results: Our final study included 138 AML patients. Sixty-seven percent received Flu/Treo30 (treosulfan 10 g/m² for 3 days, fludarabine 30 mg/m² for 5 days), consistent with Beelen's cohort, while other regimens included Thio5Treo30Flu (16%), Thio10Treo30Flu (14%), and TreoFluCy (4%). The median follow-up was 15 months (range 8–24 months). Detailed baseline characteristics are provided in the table below.One-year OS was 81% (CI 74–88), two-year OS was 73% (CI 65–81), and three-year OS was 68%. Compared to Beelen's cohort, our Flu/Treo30 subgroup (n=92) had similar 2-year OS (75% vs. 71%) and 3-year OS (69% vs. 67%). Cox regression identified acute GvHD as a significant predictor of poor OS (HR 2.78, p = 0.01). HCT-CI ≥3 trended towards poorer OS, though not statistically significant (HR 2.24, p = 0.069). NRM at 1 year was 9.4%, at 2 years 12.5%, and at 3 years 15.6% (Beelen: 14.2% at 3 years). Relapse rates were 17.3% at 1 year, 19.3% at 2 years, and 27% at 3 years (Beelen: 25.9% at 3 years). Acute GvHD by day 100 occurred in 24%, lower than Beelen's cohort (52%). Chronic GvHD at 2 years was 14% in our cohort versus 18% in Beelen et al.

Baseline characteristics	
N=	138
Age (years)	60 [53, 76]
Male	79 (57%)
ELN2017	
favorable	22 (16%)
intermediate	48 (35%)
adverse	65 (47%)
n.a.	3 (2%)
Remission	
CR1	107 (77%)
CR2 plus	19 (14%)
NR	12 (9%)
HCT-CI	
0	54 (39%)
1 - 2	45 (33%)
≥ 3	39 (28%)
Conditioning	
FluTreo30	92 (67%)
Thio10Treo30Flu	20 (14%)
Thio5Treo30Flu	22 (16%)
TreoFC	4 (2.9%)
Donor	
Matched Sibling	20 (14%)
MUD	84 (61%)
MMUD	11 (8%)
HAPLO	23 (17%)
Immunosuppression (other than CSA, MMF)	
ATG	104 (75%)
PTCy	34 (25%)
F/U [mo]	15 [8, 24]

Conclusions: Flu/Treo conditioning demonstrated favorable survival, low relapse, and NRM, and reduced rates of acute and chronic GvHD in older, comorbid AML patients. Acute GvHD was a significant predictor of poor survival, and HCT-CI ≥3 showed a trend toward worse outcomes, though not statistically significant. These findings support Flu/Treo as an effective and well-tolerated RIC regimen in a real-world setting, confirming its potential as a viable option for elderly or high-risk AML patients. Our results, consistent with Beelen's study, further advocate for Flu/Treo as a standard regimen in clinical practice for high-risk AML patients undergoing HSCT.

Disclosure: Hildegard, Greinix: honoraria for presentations at scientific meetings from Therakos, Sanofi, Daiichi Sankyo, and Stemline.
Werner, Rabitsch: speaker's honoraria from Threakos, KiteGilead, MSD; honoraria for advisory board participation from Kite Gilead, BMS, Jhnson&Johnson, Novartis, MSD; travel support from Neovii.

B175

A FAVORABLE EFFICACY-SAFETY PROFILE: TREOSULFAN-BASED CONDITIONING IMPROVES OVERALL SURVIVAL AND LOWERS RELAPSE RISK COMPARED TO BUSULFAN IN RIC ALLO-HSCT

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a potentially curative therapeutic option for patients with malignant hematologic disorders. Conditioning regimens traditionally rely on Busulfan-based protocols, whose efficacy is well established but often limited by toxicity. Treosulfan has more recently emerged as a promising alternative to Busulfan in Reduced-Intensity Conditioning (RIC) regimens, particularly for elderly or frail patients, with a potentially more favorable therapeutic profile.

Methods: We retrospectively analyzed 316 patients aged 18-75 years undergoing allo-HSCT between March 2006 and December 2023 at our Istitution. All patients received conditioning regimens containing either Busulfan or Treosulfan. In order to improve the accuracy of the comparative analysis and reduce cohort heterogeneity, the study was restricted to patients who received exclusively RIC regimens, mainly for myeloid malignancies: by doing so, we aimed to minimize confounding factors related to variations in toxicity and myeloablative intensity. Overall survival (OS) and graft-versus-host disease-free, relapse-free survival (GRFS) were estimated using Kaplan-Meier analysis. The cumulative incidence of relapse, global GVHD, acute/chronic GVHD and non-relapse mortality (NRM) were assessed using the Gray's test for between-group analysis. Multivariate analysis for OS was performed using the Cox proportional hazards regression model.

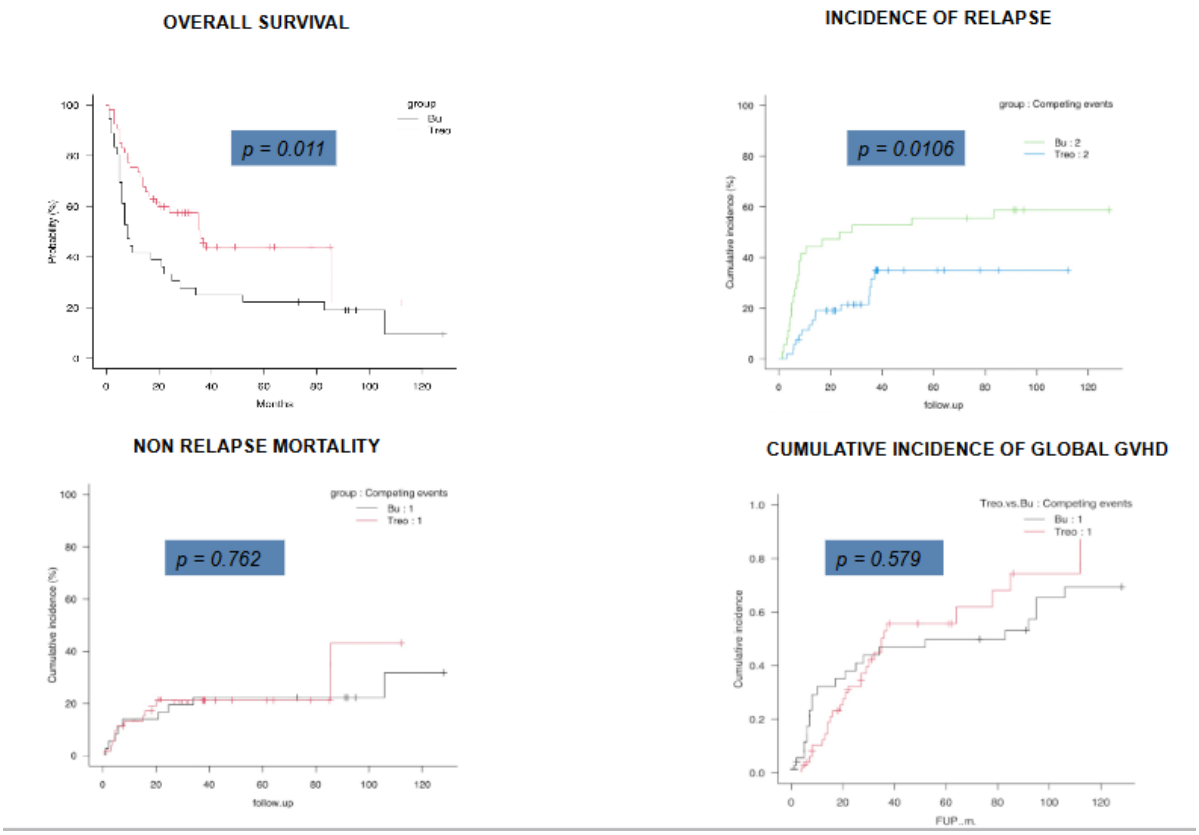
Results:

VARIABLE	OVERALL POPULATION	FB2	FT10	p-value
Patients n, (%) *N° total* *Sex M* *Sex F* *Median age at HSCT* *(Q1 – Q3)* *age at HSCT < 60 years* *age at HSCT ≥ 60 years*	90 (100) 58 (64.44) 32 (35.56) 65,4 (18,6 – 74,1) 25 (27.78) 65 (72.22)	36 (100) 23 (63.89) 13 (36.11) 64,0 (44,8 – 70,4) 10 (27.78) 26 (72.22)	54 (100) 35 (64.81) 19 (35.19) 66,3 (18,6 – 74,1) 15 (27.78) 39 (72.22)	
Main diagnosis, n (%) *AML* *MDS*	54 (60.00) 13 (14.44)	21 (58.33) 4 (11.11)	33 (61.11) 9 (16.67)	
Additional diagnosis	23 (25.56) 1 ()	11 (30.56) 1 ()	12 (22.22) 0	

B/T ALL *CML* *MM* *BPDCN* *Myelofibrosis* *MDS/MPN* *Other*	8 () 3 () 1 () 7 () 2 () 3 ()	1 () 0 1 () 7 () 1 () 0 ()	7 () 3 () 0 0 () 1 () 3 ()	
Disease status n, (%) *CR1* *>CR1* *Missing*	39 (43.33) 49 (54.44) 2 (2.22)	13 (36.11) 23 (63.89) 0 (0.00)	26 (48.15) 26 (48.15) 2 (3.70)	
Donor type n, (%) *Sex M* *Sex F* *MRD* *MUD* *UCB* *Haplo*	53 (58.89) 37 (41.11) 36 (40.00) 50 (55.56) 0 (0.00) 4 (4.44)	19 (52.78) 17 (47.22) 22 (61.11) 14 (38.89) 0 (0.00) 0 (0.00)	34 (62.96) 20 (37.04) 14 (25.93) 36 (66.67) 0 (0.00) 4 (7.41)	
Source n, (%) *PBSC* *BM*	81 (90.00) 9 (110.00)	30 (83.33) 6 (16.67)	51(94.44) 3 (5.56)	
aGVHD grade n, (%) *1* *2* *3* *4*	14 (15.56) 14 (20.57) 6 (6.67) 1 (1.11)	3 (8.33) 7 (19.44) 2 (5.56) 1 (2.78)	11 (20.37) 7 (12.96) 4 (7.41) 0 (0.00)	0.123 0.406 0.730 0.218
cGVHD grade n, (%) *Mild* *Moderate* *Severe*	5 (5.56) 10 (11.11) 6 (6.67)	4 (11.11) 4 (11.11) 1 (2.78)	1 (1.85) 6 (11.11) 5 (9.26)	0.060 1.000 0.227
GRFS n, (%) *N°* *aGVHD 3,4* *cGVHD severe* ***Relapse***	19 (33.23) 21 (8.54) 6 (5.38) ***38 (35.44)***	5 (13.89) 10 (27.78) 1 (2.78) ***21 (58.33)***	14 (25.93) 11 (20.37) 5 (9.26) ***17 (31.48)***	0.247 0.525 0.145 **0.0106**

Progression ***Death***	4 (1.90) ***57 (50.00)***	2 (5.56) ***30 (83.33)***	2 (3.70) ***27 (50.00)***	0.676 **0.001**

Our analysis included 90 patients (median age 65.4 years, range 18.6-74) who received a RIC conditioning including Fludarabine-Treosulfan (10 g/m2 for 3 days; FT10) in 54(60%) and Fludarabine-Busulfan(FB2) in 36(40%) patients, respectively (table 1).The main diagnosis was a myeloid disease (74.4%). Donors were matched related donors (MRDs) in 40% of cases, haploidentical (4.4%) or unrelated donors (55.6%). Peripheral blood was the main stem cell source.
Treosulfan-based conditioning was associated with significantly improved OS compared with Busulfan. Median OS was 8 months (95% CI: 6–22) in the Busulfan group versus 36 months (95% CI: 16–not reached) in the Treosulfan group (p = 0.011). GRFS duration was approximately four times longer in the Treosulfan group; however, despite this clinically meaningful difference, the comparison did not reach statistical significance (p = 0.247). In the Treosulfan group, the median GRFS was 34.9 (95% CI: 12.9–85.6) vs 7.9 months. Non-relapse mortality(NRM) did not differ significantly between groups (p = 0.762). By contrast, the Treosulfan cohort exhibited a significantly lower cumulative incidence of relapse (p = 0.0106), suggesting enhanced disease control. Rates of acute GVHD (grade II–IV), chronic GVHD and overall GVHD showed no statistically significant differences (p = 0.145, p = 0.525 and p = 0.579, respectively), despite differences in the temporal pattern of onset, confirming a comparable risk of GVHD associated with both regimens (figure 1). Multivariate analyses supported these findings, confirming Treosulfan as an independent predictor of improved OS without added immunologic complications .



Conclusions: Treosulfan-based conditioning demonstrated a favorable balance between efficacy and safety, showing significantly longer overall survival and a reduced risk of relapse compared with Busulfan, while maintaining similar rates of NRM and GVHD. Despite inherent methodological limitations including its retrospective design and cohort heterogeneity,these findings support Treosulfan as a valid and potentially useful option, particularly within reduced-intensity conditioning settings.

Disclosure: Nothing to declare.

B176

COMPARISON OF CARMUSTINE-, LOMUSTINE-, AND NITROSOUREA-FREE CONDITIONING REGIMENS FOR AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION IN LYMPHOMA: RESULTS FROM THE BRAZILIAN REGISTRY

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Background: Background: Conditioning regimens (CT) for autologous hematopoietic cell transplantation (auto-HCT) in lymphoma commonly include carmustine (e.g., CBV, BEAM). When carmustine is unavailable, lomustine (e.g., LEAM) is often used as an alternative. In Brazil, intermittent shortages of both agents have prompted the use of additional nitrosourea-free regimens.

Methods: Methods: We analyzed adult patients with lymphoma in complete remission who underwent auto-HCT in Brazil between 2008 and 2023 and were reported to the CIBMTR/Brazilian Registry (HCTBR). Patients were grouped according to conditioning exposure: carmustine-based, lomustine-based, or nitrosourea-free. Endpoints included disease-free survival (DFS), overall survival (OS), and early non-relapse mortality (3-month NRM). Multivariable Cox and competing-risk models adjusted for baseline clinical differences. Subgroup analyses by lymphoma subtype were performed.

Results: Results: A total of 669 patients were included: Hodgkin lymphoma (HL, n=302), large B-cell lymphoma (LBCL, n=191), and mantle cell lymphoma(MCL, n=176). CT exposure comprised carmustine-based (n=279), lomustine-based (n=216), or nitrosourea-free (n=174) regimens. Estimated 5-year DFS was similar across groups (61%, 57%, and 57%, respectively). In multivariable analysis, CT type was not significantly associated with DFS, OS, or NRM. Older age at transplant was independently associated with inferior DFS ($p<0.0001$) and OS ($p<0.0001$), and higher NRM ($p<0.0001$). Compared with HL and MCL, patients with LBCL had worse DFS ($p<0.0001$) and OS ($p=0.02$). By diagnosis, 5-year DFS was 75% for HL, 57% for MCL, and 44% for LBCL. In subgroup analyses, CT type did not influence outcomes within any lymphoma subtype.

Conclusions: In this large national cohort, outcomes after auto-HCT for lymphoma were comparable across carmustine-, lomustine-, and nitrosourea-free conditioning regimens, supporting their interchangeability when specific agents are unavailable.

Disclosure: We have no conflict of interest to declare for this study.

B178

FLUDARABINE AND TREOSULFAN MYELOABLATIVE CONDITIONING LEADS TO HIGH OS AND LOW NRM

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Background: Myeloablative conditioning regimens based on fludarabine and treosulfan (FT14) are emerging as a safe, reduced toxic alternative to busulfan-based regimens for patients with myeloid disorders undergoing an allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, real world data of this preparative regimen remain limited.

Methods: Here we report clinical data from a single center cohort in Geneva including 62 adult patients who underwent an HSCT for an hematological disorder after FT14 conditioning regimen (Fludarabine 30 mg/m2/d for 5 days and treosulfan 14 g/m2/d for 3 days), between 2019 and 2025.

Results: Overall, 62 patients were included in this retrospective study (38 with AML, 14 with MDS, and 10 with other hematological diseases). The median age at transplant was 44.5 years (range 20–63), with a median follow-up of 27 months. The majority of stem cell sources were peripheral blood stem cells (98%). Donors included sibling donors (19%), matched unrelated donors (44%), haploidentical donors (32%), and mismatched unrelated donors (5%). DRI score was low in 10%, intermediate in 74%, and high in 16% of patients. EBMT score distribution was: 1 (3%), 2 (27%), 3 (45%), 4 (18%), and 5 (7%).
At 2 years, overall survival (OS) was 85% (95% CI 75.9–95.2%), and progression-free survival (PFS) was 82.6% (95% CI 73.2–93.2%). The 2-year graft-versus-host disease-free, relapse-free survival (GRFS) was 67.8% (95% CI 56.7–81%). The 2-year cumulative incidence of relapse was 15.4% (95% CI 7.1–26.6%), while non-relapse mortality (NRM) was 1.6% (95% CI 0.1–7.6%). The cumulative incidence of grade II–IV acute GvHD at day +100 was 21% (95% CI 11.8–31.8%), and the 2-year cumulative incidence of moderate/severe chronic GvHD was 15.9% (95% CI 8.1–26.7%).

Conclusions: Our study confirms the favorable safety profile and efficacy of FT14 conditioning. Patients treated with this regimen demonstrated excellent survival, low relapse rates, and low mortality. Relapse remained the main cause of death after transplant in our cohort. Long-term toxicity requires further follow-up. Prospective randomized studies are warranted to further validate these findings.

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FS: institutional consulting fees from BMS/Celgene, Incyte, Kite/Gilead; speaker fees from Kite/Gilead,
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B179

CLINICAL STUDY OF THE TBFPTCY REGIMEN AS A CONDITIONING REGIMEN FOR ALLOGENEIC TRANSPLANTATION IN MYELOID MALIGNANCIES

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Background: Thiotepa has historically been used more frequently in conditioning regimens for umbilical cord blood transplantation, often combined with total body irradiation. It has also been part of regimens such as TBC (with busulfan and cyclophosphamide), TBM (with busulfan and melphalan), or TBF (with busulfan and clofarabine). Previous studies suggested that conditioning regimens containing thiotepa yielded suboptimal outcomes in myeloid neoplasms. Fludarabine, as a conditioning agent, has been increasingly used in reduced-intensity conditioning regimens in recent years, aiding in engraftment and immune reconstitution. The PTCY regimen, a classic method for in vivo T-cell depletion, is widely used in Western countries and is gradually gaining traction in China. To identify the most suitable conditioning regimen and dosage for older patients with myeloid malignancies, we designed a regimen combining the TBF conditioning regimen with PTCY. The related clinical study has been registered on the Chinese Clinical Trial Registry website.

Methods: Inclusion criteria: Patients aged 50 years or older with myeloid malignancies (including AML and intermediate/high-risk MDS suitable for transplantation), with an HCT-CI score < 2, and an ECOG score < 2. Patients with other types of acute leukemia and frail patients were excluded. The regimen design was as follows: Thiotepa 5mg/kg on days -8 and -7; Fludarabine 30mg/m² on days -6 to -2; Busulfan 0.8mg/kg every 6 hours on days -6 to -4; Cyclophosphamide 25mg/kg on days +3 and +4. The study planned to enroll 30 patients, and interim enrollment of 16 patients has been completed.

Results: Among all patients, there were 9 with AML and 7 with intermediate/high-risk MDS. Among the AML patients, 8 were in CR pre-transplant and 1 had NR. Among the 7 intermediate/high-risk MDS patients, 1 received chemotherapy before transplant, while the others proceeded directly to transplantation. All patients achieved successful engraftment. The median time to neutrophil engraftment was 13 days, and the median time to platelet engraftment was 13 days. The projected 1-year overall survival (OS) rate is 68.8%. No relapse occurred in any patient, resulting in a 1-year cumulative incidence of relapse (CIR) of 0%. The CMV infection rate was 31.25% (5/16), and the EBV infection rate was 37.5% (6/16). The Aspergillus infection rate was 12.5% (2/16), the Gram-positive cocci infection rate was 6.25% (1/16), and the Gram-negative bacilli infection rate was 6.25% (1/16). The incidence of acute GVHD (aGVHD) was 37.5% (6/16), and the incidence of chronic GVHD (cGVHD) was 31.25% (5/16), including one case (6.25%) of severe cGVHD. The incidence of transplant-associated microangiopathy (TMA) was 25% (4/16).

Conclusions: In the currently enrolled cohort of 16 patients, the TBFPTCY regimen demonstrated good tolerability in patients with myeloid malignancies over 50 years old. The engraftment success rate was 100%, and the post-transplant relapse rate was 0%. Interim

analysis with a follow-up of 1-12 months (median 5.6 months) showed a projected 1-year OS of 70.6%. The main adverse reactions included post-transplant infections and TMA. These results suggest that this regimen may be an effective option for preventing relapse post-transplantation in high-risk myeloid malignancy patients who can tolerate more intensive chemotherapy.

Clinical Trial Registry: ChiCTR2300074726

Disclosure: Nothing to declare

B180

COMPARISON OF TOTAL NODAL IRRADIATION (6.0-7.5 GY) VS LOW-DOSE TOTAL BODY IRRADIATION (2 GY) IN EX VIVO TCRAB-DEPLETED HAPLOIDENTICAL TRANSPLANTATION IN ADULTS WITH HEMATOLOGICAL MALIGNANCIES

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Background: Total Nodal Irradiation (TNI; 6-7.5 Gy) has been utilized in conditioning for *ex vivo* T-cell-depleted haploidentical hematopoietic cell transplantation (Haplo-HCT) to promote engraftment and to reduce graft rejection. Due to significant radiation-associated gastrointestinal (GI) toxicities, our institutional protocol was modified to substitute TNI with single-fraction, low-dose Total Body Irradiation (TBI; 2 Gy). This study compares the outcomes of these two radiation strategies.

Methods: We analyzed the outcomes of 109 patients (median age 54 years) who received Haplo-HCT with TCRαβ-depleted graft with CD45RA-depleted memory T-cell add-back (αβTCD+TMDLI) between 2017 to 2025. The conditioning regimen evolved from fractionated TNI (6-7.5 Gy in 3 fractions; n=22), to single-fraction TBI (2 Gy; n=87) from year 2000 onwards.

Results: All patients achieved sustained haematopoietic engraftment, with no difference in neutrophil or platelet recovery times. With a median follow-up of 20 months (range: 4-100), the low-dose TBI cohort demonstrated superior long-term outcomes: 5-year overall survival (82% vs. 36%, p<0.01), event-free survival (74% vs. 36%, p<0.01), and GVHD-free/relapse-free survival (84% vs. 32%, p<0.01). The cumulative incidences of grade II-IV acute GVHD, chronic GVHD, and relapse were comparable. However, the 2-year non-relapse mortality (NRM) was markedly lower with TBI (12% vs. 45%, p<0.001). TBI was also associated with significantly reduced severe mucositis (5% vs. 8%, p<0.01) and gastrointestinal toxicity (11% vs. 18%, p=0.002). On multivariable analysis, the use of TBI 2Gy (vs. TNI 6-7.5 Gy) was an independent favorable factor for NRM, OS, EFS, and GRFS. These survival benefits and the reduction in NRM remained significant after propensity score matching (21 patients per cohort).

Conclusions: In Haplo-HCT with αβTCD+TMDLI, substituting TNI with low-dose TBI (2 Gy) results in markedly improved survival outcomes and reduced non-relapse mortality, without compromising engraftment or efficacy. This regimen modification significantly lowers radiation-associated toxicity, enhances patient tolerability, and optimizes resource utilization, establishing low-dose TBI as the preferred conditioning component in this setting.

Clinical Trial Registry: NA

Disclosure: NA

B181

COMPARISON OF TREOSULFAN-THIOTEPA-FLUDARABINE VS FLUDARABINE-TREOSULFAN CONDITIONING FOR ALLOGENEIC HCT IN AML AND MDS: A SINGLE-CENTER RETROSPECTIVE EXPERIENCE

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Background: Conditioning regimen strongly influences allo-HCT outcomes, yet for treosulfan-based regimens in AML and MDS the optimal platform (single vs double-alkylator) and dose levels remain unclear. We compared fludarabine-treosulfan (FT) with thiotepa-treosulfan-fludarabine (TTF), and different treosulfan doses, to identify the regimen with the most favorable efficacy-toxicity balance.

Methods: Single-center retrospective analysis of 102 consecutive adults with AML, MDS, or MDS/MPN undergoing allo-HCT between 2016 and 2024. Conditioning was TTF (n=57) or FT (n=45). All patients received PBSC, across all donor types, and GvHD prophylaxis with ATG and/or PtCY, plus a calcineurin inhibitor and an antimetabolite. Primary endpoints were OS, PFS, EFS (including hematologic/molecular relapse, loss of donor chimerism or death), GRFS, cumulative incidence of relapse (CIR), and NRM.

Results: The FT group included older patients with higher-risk disease and lower performance status (*Table 1*). At 1 year, OS and PFS were 86% and 81% with FT vs 85% and 73% with TTF (both p>0.05). GRFS at 1 year was comparable (44% vs 56%, p>0.05). CIR at 1 year was significantly lower with FT (7% vs 20% with TTF; p=0.04). Median EFS was not reached with FT, whereas it was 52 months with TTF; 1-year EFS was 80% vs 61%, respectively (p=0.06).
Neutrophil engraftment occurred earlier with FT (median 13 vs 18 days with TTF; p<0.001). FT was also associated with less mucositis (any grade: 36% vs 61%; grade ≥3: 2% vs 28%; both p=0.01). Length of hospitalization tended to be shorter with FT (median 30 vs 36 days; p=0.08), while NRM was comparable (13% vs 8%; p=0.46).

Day-180 grade III–IV aGvHD rates were comparable (8% with FT vs 3% with TTF; p=0.40). In contrast, 1-year cGvHD incidence was higher in FT, both for any-grade (48% vs 19%) and moderate–severe forms (38% vs 6%; both p<0.05). Notably, median time to discontinuation of immunosuppression was significantly shorter after FT (127 vs 192 days; p=0.006). In multivariable analysis, the occurrence of cGvHD was independently associated with improved OS (HR 0.12; p=0.005) and PFS (HR 0.26; p=0.01). FT-based conditioning showed a trend toward reduced relapse risk (HR 0.30; 95%CI 0.08-1.1; p=0.07) and was independently associated with higher rates of any-grade cGvHD (HR 10.7; p<0.001). When comparing treosulfan dose levels (10, 12, and 14 mg/m² ×3), median survival and relapse rates were similar across groups. However, NRM was unexpectedly higher with Treo-10 compared with the other dose levels.

Table 1. Patients' and transplant characteristics	**TTF (N=57)**	**FT (N=45)**	**P**
Age at transplant, (median)	59 (24 – 74)	62 (29 – 74)	**0.04**
Sex (female): N (%)	26 (45.6%)	17 (37.8%)	0.5
Diagnosis: N (%) – AML/MDS/MDS-MPN	45 (78.9%) / 8 (14%) / 4 (7%)	31 (69%) / 13 (29%) / 1 (2%)	0.1
NGS: N (%) – Abnormal/available	21/22 (96%)	35/39 (97%)	>0.9
Karyotype: Abnormal, n (%)	18 (31.6%)	18 (40%)	0.5
Disease risk (ELN/IPSS): N (%) – High	16 (28.6%)	21 (46.7%)	**0.03**
Status at transplant (ELN 2022): N (%)			0.4
- CR1/CR≥2	28 (49%) / 15 (26.4%)	20 (44.4%) / 12 (26.7%)	
- PD/refractory	5 (8.8%)	1 (2.2%)	
- Upfront/stable disease	9 (15.8%)	12 (26.7%)	
Pre-transplant MRD	14 (25%)	7 (16%)	0.5
ECOG PS: N (%) ≥ 1	3 (5.3%)	16 (35.6%)	**<0.0**
HCT-CI: N (%) ≥ 3	24 (42.1%)	21 (46.7%)	0.8
Donor type: N (%)			0.1
- Sibling/Haploidentical	9 (15.8%) / 20 (35.1%)	7 (15.6%) / 7 (15.6%)	
- Matched/mismatch unrelated	21 (36.8%) / 7 (12.3%)	23 (51.1%) / 8 (17.8%)	
GvHD Prophylaxis: ATG / PtCY, n (%)	31 (54.4%) / 24 (42.1%)	26 (57.7%) / 16 (35.5%)	0.4

CMV status: R-/D+, n (%)	3 (5.3%)	8 (17.8%)	0.07
Median follow up (months)	30.6 (0.16 - 103.9)	12.1 (0.95 - 63.7)	**<0.0**

Conclusions: In this treosulfan-based series, FT and TTF provided comparable survival outcomes with low NRM and no graft failures. Despite being used in older, higher-risk, and less fit patients, FT was associated with lower toxicity (reduced mucositis and faster neutrophil recovery), with relapse rates at least comparable to TTF.
This favorable efficacy-tolerability profile was counterbalanced by a higher incidence of cGvHD, in the context of earlier immunosuppression discontinuation. Overall, FT emerges as a promising treosulfan platform, whereas the TTF regimen may be reserved for selected scenarios. Future work should aim to standardize immunosuppression tapering strategies, refine treosulfan dosing and better assess the long-term impact of cGvHD.

Disclosure: Nothing to declare.

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IMLIFIDASE EFFICIENTLY ABROGATES THE EFFECT OF ATLG AND THYMOGLOBULIN ON T- AND NK-CELL VIABILITY AND FUNCTION

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Background: ATLG (Grafalon) and Thymoglobulin are long-established agents in allogeneic hematopoietic stem cell transplantation (allo-HSCT), effectively preventing both graft rejection and graft-versus-host disease (GvHD). Using *ex vivo* TCRαβ/B-cell-depletion for GvHD prophylaxis in allo-HSCT, the main function of both agents is to prevent graft failure. In this context, high serum levels of ATLG/Thymoglobulin before transplant are beneficial, but hamper posttransplant immune recovery, potentially limiting the antileukemic activity of NK- and γδT-cells.
Imlifidase (Idefirix), an enzyme of *S.pyogenes*, hydrolyzes IgG in $F(ab')_2$ and Fc fragments. Therefore, using imlifidase straight before transplant may be effective in rapidly inactivating ATLG/Thymoglobulin.
Here, we analyze the potency of imlifidase to reduce ATLG/Thymoglobulin-mediated i.) T- and NK-cells lysis and ii.) inhibition of NK-cell function.

Methods: MACS-isolated $CD3^+$ T- and $CD56^+$ NK-cells from healthy donors were co-incubated (2h) with different concentrations of ATLG/Thymoglobulin alone or ATLG/Thymoglobulin pretreated with imlifidase (10 µg/ml) and assessed for Calcein release. Natural cytotoxicity of expanded NK (eNK)-cells (effectors, E) after preincubation (3.5h) with ATLG/Thymoglobulin alone or ATLG/Thymoglobulin pretreated with imlifidase was determined against K562 cells (targets, T) (E:T=10:1) in the presence of human AB serum as complement source.

Results: In the presence of 10 (100, 250, 500) µg/ml ATLG, lysis of freshly isolated Calcein-labeled T-cells (donors n=3) ranged between 0-5% (4-17%, 17-30%, 30-40%), whereas T-cell lysis was completely abrogated when incubated with ATLG pretreated with imlifidase. Compared to T-cells, exposing enriched NK-cells from identical donors (n=2-3) to the same ATLG concentrations resulted in higher lysis rates, ranging between 18-39% (44-87%, 60-87%, 69-93%) and dropping to 0-1.2% in the presence of corresponding doses of ATLG pretreated with imlifidase.
As with ATLG, Thymoglobulin-mediated T-cell lysis was also dose-dependent, reaching 0-8% (9-26%, 38-44%, 41-51%; donors n=3) in the presence of 2 (10, 100, 200) µg/ml Thymoglobulin. Lysis was markedly reduced to a maximum of only 2.3% using corresponding doses of imlifidase-pretreated Thymoglobulin. As observed with ATLG, Thymoglobulin (2, 10, 100, 200 µg/ml) induced stronger lysis of NK-cells (donors n=3) compared to T-cells, ranging from 14-24% (20-30%, 53-85%, 70-87%). Again, prior treatment of Thymoglobulin with imlifidase completely prevented lysis of NK-cells.
eNKs were generated by stimulation of PBMCs (donors n=4) with IL-2 (50-100 U/ml) and irradiated feeder cells (K562-mbIL15-4-1BBL). Lysis of K562 by untreated eNKs ranged from 60-93% and was reduced to 21-56% (0-12%) after eNK-cell incubation with 10 (100) µg/ml ATLG. However, lysis increased to 41-77% (26-62%) after preincubation with imlifidase-pretreated ATLG 10 (100) µg/ml. This effect was also true for Thymoglobulin. eNK-cell-mediated K562 lysis was decreased to 23-48% (32-45%, 7-30%, 3-20%) by pretreatment of eNKs with 2 (10, 100, 200) µg/ml Thymoglobulin, but reached 51-65% (44-68%, 32-58%, 21-55%) using imlifidase-cleaved Thymoglobulin.

Conclusions: Imlifidase markedly attenuates the impact of ATLG/Thymoglobulin on NK-cell function and abrogates ATLG-/Thymoglobulin-mediated cytotoxicity on T-/NK-cells. This effect of imlifidase is to be evaluated in a clinical study in the context of T-/B-cell-depleted allo-HSCT in order to determine whether pre-transplant application of imlifidase (e.g. on day-2) results in effective inactivation of ATLG/Thymoglobulin *in vivo* and thereby accelerates post-transplant immune reconstitution.

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SALVAGE ALLOGENEIC STEM CELL TRANSPLANTATION FOR RELAPSED/REFRACTORY AML: CLADRIBINE-BASED INTENSIVE CONDITIONING VERSUS STANDARD MYELOABLATIVE REGIMENS

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Background: Salvage allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the sole potential curative therapy for patients with relapsed or refractory (R/R) acute myeloid leukemia (AML). The intensive conditioning regimen may contribute to improved long-term survival. However, the optimal conditioning regimen remains undefined. This study aimed to compare the clinical outcomes of patients with R/R AML receiving the Cladribine-based intensive regimen (CLAG) versus those receiving a standard Bu/Cy-based MAC regimen (BUCY).

Methods: This retrospective, dual-center study screened 127 patients with R/R AML who underwent salvage allo-HSCT at the Bone Marrow Transplantation Center of the First Affiliated Hospital, Zhejiang University School of Medicine, and Zhejiang Provincial People's Hospital between July 2016 and May 2025. We excluded individuals diagnosed with acute promyelocytic leukemia, or the myeloid blast phase of chronic myeloid leukemia. Consequently, 103 eligible patients were included and divided into the CLAG cohort (n=50) and the BUCY cohort (n=53). Cladribine-based regimen consisted of cladribine 5 mg/m2/day and high-dose cytarabine 2 g/m2/day for 3 days followed by Bu/Cy-based MAC regimen. Patients without grade II-IV acute graft versus host diseases (aGVHD) received one course of prophylactic donor lymphocyte infusion (pro-DLI) at about day +90.

Results: The median patient age was 42 years, and the majority of the cohort was diagnosed with de novo AML (90.3%), while the remaining 9.7% had AML secondary to myelodysplastic syndromes. Patients in the CLAG cohort presented with a significantly higher burden of pre-transplant bone marrow blasts compared to the BUCY group (median 15% vs 11%, P=0.002). Other baseline characteristics were balanced between the two cohorts. The two cohorts had comparable median times to neutrophil engraftment (13 days; P=0.946) and platelet engraftment (14 days; P=0.736). All patients achieved complete remission and full donor chimerism by day +30 post-HSCT.
With a median follow-up of 12.3 months, the median overall survival (OS) and disease-free survival (DFS) for the entire cohort were 16.9 months and 9.8 months, respectively. No significant differences between the CLAG and the BUCY cohorts were observed in long-term outcomes. The 1- and 2-year overall survival (OS) rates for the CLAG versus BUCY cohorts were 55.4% vs. 59.0% and 45.6% vs. 43.8%, while the corresponding cumulative incidence of relapse were 39.1% vs. 33.5% and 46.0% vs. 44.0% (all P>0.5). Multivariate analysis

identified high blast burden pre-transplant, rather than the conditioning regimen, as the independent risk factor for inferior 100-day survival (HR=15.5, P=0.03). However, the CLAG cohort exhibited higher 100-day NRM (14.0% vs. 1.9%, P=0.022).
In the entire cohort, 23.3% of patients received pro-DLI, with median time of 102 (range, 52-195) days post-HSCT. On landmark analysis at day+60, pro-DLI significantly decreased risk of 2-year relapse (23.5% vs 48.3%, P=0.047). OS was longer in the DLI cohort than the non-DLI cohort (median: 28.8 months vs 18.4 months).

Conclusions: This study demonstrated that a cladribine-based intensive regimen achieved comparable clinical outcomes to standard Bu/Cy MAC regimen in salvage HSCT for R/R AML, but may increase the risk of early NRM. Furthermore, for these patients, prophylactic DLI post-HSCT effectively reduced the risk of relapse, thus improving overall survival.

Disclosure: Nothing to declare.

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TRANSFUSION BURDEN UNDER ATG AND PTCY IN ACUTE LEUKEMIA PATIENTS RECEIVING ALLOGENEIC STEM CELL TRANSPLANTATION

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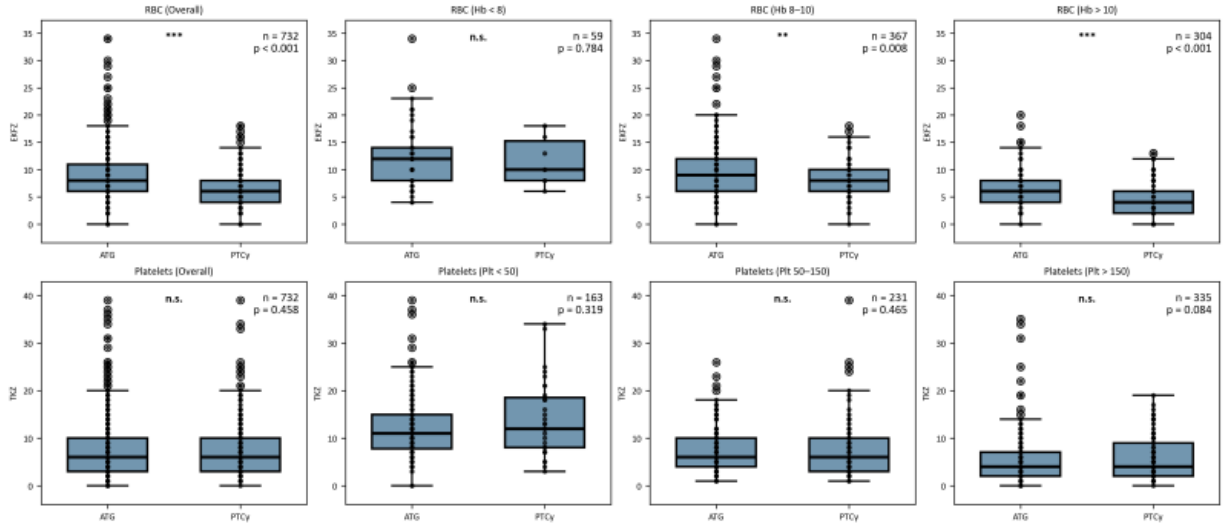
Background: Hematopoietic stem cell transplantation (HSCT) requires T-cell depletion as part of graft-versus-host disease (GvHD) prophylaxis. The advantages and disadvantages of anti-thymocyte globulin (ATG) and post-transplant cyclophosphamide (PTCy) are widely discussed. However, data directly evaluating transfusion requirements associated with these approaches is lacking. We therefore conducted a retrospective analysis of transfusion needs in patients with acute leukemia undergoing allogeneic HSCT to assess and compare transfusion requirements under ATG- and PTCy-based GvHD prophylaxis.

Methods: We included all patients with acute leukemia (AML or ALL) who underwent allogeneic HSCT at our center between November 2015 and November 2025. Exclusion criteria were age <18 years, second or later HSCT, cord blood grafts, and cases not clearly assignable to ATG or PTCy. Baseline characteristics were generated using Python library *TableOne*. Group differences were assessed using non-parametric tests for continuous variables and chi-square–based tests for categorical variables. Primary endpoints were transfusion requirements from day −7 to day +30 and time to engraftment. Transfusion differences (red blood cell and platelet units) were evaluated using the Mann–Whitney U test. Mean values with 95% confidence intervals and medians were calculated descriptively. Transfusions per inpatient day were calculated for day −7 to day +30 or until earlier discharge. Additional predefined subgroup analyses were performed.

Results: A total of 878 patients were included, with 612 receiving ATG and 266 receiving PTCy. Red blood cell (RBC) transfusion requirements differed between groups, with higher RBC use in the ATG group (median 8 vs. 6, p <0.001), while platelet transfusions were comparable (6 vs. 6, p = 0.434). Among patients who were transfusion-dependent at the beginning of the peri-transplant phase (Hb < 8 g/dl; n = 59), RBC transfusion requirements did not differ between ATG and PTCy (median 12 vs. 10 units, p = 0.784). When adjusted for inpatient duration, ATG patients required more RBC units (0.28 vs. 0.18, p <0.001) and platelet units per hospital day (0.23 vs. 0.19, p <0.001), due to shorter inpatient duration (21 vs. 27 days, p <0.001).
Leukocyte engraftment occurred at a median of 11 vs. 16 days (p <0.001) and platelet engraftment (platelets 20 x10⁹/L) at 12 vs. 21 (p <0.001) days for ATG and PTCy.
Findings were similar in the AML subgroup (n = 762), showing higher RBC use with ATG (8 vs. 7, p = 0.004) but no differences in platelet transfusions (6 vs. 7, p = 0.345) while platelet engraftment occurred later with PTCy (12 vs. 22 days, p <0.001). Transfusions per inpatient day showed similar results regarding RBC units (0.28 vs. 0.22, p <0.001) but no difference in platelet units (0,23 vs. 0.22, p = 0.628).



Conclusions: Only RBC transfusion requirements differed significantly between ATG and PTCy groups, although the clinical relevance of this difference appears limited. Overall findings suggest that the transfusion burden between the two GvHD prophylaxis strategies may be more balanced than anticipated. The later engraftment observed after PTCy accompanied by a prolonged hospital stay may offset the more frequent but shorter duration of transfusion requirements under the application of ATG.

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All other authors declare no conflicts of interest.

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TOTAL BODY IRRADIATION, BUSULFAN, FLUDARABINE WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA UNDERGOING HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Total body irradiation (TBI)-based myeloablative conditioning is considered the standard of care for pediatric acute lymphoblastic leukemia (ALL) undergoing allogeneic hematopoietic cell transplantation (HCT); however, the optimal TBI dose has yet to be defined. To reduce radiation-related long-term toxicities while preserving antileukemic efficacy, we incorporated a conditioning strategy using 8-Gy TBI combined with busulfan and fludarabine, particularly in the setting of T-cell-replete haploidentical HCT with post-transplant cyclophosphamide (PTCy) for pediatric patients with high-risk or relapsed ALL in remission.

Methods: We retrospectively reviewed the outcomes of 36 patients (median age: 7.5 years, range, 1.3-17.8) with high-risk cytogenetics (n=6) or relapsed ALL (n=30) who underwent allogeneic HCT in complete remission (CR) between 2019 and 2025. Diagnoses included B-ALL in 31 patients, T-ALL in 2 patients, and mixed phenotype acute leukemia in 3 patients. Eight patients (22.2%) had a history of prior HCT. All patients received G-CSF-mobilized peripheral blood stem cell grafts from haploidentical family donors. The conditioning regimen consisted of 8-Gy TBI administered on days -8 and -7, followed by busulfan at 130mg/m^2/day on days -6 and -5 and fludarabine at 40mg/m^2/day on days -6 to -3. Graft-versus-host-disease (GVHD) prophylaxis included PTCy at 50mg/kg/day on days +3 and +4 in combination with cyclosporine.

Results: The median age at HCT was 12.9 years (range, 2.5-22.0 years). Disease status prior to HCT included first CR in 6 patients, second CR in 23 patients, and third CR in 7 patients. The median infused cell doses were as follows: total nucleated cells (TNCs) 20.4 x 10^8/kg, CD34+ cells 6.3 x 10^6/kg, and CD3+ cells 45.8 x 10^7/kg. Neutrophil and platelet engraftment were observed in all patients and all but one patient at a mean of 15 days and 27 days post-transplant, respectively. The 100-day cumulative incidences (CI) of grades II-IV and grade III-IV acute GVHD were 51.4.0±8.2% and 13.5±5.6%, respectively. Chronic GVHD developed in 10 of 36 patients (moderate, n=9; severe, n=1), with a 3-year CI of 29.7±8.5%, and no GVHD-related mortality was observed. With a mean follow-up of 36 months (range, 3-83 months), the estimated 3-year leukemia-free survival and overall survival rates were 81.3±7.1% (6/36) and 91.3±4.8% (3/36), respectively. These survival outcomes were comparable to those of our historical cohort who underwent matched donor transplantation with a conventional 13.2-Gy TBI and cyclophosphamide-based conditioning regimen.

Conclusions: An 8-Gy TBI-based myeloablative conditioning regimen combined with busulfan and fludarabine with PTCy prophylaxis resulted in encouraging survival outcomes in pediatric patients with high-risk or relapsed ALL undergoing haploidentical HCT in remission. Future studies from our institution will explore the applicability of this conditioning strategy in matched donor transplantation, with the aim of reducing long-term radiation-related toxicities.

Disclosure: Nothing to declare

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'IMPROVING TRANSPLANT PLATFORMS': REAL-LIFE EXPERIENCE OF TREOSULFAN AS CONDITIONING FOR ALLO-HSCT IN AML AND MDS

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Background: Conditioning for allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a key part of the procedure. Age, comorbidities and, especially, the need for a second transplant make it difficult to use ablative regimens and increase morbidity and mortality. The use of treosulfan allows us to reduce toxicity while maintaining its antitumor effect.
The aim of our study is to report real-world experience with the use of treosulfan in conditioning for a-HPT in adult patients diagnosed with myelodysplastic syndrome (MDS) and acute myeloid leukaemia (AML).

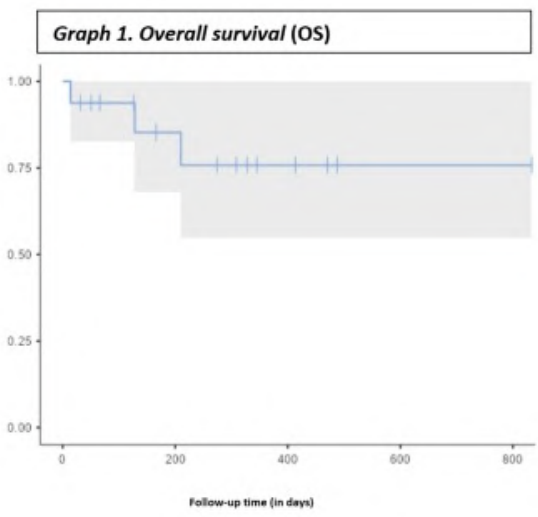
Methods: A retrospective observational study evaluating overall survival (OS), progression-free survival (PFS), toxic mortality (TMR), and the incidence of complications in all patients with AML and MDS who have received Treosulfan in the conditioning regimen for allogeneic HPT at our center from February 2023 to the present. Patients were selected based on their comorbidities and the need for a second allo-HSCT.

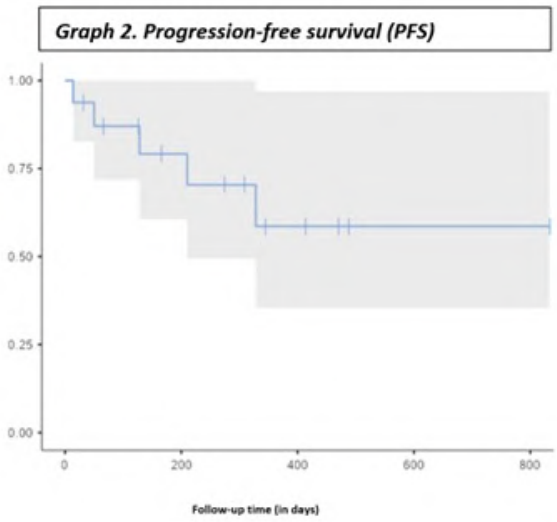
Results: Baseline characteristics are presented in Table 1. Eighteen patients were included, 62% with AML and 38% with MDS, mainly males (67%) with a mean age of 58 years (range 27–71). In 28% (5/18) an HLA-identical (HLA-i) donor was used, in 33% (6/18) an unrelated donor (URD) and in 39% (7/18) a haploidentical donor. Forty per cent of the series are second allogeneic transplants. More than half of the patients (56%) were in a situation of second CR or higher or refractoriness, and only 44% were in first complete response. Molecular alterations are described in Table 1, with the most frequent being RUNX1 (28%), DNMT3A (22%), and TP53 (16%).

Table 1. Characteristics.

Total	N= 18 patients
Average age	58 (27-71)
Gender Male Female	 12 (67%) 6 (33%)
Underlying disease AML MDS CML	 11 (62%) 6 (335) 1 (5%)
NGS/BM (AML/MDS) TP53 DNMT3A RUNX1 ASLX1 TET2/KRAS FLT3 NPM1	 2/1 2/2 2/3 1/1 1/1 1/0 1/0
Donor type HLAi DNE 10/10 DNE 9/10 Haploidentical	 5 (28%) 5 (28%) 1 (5%) 7 (395)
TPH ≥ 2	7 (39%)
Situation pre-TPH 1st CR 2nd CR pr > RR	 8 (44%) 7 (39%) 3 (17%)
Conditioning Treosulfan-Fludarabine (30 g/m2)	18 (100%)
EICR prophylaxis PTCy-Tacrolimus MTX-Tacrolimus	 16 (90%) 2 (10%)

All patients received ablative conditioning according to the Treosulfan 10 g/m² x 3 days (total dose of Treosulfan 30 g/m²) with Fludarabine regimen. Graft-versus-host disease (GVHD) prophylaxis was performed in 90% of patients with post-TPH Cyclophosphamide and Tacrolimus/Mycophenolate. No serious complications were reported during the procedure, and 22.2% of patients required some form of analgesia for muscle pain in the lower limbs. Sixty-two percent of patients developed acute GvHD, while only 10% developed grade III-IV GvHD. Twenty-eight per cent developed chronic GvHD, most (4/5) of which was mild to moderate. Two patients developed EVOH (11%); a second allo-TPH and a patient with tumor infiltration of the liver. Three patients (17%) developed IFI, all of whom were refractory. The SG was 75.8% at 2 years with an SLP of 58.6% and a median not reached. The MRT was 11.1% (2/18), exitus due to MAGIC III and IBMTR D cutaneous EICR and severe mucormycosis.





Conclusions: The conditioning regimen with Treosulfan demonstrated both efficacy in preventing disease relapse in high-risk patients (relapsed and refractory) and safety, allowing the inclusion of patients undergoing second transplants, older patients, and patients with comorbidities, without observing high rates of toxic mortality.

Disclosure: No conflict of interest.

P197

THIOTEPA, CYCLOPHOSPHAMIDE AND FLUDARABINE CONDITIONING REGIMEN FOR ADULT PATIENTS WITH NON-HODGKIN LYMPHOMA UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION: IMPACT OF DONOR MISMATCH ON OUTCOME

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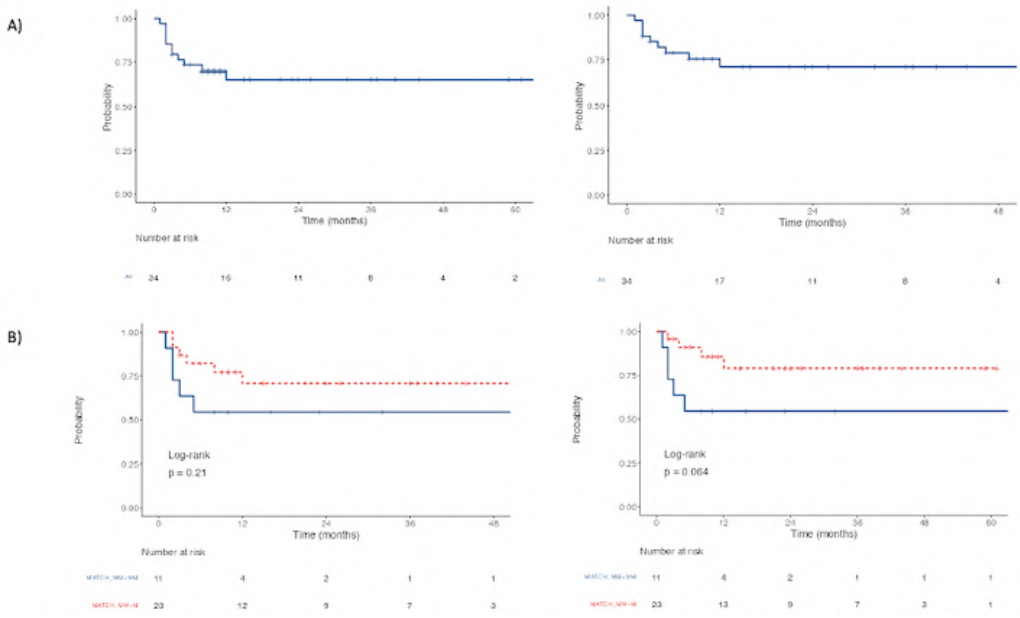
Background: Allogeneic stem cell transplantation (HSCT) still represents a potentially curative option for patients with refractory/relapsed (RR) lymphoid malignancies. Modulation of conditioning intensity is crucial for disease control with acceptable toxicity. Thiotepa, Cyclophosphamide and Fludarabine (TCF) is a low-intensity conditioning (according to the new Transplant Conditioning Intensity Index) that has demonstrated excellent balance between safety and efficacy, even if data are still limited.

Methods: In this retrospective study we analyzed all 34 consecutive adult patients (pts) affected by lymphoid malignancies who underwent HSCT following TCF conditioning at our center between January 2019 and December 2024.

Results: Median age at transplant was 59 (35-74) years and 53% of pts were male. Baseline diagnoses were: 8 (23%) T-cell lymphomas, 6 (18%) DLBCL, 6 (18%) mantle cell lymphoma, 5 (15%) follicular lymphomas, 4 (11%) Richter syndrome and 5 (15%) other histology. Median number of lines before transplant were 3 (range 1-10); 8 (23%) pts received autologous stem cell transplant, 6 (18%) pts CAR-T (3 tisagenlecleucel, 1 brexucabtagene autoleucel, 1 axicabtagene ciloleucel) and 6 (18%) bispecific antibodies (4 glofitamab, 2 mosunetuzumab). Disease status at HSCT was complete remission (CR) in 53% of pts. Donors were matched unrelated in 19 (56%) pts, matched related in 4 (11%) pts, mismatch unrelated in 9 (26%) pts and haploidentical in 2 (6%). Overall, 25 (74%) pts received ATG as GVHD prophylaxis while 9 (26%) post-transplant cyclophosphamide (PT-Cy). Graft source was peripheral blood in all pts. Median infused CD34+ and CD3+ counts were 7,37 x10^6 cells/kg (3,20-10,5) and 18,8 x10^7 cells/kg (9,69-65,4), respectively. All pts engrafted. Median time for neutrophil and platelet engraftment was 14 (range 10–22) and 15 (range 11–34) days, respectively. With a median follow up of 11,5 (1-68) months, one-year progression-free survival (PFS), overall survival (OS) and graft-relapse free survival (GRFS) were 66%, 71% and 42% respectively (Figure 1A). Eight (23%) pts died due to transplant complications: 6/8 (75%) GVHD, 1/8 (12%) infections and 1/8 (12%) other. Only one pts died due to disease progression (1/34, 3%). A trend towards better one-year OS was observed in pts transplanted from matched donors compared with mismatch donors even if not statistically significative (79% vs 54%; p=0,064) while no differences in terms of 1-year PFS (p=0,21) were recorded (Figure 1B). Deaths due to complications were higher in mismatched group (45% vs 23%, p=0,037) while relapse rate was similar (36% vs 22%, p= 0,366).

Figure 1 A) PFS and OS global B) PFS and OS comparison between Matched and Mismatched donors HSCT



Conclusions: Our data highlight the efficacy of TCF conditioning for disease control in heavily pretreated lymphomas, with 1-year PFS and OS of 66% and 71% respectively. HSCT from mismatched donors had higher complications rate (mainly GVHD, despite the prevalent use of PT-Cy GVHD prophylaxis platform) and a tendency of lower 1-year OS.

Disclosure: Nothing to declare.

P198

ENGRAFTMENT KINETICS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION: IMPACT OF CONDITIONING INTENSITY AND EARLY POST-TRANSPLANT EVENTS

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Background: Real-world data from resource-limited settings evaluating the impact of myeloablative (MYA) and reduced-intensity (RIC) conditioning on engraftment kinetics after hematopoietic stem cell transplantation (HSCT) remains scarce.

Methods: This single institution retrospective cohort study was conducted from 2022 to 2025, including adult patients undergoing conditioning regimens in the context of HSCT. Conditioning protocols were classified as MYA or RIC, and engraftment kinetics were analyzed using time to neutrophil and platelet recovery.

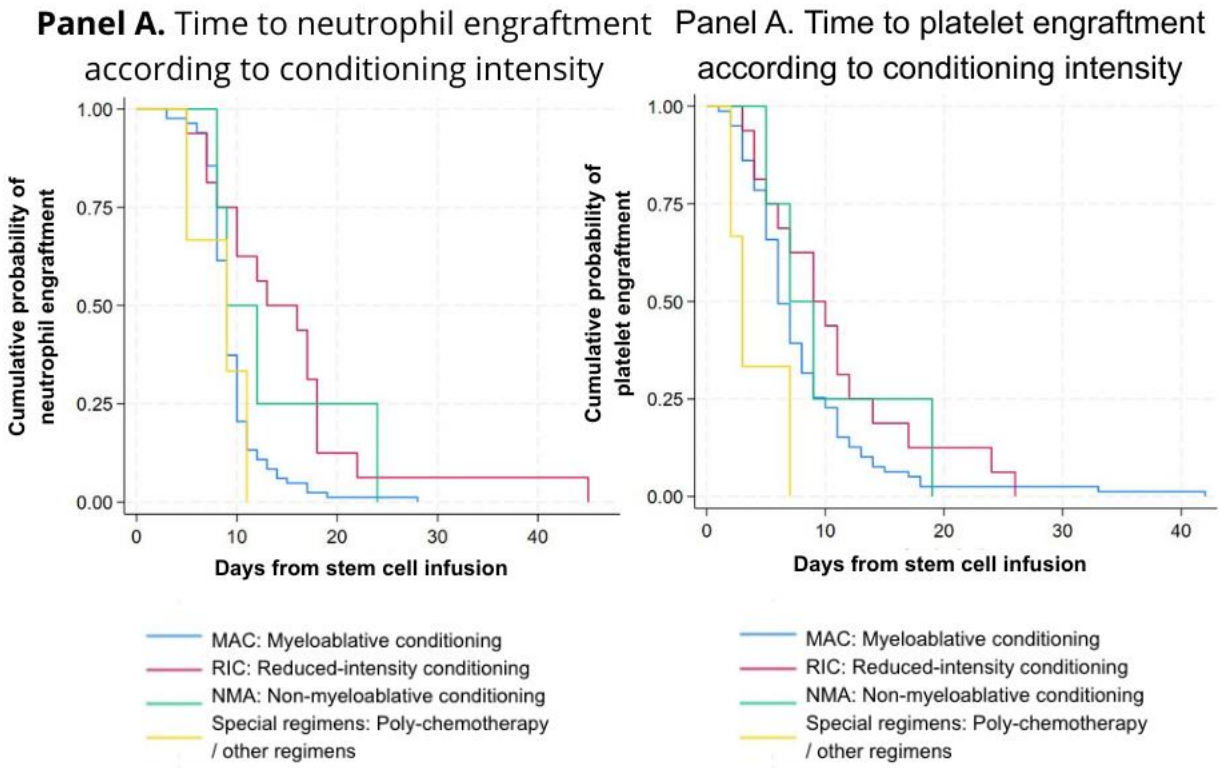
Results:

A total of 111 patients were included in the analysis, of whom 77.4% received myeloablative conditioning (MAC), 15.3% reduced-intensity conditioning (RIC), 4.5% received other non-myeloablative regimens (NMA) and 2.7% were treated with special regimens or poly-chemotherapy. Adverse events during conditioning were uncommon, with diarrhea occurring in 10 patients (9.1%) and emesis in 9 patients (8.2%). Late adverse events were more frequent, with mucositis observed in 43 patients (39.5%) and diarrhea in 79 patients (72.4%).

The most prevalent diagnosis was multiple myeloma (n=52, 46.85%), followed by mantle cell lymphoma (n=10, 9.01%) and acute myeloid leukemia (n=10, 9.01%). The mean time to neutrophil engraftment was 10.2 days (SD=5.4). Kaplan–Meier analysis showed significant differences in neutrophil engraftment kinetics according to conditioning intensity. Patients receiving myeloablative conditioning experienced earlier neutrophil engraftment compared with reduced-intensity conditioning (log-rank $p < 0.001$). In multivariable Cox regression analysis, higher CD34+ cell dose was independently associated with faster neutrophil engraftment (HR 1.005, $p = 0.014$). Other variables such as age and sex showed no significant association. Differences in engraftment kinetics were also observed according to donor type.

Mean time to platelet engraftment was 8.19 days (SD=6.27). Platelet engraftment kinetics showed greater variability across conditioning regimens. Although myeloablative conditioning appeared to be associated with earlier platelet recovery on Kaplan–Meier analysis, differences between regimens did not reach statistical significance (log-rank $p = 0.056$). This finding was consistent when comparing myeloablative versus reduced-intensity conditioning ($p = 0.13$).

Figure 1. Engraftment kinetics according to conditioning intensity



Protocol	Histology	Frequency
Abbreviated BEAM	Follicular lymphoma	4 (19.5%)
	Burkitt lymphoma	3 (14.29%)
	Mantle cell lymphoma	8 (38.1%)
BEAM	Mantle cell lymphoma	2 (100%)
Busulfan/Fludarabine/AMA	Acute myeloid leukemia	1 (100%)

Etoposide + carboplatin	Others	2 (100%)
Etoposide + carboplatin + melphalan	Others	1 (100%)
Fludarabine + melphalan	Acute myeloid leukemia	1 (100%)
Ifosfamide + carboplatin + etoposide (ICE)	Non-germinomatous germinal tumor	1 (100%)
Melphalan	Multiple myeloma	52 (92.86%)
	Hodgkin lymphoma	1 (1.79%)
	Amyloidosis	3 (5.36%)
Thiotepa + busulfan + fludarabine	Acute myeloid leukemia	3 (60%)
	Chronic myeloid leukemia	1 (20%)
	Acute lymphocytic leukemia	1 (20%)
Thymoglobulin	Non-malignant hematological diseases with bone marrow failure	1 (50%)
	Systemic sclerosis	1 (50%)
Thymoglobulin + cyclophosphamide	Non-malignant hematological diseases with bone marrow failure	1 (50%)
	Systemic sclerosis	1 (50%)

Conclusions: In this real-world cohort, conditioning intensity was a key determinant of neutrophil engraftment kinetics after HSCT, with myeloablative regimens associated with earlier neutrophil recovery compared with reduced-intensity approaches. Importantly, CD34+ cell dose emerged as an independent predictor of engraftment speed, underscoring the role of graft quality beyond conditioning intensity alone. In contrast, platelet engraftment showed greater heterogeneity and was not consistently influenced by conditioning intensity, suggesting that additional factors may modulate platelet recovery. Collectively, these findings emphasize the need for integrated optimization of both conditioning strategies and graft characteristics to improve early post-transplant outcomes in resource-limited settings where delays in engraftment may translate into increased morbidity and healthcare burden.

Disclosure: Beatriz Wills: Consultancy with Johnson, Pfizer, Astrazeneca and Roche, grants with BMS, speaker for Abvie
Rest of authors: Nothing to declare.

P199

MYELOABLATIVE CONDITIONING FOR MYELOID MALIGNANCIES WITH THIOTEPA, BUSULFAN, FLUDARABINE WITH ANTI-THYMOCYTE GLOBULIN OR POST TRANSPLANT CYCLOPHOSPHAMIDE (TBF-ATG OR TBF-PTCY) - A SINGLE CENTRE EXPERIENCE

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Background: Thiotepa-Busulphan-Fludarabine has been shown to be a highly effective myeloablative chemotherapy-only preparative regimen in patients with myeloid malignancies, avoiding the toxicities of TBI.

Methods: We analysed the outcomes of 36 consecutive patients who underwent allogeneic transplantation using the TBF backbone (Thiotepa 10 mg/m2; Busulphan 9.6mg/m2; Fludarabine 50mg/m2) at our centre. Those with HLA 10/10 matched sibling (n=4) or unrelated donors (n=17) received ATG 2.5 mg/kg on days -1 and -2 together with CSA and MMF from D-1 as GVHD prophylaxis (n= 21). Those with HLA 9/10 mismatched unrelated (n=4) or haplo-identical family donors (n=11) received PTCy (40 mg/kg on days +3 and +4) together with CSA and MMF from Day +5 (n=15).

Results: All patients received PBSC grafts with a median cell dose of 5.20 x 10^6 CD34+/kg. The median age in both ATG and PTCy groups was 35 years (17-51 yrs). The diagnoses were AML (n=16), MDS (n=4) and CML (n=4) in the ATG group and AML (n=13) and CML (n=2) in the PTCy group. The median haemopoietic comorbidity score was 0 in the ATG group and 1 in the PTCy group (range 0-6).
All patients engrafted, with a faster median time to neutrophil and platelet engraftment in the ATG group of 11 days (9-22 days) and 18 days (15-28 days), compared with 15 days (13-21 days) and 21 days (14-50 days) in the PTCy group. All patients in both groups achieved full donor chimerism at 1- and 3-months post-transplant.
All patients except one were EBV seropositive and one third were CMV seropositive. EBV reactivation requiring treatment occurred in 71% of TBF-ATG and 13% of TBF-PTCy patients whilst CMV reactivation required treatment in 14% of TBF-ATG and 20% of TBF-PTCy. BK virus haemorrhagic cystitis incidence was high requiring treatment in 33% of TBF-ATG and 40% of TBF-PTCy. There were 3 cases of VOD all in heavily pre-treated patients and one case of CRS in a haploidentical PTCy patient that required brief ITU admission for inotropic support.
At a median follow up of 24 months (5-70m) 30/36 patients (83%) are alive. In the TBF-ATG group 2y OS was 93% with 9.5% NRM at 2 years (2 infective deaths and 1 relapse) whilst in the TBF-PTCy group 2y OS was 70% with 0% 2y NRM, but 3 deaths from relapse (2 = AML and 1=CML-2CP). Acute GVHD Grade 2-3 occurred in 25% of the TBF-ATG cohort and 6% of the TBF-PTCy group with no cases of grade 4 aGVHD.

Conclusions: We conclude that the TBF platform is an effective strategy for patients regardless of donor type, with acceptable toxicity and relapse rates. We observed a higher risk of EBV reactivation in the ATG group as compared to the PTCy group likely due to slower immune reconstitution, and high symptomatic BK haemorrhagic cystitis in both groups as compared to other regimens. Although longer follow up is needed, these findings, together with the lower incidence of GVHD in the PTCy group, makes PTCy an attractive option for fully matched donors going forward.

Disclosure: Nothing to declare.

P200

FLUDARABINE AUGMENTED REDUCED INTENSITY CONDITIONING IMPROVES ENGRAFTMENT AND OUTCOMES IN ADVANCE CUTANEOUS T-CELL LYMPHOMA

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Background: Advanced stage cutaneous T cell lymphoma (CTCL), including Mycosis fungoides (MF) and Sezary syndrome (SS) are rare, usually refractory with limited curative options. Allogenic HSCT offers potential cure and Reduced Intensity Conditioning (RIC) is recommended by the EORTC-CLTG and the NCCN . Although Stanford nonmyeloablative regimen (TSEB/TLI/ATG) is well tolerated, the slow and sometimes incomplete engraftment and higher rate of primary and secondary graft failure remain a major concern. In view of these concerns we incorporated fludarabine into conditioning regimen at our center. We report a 10 year experience of allo-HSCT in advanced CTCL, comparing outcomes across conditioning approaches.

Methods: A retrospective analysis was conducted of all patients who underwent an allo-HSCT for MF/SS at a tertiary UK centre from 2015 to 2025. Data collected included disease stage, remission status, prior treatments, conditioning regimens, engraftment kinetics, transplant complications, GVHD, donor chimerism and relapse.

Results: Nine patients with advanced-stage MF/SS (stages IIB–IVB) underwent allo-HSCT (7 MF, 2 SS). The median prior systemic therapies was 6(range 3-7). At transplant, 7 patients were in CR and 2 in PR. Median follow up was 11.6 months (range 1.2- 48.9).
3 patients received the Stanford protocol and 4 patients received institutional modified Stanford protocol incorporating fludarabine (60 mg/m2). One patient without a suitable MUD underwent HAPLO RIC transplantation. One patient with bulky nodal disease received LEAM/ATG.
TSEB/TLI/ATG RIC (n = 3)
2 patients developed non-neutropenic fever and one developed neutropenic sepsis. One had CMV reactivation. Two experienced grade 1–2 acute skin GVHD. 2 patients never dropped their neutrophils <0.5 x 10^9/L and 1 patient engrafted on day 11. Day-90 donor chimerism was <95%in one evaluable patient. All relapsed, including two within 30 days, one late relapse, they all subsequently died.
Modified RIC: TSEB/TLI/ATG/Fludarabine (n = 4)
Two patients had no acute complications, while two developed non- neutropenic fever. One had CMV reactivation. Three did not drop their neutrophils < 0.5 x 10^9/L and One engrafted on day 7. Three developed grade 1 skin GVHD. By day 90, two achieved full donor chimerism and two remained in mixed. There was no evidence of graft failure. Two patients remain in

sustained remission, while two relapsed at 3 and 13 months post HSCT. All remain alive at last follow up.
Other Regimens (LEAM/ATG and Haplo-RIC; n = 2)
Both experienced early bacterial sepsis with neutropenia. Engraftment occurred on days 11 (LEAM/ATG) and 15 (HAPLO RIC). Patient undergoing LEAM conditioning developed grade 2 gut and skin GVHD. Both patients remain in remission with full donor chimerism and are alive at last follow up.

Table 1: Patient Information

Number	Diagnosis	Stage	CLIPI Risk group	Number of prior treatments	Transplant conditioning	Transplant complications	Neutrophil Engraftment	GVHD	Donor Chimerism	Disease status	Days of relapse post HSCT	Alive/ Dead
1	MF	2B	High	3	TSEB+TLI+ ATG	Sepsis, CMV reactivation	Never <0.5x 10 9/L	No	NA	Relapse	19	Dead
2	MF	IV A	High	6	TSEB+TLI+ ATG	Sepsis	Never <0.5x 10 9/L	Grade 2 Skin	NA	Relapse	24	Dead
3	MF	2B	Intermediate	6	TSEB+TLI+ ATG	Neutropenic sepsis	Day 11	Grade 2 skin	<95	Relapse	262	Dead
4	SS	IV A	High	5	TSEB+TLI+ ATG+Flu	Psudomonas exit line site infection	Never <0.5x 10 9/L	Grade 1 skin	100	Remission	NA	Alive
5	MF	2B	Low	6	TSEB+TLI+ ATG+Flu	None	Never <0.5x 10 9/L	Grade 1	100	Relapse	397	Alive

								skin				
6	MF	IVA	High	3	TSEB+TLI+ATG+Flu	Neutropenic sepsis	Never <0.5x 10 9/L	No	<95	Relapse	105	Alive
7	MF	2B	Intermediate	4	TSEB+TLI+ATG+Flu	None	Day 7	Grade 1 skin	<95	Remission	NA	Alive
8	SS	IVB	High	7	HAPLO RIC	Neutropenic sepsis	Day 15	No	100	Remission	NA	Alive
9	MF	IVA	High	7	LEAM ATG	Neutropenic sepsis	Day 11	Grade 2 skin, Gut	100	Remission	NA	Alive

Conclusions: Incorporation of fludarabine to the TSEB/TLI/ATG RIC regimen improved donor chimerism and outcomes without increasing toxicity, no graft failures were observed. HAPLO-RIC and LEAM- based conditioning regimens were feasible alternatives for patients lacking matched donors or with bulky disease. Although limited by small sample size, these findings support further prospective evaluation of incorporation of fludarabine as a reliable conditioning strategy in advanced stage CTCL.

Disclosure: We have no disclosures.

P202

TREOSULFAN-BASED CONDITIONING REGIMEN IS ASSOCIATED WITH AN INCREASED RISK OF EARLY TOXICITY AND RELAPSE IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Background: Treosulfan-based conditioning has emerged as an effective myeloablative regimen associated with reduced non-relapse mortality (NRM).
The aim of our study was to evaluate the safety and efficacy of treosulfan-based conditioning in patients with hematological malignancies (HM) who underwent allogenic hematopoietic stem cell transplantation (allo-HSCT) from matched sibling donors (MSD).

Methods: Retrospective study conducted in all consecutive patients with HM who underwent allo-HSCT from MSD between 2019 and 2024. Conditioning regimens consisted on a combination of treosulfan- thiotepa and fludarabine (TTF) for lymphoid malignancies and treosulfan-fludarabine or cyclophosphamide (FT or TreCy) for myeloid malignancies. GVHD prophylaxis consisted on cyclosporine and short course of methotrexate+/- antithymocyte globulin (ATG). Stem cell sources were bone marrow (BM) or peripheral blood stem cells.

Results: Overall, 39 patients were included with a median age of 31 years (range, 7–53). Underlying diseases were acute lymphoblastic leukemia in 31% of cases and acute myeloblastic leukemia in 56% of cases. Before allo-HSCT, 59% of patients were in CR1, 28% ≥ CR2 and refractory disease in 2 patients. Stem cell source was BM in 95% of patients. Fifteen patients received TTF (38%), 44% TreCy and 18% FT. Nine patients (23%) received ATG in addition of the standard GVHD prophylaxis. During the early phase of conditioning, 30 patients (77%) developed grade III-IV mucositis, diarrhea (77%), vomiting (64%). Skin involvement was observed in 64% of patients, consisting of diffuse erythema. Among them 3 patients developed epidermal detachment. The skin biopsy, along with the pharmacovigilance investigation, supported a treosulfan-induced drug eruption. Engraftment was achieved in all cases, with median neutrophil engraftment on day +16 and platelet engraftment on day +23. Twelve patients (31%) developed grade II-IV acute GVHD with a median time of 17 days (range, 10-100), mainly with gastrointestinal involvement (n= 11). Chronic GVHD was observed in 15% of patients, with 2 cases of extensive form. CMV reactivation was observed in 28% of patients. After a median follow-up of 7 months (range, 1–21m), the 1-year OS and EFS were 78% and 51%, respectively. Relapse occurred in 23% of patients after a median time of 2 months (range: 1–14m). NRM occurred in 3 patients after a median time of 5 months (range, 2-7m), due to severe acute GVHD in 2 patients and infectious complication in 1 patient.

Conclusions: Our experience showed that treosulfan based conditioning regimen is associated with an increased risk of skin toxicity and early relapse. A pharmacokinetic study is probably required to optimize efficacy and minimize toxicity.

Disclosure: Nothing to declare.

P203

SUCCESSFUL ABTCR-DEPLETED HAPLOIDENTICAL HSCT AFTER MINIMAL TOXICITY CONDITIONING IN AN HEAVILY PRETREATED DOWN'S SYNDROME PATIENT WITH R/R BCP-ALL

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Background: Down's syndrome (DS) patients with ALL have a significantly worse outcome compared to their non-DS counterparts due to both higher relapse risk and higher treatment-related mortality. Profound sensitivity to conventional chemotherapy can limit treatment options in these patients in case of relapsed/refractory disease, and standard myeloablative conditioning before HSCT may not be applicable due to unacceptable toxicity risk.

Methods: We here present the case of a 20-year-old female DS patient with R/R BCP ALL who could successfully be salvaged by αβTCR-depleted haploidentical HSCT from her sister after conditioning with frontline ATG 20mg/kg x3, fludarabine 30mg/m^2 x4 and TBI 2Gy, complemented by posttransplant cyclophosphamide 25mg/kg d3+4, without further GVHD prophylaxis. Shortly before transplant, the patient was diagnosed with pulmonary aspergillosis, and antifungal treatment with isavuconazol was initiated.

Results: The transplant procedure was unexpectedly well tolerated, with rapid and sustained engraftment and achievement of MRD negativity on d+30. Prophylactic DLI were given from d+62, and venetoclax 50mg/d was preemptively reintroduced on d+64, after re-emergence of low-level MRD was noticed. Pulmonary aspergillosis completely resolved under continuous isavuconazol.

Conclusions: This case shows that heavily pretreated and highly vulnerable patients can successfully be salvaged with αβTCR-depleted haploidentical HSCT after minimal toxicity conditioning. Effective lymphodepletion with frontline ATG and posttransplant cyclophosphamide enabled rapid engraftment and made further GVHD prophylaxis dispensable. Low toxicity of this regimen allowed early initiation of prophylactic DLI and reintroduction of venetoclax for promoting antineoplastic efficacy. Invasive fungal infection at the time of transplant is not necessarily a contraindication for proceeding to RIC HSCT.

Disclosure: Nothing to declare.

P204

OUTCOME OF TREOSULFAN-FLUDARABINE CONDITIONING REGIMENS: A SINGLE CENTER EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) in elderly patients remains a clinical challenge due to frailty, comorbidities, and increased susceptibility to treatment-related toxicity. Treosulfan based regimens are a particularly promising option, providing robust myeloablation while maintaining a more favourable toxicity profile than traditional myeloablative treatments either in malignancies or in non-malignant disease. Despite this growing adoption, real-world data on treosulfan-based conditioning in elderly or frail patients remain limited and warrant further investigation.
The aim of this study was to collect real-world data on the feasibility, efficacy, and safety of treosulfan in a single-centre cohort.

Methods: We conducted a retrospective analysis of all patients aged ≥18 years old who received treosulfan-based conditioning in our Institution between 2021 and 2025. Treosulfan was administered in combination with fludarabine 200 mg/m² as immunosuppressive agent. Baseline demographics, disease characteristics, comorbidities and conditioning details were collected. Outcomes of interest included engraftment kinetics, transplant-related toxicity, infectious complications, acute and chronic graft-versus-host disease (GVHD), non-relapse mortality (NRM), relapse incidence, progression-free survival (PFS), and overall survival (OS).

Results: A total of 46 patients underwent allo-HSCT with a treosulfan-based conditioning regimen between 2021 and 2025. The median age at transplant was 65 years, but two patients were younger than 35. Standard treosulfan dosage was 10 g/m², increased to 14 mg/m² in selected patients.
Median engraftment time of neutrophil (≥ 0.5 × 10^9/L) and platelet (≥ 20 × 10^9/L) was 17 and 14 days respectively. Infectious complications occurred in 16 patients within the first 100 days, two had fatal outcome. Severe mucositis (grade ≥3) was recorded in only 7 patients. 19 patients (41%) presented acute or chronic GvHD: 8 were responsive to steroid treatment but 11 required a second-line therapy.
In the whole cohort median OS was 21 months, 6 patients died for relapse, 8 for non relapse mortality. Median PFS was 15 months; relapse occurred in 9 patients and 3 of them are still alive.
Two clinically relevant cases involved two young patients (35 and 20 years old): the first had AML associated with chronic bowel disease, and the second had MDS with del(7) cytogenetic abnormality secondary to Fanconi anemia. In these cases, treosulfan was chosen to reduce systemic toxicities while maintaining effective myeloablation. Both patients are alive, in complete remission, and free from GvHD after 10 and 48 months, respectively.

Conclusions: In this real-world cohort of predominantly elderly patients, treosulfan-based conditioning showed favorable engraftment kinetics, acceptable infectious morbidity, and a low incidence of severe mucositis. Notably, fewer than half of the patients developed GvHD, although 42% of these cases were steroid-refractory. OS and NRM were consistent with expectations for an elderly transplanted population.
These findings support the feasibility and tolerability of treosulfan-based conditioning in elderly or comorbid patients undergoing allo-HSCT. The inclusion of two younger patients with complex clinical backgrounds further highlights the regimen's adaptability in selected cases. Larger studies with longer follow-up are warranted to confirm these observations and to better define the optimal treosulfan dosing strategy across different patient subsets.

Disclosure: Nothing to declare.

P205

CONDITIONING WITH FLUDARABINE, CYTARABINE, VENETOCLAX, ETOPOSIDE FOR ALLOGENEIC STEM CELL TRANSPLANT IN PATIENTS WITH ACTIVE ACUTE MYELOID LEUKEMIA

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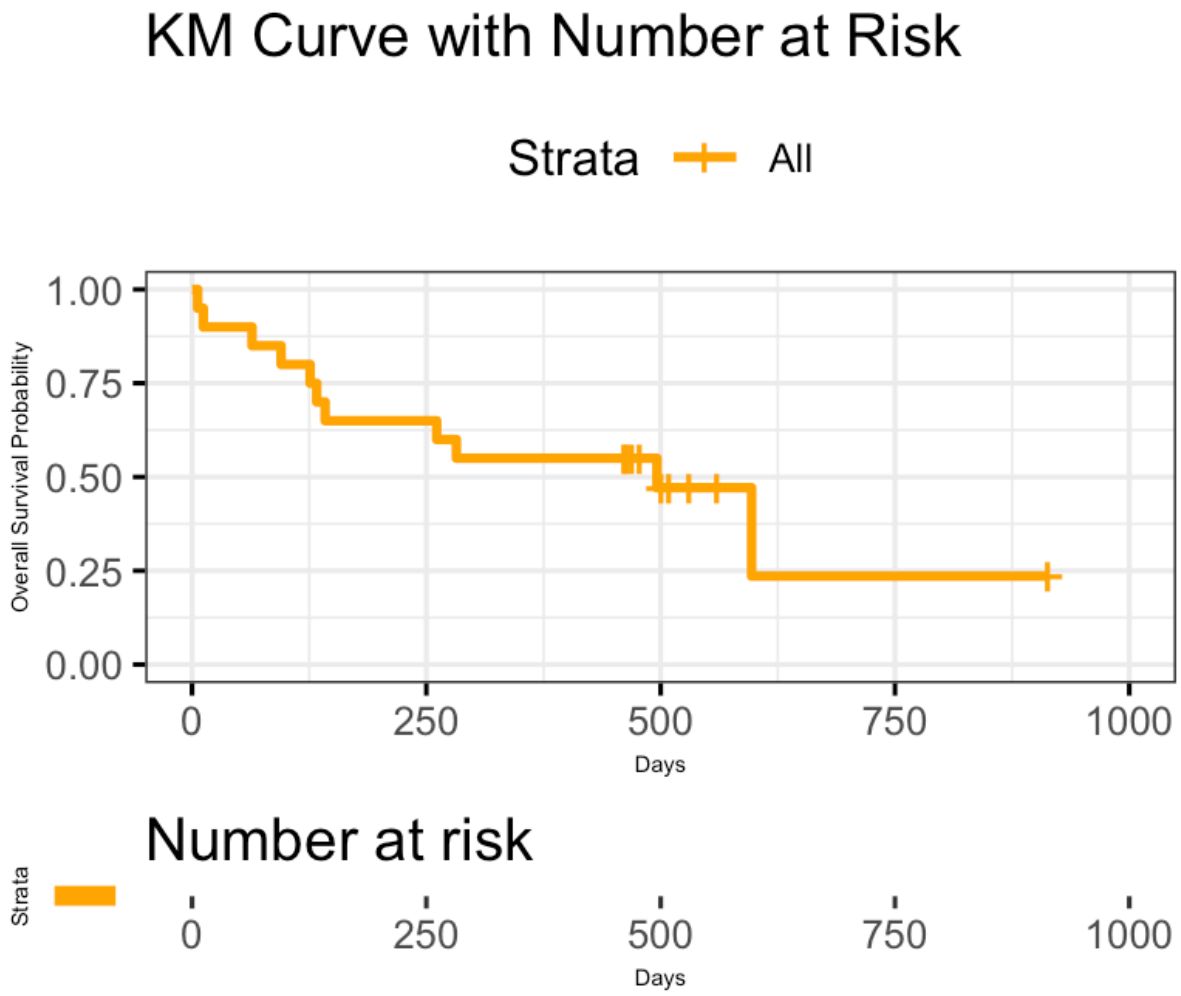
Background: AML patients are frequently refractory to initial therapy or have refractory relapses. Sequential chemotherapy followed by RIC pioneered by the German FLAMSA regimen has been safe and efficacious in these patients. Here we report the single center outcomes of modified FLAMSA(Fludarabine, Cytarabine, Venetoclax, Etoposide, Alkylating agents based RIC) – FLAVER regimen by substituting Amasacrine with Etoposide.

Methods: This was a single center observational study conducted at All India Institute of Medical Sciences, New Delhi.
FLAVER conditioning regimen consisting of Fludarabine 30mg/m^2 , Cytarabine 1500mg/m^2 , Tab Venetoclax 100 mg OD with Tab Voriconazole 200 mg BD on Days -8,-7,-6,-5,-4 with alkylating agent backbone consisting of Busulfan 3.2mg/kg on D-3,-2 and Cyclophosphamide 2000mg/m^2 on D-2 to D-1 . All patients received ATLG 10 mg/kg divided over D-4 to D-1. GVHD prophylaxis consisted of Methotrexate 15 mg/m^2 on D+1 and 10 mg/m^2 on days +3,+6,+11 cyclosporine A (from day -1 with tapering from day +100, target concentration 200-400 mcg/l), and mycophenolate mofetil 1 g/d (days -8 to +30). All patients received GCSF and Plerixafor mobilized peripheral blood stem cells.

Results: A total of 20 patients (14 males)with relapsed or refractory AML underwent FLAVER-SCT between June and September 2024. The median age was 32 years. Six (30%) patients had refractory AML, while 14 (70%) had relapsed AML. The median number of lines of therapy was 2 (1–3). 5(25%) were favorable risk, 9 (45%) intermediate risk and 6 (30%) adverse risk as per ELN classification. FLT3-ITD mutations were present in 8 (40%) patients. Prior exposure to therapy included venetoclax in 19/20 (95%), FLT3 inhibitors in 4/20 (20%), and previous allogeneic transplantation in 1/20 (5%). The median blast percentage

was 19% before conditioning. Donors included haploidentical donors in 10/20 (50%) patients and matched sibling donors in 10/20 (50%).
The CR/CRp rate at Day +30 post-allo-SCT was 90% (18/20), with MRD-negative remission in 17/18 (94.4%) of evaluable patients. The median time to neutrophil recovery was 12 days (8–18).
Grade 3–5 infectious complications occurred in 15/20 (75%) patients, and CMV reactivation was observed in 12/20 (60%). Grade 3–4 diarrhea noted in 6/20 (30%).Veno-occlusive disease was documented in 4/20 (20%).Grade 3–4 acute GVHD occurred in 5/20 (25%).Day 30 mortality was 10% (2/20).
At the data cutoff date (30 November 2025), 8 (40%) patients were alive, 5 (25%) relapsed and subsequently died, 2 (10%) died in transplant course and 4 (20%) died of transplant related complications and 1(5%) patient died of stroke. At a median follow up of 16.5 months, median OS and DFS was 16.3 and 15.6 months respectively.



Conclusions: In this single center experience, FLAVER-SCT demonstrated encouraging remission rates and manageable toxicity in patients with relapsed and active AML, a

population historically associated with poor prognosis. The high CR/CRp rate and rapid neutrophil engraftment suggests potent disease control. Despite frequent toxicities acute mortality remained acceptable with durable remissions. Larger prospective studies are warranted to validate these findings.

Disclosure: Nothing to Declare

P206

THE EFFICACY AND SAFETY OF COMBINED FLUDARABINE, BUSULFAN, AND MELPHALAN REDUCED-INTENSITY CONDITIONING (RIC) REGIMEN IN ALLOGENEIC STEM CELL TRANSPLANTATION FOR ADULTS WITH HEMATOLOGIC MALIGNANCY DISEASES

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Background: Reduced-intensity conditioning (RIC) regimen is therapeutic option for older patients or those with comorbidities undergoing allogeneic stem cell transplantation (allo-SCT). While fludarabine-based regimens (with either busulfan or melphalan) are widely used, balancing relapse incidence (RI) against non-relapse mortality (NRM) remains challenging. This study evaluated the efficacy and safety of a triple-agent RIC regimen combining Fludarabine, Busulfan, and Melphalan (Flu-Bu-Mel) in patients with malignant hematological diseases.

Methods: This retrospective study was performed using registry data from adult patients underwent allo-HCT following fludarabine (125 mg/m^2), busulfan (6.4 mg/kg) and melphalan (100 mg/m^2) conditioning regimen at Chiang Mai University hospital between September 2022 and October 2025. The primary endpoint was Overall Survival (OS). Secondary endpoints included Relapse-Free Survival (RFS), Relapse Incidence (RI), Non-Relapse Mortality (NRM), and safety profiles.

Results:

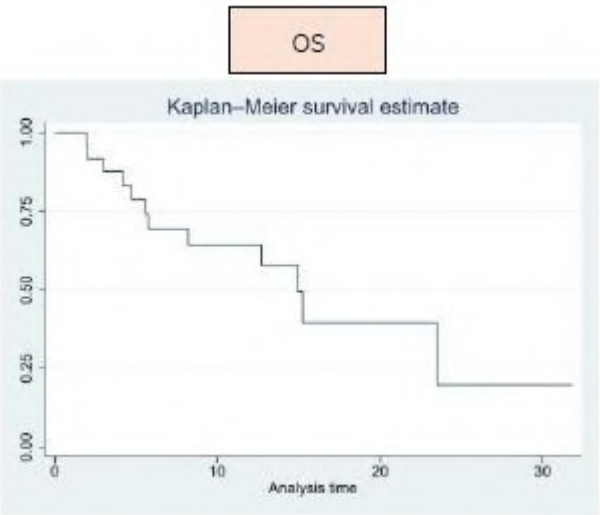
Baseline Characteristics	Total (n=25)	Related Donor (RD) (n=12)	Unrelated Donor (UD) (n=13)	P value
Patient age, median (IQR), y	40 (30-49)	47.5 (34-52.5)	24 (28-42)	0.103

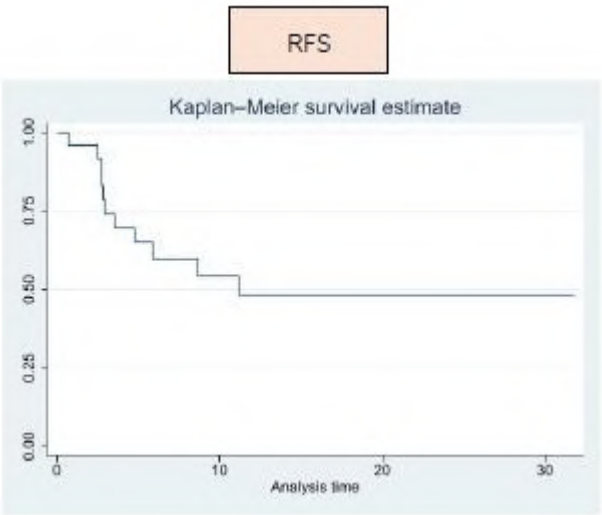
Recipient sex: male, n (%)	14 (56)	7 (58.3)	7 (53.9)	0.821
Donor sex: male, n (%)	13 (52)	7 (58.3)	6 (46.1)	0.543
Female donor to male recipient, n (%)	6 (24)	1 (8.3)	5 (38.5)	0.094
Degree of HLA-match • 10/10 • 9/10 • 8/10	21 (84.0) 3 (12.0) 1 (4.0)	12 (100.0) 0 (0) 0 (0)	9 (69.23) 3 (23.08) 1 (7.69)	0.152
Diagnosis • Acute Myeloid Leukemia (AML) • Acute Lymphoblastic Leukemia (ALL) • Myelodysplastic syndrome (MDS) • Chronic Myeloid Leukemia (CML) • Chronic Myelomonocytic Leukemia (CMML) • Myelofibrosis • Peripheral T-cell Lymphoma, not otherwise specified (PTCL, NOS) • Hodgkin Lymphoma (HL)	9 (36.0) 6 (24.0) 4 (16.0) 2 (8.0) 1 (4.0) 1 (4.0) 1 (4.0) 1 (4.0)	5 (41.7) 3 (25.0) 1 (8.3) 2 (16.7) 0 (0) 0 (0) 1(8.3) 0 (0)	4 (30.8) 3 (23.08) 3 (23.1) 0 (0) 1 (7.7) 1 (7.7) 0 (0) 1 (7.7)	0.563
Disease status before transplantation • Complete remission1 (CR) • Partial remission (PR) • Stable of disease (SD) • Refractory	21 (84.0) 1 (4.0) 3 (12.0) 0 (0)	11 (91.7) 1 (8.3) 0 (0) 0 (0)	10 (76.9) 0 (0) 3 (23.1) 0 (0)	0.220
HCT-CI score • 0 • 1-2	4 (16.0) 20	1 (8.3) 10	3 (23.1) 10 (76.9) 0 (0)	0.593

• ≥ 3	(80.0) 1 (4.0)	(83.3) 1 (8.3)		
Performance status (ECOG) • 0 • 1	17 (68.0) 8 (32.0)	8 (66.7) 4 (33.3)	9 (69.2) 4 (30.8)	>0.999
CMV status • D+/R+, n (%) • D+/R-, n (%) • D-/R+, n (%) • D-/R-, n (%)	22 (88.0) 2 (8.0) 1 (4.0) 0 (0)	10 (83.3) 2 (16.7) 0 (0) 0 (0)	12 (92.3) 0 (0) 1 (7.7) 0 (0)	0.344
Stem cell source, n (%) • G-CSF–mobilized peripheral blood stem cells (PB) • Bone marrow (BM)	25 (100.0) 0 (0)	12 (100.0) 0 (0)	13 (100.0) 0 (0)	0.876
Post grafting immunosuppression, n (%) • PTCy + Tacrolimus + MMF • Calcineurin inhibitors (CNI) + Methotrexate (MTX)	13 (52.0) 12 (48.0)	0 (0) 12 (100.0)	13 (100.0) 0 (0)	<0.001
CMV prophylaxis used (Day 10-37), n (%)	10 (40.0)	0 (0)	10 (76.92)	<0.001
Anti-thymoglobulin used, n (%)	0 (0)	0 (0)	0 (0)	-
WBC engraftment, median (IQR), day after stem cell infusion	20 (17-21)	17.5 (16-20)	21 (20-23)	0.004
Platelet engraftment, median (IQR), day after stem cell infusion	15 (13-17)	13.5 (12.5-15)	16 (14-21)	0.023

A total of 25 patients (AML n=9, ALL n=6, MDS n=4, CML blastic phase n=2, CMML n=1,

Myelofibrosis n=1, Relapsed PTCL, NOS n=1 and Relapsed cHL n=1) were analyzed. The median age was 40 years (30-49). Donors were matched related (n=12) and unrelated (n=13). Most patients (84%) were in the first complete remission (CR1) at the time of transplant. Stem cell source were G-CSF-mobilized peripheral blood stem cells (PB) (100%). Patients underwent match related allo-HCT were recieved CNI/MTX GVHD prophylaxis, while patients underwent match related allo-HCT were recieved PTCy/Tacrolimus/MMF GVHD prophylaxis. The median time to neutrophil was 17.5 and 21 days in match related and unrelated allo-HCT, respectively. The madian time to platelet recovery was 13.5 and 16 days in match related and unrelated allo-HCT, respectively.
The 1-year OS, RFS, GRFS and NRM were 68.0%, 56.0%, 28.0% and 8.3% respectively, while the Relapse Incidence (RI) was 44.0%. There was no statistically significant difference in 1-year OS between related (75.0%) and unrelated allo-HCT patients (61.5%) (p=0.673). Median OS and RFS was 14.9 (5.6-23.5) and 11.2 (2.9-NR) months, respectively.





The incidence of acute GVHD was 12.0%, and chronic GVHD was 32.0%. There was no statistically significant difference in incidence of aGVHD and cGVHD between related and unrelated allo-HCT patients (p>0.999 and 0.411, respectively).
In terms of safety, the regimen was well-tolerated. Common Grade 3-4 non-hematologic adverse events included diarrhea (12.0%), oral mucositis (8.0%), and lung infection (8.0%). There was one Grade 5 adverse event (Lung infection) (4.0%).

Conclusions: The Flu-Bu-Mel reduced-intensity conditioning regimen demonstrates a favorable safety profile with low non-relapse mortality (NRM) and acceptable toxicity in patients with hematological malignancies. However, the relapse rate remains a concern (44%). This triple-agent regimen is a feasible option for patient ineligible for myeloablative conditioning, though further studies are warranted to optimize relapse prevention.

Clinical Trial Registry: -

Disclosure: Nothing to declare.

Immune Reconstitution and Chimerism

OS05-01

COMBINED TRANSPLANTS (HEMATOPOIETIC STEM CELL AND SOLID ORGAN) TO ACHIEVE IMMUNE TOLERANCE: A EUROPEAN PEDIATRIC STUDY

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Background: One of the possible indication of allogeneic hematopoietic stem cell transplantation (alloHSCT) is the induction of immune tolerance in the setting of solid organ transplantation (SOT). Indeed, lifelong immunosuppression is associated with significant morbidity, while it does not completely prevent graft rejection. This is of particular importance in children, in whom life expectancy is long, frequently overcoming the graft survival. Although specific programs for combined transplant are active in adults, pediatric programs are lacking and data on combo transplant are scarce and anecdotal.

Methods: PDWP sub-commission COST4KIDS, aimed at studying this peculiar field in transplantation, conducted a retrospective multicenter data collection on patients receiving a combined transplant (i.e., alloHSCT + SOT) whatever the sequence of the transplants, in 4 countries, namely Italy, UK, Spain and Germany.

Results: We identified 30 transplants combined with alloHSCT: 20 liver, 7 kidneys and 3 multivisceral transplants (gut+liver). Median age at first transplant was 6.1 years (interquartile range, IQR, 4.6-11.1). The donor was the same for both the transplant in 12 cases (6 kidney and 6 liver), while it differed (mainly being a cadaveric donor) in all other cases. Regarding the timing of HSCT/SOT, HSCT preceded SOT in 9 cases [7 kidneys and 2 liver transplants; median time 16 months (IQR 11-19)], while it followed in 21 cases [median time 10.2 months (IQR 3-22)]. Indication to SOTs varied (details in Table 1); in general, there were two main scenarios: 1) liver transplant for hepatic failure due to nonAtoE-viral hepatitis from a cadaveric donor, followed by alloHSCT (from a different donor) because of severe aplastic anemia developing after SOT (11 cases); 2) alloHSCT for an hematological indication, followed by SOT (kidney or liver, frequently from the same HSC donor) because of organ failure as complication of alloHSCT (9 cases). Eleven patients (36.6%) received a fully-myeloablative conditioning, one none, while the others a reduced-intensity conditioning. All

patients, including those who underwent SOT after HSCT from the same donor of HSC, received immunosuppression after the SOT. Importantly, 11 patients out of 30 (36.6%), were able to safely discontinue immunosuppression. In details, 6 liver transplant (who received an HSCT after SOT) and 5 kidney transplant (who received an HSCT before SOT) stopped IS after a median of 150 days after the last transplant (IQR 60-470) without occurrence of graft rejection. In 3 cases the donor of SOT and alloHSCT was different. Infectious complications (including bacterial, viral and fungal infections) after both HSCT and SOT and surgical complications after SOT were frequent, reflecting the heavily immunocompromised state of these patients and the complexity of this kind of program. With a median follow-up of 4.8 years (IQR 2.5-6.6) 24 patients are alive with conserved organ function.

Indication to SOT		**Number**		**Indication to alloHSCT**	**Number**
Liver	hepatic failure due to nonAtoE-viral hepatitis	11		aplastic anemia	13
	hepatic failure due to adenovirus	1		acute leukemia	6
	hepatoblastoma	4		Hodgkin lymphoma	1
	autoimmune hepatitis	1		Shwachman-diamond syndrome	1
	alpha-1 antitrypsin deficiency	1		hemophagocytic lymphohistiocytosis	1
	liver failure due to secondary HLH	1		severe combined immunodeficiency	1
	iron overload	1		beta-thalassemia	1
Kidney	ESRD due to TMA	2		concomitant to favor immune tolerance	6
	interstitial nephritis	2			
	glomerular sclerosis	1			
	glomerulonephritis	1			
	SIOD	1			
Multivisceral	short bowel syndrome due to malrotation and volvulus	2			
	epithelial dysplasia	1			

Conclusions: Despite a complex scenario, with different indications, timing of transplants, donor employed and immunosuppressive regimens used, these data indicates that HSCT can induce immune tolerance also in the pediatric setting. Long-term data on organ function and chimerism/immune recovery will help in further refining this kind of interventions.
Perspective studies and dedicated programs in children are urgently needed.

Disclosure: None related to this abstract.

OS05-02

EARLY IMMUNE RECOVERY IN MISMATCHED UNRELATED DONOR PERIPHERAL BLOOD STEM CELL TRANSPLANTATION USING REDUCED-DOSE POST-TRANSPLANTATION CYCLOPHOSPHAMIDE AS GRAFT-VERSUS-HOST DISEASE PROPHYLAXIS: RESULTS FROM THE OPTIMIZE TRIAL

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Background: The ACCESS trial (NCT04904588) showed favorable combined one-year overall survival (81%) after mismatched unrelated donor (MMUD) hematopoietic cell transplantation (HCT) in 145 adult patients using post-transplantation cyclophosphamide (PTCy, 50 mg/kg Days 3&4) (PMID 40523209). However, 87 (60%) patients [42 (56%) receiving myeloablative, MAC (n=75) and 45 (64%) receiving non-myeloablative/reduced intensity conditioning, NMA/RIC (n=70)] experienced 275 clinically significant infections (CTCAE Grade 2-5) within the first 100 days (D100) [n=72 MAC, n=203 RIC/NMA]. The OPTIMIZE trial (NCT06001385) using reduced dose (RD) PTCy (25 mg/kg D3&4) aims to attenuate infection burden while maintaining graft-versus-host disease (GvHD) prevention. Herein, we describe immune reconstitution (IR) and cumulative incidence of infection by D100 following MMUD HCT in a subset of patients with available data enrolled in OPTIMIZE.

Methods: Correlative data was restricted to 69 adult patients enrolled on OPTIMIZE with available donor chimerism (D28, 100), IR (D28, D56, 100), and infection data by D100. Unsorted bone marrow or peripheral blood (PB) CD3+ donor chimerism analyses were performed at sites, while IR analyses were performed at a central reference laboratory. Absolute numbers of immune cell populations (mean ± SEM) were calculated by multiplying the percentage of a gated cell population by white blood cell count (cells/μL) from the same PB sample. Infections were graded using Blood and Marrow Transplant Clinical Trials Network (BMT CTN) criteria. Exact binomial and complementary log-log confidence intervals were

computed around estimates of donor chimerism and cumulative incidences of infection, respectively.

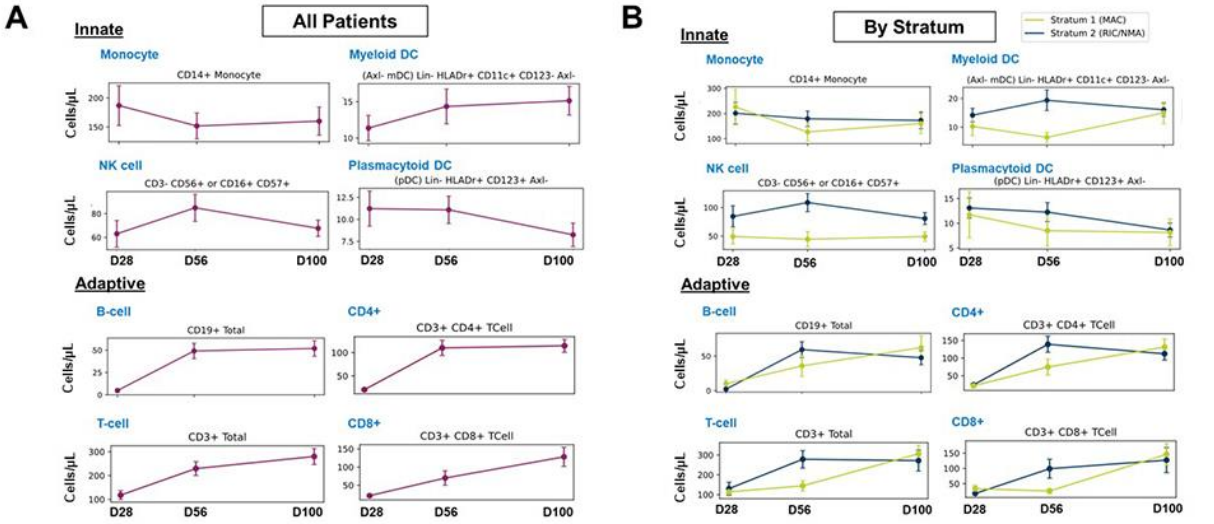
OPTIMIZE Sample Contributors:

Site	PI	PI Email	No. Pts
10047 University of Pennsylvania	Shannon McCurdy	shannon.mccurdy@pennmedicine.upenn.edu	5
10065 University of Miami	Antonio Jimenez Jimenez	amjimenez@med.miami.edu	2
10117 Fred Hutch	Masumi Ueda Oshima	mueda@fredhutch.org	6
10134 Karmanos	Dipenkumar Modi	modid@karmanos.org	2
10140 Dana Farber	Mahasweta Gooptu	mahasweta_gooptu@dfci.harvard.edu	10
10143 City of Hope	Monzr Al Malki	malmalki@coh.org	13
10151 MD Anderson	Betul Oran	boran@mdanderson.org	4
11113 University of Virginia	Karen Ballen	KB3TC@uvahealth.org	8
11188 University of Minnesota	Mark Juckett	juck0001@umn.edu	10
11380 Oregon Health and Science University	Rachel Cook	coora@ohsu.edu	10

Results: Median patient age by stratum was 41 (19-64) and 68 (42-78) years for MAC (n=26) and RIC/NMA (n=43) recipients, respectively. The most common conditioning regimens were Busulfan/Fludarabine (Flu) (46%) and Flu/total body irradiation (TBI) (42%) for MAC recipients and Flu/Melphalan (51%) and Flu/Cyclophosphamide/TBI (21%) for RIC/NMA recipients. The percentage of patients with ≥95% donor chimerism at D28 and D100 were 75.4% (95% CI 63.5-84.9) and 79.7% (95% CI 68.3-88.4), respectively. Donor chimerism did not differ by conditioning intensity (data not shown). Median time to absolute neutrophil recovery (≥500/µl) for all patients was 14 days (13-15) and did not differ by conditioning intensity (data not shown). In general, mean absolute numbers of immune cells increased from D28 to D100 except for monocytes, which decreased after D28 (**Figure 1A**).

Natural killer and plasmacytoid dendritic cells decreased after D56, while B- and T-cell increased to 50 cells/µl by D56. Patients receiving MAC had slower IR versus RIC/NMA recipients (**Figure 1B**). By D100, 22 (30%) patients [n=11 per stratum] experienced 35 BMT CTN Grade 2-3 infections [n=18 MAC, n=17 RIC/NMA]. Cumulative incidence of BMT CTN Grades 2-3 infection for all patients by pathogen type are shown in **Figure 1C**. Cumulative incidences of BMT CTN Grades 2-3 infections were higher in MAC versus RIC/NMA recipients, with most infections occurring by D28 (**Figure 1D**).

Figure 1. Innate and Adaptive Immune Cell Recovery and Cumulative Incidence of Infection



C

Cumulative Incidence (95% CI) of First BMT CTN Grade 2-3 Infection by Pathogen Type			
	D28	D56	D100
All Pathogens	21.3% (12.9-31.2)	26.7% (17.2-37.1)	33.5% (23.0-44.2)
Bacterial	10.7% (5.0-18.9)	12.0% (5.9-20.5)	16.1% (8.8-25.3)
Viral	12.0% (5.9-20.5)	17.3% (9.7-26.7)	20.0% (11.8-29.8)

No fungal infections reported. Competing events included second transplant, death, early termination, and loss to follow-up.

D

Cumulative Incidence (95% CI) of First BMT CTN Grade 2-3 Infection By Strata			
Stratum (No. pts)	D28	D56	D100
MAC (n=26)	26.9% (11.7-44.9)	34.6% (17.1-52.9)	42.3% (23.0-60.4)
RIC/NMA (n=43)	16.3% (7.1-28.8)	18.6% (8.6-31.5)	25.8% (13.7-39.6)

Competing events included second transplant, death, early termination, and loss to follow-up.

Conclusions: OPTIMIZE is the first MMUD trial using RD PTCy to describe donor-derived immune recovery and its association with infection. Preliminary findings suggest differences in IR based on conditioning intensity with MAC recipients having slower IR and higher cumulative incidence of infection.

Clinical Trial Registry: OPTIMIZE NCT06001385
https://clinicaltrials.gov/study/NCT06001385

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OS05-03

SYSTEMS BIOLOGY APPROACH REVEALS BDNF AS A DRIVER OF B-CELL REGENERATION

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Background: Prolonged B-cell aplasia, observed after allogeneic hematopoietic stem cell transplantation (HSCT) and CD19 directed immunotherapies, impairs protective immune responses against cancer, infections, and vaccines. In contrast to the myeloid and erythroid lineages, which can be supported using G-CSF and erythropoietin, there is currently no therapeutic strategy available to promote B-cell development. Here, we utilized a system biology approach to discover drivers for B lymphopoiesis in the human Bone Marrow (BM).

Methods: We analyzed single cell RNA sequencing (scRNA-seq) data from healthy human BM samples and applied the CellAllign algorithm to compare B-cell developmental trajectories across individuals. We quantified circulating proteins in patients treated with B-cell depleting therapies using multiplex protein assays. Putative drivers identified through these analyses were evaluated in single cell stimulation assays and in an in vitro co culture system modeling B-cell development from CD34+ progenitor cells.

Results: By mapping the BM intercellular communication landscape using scRNA-seq datasets, we identified multiple microenvironment derived signals predicted to interact with and influence early B-cell progenitors. Our computational analyses highlighted a subset of putative drivers enriched in stromal and niche populations positioned to support B-cell maturation. To refine this list, we incorporated information from several orthogonal datasets, including transcriptional signatures associated with age impaired B lymphopoiesis, differences in developmental trajectory dynamics across individuals, and regulatory patterns emerging from mesenchymal stromal cells. We also examined plasma protein profiles from patients who had undergone B-cell depleting therapies, which provided an additional layer of evidence for factors that may influence B-cell regeneration in vivo.
Across these analyses, several high confidence candidates emerged. Functional single cell stimulation assays demonstrated that these candidates activated distinct transcriptional programs related to B-cell development, including pathways involved in lineage proliferation, differentiation and survival. Different putative drivers influenced non overlapping sets of genes, suggesting that multiple regulatory mechanisms converge to shape human B lymphopoiesis. Among the prioritized molecules, brain derived neurotrophic factor (BDNF) consistently showed strong and reproductive ability to activate B-cell developmental pathways.
To assess its functional relevance, we tested BDNF in an in vitro co culture system that

models early human B-cell development from CD34+ hematopoietic stem and progenitor cells. In this biological system, BDNF exposure led to a marked increase in the generation of early B-cell progenitors. The enhancement of differentiation was observed across multiple donors, demonstrating that the effect of BDNF is robust and not donor specific. Together, these results identify BDNF as a previously unrecognized driver of human B-cell development and validate our multi-layered approach for discovering new regulators of hematopoiesis.

Conclusions: Our findings reveal new regulators of human B lymphopoiesis and suggest potential therapeutic strategies for enhancing B-cell development in clinical settings. By integrating single cell genomics, proteomics, computational alignment, and functional in vitro assays, we establish a framework for dissecting complex developmental processes in the BM. This integrative approach provides a scalable template for identifying accelerators of additional immune lineages and advancing system level understanding of human immune regeneration following HSCT.

Disclosure: Nothing to declare

OS05-04

COMPARISON OF IMMUNE RECONSTITUTION AND INFECTION-RELATED OUTCOMES WITH PT-CY VERSUS ATG AFTER MUD TRANSPLANTATION FOR HIGH-RISK MYELOID MALIGNANCIES

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Background: Post-transplant cyclophosphamide (PT-Cy) and anti-thymocyte globulin (ATG) are widely used T-cell depletion strategies in matched unrelated donor (MUD) allogenic hematopoietic cell transplantation (allo-HCT). However, no consensus exists regarding the recommended approach. Assessing how these strategies affect immune reconstitution (IR) and infection rates may help define a decision-making algorithm.

Methods: We retrospectively analyzed the timing and dynamics of IR in a two-center study of allo-HCT from MUD following intermediate- or high-intensity conditioning for high-risk myeloid malignancies. GVHD prophylaxis differed by center (ATG 30 mg/kg plus calcineurin inhibitors versus PT-Cy 100 mg/kg plus rapamycin). Immune monitoring was performed monthly throughout the first year after allo-HCT by flow cytometry with quantification of $CD3^+CD4^+$ and $CD3^+CD8^+$ T cells, $CD19^+$ B cells, and $CD56^+CD16^+$ NK cells. IR was defined as sustained recovery of $CD3^+CD4^+$ T-cells >200/µL and $CD19^+$ B-cells >50/µL.

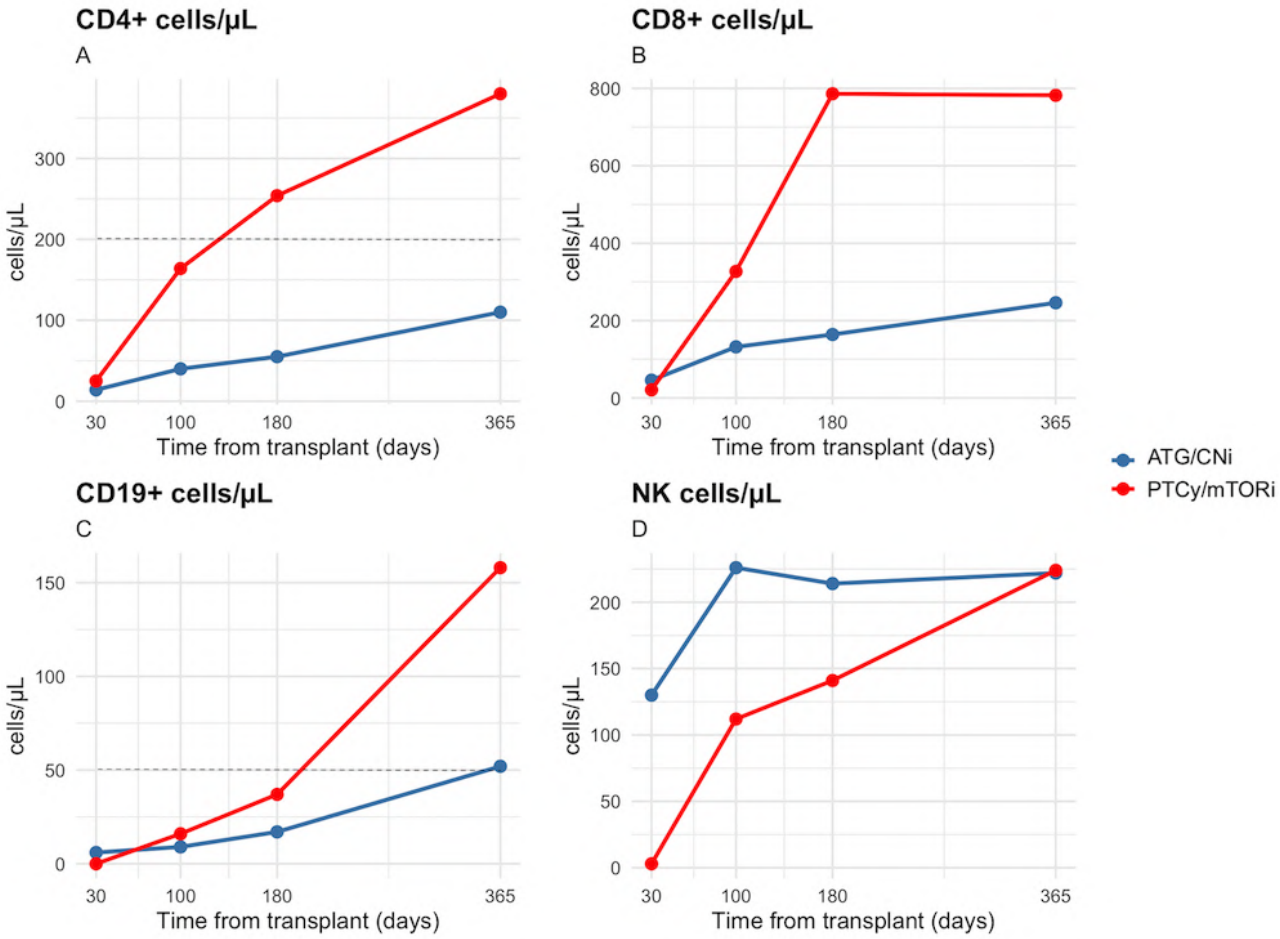
Results: Overall, 204 patients were included, 154 (75.5%) receiving ATG and 50 (24.5%) receiving PT-Cy. The cohorts were comparable, except for a higher proportion of patients

with high EBMT risk score among those in the ATG group (p<0.001), and more high-risk recipient/donor CMV matching in the PT-Cy group (p<0.001) (**Table1.docx**). The 1-year cumulative incidence (CI) of IR was 41% in the PT-Cy arm versus 7% in the ATG arm (p<0.0001), increasing at 18 months to 53% and 16%, respectively. Multivariable analysis—adjusting for recipient/donor age, EBMT risk score, conditioning intensity, and CMV serology—confirmed this association (SHR 0.40, 95%CI 0.22–0.70; p=0.001). IR dynamics differed: $CD3^+CD4^+$, $CD3^+CD8^+$, and $CD19^+$ recovery were faster with PT-Cy, whereas NK cells peaked earlier with ATG, converging between the two populations by one year (**Figure 1**). Coherent with IR kinetics, the incidence of severe infections requiring re-hospitalization within six months from allo-HCT was higher in the ATG cohort (36.4% versus 8.2%; p<0.001). Among these episodes, fungal infections were observed exclusively with ATG (17.9%). Bacterial infections during the first six months post-transplant were more common among PT-Cy recipients (75% versus 39.3% in the ATG group). Finally, viral infections requiring hospitalization in the first six months were observed in both cohorts (50% in PT-Cy versus 35.7% in ATG). Notably, clinically relevant CMV reactivations within 1 year from transplant were more frequent after ATG, with an incidence of 24.7% versus 12% in the PT-Cy cohort (p=0.09). EBV reactivations were restricted to the ATG arm throughout follow-up (22.1%).

Consistent with these findings, 100-day transplant-related mortality (TRM) was 2% in the PT-Cy group and 9% in the ATG cohort (p<0.001), rising to 28.6% at 1 year in ATG while remaining 2% in PT-Cy. Infectious TRM accounted for 6% at 100 days and 15.6% at 1 year after allo-HCT in the ATG arm, whereas no infectious deaths occurred in PT-Cy-receiving patients (p=0.0011).

	ATG N = 154	**PTCy** N = 50	**p-value**
Male Gender, n (%)	93 (60%)	30 (60%)	>0.9
Age at transplant, median (IQR)	61 (54–66)	57 (45–65)	0.073
Baseline disease, n (%)			0.3
AML	101 (66%)	40 (80%)	
MDS, MPN, MDS/MPN	53 (34%)	10 (20%)	
EBMT risk score (categories), n (%)			**<0.001**
Low (0–2)	15 (9.7%)	5 (10%)	
Intermediate (3–4)	73 (47%)	41 (82%)	
High (5–7)	66 (43%)	4 (8.0%)	
Donor age, median (IQR)	31 (25–37)	27 (23–35)	0.052
CMV serostatus (R/D), n (%)			**<0.001**

	ATG N = 154	**PTCy** N = 50	**p-value**
High risk (+/+,+/-)	61 (40%)	44 (88%)	
Intermediate risk (-/+)	24 (16%)	1 (2.0%)	
Low risk (-/-)	69 (45%)	3 (6.0%)	
Female Donor/Male Recipient, n (%)	0 (0%)	0 (0%)	
Transplant Conditioning Intensity, n (%)			0.2
Intermediate	116 (75%)	33 (66%)	
High	38 (25%)	17 (34%)	
Median follow-up (month), median (IQR)	23 (7–48)	41 (30–53)	**<0.001**



Conclusions: In this retrospective study, the PT-Cy + rapamycin platform was associated with a faster and more sustained IR, a lower incidence of infection-related hospitalizations, and a lower infectious TRM. These potentially clinically meaningful findings warrant validation in prospective, randomized studies.

Disclosure: **Nothing to declare.**

OS05-05

THREE-MONTH CHIMERISM-TRIGGERED PRE-EMPTIVE DONOR LYMPHOCYTE INFUSIONS IMPROVE OUTCOMES IN T-CELL-DEPLETED ALLOGENEIC STEM CELL TRANSPLANTS FOR HAEMATOLOGICAL MALIGNANCIES

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Background: The importance of three-month (3-mo) chimerism as a trigger for pre-emptive donor lymphocyte infusion (DLI) remains unknown. Herein, we present a multicentre study on this topic across T-cell-depleted (TCD) allogeneic stem cell transplantation (allo-SCT) for various haematological malignancies. This study aims to evaluate the impact of 3-mo chimerism-triggered DLI on 2-year overall survival (OS), progression-free survival (PFS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM) and graft-versus-host disease-free/relapse-free survival (GRFS).

Methods: This retrospective multicentre study included 649 patients from five centres who received TCD allo-SCT. Patients who relapsed (n=43) or died (n=73) before 3-mo were excluded. The median age was 56.7 years (range 16.5-76.9), with 59.7% males. Disease lineage included myeloid (n=378) and lymphoid (n=151). Donor types included unrelated (n=411) and sibling (n=115). Median follow-up estimated using the reverse Kaplan-Meier method was 34.6 months. Mixed donor chimerism was defined as 5-95% donor cells. Full donor chimerism was defined as >95%. OS, PFS and GRFS were calculated using univariate and multivariable Cox proportional hazards models. For GRFS analysis only, patients with MC who developed GVHD before 180 days and subsequently did not receive DLI were excluded. CIR and NRM were assessed with Fine-Gray competing-risks regression for both univariate and multivariable analyses. Multivariable models adjusted for age, sex, disease lineage, cytogenetic risk, cytomegalovirus serostatus, donor type, and presence of acute graft-versus-host disease.

Results: Among individuals with 3-mo mixed chimerism (MC) in whole blood (WB), univariate analysis showed improved PFS (HR 0.46, 95% CI 0.22–0.98, p=0.04) and GRFS (HR 0.34, 95% CI 0.16-0.72, p=0.0049) with DLI, but no significant effect on OS, CIR or NRM. Those with MC in T-cell (TC) subset showed improved OS (HR 0.48, 95% CI 0.25–0.90, p=0.023) and GRFS (HR 0.48, 95% CI 0.28-0.83, p=0.0078) with DLI, but no significant effect on PFS, CIR or NRM.
Multivariable analysis in the MC WB cohort found that pre-emptive DLI was significantly associated with improved PFS (HR 0.10, 95% CI 0.025–0.44, p=0.002), OS (HR 0.078, 95% CI 0.012–0.52, p=0.008), GRFS (HR 0.048, 95% CI 0.0089-0.26, p=0.00042) and reduced CIR (HR 0.14, 95% CI 0.03-0.68, p=0.014), with no effect on NRM. In the MC T-cell cohort, DLI significantly improved OS (HR 0.26, 95% CI 0.08-0.77, p=0.016) and GRFS (HR 0.26, 95% CI 0.11-0.62, p=0.0026), without affecting NRM.

Conclusions: Pre-emptive DLI in patients with 3-mo MC following T-cell-depleted allo-SCT is associated with improved survival outcomes. In WB MC, DLI significantly improves 2-year PFS and OS due to reduced CIR without negatively impacting GRFS or NRM. In TC MC, DLI was associated with improved OS, without impaired GRFS or increased NRM. These findings support the use of 3-mo chimerism measurement as an indication for pre-emptive DLI. Prospective studies integrating chimerism subsets with measurable residual disease are warranted to optimise post-transplant intervention strategies.

Disclosure: Nothing to declare.

OS05-06

EVALUATION OF FACTORS THAT MAY INFLUENCE CHIMERISM IN HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SICKLE CELL DISEASE

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Background: Monitoring post-transplant chimerism in hematopoietic stem cell transplantation (HSCT) for sickle cell disease (SCD) is essential to guide immunosuppression management. Maintaining a minimum donor chimerism threshold of approximately 20–30% is crucial for long-term disease control. Identifying factors associated with the achievement and maintenance of complete chimerism (CC) remains an important objective.

Methods: We conducted a single-center analytical study including patients with SCD who underwent HSCT from an HLA-identical sibling donor between May 2010 and May 2025. Bone marrow was used as the stem cell source in all cases. Transfusion therapy was initiated 3 months before HSCT, and since 2015, hydroxyurea was started or intensified 1 month pre-HSCT to maintain reticulocyte counts below 100,000/mm³. Conditioning regimens consisted of busulfan, cyclophosphamide, and alemtuzumab until January 2015, and thiotepa, treosulfan, fludarabine, and anti-thymocyte globulin thereafter.
Donor/recipient chimerism was assessed in unfractionated peripheral blood (PB) and T lymphocytes (LT) at months +1, +12, and at last follow-up; bone marrow was additionally analyzed at month +1. CC was defined as ≥95% donor cells, mixed chimerism (MC) as ≥5% to <95%, and autologous reconstitution as <5%. Epidemiological, clinical, and analytical data were collected. Results are presented as medians (p25–p75) or percentages. Statistical analyses included chi-square or Fisher's exact tests, Wilcoxon signed-rank test, log-rank test, and mixed-effects regression models, with significance set at $p<0.05$.

Results: A total of 63 HSCTs were performed in 62 patients, with a median age of 6.45 years (3.07–9.82). Eleven patients received the first conditioning regimen and 52 the second. At month +1, 52 patients (82.5%) achieved CC in PB, while 11 had MC. At year +1, 40 patients (67.8%) maintained CC and 19 had MC; 2 of these showed recipient chimerism >80% with reappearance of SCD symptoms. At last follow-up, 41 patients (65.1%) remained in CC and 22 in MC, including 4 with >80% recipient chimerism. Among these, one patient experienced vaso-occlusive crisis and subsequently achieved CC after a second HSCT, one was lost to follow-up, one died due to refractory EBV-associated hemophagocytic lymphohistiocytosis, and one remains asymptomatic.
Higher pre-HSCT hemoglobin levels ($p=0.035$) and lower reticulocyte counts ($p=0.043$) were significantly associated with CC at last follow-up (Table 1). Pre-HSCT hemoglobin also showed a trend toward association with CC at year +1 ($p=0.052$). Mixed-effects regression models demonstrated that increasing time and higher pre-HSCT hemoglobin were associated with progressive decreases in donor chimerism in PB (Picture 1A) and LT (1B). Similar associations were observed for reticulocyte and fetal hemoglobin levels in PB chimerism (1C-D).

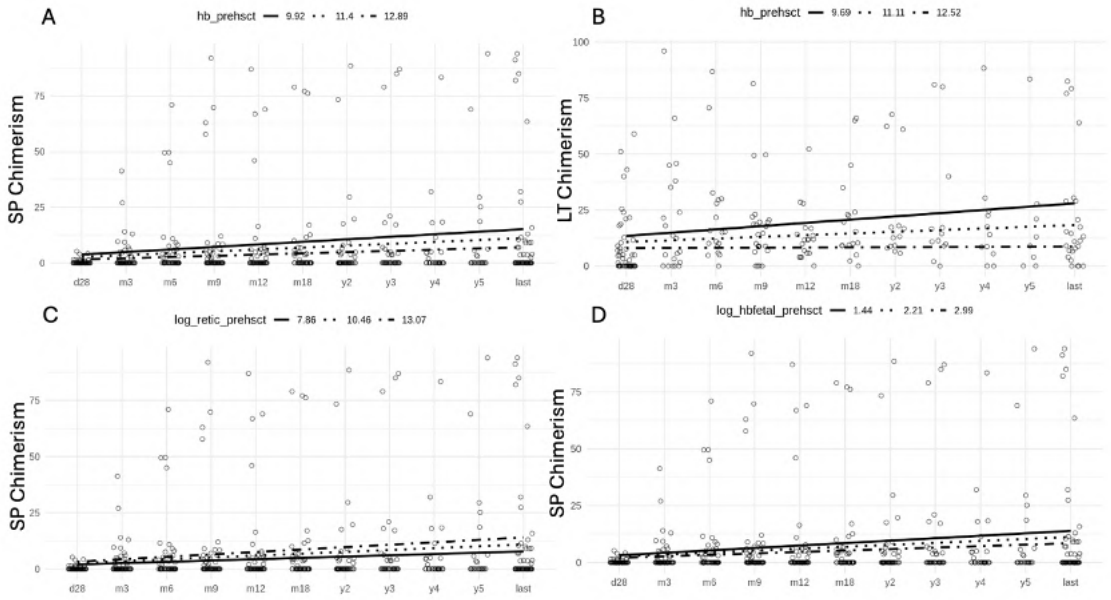
Table 1. Pre-HSCT factors and complete chimerism in PB at last follow-up

	Complete Chimerism Yes (N=41)[1]	Complete Chimerism No (N=19)[1]	
Pre-HSCT Ferritin (ng/ml)	640 (401, 964)	612 (225, 821)	0.3[2]
Pre-HSCT LDH (UI/L)	342 (281, 448)	351 (283, 441)	0.8[2]
Pre-HSCT HbS (%)	21 (14, 28)	23 (18, 37)	0.2[2]
Pre-HSCT HbF (%)	11 (6, 16)	11 (8, 14)	>0.9[2]
Pre-HSCT Hemoglobin (g/dl)	11.75 (10.7, 12.9)	10.90 (10.4, 11.7)	**0.035[2]**

Table 1. Pre-HSCT factors and complete chimerism in PB at last follow-up			
Pre-HSCT Reticulocytes (/mm^3)	73,800 (26,400, 129,100)	138,800 (45,100, 223,400)	**0.043**[3]
Pre-HSCT Dose Hydrea (mg/kg)	28.0 (25.0, 30.0)	28.0 (20.0, 30.0)	>0.9[2]
Splenectomy	4 (9.8%)	4 (21%)	0.2[4]
Pre-HSCT Chelation	10 (24%)	5 (26%)	>0.9[4]

[1] Median (p25, p75); n (%)
[2] Wilcoxon rank sum test
[3] Wilcoxon rank sum exact test
[4] Fisher's exact test

Picture 1. Longitudinal analysis of chimerism levels and hemoglobin (A+B), reticulocyte (C), and fetal hemoglobin (D) values prior to HSCT



Conclusions: Adequate pre-HSCT preparation, characterized by higher hemoglobin levels and lower reticulocyte counts, was associated with improved chimerism outcomes in this cohort. These findings warrant confirmation in larger, prospective studies.

Disclosure: Nothing to declare.

OS05-08

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PHARMACOLOGICAL MODULATION OF PROTEOSTASIS AS A STRATEGY TO BOOST THYMIC REGENERATION AND T CELL IMMUNITY

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Background: Thymic function is highly vulnerable to injury from cancer treatments, infections, and graft-versus-host disease (GvHD), leading to impaired T-cell development and reduced immune surveillance. Prolonged thymic insufficiency exposes patients, particularly those receiving allogeneic hematopoietic cell transplantation (allo-HCT), to increased risks of infection and poor outcomes. Recently, better thymic function has also been associated with improved response to immune checkpoint inhibitors in cancer patients, underscoring the broader relevance of thymic health for immunotherapy success. Effective strategies to restore thymic function remain limited. We aimed to identify novel thymic-boosting approaches based on pharmacological induction of *Foxn1*, a key transcription factor regulating thymic epithelial cell (TEC) function and regeneration.

Methods: We developed a dual-luciferase reporter assay to screen 1,530 FDA-approved compounds for their ability to enhance FOXN1 activity in murine cortical TECs (Fig.1A). Compounds were evaluated for efficacy and toxicity (IC50, IG50), and top candidates were tested in mice subjected to sub-lethal total body irradiation (SL-TBI). Mechanistic studies included molecular profiling and flow cytometry to assess thymocyte development, TEC recovery, and signaling pathways.

Results: Proteasome inhibition emerged as a potent and previously unrecognized mechanism for regulating *Foxn1* transcription via proteotoxic stress and chromatin remodeling at its regulatory regions. Among the hits, the antiparasitic drug nitazoxanide (NTZ) induced proteasome inhibition and Foxn1 expression without cytotoxicity, unlike other proteasome inhibitors. Mechanistically, NTZ triggered endoplasmic reticulum (ER) stress and ATF4-mediated unfolded protein response (UPR), ultimately engaging autophagy as a compensatory survival mechanism. Consistently, pharmacological activation of UPR with salubrinal increased *Foxn1* and *Atf4* expression, and several other hits from our screen were known ER stress inducers, supporting the notion that *Foxn1* induction reflects a broader stress-related mechanism linked to alterations in cellular proteostasis. NTZ upregulated *Foxn1* and its downstream target Dll4, a key gene crucial for T cell commitment and expansion, in murine TECs as well as human primary TECs derived from pediatric thymic tissue (Fig.1B). In vivo, NTZ significantly accelerated thymic recovery after SL-TBI, restoring all thymocyte subsets, mature $CD4^+$ and $CD8^+$ T cells, and TEC compartments without impairing positive or negative selection (Fig.1 C-E). Analysis of TCRβ/CD69 and TCRβ/CD5 profiles confirmed normal progression through selection checkpoints, while CD24 expression on single-positive thymocytes indicated preserved deletion and maturation dynamics. Regulatory T cells ($CD4^+CD25^+Foxp3^+$) increased proportionally, maintaining stable frequency

within the CD4 compartment. TEC recovery was accompanied by reduced apoptosis (Fig.1F) and induction of *Foxn1* and its targets (*Dll4*, *Psmb11*) in cTECs alongside UPR genes *Atf4* and *Xbp1*, while *Aire* expression remained unchanged, suggesting preserved central tolerance.

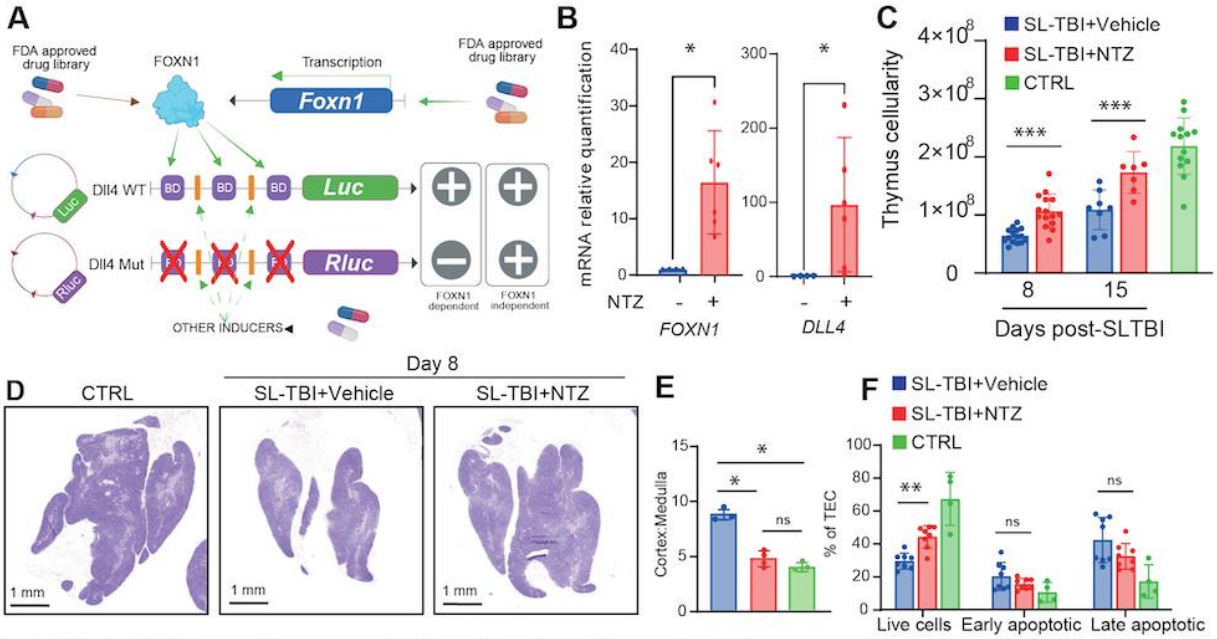

FIGURE1. (A) Schematic representation of the high-throughput drug screening system. (B) Stimulation of human primary TECs with NTZ and assessment of Foxn1 and Dll4 expression by qPCR. (C) Young C57BL/6 mice received SL-TBI and were treated with vehicle or NTZ. Total thymic cellularity was assessed at days 8 and 15 post-SL-TBI. (D) Representative H&E staining of thymus from control and sublethally irradiated mice, treated or not with NTZ. (E) Quantification of cortical to medulla ratio. (F) Evaluation of Annexin V in TECs 7 days after SL-TBI in vehicle- and NTZ-treated mice.

Conclusions: Our findings uncover proteotoxic stress as a novel mechanism regulating *Foxn1* expression and position NTZ as a promising thymic regenerative therapy that accelerates recovery without disrupting physiological T-cell selection or tolerance. Evaluation of T-cell recovery in clinically relevant HSCT mouse models is ongoing, supporting the translational potential of our study for allo-HCT recipients and individuals with thymic insufficiency due to aging, infections, or anti-neoplastic therapies.

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OS17-06

PROPHYLACTIC MEMORY DLI ENHANCES IMMUNE RECOVERY AND DISEASE-FREE SURVIVAL AFTER ALLOGENEIC HCT

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Background: Memory T selected cells ($CD45RA^-/RO^+$) as donor lymphocyte infusion are less capable of producing alloreactivity and graft versus host disease (GvHD) compared with naïve T cells. The objective of this study was to evaluate the safety and efficacy of memory donor lymphocyte infusion (mDLI; $CD45RA^-/RO^+$) following allogeneic hematopoietic cell transplantation (HCT).

Methods: A total of 108 children (median age: 9.69 years; IQR: 4.5–13.16) diagnosed with malignant (74%) or non-malignant diseases (26%) received 864 mDLI infusions, administered either "as needed" or as a "prophylactic regimen". Patients received haploidentical grafts (48%), matched related donor (MRD) grafts (14%), matched unrelated donor (MUD) grafts (23%), and mismatched unrelated donor (MMUD) grafts (14%). Graft manipulation included CD45RA depletion (51%), TCRαβ depletion (37%), and unmanipulated grafts (11%). Each patient received monthly a median of seven infusions (IQR: 3–13) with a median dose of 1.65×10^7/kg $CD45RO^+$ cells, including 1.22×10^6/kg $CD3^+CD45RO^+$ and 1.6×10^3/kg $CD3^+CD45RA^+$.

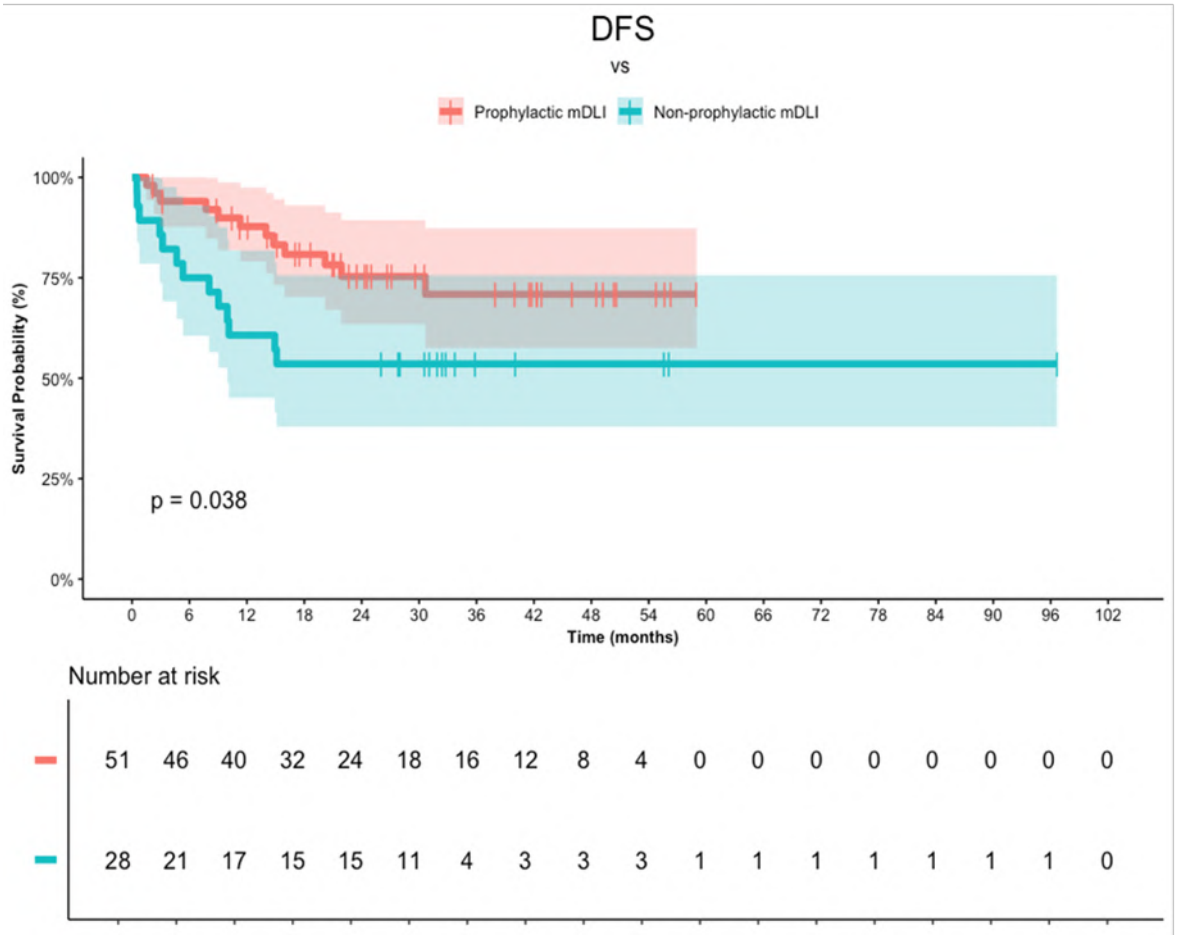
Results:

	mDLI 1	mDLI 2	mDLI 3	mDLI 4	mDLI 5	mDLI 6	mDLI 7	mDLI 8	mDLI 9	mDLI 10	mDLI 11	mDLI 12	mDLI 13
Day after HCT, median (IQR)	35 (49)	61 (63)	83 (60)	105 (78)	130 (102)	162 (92)	186 (110)	217 (169)	239 (180)	270 (179)	293 (157)	300 (165)	351 (189)

mDLI dose CD3CD45RO$^+$ x10^6/kg, median (IQR)	3.92 (9)	1.2 (9)	1.43 (9)	1.25 (9)	1.27 (9)	1.21 (9)	1.15 (8)	1.15 (8)	1.15 (8)	1.22 (8)	1.15 (9)	1.19 (9)	1.07 (8)
de novo GvHD>1, %	9	9	2	6	2	0	0	4	0	0	3	0	0
worsened GvHD>1; %	17	12	13	4	16	19	0	8	0	0	0	0	0
Patients taking immunoppressi on, %	63	59	52	49	44	38	47	40	44	45	36	26	32
CD4$^+$ x10^9/L	0.09			0.14			0.19						0.39
CD4$^+$ >0.05 x10^9/L, %	58			71			87						96
CD4$^+$ >0.2 x109/L, %	25			36			44						78

De novo acute graft-versus-host disease (aGvHD) occurred in 13 patients (17%) (36 of 599 infusions), with 8 patients (10%) experiencing grade II-IV. Among patients with pre-existing GvHD, worsening was observed after in 6 patients (17%) (29 of 229 infusions) with previously had GvHD II-IV. Patients with acute myeloid leukemia (AML) had a higher risk of GvHD worsening compared with those with acute lymphoblastic leukemia (ALL) ($p = 0.003$). Viral load clearance was achieved in 17%, 58%, 20%, 67%, 24%, and 8% of patients with CMV, EBV, HHV6, parvovirus, ADV, and BK virus, respectively. Reduction in viral load was statistically significant for EBV ($p = 0.02$) and approached significance for CMV ($p = 0.07$). Immune recovery was faster in the prophylactic mDLI group, evident as early as day 30 for total lymphocytes x 10^9/L (0.76 vs. 0.45, $p = 0.02$), T cells x 10^9/L (0.336 vs. 0.19, $p = 0.02$), and CD4$^+$ T cells x 10^9/L (0.112 vs. 0.06, $p = 0.05$). At day 90, B-cell x 10^9/L were higher (0.055 vs. 0.002, $p = 0.03$), and this difference persisted at day 180 (0.464 vs. 0.290, $p = 0.02$). NK cell recovery was also superior at day 180 (0.21 vs. 0.13, $p = 0.04$) and day 360 (0.25 vs. 0.15, $p = 0.007$).
Four-year overall survival (OS) and disease-free survival (DFS) for the entire cohort were 77% (95% CI: 69–87%) and 65% (95% CI: 55–78%), respectively. Patients receiving prophylactic mDLI had a four-year DFS of 71% (95% CI: 58–87%) compared with 54% (95% CI: 38–76%) in the non-prophylactic group (p=0.038).

Figure 1. Disease free survival comparing prophylactic mDLI vs non-prophylactic mDLI



Conclusions: mDLI is feasible and safe, with a relatively low risk of severe GvHD—even in patients with active GvHD. Importantly, mDLI was associated with significant clinical benefits, including improved control of EBV and CMV viremia, accelerated immune reconstitution, and enhanced DFS.

Disclosure: Nothing to declare

B186

IMMUNE RECONSTITUTION DURING MAINTENANCE THERAPY WITH AZACITIDINE AFTER ALLOGENEIC HCT

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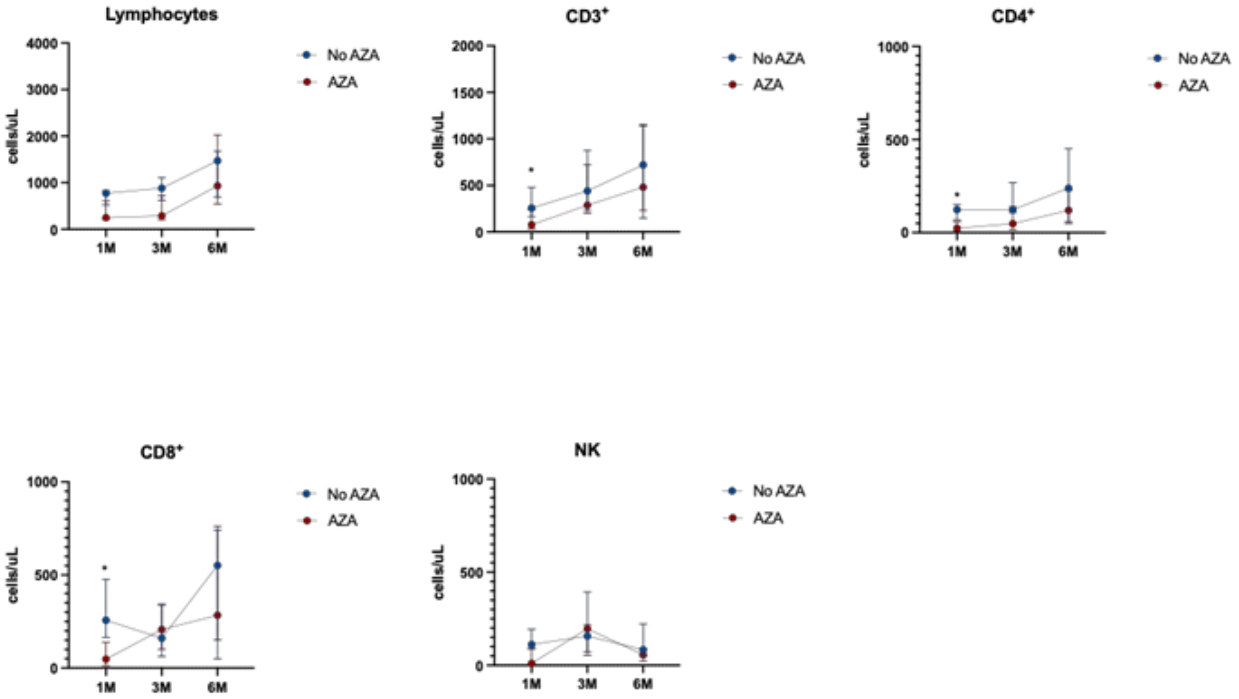
Background: Azacitidine is increasingly used as post-transplant maintenance to reduce relapse after allo-HCT. While its efficacy has been studied, data on early immune reconstitution, especially in pediatric patients, are limited. Assessing immune recovery during azacitidine is essential to evaluate its safety and feasibility.

Methods: We retrospectively analyzed immune reconstitution in 18 pediatric allo-HCT patients, comparing those receiving azacitidine maintenance (AZA, n=7) with controls (n=11). Patient characteristics, transplant variables, and immune subsets were assessed at 1, 3, and 6 months post-transplant by flow cytometry, focusing on T cells (CD3, CD4, CD8), total lymphocytes, NK cells, and $CD4^+CD8^+$ T cells. Counts were evaluated before azacitidine (1 month) and during maintenance.

Results:

Patients in the AZA group were younger (mean age 5.7 vs. 9.2 years) and more frequently diagnosed with JMML (71.4%), whereas all control patients had AML. GVHD prophylaxis differed, with more frequent ATG use in the AZA group and predominance of post-transplant cyclophosphamide in the control group. AZA was administered every 24 hours for 5 consecutive days, starting no earlier than day +40, and repeated every 40 days; in AML patients, it was combined with venetoclax. Treatment exposure ranged from 2 to 11 cycles, with fewer cycles in patients who discontinued due to GVHD or treatment-related mortality. In the AZA group, 4 patients developed grade II–IV acute GVHD: gut grade II (n=1), gut grade IV (n=2), and liver grade III (n=1), with 3 experiencing grade III–IV GVHD and one developing chronic GVHD (eye, skin). In the control group, 4 patients developed grade II–IV acute GVHD: skin/liver grade II (n=1), gut grade II (n=1), skin/gut grade II (n=1), and gut/skin grade III (n=1); only 1 patient experienced grade III–IV GVHD, and 3 developed chronic GVHD (skin/lung or skin/intestine). Infectious complications included Pseudomonas aeruginosa and EBV reactivation in 2 AZA patients, and parvovirus plus 4 CMV reactivations in 5 controls.
Referring to Table 1 and Figure 1, at 1 month post-transplant, prior to azacitidine, total lymphocyte counts were lower in the AZA group (median 249.5 vs. 770 cells/μL, p=0.0047), including $CD3^+$, $CD4^+$, and $CD8^+$ T cells. After AZA initiation, no significant differences were observed at 3 or 6 months. $CD4^+$ and $CD8^+$ T-cell differentiation showed transient early differences that normalized over time. NK cell frequencies converged by 6 months. Double-positive $CD4^+CD8^+$ T cells were increased at 1 month in the control group (p = 0.0007) but remained similar at later time points. Mean $CD3^+CD4^+$ T-cell counts at day +100 exceeded 50 cells/μL in both groups (78.4 vs. 119.2), with no significant differences at later time points.



	n	AZA group 7 (%)	control group 11 (%)	*P value*
	Age (mean)	5,7 years	9,2 years	*0,15*
	Diagnosis JMML AML	 5 (71.4%) 2 (28.6%)	 - 11 (100%)	*0,0025*
	Conditioning TTF TBF BU-CY-MEL BU FLU MEL	 1 (14.3%) - 5 (71.4%) 1 (14.3%)	 1 (9.1%) 5 (45.5%) 5 (45.5%) -	*(Bu vs Treo 0.99)*
	Prophylaxis **GVHD** CNI only ATG Pt-CY Pt-CY+ Abatacept	 2 (28.6%) 4 (57.1%) - 1 (14.3%)	 3 (27.3%) 1 (9.1%) 6 (54.5%) 1 (9.1%)	

	Donor Haplo MUD sibling	1 (14.3%) 4 (57.1%) 2 (27.3%)			5 (45.5%) 3 (27.3%) 3 (27.3%)			*(Haplo vs MUD 0.26)*		
	Source BM PB	5 (71.4%) 2 (28.6%)			8 (72.7%) 3 (27.3%)			*0,89*		
		1 m	**3 m**	**6 m**	**1 m**	**3 m**	**6 m**	***1 m***	***3 m***	***6 m***
	Lymphocytes/uL (median)	249,5	545,8	930	770	880	1470	***0,0047***	*0,29*	*0,94*
	CD3/uL **(median)** T γδ (%) T reg (%)	76,93 1 0,3	286,9 2,3 1	481,015 2 1,2	257,4 1,95 1,1	425,04 0,8 1,4	720,38 1,2 2,1	***0.0065*** *0,5* *0,02*	*0.67* *0,15* *0,58*	*0.99* *0,46* ***0,01***
	CD4 **/uL(median)** CM (%) Naïve (%) EM (%) TEMRA (%)	24 14,5 0,8 3.15 0,75	78,42 2,9 0 15,2 0	119,87 0,5 0 14,7 1,4	123,2 7,2 2,4 4,5 1,55	119,2 3,4 0 20,9 1,2	238,43 3,4 0,1 13 0,4	***0,0064*** *0,54* *0,83* *0,79* *0,40*	*0,31* *0,94* *0,48* *0,81* *0,24*	*0,28* *0,17* *0,39* *0,77* *0,91*
	CD8 **/uL(median)** CM (%) Naïve (%) EM (%) TEMRA (%)	48 2,4 2,8 7,55 6,25	206,70 2,9 0 15,2 0	283,46 2,1 0,5 25,2 19,9	122,12 1,5 1,3 13,8 13,8	160,83 3,4 0 20,9 1,2	551,07 0,8 1,3 14,9 12	***0,031*** *0,93* *0,99* *0,25* *0,39*	*0,48* *0,94* *0,48* *0,81* *0,24*	*0,99* *0,17* *0,39* *0,77* *0,91*
	NK/uL **NK/T (%)**	10,47 4,55	195,9 3,2	56,29 6,2	128,1 2,1	157,35 8	83,76 1,6	***0,034*** *0,78*	*0,81* *0,23*	*0,30* *0,11*
	CD4+8+ (%)	0,68	2,9	3,53	4,4	1,01	5,025	***0,0007***	*0,94*	*0,82*

Table 1

Conclusions: In this pediatric limited cohort, azacytidine maintenance therapy was not associated with sustained impairment of immune reconstitution after allo-HSCT. Although initial differences were observed prior to the start of maintenance, immune recovery trajectories during azacytidine exposure were comparable to those of controls, supporting its feasibility in the post-transplant setting. Larger prospective studies are warranted to determine the clinical significance of these immune findings.

Disclosure: Nothing to declare

B187

PREVALENCE AND LONG-TERM CLINICAL IMPACT OF SELECTIVE IGA DEFICIENCY FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PRIMARY IMMUNODEFICIENCY: A RETROSPECTIVE COHORT ANALYSIS

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Background: While T-cell recovery after hematopoietic stem cell transplantation (HSCT) for inborn errors of immunity (IEI) is well-documented, long-term B-cell reconstitution and associated humoral deficits remain inadequately characterized. Selective IgA deficiency (sIgAD) is a recognized potential sequela, but its frequency, predisposing transplant-related factors, and long-term clinical impact in IEI patients surviving >5 years post-HSCT are poorly defined.

Methods: We conducted a single-center, retrospective cohort study of patients with IEI who underwent HSCT between January 2010 and December 2020 and survived >5 years. Exclusion criteria included prior gene or thymus transplantation, death, or loss to follow-up within five years. Data extracted included IEI diagnosis, transplant details (donor, stem cell source, conditioning intensity, serotherapy), post-HSCT complications (acute/chronic GvHD), and long-term outcomes (>5 years): recurrent infections, autoimmunity, and detailed immune reconstitution (lymphocyte subsets, B-cell phenotypes, vaccination responses). We specifically analysed prolonged steroid use (>3 months) and post-HSCT rituximab as risk factors for sIgAD and subsequent morbidity.

Results: From 246 patients (251 transplants), 151 met inclusion criteria (median transplant age 3 years, median follow-up 8 years). Twenty-five of 151 patients (16.5%) fulfilled ESID criteria for sIgAD (IgA <0.07 g/L). Underlying IEIs were heterogeneous, including SCID (n=8), CD40L deficiency (n=3), Wiskott-Aldrich syndrome (n=3), and others. Most sIgAD patients (72%) received reduced-intensity conditioning (RIC), primarily with Treosulfan or Melphalan. Alemtuzumab serotherapy was used in 17/25 (68%). Acute GvHD occurred in 15 patients. Post-HSCT, 52% (13/25) received systemic steroids for >3 months and 32% (8/25) received rituximab. At >5 years post-HSCT, 28% (7/25) had recurrent upper respiratory infections, and 36% (9/25) developed autoimmunity, most commonly thyroid disease (n=4), emerging a median of 2 years after sIgAD diagnosis. At last follow-up (median 8 years), all patients were immunoglobulin-independent and off immunosuppression. Immune profiling revealed a mean absolute B-cell count of ~0.35 $\times 10^9$/L, with class-switched memory B cells deficient in 13/25 patients.

Conclusions: sIgAD is a prevalent (16.5%) long-term complication in IEI survivors after HSCT, marking incomplete B-cell reconstitution. A significant proportion of these patients experience substantial morbidity, including recurrent infections and a high burden of autoimmune disease, despite eventual cessation of immunoglobulin replacement and immunosuppression. The frequent association with RIC, alemtuzumab use, prolonged steroids, and rituximab suggests a complex interplay of conditioning, immune manipulation, and ongoing dysregulation in its pathogenesis. These findings identify post-HSCT sIgAD as a clinically important marker for heightened risk of immune dysregulation, necessitating lifelong, targeted surveillance for autoimmune and infectious complications in this subgroup of long-term survivors.

Disclosure: Nothing to declare.

B188

CHARACTERIZING THERAPEUTIC ENDPOINTS AND EFFICACY OF PRE-EMPTIVE DONOR LYMPHOCYTE INFUSION FOR MIXED LYMPHOID CHIMERISM POST-ALLOGENEIC STEM CELL TRANSPLANT: A FOUR-YEAR SINGLE-CENTRE RETROSPECTIVE ANALYSIS

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Background: Donor lymphocyte infusion (DLI) is a powerful allogeneic immunotherapy to augment graft-versus-tumour effects mediated by donor-derived CD3+ lymphocytes. In the setting of mixed lymphoid chimerism (MC) — strongly associated with post-transplant relapse — pre-emptive DLI (preDLI) is an effective tool for enhancing donor lymphocyte activity, ultimately reducing relapse and mortality. DLI is fraught by off-tumour cytotoxicity, primarily manifesting as graft-versus-host disease (GvHD), which may mandate cessation of therapy. Here, we describe the therapeutic endpoints encountered by a cohort of patients (n=37) receiving preDLI for MC in a Scottish tertiary centre. Secondarily, we determine overall response rate (ORR); quantify GvHD-associated morbidity and mortality; and examine overall survival.

Methods: Retrospective single-centre study comprising patients receiving preDLI between 1st January 2021 to 27th March 2025, with the specific indication being MC (donor lymphoid fraction <90% by PCR-STR). Patients demonstrating concurrent haematological relapse were excluded. Final date of data collection was 1st July 2025, at which point n=34 had achieved a therapeutic endpoint, with 3 awaiting further decision. Data obtained by interrogation of the electronic patient record, with analysis in Microsoft Excel and R.

Results: The median age at preDLI initiation was 54 years [range 20-66]. Indication for SCT was myeloid disease in 78%, chiefly AML and high-risk MDS [n=25], with lymphoid disorders in 22%. Matched sibling (49%) and volunteer unrelated donors (51%) were of equal

frequency. Median days from HSCT to preDLI was 233 [range 126 – 517]. The most frequent starting dose was 1x10e6 CD3+ cells, with titration to a maximum of 3x10e7 cells. 73% of patients received a single dose, with 11% receiving two doses and 16% three or more fractions.
DLI endpoints can be stratified between those due to patient death (n=2) and endpoints at which the patient was alive at the decision to cease DLI (n=35). The ORR was 81%, defined as attainment of ≥ 90% donor lymphoid chimerism. The median time to attaining this endpoint was 173 days. Of the subset attaining this endpoint, 60% did not experience any GvHD; the remaining 40% experienced at least one episode of GvHD, triggering cessation of DLI. Only a single patient who received a single dose of DLI but stopped due to GvHD ultimately failed to augment their donor lymphoid fraction. One patient also achieved the clinically significant endpoint of resolution of anti-D mediated haemolysis, despite failure to attain target lymphoid chimerism. We recorded 21 discrete episodes of GVHD, primarily cutaneous. The two-year OS for patients in this cohort from first DLI dose is 84.7%, with median survival not yet reached.

Conclusions: PreDLI is an effective strategy for overcoming mixed chimerism, with an ORR in this cohort comparable to published studies [50-71%], of which a limited number are available for this specific indication. Acute GvHD is a significant attendant risk, with the incidence at any grade commensurate with that in the published literature. We describe a low treatment-related mortality of 2.8% (one patient) in this cohort, with GvHD preceding attainment of ≥90% donor lymphoid chimerism in 91% of affected patients.

Disclosure: Nothing to declare.

B189

BONE MARROW ASPIRATIONS (BMAS) AFTER DONOR LYMPHOCYTE INFUSION (DLI): ARE ROUTINE FOLLOW-UPS NECESSARY FOR ALL PATIENTS?

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Background: Donor lymphocyte infusion (DLI) is frequently administered after allogeneic haematopoietic stem cell transplantation (allo-HSCT), particularly following reduced-intensity conditioning (RIC) and in patients with complex disease profiles. However, there is no consensus on the optimal timing or frequency of post-DLI bone marrow aspirations (BMAs) to assess disease response and donor chimerism. Historically, the South Wales Bone Marrow Transplant (SWBMT) Programme performed BMAs at 1, 2, and 3 months post-DLI. This audit evaluated whether routine BMAs at fixed intervals are clinically necessary, identified subgroups who may benefit from reduced monitoring, and assessed the role of multidisciplinary team (MDT) review in guiding follow-up care.

Methods: We retrospectively reviewed 80 patients who received DLI between 2021 and 2025. The cohort included 45 males and 35 females, median age 59 years (range: 24–71). Inclusion criteria were receipt of DLI following allo-HSCT, availability of follow-up data including remission status at 1–3 months post-DLI, peripheral blood T-cell (PBT) and bone marrow (BM) chimerism results, and documentation of MDT discussions. Mixed chimerism (MC) is defined as <95% donor.

Underlaying diagnosis	AML (40%) MDS (15%) B-ALL (11%) Other (34%)
Conditioning regimens used	FMC (44%) FTreoATG (20%) Other (36%)

Results: **Group 1** (Mixed BM and PBT chimerism): 84% showed lower PBT chimerism compared with BM, with PBT providing the most clinically informative results in 88% of cases. No patients achieved full donor chimerism by week 4, indicating that assessment at this early time point is not meaningful. Maximum response to DLI was typically observed by week 12 in 72% of patients. Despite this, only 25% were discussed in MDT meetings with a documented management plan.
Group 2 (isolated mixed PBT chimerism): 72% underwent at least one BMA in the first three months post-DLI. 77% remained in complete remission with full donor BM chimerism, suggesting PBT monitoring alone may have sufficed. 23% demonstrated minor declines in bone marrow chimerism, with an average reduction of 15%; however, this did not correlate with disease progression. Importantly, all patients monitored exclusively by PBT were discussed in MDT meetings, supporting a non-invasive monitoring strategy.
Group 3 (MRD-positive subgroup): This complex cohort required MDT or consultant-led management. Within this group, 21% remained MRD-positive despite full donor chimerism in both PBT and BM. A small proportion achieved MRD negativity (12% by week 4, 12% by week 12). However, 17% experianced frank relapse, while another 17% remained persistently MRD-positive with declining BM chimerism. Additionally, 21% achieved MRD negativity but continued to show mixed donor chimerism, highlighting the heterogeneity and challenges of this subgroup.

Conclusions: A uniform, one-size-fits-all approach to post-DLI bone marrow monitoring is unsuitable. Evidence supports a risk-adapted strategy: BMAs can be reduced for low-risk patients, particularly those in complete remission with isolated mixed PBT chimerism or a greater decline in PBT compared with bone marrow. As responses are rarely evident at 4 weeks post-DLI, early assessment should be reserved for high-risk cases. MDT discussion is strongly recommended to ensure consistent, individualised care. In line with this, the SWBMT Programme has updated its protocol to minimise unnecessary BMAs and adopt a tailored, MDT-led follow-up approach.

Disclosure: Nothing to declare

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LETERMOVIR PROPHYLAXIS RESHAPES EARLY IMMUNE RECONSTITUTION AND CMV/EBV REACTIVATION DYNAMICS AFTER ALLOGENEIC HSCT

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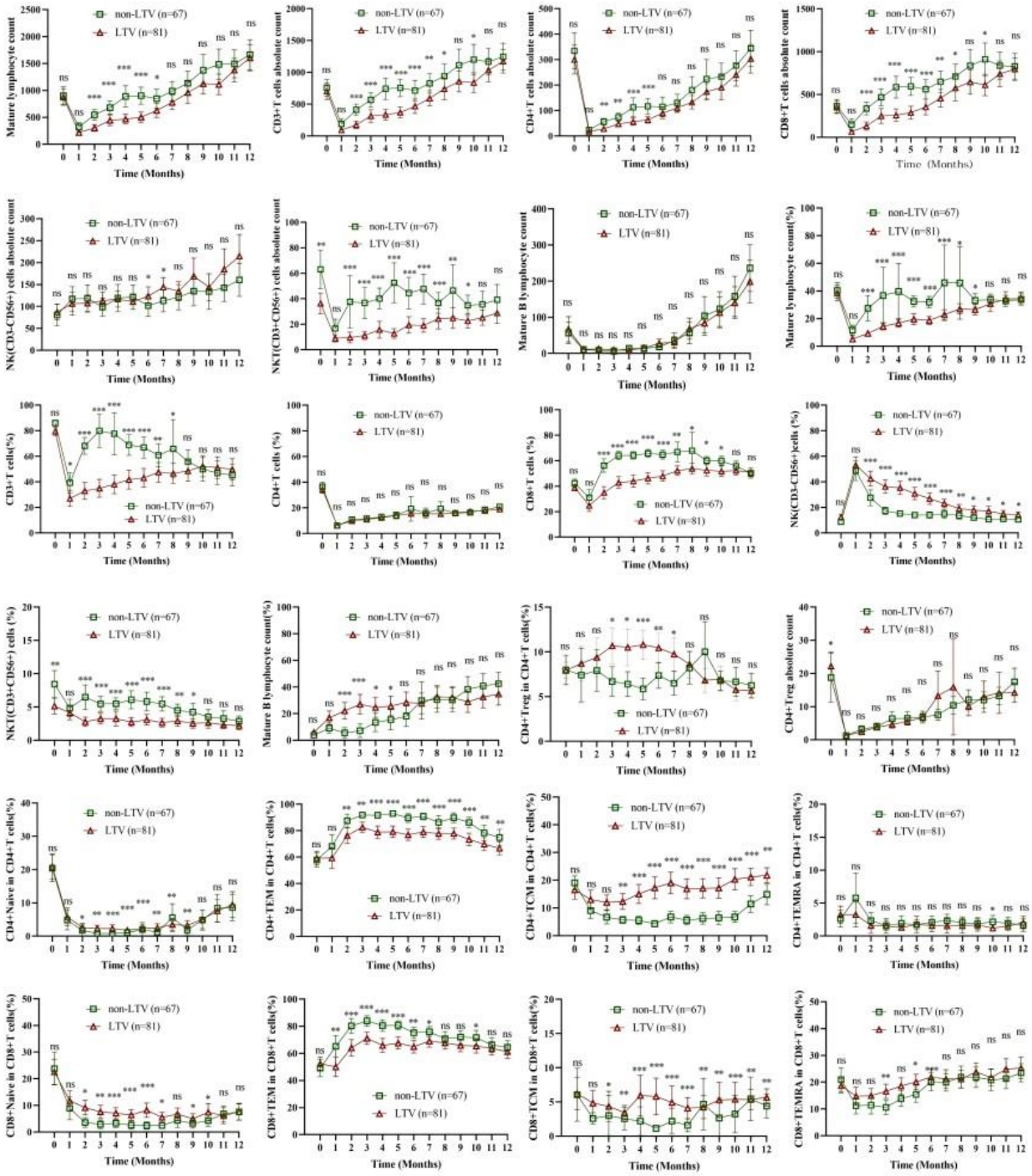
Background: With Letermovir (LTV) redefining CMV prophylaxis in allo-HSCT, its broader effects on early immune reconstitution have become an important but underexplored issue. This study characterized immune reconstitution patterns associated with LTV prophylaxis.

Methods: We retrospectively analyzed 148 allo-HSCT recipients treated at Beijing Ludaopei Hospital between April 2021 and December 2024. Clinical and virologic data were systematically reviewed, and patients were categorized into a pre-emptive therapy group (PET, n = 67) or a Letermovir prophylaxis group (LTV, n = 81). Peripheral blood lymphocyte subsets were monitored by flow cytometry at baseline and monthly for 12 months post-transplant to assess longitudinal immune reconstitution.

Results: ***Survival and CMV/EBV Reactivation***
At a median follow-up of 28.1 months (range, 6.5–49.1), 2-year OS (83.6% vs 82.4%) and NRM (10.5% vs 10.1%) were comparable between the PET and LTV groups (all $P > 0.05$). Within 180 days, LTV prophylaxis markedly reduced CS-CMV infection (61.2% vs 12.4%, $P < 0.001$), delayed CMV activation (median 25 vs 122 days, $P < 0.001$), and shortened infection duration (34 vs 19 days, $P = 0.017$), while peak viral load (1200 vs 1450, $P = 0.240$) and CMV disease (2.0% vs 1.2%, $P = 0.341$) remained similar. EBV activation was higher in the LTV group (14.9% vs 27.2%, $P = 0.083$), but infection duration (26 vs 18 days, $P = 0.179$), peak viral load (1850 vs 1600, $P = 0.984$), and EBV-PTLD incidence (2.99% vs 2.47%, $P = 0.847$) were comparable. In Fine–Gray competing-risk models, LTV independently reduced CS-CMV infection (HR = 0.16, 95% CI 0.08–0.35, $P < 0.001$), whereas CS-EBV infection was independently associated with rATG exposure (HR = 2.50, 95% CI 1.04–6.06, $P = 0.042$) and LTV prophylaxis (HR = 2.63, 95% CI 1.02–6.77, $P = 0.046$).
Immune Reconstitution Dynamics (Figure 1)
Pre-transplant immune baselines were comparable between groups. During the LTV usage period (+2 to +6 months post-transplant), the LTV group displayed significantly lower levels of total lymphocytes, $CD3^+$ T cells, $CD8^+$ T cells, NKT cells (counts and percentages), $CD4^+$ T-cell absolute counts, and NK-cell percentages (all $P < 0.05$). The proportion of B cells was consistently higher in the LTV group across multiple time points. After +6 months, these differences were no longer observed .
At later time points, LTV recipients showed a distinctive T-cell maturation profile, including higher $CD4^+$ T-cell Treg proportions and elevated CD4/CD8 ratios ($P < 0.05$). The percentages of $CD4^+$ and $CD8^+$ naïve T cells, central memory (TCM) subsets, and $CD8^+$ TEMRA subsets were significantly increased, whereas effector memory (TEM) proportions in both $CD4^+$ and $CD8^+$ compartments were significantly reduced ($P < 0.05$).

Figure 1. Longitudinal immune reconstitution between the PET and LTV groups



Conclusions: HSCT recipients receiving LTV prophylaxis exhibited a unique pattern of immune reconstitution characterized by early suppression of T cell numbers. However, by avoiding CMV-driven abnormal immune activation and exhaustion, they retained T cell TCR

diversity, indirectly preserving robust T cell reserve capacity. This configuration is more conducive to the recovery of immune reconstitution in later stages.

Disclosure: Nothing to declare

B191

DEEP IMMUNOPHENOTYPING IDENTIFIES DIFFERENTIAL IMMUNE PROFILES IN RECIPIENTS OF DONOR LYMPHOCYTE INFUSIONS

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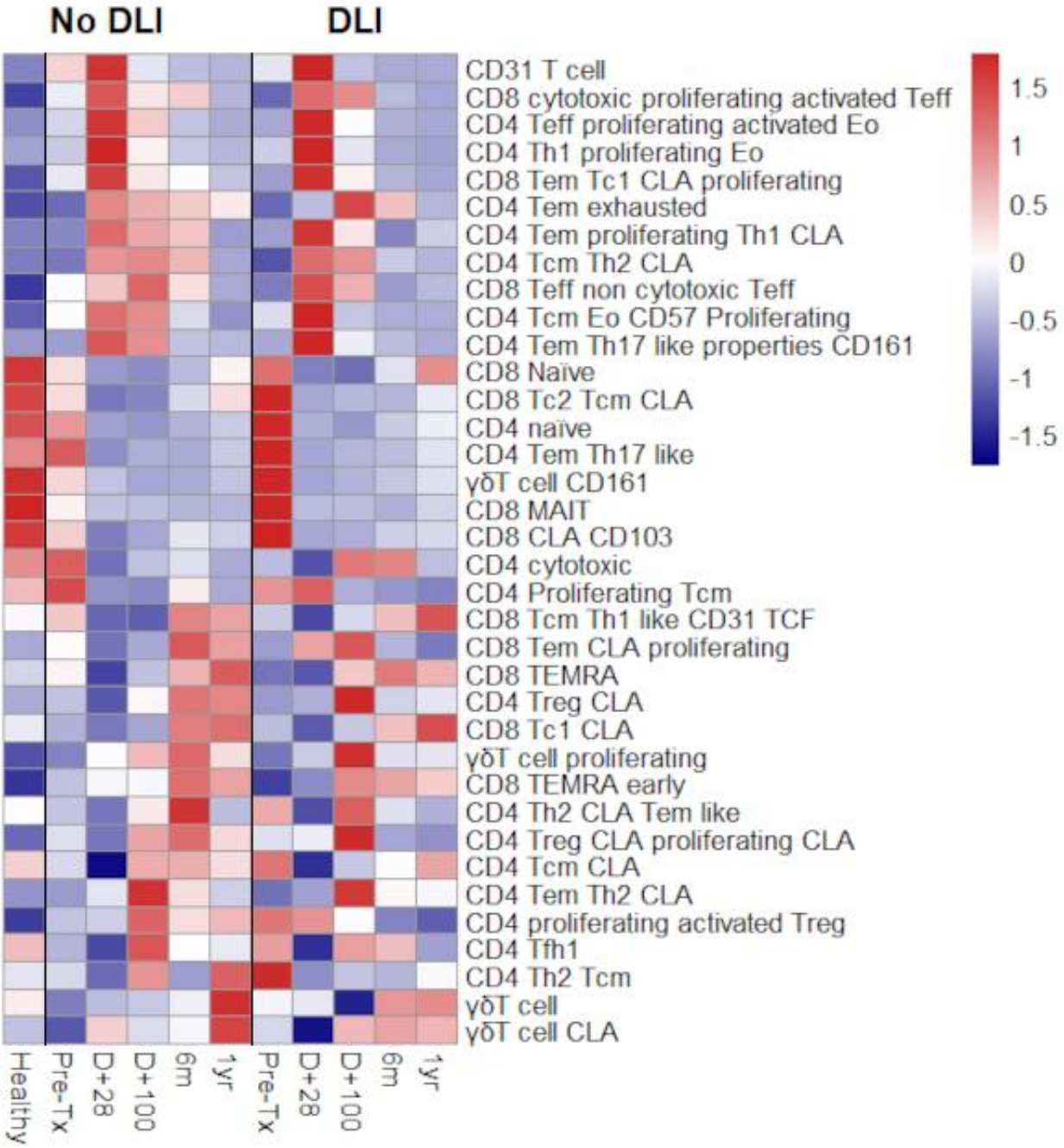
Background: Donor lymphocyte infusions (DLI) are routinely administered post-allogeneic haematopoietic cell transplant (HCT) to prevent or treat relapsed disease. Despite this, little is understood regarding optimal DLI strategy for relapse prevention or the immunological consequences of DLI in the patient.
PRO-DLI (NCT02856464) was the first clinical trial globally to compare prophylactic versus pre-emptive DLI in patients with Acute Myeloid Leukaemia or Myelodysplastic Syndrome undergoing reduced intensity conditioned (RIC) HCT with alemtuzumab for Graft-versus-Host Disease (GvHD) prophylaxis. Using the extensive PRO-DLI sample biobank, we sought to examine the effect of DLI on immune reconstitution.

Methods: Peripheral blood mononuclear cells sequentially collected from 61 patients (median age 63 years, range 25 – 71 years; total 266 samples) were analysed using cytometry by time-of-flight (44 markers identifying T-, NK- and B-cell subsets). Patients were randomised in the experimental arm of PRO-DLI to early withdrawal of immune suppression (IS) and up to 4 prophylactic DLI from D+100, or a restricted DLI approach, only for mixed myeloid chimerism or detection of measurable residual disease (control arm). We analysed patients with a minimum of 3 samples collected at the following timepoints: pre-HCT, D+28, D+100 (prior to any DLI) and D+180 and D+365 (post-DLI in those who received it). Twenty-four patients in our cohort received DLI and 37 did not. Unsupervised clustering using the R package CATALYST identified 36 unique T-cell clusters, phenotypically identified and analysed using R packages and FlowJo.

Results: The early post-transplant patient immune profile was characterised by low frequencies of naïve CD4+ and CD8+ T-cells and marked expansion of effector and memory T-cells early post-HCT (D+28), which decreased over time. The patients' immune repertoires remained profoundly different from healthy volunteers even at 1 year, with limited recovery of naïve T-cells, likely secondary to the depletion of T-cells mediated by alemtuzumab and age-associated thymic involution.
A rapid and sustained increase in CD8+ T-effector memory cells re-expressing CD45RA

(TEMRA) from D+100 correlated with early withdrawal of immune suppression and DLI: median subset abundance = 31.7% (IQR 37.4%) compared with 4.8% (IQR 13.3%) in those not receiving DLI, FDR p-value = 0.008. Differences in immune recovery in those who did/did not receive DLI continued to be seen at 6 and 12 months post-HCT. We also noted marked expansion in naïve CD4+ and CD8+ T-cells in DLI recipients with cytomegalovirus (CMV)

reactivation (CD4+ FDR p-value = 0.023, CD8+ FDR p-value =0.0034).



Conclusions: We have developed an immunophenotypic atlas of immune recovery in the presence or absence of DLI after alemtuzumab-based RIC HCT. The effects of T-cell depletion are profound and long-lasting, even up to 1 year post-HCT. Early withdrawal of IS followed by DLI leads to identifiable changes in the immune repertoire; CMV reactivation appears also to shape the subsequent immune repertoire after DLI, favoring recovery of naïve T-cells. It is known that confounding clinical variables such as relapse, CMV and GvHD can impact immune subsets, and are being further explored in multivariate analysis of the dataset.

Disclosure: Nothing to declare

B192

BONE MARROW GRAFTS SUPPORT BROADER EARLY T-CELL AND ANTIVIRAL REPERTOIRE RECOVERY AFTER HAPLOIDENTICAL HSCT WITH PTCY

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Background: Post-transplant cyclophosphamide (PTCy) is a widely employed GvHD prophylaxis for Haploidentical hematopoietic stem cell transplantation (HSCT) and more recently transplants from other donor sources. Although this platform ensures effective GVHD control, it is associated with delayed immune reconstitution, particularly within the T-cell compartment, resulting in increased susceptibility to infections such as CMV and EBV. While bone marrow (BM) was initially the standard graft source, many centers have transitioned to peripheral blood stem cells (PBSC). Although clinical differences between BM and PBSC are well described, their respective effects on immune recovery and T-cell repertoire dynamics in the PTCy setting remain unexplored.

Methods: We retrospectively analyzed 70 patients who underwent haploidentical HSCT with uniform PTCy prophylaxis, including 31 BM and 39 PBSC recipients. Peripheral blood was collected at days +30, +100, +180, and +365. Flow cytometry quantified absolute T-cell counts, differentiation subsets (naïve, central memory, effector memory, TEMRA), and activation, exhaustion, and senescence markers. T-cell receptor sequencing (TCRseq) was performed using the LymphoTrack TRB Assay (Invivoscribe) to assess global repertoire diversity, clonotype richness, and CMV- and EBV-specific clonotypes.

Results: Absolute $CD4^+$ and $CD8^+$ counts were comparable between BM and PBSC recipients across all time points over the first year after allogeneic HSCT. Similarly, the distribution of naïve, memory, TEMRA, as well as the expression of activation, exhaustion, and senescence markers, evolved similarly in both groups.
Global TCR repertoire diversity as measured by the squared Simpson's index increased progressively over the first year and did not differ significantly between graft sources at

months 1, 3, 6, or 12 (p = 0.82, 0.59, 0.45, and 0.54, respectively). In contrast, clonotype richness showed clear early differences: BM recipients displayed significantly higher numbers of unique clonotypes at months 1 and 3 (p = 0.0087 at both time points). These differences diminished thereafter and were no longer detectable at months 6 and 12 (p = 0.63 and 0.79).
Virus-specific analyses showed a parallel pattern. CMV-specific clonotype richness was significantly higher in BM recipients at months 1 and 3 (p = 0.0013 and 0.0087), converging with PBSC recipients by months 6 and 12 (p = 0.43 and 0.79). EBV-specific repertoires showed similarly greater richness in BM recipients early (p = 0.013 at month 1 and 0.02 at month 3), with no significant differences later (p = 1 and 0.85).

Conclusions: In haploidentical HSCT with PTCy, bone marrow and peripheral blood grafts support similar quantitative and phenotypic T-cell recovery. However, bone marrow transplantation is associated with broader early global clonotype richness and greater diversification of CMV- and EBV-specific repertoires. These findings indicate that graft source influences the qualitative breadth of early T-cell immune recovery despite comparable numeric and phenotypic reconstitution.

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SML: consulting fees for advisory board from AdBoard Vertex; Travel support from Neovii, BeiGene, Gilead, Jazz, Sanofi and AstraZeneca all via the institution.
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B193

A RANDOMIZED PILOT TRIAL OF CLOSTRIDIUM BUTYRICUM MIYARI 588 IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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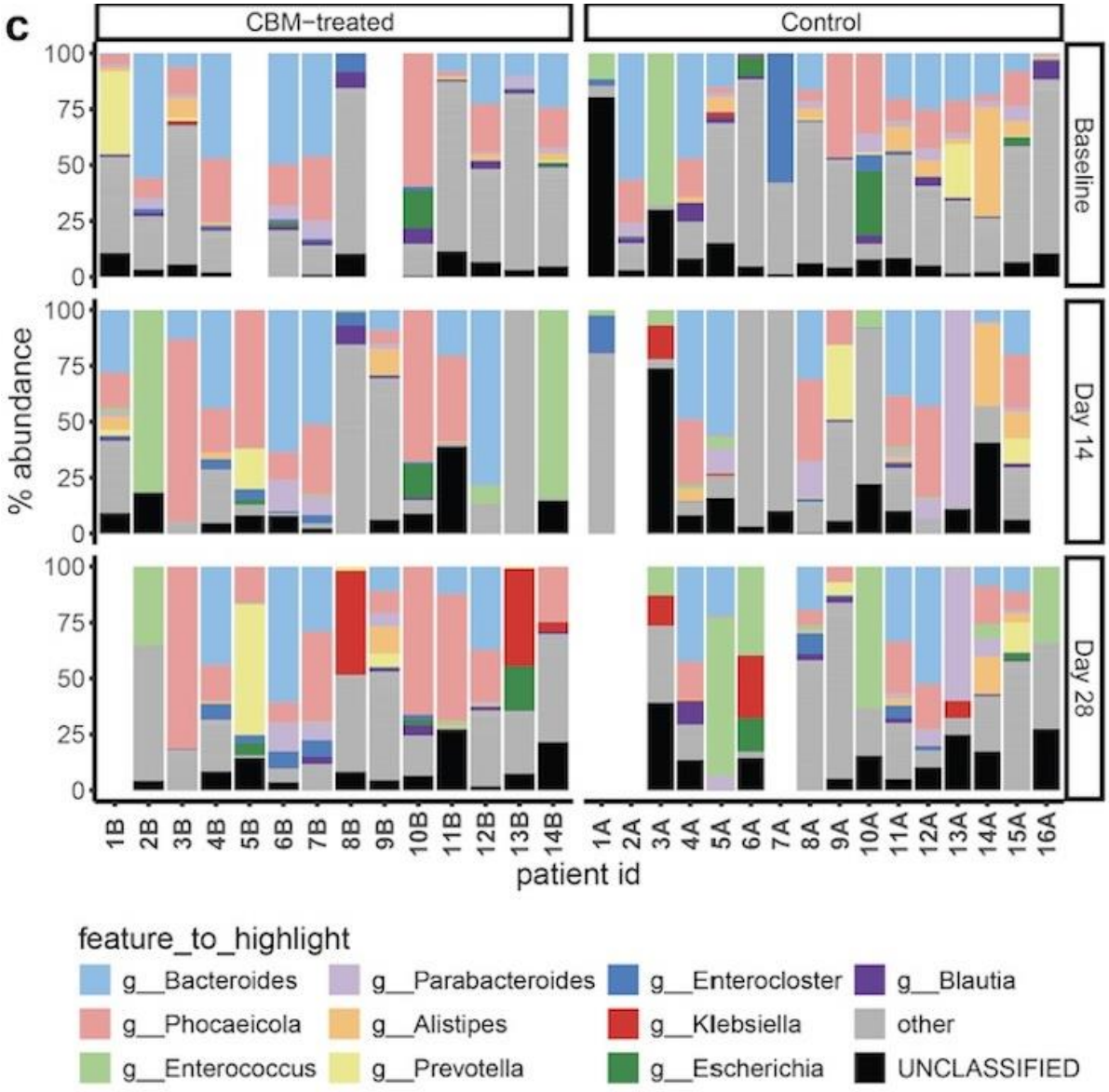
Background: *Clostridium butyricum* MIYAIRI588 (CBM588) is a butyrate-producing live biotherapeutic product that supports colonic health by regulating epithelial growth, fluid balance, and inflammation. In murine models of antibiotic-induced dysbiosis, CBM588 administration enhanced intestinal barrier function and increased abundance of Bifidobacterium, Lactobacillus, and Lactococcus species within the gut microbiome.

Methods: In this pilot study (NCT03922035), we assessed the safety, feasibility, and preliminary efficacy of CBM588 in adults undergoing reduced-intensity allogeneic hematopoietic cell transplantation (HCT). Following a six-patient safety lead-in, 30 patients were randomized 1:1 to standard supportive care alone or with CBM588 (160 mg twice daily, day −8 to discharge). Median age was 66 years; most patients (61%) had leukemia. Fludarabine/melphalan conditioning and tacrolimus/sirolimus GVHD prophylaxis were used; grafts were from matched related (n=14) or unrelated donors (n=22). Correlative studies included 16S rRNA gene amplification, shotgun DNA metagenomics sequencing, metabolomic profiling, cytokine profiles, and flow-cytometry.

Results: We enrolled 36 patients (21 were female) at the median age of 66 years (range: 34-77). All CBM588-treated patients tolerated therapy, with 90.5% completing ≥14 days. One serious adverse event occurred in the CBM588 arm versus five in controls. Acute GVHD occurred in 26.7% of CBM588 patients versus 33% of controls; lower GI-GVHD was less frequent in the CBM588 group (7.1% vs. 31.3% as treated). One-year chronic GVHD was 37% versus 44%, and 100-day non-relapse mortality was 0% versus 7% in controls. One-year OS and RFS were 67% (95%CI: 0.20 - 0.90) and 50% (95% CI: 0.11 - 0.80) for safety lead-in, 87% (95% CI: 0.56 - 0.95) and 73% (95% CI: 0.44 - 0.89) for CBM588 arm, and 80.0% (0.50-0.93) and 80.0% (0.50-0.93) for the control arm, respectively.
Fecal microbiome composition is shown in Figure. CBM588 restored gut microbiome diversity by Day +28 and enriched microbial pathways involved in lipopolysaccharide and aerobactin biosynthesis. Interestingly, lower baseline calorie and protein intake was associated with reduced microbiome diversity and higher lower GI-GVHD. Acute GVHD was associated with early reductions in fecal short-chain fatty acids. We observed lower levels of select cytokines in the CBM588 group compared with controls, including IL-2 on Days +7 and +14, and RANTES and IL-6 on Day +14 (p = 0.006, 0.02, 0.05, 0.09, respectively, unadjusted for multiple testing). GVHD-associated biomarkers (Reg3a, ST2, and TNF-R1) measured on Day +30 were numerically higher in the control group, though differences did not reach statistical significance (p = 0.2, 0.18, 0.3, respectively). Multi-color flow cytometry showed no clear polarization of systemic immune subsets seen in the CBM588 group vs. control group on Days +30, +60, or +100 post-transplant, with the exception of reduced CD69+CD8+ T cells in the CBM588 group on Day +60 and increased intermediate monocytes on Day +100 in the same group.

Intent to Treat	**Lead-in (N=6)**	**CBM588 (N=15)**	**Control (N=15)**
Overall acute GVHD Grade 2-4 Grade 3-4	1 (16.7%) 1 (16.7%)	3 (20%) 1 (6.7%)	5 (33.3%) 0 (0%)

Lower GI GVHD			
Stage 1 Stage 2 Stage 3	0 (0%) 0 (0%) 1 (16.7%)	0 (0%) 1 (6.7%) 1 (6.7%)	1 (6.7%) 3 (20%) 0 (0%)
Total GI GVHD	2 (33.3%)	2 (13.3%)	4 (26.7%)
As Treated	**Lead-in (N=6)**	**CBM588 (N=14)**	**No CBM588 (N=16)**
Overall acute GVHD Grade 2-4 Grade 3-4	1 (16.7%) 1 (16.7%)	3 (21.4%)	
Lower GI GVHD	1 (16.7%)	1 (7.1%)	5 (31.3%)



Conclusions: CBM588 administration is safe, feasible, and modulates gut microbiome composition and function in HCT recipients, improving microbial diversity and trending toward reduced lower GI GVHD. Nutritional status strongly impacts microbiome dynamics and GVHD risk. Our data strongly support further investigation of microbiome-targeted interventions to improve transplant outcomes.

Clinical Trial Registry: NCT03922035
https://www.clinicaltrials.gov/study/NCT03922035?term=NCT03922035&rank=1

Disclosure: Miyarisan: partial research funding.

B194

DETERMINANTS OF ENGRAFTMENT INSTABILITY IN SICKLE CELL DISEASE: IDENTIFYING MODIFIABLE AND EARLY PREDICTORS OF MIXED CHIMERISM AFTER CURATIVE TRANSPLANTATION

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Background: Mixed donor chimerism (MC) is a clinically consequential outcome after hematopoietic stem cell transplantation (HSCT) for sickle cell disease (SCD). Although stable MC may maintain disease control, declining donor myeloid chimerism predicts graft failure, autologous recovery, and recurrence of SCD complications. Recent reports also link persistent host hematopoiesis and MC to expansion of pre-existing clonal hematopoiesis and elevated post-transplant malignancy risk in SCD, underscoring the need to identify early predictors of chimerism instability. However, determinants of MC after myeloablative matched sibling donor (MSD) HSCT, currently the most widely used curative approach in children and young adults, remain poorly defined. We conducted a single center analysis to identify biological and early post-transplant predictors of MC at one year.

Methods: We retrospectively analyzed 67 pediatric and young adult SCD patients who underwent myeloablative (busulfan/cyclophsophamide/Campath) MSD HSCT at a single center (2001–2024). MC was defined as <95% donor myeloid chimerism at ~day +365. Variables included demographics, SCD genotype, organ function, pre-transplant chest imaging, conditioning metrics (including busulfan AUC), graft characteristics, early complications, and serial lineage-specific chimerism at standardized timepoints. Univariate analyses used t-tests, Wilcoxon rank-sum, χ^2, or Fisher's exact tests. The primary objective was to identify predictors of MC at one year.

Results: MC occurred in 33/67 patients (49%).
Pre-transplant factors:
• Abnormal chest imaging including airway inflammation, parenchymal scarring, atelectasis, or splenomegaly was strongly associated with MC: 6/6 (100%) with abnormal imaging developed MC vs. 27/61 (44%) with normal imaging (Fisher p = 0.011).
• HbSS genotype demonstrated a non-significant trend towards MC compared to HbSC or HbSβ-thalassemia (Fisher p = 0.0822), consistent with greater inflammatory and hematopoietic stress in severe SCD.
• Older donor age demonstrated a non-significant trend towards MC (p = 0.06729).
Transplant-related factors:
• Higher busulfan AUC demonstrated a non-significant trend toward MC (Wilcoxon p = 0.08523), though interpretation was limited by small sample size (n = 30).
Post-transplant engraftment kinetics:
• Day +60 donor myeloid chimerism was a strong early predictor of MC, with significantly

lower levels in patients who later developed MC (p = 0.04959).
• Days +100, +120, +180, and +270 myeloid chimerism were also significantly lower among MC patients, demonstrating divergence of donor–host hematopoietic dominance early after transplant.
Interpretation:
These findings support a biologically coherent model in which baseline pulmonary abnormalities predispose to impaired donor marrow dominance despite uniform myeloablative conditioning. Early donor myeloid chimerism, especially at day +60, is a powerful, actionable biomarker of long-term graft stability. The association between MC and environments that preserve host hematopoiesis resonates with emerging literature linking graft instability to increased risk of clonal expansion and hematologic malignancies in SCD survivors.

Conclusions: Abnormal pre-transplant chest imaging and early donor myeloid kinetics are the strongest predictors of MC after myeloablative MSD HSCT. Incorporating **d**ay +60 chimerism thresholds into clinical decision-making may enable risk-adapted monitoring and pre-emptive interventions to prevent graft failure and mitigate long-term malignant risk. Prospective multicenter validation is needed to inform standardized chimerism surveillance strategies for SCD transplantation.

Disclosure: Ngwube, Alexander : Vertex Therapeutics (paid consultant one-time, ended November 2025) and Beam Therapeutics (paid consultant one-time, ended December 2025) All other authors, including myself, have nothing to declare.

B195

DIFFERENTIAL IMMUNE RECONSTITUTION ACROSS AGE GROUPS AFTER ALLO-HSCT: A LONGITUDINAL ANALYSIS OF PEDIATRIC, ADULT, AND ELDERLY PATIENTS

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Background: Age is a major determinant of immune reconstitution after allogeneic HSCT. However, high-resolution longitudinal comparisons across age groups remain limited.

Methods: We retrospectively analyzed 148 patients who underwent allo-HSCT for hematologic malignancies between April 2021 and December 2024. Patients were stratified into pediatric (≤18 years, n=38), young adult (19–54 years, n=84), and elderly (≥55 years, n=26) cohorts. Lymphocyte subsets were monitored monthly for 12 months post-transplant using multiparameter flow cytometry.

Results: Baseline disease duration and follow-up were comparable across pediatric, young adult, and elderly groups (Table 1). Three-year OS decreased with age—87.9% , 86.0% , and 64.0% , respectively (P=0.012)—while 3-year NRM rose accordingly at 2.78% , 10.27%

, and 23.87% (P=0.05) (Figure 1). Elderly patients were exhibited later CMV reactivation (P<0.05).

Early after HSCT (≤3 months), total lymphocyte counts and $CD3^+$ T-cell counts recovered fastest in children and slowest in elderly patients, with convergence across groups by +6 months (P>0.05). $CD4^+$ T-cell reconstitution showed the clearest age gradient: from +2 months onward, children had higher $CD4^+$ T-cell counts than young adults and elderly patients (41 vs. 19 vs. 21/μL; P=0.006) , a pattern maintained at +12 months (318 vs. 240 vs. 205/μL; P=0.106). $CD4^+$ T-cell percentages were also significantly higher in children at most time points (months 1, 2, 4, 7–12; all P<0.05) .

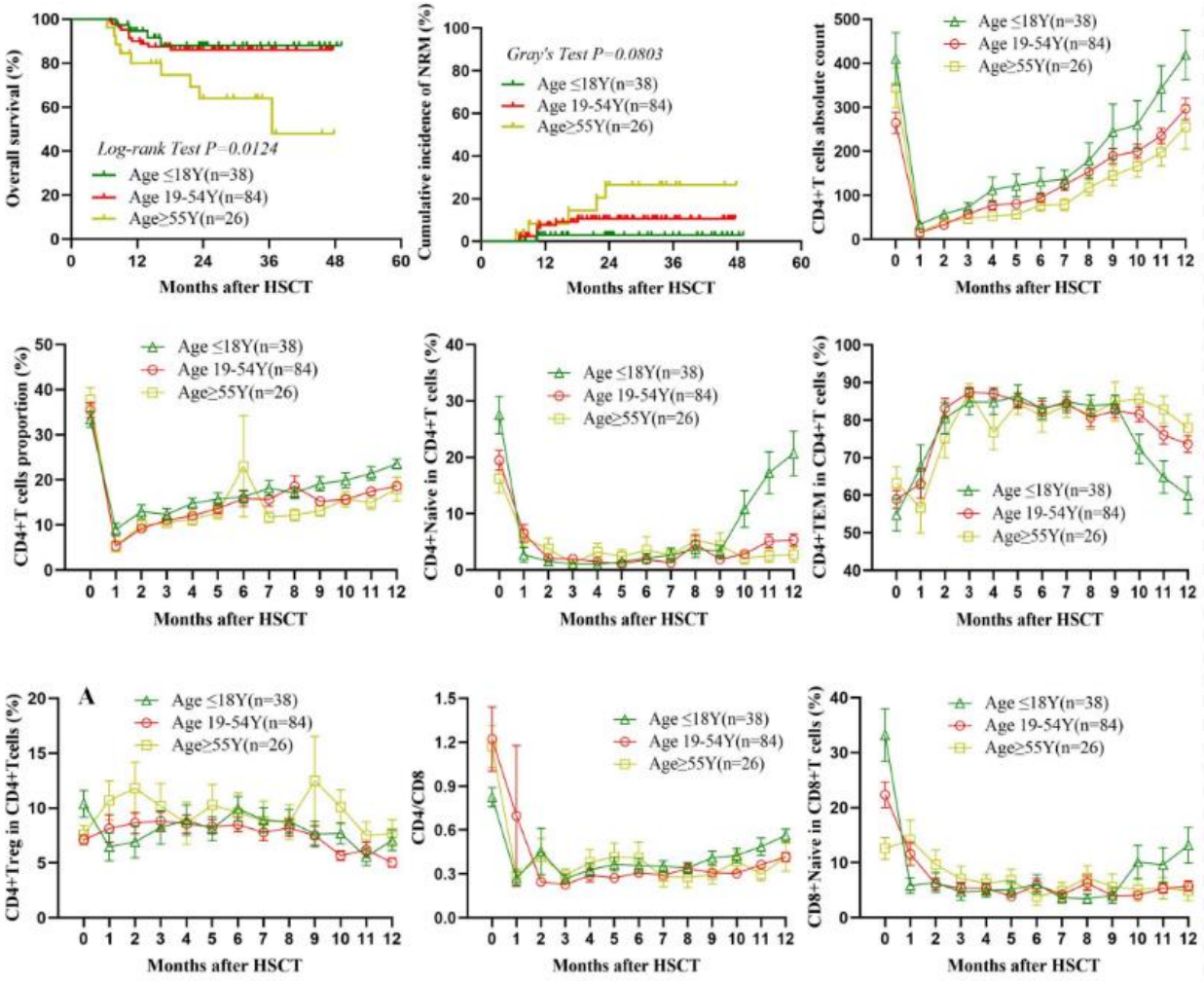
In late recovery (≥+10 months), children maintained the highest naïve $CD4^+$ T-cell proportion (+12 months: 8.94% vs. 2.04% vs. 0.91%; P=0.003), whereas elderly patients showed the highest effector-memory $CD4^+$ fractions (+12 months: 64.6% vs. 75.38% vs. 77.98%; P=0.038). Other $CD4^+$ subsets did not differ significantly. $CD8^+$ T-cell counts and percentages were broadly similar across groups. Naïve $CD8^+$ T cells were initially lowest in children but exceeded older groups by +12 months (7.25% vs. 3.32% vs. 1.59%; P=0.028). Central-memory $CD8^+$ T cells differed only at +5 months, with higher levels in the elderly (2.34% vs. 0.75% vs. 1.09%; P=0.042). Effector-memory and terminally differentiated $CD8^+$ subsets were comparable across age groups.Children had higher $CD4^+/CD8^+$ ratios at +5, +11, and +12 months (P=0.026, 0.023, 0.001). Elderly patients showed greater immunosuppression, with higher Treg levels at +10 and +12 months (7.07% vs. 6.72% vs. 4.88%, P=0.011; 6.04% vs. 5.66% vs. 4.51%, P=0.013). B-cell counts remained low early and partially recovered by +12 months with no significant differences (153.0 vs. 125.0 vs. 134.5; P=0.837), though elderly patients tended toward higher mature B-cell proportions (+12 months: 58.55% vs. 28.48% vs. 18.61%; P=0.323). NK-cell recovery was similar across groups.

Table 1. Baseline characteristics between groups

Variables	pediatric (≤18 years, n=38)	young adult (19–54 years, n=84)	elderly (≥55 years, n=26)	P-value
Age(Y)	13 (8,16)	36 (31,44)	58 (57,62)	<.001
MNC($\times 10^8$/kg)	10.03 (7.60,10.94)	7.58 (5.69,10.23)	7.85 (6.55,9.81)	0.053
CD34($\times 10^6$/kg)	5.02 (4.02,7.01)	7.00 (5.00,9.00)	6.52 (5.07,9.99)	0.032
WBCengraftment (Day)	12 (11,14)	13 (12,16)	14 (12,15)	0.075
PLTengraftment (Day)	13 (10,16)	14 (11,19)	13 (11,19)	0.515
Donor (MUD/Haplo)	11/27	41/43	14/12	0.072

CR status (CR/NR)	31/7	54/30	10/16	0.002
TBI-based/BU-based	20/18	26/58	4/22	0.006
rATG/ATLG	15/23	22/62	16/10	0.004
Ⅱ-Ⅳ aGVHD	15 (39.47)	18 (21.43)	6 (23.08)	0.102
Moderate-severe cGVHD	7 (18.42)	14 (16.67)	2 (7.69)	0.463
CS-CMVi (Day)	26(18,42)	26 (23,39)	50 (39,164)	0.022
CS-EBVi (Day)	51 (42,58)	60 (49,73)	63 (57,148)	0.248

Figure 1. Outcomes and longitudinal immune reconstitution between groups



Conclusions: Children demonstrated more efficient thymic output and immune reserve after allo-HSCT, reflected by faster $CD4^+$ T-cell recovery, higher $CD4^+/CD8^+$ ratios, and sustained enrichment of naïve $CD4^+$ T cells. In contrast, elderly recipients exhibited features of immune exhaustion and suppression—including higher $CD4^+$ TEM fractions, reduced naïve T-cell pools, early $CD8^+$ T-cell predominance, and elevated late-phase Treg levels—consistent with age-related thymic involution and cumulative antigen exposure.

Disclosure: Nothing to declare

B196

IMMUNE RECONSTITUTION AFTER HAPLOIDENTICAL PBSCT IN PAEDIATRIC B AND T-ALL: A COMPARATIVE STUDY OF PATIENTS WITH AND WITHOUT PRIOR CAR-T THERAPY

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Background: The impact of prior CAR-T therapy on post-transplant immune reconstitution in paediatric ALL remains poorly characterised. Because lymphodepletion and CAR-T therapy induce prolonged immune perturbations, understanding their influence on immune recovery after HSCT is clinically relevant.

Methods: We conducted a retrospective analysis of paediatric patients with ALL who underwent haploidentical peripheral blood stem cell transplantation (PBSCT) at the National University Hospital, Singapore (2019–2024). Immune recovery was assessed using CD4, CD8, and CD20 subsets closest to Day (D)60 (51–72 days), D100 (89–114), and D200 (151–220), with no statistically significant difference in sampling windows between groups. Significant infections were defined as viral infections requiring treatment or hospitalisation, bacterial infections requiring intravenous antibiotics, and invasive fungal infections. Time to IgG normalisation was the first time IgG was within age-adjusted norms without IVIG support. Statistical analyses included t-tests, Mann–Whitney U and Fisher's exact tests, and Kaplan–Meier analysis.

Results:

Twenty-two patients met inclusion criteria: 10 in the HSCT with prior CAR-T group and 12 in the HSCT-only group. CAR-T products were manufactured at National University of Singapore using autologous T cells (CD19 or CD19/CD22 for B-ALL; CD7 for T-ALL) and infused after fludarabine/cyclophosphamide lymphodepletion. CAR-T recipients proceeded to haploidentical HSCT at a mean of 175 days (range 60–471). GVHD prophylaxis consisted of ex-vivo CD3/CD45RA depletion in all, except one HSCT-only patient, who received post-transplant cyclophosphamide.
Age (Table 1) and sex distribution were similar between groups (female: 40% vs 25%; p = 0.65). One patient had T-ALL in the HSCT with prior CAR-T group and two in the HSCT-only group; the remainder had B-ALL. The HSCT with prior CAR-T cohort had more multiply relapsed patients, trending toward significance (p = 0.055). CD34 (15.77×10^6/kg vs 17.68×10^6/kg; p = 0.66) and CD45RO doses (19.61×10^6/kg vs 16.86×10^6/kg; p = 0.32) were comparable. Myeloablative conditioning (ATG/fludarabine/treosulfan/thiotepa/melphalan/rituximab) was used in 90% vs 83% (p = 1.00). Median neutrophil (13 vs 12 days; p = 0.89) and platelet engraftment (13.5 vs 12.5 days; p = 0.55), and rates of grade III–IV acute GVHD (10% vs 8.3%) and chronic GVHD (20% vs 16.7%) were similar.
Immune reconstitution findings are shown in Table 1 and Figure 1. Although not statistically significant (all p > 0.1), HSCT with prior CAR-T patients displayed a higher number and frequency of clinically significant infections than HSCT-only patients. CD4, CD8, and CD20 recovery at D60, D100, and D200 were similar, though missing data from retrospective, non-protocolised sampling limited interpretation. CD20 remained 0 cells/μL at D60 and D100 in

all patients. Time to CD4 >100/μL at D60, CD4 >200/μL at D100, and time to IgG normalisation were comparable (log-rank p = 0.81).

Table 1. Characteristics and immune reconstitution parameters of those who received HSCT + prior CAR-T and HSCT only.

Variable	HSCT + Prior CAR-T (n=10)	HSCT Only (n=12)	p value [a] = Mann-Whitney U [b] = Fischer's exact
Age in months (median, IQR)	106.5 (72-189)	87 (70-133)	0.43[a]
Complete Remission	CR1 = 3 CR2 = 3 CR3 = 3 CR4 = 1	CR1 = 9 CR2 = 3	0.055[b]
Number of significant infections per patient	0 infections = 3 patients 1 infection = 2 patients 2 infections = 3 patients 3 infections = 1 patient 4 infections = 1 patient	0 infections = 6 patients 1 infection = 2 patients 2 infections = 4 patients	0.236[b]
CMV reactivation	40% (n=4)	41.67% (n=5)	1.000[b]
Adenovirus	30% (n=3)	8.33 (n=1)	0.293[b]
EBV reactivation	10% (n=1)	0%	0.455[b]
Other viral infections	40% (n=4)	8.33% (n=1)	0.135[b]
Invasive fungal infections	20% (n=2)	8.33% (n=1)	0.571[b]
Bacterial infections	20% (n=2)	16.67% (n=2)	1.000[b]
CD4 >100 by D60	44.44% (n=4, missing 1)	45.45% (n=5, missing 1)	1.000[b]

CD4 > 200 by D100	33.33% (n=3, missing 1)	30% (n=3, missing 2)	1.000[b]
CD4 at D60 (median, IQR)	53 (37-137) (missing 5)	34 (24-45) (missing 7)	0.6015[a]
CD8 at D60 (median, IQR)	158 (83-241) (missing 5)	62 (50-140) (missing 7)	0.4647[a]
CD4 at D100 (median, IQR)	125 (61-181) (missing 1)	107 (38-293) (missing 2)	0.9674[a]
CD8 at D100. (median, IQR)	241 (71-776) (missing 1)	284 (84-408) (missing 2)	0.8703[a]
CD 4 at D200 (median, IQR)	668 (350.5-902.5) (missing 2)	433 (89-537) (missing 2)	0.2135[a]
CD8 at D200. (median, IQR)	564 (202 – 1936) (missing 2)	306 (194-434) (missing 2)	0.5338[a]
CD20 at D200 (median, IQR)	137 (17-227) (missing 2)	104 (61-147) (missing 2)	0.2858[a]

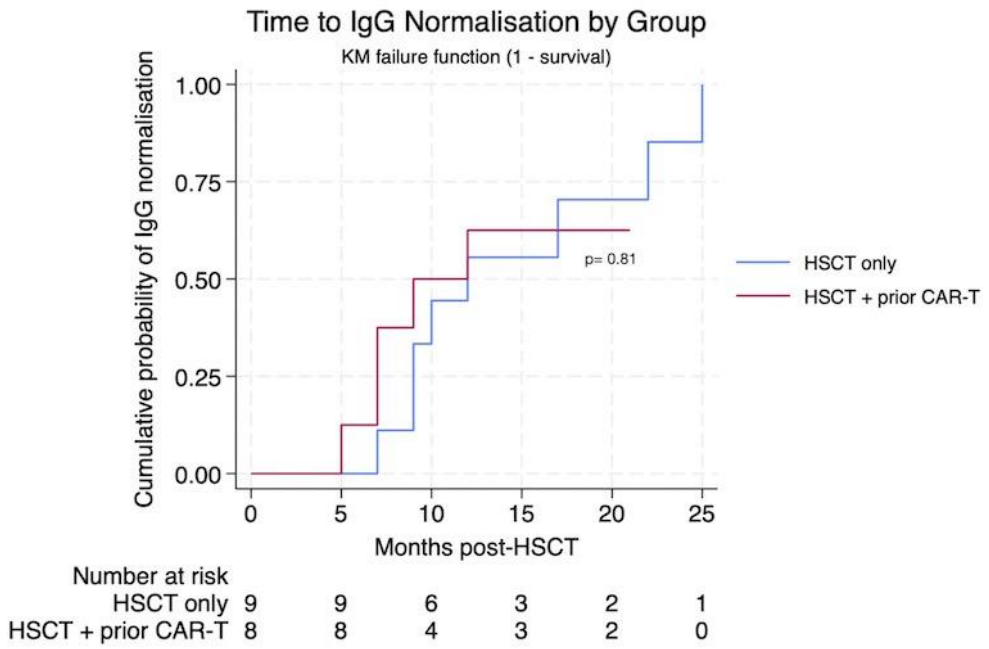

Figure 1. Time to IgG Normalisation After Haploidentical HSCT in Patients With and Without Prior CAR-T Therapy.

Kaplan–Meier failure curve showing time to IgG normalisation after haploidentical HSCT in patients with and without prior CAR-T therapy. Failure was defined as achievement of age-adjusted normal serum IgG without IVIG support. Patients who did not normalise IgG were censored at last follow-up. No significant difference was observed between the CAR-T + HSCT and HSCT-only groups (log-rank p = 0.81). Median time to IgG normalisation was 9 months in HSCT + Prior CAR-T group, and 12 months in HSCT only group

Conclusions:

Immune reconstitution, engraftment, GVHD, and IgG recovery were similar between groups. However, HSCT with prior CAR-T patients had a higher burden of clinically significant infections—a clinically meaningful trend despite lack of statistical significance, likely driven by small sample size. These findings highlight a potential vulnerability in CAR-T–bridged patients and should be validated in larger studies.

Clinical Trial Registry: none

Disclosure: None

B197

DAY 30 MIXED DONOR CHIMERISM DOES NOT PREDICT RELAPSE IN ALLOGENEIC STEM CELL TRANSPLANTATION FOR AML AND MDS

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Background: Hematopoietic stem cell transplantation (HSCT) remains the only curative option for patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS) due to the graft-versus-tumor effect. Post-transplant chimerism monitoring allows evaluation of graft engraftment and residual host hematopoiesis. Recent studies suggest that mixed chimerism at day +30 may be associated with higher relapse risk, but results are inconsistent. We aimed to clarify this uncertainty.

Methods: This retrospective, observational, single-center study included 171 adults (18–75 years) with AML (n = 116) or MDS (n = 55) who underwent HSCT between January 2018 and June 2025. All patients received post-transplant cyclophosphamide for graft-versus-host disease (GVHD) prophylaxis. Chimerism was measured using two techniques: quantitative PCR (qPCR) via STR fragment analysis (January 2018–December 2021, n = 71) and digital PCR (dPCR) targeting donor- and recipient-specific DNA sequences (informative indels, CNVs, or Y-chromosome sequences in sex-mismatched transplants, January 2022–July 2025, n = 100). Complete chimerism was defined as ≤0.1% recipient DNA; >0.1% was considered mixed. Overall survival (OS) and relapse-free survival (RFS) were estimated with Kaplan–Meier curves. Cox regression models explored prognostic factors for OS and RFS.

Results: The characteristics of the sample are shown in **Table 1**. Mixed chimerism at day 30 was not associated with increased relapse risk or impaired RFS with either qPCR [HR 1,03 (95% IC, 0,40-2,67); p 0,94] or dPCR [HR 1,11 (95% IC, 0,36-3,45); p 0,85]. In contrast, mixed chimerism at days 60 and 90 with dPCR [HR 5,16 (95% IC, 1,37-19,46); p 0,01] [HR 3,66 (95% IC 1,03-13,0); p 0,04] and qPCR [HR 3,05 (95% IC 1,07-8,6); p 0,03] [HR 4,28 (95% IC 1,39-13,16); p 0,01] were independently associated with higher relapse risk and worse RFS (**figure 1**). Nearly twice as many patients with complete chimerism at day 90 developed chronic GVHD compared to those with mixed chimerism. Myeloablative conditioning was associated with a lower probability of mixed chimerism at day 90 [OR 0,30 (95% IC, 0,10-0,78); p 0,01].

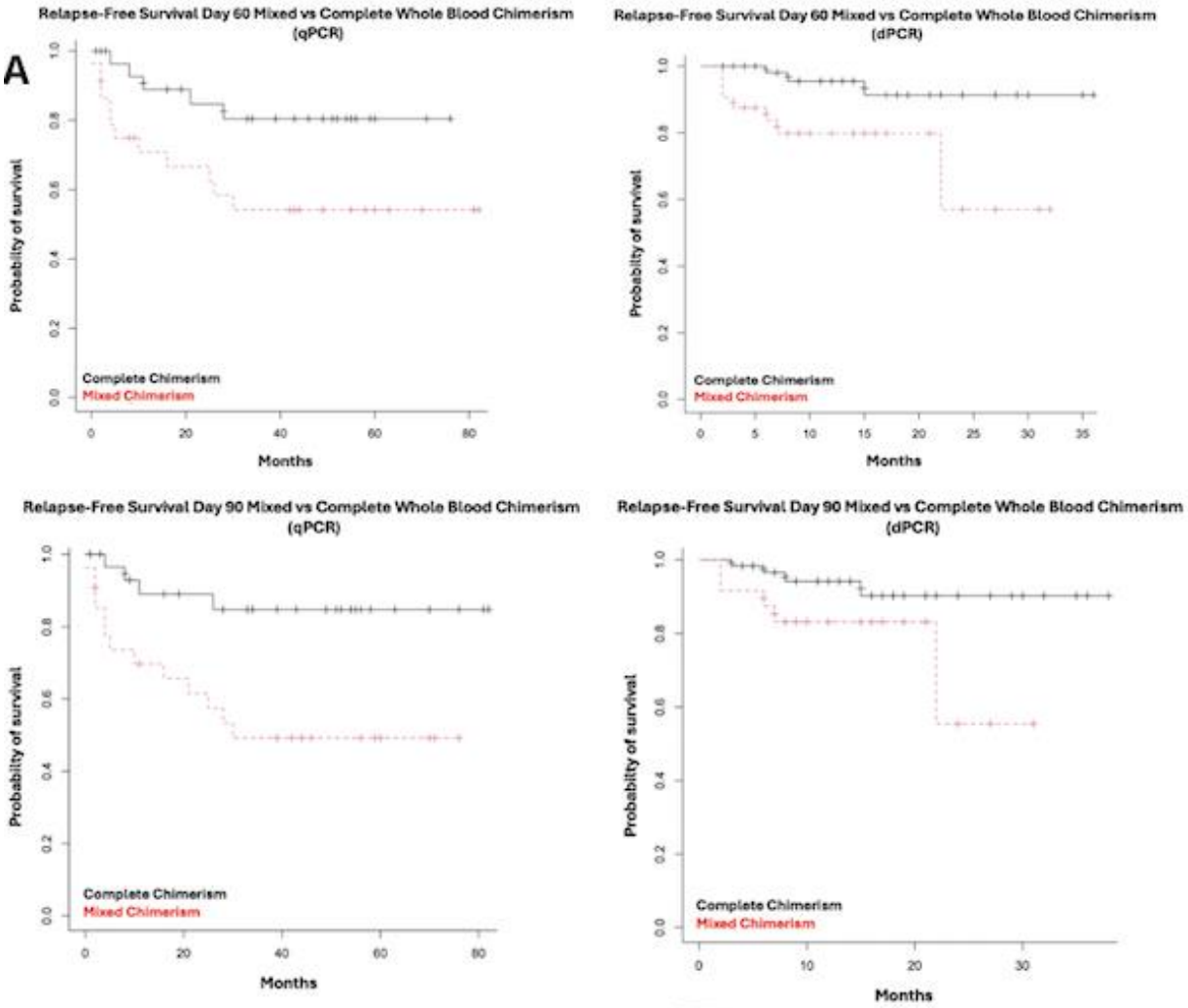
Table 1. Patient Characteristics

Variable		*Results*
N		171

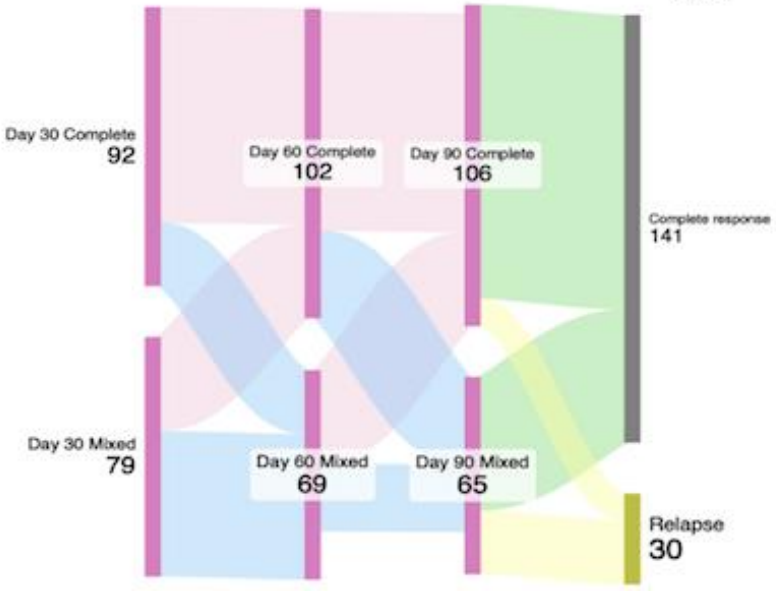
Table 1. Patient Characteristics

Age (years)	Median (Range)	55 (52-56)
Gender -- n(%)	Female / Male	91 (53,22) / 80 (46,78)
Graft Source -- n(%)	PBSC / BM	170 (99,42) / 1 (0,58)
Diagnosis -- n(%)	AML / MDS	116 (67,84) / 55 (32,16)
EBMT Risk Score	Median (Range)	3 (3-4)
Disease Status -- AML -- n(%)	CR1 / CR2 / Persistence of disease	90 (77,59) / 9 (7,76) / 17 (14,66)
Disease Status -- MDS -- n(%)	CR1 / Persistence of disease	14 (25,45) / 41 (75,55)
Donor Source -- n(%)	MmUD / MUD / Haploidentical / MRD	5 (2,92) / 27 (15,79) / 73 (42,69) / 66 (38,60)
Conditioning intensity -- n(%)	MAC / RIC	123 (72,35) / 47 (27,65)
GVHD Prophylaxis -- n(%)	PTCy + Tacrolimus + MMF	171 (100)
aGVHD -- n(%)	Yes / No	53 (31,17) / 117 (68,82)
Max Grade aGVHD -- n(%)	1 / 2 / 3 / 4	21 (12,35) / 13 (7,64) / 10 (5,88) / 9 (5,29)
cGVHD -- n(%)	Yes / No	51 (30) / 119 (70)
Grade cGVHD -- n(%)	Mild / Moderate / Severe	26 (15,29) / 14 (8,23) / 11 (6,47)
Relapse -- n(%)	Yes	30 (17,96)

A


Relapse-Free Survival Day 60 Mixed vs Complete Whole Blood Chimerism (qPCR)
Probability of survival
Complete Chimerism
Mixed Chimerism
Months
Relapse-Free Survival Day 60 Mixed vs Complete Whole Blood Chimerism (dPCR)
Probability of survival
Complete Chimerism
Mixed Chimerism
Months
Relapse-Free Survival Day 90 Mixed vs Complete Whole Blood Chimerism (qPCR)
Probability of survival
Complete Chimerism
Mixed Chimerism
Months
Relapse-Free Survival Day 90 Mixed vs Complete Whole Blood Chimerism (dPCR)
Probability of survival
Complete Chimerism
Mixed Chimerism
Months

B


Day 30 Complete
92
Day 60 Complete
102
Day 90 Complete
106
Complete response
141
Day 30 Mixed
79
Day 60 Mixed
69
Day 90 Mixed
65
Relapse
30

Conclusions: Mixed chimerism at days 60 and 90 measured by qPCR and dPCR was associated with increased relapse risk, consistent with previous reports. Early mixed chimerism at day 30 was not linked to higher relapse risk or worse OS/RFS. These findings highlight the dynamic nature of post-transplant chimerism and underscore the prognostic value of serial monitoring beyond early single measurements.

Disclosure: Nothing to declare.

B198

PROLONGED HYPOGAMMAGLOBULINEMIA IN PATIENTS WITH INBORN ERRORS OF IMMUNITY (IEI) AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT)

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Background: Prolonged hypogammaglobulinemia in pediatric patients with IEI after allogeneic HSCT causes increased susceptibility to infections, increases frequency of hospitalizations and thus requires regular immunoglobulin replacement therapy, which significantly reduces quality of life.

Methods: Included were 97 patients with IEI who received HSCT in our Center between 2012 and 2021. Prolonged hypogammaglobulinemia was defined as serum immunoglobulin G levels below 4 g/L, lasing longer than 3 years after allogeneic HSCT. Excluded were patients with chronic graft-versus-host disease, as well as patients receiving immunosuppressive therapy for any reason.

Results: Median time after HSCT was 6,6 years (range 4,7-11,8). 19 patients had prolonged hypogammaglobulinemia after HSCT. Median IgG – 3 g/L (0,7-4,7). Of 19 patients with prolonged hypogammaglobulinemia 10 had B-lymphocytes > 200 cells/μl, 9 patients - < 200 cells/μl. In all patients with B-lymphocytes > 200 cells/μl, a decrease in memory B-cells of less than 5% was observed.
Mixed chimerism was observed in 12/19 patients (63%) hypogammaglobulinemic patients had mixed chimerism, whereas in the rest of the IEI patients in was 24% (19/78).
In the 10 patients with B-lymphocyte >200 cells/μL, split chimerism with mixed origin in T-lymphocyte and myeloid lineages was seen in 5/10, 5/10 had complete donor chimerism in all lineages.
9/19 (47%) patients received B-depletion (rituximab/bortezomib) in early post-transplant period to treat autoimmune hemolytic anemia (6) and EBV lymphoproliferative disorder (3). In the rest of the IEI group B-depletion was used in 5/78(6%) of patients.

Conclusions: Patients with mixed chimerism, receiving B-depletion after HSCT need thorough monitoring due to increased risk of prolonged hypogammaglobulinemia.

The role of factors influencing B-lymphocyte reconstitution and humoral immunity in IEI patients after HSCT requires further investigation.

Disclosure: Nothing to declare.

B199

THREE-MONTH WHOLE BLOOD AND T-CELL CHIMERISM INDEPENDENTLY PREDICT RELAPSE AND SURVIVAL FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTS FOR HAEMATOLOGICAL CANCERS: A MULTICENTRE ANALYSIS

Rebecca Goodhew[1], *Mahmoud Bokhary*[1], *Rawya Hussein*[2], *Jamie Macleod*[1], *Lucy Rose*[1], *Amardass Dhami*[1], *Angeliki Georgopoulou*[3], *Eleftheria Sagiadinou*[3], *Rebecca Hallam*[4], *Maria Mazza*[4], *Rik Lewin*[2], *Hussein Jabbar*[1], *Graham Mcilroy*[5], *Rebecca Lloyd*[5], *Claire Horgan*[5,6], *Bhuvan Kishore*[5], *Richard Lovell*[5], *Elisa Roldan Galvan*[1], *Sebastian Francis*[1], *Harpreet Kaur*[1], *Jose Aspa*[1], *John Snowden*[1], *Paul Player*[2], *Alexandros Spyridonidis*[3], *Rachel Protheroe*[4], *Emmanouil Nikolousis*[5,7], *Maria Liga*[3], *Alexandros Kanellopoulos*[1,5]
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Background: Donor chimerism is routinely assessed after allogeneic stem cell transplant (allo-SCT). However, the utility of single-timepoint chimerism measurements to predict patient outcomes and guide treatment remains unclear. This study aims to evaluate whether three-month (3-mo) whole blood (WB) or T-cell (TC) mixed donor chimerism predicts cumulative incidence of relapse (CIR), overall survival (OS), progression-free survival (PFS) and acute graft-versus-host disease (aGVHD).

Methods: This retrospective study included 769 patients who received allo-SCT at one of five centres (Sheffield, Leicester, Patras, Bristol or Birmingham) for haematological malignancy. Patients who relapsed or died before 3-mo (n=116) were excluded, leaving 653 patients for analysis. The median age was 56.1 years (range 16.5-76.9), 60.1% of patients were male. Disease lineage included myeloid (n=474), lymphoid (n=174), mixed phenotype (n=3) and undifferentiated (n=2). Donor types included unrelated (n=454), sibling (n=119) and haploidentical (n=72). Median follow-up time estimated using the reverse Kaplan-Meier method was 32.3 months. Mixed donor chimerism was defined as 5-95% donor cells. Full donor chimerism was defined as >95%. OS and PFS were analysed using univariate and

multivariate Cox proportional hazards models. CIR was evaluated using Fine-Gray competing-risks regression. Multivariate models adjusted for age, sex, lineage, cytogenetic risk, cytomegalovirus serostatus, donor type and conditioning regimen. Association between 3-mo donor chimerism and the incidence and severity of aGVHD were assessed using chi-squared tests.

Results: In univariate analysis, mixed 3-mo WB chimerism was associated with inferior 2-year PFS (HR 1.57, 95% CI: 1.13-2.19, p=0.007), OS (HR 1.53, 95% CI: 1.06-2.21, p=0.02) and significantly higher CIR (HR 1.70, 95% CI 1.14-2.53, p=0.0089) compared with full donor WB chimerism. In contrast, mixed TC chimerism had no effect on 2-year PFS (p=0.65), OS (p=0.81) or CIR (p=0.28).
In multivariate analysis, WB mixed chimerism remained an independent predictor of worse PFS (HR 1.75, 95% CI: 1.18-2.58, p=0.0051), OS (HR 1.60, 95% CI: 1.03-2.47, p=0.035) and CIR (HR 1.83, 95% CI 1.13-2.96, p=0.013). TC mixed chimerism showed no independent effect on PFS (HR 1.05, 95% CI: 0.68-1.63, p=0.82), OS (HR 0.98, 95% CI: 0.60-1.60, p=0.93) or CIR (HR 1.69, 95% CI 0.97-2.92, p=0.062).
Patients achieving full donor WB or TC chimerism at 3-mo were more likely to develop aGVHD (p=0.030 and p= 0.0000013 respectively). 3-mo WB and TC chimerism did not predict aGVHD grade (p=0.79 and p=0.86 respectively).

Conclusions: In this large, retrospective multi-centre study, 3-mo WB chimerism is a strong predictor of relapse and survival following allo-SCT for haematological malignancy.

Disclosure: Nothing to declare

B200

SUCCESSFUL TREATMENT OF TRANSPLANTED PID PATIENTS WITH SPLIT CHIMERISM USING CD34+POSITIVELY-SELECTED HSPCS AFTER CONDITIONING WITH REDUCED-TOXICITY TARGETED BUSULFAN ALONE

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Background: Split chimerism with high donor T-cells chimerism but low myeloid chimerism may emerge as a consequence of failure to engraft or waning graft function. Despite the absence of graft rejection this state may hamper the long-term success of allo-HSCT, e.g. by recurrence of underlying disease or disturbances of immune function. Thus a secondary transplant with considerable risks may be necessary.

Methods: Here we report on 3 patients with primary immunodeficiencies (PID) (CGD, IPEX syndrome and XIAP deficiency) who successfully engrafted after a Treosulfan-based allo-HSCT. Patient 4 (SCID, cg-deficiency) was treated with an allo-graft after ATG-only conditioning and exclusively engrafted with donor T cells. In patients 1-3 a relevant decline

(<10%) of myeloid DC was observed within 9-18 months post-HSCT while lymphoid DC remained stable. A second allo-HSCT with CD34+-selected PBSC from the original donor was performed 11-178 months after the first procedure. The conditioning regimen consisted of targeted busulfan (cAUC 60-68mgxh/L) as a single-agent . No immunoablative component was applied. Transient immunosuppression consisted of tacrolimus (3 patients) or ruxolitinib (1 patient).

Results: Administration of targeted busulfan followed by CD34+ selected PBSC grafts from the original donor (9/10 MMUD, 10/10 MSD, 10/10 MUD, haplo) lead to rapid surge of myeloid DC and resulted in functional correction of the underlying disease. Neutrophil and thrombocyte engraftment occurred between day+15 to +23 and day+11 to+16, respectively. Minimal transfusion necessity was noted in two patients. Tacrolimus was stopped between day+39 to +47 and ruxolitinib in P4 tapered off until day +71. No opportunistic infections or virus reactivations occurred. Mucositis was mild, No patient required parenteral nutrition. Length of hospital stay ranged from 28-32 days. Except for a palmar erythema in 1 patient, no signs for acute or chronic GvHD was observed over the follow-up period of 18–56 months. While a mild dip in numbers and function was observed imposed by busulfan, T cells persisted throughout the procedure and recovered numerically and functionally within 3 months post-HSCT. In vitro evidence demonstrates the dose-dependent and transient effect of busulfan on T-cell proliferation, while their activation is not affected.

Conclusions: Treosulfan-based conditioning failed to induce durable myeloid engraftment in three patients, while patient 4 with SCID never achieved myeloid engraftment after serotherapy-only conditioning. The persistent T-cell DC in all patients excluded a graft rejection. As hematopoiesis was normal in all patients a stem cell boost with CD34-selected donor HSPCs was deemed unsuccessful to restore DC in the myeloid compartment. Busulfan is considered to exert mild if any lymphotoxic effects. We thus examined the effects of a reduced-dose busulfan-only regimen followed by infusion of highly purified HSPC grafts on myeloid engraftment and the existing immune system. We demonstrate, that this regimen is not only well tolerized (minor toxicity, rapid engraftment, no GvHD, no viral reactivation) but also highly effective in establishing durable full-donor myeloid chimerism and spares existing immune function in patients. This concept may provide a valuable treatment option for post-HSCT patients with split chimerism in need of a durable cure.

Disclosure: Nothing to declare.

B201

FROM IMMUNODEFICIENCY TO MALIGNANCY: SUCCESSFUL ALLOGENEIC HSCT IN NIJMEGEN BREAKAGE SYNDROME WITH LATE RELAPSE T-ALL

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Background: Nijmegen breakage syndrome (NBS) is a rare autosomal recessive disorder characterized by chromosomal instability, microcephaly and combined immunodeficiency caused by a homozygous mutation in the NBS1 gene. Affected patients have a markedly increased risk of haematological malignancies. Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is a potential curative option, but has been rarely reported in NBS. We report a case of successful allo-HSCT in a young adult with NBS and late relapse of T-cell acute lymphoblastic leukaemia (T-ALL).

Methods: A 20-year-old male with genetically confirmed NBS (homozygous NBS1 658del5 mutation) and a history of frequent infections had been diagnosed with primary immunodeficiency at 3 years of age based on a characteristic phenotype, recurrent respiratory infections and reduced serum immunoglobulin levels. At 12 years he developed TIII-variant T-ALL and achieved complete remission after therapy according to the ALL-MB-2008 protocol. He was admitted electively for intravenous immunoglobulin replacement when routine blood tests revealed leukocytosis (WBC 38 × 10^9/L) with 65% blasts and mild thrombocytopenia. Bone marrow examination showed 87.9% MPO-negative blasts with an immunophenotype consistent with TIII cortical T-ALL (EGIL high-risk). Cytogenetics revealed a complex karyotype with derivative chromosomes; FISH demonstrated ETV6 (12p13) deletion, partial TP53 deletion, biallelic CDKN2A (9q21) deletion with duplication of 9q21, and ABL (9q34) duplication, while screening for common fusion transcripts (AML1-EVI1, MLL/AF9, BCR-ABL p210/p190, ETV6-RUNX1, E2A/PBX1, MLL/ENL, IKZF1) was negative. MRI at relapse identified a bulky anterior mediastinal mass (128 × 103 × 139 mm). Reinduction therapy was given according to the ALL-2016 protocol. Minimal residual disease (MRD)-negative status was achieved after the first induction phase and maintained at the time of allo-HSCT. The patient subsequently underwent allo-HSCT from a fully HLA-matched unrelated donor using Flu150+Bu8 conditioning. Graft-versus-host disease (GVHD) prophylaxis consisted of post-transplant cyclophosphamide, cyclosporine A and mycophenolate mofetil.

Results: Neutrophil engraftment occurred on day +17 and platelet engraftment on day +26. Early post-transplant complications were limited to grade I acute cutaneous GVHD, which resolved with topical glucocorticoids. Bone marrow assessments showed complete donor chimerism at all time points. At 6 months post-transplant, the patient demonstrated an increase in normal serum immunoglobulin levels and recovery of T-cell immunity. Molecular testing no longer detected the NBS1 mutation in blood.

Table 1. Dynamics of cellular and humoral immune reconstitution in a patient with ALL and Nijmegen syndrome before allo-HSCT and in the early post-transplant period.

Parameter	Before allo-HSCT	Day +90 after allo-HSCT	Day +180 after allo-HSCT
IgM (ref. 0.4–2.3), g/L	0.02	0.29	0.76
IgG (ref. 7–16), g/L	0.4	9.95	10.2
IgA (ref. 0.7–4), g/L	0.01	0.03	0.23

Parameter	Before allo-HSCT	Day +90 after allo-HSCT	Day +180 after allo-HSCT
CD3+, ×10³/μL	0.48	1.32	1.95
CD3+CD4+CD8−, ×10³/μL	0.14	0.29	0.4
CD3+CD8+CD4−, ×10³/μL	0.23	1.0	1.55

Conclusions: This case illustrates the feasibility and efficacy of allo-HSCT in a young adult with NBS, achieving simultaneous treatment of combined immunodeficiency and high-risk relapsed T-ALL. Given the very high risk of haematological malignancies in NBS, early consideration of allo-HSCT at the stage of confirmed immunodeficiency, before malignant transformation, may be warranted. Multicentre studies are needed to define optimal indications, timing and transplant strategies in this rare but high-risk population.

Disclosure: Nothing to declare

B202

CLINICAL SIGNIFICANCE OF DONOR–RECIPIENT ABO MISMATCH IN SURVIVAL AND IMMUNE RECONSTITUTION AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION - SINGLE CENTRE EXPERIENCE (CIC 1085)

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Background: The clinical relevance of donor–recipient ABO incompatibility in allogeneic hematopoietic stem cell transplantation (allo-HSCT) is debated. While mismatch may increase transfusion burden and hemolytic risk, its association with survival and immune reconstitution remains unclear. This study evaluates outcomes according to ABO mismatch type in a single-center cohort.

Methods: A retrospective analysis was performed in 114 allo-HSCT recipients treated at the transplant department of the clinic of Haematology, University Hospital "St. Marina", Varna, Bulgaria (CIC 1085). Recipient and donor ABO groups were standardised and classified as compatible, major mismatch, minor mismatch, or bidirectional mismatch. Outcomes included follow-up duration, overall survival (OS), relapse-free survival (RFS), immune reconstitution (ALC, CD4+, CD8+HLA-DR+CD38+, NK, CD19 at days +100/+180/+270), and transfusion requirements. Kruskal–Wallis and χ^2 tests were used for comparisons.

Results: ABO compatibility categories included compatible (n=59), major mismatch (n=16), minor mismatch (n=22), and bidirectional mismatch (n=17). Median follow-up duration did

not differ significantly among groups (p=0.89). Overall survival (OS) was numerically higher in ABO-compatible transplants (56%) compared with major (40%), minor (47%), and bidirectional mismatches (36%), although this difference was not statistically significant (p=0.51). RFS was comparable among compatible, major, and minor mismatch groups (62.5, 63.4%, and 63.6%) and lower in the bidirectional mismatch group (47.1%), without reaching statistical significance (p=0.68). Notably, recipients of ABO-identical grafts required significantly fewer red blood cell transfusions (median 3 units, IQR 2–3) compared with those receiving minor (median 5 units), major (median 6 units), or bidirectional mismatched grafts (median 7 units; Kruskal–Wallis p<0.001), demonstrating a clear association between ABO incompatibility and increased transfusion burden. Immune reconstitution kinetics showed substantial overlap across all groups, with no consistent or clinically meaningful delay attributable to any mismatch category. Immune recovery analyses demonstrated no significant effect of ABO mismatch on the kinetics of lymphocyte subset reconstitution. Absolute lymphocyte count (ALC) recovery at days +30, +100 and +180 progressed in parallel across all ABO categories, and ABO incompatibility was not associated with delayed ALC normalization (Cox HR 1.08, 95% CI 0.82–1.41; p=0.56). CD4+ T-cell reconstitution showed modest numerical variation, with compatible transplants displaying slightly higher median CD4+ values at day +100; however, ABO status did not predict time to CD4+ ≥200/µL (HR 1.12, 95% CI 0.79–1.58; p=0.48). Activated CD8+HLA-DR+CD38+ T-cell levels exhibited the expected early post-transplant elevation in all groups without ABO-specific differences (Kruskal–Wallis p=0.61), and time to CD8+ recovery ≥150/µL was unaffected (HR 0.94; 95% CI 0.66–1.32; p=0.71). NK-cell expansion, typically rapid, showed nearly identical trajectories across compatibility groups, with no delay attributable to ABO mismatch (HR 1.05; p=0.78). Late B-cell (CD19+) recovery demonstrated substantial interpatient variability but no clustering by ABO type (Kruskal–Wallis p=0.67; HR 1.09, p=0.64). Overall, ABO mismatch was not an independent determinant of early T-, B- or NK-cell immune reconstitution following allo-HSCT.

Conclusions: ABO incompatibility did not significantly affect OS, RFS or immune reconstitution, but was strongly associated with increased transfusion requirements. ABO mismatch should not limit donor selection when HLA compatibility is prioritized, although higher transfusion needs should be anticipated.

Disclosure: Nothing to declare.

P208

B-CELL IMMUNE RECONSTITUTION AFTER ALLO-HSCT IN PEDIATRIC PATIENTS: PRELIMINARY RESULTS FROM A LONGITUDINAL FLOW CYTOMETRY ANALYSIS

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Background: Immune reconstitution is a critical determinant of HSCT outcomes. While most monitoring strategies focus on T-cell recovery, B-cell reconstitution remains less investigated. According to EUROClass (Wehr et al.,2008) and our pediatric reference data (Sozonova et al.,2025), switched memory B-cell levels <5% indicate impaired or incomplete maturation, whereas ≤2% reflect a severely deficient memory compartment. A reliable surrogate of functional humoral immunity after HSCT has not been fully established; however, the recovery of class-switched memory B cells is increasingly recognized as a key indicator of effective germinal center activity and long-term antibody competence. Here we present preliminary results of our prospective study at 1.5 years follow-up, aiming to characterize B-cell maturation dynamics in pediatric patients after HSCT.

Methods: The interim analysis of our prospective study included 51 pediatric patients that underwent HSCT for hematological malignancies (median age 9 years).
Peripheral blood(PB) samples were collected at days 30, 60, 100, 180, 365, and 540 after HSCT. B-cell subpopulations were analyzed by FC using the DURAClone IM B Cells Tube (Beckman Coulter) when absolute B-cells count exceeded 50cells/μl. The following subsets were assessed: naive, transitional, natural effector, IgM-only, switched memory, plasmablasts, plasma cells. In four patients B-cell precursors (pro-B, pre-BI, pre-BII and immature subsets) were assessed in the bone marrow(BM) samples at days 30 and 100 after HSCT according to EuroFlow recommendations.

Characteristics	**Number of patients (%)**
Diagnosis B-ALL	21 (41%)
T-ALL	5 (10%)
AML	16 (31%)
aBLL	4 (8%)
MDS	5 (10%)
Type of donor Haploidentical	31 (61%)
MSD	13 (25%)
MUD	7 (14%)

Source of stem cells BM	41 (80%)
PBSC	10 (20%)
Conditioning regiment Flu+VP+Treo	16 (31%)
Flu+Thio+Treo	4 (8%)
Flu+VP+TBI	22 (43%)
Flu+Thio+TBI	2 (4%)
Flu+VP+TMLI	4 (8%)
Flu+VP+Bu	1 (2%)
Flu+Timo+Treo+Rituximab	1 (2%)
Flu+VP+Treo+Timo	1 (2%)
GvHD prophylaxis Cyclophosphamide, vedolizumab, abatacept, baricitinib/ruxolitinib	23 (45%) / 28 (55%)

Results: Ten patients (19,6%) were excluded due to disease relapse, graft rejection or tyrosine kinase inhibitors, anti-CD20 or adoptive cell therapy.
Because B-cell maturation is initiated in the bone marrow through tightly regulated transitions from pro-B to pre-B and immature stages, assessing BM precursors provides essential upstream insight into the capacity for downstream peripheral B-cell reconstitution. Consistently, at day 30 the BM samples demonstrated predominance of pre-BI subset (72.6–86.6%) while median absolute B-cell count in PB was 1cell/µl (range 0–33). By day 100, the distribution had shifted toward pre-BII (41.6–51%) and immature (24–37%) populations, accompanied by an increase in PB B-cell count to 143cells/µl (0–892).
All patients demonstrated B-cell recovery by one year (median 480cells/µl, range 128–1148). Among B-cell subsets, the emergence of naive (median 89% at 1.5 years) and natural effector cells (median 3.6% at 1.5 years) followed by the reconstitution of switched memory B cells most closely reflects successful maturation and functional humoral recovery. At 1.5 years post-HSCT, switched memory B-cells remained markedly deficient (median 2.3%, range 0.9-5.7%), with most patients below age-adjusted lower limits and a half of patients persisting at ≤2%, consistent with severely impaired GC-dependent maturation. Only three patients achieved >5% and >25cells/µl of switched B-cells: one – at the 1-year follow-up, two – at 1.5-years, B-cell receptor repertoire assessment is currently in progress for these patients.

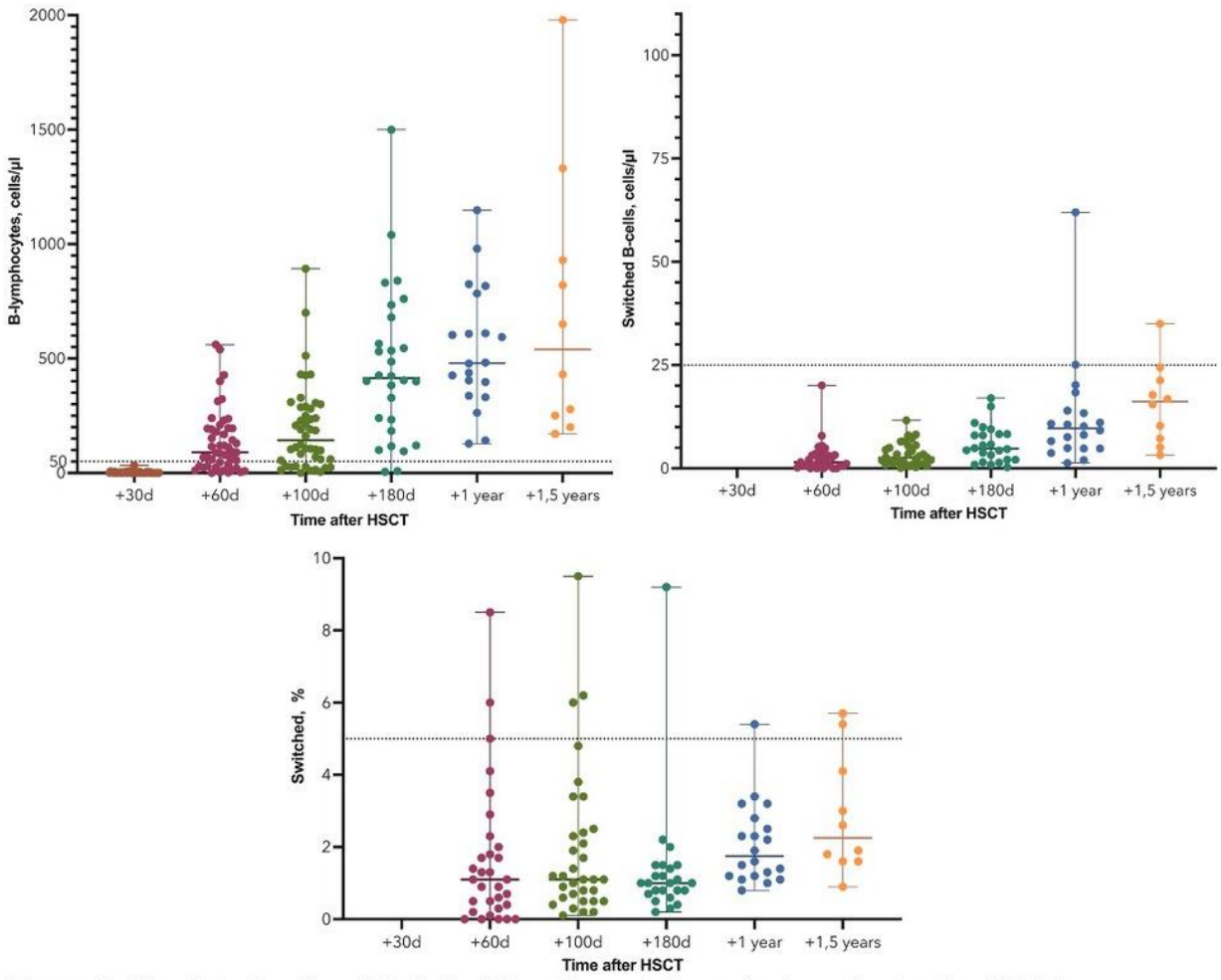

Figure 1. Absolute B-cell and Switched B-cell count dynamics in patients after HSCT.

Conclusions: The data obtained through detailed FC assessment of lymphocyte subpopulations, combined with immunoglobulin profiling, B-cell receptor repertoire analysis and clinical data will help establish a comprehensive and robust framework for evaluating humoral immune competence after HSCT. The observed delay in switched memory B-cell recovery directly impacts clinical decisions regarding IgRT continuation, prophylaxis withdrawal and vaccination readiness.

Disclosure: Nothing to declare.

P209

IMMUNE RECONSTITUTION DYNAMICS AND CLINICAL CORRELATES AFTER PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE-CENTER REAL-WORLD EXPERIENCE

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Background: Hematopoietic stem cell transplantation (HSCT) is a curative treatment for a wide range of malignant and non-malignant diseases in children. Successful immune reconstitution (IR) after HSCT is a critical determinant of long-term outcomes, as delayed or impaired IR is associated with severe infections, graft-versus-host disease (GVHD), mixed chimerism, disease relapse, and secondary malignancies. However, real-world data describing immune recovery patterns and their clinical implications in pediatric HSCT recipients remain limited.
The aim of this study was to comprehensively evaluate post-transplant immune reconstitution in children undergoing HSCT, to characterize lymphocyte subset recovery, and to explore the associations between immune parameters, chimerism status, and GVHD.

Methods: This retrospective single-center study included pediatric patients (<18 years) who underwent autologous or allogeneic HSCT between March 2019 and June 2023 at the Pediatric Bone Marrow Transplantation Unit of University of Health Sciences Ümraniye Training and Research Hospital. Patients who received a second transplant, died within the first year post-transplant, or were lost to follow-up before one year were excluded.
Immune reconstitution was assessed using lymphocyte subset analysis (CD3+, CD4+, CD8+, CD19+, CD16+/56+ cells) and correlated with chimerism status and clinical outcomes. Statistical analyses were performed using IBM SPSS version 25.0, with $p<0.05$ considered statistically significant.

Results: A total of 55 patients were analyzed, of whom 52.7% were male. The mean age at transplantation was 81.3±68.0 months. Allogeneic HSCT was performed in 49 patients (89.1%), while 6 patients (10.9%) received autologous HSCT. Indications included non-malignant diseases in 67.3% and malignant diseases in 32.7% of patients. Bone marrow was the stem cell source in 65.5%, and peripheral blood in 34.5% of cases.
Significant associations were observed between immune reconstitution parameters and chimerism status. Patients with low CD3+ T-cell counts had a significantly higher rate of mixed chimerism (<95%) compared to those with normal CD3+ counts (50% vs. 14.6%, $p=0.044$). Similarly, low CD4+, CD8+, and CD19+ cell counts were each significantly associated with increased rates of mixed chimerism ($p=0.022$, $p=0.023$, and $p=0.023$, respectively).
Furthermore, a low CD16+/56+ (NK cell) percentage was significantly associated with a higher incidence of GVHD (71.4% vs. 20.8%, $p=0.013$).

Conclusions: Our findings demonstrate that delayed or impaired immune reconstitution, particularly involving T- and B-cell compartments, is strongly associated with mixed chimerism and GVHD in pediatric HSCT recipients. Systematic monitoring of lymphocyte

subsets may enable early identification of high-risk patients and support individualized post-transplant management strategies. These results underscore the clinical relevance of immune reconstitution profiling in improving long-term outcomes after pediatric HSCT.

Disclosure: None

P211

IMMUNE RECONSTITUTION ASSESSMENT IN PATIENTS WITH CHRONIC GRAFT VERSUS HOST DISEASE

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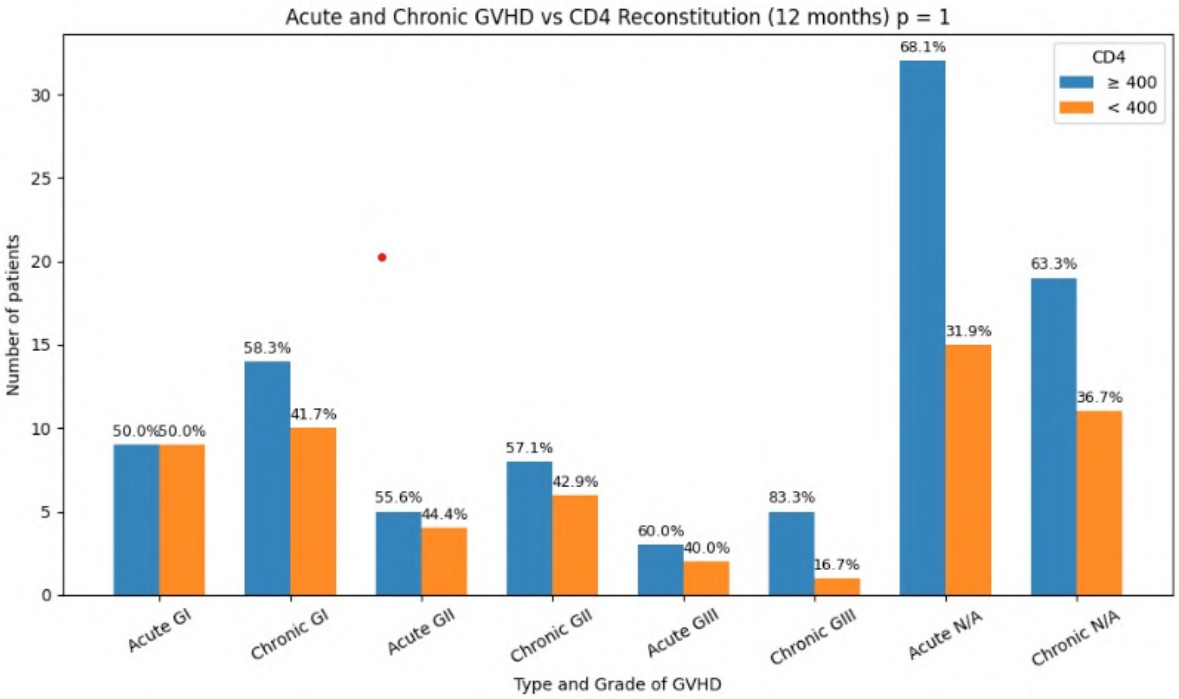
Background: Bone marrow trasplantacion (BMT), also know as Hematopoietic Stem Cell Trasplantation, is a therapeutic process which is fundamental in many malignant and non-malignant diseases, also in oncologic and autoinmune diseases. Graft-versus-host disease (GVHD) is a main complication following BMT, either acute or chronic. This condition can affect multple organs and systems, impacting the patient´s quality of life and long-term survival. GVHD is characterized by an immune response of the alloreactive T lymphocytes. Immune reconsitution is the process in which the immune systeme recovers following BMT and depends on factors such as the graft source, conditioning regiment – myeloablative (MAC) or reduced-intensity conditionin (RIC), the inmunosupresion agents, donor age and sex, graft failure and/or dysfunction, among others. This process involves de recovery of B, T and NK cells. This evaluation is performed through lymphocyte subpopoulation, a blood analysis. Poor immune reconsitution is associated with an incresed risk of infections, relapse and progression of GVHD; therefore; its monitoring and study are of great importance.

Methods: A single-center, retrospective, observational study was conducted in patients who underwent allogeneic BMT and subsequently developed chronic GVHD, compared with those who did not develop GVHD and those who developed acute GVHD, from 2017 to 2024. Clinical, demographic, and laboratory data were collected to analyze the timing of immune reconstitution, taking into account conditioning regimen, transplant type (haploidentical or HLA-identical), donor-related factors, and post-transplant complications that may impact immune recovery.

Results: A statistically significant trend (p=0.0532) was observed between transplant type and immunosuppression at 6 months. Patients with HLA-identical transplants and those using methotrexate-based regimens showed a trend toward better CD4 recovery (53.6% in the >400 group vs. 31.4% in the <400 group). Conversely, post-transplant cyclophosphamide use (common in haploidentical transplant recipients) was more frequent in the group with insufficient reconstitution (68.6%).
Also in the analysis based on our data base, we observed that immune reconstitution is affected by different variables; the most relevant was de association with acute GVHD.

Although there were other items with important significance like CMV reactivation and bacterial infections.

Variable	Total (N=79)	>400 CD4/mcl 6 months (N=28)	<400 CD4 months (N=51)	P Value	>400 CD4/mcl 12months (N=49)	<400 CD4/mcl 12 months (N=30)	P Value
Age	33 (25.5-43)	31.5 (26.25-42)	34 (25.5-44.5)	0.7466	32 (26-41)	39.5 (25.5-48)	0.4334
HLA Identical trasplant HLA Haploidentical trasplant	48 (60.8) 31.39.2	13 (46.4) 15 (53.6)	35 (68.6) 16 (31.4)	0.0532	27 (55.1) 22 (44.9)	21 (70) 9 (30)	0.1881
CMV reactivation Present Absente	49 (62) 30 (38)	20 (41.4) 8 (26.6)	29 (56.9) 22 (43.1)	0.202	32 (65.3) 17 (34.7)	17 (56.7) 13 (43.3)	0.4426
Inmunosupresion Cs + MMF +MTX (HLA Identical) Cs + MMF + CyPT (HLA Haploidentical)	31 (39.2) 48 (60.8)	15 (53.6) 13 (46.4)	16(31.4) 35 (68.6)	0.0532	22 (44.9) 27 (55.1)	9 (30) 21 (70)	0.1881
Acute GVHD Present Absent	46 (58.2) 33 (41.8)	18 (64.3) 10 (35.7)	28 (54.9) 23 (45.1)	0.418	31 (63.3) 18 (36.7)	15(50) 15 (50)	0.2459
Chronic GVHD Present Abscent	30 (38) 49 (62)	13 (46.4) 15 (53.6)	17 (33.3) 34 (66.7)	0.2513	19 (38.8) 30 (61.2)	11 (36.7) 19 (63.3)	0.8513



Conclusions: In this work we can confirm that immune reconstitution is a dynamic process in which every variable have a role in this process. Now that cyclophosphamide is being used post-transplant in HLA-identical patients, it will be interesting to evaluate immune reconstitution with this therapy and compare it to the methotrexate standard.

Disclosure: Nothing to declare.

P212

PRELIMINARY ANALYSIS OF B-CELL IMMUNORECONSTITUTION IN CHILDREN WITH HEMATOLOGICAL MALIGNANCIES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE

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Background: Allogeneic HSCT is a curative treatment for severe pediatric hematologic and immunologic diseases; however, delayed immune reconstitution remains a major contributor

to post-transplant morbidity. B-cell recovery is particularly slow and often functionally insufficient, increasing the risk of prolonged hypogammaglobulinemia and recurrent infections. Multiple transplant-related factors including GVHD, prolonged immunosuppression, prior B-cell targeted therapy, and conditioning intensity may further disrupt B-cell maturation. Despite numerical recovery within the first year, full restoration of humoral immunity may be delayed. Understanding determinants of impaired B-cell reconstitution after allo-HSCT with post-transplant cyclophosphamide (PTCy) remains essential for optimizing long-term immune recovery.

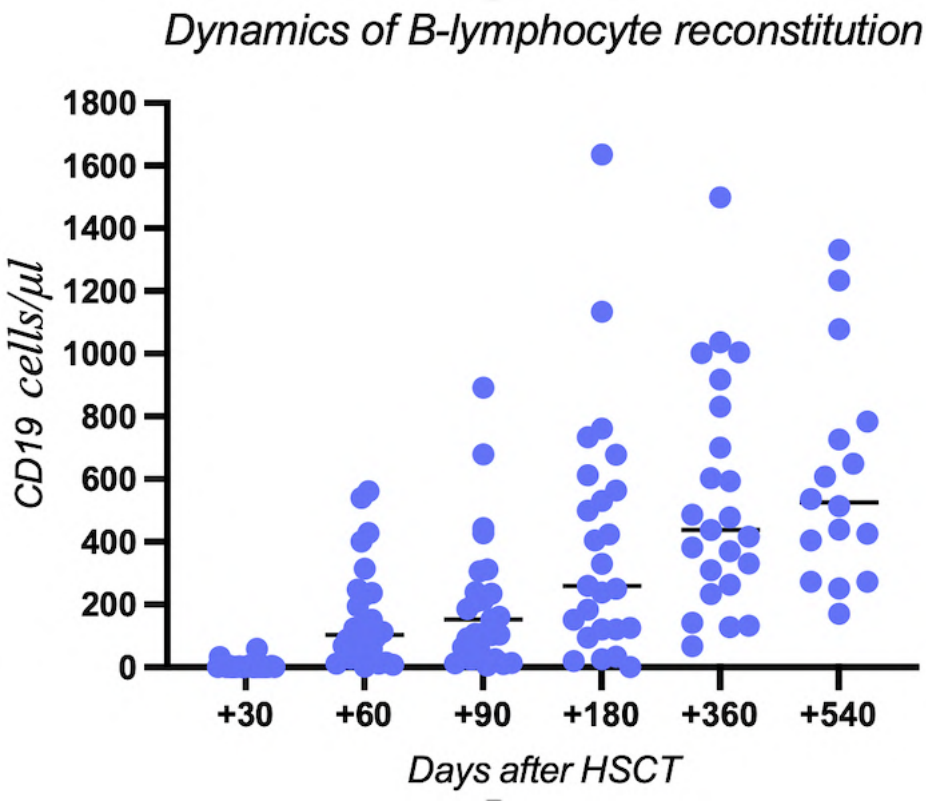
Methods: Here we demonstrate the analysis of 36 pediatric patients with acute leukemias who underwent allo-HSCT with PTCy in 2024 and reached the 1-year or longer milestone. The median age was 9 years (range 1–17 years), 27 boys, 9 girls, 18 ALL, 13 AML, 2 ABLL, 3 MDS. Patients characteristics are presented at Table 1. Seven of 27 children received blinatumomab, 1 - inotuzumab, and 1 got CAR-T cells prior to allo-HSCT. Immunophenotyping was performed by flow cytometry (CytoFLEX, Beckman Coulter). Nine patients were excluded due to relapse, adoptive cell therapy, severe complications or aplasia requiring donor cell infusion, leaving 27 in the final analysis. Detailed B-cell phenotyping ≥ 1 year post-transplant was performed in 17 patients.

Table 1. Patients characteristics

Characteristics	Number of patients (%)
Diagnosis	
ALL (B/T)	18 (50%) (14/4)
AML	13 (36%)
ABLL	2 (6%)
MDS	3 (8%)
Type of donor	
Haploidentical	22 (61%)
MUD	7 (19.5%)
MSD	7 (19.5%)
GVHD prophylaxis	
Baricitinib + Abatacept + Vedolizumab	24 (67%)
Ruxolitinib + Abatacept + Vedolizumab	12(33%)
Conditioning regimen	
TBI-based/TMLI-based (12 Gr) + VP/Thiotepa	18 (50%) (17/1)

Treo-based + VP/Thiotepa	16 (44%) (15/1)
Rituximab in conditioning	2 (6%)
Source of stem cells	
BM	31 (86%)
PBSC	5 (14%)

Results: All patients engrafted in time and had full donor chimerism. Among 27 patients, 12 (44%) developed acute GVHD: grade 1-2 in 75%, grade 3 in 25%. Chronic GVHD was observed in 5 patients (18%). Eight of children with GVHD (57%) received prolonged systemic immunosuppressive therapy (≥ 3 months). Rituximab was employed only in one case of immune-related complications (AIHA). Four of 27 patients (15%) had CMV-viremia. No other serious infections were detected, only a few respiratory episodes. Detailed B-cell phenotyping at ≥1 year after allo-HSCT has been done in 17 patients, in 7 cases switched B-memory cells (IgD-IgM-CD27+) did not exceed 2%, but nobody of them required replacement immunoglobulin therapy. The immunoglobulin M level was within reference values at more than 6 months in almost all patients.
In one (4%) of 27 patients, B-lymphocyte levels reached 50 cells/μL by day +30 after HSCT, in 70% by day +60, in 4% - +90 day, in 8% - +180 day, and in 14% - +360 post-HSCT (Figure 1). Only the patient who received rituximab post-HSCT underwent regular replacement therapy; the remaining patients underwent single intravenous immunoglobulin (IVIG) infusions as indicated (IgG <4 g/L) until B-cell immunoreconstition occurred (first 3 months after HSCT). No-one received replacement therapy with SCIG.
Figure 1. Kinetics of B-lymphocyte recovery.



Conclusions: Allo-HSCT with PTCy as GVHD prophylaxis supports an adequate quantitative and functional B-cell recovery in most pediatric recipients, despite a subset exhibiting persistently low switched memory B-cell levels. No patients required immunoglobulin administration, warranting investigation into the minimum number of switched B cells required for protective clinical efficacy. Further studies are needed to characterize B-cell repertoire evolution and to define transplant-related factors influencing long-term immune competence.

Disclosure: Nothing to declare.

P213

TÜRKİYE TRANSPLANT CENTRES CHIMERISM APPROACH SURVEY STUDY

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Background: Monitoring donor chimerism after allogeneic haematopoietic stem cell transplantation (Allo-HSCT) is important in terms of engraftment and relapse. Chimerism testing practices may vary from centre to centre. In this study, a survey was conducted targeting transplant centres with Allo-SCT experience in Turkey, and the results were evaluated.

Methods: A survey consisting of 15 questions, some multiple-choice and some open-ended, was conducted for paediatric and adult transplant centres in Turkey with allo-SCT experience(Survey link: **https://forms.gle/1Mg4wAs4z1inHUVv7**). Prior to the study, approval was obtained from the Non-Interventional Clinical Research Ethics Committee of Aydın Adnan Menderes University (2025/72) and announced on the official website of the Turkish Haematology Association. The opinions of the participants who completed the questionnaire regarding the test practice and the questionnaire itself were also obtained from the doctors who wished to provide feedback through an open-ended question.

Results: The study included 30 centres consisting of 17 (56.7%) university hospitals, 3 (10%) teaching and research hospitals, 1 (3.3%) city hospital, and 9 (30%) private hospitals. Of these centres, 23 centres (76.7%) actively perform Allo-SCT on adult patients, and 7 centres (23.3%) actively perform Allo-SCT on paediatric patients. Twenty (66.7%) centres perform related, unrelated, and haploidentical allo-SCT. Six (20%) centres can also perform cord blood-derived Allo-SCT in addition to these. The proportion of centres capable of performing haploidentical Allo-SCT is 90%. Regarding the timing of chimeric state testing, 17 (56.7%) centres have adopted testing within the first month post-transplant, followed by testing at 3 months, 6 months, and 1 year. Regarding the time to achieve chimerism, 21 (70%) centres reported obtaining results within the first 15 days, while 8 (26.7%) centres reported obtaining results between 16 and 30 days. Regarding the cell source, 14 (46.7%) centres used only peripheral blood, while 16 (53.3%) centres used peripheral blood and/or bone marrow. Twenty-three (76.7%) centres do not examine chimerism in a specific population; 5 (16.7%) centres examine the T-cell series, and 2 (6.7%) centres examine the CD34 cell population. The most frequently used method for chimeric state research is short tandem repeats (STR) (50%). Twenty cases (66.7%) stated that they obtained the test result from an accredited laboratory. Twenty-six (86.7%) centres stated that they did not use the HLA relapse loss test.

Conclusions: This survey study, which aims to determine the practices of centres performing allo-SCT in Türkiye regarding chimerism, provides results that will guide future, larger-scale studies. The proliferation of international studies involving a larger number of centres and determining more parameters will improve clinicians' approach to performing and interpreting chimerism tests.

Disclosure: Nothing to declare

Paediatrics – Clinical

OS04-04

PERI-TRANSPLANT GUT MICROBIOME INJURY AND ENTEROCOCCUS FAECIUM DOMINATION ARE ASSOCIATED WITH INCREASED MORTALITY IN PEDIATRIC ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) is a potentially curative therapy for a wide range of pediatric diseases, yet transplant-related complications remain a major cause of morbidity and mortality. Increasing evidence from adult cohorts suggests that gut microbiome diversity and composition influence post-transplant outcomes; nevertheless, pediatric patients have distinct age-related characteristics in microbiome development, immune maturation, and transplant indications. The contribution of gut microbiome dynamics to outcomes after pediatric allo-HCT remains insufficiently understood.

Methods: We conducted a longitudinal, multicenter study of pediatric patients receiving allo-HCT at Memorial Sloan Kettering Cancer Center (New York, USA), Bambino Gesu Children's hospital (Rome, Italy), and Boston Children's Hospital (Boston, USA). Stool samples were collected from day −30 to 2 years post-transplant. Shotgun metagenomic sequencing with external microbial spike-in controls was used to quantify microbiome composition and absolute abundance across kingdoms. Associations between clinical variables, microbiome features, and transplant outcomes were systematically evaluated.

Results: A total of 349 patients were enrolled, contributing 1,699 stool samples. Median age at transplantation was 8.1 years (IQR 4.2–14.1), and 66% underwent allo-HCT for malignant indications. Females accounted for 36% of the cohort (n=124). T-cell depletion (TCD) was applied in 110 allografts (32%), including alpha/beta TCD in 81 patients. Bone marrow was the most frequently used stem cell source (n=207, 59%), followed by peripheral blood stem cells (n=122, 35%) and umbilical cord blood (n=16, 5%). Most patients (94%) underwent allo-HCT for the first time, while a minority received a subsequent transplant. After a median follow-up of 2.6 years (IQR 1.7–3.8), relapse occurred in 42 patients, corresponding to 18% of those transplanted for malignant indications. Acute GVHD occurred in 31% of the cohort, and overall mortality was 17%, with non-relapse mortality accounting for 6% of deaths.

During the peri-transplant period, gut microbiome α-diversity declined significantly after transplantation (median Simpson reciprocal index 4.0 pre-HCT vs. 2.1 post-HCT, p<0.001), accompanied by an approximately five-fold reduction in total bacterial load. Younger age (<3 years), malignant indication, and use of TCD grafts were associated with lower α-diversity over time (p<0.001). Across the peri-transplant period, bacterial absolute abundance varied significantly by transplant center and underlying disease indication (p<0.001). Microbiome composition analysis revealed frequent low-diversity states, with taxonomic domination (≥30% relative abundance) observed in 97% of patients by day +28. Among dominant taxa, Enterococcus was most frequently observed (26% of samples), followed by Streptococcus (9%). Multivariable analyses were performed to explore clinical determinants of microbiome domination. Malignant disease and piperacillin/tazobactam prophylaxis were associated with increased *Enterococcus* domination and abundance.
In multivariable Cox analysis of first-time recipients (n=192), greater gut microbiome α-diversity during the peri-engraftment period predicted lower all-cause mortality (HR 0.40, 95% CI 0.17–0.95; p=0.038). FLORAL was implemented to identify gut microbiome taxa associated with outcomes, which identified *Enterococcus faecium* as positively associated with mortality.

Conclusions: This multicenter study demonstrates pronounced age- and center-related heterogeneity in the pediatric HCT microbiome. Reduced α-diversity and Enterococcus faecium domination were associated with increased mortality, supporting the prognostic importance of peri-transplant microbiome characteristics.

Disclosure: Declaration of interests Dr. M.R.M.v.d.B has received research support and stock options from Seres Therapeutics and stock options from Notch Therapeutics and Pluto Therapeutics; has received royalties from Wolters Kluwer; has consulted, received honoraria from, or participated in advisory boards for Seres Therapeutics, Rheos Medicines, Ceramedix, Pluto Therapeutics, Thymofox, Garuda, Novartis (spouse), Synthekine (spouse), Beigene (spouse), and Kite (spouse); has IP licensing with Seres Therapeutics and Juno Therapeutics; and holds a fiduciary role on the Foundation Board of DKMS (a nonprofit organization). V.E. was supported by grants from the Amy Stelzer Manasevit Research Program, the Italian Association for Cancer Research, and by the Italian Ministry of Health with "Current Research funds. L.F. was supported by grants from AIRC (Special Program Metastatic disease: the key unmet need in oncology 5 per mille 2018 Project Code 21147 and Accelerator Award 2017 INCAR); Ministero dell'Istruzione, dell'Università e della Ricerca, PRIN ID 2017 WC8499_004; Ministero della Salute, RF-2016-02364388.

OS10-08

HLA-DRB1 MISMATCHING ENHANCES GVL EFFECT IN PEDIATRIC ACUTE LEUKEMIA UNDERGOING G-CSF/ATG-BASED HAPLOIDENTICAL TRANSPLANTATION : THE CRITICAL ROLE OF POSITION 86 DIMORPHISM

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Background: The impact of HLA-DRB1 mismatching in haploidentical hematopoietic stem cell transplantation (haplo-HSCT) is increasingly recognized in post-transplant cyclophosphamide (PTCy) platforms. Recent investigations led by Petersdorf et al. demonstrated that the amino acid dimorphism at position 86 (p86) of the HLA-DRB1 antigen-binding groove—specifically the Glycine/Glycine (GG) genotype—predicts reduced relapse after haplo-HSCT with PTCy. However, this immunogenetic association remains understudied in pediatric patients treated with the G-CSF/ATG-based protocol (the Beijing Protocol).

Methods: A total of 690 pediatric patients who received haplo-HSCT (5–8/10 HLA matched) with G-CSF/ATG-based conditioning across multicenters in China from 2015 to 2023 were included in this retrospective study. The overall cohort had a median age of 9 years (IQR: 5–13 years), and was composed of 347 AML patients and 343 ALL patients. In terms of disease status at transplantation, 72 cases were categorized as refractory/relapsed (RR) disease, while the remaining 618 were classified as non-RR cases. We evaluated the association between HLA-A/B/C/DRB1/DQB1 matching and clinical outcomes—including disease-free survival (DFS), overall survival (OS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM) and relapse-related mortality (RRM)—using Cox regression models. Additionally, we investigated the immunomodulatory impact of the DRB1 p86 dimorphism (Glycine/Valine), specifically evaluating the prognostic value of DRB1 mismatching within patient GG, GV, and VV subgroups.

Results: HLA-DRB1 matching was significantly associated with inferior outcomes compared to mismatching in the non-RR cohort (Fig. 1a). This effect was not observed in the RR cohort (Fig. 1b). In the non-RR cohort (Fig. 1c), patients matched at DRB1 exhibited lower DFS (HR=1.95, p=0.0002) and OS (HR=1.92, p=0.0021). This survival disadvantage was primarily attributed to a higher cumulative incidence of relapse (HR=2.11, p=0.0006) and

RRM (HR=2.25, p=0.0033), with no significant difference in NRM (HR=1.62, p=0.1484). Structural stratification revealed that the protective effect of DRB1 mismatching is modulated by p86 dimorphism in a disease-specific manner. While the impact of DRB1 mismatch within the p86-GG subgroup showed only marginal association with RRM in the overall cohort (p=0.0472), disease-specific stratification revealed distinct patterns. In AML (Fig. 1d), the DFS benefit was pronounced in the p86-VV subgroup (p=0.0018). Notably, although the p86-GV subgroup showed a significant reduction in relapse risk (p=0.03), it failed to achieve a statistical improvement in DFS. In contrast, in ALL (Fig. 1e), the protective efficacy was prominent in the p86-GV genotype (predicting superior DFS, p=0.0224, and lower RRM, p=0.0305). In multivariate analysis, DRB1 mismatch was identified as an independent predictor of DFS, whereas mismatches at other loci showed no significant association.

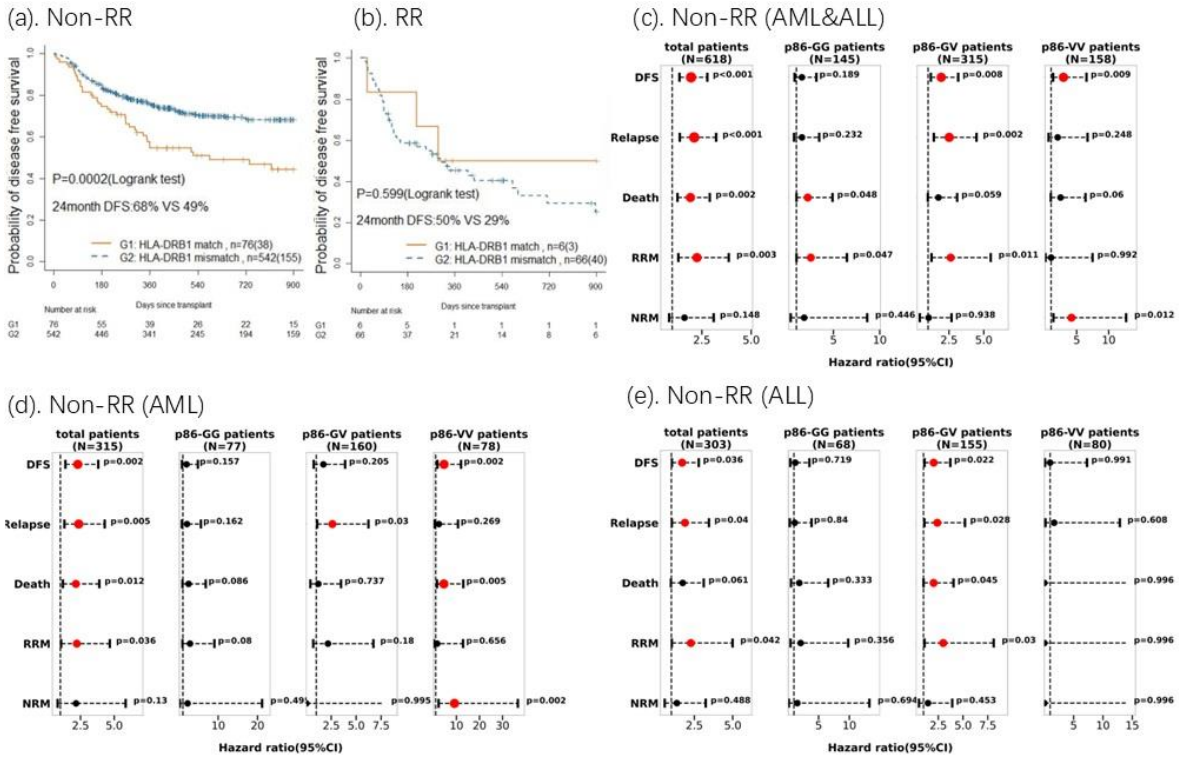

Figure 1. **HLA-DRB1 matching-associated DFS Kaplan-Meier curves and risks stratified by patient amino acid dimorphism at position 86 of DRB1.** (a),(b) Kaplan-Meier curves of DFS for the non-RR and RR subgroups. (c) Forest plot of risks for non-RR (AML&ALL). (d) Forest plot of risks for non-RR (AML). (e) Forest plot of risks for non-RR (ALL).

Conclusions: This multicenter study suggests that HLA-DRB1 matching generally attenuates GVL efficacy in pediatric patients with lower tumor burden (non-RR) undergoing haplo-HSCT. Furthermore, our data indicate that the outcomes are significantly modulated by the Valine/Glycine dimorphism at position 86 . While the survival advantage of DRB1 mismatching is mainly attributed to enhanced GVL, the distinct patterns observed (especially in the p86-VV subgroup) imply that p86 dimorphism also alters immunogenicity, thereby influencing the risk of NRM. These findings highlight the utility of integrating p86 polymorphism into donor selection strategies.

Disclosure: Nothing to declare

OS14-04

TCR ALPHA/BETA DEPLETION IN HAPLOIDENTICAL TRANSPLANTATION FOR PEDIATRIC PATIENTS

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Background: TCRαβ-depleted haploidentical HSCT is effective for children without matched donors across benign and malignant diseases. Ex-vivo T-cell depletion of graft- versus -host disease (GvHD) causing subsets- TCR αβ and CD45RA cells – and adoptive transfer with memory (CD45RO) cells have significantly improved the outcomes with low GvHD rates and acceptable viral reactivation.

Methods: We retrospectively analyzed 397 pediatric patients who underwent TCR αβ depleted haplo-HSCTs from January 2013 to September 2025 in a tertiary care center for benign (n= 332) and malignant (n=65) indications. The stem cell product underwent ex-vivo depletion of CD19 (n=46) or CD45RA (n= 350) along with TCR αβ depletion. Patients with CD45RA depletion were given sequential donor lymphocyte infusion (DLI) of CD45RO cells post–transplant.

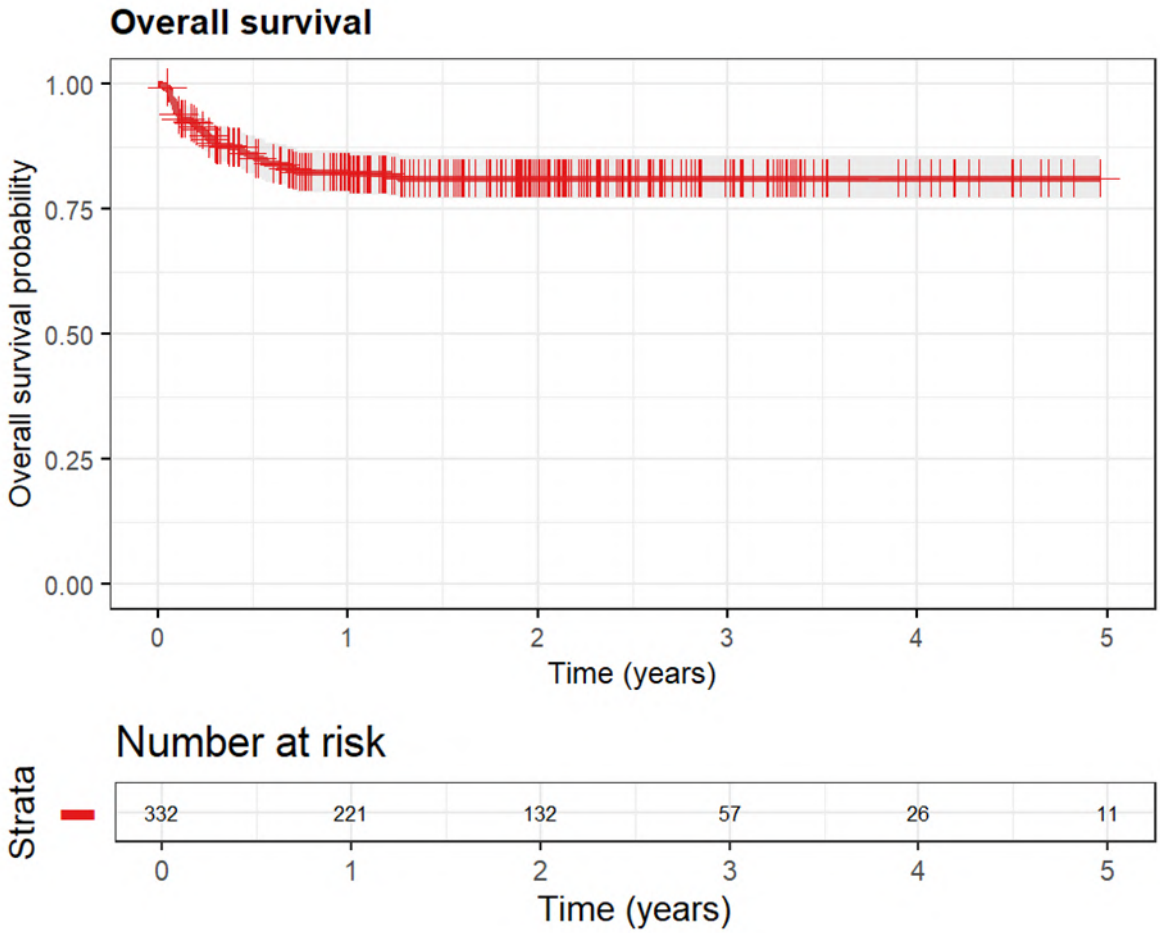
Results: Cohort characteristics: Median age – 6.08 years with 61% males and 39% females. Benign transplants included transfusion dependent thalassemia (n=253), metabolic disorders (n=32), primary immunodeficiencies (n=26), inherited bone marrow failure syndromes (n=12). Malignant indications included high risk or relapsed acute lymphoblastic leukemia (n=43), high risk or relapsed acute myeloid leukemia (n=14), juvenile myelomonocytic leukemia (n=3) –and other rare hematolymphoid malignancies (n=5).
Transplant procedure: Conditioning regimen used was predominantly myeloablative in 75% and reduced-toxicity in 23% transplants. T haplo-HSCT grafts were of parental origin in 94 %, siblings in 4 % and other relatives in 2 %. Immunosuppression with calcineurin inhibitors given typically for a month. Median CD34 cell dose was 15.4 X 10^6 cells/kg, TCRαβ dose, 0.02 x 10^6 cells/kg, and TCRγδ dose, 10.55 x 10^6 cells/kg.
Transplant outcomes: Median time to both neutrophil and platelet engraftment was 11 days. Graft failure occurred in 31 (7.8%) patients, primary in 24, secondary in 7. Six percent of benign transplants had graft failure. Incidence of acute grade III –IV was 5.5% with 5.1% in benign and 7.7% in malignant transplants. The incidence of any chronic GVHD was 16.8 %, with severe disease in 2.6%.
The incidence of viral reactivation was 54 %, with clinically significant CMV infection in 40 %, adenoviral infection in 13%, and symptomatic BK viral reactivation in 9 %. Twenty percent had bacterial infection and 3% had probable fungal infection. Eighty patients (20%) died in this cohort. Cause of mortality led with infections in 55% (half of whom had proven bacterial sepsis), graft rejection in 21 % and GvHD in 10%. Cumulative incidence of relapse in malignant transplants was 18.5%.

With a median follow up of 18 months, OS and EFS in benign transplants were 81.2% and 79.1% respectively and in malignant transplants was an OS of 65% and EFS of 48%.

Table 1: Transplant characteristics and patient outcomes	
CHARACTERISTICS OF BENIGN PEDIATRIC TRANSPLANTS	
Indications [N(%)]	
Transfusion dependent hemolytic anemias	**261**
Transfusion dependent thalassemia	253
Sickle cell anemia	5
Congenital dyserythropoietic anemia type II	1
Unstable hemoglobin disease	2
Inborn errors of immunity	**26**
Chronic granulomatous disease	5
Congenital neutropenia	2
Severe combined immunodeficiency	2
Primary or secondary HLH	8
Wiskott – Aldrich syndrome	2
Leukocyte adhesion deficiency	Type 1 (3), type 3(1)
Others –	IL-10 related VEO-IBD (1), CVID (1), MSMD (1)
Inherited bone marrow failure syndromes	**12**
Fanconi anemia	9
Others	Dyskeratosis congenita (1), CAMT(1), DBA (1)
Metabolic disorders	**32**
Mucopolysaccharidoses	19 (Type I- 5, II-6,IV- 4, VI-4)
Malignant osteopetrosis	6
X- linked adrenoleukodystrophy	4 Neiman Pick type A (1), type C (1), alpha mannosidosis (1)
Others –	
Other miscellaneous benign indications	Severe aplastic anemia (1)
Conditioning [N(%)]	Myeloablative 235 (71%) Reduced toxicity 86(26%), Reduced intensity (3%)
Graft rejection [N(%)]	24 (7.2%) Primary 18 (5.4%), secondary 6 (1.8%)
Mixed chimerism (n=298)	23 (7.7%)
Veno-occlusive disease (VOD) [N(%)]	71 (21.4%), Severe/very severe VOD 25 (7.5%)
Infections[N(%)]	
Clinically significant CMV infection	127 (38.3%)
Any viral reactivation	176 (53%)
Any infections (bacterial/fungal/viral)	211 (63.5%)

Table 1: Transplant characteristics and patient outcomes	
Acute GvHD [N (%)] Grade II- IV Grade III-IV	 70 (21%) 17 (5.1%)
Chronic GvHD [N (%)] (n=290) Mild Moderate Severe	17.5% 14.1% 1% 2.4%
Transplant related mortality (TRM) Cause of TRM	59 (17.8%), Early – 36 , Late - 23 Infections – 39, Rejection – 12, GvHD – 4, Others – severe VOD -4
MALIGNANT TRANSPLANTS	
Indications Acute lymphoblastic leukemia Acute myeloid leukemia Juvenile myelomonocytic leukemia Others	 43 CR1 (11), CR2 (29), >CR2 (1), post CART (2) 14 , High risk (8), relapsed (6) 3 Chronic myeloid leukemia(2), R/R Hodgkin lymphoma (2), Mixed phenotype Acute leukemia (1)
Conditioning	41 (Myeloablative – TBI based) 24 (MAC – chemotherapy based)
Graft rejection [N(%)]	7 (10.8%), Primary 6 (9.3%), secondary (1.5%)
Veno-occlusive disease (VOD) [N(%)]	5 (7.6%), Severe/very severe VOD 3 (4.6%)
Infections[N(%)] Clinically significant CMV infection Any viral reactivation Any infections (bacterial/fungal/viral)	 32 (49%) 39 (60%) 42 (63%)
Acute GvHD [N (%)] Grade II- IV Grade III-IV **Chronic GvHD [N (%)] (n=49)** Mild Severe	 17 (26%) 5 (7.6%) 6 (12.2%), 4 (8.2%) 2 (4%)
Transplant related mortality (TRM) Cause of TRM	21 (32.3%), Early – 13, Late - 8 Infections – 5, Rejection – 5, GvHD – 4, relapse – 4, Others – 3

Table 1: Transplant characteristics and patient outcomes	
IL-10 related VEO-IBD: IL-10 related very early onset inflammatory bowel disease, CVID: combined variable immunodeficiency, MSMD: mendelian susceptibility to mycobacterial diseases, CAMT: congenital megakaryocytic thrombocytopenia, DBA : diamond blackfan anemia, R/R: Relapsed/refractory	



Conclusions: TCRαβ depleted Haplo-HSCT is a curative option for various transplant indication in pediatric patients with low incidence of GvHD, graft failure and early engraftment. Viral reactivation and infectious complications remain a concern. Affordable antiviral prophylaxis and virus-specific cytotoxic T-lymphocytes will improve early-TRM.

Clinical Trial Registry: None.

Disclosure: None.

OS18-06

IMMUNE CELL THERAPY AFTER TCRAB$^+$/CD19$^+$-DEPLETED HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN RELAPSED HIGH-RISK NEUROBLASTOMA: A PHASE 2 SINGLE-CENTER STUDY

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Background: Despite recent advances in immunotherapies in neuroblastoma(NB), the prognosis of relapsed high-risk(HR) patients remains dismal, with historical 5-year survival rates below 20%.
Recently, treatment of relapsed patients with a combination of chemotherapy and dinuximab-β immunotherapy has proven effective in inducing high response rates; however, these responses tend to wane over time, pointing the need for effective consolidation therapies to enhance immunological control of the disease.
At IRCCS Gaslini, a prospective, single-center phase 2 clinical trial with immune-Cell therapy is ongoing in this patient population, aiming to report the feasibility and activity of the proposed approach.

Methods: Eligible patients included those with relapsed HR-NB achieving at least stable disease per INRC criteria and having an available haploidentical parental donor suitable for peripheral blood stem cell harvest. Among parental donors, selection followed an algorithm that integrated the donor's KIR phenotype, NK alloreactivity, the percentage of circulating donor-derived NK cells, and their in-vitro degranulation and cytotoxicity against NB cell lines, both alone and in the presence of anti-GD2 mAb. The treatment protocol consists of a sequential approach involving TCRαβ$^+$/CD19$^+$-depleted haploidentical hematopoietic stem cell transplantation (haplo-HSCT), followed by five courses of post-transplant immunotherapy with dinutuximab beta. Starting from the second course, donor-derived natural killer cell

infusions(NKIs) are administered prior to each cycle (Table 1).

Table 1	
Inclusion criteria	1. Relapsed neuroblastoma after first-line therapy; 2. Disease response ≥ stable disease (according to INRC criteri 3. Age between 0 and 25 years; 4. Availability of a haploidentical family donor eligible for PBS
Donor selection and management	- KIR phenotyping, NK alloreactivity assessment, percentage c vitro degranulatiobn and cytotoxicity in the presence of anti-C - One (or two) lymphocytoapheresis sessions for NK cell manu - G-CSF–mobilized PBSC collection.
Haploidentical HSCT	**Conditioning regimen:** Thiotepa, Fludarabine, Melphalar **In vivo T/B-cell depletion:** ATG, Rituximab. **Graft manipulation:** Negative selection of TCRαβ⁺/CD
ImmunoCell therapy	**Dinutuximab beta:** 5 courses from day +35, every 35 days, 1 **NK cell infusions (NKI):** from the 2nd to the 5th course, cell d
Disease Response Evaluation Schedule	1st: after haplo-HSCT and the first 2 courses of immunotherap 2nd: after the 5th course of immunotherapy 3rd: every 3 months during the first year afetr haploHSCT 4th: every 6 months from the second year after haploHSCT
Immunomonitoring	- Immunophenotyping of circulating immune cells. - Cytokine profiling during immunotherapy. - In vitro evaluation of NK cell functional activity.

Results: As of this report, eight patients have undergone haplo-HSCT. Cellular product manufacturing (TCRαβ⁺/CD19⁺-depleted grafts;NK cells) was successful in all cases, meeting

predefined release criteria. Engraftment was achieved in 7/8 patients, with full donor chimerism. One patient experienced primary graft rejection and was excluded from the protocol. No grade >2 acute or chronic graft-versus-host disease (GvHD) was observed. Among the seven engrafted patients, six have completed the post-transplant immunoCell therapy program, and one is about to begin it. A total of 24 immunotherapy courses were administered post-transplant so far, 17 of which included NKIs, and 12 were completed via home care. Twenty-nine adverse events were reported, all graded <3 (mild to moderate, CTCAE v5.0).
At the end of the treatment, all patients achieved a complete disease response (INRC). Among the six patients with at least 1 year of follow-up, five are alive at a median follow-up of 2.1 years (0.99–2.7) (OS 83%). Two patients are disease-free at 1 and 2.7 years after haplo-HSCT, respectively; two experienced local relapse at 10 and 11 months after haplo-HSCT and started local radiotherapy plus temozolomide, which is ongoing; and one patient developed a local relapse 13 months after haplo-HSCT and achieved a second complete remission following local radiotherapy, topotecan, and consolidation with anti-GD2 CAR-T therapy, remaining stable 14 months after relapse. Only one patient died due to disease progression, 5 months after a metastatic relapse that occurred 20 months post–haplo-HSCT.

Conclusions: Preliminary data demonstrate the feasibility and safety of haplo-HSCT followed by immunotherapy with dinutuximab beta and NK cell infusions in relapsed HR neuroblastoma. This approach shows promise for improving immune control of disease. Long-term efficacy will be assessed with a larger cohort and extended follow-up.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

OS21-01

HAPLOIDENTICAL STEM CELL TRANSPLANT WITH TCR-ALPHA/BETA DEPLETION IN TRANSFUSION DEPENDENT THALASSEMIA POST PRE TRANSPLANT IMMUNOSUPPRESSION

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Background: Haploidentical hematopoietic stem cell transplantation (Haplo-HSCT) is an option for treating patients of transfusion-dependent thalassemia (TDT) who lack a full-matched donor. Ex-vivo T-cell depletion of graft-versus-host disease (GvHD) causing subsets-TCR αβ and adoptive transfer with memory (CD45RO) cells have significantly improved the outcomes of haploidentical HSCT.

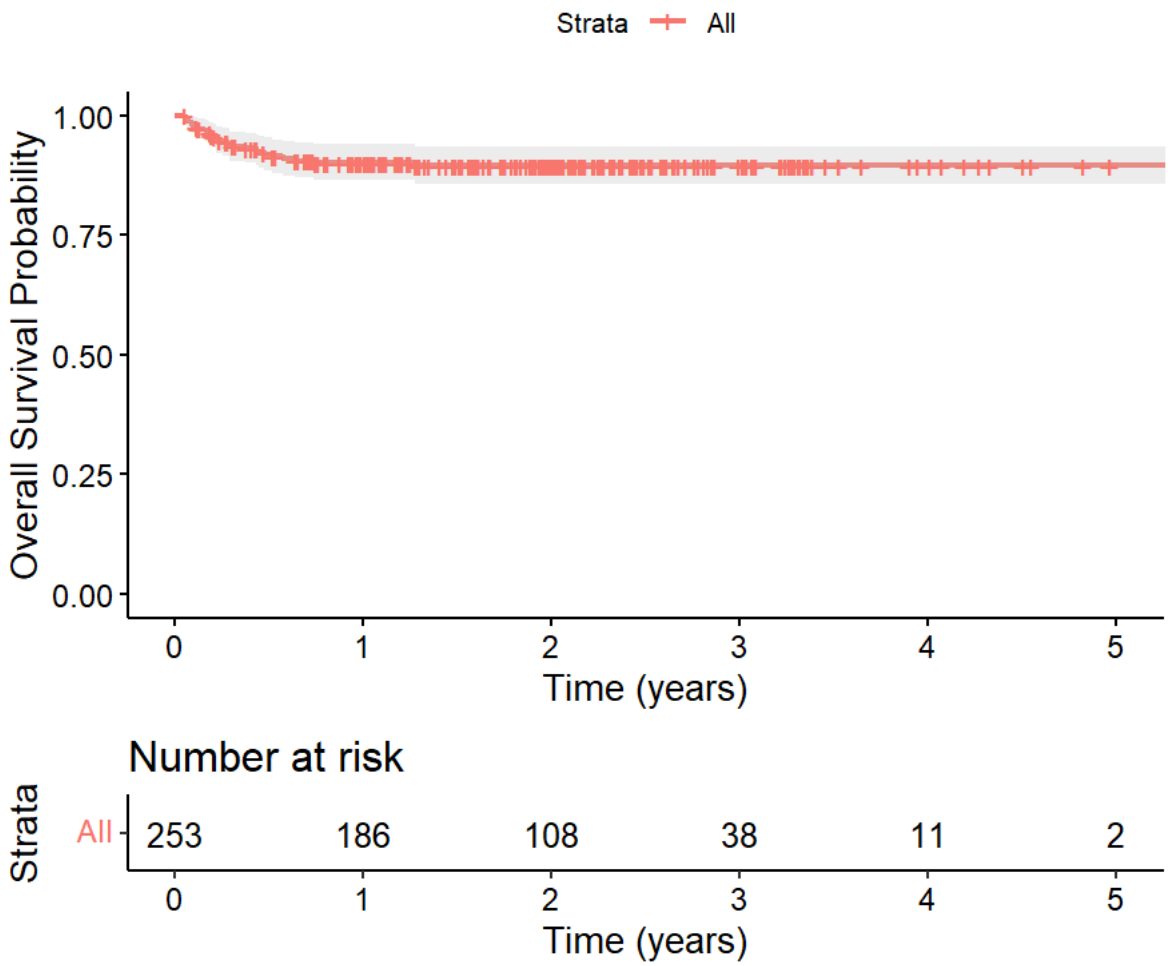
Methods: We prospectively followed up 253 pediatric patients of TDT who underwent TCR αβ depleted haplo-HSCTs from January 2013 to September 2025. The stem cell product underwent ex-vivo manipulation with depletion of CD19 (n=13) or CD45RA (n=240) along

with TCR αβ depletion. Patients with CD45RA depletion were given sequential donor lymphocyte infusion (DLI) of CD45RO cells post–transplant.

Results: Cohort characteristics: Two hundred fifty – three patients with median age of 6.5 (IQR 4.08-10.25) years, 59% males and 41% females. Thirty-four (13.5%) patients were categorized as Pesaro Class I, 150 (59.2%) to class II, and 69 (27.3%) to Class III. Ninety-six percent were CMV serostatus positive. Only 5% of transplants were CMV serostatus mismatched.
Transplant procedure: All patients received pretransplant immunosuppression with 3 cycles of Cyclophosphamide, Fludarabine and Dexamethasone. Myeloablative conditioning with Fludarabine, Busulfan and Cyclophosphamide was used in 195 patients. 58 patients received reduced toxicity- conditioning with Treosulfan. Total body irradiation (TBI) of 2 Gy employed in children older than 3 years (n=164). ATG was used as a strategy to minimize graft rejection and GvHD in younger children, and in Pesaro Class III (n=89). T haplo-HSCT grafts were of parental origin in 93%, siblings in 5% and other relatives in 2%.
Immunosuppression with calcineurin inhibitors given typically for a month.
Transplant characteristics: Median CD34 cell dose was 15.3 X 10^{6} cells/kg. Median time for both neutrophil and platelet engraftment was 11 days. Graft failure occurred in 15 (5.9 %). Incidence of veno-occlusive disease was 29% in Busulfan group and only 7% in Treosulfan ($p < 0.001$).
The incidence of viral reactivation was 50.2%, with clinically significant CMV infection in 34%, adenoviral infection in 12%, and symptomatic BK viral reactivation in 11%. Nineteen percent had proven bacterial infection and 4% had proven or probable fungal infection. Use of ATG was not significantly associated with any infection or viral reactivation.
Acute GVHD grade II- IV in 23.7%, grade III –IV in 5.1 %. The incidence of any chronic GVHD was 18.6%, of which 2.2% was severe.
Twenty-five patients died, with 15 early transplant-related mortality. Infections remained the biggest killer (56%, with bacterial sepsis in three-fourth), followed by graft rejection (24%), severe VOD (16%) and GvHD (4%). With a median follow-up of 22 months the overall survival (OS) at 3 years was 89% and thalassemia-free survival (TFS) at 3 years was 86 %. TFS was 94%, 86%, and 84% in Pesaro Class I, Class II and Class III (p=0.38).

Table 1: Transplant and outcome characteristics		
Characteristics	Descriptive statistics	P value
Donor [N (%)] Male Female	 193 (76%) 60 (24%)	
Median CD34 [median (IQR)]	15.3 x 106 cells/kg (12.12 - 19.45)	
TCR AB dose [median (IQR)]	0.02 x 106 cells/kg (0.01 – 0.04)	
TCR gamma-delta dose [median (IQR)]	9.8 x 106 cells/kg (5.38 – 18.8)	

Table 1: Transplant and outcome characteristics		
Conditioning regimen [N (%)] Busulfan Treosulfan	 195 (77%) 58 (23%)	
Median days to neutrophil engraftment [median (IQR)]	11 (10-12 days)	
Median days to platelet engraftment [median (IQR)]	11 (10 –13 days)	
Rejection [N (%)] Primary Secondary	15 (5.9%) 11 (4.3%) 4 (1.6%)	
Mixed chimerism [N (%)] Busulfan group Treosulfan group	18 out of 232 assessed (7.8%) 17 /169 (10%) 1/51 (2%)	 0.08
Use of ATG [N (%)] Yes No Any infection (ATG vs. No ATG) Viral reactivation (ATG vs. No ATG)	 89 (35%) 164 (65%) 62.1% vs. 57.1% 58.4% vs 46%	 0.36 0.06
Chronic GvHD [N (%)] Mild Moderate Severe	43 out of 231 assessed (18.6%) 36 (15.6%) 2 (0.8%) 5 (2.2%)	



Conclusions: TCR-αβ depleted haplo-HSCTs offer an excellent curative option for TDT patients with acceptable survival and low rates of graft failure and GvHD. CD45RO DLIs are an effective strategy to enhance immune reconstitution and combat the expected viral reactivation in T-cell depleted haplo-HSCT.

Clinical Trial Registry: None.

Disclosure: None.

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Paed3-01

COMPARATIVE OUTCOMES AFTER SEROTHERAPY WITH ATLG-GRAFALON OR ATG-THYMOGLOBULIN IN PEDIATRIC ALL PATIENTS GIVEN MUD ALLOGENEIC HSCT: FINDINGS FROM THE INTERNATIONAL PROSPECTIVE FORUM STUDY

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Background: Serotherapy with anti-T lymphocyte globulins (ATG) is used to prevent severe acute and chronic GVHD and rejection after unrelated-donor HSCT. The two main ATGs – ATLG-Grafalon® (Neovii) and ATG-Thymoglobulin® (Sanofi) – are polyclonal antibodies generated by immunizing rabbits with Jurkat T-cells or human thymocytes, respectively. Both are lymphodepleting yet differ in antibody quantity, antigen recognition, and effects on lymphocyte subsets. This study compares outcomes of children with ALL who received Grafalon or Thymoglobulin before matched-unrelated-donor (MUD) HSCT in the prospective international ALL SCTped 2012 FORUM1 trial.

Methods: Patients were transplanted from a 9/10 or 10/10 MUD and received serotherapy with either Grafalon (45 mg/kg total) or Thymoglobulin (7.5 mg/kg total) from d-3 to d-1. Patients ≥4 years were conditioned with either total-body irradiation (TBI 12Gy and etoposide, cohort1) or chemo-conditioning with either busulfan or treosulfan combined with thiotepa and fludarabine (cohort2). All patients <4 years received chemo-conditioning (cohort3).

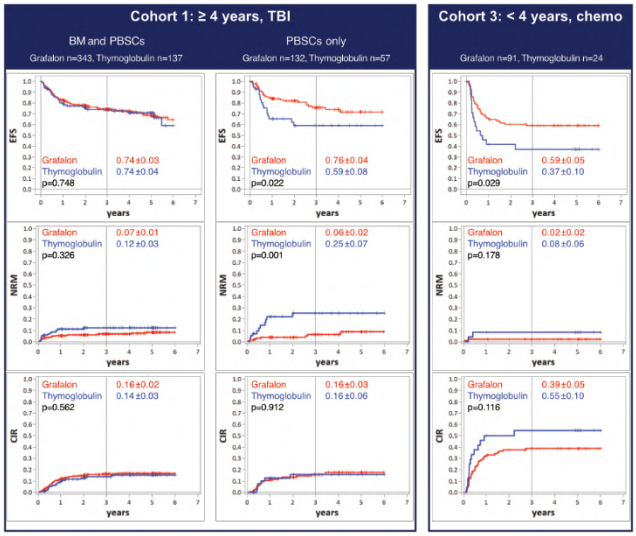
Results: Within each cohort, Grafalon and Thymoglobulin groups were evenly matched in disease and transplant characteristics.
In cohort1 (≥4y TBI) we observed similar 3-year overall (OS) and event-free survival (EFS) of 84% vs 78% and 74% vs 74% with Grafalon (n=343) and Thymoglobulin (n=137), respectively. 3-year incidence of relapse (CIR) was comparable (16% vs 14%), as was non-relapse mortality (NRM) (7% vs 12%). After Grafalon, there was a trend toward faster lymphocyte recovery at day 28, while platelet engraftment was delayed (p<0.0001). 100-day cumulative incidence of CMV and EBV infection/disease was lower after Grafalon (26% vs 46%, p<0.001). We observed no difference in grade ≥2 acute GVHD at day 100 (28% vs 34%), but a lower 3-year incidence of any chronic GVHD after Grafalon (8% vs 16%, p=0.015). Although outcomes were comparable for bone-marrow grafts, substantial differences were seen with PBSCs (n=189): 3-year NRM was lower after Grafalon (6% vs 25%, p=0.001) with similar CIR, resulting in a higher 3-year OS (85% vs 66%, p=0.012) and EFS (76% vs. 59%, p=0.022)
In cohort2 (≥4y chemo-conditioning) no significant differences were seen between the two serotherapies (n=139 vs n=48) regarding OS, EFS, CIR or NRM, as well as engraftment, GVHD and infection.
In cohort3 (<4y chemo-conditioning, n=91 vs n=24) we observed higher 3-year EFS (59% vs 37%, p=0.029) and a trend towards higher 3-year OS (76% vs 60%) after Grafalon. Comparable, high rates of relapse (39% vs 55%) and low NRM (2% vs 8%) were seen in both groups. No difference was observed in rates of engraftment, GVHD, or infection.

	Cohort 1 **≥ 4 years, TBI conditioning** TBI 12Gy & etoposide					**Cohort 2** **≥ 4 years, chemo-conditioning** fludarabin, thiotepa, busulfan or treosulfan					**Cohort 3** **< 4 years, chemo-conditioning** fludarabin, thiotepa, busulfan or treosulfan				
	Grafalon		**Thymo**			**Grafalon**		**Thymo**			**Grafalon**		**Thymo**		
	n	%	n	%	p-value	n	%	n	%	p-value	n	%	n	%	p-value
All	343		137			139		48			91		24		
Sex male female	226 117	66% 34%	86 51	63% 37%	0.336	84 55	60% 40%	31 17	65% 35%	0.864	47 44	52% 48%	9 15	38% 63%	0.357
Immunephenotype BCP	239	71%	111	81%	0.184	99	71%	34	71%	0.871	68	76%	21	88%	0.508

T-ALL other	78 21	23 % 6%	22 4	16 % 3%		35 5	25 % 4%	12 2	25 % 4%		17 5	19 % 5%	3 0	13 % 0%	
Stem-cell source BM PBSC	21 1 13 2	62 % 38 %	80 57	58 % 42 %	0.582	94 45	68 % 32 %	35 13	73 % 27 %	0.405	63 28	69 % 31 %	1 9 5	79 % 21 %	0.191
Remission CR1 CR2 CR3 > CR3	15 3 16 1 23 4	45 % 47 % 7% 1%	57 60 16 1	43 % 45 % 12 % 1%	0.381	73 53 12 1	53 % 38 % 9% 1%	2 2 2 4 2 0	46 % 50 % 4% 0%	0.319	75 16 0 0	82 % 18 % 0% 0%	1 7 7 0 0	71 % 29 % 0% 0%	0.337
pre-transplant MRD < 10^{-4} > 10^{-4}	22 7 48	83 % 17 %	73 23	76 % 24 %	0.373	68 % 29 %	70 % 30 %	3 5 9	80 % 20 %	0.490	45 22	67 % 33 %	1 4 9	61 % 39 %	0.859
HLA match 9/10 10/10	88 18 5	32 % 68 %	43 65	40 % 60 %	0.297	32 89	26 % 74 %	1 3 3 4	28 % 72 %	0.754	29 45	39 % 61 %	8 1 4	36 % 64 %	0.286
CMV donor/patient neg/neg neg/pos pos/neg pos/pos	94 82 35 12 5	28 % 24 % 10 % 37 %	36 38 13 56	27 % 21 % 10 % 42 %	0.766	35 32 22 47	26 % 24 % 16 % 35 %	2 0 9 4 1 5	42 % 19 % 8% 31 %	0.239	33 13 13 29	38 % 15 % 15 % 33 %	3 8 2 1 0	13 % 35 % 9% 43 %	0.170
EBV donor/patient neg/neg neg/pos	24 33 42	7% 10 % 13	6 9 16 81	5% 7% 12 %	0.681	7 11 19 67	5% 8% 14 %	3 3 8	6% 6% 17 %	0.934	6 11 11 42	7% 13 % 13	2 1 4	9% 4% 17 %	0.567

pos/neg pos/pos	19 1	% 57 %		61 %			49 %	3 3	69 %			% 48 %	1 4	61 %	

Conclusions: In patients ≥4y who received TBI-based conditioning – current standard of care – outcomes were excellent following either serotherapy. Differences emerged only for PBSC grafts, where Thymoglobulin was associated with higher NRM and lower OS and EFS. Among patients >4y conditioned with chemotherapy, outcomes did not differ by serotherapy. In patients <4y – characterized by higher risk of relapse – we observed higher EFS after Grafalon. Taken together, our data suggest that Grafalon may be preferable in those ALL patients at higher risk of NRM (PBSC transplant recipients ≥4y) or relapse (children <4y).



Clinical Trial Registry: https://clinicaltrials.gov/study/NCT01949129
NCT01949129

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Tayfun Güngör: Novartis, MSD, Neovii, Jazz, Vertex
Marianne Ifversen: Novartis, Vertex
Franco Locatelli: speakers bureau: Miltenyi, Amgen, Novartis, BMS, Medac, GILEAD, SOBI; advisory board: Amgen, Novartis, Sanofi, Vertex
Christina Peters: Amgen, Jazz, Novartis, Medac, Neovii, Pfizer, Vertex
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Cécile Pochon: Amgen, Gilead, Medac, Servier, Jazz Pharmaceuticals, Novartis, Neovii, Pierre Fabre
All other authors declare no conflict of interest.

Paed3-02

HIGH INCIDENCE OF RELAPSE AFTER HAEMATOPOIETIC STEM CELL TRANSPLANTATION CONFERS A POOR PROGNOSIS IN PAEDIATRIC GLIS2+ AML- AN EBMT PAEDIATRIC DISEASES WORKING PARTY STUDY

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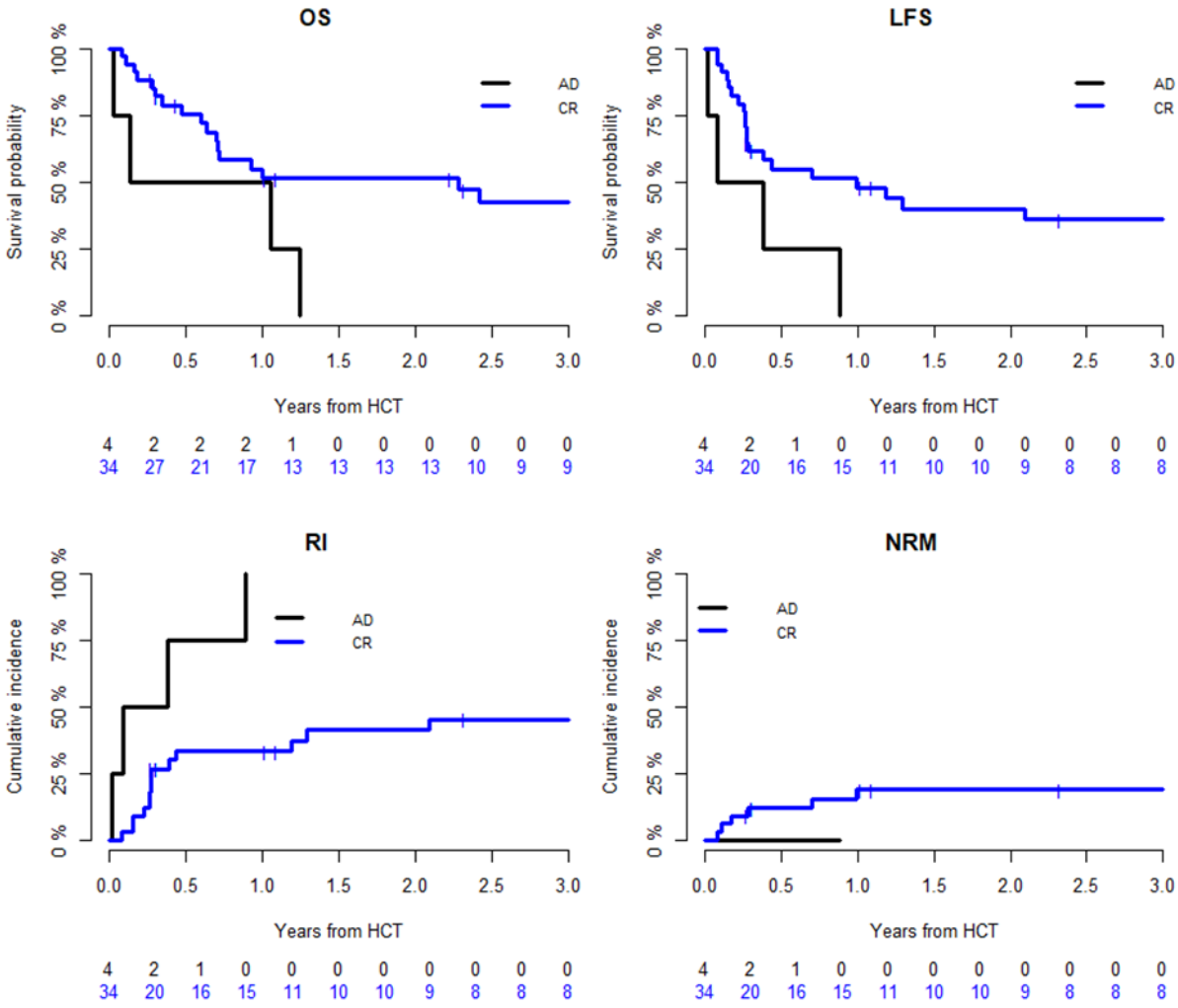
Background: The *CBFA2T3–GLIS2* fusion gene characterizes a paediatric-specific subtype of AML occurring in infants, toddlers and very young children. It is the most frequent chimeric oncogene identified in non–Down syndrome acute megakaryocytic leukaemia and is associated with an extremely poor clinical outcome.

Methods: In this retrospective study, we analyzed outcomes of children undergoing allogeneic haematopoietic stem cell transplantation (alloHSCT) for GLIS2+ AML between

2013 and 2024 at EBMT centres. The primary objectives were to assess overall survival (OS) and leukaemia-free survival (LFS).

Results: Thirty-eight patients (20 female,18male) were included. The majority (30/38, 78.9%) were under 3 years of age at presentation. Isolated bone marrow disease was the most common presentation (20/29, 69%; data missing for 9 patients). Median age at alloHSCT was 1.8 years (range 0.7–17.5). Thirty-two patients (84%) underwent transplantation in CR1, two in CR2, and four had active disease at alloHSCT. Among patients in CR, MRD was negative in 19/22 (data missing for 12).
All patients received myeloablative conditioning, predominantly Busulfan-based regimens (31/38, 81.6%). Serotherapy with ATG was given in 21 patients, while 17 received none. Most children received ciclosporin (± MMF/MTX) as GVHD prophylaxis. Donors included matched and mismatched unrelated donors (29/38, 76%), matched related donors (3/38, 8%), and HLA haploidentical family donors (6/38, 16%). Cord blood was the predominant stem cell source (16/37, 43%; one missing), followed by bone marrow (14/37, 38%) and peripheral blood (7/37, 19%).
At a median follow-up of 3.2 years (95% CI 2.2–4.7), the 2-year probability of OS and LFS was 44.9% (27.7–60.7) and 35.2% (19.7–51.2) respectively. All 4 patients transplanted with active disease relapsed and died. Relapse was the major cause of treatment failure (48.1%, 30.2–63.9). The day-100 incidence of grade II–IV and grade III–IV acute GVHD was 41.2% and 17.6%, respectively. The 2-year incidence of chronic GVHD was 11.6% (2.6-28). Non-relapse mortality at 2 years was 16.7%. The 2-year cumulative incidence of second alloHSCT was 13% (3.9–27.8).

Overall Survival, Leukaemia Free Survival and Relapse Incidence



Conclusions: In the largest cohort to date of children with GLIS2+ AML undergoing alloHSCT, outcomes are confirmed to be poor, with relapse being the predominant cause of treatment failure. This occurred despite most patients being in CR at transplantation and despite a high incidence of significant GVHD. These findings highlight an urgent need for targeted post-transplant therapies, such as the anti–folate receptor-α antibody–drug conjugate luveltamab tazevibulin (STRO-002) or CAR-T cells targeted against this target, in this high-risk group.

Clinical Trial Registry: Not applicable

Disclosure: Herbert Pichler- Travel grants from Jazz Pharmaceuticals

Paed3-03

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REGISTRY-BASED, PAIR-MATCHED ANALYSIS COMPARING A/B T-/CD19-CELL DEPLETION AND POST-TRANSPLANT CYCLOPHOSPHAMIDE IN HLA-HAPLOIDENTICAL HSCT FOR CHILDREN WITH ACUTE LEUKEMIA: AN EBMT PDWP STUDY

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Background: TCRαβ/CD19-cell depletion (TCRαβ-depl) and post-transplant cyclophosphamide (PT-Cy) are the two most used platforms for haploHSCT in children. Despite their wide use, however, neither direct prospective comparison, nor retrospective analysis is available for children affected by acute leukemia (AL). The EBMT-PDWP conducted a registry study to compare the outcomes of patients given either of these two approaches.

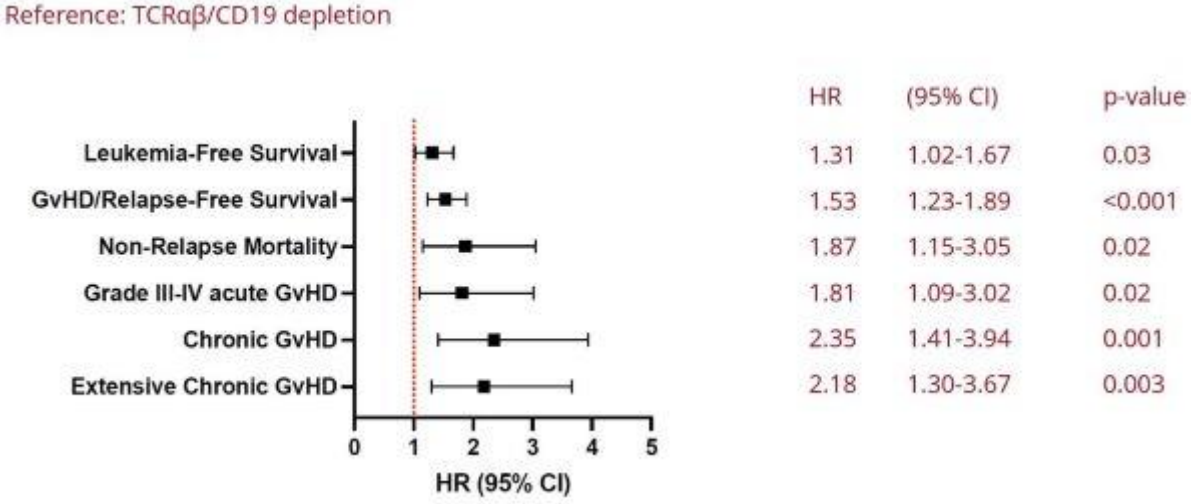
Methods: All patients affected by AML or ALL, transplanted from an HLA-haploidentical donor with either of the 2 techniques between 2010 and 2022 and registered in the EBMT database were considered. Among more than 1000 patients, a 1:1 matched-pair analysis was performed, using type of disease (AML or ALL) and disease status (complete remission, CR, or non-CR) for exact matching, and patient age and sex, disease risk index (DRI), Lansky score, donor sex, and use of total body irradiation (TBI) in the conditioning regimen for propensity score matching (caliper set=0.2). The impact of the two approaches was estimated using a Cox model with a cluster effect on matching subgroups.

Results: The final cohort was composed of 506 patients (253 patients per group), the median year of HSCT being 2019 (range, January 2010-December 2022); median age at HSCT was 8.4 years (range, 0.4-18). Details on patients and transplant characteristics are

reported in Table 1. Because of the difference in the 2 approaches, as expected, PT-Cy patients received a significantly lower number of $CD34^+$ cells/kg and more $CD3^+$cells/kg. All other transplant variables were comparable between the 2 groups, except for a slightly younger donor age.The median follow-up for surviving patients was 4.4 years. Projected 4-yr relapse incidence and non-relapse mortality (NRM) were 37.1% and 13.4%, respectively. Regarding acute graft-versus-host disease (GVHD), the overall cumulative incidence of grade III-IV GVHD and extensive chronic GVHD were 10.1% and 14.6%; in the TCRαβ-depl group, the cumulative incidence of grade III-IV acute GVHD and extensive chronic GVHD were 7.2% and 10%, respectively, while in children receiving PT-Cy they were 13.1% and 19.5%. The 4-yr overall survival (OS) and leukemia-free survival (LFS) for the TCRαβ-depl and PT-Cy group were 58.5% versus 52.8%, and 54.4% versus 44.8%, respectively. The GVHD/relapse-free survival (GRFS) in the 2 groups were 46.7% for TCRαβ-depl and 30.8% for PT-Cy, respectively. The Cox model (Figure 1) showed that, using TCRαβ- depl as reference population, patients receiving PT-Cy had higher NRM, grade III-IV acute GVHD, chronic GVHD and extensive chronic GVHD, as well as worse LFS and GRFS. In particular, PT-Cy recipients had a higher incidence of death due to GvHD, infections and graft failure.

	Pair-match cohort n=506	TCRαβ-HSCT n=253	PTCY-HSCT n=253	*P-value*
Median age at HSCT (range), y	8.4 (0.4-18)	8.2 (0.4-17.8)	8.6 (0.5-18)	*pair-match factor*
Diagnosis, n (%) ALL AML	278 (54.9) 228 (45.1)	139 (54.9) 114 (45.1)	139 (54.9) 114 (45.1)	*pair-match factor*
Disease status at HSCT, n (%) CR1 CR2 Other CR Active disease	206 (40.7) 180 (35.6) 38 (7.5) 82 (16.2)	104 (41.1) 91 (36) 17 (6.7) 41 (16.2)	102 (40.3) 89 (35.2) 21 (8.3) 41 (16.2)	*n.t.*
Stem cell source, n (%) BM PB	207 (40.9) 299 (59.1)	5 (2) 248 (98)	202 (79.8) 51 (20.2)	*<0.001*
Median infused nucleated cells (range) $x10^8$/Kg	8.2 (0-1119)	8.2 (0-73.8)	8.2(0-1119)	*0.59*
Median infused $CD34^+$ cells (range) $x10^6$/Kg	8.7 (0-4016)	11.4 (2-4016)	5.8 (0-77)	*<0.001*

Use of TBI in conditioning regimen, n (%) No Yes	338 (66.8) 168 (33.2)	164 (64.8) 89 (35.2)	174 (68.8) 79 (31.2)	*pair-match factor*
Additional GvHD prophylaxis, n (%) No Yes	164 (32.4) 342 (67.6)	162 (64) 91 (36)	2 (0.8) 251 (99.2)	*n.t.*
Median donor age (range), years	37.0 (5.7-59.3)	38.2 (6.7-59.3)	36 (5.7-55.5)	*<0.001*
Median year of HSCT (range)	2019 (2010-2022)	2019 (2010-2022)	2018 (2010-2022)	*Pair-match factor*



Conclusions: This large retrospective, registry-based study shows that both platforms are a suitable option for children with AL needing HSCT and lacking a suitable HLA-matched donor or with an urgent transplant indication. Notably, the TCRαβ-depl platform is characterized by lower incidence of severe acute and chronic GVHD, lower risk of NRM and better LFS and GRFS as compared to PT-Cy. Pharmacoeconomic studies are needed to further elucidate the differences between the two platforms in children with AL.

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Marta Gonzalez-Vincent: reports personal fees (Consultancy) from SANOFI
Gaurav Kharya: reports personal fees (Consultancy) from Cellogen Therapeutics
Selim Corbacioglu: reports personal fees (Consultancy) from Vertex Pharmaceuticals
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Paed3-05

IMPROVED ENGRAFTMENT FOLLOWING A TREOSULFAN-FLUDARABINE CONDITIONING REGIMEN COMPARED TO THIOTEPA-FLUDARABINE IN PATIENTS WITH REFRACTORY CYTOPENIA OF CHILDHOOD

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Background: Refractory cytopenia of childhood (RCC) is a well-defined subgroup of pediatric bone marrow (BM) failure, characterized by persistent peripheral cytopenia, dysplasia, and a distinctive BM histology. It can successfully be treated with hematopoietic stem cell transplantation (HSCT). Following the observation of a high rate of graft-failure (GF) after HSCT with a conditioning regimen consisting of thiotepa (Thio) and fludarabine (Flu), a treosulfan (Treo)-Flu regimen had been introduced in our study group.

Methods: We analyzed 373 patients with RCC and normal karyotype enrolled in EWOG-MDS and transplanted between 2007 and 2024 following conditioning with Thio-Flu (n=239) or Treo-Flu (n=134). Median age was 10.4 years (0.8-22.8), and donors were matched siblings (MSD, n=95), 10/10 HLA-matched unrelated donors (MUD, n=190) or 9/10 HLA-matched unrelated donors (MMUD, n=88). There was no difference in donor distribution in the two groups. The main stem cell source was BM (BM 81% vs peripheral blood (PB) 19%) with a higher use of PB in the Treo-Flu group (Treo-Flu 27% PB vs Thio-Flu 15% PB, p=<0.01). Different types of serotherapy were used in unrelated HSCT (ATG Grafalon 88%, Thymoglobulin 7%, alemtuzumab 5%), and 36% of MSD recipients received ATG (ATG Grafalon 82%, Thymoglobulin 18%).

Results: Five-year overall survival (OS) was 0.94 (0.91-0.97) and 0.96 (0.92-1.00) for the Thio-Flu and Treo-Flu group (p=n.s.), respectively. There were significant differences in the incidence of GF (Thio-Flu 0.17 [0.13-0.23] vs Treo-Flu 0.09 [0.04-0.21], p<0.01) and moderate/severe chronic GvHD (cGVHD) (Thio-Flu 0.16 [0.12-0.22] vs Treo-Flu 0.08 [0.04-0.141], p=0.03) resulting in a better cGvHD-GF-free-survival (cGRFS) in the Treo-Flu group (Thio-Flu 0.74 [0.68-0.80] vs Treo-Flu 0.84 [0.75-0.93], p<0.01). The impact of the conditioning regimen on cGRFS was confirmed in multivariate analysis (Thio-Flu vs Treo-Flu relative risk (RR) 2.04, p< 0.01). Additional factors associated with an inferior cGRFS were the use of a MMUD (9/10) compared to a MUD or MSD (MMUD vs MUD RR 1.76, p=0.03; MSD vs MUD RR 1.07, p=n.s.) and a CMV positive recipient (CMV pos vs. CMV neg RR 1.64; p=0.04). In MSD-HSCT the addition of ATG to the conditioning did not result in a difference in GF, aGVHD, cGVHD or OS. In contrast, the use of a higher dose of ATG was associated with a higher incidence of GF and cGVHD resulting in a lower cGRFS in patients conditioned with Thio-Flu for unrelated donor HSCT (ATG Grafalon 60 mg/kg vs 45 mg/kg 0.68 [0.58-0.78] vs 0.80 [0.70-0.90], p< 0.01).

Conclusions: Although both regimens offered an excellent OS for patients with RCC, the Treo-Flu regimen resulted in superior engraftment and lower rates of cGVHD. Serotherapy provided no benefit in MSD-HSCT and a higher-dose ATG Grafalon adversely affected outcomes in unrelated HSCT with Thio-Flu likely through impaired immune reconstitution.

Comprehensive evaluation of long-term consequences, including fertility outcomes, is required.

Disclosure: Nothing to declare.

Paed3-06

IMPACT OF EX-VIVO T-CELL DEPLETION IN UNRELATED DONOR HSCT FOR PEDIATRIC MALIGNANT DISEASES: A MULTICENTER RETROSPECTIVE COMPARATIVE STUDY ON BEHALF OF SPANISH GETH-TC PED GROUP

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Background: Ex-vivo selective T-cell depletion (TCD) has emerged as a strategy to reduce graft-versus-host disease (GvHD) while preserving immune recovery. Although widely implemented in haploidentical transplantation, evidence in unrelated donor (URD) pediatric HSCT remains limited.

Methods: We performed a retrospective observational study across GETH-TC pediatric transplant centers including patients transplanted between 2016–2023. Eligible patients had malignant diseases and received a URD HSCT (9/10 or 10/10 HLA match). Two groups were analyzed: ex-vivo TCD (αβ or CD45RA$^+$) versus conventional non-manipulated grafts. Outcomes included engraftment, acute and chronic GvHD, infections, relapse, TRM, overall survival (OS), disease-free survival (DFS), and GvHD-/relapse-free survival (GRFS). Survival was calculated using Kaplan–Meier; cumulative incidences were analyzed in a competing-risk framework using Gray's test; prognostic factors were evaluated with Cox regression.

Results: A total of 96 patients were included: 49 conventional HSCT and 47 TCD (24 αβ; 23 CD45RA$^+$). Baseline characteristics were largely balanced.
Engraftment: TCD significantly accelerated neutrophil and platelet recovery (median 11 vs 20 days and 12 vs 22 days, both p <0.001). Mixed chimerism was more frequent in TCD (34.8% vs 8.5%, p = 0.002).
Acute and chronic GvHD: TCD reduced the incidence of any-grade aGvHD (46.8% vs 77.6%, p = 0.002). Cumulative incidence of grade II–IV aGvHD showed a non-significant trend toward reduction with TCD (12-month: 37% vs 57%, p = 0.068). Chronic GvHD rates were similar between groups (27.7% vs 24.5%, p = 0.72).
Infectious complications: TCD patients had fewer infections between days 101–180 (14.6% vs 35.6%, p=0.026) and beyond day +365 (2.8% vs 29.3%, p = 0.002).

Relapse and TRM: Relapse cumulative incidence was identical in both groups (18% at 48 months, Gray p = 0.9). TRM at 12 months showed no significant differences (14% vs 11%, p = 0.4).
Survival: Overall survival (OS) and disease-free survival (DFS) did not differ significantly between groups. At 48 months, OS was 80% in the TCD cohort and 61% in the conventional cohort, without reaching statistical significance (p = 0.08). DFS showed a similar pattern, with 69% vs 60% survival at 48 months (p = 0.4). GRFS was also comparable between groups (approx. 50% at 48 months, p > 0.9).
In multivariate Cox analysis for DFS, several disease-related factors emerged as independent predictors: T-ALL diagnosis (HR 6.71, p = 0.016) and disease status ≥CR2 showed worse outcomes (CR2: HR 6.48; ≥CR3: HR 5.60; both p = 0.02). Conversely, negative molecular status (HR 0.37, p = 0.022) and RIC conditioning (HR 0.31, p=0.033) were associated with improved DFS.

Conclusions: In this multicenter real-world pediatric cohort, ex-vivo TCD in URD-HSCT was associated with a reduction in early post-transplant complications—particularly acute GvHD and selected infectious events—while maintaining comparable rates of relapse, TRM, OS, DFS and GRFS relative to conventional grafts. These findings support the safety of ex-vivo TCD approach in pediatric malignant indications, although definitive benefits cannot be established from this retrospective cohort.

Disclosure: No conflict of interest to declare

Paed3-07

REAL-WORLD OUTCOMES OF MESENCHYMAL STROMAL CELL THERAPY IN HEAVILY PRE-TREATED PAEDIATRIC PATIENTS WITH REFRACTORY ACUTE GRAFT-VERSUS-HOST DISEASE

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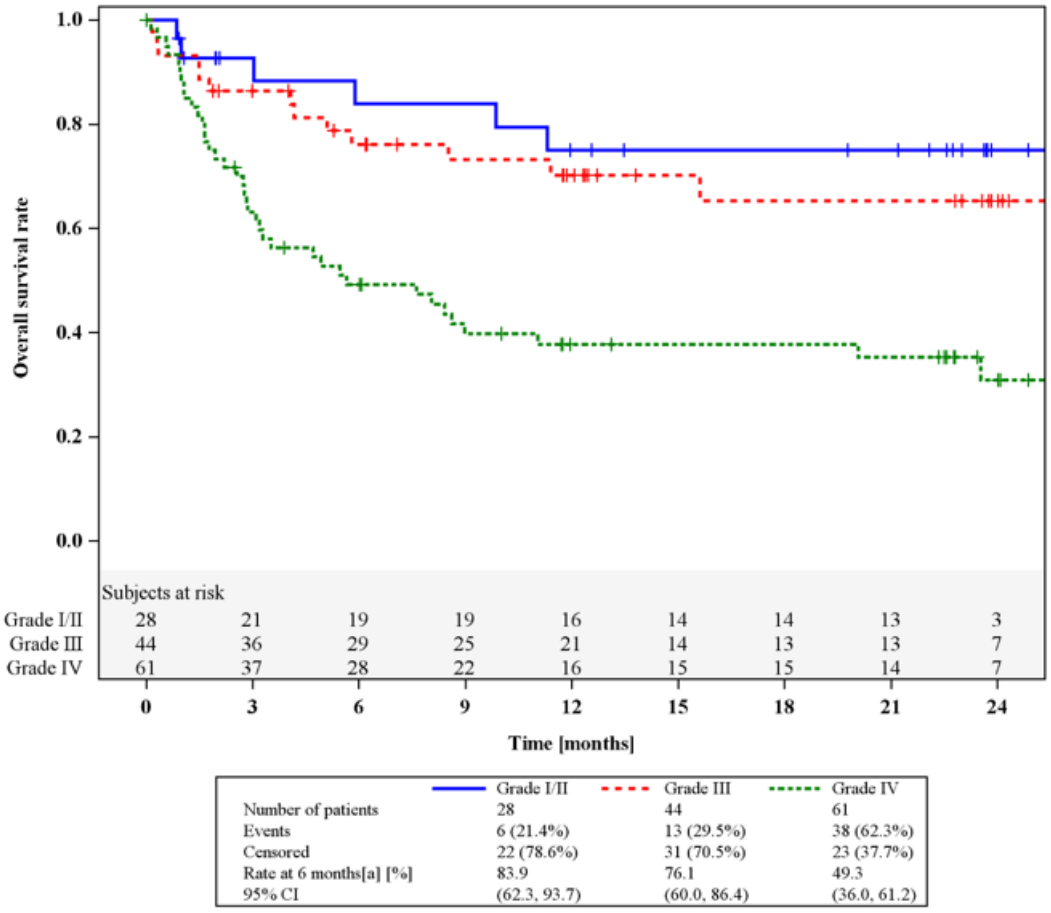
Background: Patients with aGvHD who fail to respond to steroids and/or ruxolitinib face a poor prognosis.

Methods: We conducted a retrospective analysis of real-world data from 140 paediatric aGvHD patients who received the random-donor mesenchymal stromal cell (MSC) preparation MSC-FFM, manufactured from pooled human allogeneic bone marrow-derived mononuclear cells of 8 different donors. The product is distributed via Hospital Exemption in Germany (under the name Obnitix®) and Named Patient Use elsewhere. MSC-FFM is administered as an intravenous infusion; at a recommended dose of 1 to 2 million MSCs/kg BW in 4 once-weekly doses. At baseline, 60.0% had an underlying malignant disease and were severely ill, with 31.4% Grade III and 44.3% with Grade IV aGvHD. Most Grade III/IV cases had lower GI involvement. Patients received a median of 3.5 (maximum: 11) prior lines of therapy; 54.3% were pre-treated with ruxolitinib. The majority (72.9%) received 1 to 2 million MSCs/kg BW and 67.1% received 4 to 6 infusions. Treatment response was assessed at Days 28 and 60.

Results: At Day 28, the overall response rate (OR) was 62.9%, (complete response [CR]: 22.1%, partial response [PR]: 40.7%) with rates of 74.1%, 75.0%, and 53.2% for Grade II, III, and IV aGvHD, respectively. At Day 60 the overall response rate, and in particular CR, improved for all grades to 66.9% (CR: 44.9%, PR: 22.1%). The organ stage in patients with skin, liver, lower gut, and upper gut involvement improved at Day 28 in 69.4%, 57.5%, 58.6%, and 39.5% of the patients, respectively. Response and survival were better in patients with non-malignant disease compared to patients with a malignant disease. Younger patients showed a trend toward better responses and survival. Patients with Grade III and IV, pre-treated with ruxolitinib, had an OR at Day 28 of 63.5% and at Day 60 of 59.7%, and overall survival rates at 6 and 12 months of 61.0% vs 50.3%, respectively.
Overall survival correlated with overall response at Day 28, with 72.9% and 64.2% in responders and 49.1% and 39.7% in non-responders at 6 and 12 months, respectively. Survival probability at 6 months in patients with Grade I/II was 83.9%, Grade III 76.1%, and Grade IV 49.3% (Figure 1).
Four adverse drug reactions were reported in 3 patients (3 serious, 1 non-serious). The good safety profile of MSC-FFM was consistent with prior MSC reports. Most frequently reported causes of death were GvHD (20.9%) and infections (18.4%), with GvHD-related deaths more common in patients pre-treated with ruxolitinib (26.3% vs 14.3%).

Figure 1: → **Kaplan-Meier estimates of overall survival by aGvHD grade prior to first infusion (paediatric aGvHD patients with aGvHD assessment prior to first infusion)**



	Grade I/II	Grade III	Grade IV
Number of patients	28	44	61
Events	6 (21.4%)	13 (29.5%)	38 (62.3%)
Censored	22 (78.6%)	31 (70.5%)	23 (37.7%)
Rate at 6 months[a] [%]	83.9	76.1	49.3
95% CI	(62.3, 93.7)	(60.0, 86.4)	(36.0, 61.2)

[a] based on Kaplan-Meier estimates

Conclusions: Despite limitations of real-world data, MSC-FFM demonstrated good responses with a favourable safety profile in treatment-refractory paediatric aGvHD patients, including those previously exposed to ruxolitinib. Favourable prognostic factors for overall survival are young age, low-grade aGvHD, response at Day 28, and a non-malignant disease. A prospective randomised trial BALDER (NCT06075706) is underway to clarify the efficacy and safety of MSC-FFM in the treatment of steroid-refractory paediatric aGvHD.

Disclosure: Peter Bader receives patent and royalties for MSC-FFM from medac GmbH. Elena Osswald, Michael Tribanek, and Maria Lazarou-Wild are all employees of medac GmbH. The remaining authors declare no conflicts of interest.

Paed3-08

ADAPT TO ENDURE: SUSTAINING PEDIATRIC HCT THROUGH WARTIME DISRUPTION IN UKRAINE

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Background: Healthcare reforms in 2019 expanded hematopoietic cell transplantation (HCT) in Ukraine with the promising growth of transplant activity nationwide. To date, the National Specialized Children's Hospital "Ohmatdyt" (NSCH) remains Ukraine's largest pediatric hematology-oncology (PHO) center, offering comprehensive care with its expert reference laboratory and all types of HCT available. It was the first in Ukraine to perform a matched unrelated donor transplant in a 2-year-old with ADA-deficiency during the COVID-19 pandemic.
The full-scale war in 2022 triggered a humanitarian crisis that severely disrupted the healthcare system, with the PHO sector among the most affected. Evacuation efforts, most notably the St. Jude Global SAFER Ukraine initiative, enabled around 1,400 children to continue care abroad. However, resource constraints, safety concerns, mass migration, and a sharp decline in newly diagnosed cases pushed Ukraine's pediatric HCT program to the verge of collapse.
Here we present the first comprehensive analysis of transplant activity in Ukraine during wartime, focusing on the experience of the largest PHO/HCT facility and highlighting epidemiologic shifts, challenges, and key insights for pediatric transplant centers.

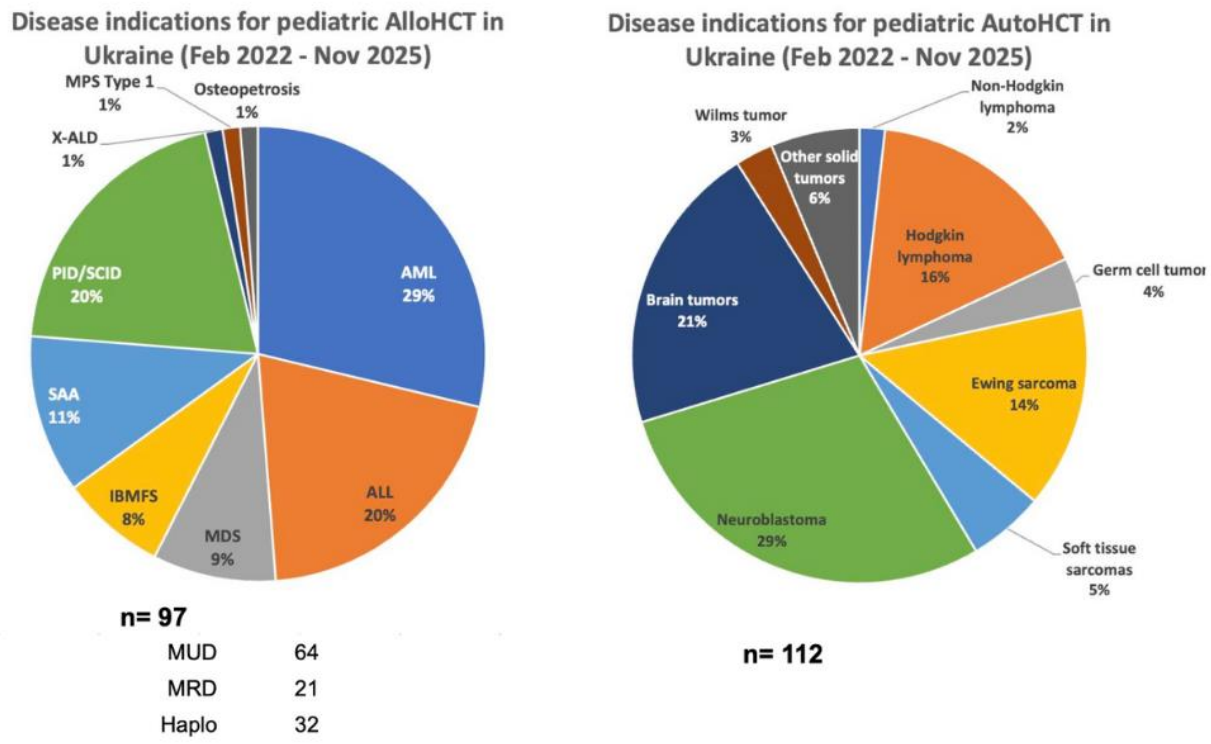
Methods: We retrospectively analyzed national HCT data from February 2022 to November 2025, obtained upon request from the Specialized State Institution 'Ukrainian Transplant Coordination Center' (UTCC), established in mid-2021 to oversee quality control, data collection, and nationwide transplant coordination. UTCC provided annual transplant volumes, the number of operating centers, and HCT distribution by donor type, stratified by pediatric (<18 years) and adult (≥18 years) populations. Data prior to 2022 on pediatric HCT activity were extracted from the internal registry of NSCH's HCT program. All data were analyzed descriptively to evaluate patient demographics and year-by-year trends, with institutional adaptation strategies described in the Results and Summary sections.

Results:

As of December 2025, 13 HCT centers were operating in Ukraine, six of which were formally accredited for transplant activity. Among these, only two performed allogeneic HCT, with NSCH contributing the majority. Expanding transplant eligibility to adult patients allowed more individuals to receive life-saving care while reinforcing NSCH's institutional resilience (see Table 1)

Table 1.				
Year	**Location**	**Total # HCT**	**Total # HCT in children (%)**	**Total # AlloHCT in children (%)**
2022	Ukraine	200	24 (12%)	17
	NSCH	36	17 (47%)	17 (100%)
2023	Ukraine	342	53 (15%)	21
	NSCH	64	32 (50%)	20 (95%)
2024	Ukraine	404	58 (14%)	27
	NSCH	81	36 (44%)	26 (96%)
2025 (Jan-Nov)	Ukraine	443	74 (17%)	34
	NSCH	96	46 (48%)	33 (97%)
Total	Ukraine	1389	209	99
	NSCH	**277**	**131**	**94**
	%	**19,94%**	**62,68%**	**96,91%**

Epidemiologic shifts in pediatric HCT are also notable, with an unusual predominance of acute myeloid leukemia over acute lymphoblastic leukemia - a likely consequence of evacuation programs prioritization patterns towards advanced therapeutic options that are unavailable in Ukraine.



AML - acute myeloid leukemia, **ALL** - acute lymphoblastic leukemia, **PID/SCID** - primary/severe immunodeficiency syndrome, **SAA** - severe aplastic anemia, **IBMFS** - inherited bone marrow failure syndrome, **MDS** - myelodysplastic syndrome, **MPS** - mucopolysacharridoses, **X-ALD** - x-linked adrenoleukodystrophy; **MUD** - matched unrelated donor, **MRD** - matched related donor, **Haplo** - haploidentical

Conclusions:

NSCH leveraged its HCT expertise, crisis management skills, and global partnerships to maintain and expand transplant activity during wartime, becoming a key contributor to Ukraine's national program, covering nearly all pediatric alloHCT and accounting for one-fifth of the country's total volume. Recognizing the fragility of evacuation-based strategies in prolonged crises, NSCH swiftly adapted by extending services to adult patients. This move required complex legislative approvals, additional staff training, and standardization of practices. Collaborations with global institutions such as St. Jude Global and European clinics

enabled evacuation in acute phase patient access to advanced therapies like CAR-T cell treatment abroad. This experience highlights the importance of cross-disciplinary collaboration, international partnerships, and flexible adaptation in sustaining healthcare services in countries affected by war.

Disclosure: Nothing to disclose

Paed4-06

MANAGEMENT AND OUTCOMES OF PEDIATRIC TA-TMA AFTER ALLOGENEIC HCT: A UK MULTICENTER RETROSPECTIVE STUDY

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Background: Transplantation-associated thrombotic microangiopathy (TA-TMA) is a severe complication after hematopoietic stem cell transplantation (HCT), associated with high morbidity and mortality. Treatment remains controversial, often guided by complement inhibitors, but access is limited by cost, monitoring requirements, and lack of randomized trials. Defibrotide may protect small-vessel endothelium from TA-TMA-related damage.To describe management and outcomes of TA-TMA in a pediatric cohort and evaluate treatment strategies.

Methods: This retrospective study by the UK Pediatric Hematopoietic Stem Cell Transplantation Group analyzed 42 patients (from 55 cases) across seven centers who developed TA-TMA after HCT between January 2016 and May 2025.

Results:

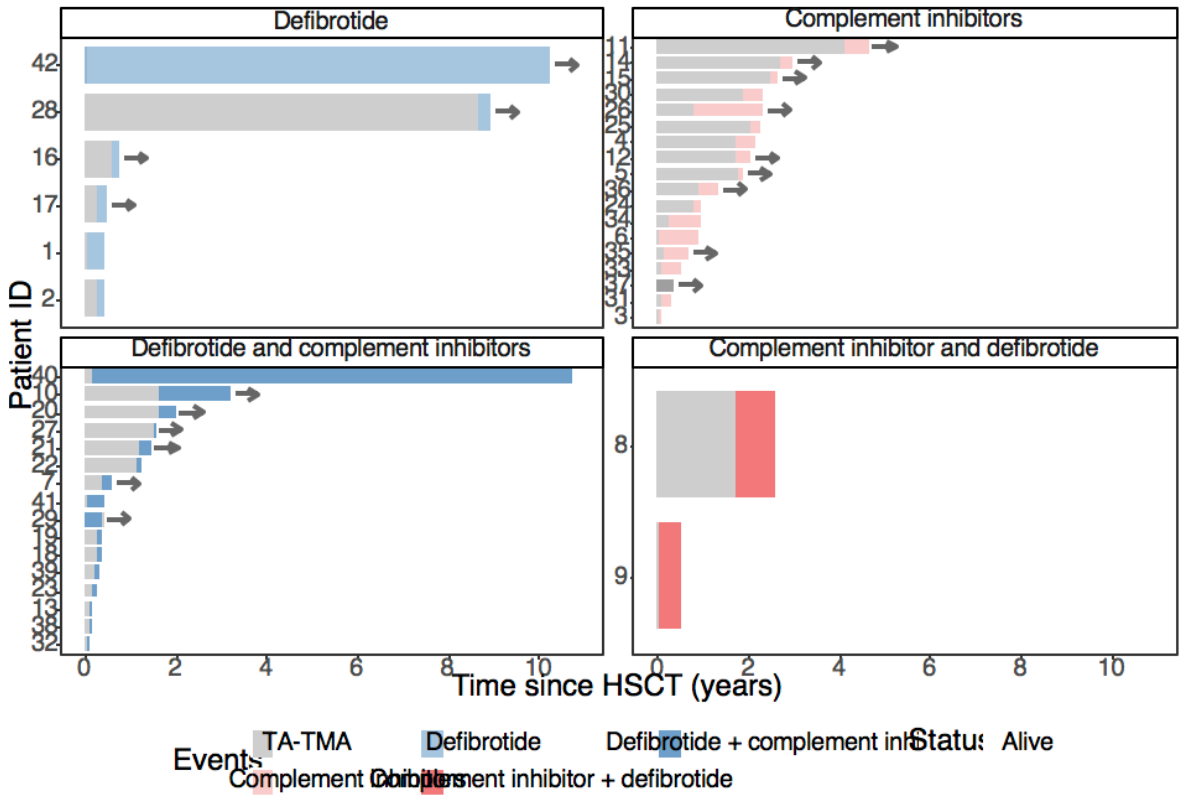
N/N all data completed	55/42
Gender, Male/Female and age, median (IQR)	27/15 and 8 (9)

Disease, malignant/non-malignant	15/40
Donor, MRD/MUD/MMUD/CB/Haplo	11/15/3/8/5
Source, BM, PB, CB	23/11/8
Conditioning, MAC/RTC/RIC	20/11/11
GvHD II-IV, n (%)	26 (62)
Virus reactivation, CMV/EBV/ADV	10/9/14
Day TA-TMA after HCT, median (IQR)	108 (132)
De novo anemia/ thrombocytopenia	28/29
Schystocytes, n (%)	34 (81)
HBP, n (%)	38 (90)
sC5b9 ng/ml, median (IQR)	434 (229)
sC5b9 greater than ULN, n (%)	21 (50)
rUPCR ≥1g/mmol, median (IQR)	0.65 (1)
rUPCR ≥1g/mmol, n (%)	14 (33)
LDH (U/L), median (IQR)	848 (884)
LDH ≥2x ULN, n (%)	33 78)
2/5-year OS (CI95%)	62 (46-84)/21 (8-53)
Alive, n (%) and follow up, median (IQR)	19 (45) and 745 (1046)

The cohort included 42 patients (median age, 8 years; interquartile range [IQR], 9) who underwent either a first (n=39) or second (n=3) allogeneic HCT for malignant (n=14) or

nonmalignant (n=28) conditions. Donors were matched in 26 cases (11 related) and mismatched in 16 cases, including 5 haploidentical and 8 cord blood transplants. Pharmacological graft-versus-host disease (GvHD) prophylaxis was administered in 41 of 42 transplants, predominantly with calcineurin inhibitors (n=37). Acute GvHD grade > I occurred in 26 patients (62%), with a median onset at day 39 (IQR, 66) post-HCT. The median time to TA-TMA diagnosis was 108 days (IQR, 132).
Extra-renal involvement was observed in 28 patients (66%), including pulmonary (n=21), serositis (n=16), central nervous system (n=11), and gastrointestinal (n=8) manifestations. Biopsies confirmed TA-TMA in renal (n=11), pulmonary (n=6), and gastrointestinal (n=2) sites. Twenty-eight patients (66%) required admission to the pediatric intensive care unit for a median of 11 days (IQR, 28), primarily for respiratory support (n=22), inotropic therapy (n=9), and renal replacement therapy (n=10).
Regarding treatment, 6 patients (14%) received defibrotide alone; 18 (43%) received complement inhibitors (predominantly eculizumab, with one case each of ravulizumab and nomacopan); 16 (38%) received defibrotide followed by a complement inhibitor (including one concomitant administration); and 3 (5%) received complement inhibitors followed by defibrotide. The median number of eculizumab doses was 8 (IQR, 12), and the median duration of defibrotide therapy was 16 days (IQR, 35). Soluble C5b-9 (sC5b-9) was elevated in 21 of 31 patients tested (57%; median, 434 ng/mL). Among these, complement inhibitors achieved an overall response rate (ORR) of 63% (7 responders, including 4 complete remissions [CR]); defibrotide achieved an ORR of 70% (including 3 CR). In patients with normal sC5b-9, complement inhibitors achieved 3 CR and 1 partial remission (PR), while defibrotide achieved 2 PR. All unresolved TA-TMA cases were fatal. Overall, 27 patients (63%) responded, and 16 (38%) achieved CR. At last follow-up, 19 patients (45%) were alive. Five-year overall survival was 21% (95% CI, 7.9–53.4%). Causes of death included TA-TMA (65%), GvHD (9%), infection (9%), and relapse (17%).

Conclusions: TA-TMA is a highly aggressive complication following HCT. Both defibrotide and complement inhibitors demonstrated similar ORR; however, complement inhibitors achieved more CR across sC5b-9 strata. Complement inhibitors should be considered first-line therapy, even when sC5b-9 levels are not elevated. Defibrotide remains a reasonable alternative when complement inhibitors are not immediately available, particularly in complement-driven TA-TMA.



Disclosure: Nothing to declare

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COMPARATIVE ANALYSIS ON ANTI-THYMOCYTE GLOBULIN (ATG) *VS* ANTI-T-LYMPHOCYTE GLOBULIN (ATLG) IN PEDIATRIC PATIENTS WITH MALIGNANT DISEASES RECEIVING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE STUDY

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Background: Owing to different manufacturing processes, anti-thymocyte globulin (ATG) and anti-T-lymphocyte globulin (ATLG) diverge in ligand specificities, potency, dosing, and pharmacokinetics.

Methods: We retrospectively compared the global outcome of a cohort of pediatric patients (n=117) with malignant diseases undergoing allogeneic hematopoietic stem cell

transplantation receiving either ATG (n=82) or ATLG (n=35) as part of GvHD prophylaxis (see Table 1 Patient and Transplant Characteristics).

Table 1 Patient and Transplant Characteristics

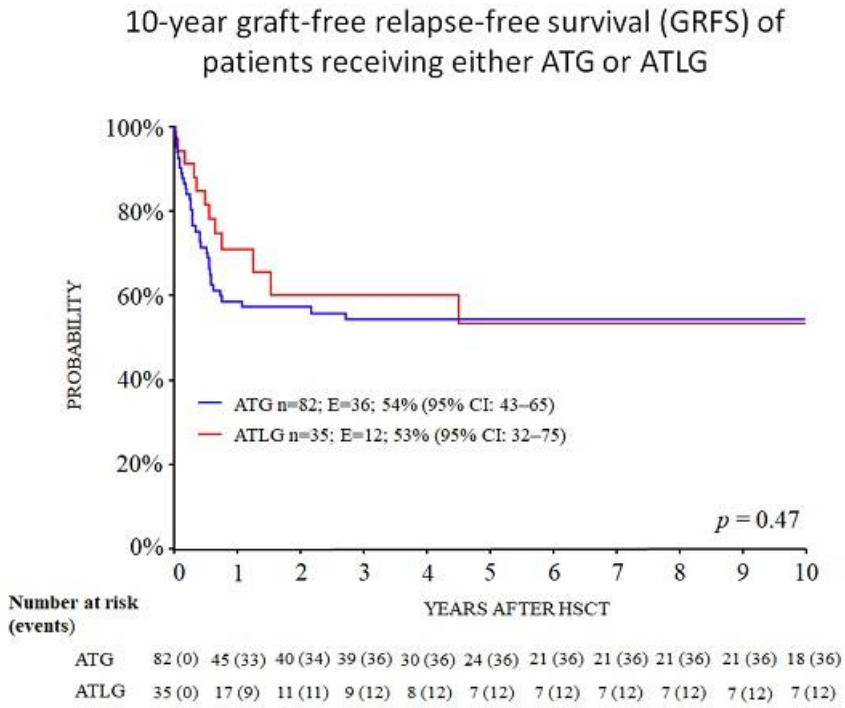
Variable	**ATG** (n = 82)	**ATLG** (n = 35)	***p*-value**
Sex, [n (%)] Male Female	 45 (55%) 37 (45%)	 18 (51%) 17 (49%)	0.88
Age at transplantation, median (range), years	10.3 (0.6–24.9)	12.6 (1.1–21.3)	0.19
Disease, [n (%)] ALL AML NHL MDS	 44 (54%) 28 (34%) 3 (4%) 7 (8%)	 19 (54%) 12 (34%) 2 (6%) 2 (6%)	0.82
Disease Risk Index (DRI), [n (%)] Intermediate High Very high	 40 (49%) 39 (48%) 3 (3%)	 17 (49%) 14 (40%) 4 (11%)	0.25
Disease phase at time of transplantation CR1 ≥CR2 or active disease at HSCT	 50 (61%) 32 (39%)	 17 (49%) 18 (51%)	0.29
Graft source, [n (%)] BM PBSC	 52 (63%) 30 (37%)	 16 (46%) 19 (54%)	0.11
Conditioning regimen TBI-based Busulfan-based Treosulfan-based	 43 (52%) 25 (31%) 14 (17%)	 21 (60%) 6 (17%) 8 (23%)	0.34
Donor type, [n (%)] Unrelated (MUD or MMUD) HLA-identical sibling	 80 (98%) 2 (2%)	 32 (91%) 3 (9%)	0.31
HLA-matched, [n (%)] 10/10 9/10 8/10	 47 (57%) 31 (38%) 4 (5%)	 27 (77%) 8 (23%) 0 (0%)	0.19

Table 1 Patient and Transplant Characteristics

Infused CD34⁺ cells, median (range)	7.1 (1.4–41.9)	7.4 (1.9–27.1)	0.65
Infused mononuclear cells, median (range)	8.1 (0.9–29.1)	8.5 (2–44)	0.50
Donor-patient sex matched, [n (%)] Female–male Female–female Male-female Male-male	 22 (27%) 15 (18%) 16 (20%) 29 (35%)	 13 (37%) 4 (11%) 6 (17%) 12 (35%)	0.64
CMV serostatus, [n (%)] Positive Negative	 54 (66%) 28 (34%)	 18 (52%) 17 (49%)	0.14
Blood type, [n (%)] No ABO mismatch Major ABO incompatibility Minor ABO incompatibility Bidirectional ABO incompatibility	 25 (30%) 21 (26%) 29 (35%) 7 (9%)	 17 (49%) 10 (29%) 4 (11%) 4 (11%)	0.06

Results: The median follow-up for the whole study population was 5.9 years (IQR 2.9–12.4), with no differences between the two groups [ATG 9.9 years (IQR 4.3–11.9), ATLG 1.7 years (IQR 1.3–13.9) (p = 0.33)]. The primary, composite endpoint of ten-year graft-free relapse-free survival (GRFS) was 54% (95% confidence interval [CI]: 43–65%) in ATG patients and 53% (95% CI: 32–75%) in ATLG patients (p = 0.47) (see Figure 1). In multivariable analysis only patient age showed a statistical impact on the rate of GRFS, with younger recipients having a better graft-free relapse-free survival compared to the older counterpart (HR 1.97, 95% CI: 1.08–3.58, p = 0.03). The ten-year overall survival (OS) was 64% (95% CI: 54–75%) in the ATG group and 72% in the ATLG group (95% CI: 55–90%) (p = 0.41). The ten-year event-free survival (EFS) was 64% (95% CI: 53–74%) among patients receiving ATG and 67% (95% CI: 48–87%) among patients given ATLG (p = 0.42). The ten-year cumulative incidence of relapse did not differ in the two study populations, being 25% (95% CI: 17–36%) for the ATG group and 27% (95% CI: 13–54%) for the ATLG group (p = 0.74). The 100-day cumulative incidence of grade III-IV acute GvHD was 9% (95% CI: 4–18%) among patients receiving ATG and 6% (95% CI: 1–22%) in patients receiving ATLG (p = 0.58). Statistical significance was observed neither for the cumulative incidence of ten-year non-relapse mortality (NRM) [ATG group 15% (95% CI: 9–25%), ATLG group 6% (95% CI: 1–22%) (p = 0.23)] nor for the cumulative incidence of chronic GvHD [ATG cohort 11% (95% CI: 6–20%), ATLG cohort 21% (95% CI: 10–43%) (p = 0.29)]. The 500-day cumulative incidence of viral infections/reactivations was significantly lower among patients treated with ATLG [41% (95% CI: 26–64%)] compared to those receiving ATG [81% (95% CI: 70–94%)] (p = 0.0003). Such a protective effect towards viral infections/reactivations was confirmed by multivariable analysis. With the exception of $CD16^{+}CD56^{+}$ NK cell immune reconstitution at one year post-transplant (ATG: median 211 cells/μL, ATLG: median 113 cells/μL, p = 0.006), ATG and ATLG patients showed a similar

immune recovery at different timepoints.



Conclusions: ATG and ATLG produce similar outcomes in terms of graft-free relapse-free survival, overall survival, event-free survival, acute and chronic GvHD, relapse, non-relapse mortality and immune reconstitution. Notably, ATLG is strongly associated with a reduced rate of viral infections/reactivations. Future randomized and prospective studies may aid in better defining the optimal dosing and pre- and post-transplant exposure to ATG and ATLG, aiming at improving the transplant-related outcomes.

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B204

PRETRANSPLANT ENDOTHELIAL ACTIVATION AND STRESS INDEX (EASIX) PREDICTS NON-RELAPSE MORTALITY AFTER ALLO-HSCT IN A MULTICENTRIC PEDIATRIC ALL COHORT WITH INCREASING RISK FOR OLDER PATIENTS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for many children with acute lymphoblastic leukemia (ALL); however, non-relapse mortality (NRM) remains a substantial limitation. Reliable early prognostic tools to identify patients at increased risk are therefore needed. The Endothelial Activation and Stress Index (EASIX; LDH × creatinine / thrombocyte count) has been shown to predict post-transplant outcomes in adults and, in our pediatric single-center preliminary analysis, NRM and overall survival (OS). To validate these findings, we conducted the present multicenter study.

Methods: We retrospectively analyzed 206 patients with ALL who underwent allo-HSCT within the FORUM-trial at five pediatric transplant centers (Frankfurt/Main, Paris, Prague, Vienna, Wroclav). Pre-HSCT EASIX was computed at prespecified time points (days −30, -3 and 0). Patients were stratified by cohort-median EASIX at each time point. Primary endpoints were OS and NRM, event-free survival (EFS) was secondary. Kaplan–Meier and log-rank tests compared survival; NRM was analyzed with competing risks methods.

Results:

Table: Patient and transplant characteristics						
	N	%				
Total	206	100%				Total
Male	127	62%				Remission status
Female	79	38%				CR1
			%EASIX	%EASIX	p-value	CR2
Age at HSCT			low	high		>CR2
						Immunophenotype
<4 years	31	15%	27%	4%		BCP
4-10 years	84	41%	44%	38%	<0,001	T-ALL
10-14 years	43	21%	19%	22%		other
>14 years	48	23%	10%	35%		Stem cell donors
Conditioning Regimen						MUD
TBI/VP16	136	66%	58%	74%		MSD

FLU/THIO/BU	26	13%	15%	10%	0,069	MMD
FLU/THIO/TREO	44	21%	27%	16%		Blinatumomab prior to HS
Stem cell source						aGVHD
BM	126	61%	68%	55%		Grades II-IV
PBSCs	75	36%	27%	45%	0,003	Grades III-IV
CB	5	3%	5%	0%		cGVHD

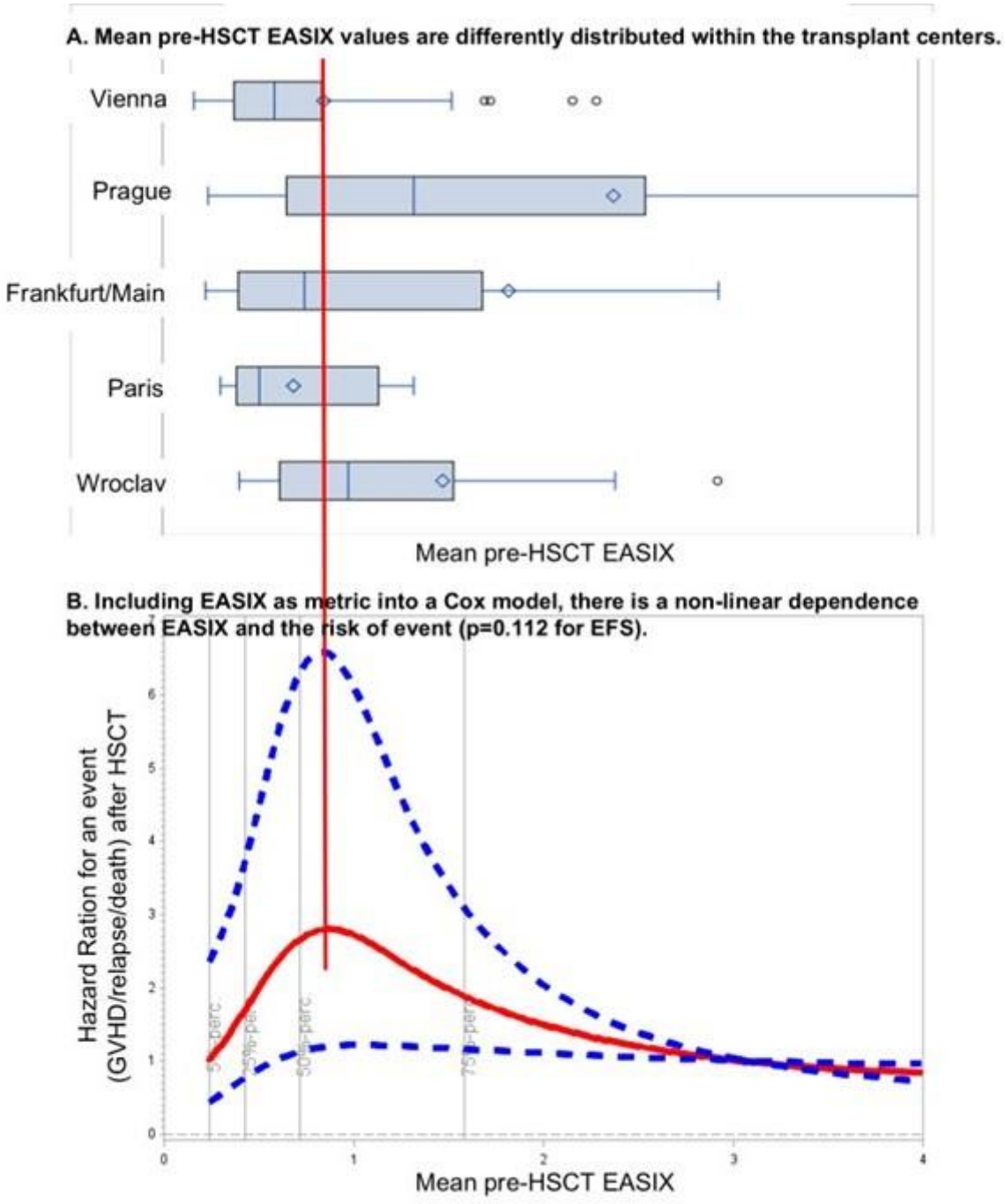

Figure A/B: Only for low EASIX values there is a positive linear dependence between pre-HSCT EASIX and risk.

HSCT was conducted predominantly from matched unrelated donors (74%) with bone marrow as stem cell source (61%) and TBI-containing conditioning regimen (66%). Fifty-six percent of patients were transplanted in first complete remission; the underlying ALL was a

precursor B-cell ALL in 73%. In terms of patient characteristics, immunophenotype and remission status did not correlate significantly with EASIX. An adverse effect of TBI-containing conditioning was borderline significant. Increasing age and peripheral blood as stem cell source were significantly associated with a higher risk of elevated EASIX values (Table).
When patients were dichotomized by mean pre-HSCT EASIX (day−30 to day0), the 5-year NRM was 4% in the low-EASIX group compared with 15% in the high-EASIX group (p = 0.019). Mean pre-HSCT EASIX was not associated with 5-year OS. In contrast, EASIX measured at day −3 showed a clearer separation in outcomes, with a 5-year OS of 72% in the low-EASIX group compared with 84% in the high-EASIX group, indicating a trend toward significance (p = 0.072). The association between mean pre-HSCT EASIX and 5-year EFS observed in the single-center study was not confirmed in the multicenter cohort. However, modeling EASIX as a continuous variable suggested a non-linear relationship with event risk (p = 0.112), indicating that any adverse association may be limited to cohorts with lower mean EASIX values (Figure).
Notably, substantial inter-center variability in mean pre-HSCT EASIX values was observed across the five transplant centers (Figure).

Conclusions: In this multicenter pediatric ALL transplant cohort, elevated pre-HSCT EASIX robustly identified patients at increased risk of NRM, thereby confirming our previous single-center findings. Variability in results across transplant centers may reflect differences in national patient populations and center-specific transplant procedures including supportive care. The analysis including modifications of the EASIX-score as well as post-transplant values is ongoing. The observation of higher pre-HSCT EASIX values in older patients is consistent with the increased NRM reported in adolescents and young adults in the FORUM trial. Prospective integration of EASIX into pediatric pretransplant assessment and early post-transplant monitoring is feasible and may facilitate more effective risk-adapted supportive care.

Disclosure: Nothing to declare.

B205

IMPACT OF RECIPIENT AGE AND CYCLOSPORIN A TARGET LEVEL ON MIXED CHIMERISM AFTER TREOSULFAN-BASED MATCHED FAMILY DONOR HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SICKLE CELL DISEASE

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Background: HSCT is the only widely available curative treatment option for sickle cell disease (SCD), with HLA-matched sibling donor (MSD)-HSCT representing the standard-of-care. We aimed to evaluate outcome of transplant activity for SCD in Germany in recent years across all donor types and conditioning regimens.

Methods: We analysed overall (OS), SCD-free (SFS), and persistent chronic GVHD SCD-free (GSFS) rates as well as risk factors for mixed chimersim (MC) in a retrospective, multicentre analysis of the German paediatric stem cell transplantation and SCD registries, including 146 patients receiving a first HSCT between 2011 and 2022.

Results: The table shows transplant characteristics and outcome according to donor. All patients received reduced-toxicity protocols (RTPs), which were predominantly treosulfan-fludarabine-thiotepa-based (69.9%). Four-year OS and GSFS did not differ significantly between conditioning regimens (treosulfan-based: 97.1% and 82.8%; busulfan-based: 95.2% and 89.2%; melphalan-based: 100.0% and 77.8%). Matched family donor (MFD)-HSCT (88 MSD; 5 other MFD) showed a tendency towards better 4-year-OS (98.9%, p=0.09, table) and represented a protective factor for inferior SFS (91.6%, HR=0.38, p=0.04) and GSFS (91.6%, HR=0.26, p=0.002,), whereas reduced myeloablation (treosulfan 36g/m^2 or without thiotepa) acted as risk factor (SFS: HR=3.4, p=0.03; GSFS: HR=4.3, p=0.005). Multivariate Cox regression analysis identified MUD (HR=27.9, p=0.003), MMUD (HR=14.5, p=0.002) and Ferritin ≥2500µg/l (HR=32.2, p=0.001) as hazard factors for aGVHD II-IV (N=20, table), with a trend towards older recipient age (≥12 years; HR=3.7, p=0.07). Graft failure (GF, N=17) predominantly occurred in treosulfan-based regimens (4-y-cumulative incidence: treosulfan 12.4%, busulfan 3.0%, p=0.14) and frequently in patients undergoing reduced myeloablation (p=0.005). Likewise, MC below 75% appeared more frequently in treosulfan-based regimens (32.4%) compared to busulfan (8.8%, p=0.007). 16 patients received donor lymphocyte infusions, all after treosulfan-based conditioning.
We performed multivariate logistic regression analysis to assess the risk of MC at day+30, +60 (<95% donor chimerism (DC)) and day+100, +180 and +365 post HSCT (<75% DC). Serotherapy with Thymoglobulin® was main risk factor at day+30 (p=0.04). This corresponded to a faster reduction (median day: Thymoglobulin® 73, ATG-Fresenius 124 (p<0.001)) and discontinuation (Thymoglobulin® 115, ATG-Fresenius 162 (p<0.001)) of calcineurin inhibitors in this subgroup. High mean targeted trough level of cyclosporine A (CSA≥150µg/l) combined with MFD-HSCT represented main risk factor at day+60 (p=0.03) and day+100 (p=0.01). From day+100 onwards, young recipient age at transplant (<6 years) was significantly associated with drop in DC to <75% (day+100: p=0.02; day+180: p=0.005; day+365: p=0.004) as well as reduced myeloablation (day+180: p=0.05; day+365: p=0.02). These risk factors originate from a homogenous subgroup of

treosulfan(42g/m^2)-fludarabine-thiotepa-ATG-based MFD-HSCTs (N=62; Thymoglobulin® (day+30: p=0.18); CSA≥150µg/l (day+60: p=0.03; d+100: p=0.03); age<6 years (day+180: p=0.02; day+365: p=0.02)). This subgroup was characterised by minor GvHD problems (no aGvHD III-IV, 4.8% aGvHD II; 1.6% temporary mild cGVHD).

	MFD (N=93), n (%)	**MUD (N=17), n (%)**	**MMUD 9/10 (N=19), n (%)**	**Haploidentical (N=17), n (%)**	**Descriptive *P***
Median patient age, years median (range)	9.4 (1.8-19.0)	14.2 (1.7-19.5)	10.8 (2.5-16.7)	12.9 (4.3-23.4)	0.01
Male patient sex, n (%)	57 (61.3)	10 (58.8)	10 (52.6)	9 (52.9)	0.86
Pre-transfusion/apheresis None Erythroyte concentrate only Single Apheresis/Exchange Repeated Apheresis/Exchange	12 (12.9) 7 (7.5) 55 (59.1) 19 (20.4)	2 (11.8) 1 (5.9) 9 (52.9) 5 (29.4)	1 (5.3) 4 (21.1) 10 (52.6) 4 (21.1.)	0 (0.0) 0 (0.0) 8 (47.1) 9 (52.9)	0.14
Pre-conditioning, n (%) None Hydroxyurea +/- other	15 (16.1) 78 (83.9)	0 (0.0) 17 (100)	2 (10.5) 17 (89.5)	2 (11.8) 15 (88.2)	0.37
Serotherapy, n (%) ATG Fresenius ATG Thymoglobulin® Alemtuzumab Unknown	59 (64.1) 32 (34.8) 1 (1.1) 1	8 (47.1) 9 (52.9) 0 (0.0) 0	12 (63.2) 3 (15.8) 4 (21.1) 0	11 (64.7) 0 (0.0) 6 (35.3) 0	< 0.001
Conditioning regimen, n (%) Treosulfan-fludarabine based Busulfan-fludarabine based Melphalan-fludarabine based	67 (72.0) 20 (21.5) 6 (6.5)	11 (64.7) 4 (23.5) 2 (11.8)	12 (63.2) 7 (36.8) 0 (0.0)	13 (76.5) 3 (17.6) 1 (5.9)	0.64
Myeloablation, n (%) Normal	88 (94.6) 5 (5.4)	13 (76.5) 4 (23.5)	18	16 (94.1) 1 (5.9)	0.09

Reduced (treosulfan 36g/m^2 or without thiotepa)			(94.7) 1 (5.3)		
Stem cell source, n (%) Bone marrow only Unmanipulated PBSC PBSC with CD34-selection and T-cell add-back PBSC with CD3/CD19- or αβ-depletion	92 (98.9) 1 (1.1) 0 (0.0) 0 (0.0)	10 (58.8) 5 (29.4) 2 (11.8) 0 (0.0)	9 (47.4) 1 (5.3) 4 (21.1) 5 (26.3)	6 (35.3) 0 (0.0) 0 (0.0) 11 (64.7)	<0.001
GvHD prophylaxis, n (%) Cyclosporine A + methotrexate Cyclosporine A + mycophenolate mofetil Tacrolimus + mycophenolate mofetil Cyclosporine A + methotrexate + other PostCy + tacrolimus + mycophenolate mofetil other	56 (60.2) 32 (34.4) 1 (1.1) 2 (2.2) 0 (0.0) 2 (2.2)	12 (70.6) 5 (29.4) 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0)	7 (36.8) 9 (47.4) 0 (0.0) 3 (15.8) 0 (0.0) 0 (0.0)	0 (0.0) 4 (23.5) 6 (35.3) 0 (0.0) 6 (35.3) 1 (5.9)	< 0.001
Mean targeted trough level of Cyclosporine A, µg/l, n (%) ≤100 101-149 ≥150 Not applicable	14 (15.4) 57 (62.6) 20 (22.0) 2	0 (0.0) 14 (82.4) 3 (17.6) 0	0 (0.0) 14 (73.7) 5 (26.3) 0	0 (0.0) 3 (75.0) 1 (25.0) 13	0.30
Median time to neutrophil count >0.5/nl, days (range)	22 (9-42)	19 (10-34)	17 (11-26)	18 (12-24)	0.15
Median time to platelet count >20/nl, days (range)	23 (7-84)	20 (10-66)	18 (14-62)	17 (7-33)	0.20
Central nervous system complications, n (%)	6 (6.5)	3 (17.6)	2 (10.5)	3 (17.6)	0.18
Graft failure, n (4-year probability, %)	8 (7.3)	3 (17.6)	2 (10.5)	4 (23.5)	0.13

Acute GvHD II-IV, n (1-year probability, %)	6 (6.5)	7 (41.2)	6 (33.8)	1 (7.1)	<0.001
Moderate and severe chronic GvHD, n (4-year probability, %)	1 (1.1)	3 (18.1)	2 (11.1)	0 (0.0)	0.005
4-y overall survival, %	98.9	94.1	86.8	100.0	0.09
4-y sickle cell disease (SCD)-free survival, %	91.6	76.5	81.3	76.5	0.09
4-y persistent cGvHD- and SCD-free survival, %	91.6	64.2	76.6	70.6	0.004

Conclusions: The results of our detailed, multicentre data analysis confirm excellent OS across all donor types, but significantly better GSFS after MFD HSCT for SCD. We identified risk factors (Thymoglobulin®, CSA≥150µg/l, age<6 years, reduced myeloablation) for the development of MC in treosulfan-based conditioning regimens. These data should assist in risk-adapted optimization of RTPs especially in the setting of MFD-HSCT.

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B206

OUTCOMES OF PATIENTS WITH AML UNDER 18 YEARS WHO RELAPSE WITHIN 6 MONTHS FROM ALLOGENEIC HSCT- A RETROSPECTIVE STUDY FROM THE EBMT PDWP

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Background: Allogeneic haematopoietic stem cell transplantation (HSCT) is the treatment of choice to cure high risk and relapsed or refractory paediatric AML, however, relapse remains the leading cause of treatment failure. Outcomes for children who relapse after HSCT have been poor historically, particularly for those who experience early relapse (i.e. within 6 months after the allograft), yet data specifically evaluating early relapse in the paediatric AML setting is very limited. We sought to evaluate outcomes for children with AML who relapse within 6 months post-transplant in the largest international registry-based study focusing on this cohort to date.

Methods: We conducted a retrospective study from the EBMT Paediatric Diseases Working Party (PDWP) of all patients transplanted in complete remission (CR) for AML, and aged under 18 years at time of transplant, who relapse within 6 months post first allo-HSCT, over a 15-year study period from 2010-2024. Overall survival (OS) was evaluated from date of relapse post HCT to death or last follow-up. A Cox multivariable model was used to evaluate factors influencing OS.

Results: 469 patients were included in analysis, 288 in CR1 and 181 in CR2 or more, median follow up was 3.2 years after relapse (95%CI 2.1-4.1). The median age for the entire cohort was 6.0 years, (range 1.1-14.8) and 190 were female. Overall survival at 1- and 3-years post relapse was 15.4% (95%CI 12.1-19.2) and 9.1% (95%CI 6.4-12.4) respectively, figure 1. Time from HSCT to relapse, Lansky performance status, and year of HSCT were all shown to adversely impact outcomes on multivariable analysis, table 1.
The 3y cumulative incidence of allo HSCT post relapse was 14.3%, corresponding to 61 pts. Median time of second allo HSCT after relapse was 105 days. At time of second allo HSCT, 31 were transplanted in CR and 27 in active disease (3 missing).
Three patients have no follow-up after the second allo HSCT. Regarding the 58 remaining patients: 1- and 3- year OS was 45.9% (95%CI 32.1 - 58.7) and 30.3% (95%CI 18 - 43.5), respectively. 1- and 3- year leukaemia free survival (LFS) was 34.1% (95%CI 21.7 - 46.9) and 24.6% (95%CI 13.5 - 37.4), respectively.1- year relapse incidence (RI) 53% (95%CI

38.6 - 65.5) and 3-year RI was 60.3% (95%CI 45 - 72.6). Non relapse mortality (NRM) was 12.9% at 1 year (95%CI 5.5 - 23.3) and 15.1% (95%CI 6.9 - 26.3) at 3 years.

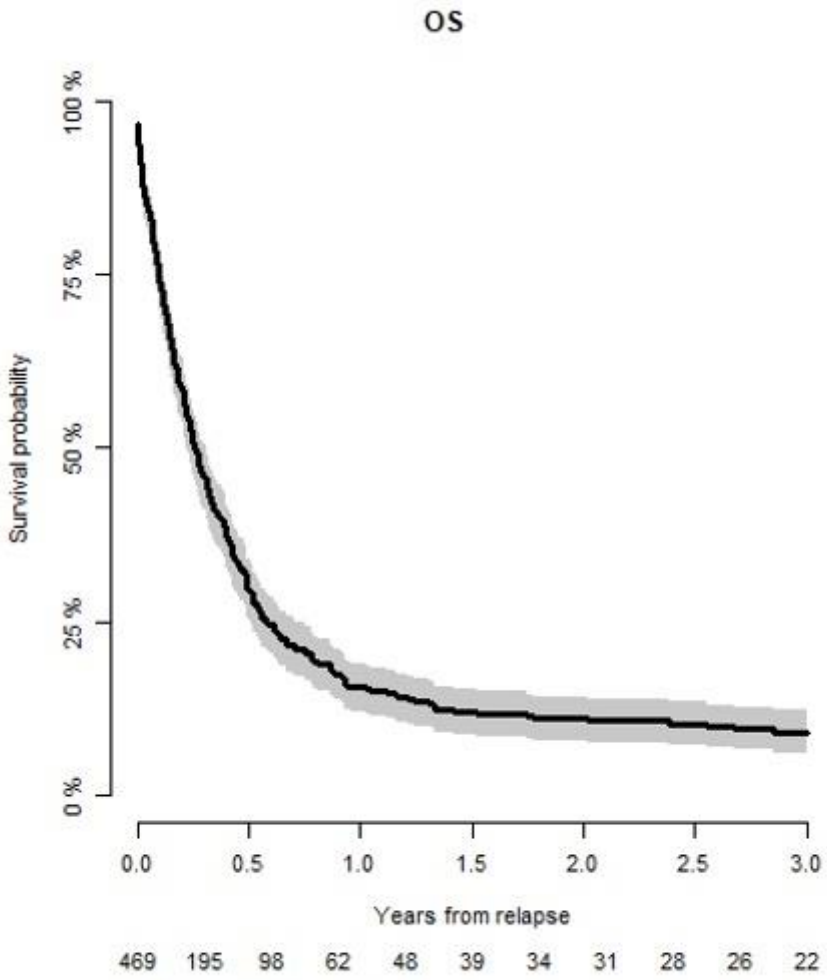

Figure 1: OS of entire cohort

Table 1: Multivariable Cox model on OS

Variables	Parameters	HR (95% CI)	P value
Time from HSCT to relapse	4 to 6 months	1	
	Within 3 months	1.20 (1.21-1.87)	<0.001

Lansky	90 and 100	1	
	≤80	1.43 (1.12-1.84)	0.004
Year of HSCT (5y unit)	After 2016	1	
	Before 2016	1.29. (1.04-1.60)	0.03
Donor type	Matched related	1	
	Mismatched related	1.24 (0.89-1.73)	0.19
	Unrelated donor	1.11 (0.85-1.45)	0.43
	CB	1.38 (0.99-1.82)	0.052
Disease status at HSCT	CR1	1	
	CR2+	1.02 (0.8201.28)	0.85
Age at HSCT (5y unit)		1.04 (0.95-1.14)	0.4
ELN 2022 cyto	Fav/int	1	
	Adverse	0.80 (0.62-1.04)	0.1
	Missing	0.83 (0.64-1.07)	0.14

Conclusions: Our study, representing the largest reported cohort of this specific population to date, shows that outcomes of children with AML who relapse within 6 months after allogeneic HSCT are abysmal using standard transplant approaches. This remains true regardless of whether transplantation occurred in first or second remission. These data highlight the urgent need for innovative and experimental therapeutic strategies to be explored in this setting and serve as a benchmark for future prospective trials evaluating novel approaches to improve outcomes.

Clinical Trial Registry: n/a

Disclosure: Nothing to declare.

B207

COMPARISON OF BONE MARROW VS PERIPHERAL BLOOD STEM CELLS FOR HAPLOIDENTICAL HSCT WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE IN CHILDREN: A CIBMTR ANALYSIS

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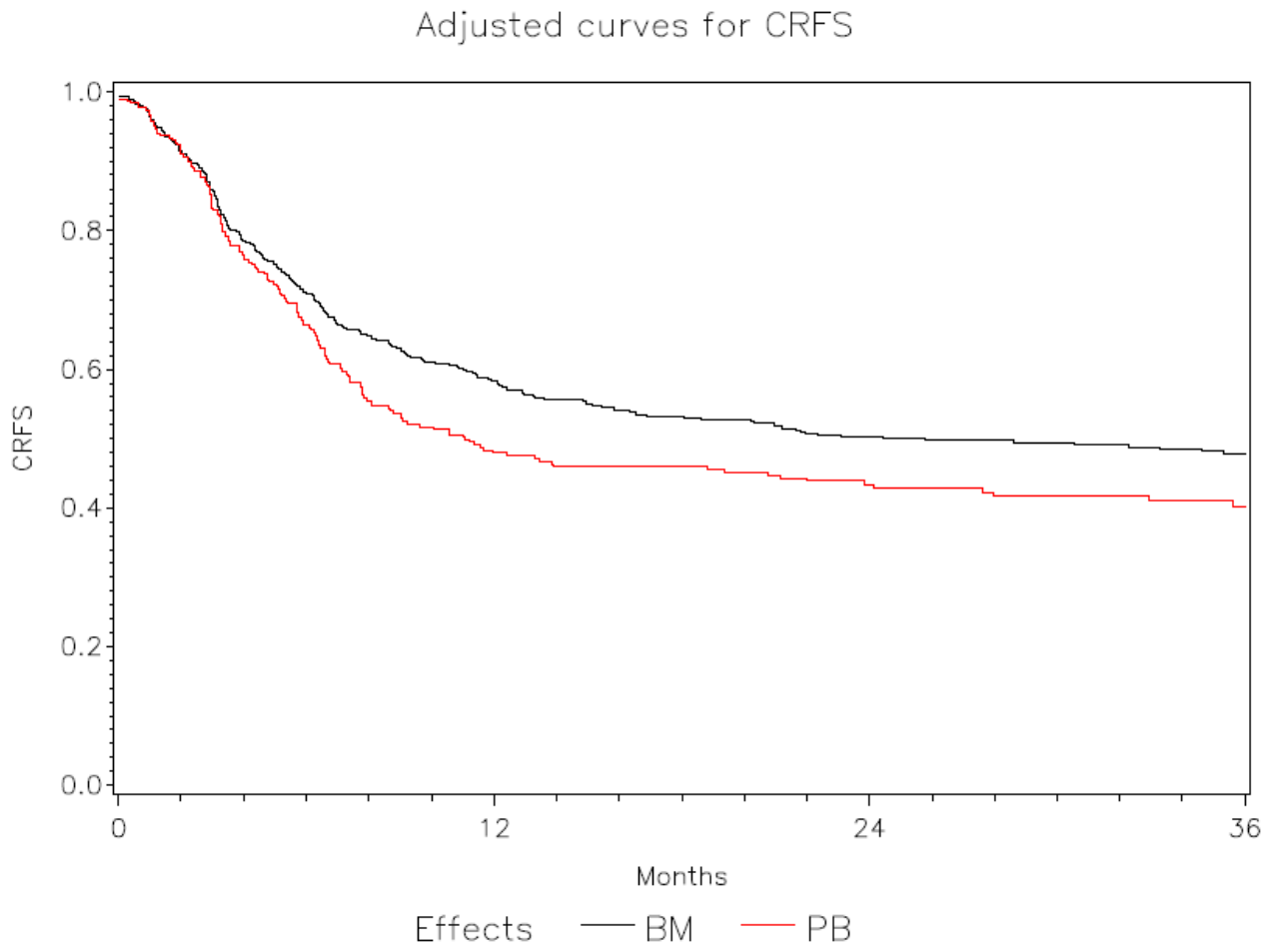
Background: Post-transplant cyclophosphamide has dramatically changed the landscape of hematopoietic cell transplant (HCT) for adults with malignancies, significantly reducing GVHD rates when either BM or PBSC is used as a graft source. In many pediatric programs, bone marrow (BM) remains the preferred graft source due to low rates of graft-versus-host disease (GVHD) when calcineurin inhibitor-based prophylaxis is used; data using peripheral blood stem cells (PBSC) grafts for children in the PTCy setting is limited. We aimed to compare outcomes between BM and PBSC grafts in pediatric patients with hematological malignancies receiving PTCy based haploHCT.

Methods: Children ≤21 years (y) with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) who received their first myeloablative haploHCT with PTCy between 2015-2022 were identified in the CIBMTR registry. Primary outcome was chronic graft-versus-host disease-free relapse free survival (CRFS) defined as patients who have not experienced extensive cGVHD or relapse of their primary disease at 2 years post-HCT. Secondary outcomes were overall survival (OS), incidence of relapse and acute/chronic GVHD. Survival was estimated using Kaplan-Meier analysis and graft sources compared using log-rank testing. Multivariable analysis assessed the effect of graft source on outcomes, adjusting for other significant covariates (variables tested: recipient age, donor relationship, disease, disease status, conditioning regimen, year of transplant, and disease risk index scoring). Statistical significance was defined as $p < 0.05$.

Results: In our cohort of 836 patients, 532 patients received BM, 304 PBSC. Demographics were comparably, except for an older age receiving PBSC (median age for PBSC 15.3 vs 9.7 for BM; $p<0.01$).
Although there was no difference in CRFS by graft source (PBSC 44.4% vs BM 49.8% at 2 years, p=0.101), cGVHD was significantly higher in those receiving PBSC, particularly extensive cGVHD (PBSC 26.6% vs BM 13.4%; p=<0.001). There was no difference in the incidence of grade 3-4 aGVHD (PBSC 3.6% vs BM 3.3%; p=0.835). The cumulative incidence of relapse was lower with PBSC grafts (PBSC 21.9% vs BM 29.5%; p=0.045), but the OS was similar (PBSC 71.2% vs BM 70.9%; p=0.360).
Multivariate analysis showed inferior CRFS with PBSC (HR 1.23; 95% CI 1.01-1.58; p=0.04). OS (HR 0.93; 95% CI: 0.72-1.21; p=0.60) and DFS (HR 0.98; 95% CI: 0.77-1.25; p=0.89) were comparable for both stem cell sources. The decrease in CRFS was due to the increased incidence of extensive cGVHD (HR: 1.89; 95% CI: 1.46-2.46; p=<0.0001) with PBSC. There were no differences in incidence of grade 3-4 aGVHD (PB HR: 1.67; 95% CI: 0.70-3.97;

p=0.25); relapse (PB HR: 0.88; 95% CI: 0.65-1.17; p=0.37) and transplant related mortality (PB HR: 1.23; 95% CI: 0.82-1.83; p=0.32).

Conclusions: In this large contemporary comparison of BM and PBSC grafts in haploHCT utilizing PTCy, the use of PBSC conveys a higher risk of cGVHD with mildly inferior CRFS. This suggests that PTCy does not fully mitigate the PBSC associated cGvHD risk. Patients receiving PBSC had a lower relapse rate in univariate analysis, but this finding did not persist when other covariates were adjusted for in multivariate analysis. Prospective studies are needed to further optimize haploHCT for pediatric patients.



Disclosure: A.S. has received consultant fees from Medexus Inc, Vertex Pharmaceuticals, Sangamo Therapeutics, Editas Medicine, BioLineRx, Gamida Cell, RGenta Therapeutics and Bristol Myers Squibb; is a medical monitor for the CSIDE clinical trial for which he receives financial compensation; has received honoraria from Blackwood CME; and is the St. Jude Children's Research Hospital site principal investigator of clinical trials for genome editing of sickle cell disease sponsored by Vertex Pharmaceuticals/CRISPR Therapeutics (NCT03745287), Novartis Pharmaceuticals (NCT04443907), and Beam Therapeutics

(NCT05456880). The industry sponsors provide funding for the clinical trial, which includes salary support paid to the institution. A.S. has no direct financial interest in these therapies. These conflicts are managed through the compliance office at St. Jude Children's Research Hospital in accordance with their conflict-of-interest policy.

B208

EFFICACY ANALYSIS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC ACUTE MYELOID LEUKEMIA: A 15-YEAR CLINICAL STUDY FROM CHINA

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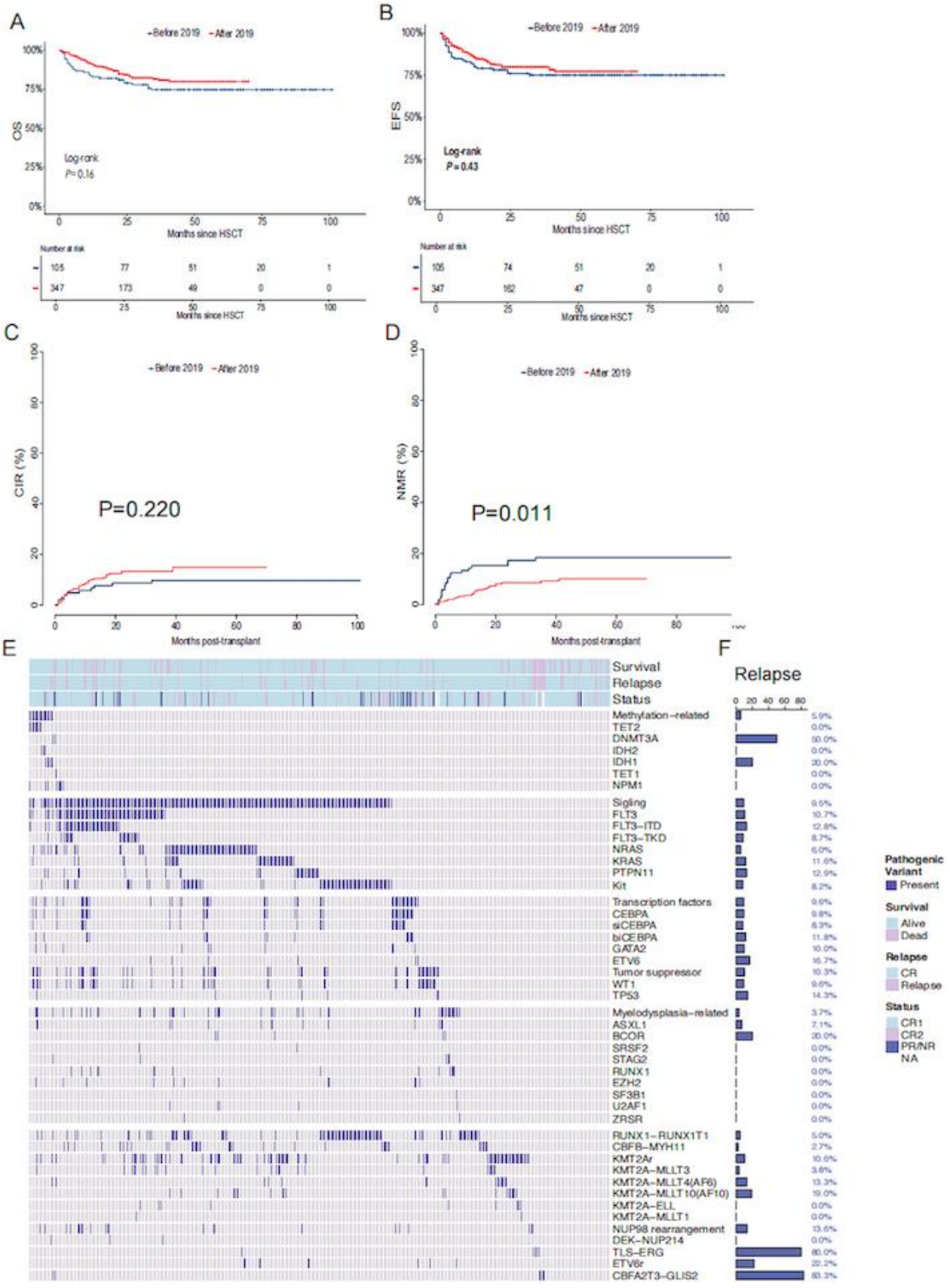
Background: In recent years, transplantation techniques for pediatric acute myeloid leukemia (AML) have advanced significantly; however, post-transplant relapse remains the primary challenge affecting prognosis. This study aims to analyze the evolution of transplant outcomes over 15 years and explore the impact of specific molecular subtypes and clinical factors on relapse.

Methods: A retrospective analysis was conducted on 452 children with AML who underwent their first allo-HSCT at the Children's Hospital of Soochow University between 2011 and 2025. Patients were divided into two groups based on the transplant era (pre-2019 vs. post-2019). Outcomes, including overall survival (OS), event-free survival (EFS), cumulative incidence of relapse (CIR), non-relapse mortality (NRM), and incidence of acute graft-versus-host disease (aGVHD), were compared between the groups. Furthermore, based on clinical data such as molecular characteristics at initial diagnosis, response to chemotherapy, and donor-recipient profiles, multivariate analysis was performed to identify independent prognostic factors.

Results: Among the 452 patients (248 males, 204 females), the median age was 90 months (range: 4.7-205). There were 105 transplants performed before 2019 and 347 after 2019. The two groups showed no significant differences in baseline characteristics, including peripheral blood counts at diagnosis, age at transplant, gender, nutritional status, blood group compatibility, or donor-recipient gender. Notably, the post-2019 era saw an increase in haploidentical transplants and a decrease in cord blood transplants. With a median follow-up of 27 months (range: 1-101) post-transplant, patients transplanted after 2019 showed trends towards improved 3-year OS (81.5% vs. 74.6%, P=0.16) and EFS (79.8% vs. 75.0%, P=0.43), significantly lower NRM (9.2% vs. 18.4%, P=0.011), and a significantly reduced incidence of grade 2-4 aGVHD (10.5% vs. 26.0%, P<0.001). However, CIR did not show significant improvement (13.3% vs. 9.7%, P=0.220). Molecular analysis revealed that patients with*CBFA2T3::GLIS2* or *TLS::ERG* fusion genes derived minimal benefit from transplantation, with post-transplant relapse rates exceeding 80%. Patients with *KMT2A::AF10* rearrangement had limited benefit (relapse rate 19.0%, 4/21), while those

with spliceosome mutations showed excellent outcomes (relapse rate 4.2%, 1/54). Multivariate Cox analysis identified myeloid sarcoma (vs. non-M7, HR=9.0, P=0.045), M7 (vs. non-M7, HR=8.112, P=0.001), failure to achieve remission after first induction (NR vs. CR/CRi, HR=2.433, P=0.045), and non-complete remission status pre-transplant (PR/NR vs. CR1, HR=3.237, P=0.017) as independent risk factors for poorer OS. Transplantation in the post-2019 era (HR=0.262, P=0.004) was a protective factor for OS. For relapse-free survival (RFS), M7 (vs. non-M7, HR=8.379, P=0.001) and pre-transplant PR/NR status (HR=3.427, P=0.005) were risk factors, while transplantation post-2019 (HR=0.346, P=0.018) and younger donor age (HR=1.03, P=0.038) were protective factors.


A
Before 2019
After 2019
OS
Log-rank
P= 0.16
Months since HSCT
Number at risk
105 77 51 20 1
347 173 49 0 0
B
Before 2019
After 2019
EFS
Log-rank
P = 0.43
Months since HSCT
Number at risk
105 74 51 20 1
347 162 47 0 0
C
Before 2019
After 2019
CIR (%)
P=0.220
Months post-transplant
D
Before 2019
After 2019
NMR (%)
P=0.011
Months post-transplant
E
Survival
Relapse
Status
Methylation-related
TET2
DNMT3A
IDH2
IDH1
TET1
NPM1
Signling
FLT3
FLT3-ITD
FLT3-TKD
NRAS
KRAS
PTPN11
Kit
Transcription factors
CEBPA
siCEBPA
biCEBPA
GATA2
ETV6
Tumor suppressor
WT1
TP53
Myelodysplasia-related
ASXL1
BCOR
SRSF2
STAG2
RUNX1
EZH2
SF3B1
U2AF1
ZRSR
RUNX1-RUNX1T1
CBFB-MYH11
KMT2Ar
KMT2A-MLLT3
KMT2A-MLLT4(AF6)
KMT2A-MLLT10(AF10)
KMT2A-ELL
KMT2A-MLLT1
NUP98 rearrangement
DEK-NUP214
TLS-ERG
ETV6r
CBFA2T3-GLIS2
F
Relapse
Pathogenic Variant
Present
Survival
Alive
Dead
Relapse
CR
Relapse
Status
CR1
CR2
PR/NR
NA

Conclusions: Advances in transplantation techniques, particularly the optimization of haploidentical protocols, have significantly reduced NRM and severe aGVHD, contributing to a trend towards improved survival in pediatric AML. However, relapse remains a major challenge. Patients with specific molecular subtypes (e.g., *CBFA2T3::GLIS2, TLS::ERG*) have extremely poor outcomes, whereas those with spliceosome mutations derive significant benefit. Additionally, myeloid sarcoma, M7, and failure to achieve complete remission prior to transplant are important adverse prognostic factors. Selecting younger donors may help improve RFS.

Disclosure: Nothing to declare.

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THE COMBINATION OF VENETOCLAX AND DECITABINE AS MAINTENANCE THERAPY AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CHILDREN WITH VERY HIGH-RISK ACUTE MYELOID LEUKEMIA

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Background: Relapse of AML remains the leading cause of treatment failure and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Venetoclax combined with decitabine has shown efficacy as post-HSCT maintenance therapy in adult AML, but pediatric data are scarce. This retrospective case series evaluates venetoclax/decitabine maintenance as an individualized post-HSCT strategy in children with AML and very high-risk (VHR) for post-HSCT relapse.

Methods: We retrospectively analyzed 12 pediatric AML patients treated between March 2022 and November 2025 at two German HSCT centers (Charité Universitätsmedizin Berlin and Universitätsklinikum Tübingen). Eligibility criteria defined VHR-AML by adverse cytogenetics, refractory disease, relapse after prior allo-HSCT, and/or minimal residual disease (MRD) reappearance post-HSCT.
The maintenance regimen was adapted from Wei et al. (Cancer Science, 2021). Therapy was initiated between day +45 to +200 after HSCT, in the absence of active infection, grade III–IV acute GvHD, or relevant transplant-related toxicities. Each 21-day cycle consisted of decitabine 15 mg/m² on days 1–3 and venetoclax up to 200 mg daily on days 1–21 (dose-adjusted for body weight and drug interactions). Cycles were repeated every 8 weeks for up

to 10 cycles or a maximum of 24 months post-HSCT. Dose modifications were applied for cytopenias.
Primary endpoints were relapse-free survival (RFS) and overall survival (OS), calculated from the day of last HSCT. Secondary endpoints included non-relapse mortality, incidence and severity of acute and chronic GvHD, feasibility, and tolerability. Analyses were performed both intention-to-treat and per protocol (>2 cycles).

Results: Median age at diagnosis was 5.7 years (range 2 months–15 years). Patients were heavily pretreated, including multiple chemotherapy lines, targeted agents, and prior HSCTs. Disease status before HSCT was heterogeneous: 6/12 patients (50%) proceeded to transplantation in CR, whereas 6 patients had refractory disease (2/12, 16.7%) or empty marrow (4/12, 33%), reflecting advanced, therapy-resistant disease.
Conditioning regimens were treosulfan- (6/12, 50%), melphalan- (4/12, 33%) or busulfan- -based (2/12, 16.7%). Median time from HSCT to maintenance initiation was 96 days (range 45-209 days). Six patients (50%) completed all planned cycles, four (33%) remain on therapy, and two patients discontinued early, one due to relapse, another due to withdrawal of health insurance reimbursement. Two patients additionally received DLI. Eleven out of 12 evaluable patients (92%) completed >2 cycles.
The most common grade III adverse events were febrile neutropenia or fever without neutropenia where patients had to be hospitalized (9 events), all transient and reversible. No grade IV toxicities and no severe (≥grade III) acute or chronic GvHD were observed.
At a median follow-up of 24 months, 2-year RFS was 83% (10/12) in the intention-to-treat analysis and 91% (10/11) in patients receiving >2 cycles. Corresponding OS rates were 92% (11/12) and 100% (11/11), respectively.

Table 1. Demographic and clinical characteristics.
Abbreviations: AML - acute myeloid leukemia; N - sample size; VENDEC - combination of venetoclax and decitabine; HSCT – hematopoietic stem cell transplantation; VHR – very high risk; MRD - minimal residual disease; CR – complete remission; MUD – matched unrelated donor; MSD – matched sibling donor; MMFD – mismatched family donor.

AML subtype, N (%)	M1	3 (25)
	M2	1 (8)
	M4	5 (42)
	M5	3 (25)
Indications for VENDEC, N (%)	Primary refractory	7 (58)
	Relapse after prior HSCT	3 (25)
	VHR-Cytogenetics	1 (8)

Table 1. Demographic and clinical characteristics.
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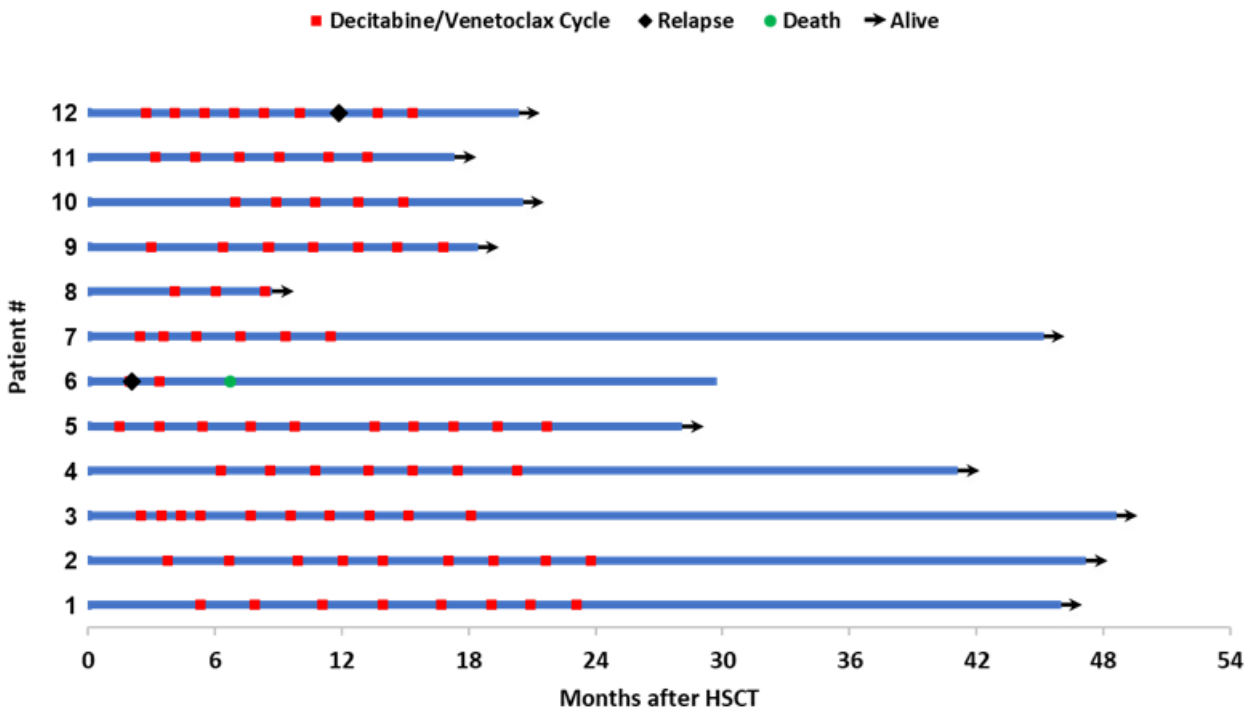
	MRD-Persistence	1 (8)
Prior HSCT, N(%)	0	8 (67)
	1	4 (33)
Remission status before HSCT, N (%)	Empty marrow	4 (33)
	Persistent blasts	2 (17)
	CR with pos. MRD	2 (17)
	CR with neg. MRD	4 (33)
Donor Type, N (%)	9/10 MUD	1 (8)
	10/10 MUD	4 (33)
	MSD	2 (17)
	5/10 MMFD (Haplo)	5 (42)
Number of VENDEC cycles, N	Median (Range)	7 (1-10)



Conclusions: Venetoclax plus decitabine appears feasible and well tolerated as post-HSCT maintenance in children with VHR-AML, with encouraging survival outcomes compared with an expected EFS of <30% in this population. Despite limitations related to small sample size and retrospective design, these data support prospective studies to define personalized, risk-adapted maintenance strategies in pediatric AML.

Disclosure: Nothing to declare.

B210

MMUD VS MATCHED DONORS IN PEDIATRIC HSCT SETTING: TIME TO RE-THINK GVHD PROPHYLAXIS STRATEGIES?

EBMT 52nd Annual Meeting
Madrid, Spain
22-25 March 2026
#EBMT26
Advancing the Art of Patient Care

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Background: The use of Mismatched unrelated donors (MMUD), a subgroup of the so-called "alternative donors", although increasingly widespread in adult and pediatric HSCT, raises concerns about transplant outcome, since GvHD risk might be increased. Optimizing GvHD prophylaxis in MMUD HSCT is crucial, especially in hematological disease where no graft-versus-leukemia effect is of interest.The present study aims to detect any differences in transplant outcomes according to the donor used (MMUD vs matched) in a single Institution's pediatric dataset.

Methods: A large cohort of pediatric patients, who underwent MUD HSCT for malignant and non-malignant disease with an homogeneous GvHD prophylaxis regimen (r-ATG, Ciclosporin A and short course Methotrexate) was reviewed. Patients were categorized according to stem cell donor as "Matched" (10/10 HLA matching at loci HLA-A, B, C, DRB1, DQB1) or "MMUD" (9/10 or lower HLA matching at the same loci) and and the groups were compared in terms of engraftment times, acute and chronic GvHD prevalence, transplant-related mortality (TRM) and OS and EFS, considering relapse and graft failure as events. Patients were not censored according to the number of transplants (1 or > 1). Groups were compared for categoric variables using the Chi-squared test with Yates correction. The probability of OS and DFS was estimated using the Kaplan–Meier method. NRM, relapse incidence and GvHD occurrence were expressed as cumulative incidence (CI) curves. The log-rank test was used to estimate differences between curves.

Results:

Patients' characteristics are summarized in Table 1.

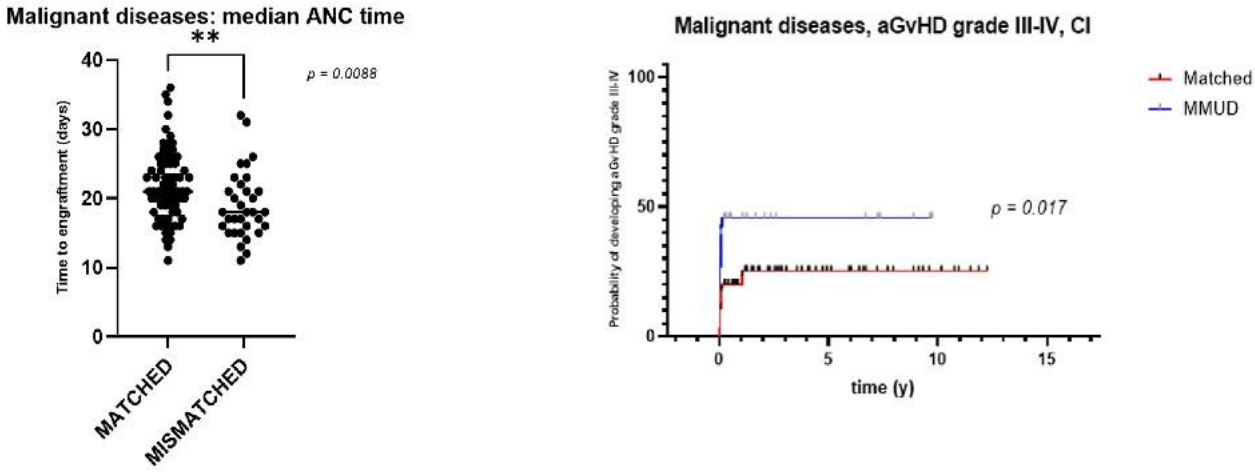
TABLE 1.

		a) Malignant diseases				**b) Non-malignant diseases**	
		MMUD	**MATCHED**			**MMUD**	**MATCHED**
n° transplants 108		33/108 (30.6%)	75/108 (69.4%)	47		18/47 (38.3%)	29/47 (61.7%)
n° patients 106		33	73	45		18	27
median age at HSCT (years)		11.1	9			7.9	7.4
Underlying disease	**ALL**	17/33 (51.5%)	48/75 (64%)		**SAA**	7/18 (38.9%)	8/29 (27.6%)

	AML	9/33 (27.3%)	14/75 (18.7%)		**Immunodeficiency**	5/18 (27.8%)	8/29 (27.6%)
	other (NHL, MDS)	7/33 (21.2%)	13/75 (17.3%)		**Hemoglobinopathies**	2/18 (11.1%)	3/29 (10.3%)
					Metabolic disease	2/18 (11.1%)	6/29 (20.7%)
					other (FA, other BMFs)	2/18 (11.1%)	4/29 (13.8%)
median engraftment time ANC (days)		18	21			24	23
median engraftment time PTL (days)		24	25			29	25
aGvHD any grade		24/33 (72.7%)	47/75 (62.7%)			5/18 (27.8%)	11/29 (37.9%)
aGvHD gr. III-IV		15/33 (45.4%)	18/75 (24%)			1/18 (5.6%)	4/29 (13.8%)
cGvHD		6/33 (18.18%)	16/75 (21.3%)			0/18	2/29 (6.9%)
cGvHD severe		2/33 (6%)	5/75 (6.6%)			0/18	1/29 (3.4%)
death		10/33 (30.3%)	23/73 (31.5%)			2/18 (11.1%)	2/27 (7.4%)
relapse		6/33 (18.18%)	21/73 (28.7%)	**graft failure**		1/18 (5.6%)	4/29 (13.4%)
death due to TRM		6/10 (60%)	7/23 (30.4%)			2/2 (100%)	2/2 (100%)
death due to relapse		4/10 (40%)	16/23 (69.6%)				

108 MUD HSCT were performed in 106 patients affected by malignant disease in a 15 year interval, with the main indication being ALL. The majority (nearly 70%) were transplanted from a matched donor. In the same timespan, 47 MUD HSCT were performed in 45 patients with non malignant disease, mostly severe aplastic anemia (AAS) and immunodeficiencies. 61.7% of them received HSCT from a matched donor. ANC recovery time resulted significantly shorter in the Matched group for malignant diseases (p = 0.0088, figure 1a), while no difference was observed for platelets recovery. This finding was not confirmed for non-malignant diseases. CI of grade III-IV aGvHD was significantly higher in the MMUD group for malignant diseases (p = 0.017, figure 1b) , while no difference was observed in OS, EFS, CI of cGvHD and TRM either in malignant and non-malignant diseases.

Figure 1
a) b)



Conclusions: Our data show that the use of MMUD donors is associated with higher probability of severe aGvHD in malignant diseases. This does not result in an increased TRM, suggesting that GvHD can be successfully cured, but such observation raises the question whether our own GvHD prophylaxis policy in pediatric patients undergoing HSCT from MMUD donors should be modified, i.e. with the use of PT-Cy and Abatacept, as many adult centers are already doing even outside the haplo-setting.

Disclosure: Nothing to disclose.

B211

BELUMOSUDIL USE FOR CHRONIC GRAFT-VERSUS-HOST DISEASE IN CHILDREN: EXPERIENCE FROM THE PEDIATRIC SUBCOMMITTEE OF THE SPANISH GROUP FOR HSCT AND CELL THERAPY (GETH)

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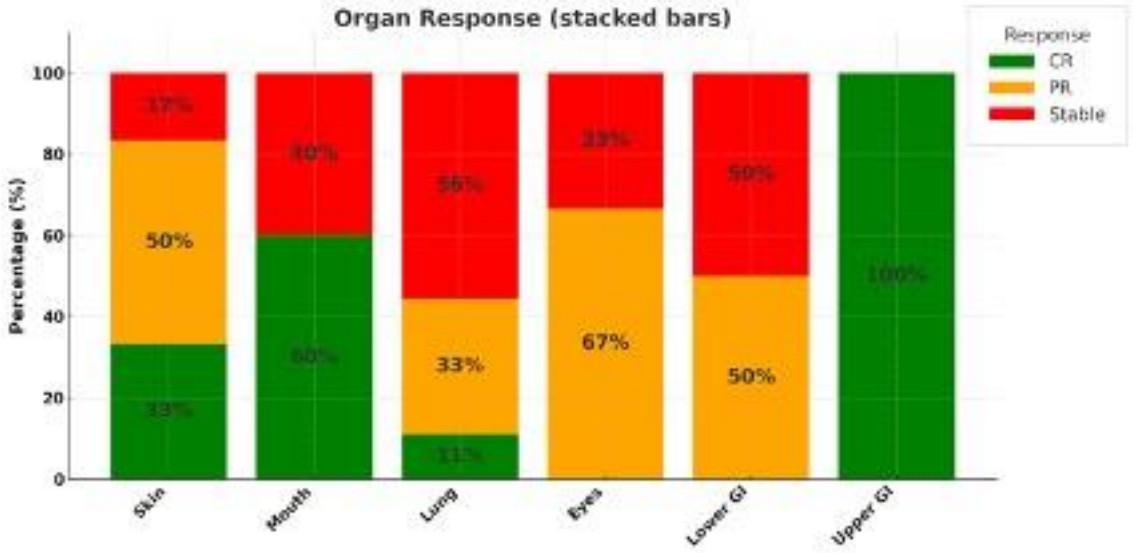
Background: Belumosudil is a selective inhibitor of the kinase ROCK2 (Rho-associated coiled-coil kinase 2), approved by FDA for the treatment of chronic GVHD in patients 12 years of age or older who have received at least two prior lines of therapy. In children, experience is limited to clinical case reports because it is still in the trial phase.

Methods: We conducted a retrospective study including 15 children in 8 Spanish centers within the Pediatric group of GETH who received belumosudil as third or subsequent line for cGVHD treatment between May 2023 and August 2025.

Results: Median age at belumosudil start was 14 years (range, 11-20) and half of patients were boys. Most of patients have acute leukemia (5 AML and 4 ALL) and the remainder six patients have a non-malignant disease. Nine children were transplanted from a HLA-identical donor and 6 from an haploidentical donor. GVHD prophylaxis consisted of cyclosporine and methotrexate in 6 cases, post-transplant cyclophosphamide in 6 cases, and T-cell depletion in 3 cases. Median time from allo-HSCT to belumosudil start was 3 years (range, 1-10 years) and median time from cGVHD diagnosis to belumosudil start was 2 years (range, 5 months-10 years). At belumosudil start, cGVHD was moderate in 9 and severe in 6 patients according to 2014 NIH criteria. Patients had received a median of 4 prior lines of therapy for cGVHD (range, 2-8) including steroids in 15, ruxolitinib in 14, extracorporeal photopheresis in 12, mesenchymal cells in 5 and ibrutinib in 4 patients.
Median follow-up after belumosudil treatment was 7 months (range, 3-30)**.** Twelve patients received 200 mg/d, 2 patients 400 mg/d and 1 patient 200 mg/48h**.** Two patients discontinued treatment after a median of 4 months, 1 because lack of efficacy and 1 due to suspected adverse events**.** Overall survival was 92%. Only one patient died by IFI.
Overall response rate (ORR) was 60%**,** all were partial responses. There were no cases of progression. Median time to response was 6 months. Nine children discontinued their concomitant treatments. The best responses were achieved in the skin, mouth, and upper gastrointestinal tract (Figure 1). It is important to highlight the overall lung response of 44%.



Conclusions: In pediatric patients, belumosudil treatment was safe and cGVHD response was obtained in 60% of cases. Now it is necessary to determine the appropriate dosage in children through clinical trials.

Disclosure: Nothing to declare.

B212

A PILOT MULTICENTRE FEASIBILITY STUDY OF REAL-TIME PHARMACOKINETIC-GUIDED FLUDARABINE DOSING IN CHILDREN RECEIVING CD19-DIRECTED CAR T-CELL THERAPY FOR RELAPSED/REFRACTORY B-CELL LEUKAEMIA

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Background: Tisagenlecleucel, a CD19-directed CAR T-cell therapy, has transformed the treatment of relapsed or refractory (R/R) paediatric B-cell acute lymphoblastic leukaemia (ALL). In the UK paediatric cohort, ~90% of patients achieve complete remission following CAR T-cell infusion but ~50% of responders subsequently experience treatment failure including frank/MRD relapse or loss of B-cell aplasia. Lymphodepleting chemotherapy with

fludarabine and cyclophosphamide is critical for promoting CAR T expansion and persistence. Prior studies have demonstrated that achieving minimum fludarabine exposure thresholds (cumulative area under the curve (cAUC) >14mg.h/L) enhances patient outcome. In children, substantial interpatient variability in fludarabine pharmacokinetics is observed when body surface area (BSA)–based dosing is utilised, therefore therapeutic drug monitoring (TDM) to individualise exposure may improve patient outcomes.

Methods: Children (<18 years) with R/R B-ALL receiving CAR T-cell therapy were prospectively enrolled in the NCCPG TDM 2018 clinical trial across 3 paediatric CAR T-cell treatment centres in the UK (Newcastle, Manchester, UCL). All patients received standard lymphodepletion consisting of fludarabine (30mg/m^2 on days -6, -5, -4 and -3) and cyclophosphamide (500mg/m^2 on days -6 and -5). Fludarabine was given over 30 minutes and PK samples were taken at 0, 1, 3 and 6 hours post end of fludarabine infusion. A fully validated liquid chromatography-tandem mass spectrometry assay was used to measure fludarabine concentrations. PK analysis was conducted using a 3-compartment population PK model using InsightRX. Real-time analysis was conducted to enable dose adjustments of 3rd and 4th fludarabine doses to target a cAUC of 16-20mg.h/L. For a subset of patients, further PK analysis was conducted on day 4 following dose adjustment.

Results: Twenty-one patients were included with a median age of 13.2 years (range 1.3 - 18). All except one (Obicel) received tisagenlecleucel. The median cAUC was 18.1 (10.2-26mg.h/L) (Table 1). Nine patients (43%) achieved exposures <16mg.h/L, increasing the risk of CAR T failure. Eight patients (38%) achieved exposures >20mg.h/L, increasing the risk of drug toxicity. Required dose adjustments to target a cAUC of 18mg.h/L ranged from 59.7 - 187% of the total protocol dose and all dose adjustments were implemented in real-time. Three patients underwent additional TDM to validate dose adjustments, with final predicted AUCs within 6% of the targeted exposure (figure 1B).
Model-predicted exposures (median 15.4 (13.2 - 25.6mg.h/L) were significantly different from the measured-predicted exposures after incorporating concentration-time data into the model (median 18.1 (10.2 - 26mg.h/L) ($p<0.05$) with no pattern of over or under prediction. Had model-based dosing (MBD) alone been utilised, potentially suboptimal exposures would have been missed for 10/21 patients (47%).

Table 1

	Patient Age (Years)	
	1-13 (n= 10)	**³ 13 (n= 11)**
Weight (kg), Median (range)	23.1 (9.2 - 49.8)	42.5 (21.1 - 71.6)
BSA (m^2), Median (range)	0.88 (0.46 - 1.4)	1.35 (0.82 - 1.88)

Creatinine (mmol/L), Median (range)	27.5 (10 - 47)	41 (16 - 60)
cAUC (mg.h/L), Median (range)	17 (10.2 - 24)	18.1 (13.2 - 26)
Patients with cAUC 16-20 mg.h/L n (%)	2 (20)	2 (18)
Patients with cAUC <16 mg.h/L n (%)	5 (50)	4 (36)
Patients with cAUC >20 mg.h/L n (%)	3 (30)	5 (45)
MBD dosing cAUC (mg.h/L), Median (range)	15 (13.2-29.9)	15.7 (14.6-25.6)
Percentage difference between measured PK and MBD cAUC, Median (range)	6.4 (-22.7 - 69.6)	8.1 (-12 - 64)

Figure 1

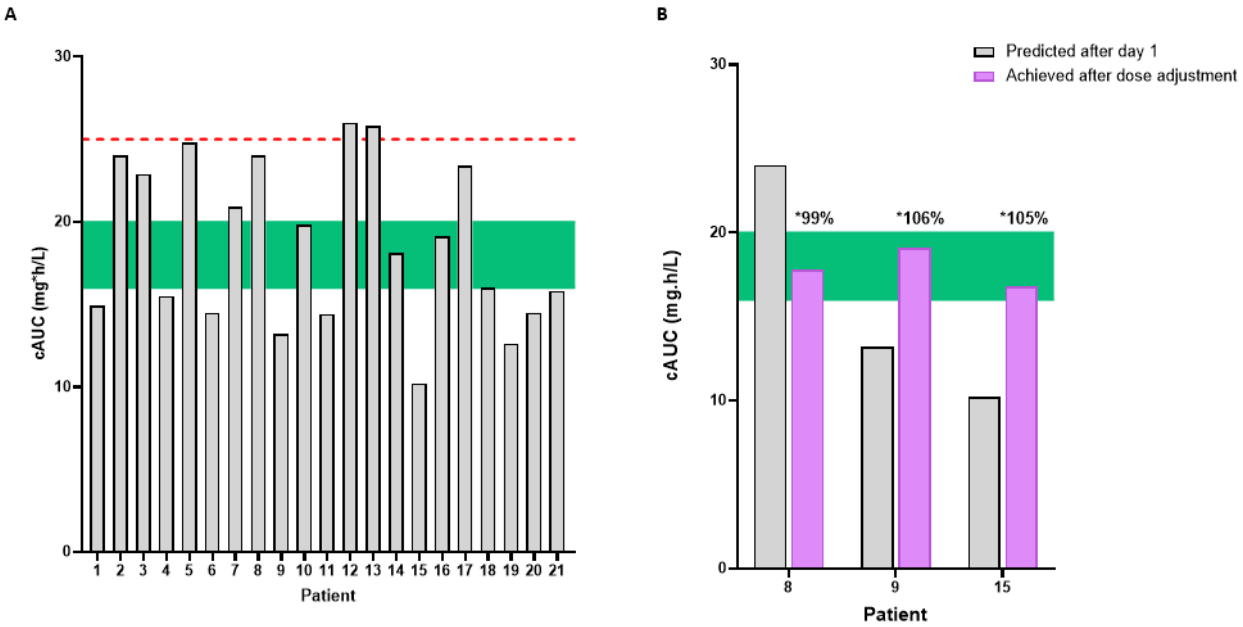

*Figure 1 A) cAUC achieved at a dose of 30 mg/m2/day x 4 (mg.h/L) (n=20). Shaded green area represents the proposed therapeutic window. Red dashed line represents a potential exposure toxicity threshold. B) cAUC achieved for 3 patients on day 1 and day 4 of treatment following a dose adjustment. *Indicates the % of the target AUC achieved following dose adjustment.*

Conclusions: These pilot data indicate considerable interpatient variability in fludarabine exposure in paediatric patients with R/R B-ALL receiving CAR T-cell therapy. BSA and model-based precision dosing were insufficient to reliably achieve target exposures, demonstrating the need for adaptive dosing strategies. Real-time therapeutic drug monitoring is feasible. Building on these findings, a dedicated clinical trial (Goldilocks) is now opening across all UK paediatric CAR T centres to implement real time PK-guided fludarabine dosing for children undergoing CD19-directed CAR T-cell therapy.

Clinical Trial Registry: NCCPG TDM 2018 - ISRCTN10139334 - https://www.isrctn.com/ISRCTN10139334
Goldilocks – ISRCTN10473740 - https://www.isrctn.com/ISRCTN10473740

Disclosure: Nothing to declare

B213

SURFACTANT PROTEIN D IN PLASMA MAY PREDICT BRONCHIOLITIS OBLITERANS AFTER PEDIATRIC HSCT

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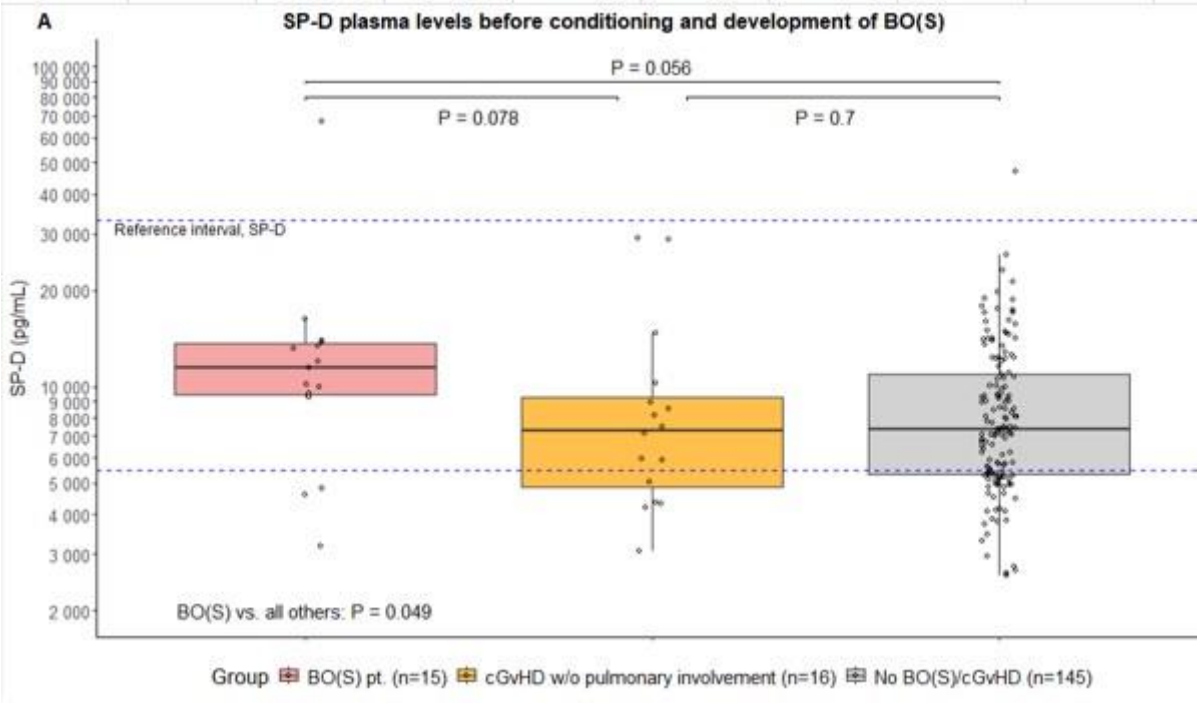
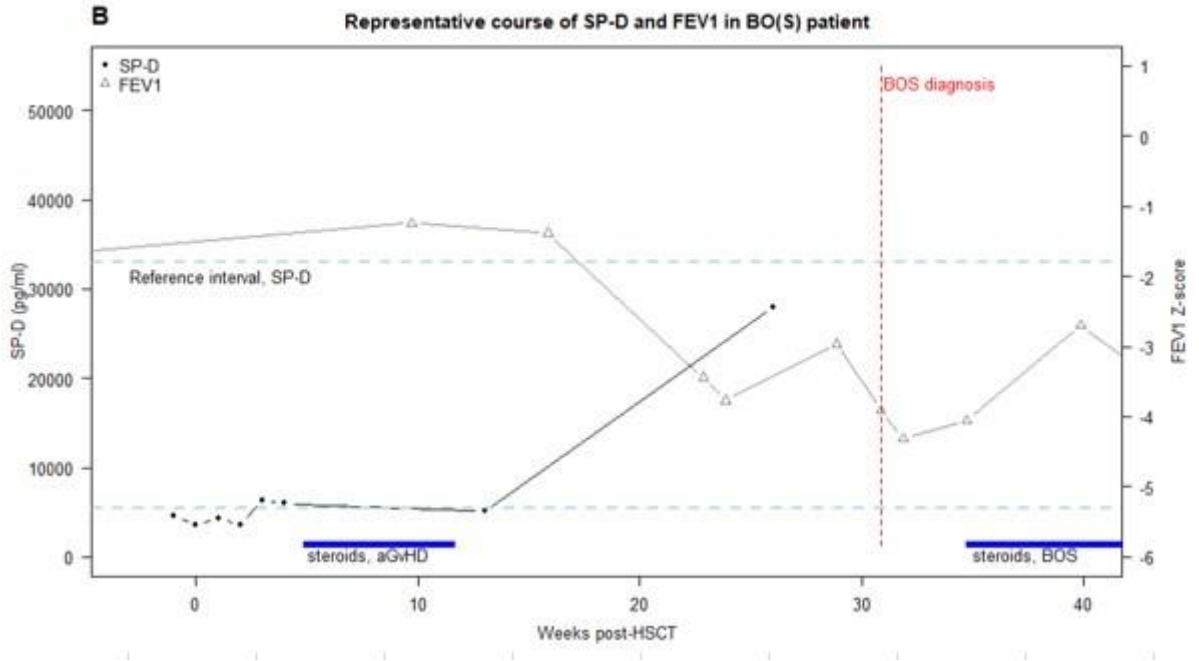
Background: Bronchiolitis obliterans and bronchiolitis obliterans syndrome (BO(S)) are severe and potentially life-threatening pulmonary complications after HSCT. Early treatment is crucial to prevent irreversible lung damage, but definitive diagnosis relies on invasive procedures such as lung biopsy and/or HRCT combined with pulmonary function tests - methods that can be challenging in young children and may fail to detect early disease. This calls for less invasive diagnostic tools, including biomarkers.
Surfactant protein D (SP-D), a component of the pulmonary innate immune system, shows elevated plasma levels during viral lower respiratory tract infections and exacerbations of COPD. We investigated SP-D as a potential biomarker for BO(S) in pediatric HSCT.

Methods: We prospectively included 178 children undergoing their first HSCT from 2010-2023 (Table), and 200 healthy children as controls (median age (range): 11.7 years (6-18.8)). BO(S) diagnosis was based on modified NIH guidelines and defined as either cGvHD in lung biopsies or the combination of >10% decrease in FEV1 from baseline, FEV1/FVC <0.7, and air trapping on HRCT.
Plasma levels of SP-D were measured by Luminex before conditioning and on days 0, +7, +14, +21, +30, +60, +90, +180 and +365 post-HSCT.

Results: Pre-conditioning SP-D levels were significantly lower in HSCT recipients than in healthy children (7620 vs. 12898 pg/mL, P<0.0001), although variability was high in both groups. SP-D levels were not associated with age, sex, diagnosis, conditioning regimen, donor type, or graft type at any timepoint.

Children who developed aGvHD grade II-IV, (n=56), had significantly higher SP-D levels pre-conditioning, and on day 0 and +14 compared to patients with aGvHD grade 0-I (pre-conditioning: 9209 vs. 7347, p=0.026), but not at later time points. SP-D levels were influenced by use of systemic corticosteroids, declining after initiation of treatment and increasing after discontinuation. Of the patients with aGvHD grade II-IV, 12 (21.4%) later developed BO(S) (P=0.0001).
15 patients (8.4%) developed BO(S) at median day +181 (range: 70-342) post-HSCT; including two fatal outcomes. Pre-conditioning SP-D levels were significantly elevated in patients who later developed BO(S) compared to those who did not (P=0.049) and patients who developed cGvHD without pulmonary involvement (P=0.078) (figure A). No association was found between pre-conditioning SP-D levels and pre-existing or current respiratory disease, including active infection, radiological abnormalities, and FEV1 Z-score (all P≥0.05). In patients with BO(S), post-HSCT SP-D levels and FEV1 Z-scores showed a tendency towards inverse correlation (Figure B). Leading up to the BO(S) diagnosis, SP-D levels increased in patients not actively treated with steroids (n=7). In all BO(S) patients, SP-D levels generally declined after initiation of steroid treatment, except for the two fatal cases where SP-D levels initially fell but subsequently rose again.





Characteristics	N=178

Recipient age (years), median (range)	8.7 (1.1-17.9)
Female recipient sex, no. (%)	71 (39.9%)
Diagnosis, no. (%)	24 (13.5%)
AML	47 (26.4%)
ALL	34 (19.1%)
Other malignant	36 (20.2%)
PID	15 (8.4%)
SAA	22 (12.4%)
Other benign	
Graft type, no. (%)	143 (80.3%)
Bone marrow	26 (14.6%)
Peripheral blood	9 (5.1%)
Umbilical cord blood	
Donor match, no. (%)	40 (22.5%)
MSD (10/10) or MMRD (9/10)	111 (62.4%)
MUD (10/10 or 9/10)	17 (9.6%)
Haplo-identical parent (5/10)	10 (5.6%)
UCB	
Conditioning regimen, no. (%)	
12 Gy TBI + VP16/Cy	35 (19.7%)
Cy + Bu + Mel	36 (20.2%)
Flu + Thio + Bu/Treo	42 (23.6%)
Other chemotherapy-based regimes (MAC)	45 (25.3%)
RIC (Cy / Cy+Flu / TBI 2 Gy + Cy)	20 (11.2%)

Anti-thymocyte globulin as part of conditioning, no. (%)	141 (79.2%)
Sex mismatch (female donor to male recipient)**, no. (%)**	39 (21.9%)
Pulmonary function prior to HSCT (n=110), median (range) FEV1 (Z-score) FVC (Z-score)	-0.92 (-3.59 – 5.55) -0.66 (-3.75 – 3.34)

Conclusions: Elevated plasma levels of SP-D before conditioning were associated with the development of BO(S), but not cGvHD without pulmonary involvement, nor pre-exiting pulmonary disease. These findings suggest that elevated SP-D pre-conditioning may reflect low-grade pulmonary inflammation that either directly or indirectly predisposes to BO(S) and indicate that SP-D may be a potential biomarker for the risk of BO(S) in pediatric HSCT.

Disclosure: None.

B214

HAPLOIDENTICAL HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN USING CD3/CD19 DEPLETED GRAFTS: RESULTS OF A MULTICENTRE PHASE I/II STUDY

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Background: The objective of our study was to investigate the clinical feasibility of haploidentical hematopoietic stem cell transplantation (HSCT) in children using CD3+ and CD19+ depletion of the graft, combined with a reduced-toxicity conditioning regimen. We aimed to assess the effects of both the depletion method and the conditioning regimen on

transplant success, toxicity and potential complications. As survival rates improve, late effects of transplants become increasingly significant and must be considered when evaluating the transplant approach.

Methods: Between 2003 and 2013, children and adolescents with both malignant and non-malignant diseases were included in the study and underwent transplantation at seven centers in Germany and Austria. CD3+ and CD19+ depletion of PBSC grafts was performed using the CliniMACS system with magnetic microbeads. A primarily melphalan-based conditioning protocol with reduced toxicity was applied, alongside standard conditioning protocols. In 2024, aftercare clinics, as well as patients and their families, were contacted to assess late effects.

Results: A total of 157 transplants were performed as part of the study. Stable engraftment was achieved in 85% of patients (primary engraftment 95.5%, secondary graft failure 10.8%). Natural killer (NK) cells recovered rapidly, reaching a mean of 300/µl by day +14, while CD3+ cells recovered more slowly, reaching 186/µl after 3 months. The cumulative incidence (CI) of aGvHD III-IV° was 6.4%. Among patients with malignant disease, 55.5% experienced relapse, which was particularly influenced by pre-transplant remission status. Event-free survival at 1 year was 34%, with relapses being the most frequent event. Non-relapse mortality at 1 year was 7.9%. Reactivation of CMV or ADV in the blood was detected in 17.2% and 10.8% of patients, respectively, but less than half developed clinical symptoms. In the long term, serious infections barely occurred. Overall survival was 40%, with a median follow-up of over 12 years. Long-term sequelae were not increased compared to allogeneic HSCT from matched donors. On the contrary, reduced conditioning toxicity and the avoidance of TBI might have reduced certain late sequelae (CI of secondary malignancies 7.7%).

Conclusions: Haploidentical HSCT with CD3/CD19-depleted grafts is feasible and safe in children. Graft manipulation was effective, resulting in low levels of transplanted CD3+ cells, which led to a reduced incidence of critical aGvHD. Rigorous monitoring for viral reactivation, combined with pre-emptive therapy, largely prevented clinical disease. Immune reconstitution was satisfactory, and, in the long term, a functioning immune system derived from the donor was established.
The conditioning regimen was well tolerated, even in heavily pre-treated patients, with a low non-relapse mortality. It also appeared to be beneficial in the long term, including a reduced risk of developing secondary malignancies.
For high-risk patients who did not achieve remission pre-transplant and for those with solid tumors, our regimen was insufficient to reduce relapse risk. However, for patients with adequate remission status it might be suitable. Since prolonged post-transplant immunosuppression is no longer required, our approach represents an optimal platform for several pre-emptive strategies to prevent relapse. These results strongly support the potential role of this haplo-HSCT approach and its evolution, including TCR-alpha/beta and CD45RA depletion.

Clinical Trial Registry: NCT01919866

Disclosure: Nothing to declare.

B215

EMAPALUMAB FOR THE TREATMENT OR PROPHYLAXIS FOR GRAFT FAILURE AFTER HSCT IN CHILDREN

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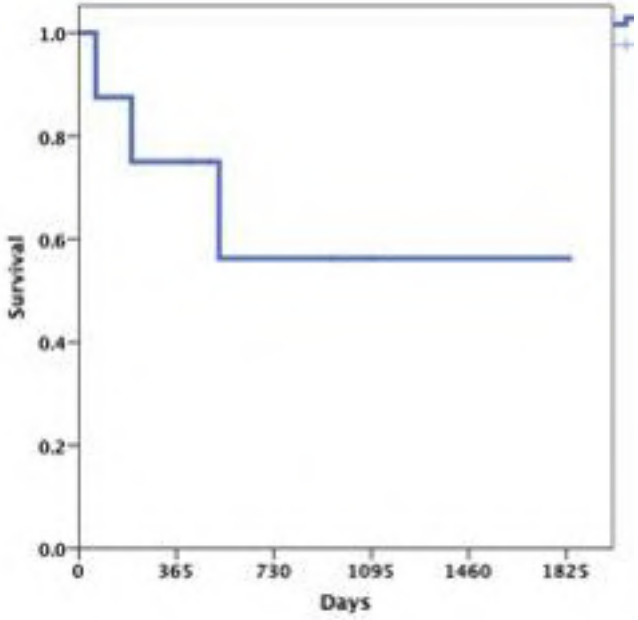
Background: Graft failure (GF) is a severe complication of allogeneic hematopoietic stem cell transplantation (HSCT) and leads to inferior overall survival (OS). The mechanisms involved in this phenomenon are still not completely understood. Interferon gamma (IFNγ) is particularly elevated in graft rejection and prior studies report the essential contribution of IFNγ in this phenomenon. Emapalumab is a fully human IgG1 monoclonal antibody directed against IFN γ and was approved in 2018 by the FDA for primary HLH who have refractory, recurrent or progressive disease or intolerance with conventional HLH therapy. Preliminary efficacy findings suggest Emapalumab merits further study as a potential graft rejection therapy.

Methods: We perform a retrospective study including pediatric patients undergoing HSCT who were treated with emapalumab either as prophylaxis or as treatment for primary or secondary GF since 2022 to 2024. Seven children with a median age of 10 years (range: 2-15) were included. Three was diagnosed of ALL, two of AML and two patients were diagnosed of non-malignant disease. Six patients underwent an haploidentical T-cell depleted peripheral blood transplant and the other one received a bone marrow HLA-identical unrelated donor (UD) transplant. Conditioning regimen was myeloablative in 6 cases and reduce toxicity in one child. Emapalumab was administered for treatment in six patients (5 with secondary GF and 1 with primary GF) and for prophylaxis in the other one with a history of previous GF secondary to HLH. Patients in the "treatment group" (n=6) received Emapalumab once signs and symptoms of graft rejection appeared associated with methylprednisolone and G-CSF. Hemophagocytosis was seen in the bone marrow in 4/6 patients and median ferritine levels at the time of graft failure diagnosis was 6378 ng/ml (range:2358-14255). The other child received Emapalumab for prophylaxis immediately after the graft infusion of the second transplant and continued twice a week until sustained engraftment.

Results: In the treatment group 50% (3/6) of HSCTs achieved engraftment after Emapalumab, while graft rejection occurred in the remaining three patients who received another allogeneic transplantation. In these 3 children Emapalumab was administered for prophylaxis in the second transplant and they all achieved engrafment and full donor chimerism. Across the entire group, the median Emapalumab dose was 3 mg/kg (range 1-6) and the median number of doses was 10 (range 2–26). Emapalumab was well-tolerated in all the cohort. With a median follow-up of 32 months, the overall survival (OS) was 57±10%.

Two patients died from relapse and one from thrombotic microangiopathy.



Conclusions: Currently, there is no effective treatment for graft failure other than a second-transplant. Therefore, Emapalumab could be effective in some patients avoiding the morbidity and mortality associated with a second HSCT. Prospective studies with a larger number of patients are needed to evaluate the efficacy and safety of this drug.

Disclosure: Nothing to declare

B216

TREOSULFAN OR BUSULFAN: DETERMINANTS OF RELAPSE RISK WITH DIFFERENT CONDITIONING REGIMEN IN CHILDREN WITH ACUTE MYELOID LEUKEMIA

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Background: Treosulfan-based (TREO) conditioning regimens have increasingly been adopted in pediatric acute myeloid leukemia (AML) undergoing hematopoietic stem cell transplantation (HSCT) as an alternative to busulfan-based (BU) protocols, with the aim of reducing treatment-related toxicity while maintaining anti-leukemic efficacy. Specifically,

children > 12 years-old historically showed higher risk of non-relapse mortality (NRM) with intensive BU-based protocols. However, comparative evidence on post-transplant outcomes remains limited.

Methods: We retrospectively evaluated outcomes of patients with AML undergoing their first allogeneic HSCT at Fondazione IRCCS San Gerardo dei Tintori (Monza, Italy) between 2011 and 2025. BU containing regimens included BuCyMel, BuFlu, BuFluTT and BuCy. TREO containing regimen included TreoFluTT and TreoFlu. Cox proportional-hazards models were used for multivariable analysis. Cumulative incidence of relapse and NRM were calculated using competing-risks methods with Gray's test. Stringent complete remission (sCR) was defined as morphologic CR with negativity for residual disease (MRD) by flow cytometry or PCR. Any MRD positivity was classified as no sCR. cGRFS was defined as time to chronic GVHD, relapse or death.

Results: A total of 77 children met inclusion criteria (median age 9 years, range 0.5–17), with a median post-transplant follow-up of 4.3 years (IQR 1.4–8.7).
Characteristics of the two groups are depicted in Table 1 (BU: n=57; TREO: n=20).

Variable	**Total[1] (n=77)**	**BU-based (n=57)**	**TREO-based (n=20)**	**p-value**
Sex				>0.999
M	44 (57%)	33 (58%)	11 (55%)	
F	33 (43%)	24 (42%)	9 (45%)	
Age at HSCT	9 [3–14]	7 [3–13]	12 [7–16]	0.050
Year of HSCT	2017 [2015–2021]	2016 [2014–2020]	2020 [2020–2022]	0.036
Phase at HSCT				0.442
CR1, MRD–	55 (71%)	40 (70%)	15 (75%)	
CR2, MRD–	8 (10%)	5 (8.8%)	3 (15%)	
No sCR	14 (18%)	12 (21%)	2 (10%)	
Donor type				0.304
Matched	64 (83%)	49 (86%)	15 (75%)	
Mismatched	13 (17%)	8 (14%)	5 (25%)	

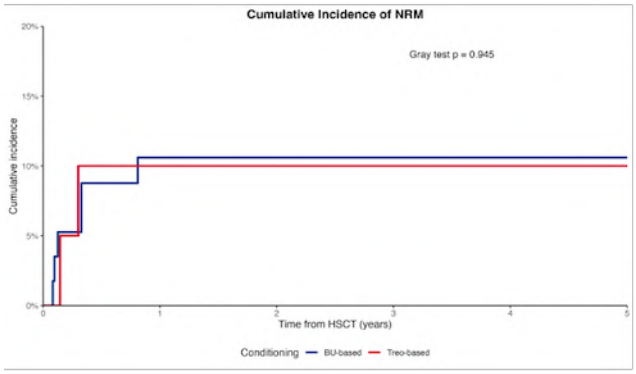
Stem cell source				0.647
BM	71 (92%)	53 (93%)	18 (90%)	
PB	6 (7.8%)	4 (7.0%)	2 (10%)	
[1]n (%); Median [Q1–Q3]				

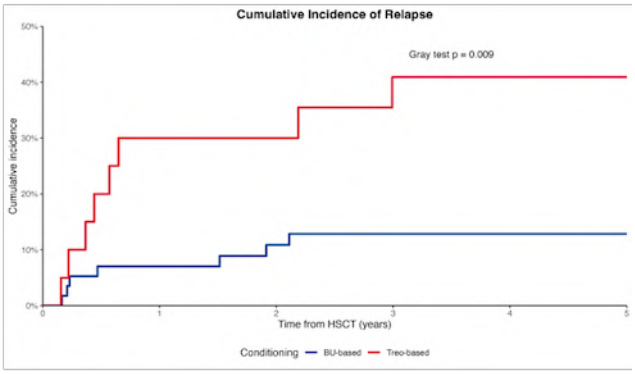
Patients were comparable within the 2 groups for remission status at HSCT, donor matching and stem cells source. Patients receiving TREO were significantly older (median 12 vs 7 years, p=0.05) than those receiving BU. HSCT outcomes showed no significant differences in time to neutrophils/platelet engraftment and risk of aGvHD and cGvHD. 3-year OS was 82.0% (95% CI 72.5–92.8) for BU and 64.6% (95% CI 46.6–89.6) for TREO (p=0.15). 3-year EFS was 76.5% (95% CI 66.1–88.6) for BU and 49.1% (95% CI 31.2–77.3) for TREO (p=0.027). Competing-risks analysis showed a higher 3-year cumulative incidence of relapse in the TREO group (40.9% vs 12.9%; p=0.009), while non-relapse mortality was similar between groups (10.6% vs 10.0%; p=0.945). In multivariable Cox models, conditioning regimen was not significantly associated with OS (HR 2.09, 95% CI 0.78–5.59; p=0.14), however TREO was associated with a lower EFS (HR 2.85, 95% CI 1.19–6.83; p=0.019). 3-year cGRFS was 67.6% (95% CI 56.3–81.2) for BU and 44.4% (95% CI 27.1–72.9) for TREO (p=0.06). sCR status was the strongest independent predictor across all models (OS: HR 2.51, p=0.009; EFS: HR 2.35, p=0.007; GRFS: HR 1.85, p=0.041), whereas age and donor type did not show independent associations with outcomes.

Conclusions: In our cohort, TREO was preferentially used in older patients, and NRM remained comparable between regimens. This observation is consistent with historical reports of higher TRM with BU in adolescents. However, patients receiving TREO had a lower EFS due to a higher cumulative incidence of relapse. Strategies to prevent relapse, including achieving deep remission before HSCT, are highly needed in this subgroup of patients. Confirmation of these findings will require larger multicenter cohorts and randomized studies comparing treosulfan and busulfan.

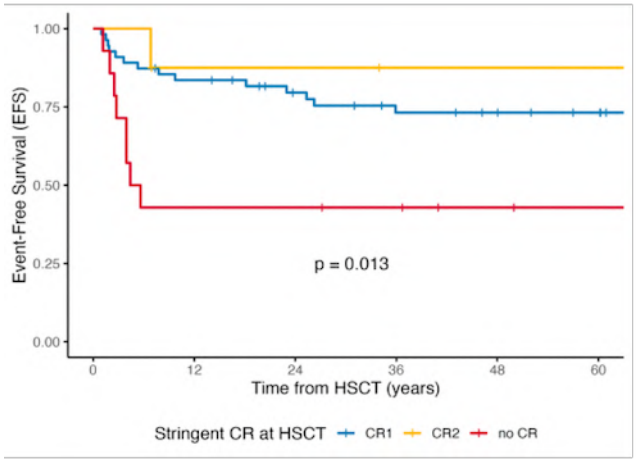
Figure 1.

A. Cumulative incidence of Relapse/NRM.





B. EFS by Stringent CR



Disclosure: Adriana Balduzzi: speaker's bureau fees from Medac.

B217

PROADRENOMEDULLIN (PRO-ADM) FOR EARLY IDENTIFICATION OF INFECTIOUS AND TRANSPLANT-RELATED COMPLICATIONS AFTER PEDIATRIC HCT: A PROSPECTIVE, MULTICENTER, OBSERVATIONAL STUDY

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Background: Infections (IDs) and transplant-related complications (TRCs)—including acute GVHD, sinusoidal obstruction syndrome, engraftment/pre-engraftment syndromes, transplant-associated thrombotic microangiopathy, cytokine release post-ATG/ATLG or PTCy—are leading causes of morbidity after pediatric allogeneic HCT and are closely linked to endothelial damage. Differentiating TRCs/IDs from benign 99febrile neutropenia (FN) in the early stages is challenging. Mid-regional proadrenomedullin (Pro-ADM), an endothelial biomarker, improves risk assessment in pediatric FN; however, evidence in HCT is limited.

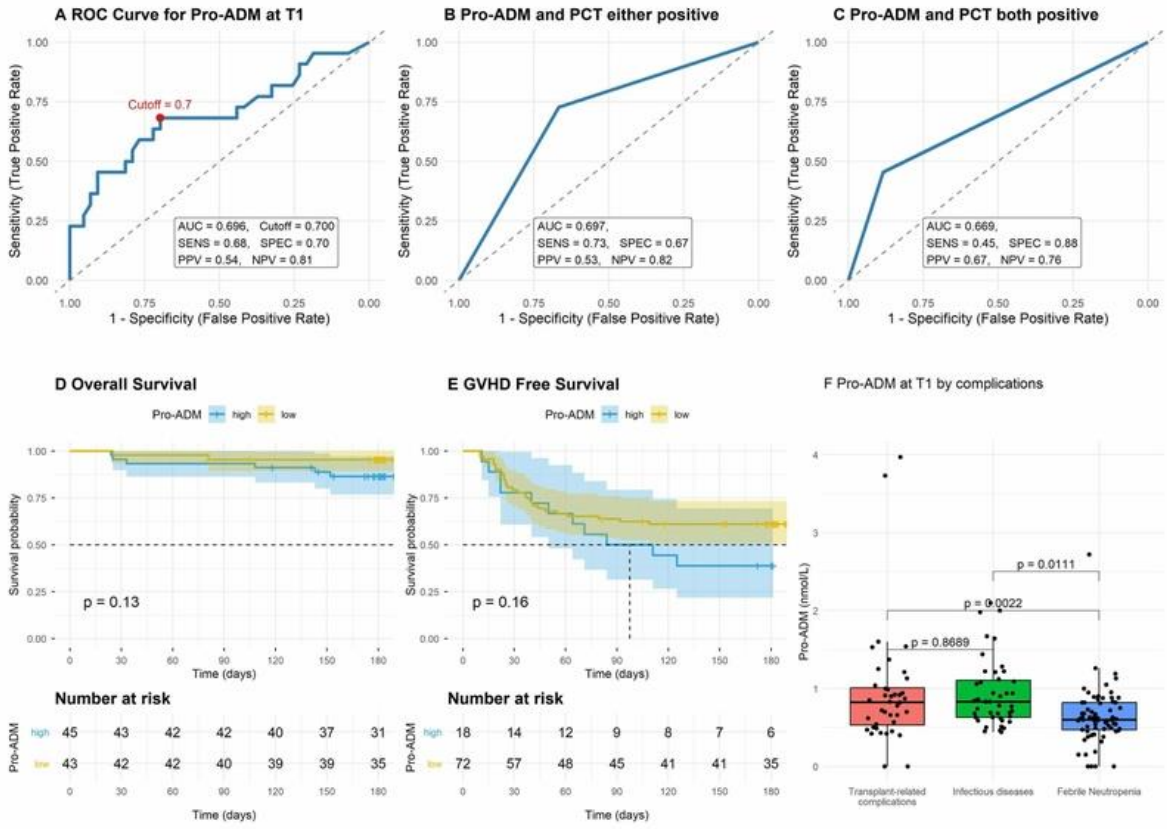
Methods: A multicenter, prospective, observational trial (NCT05523336) involving pediatric allogeneic HCT recipients with serial biomarker sampling. 99 patients enrolled, including 6 screening failures. Pro-ADM (nmol/L) and PCT levels were measured at baseline (before conditioning) and at three predefined time points (T1, T2, T3: days 0, 3, 10) when complications occurred. These were classified as TRCs, IDs, and FN, according to protocol-defined criteria. Linear mixed-effects models with patients as a random effect and Tukey-adjusted pairwise comparisons evaluated biomarker differences among complication types. ROC analyses at T1 assessed Pro-ADM alone and combined Pro-ADM+PCT strategies (either biomarker positive; both positive). Overall survival (OS) and GVHD-related survival were analyzed using Kaplan–Meier curves, stratified by high versus low Pro-ADM, with cutoff points determined via the maximally selected rank statistics.

Results: We examined 98 transplants (see Table 1 for patients' characteristics).

Patients' Characteristics	**1st HCT (N = 89)[1]**	**2nd HCT (N = 9)[1]**
Age ≤ 10 years	46 (50%)	2 (40%)
Malignancy	63 (68%)	5 (100%)
Disease status before HSCT		
CR1	35 (39.4%)	0 (0%)
CR2/CR3	11 (12.3%)	7 (77 %)
Persistent disease	43 (48.3%)	2 (22 %)

Patients' Characteristics	1st HCT (N = 89)[1]	2nd HCT (N = 9)[1]
Myeloablative conditioning regimen	79 (89%)	9 (100%)
Donor		
MFD	16 (18%)	0 (0%)
MMUD/Haplo	24 (27%)	2 (22%)
MUD	49 (55%)	7 (78%)
Stem cell source		
BM	50 (57%)	4 (44%)
PBSC	39 (43%)	5 (55%)
GVHD prophylaxis including ATG	57 (63%)	5 (55%)
GVHD prophylaxis including PTCY	17 (20%)	4 (44%)
[1]n (%)		

We analysed 40 TRCs, 44 IDs, 69 FN episodes. Across serial episodes, median (IQR) Pro-ADM at T1 was higher in TRCs and IDs than in FN: 0.83 (0.52-1.02) and 0.83 (0.63-1.12) versus 0.60 (0.47-0.82) (TRCs vs FN p=0.0022, IDs vs FN p=0.011). At T2, medians were 0.66 (0.52-1.00), 0.79 (0.62-0.92), and 0.55 (0.44-0.65) (TRCs vs FN: p=0.033); at T3, no significant difference was observed. Baseline Pro-ADM levels did not significantly differ among patients with subsequent TRCs, IDs, or FN. ROC analysis at T1 showed Pro-ADM alone had an AUC of 0.696 with a cutoff of 0.70 nmol/L (sensitivity 0.68; specificity 0.70; positive predictive value, PPV 0.54; negative predictive value, NPV 0.81). Combining Pro-ADM and PCT using a either positive rule did not significantly improve performance, whereas the both positive rule approach increased specificity (0.88) and PPV (0.67) while reducing sensitivity (0.45). Time-to-event analyses showed no significant difference in OS between high and low Pro-ADM groups; the cutoff matched the median biomarker value. Similarly, no significant difference was found for the GVHD-related survival endpoint (Figure 1).



Conclusions: In pediatric HCT, Pro-ADM and PCT are practical serial biomarkers that exhibit distinct patterns by episode type. Early measurement of Pro-ADM (T1) offers moderate yet clinically meaningful discrimination between TRCs/IDs and FN. Combining Pro-ADM with PCT in a series approach significantly enhances specificity and PPV for relevant complications, thereby identifying a high-risk group of patients who require closer monitoring and additional diagnostics. Conversely, low Pro-ADM levels support a more conservative treatment approach. Although no impact on short-term survival was observed, these results support the addition of Pro-ADM to early post-HCT assessment protocols and highlight the need for validation in larger cohorts and for future risk-based intervention studies.

Clinical Trial Registry: NCT05523336; https://clinicaltrials.gov/study/NCT05523336

Disclosure: No conflict of interest to disclose.

B218

REAL-WORLD EXPERIENCE WITH ISAVUCONAZOLE IN ALLOGENEIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS IN SPAIN

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Background: Fungal infections remain one of the main complications in patients undergoing hematopoietic stem cell transplantation (Alo-HSCT). Isavuconazole (ISV) is a next-generation broad-spectrum triazole that has been recently approved for the treatment for invasive aspergillosis and mucormycosis (when Amphotericin B is not appropriate) in children aged >1 year. The objective of our study is to share our national experience in terms of effectiveness and safety with the use of this drug in pediatric population undergoing Alo-HSCT, both in treatment and in prophylaxis for invasive fungal infections.

Methods: We present a retrospective, multicenter and observational study conducted in 12 hospitals of Spanish Group of HSCT and Cell Therapy (GETH-TC). Our objective was to evaluate the efficacy and safety of ISV use in patients <21 years undergoing Alo-HSCT from January 2019 to June 2025. One hundred patients (63 male, 37 female) with a median of 11 years (range:1-21) were included. The main diagnoses were ALL (36 %), non-malignant disease (34%), and AML (22%). Regarding the type of donor, 44 patients received an haploidentical transplantation, 23 match unrelated donor, 20 matched related donor and 13 mismatched unrelated donor. Most of patients received a mieloablative conditioning regimen (66%) and ICT was administered in 24% of the patients. For 80% was the first Alo-HSCT.

Results: In 70% of patients ISV was used as treatment and in 30% as prophylaxis. Thirty patients had acute graft versus-host-disease (aGVHD) and 20 had chronic GVHD when ISV was started. In the treatment group a total of 70 patients were included. The main reasons for selecting ISV were as second-line treatment due to toxicity with prior treatments (37%) but up to 30% of patients ISV was selected as first-line treatment. Infections were classified as probable in 33 patients (47%), possible in 27 patients (38%) and proven in 10 patients (14%). The most frequent diagnoses were Invasive Aspergillosis (n = 41; 58%). At the end of ISV treatment, 56 of 70 (80%) patients presented with a favourable response (51 complete response and 5 parcial). In the prophylaxis group a total of 30 patients were included, 17 (56%) as primary prophylaxis and 13 (44%) as secondary. Reasons for selecting ISV were a more favorable toxicity profile in 19 patients (63%). The rate of breakthrough IFI was 10% (n = 3). Therapeutic drug monitoring was performed in 69/100 patients. The median ISV dose to reach adequate levels was 6 mg/kg/day (range 2,6-16,6). In 33 patients, the dose had to be increased. Adverse events were reported in 11 patients

(11%) and 9 of them had interrupt the treatment because of it. With a median follow-up of 30 months for the HCST, the overall survival (OS) was 55±11% and only one patient died of invasive fungal infection.

Conclusions: In our experience, ISV appears to be safe and effective for treatment and prophylaxis of IFI in paediatric patients and shows a favorable toxicity profile. A significant proportion of patients showed ISV plasma levels out of the therapeutic range, highlighting the importance of monitoring levels in this population.

Disclosure: Nothing to declare.

B219

BANDICOOT: AN ADAPTIVE PLATFORM TRIAL DESIGNED TO IMPROVE THE COMPLICATIONS, COST-EFFECTIVENESS AND HEALTH OUTCOMES FOR CHILDREN RECEIVING A STEM CELL TRANSPLANT

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Background: Multiple challenges face haematopoietic stem cell transplant (HCT) clinical researchers, many of which are unique to this field. Importantly, traditional two-arm randomised trials using frequentist analysis might no longer be fit for purpose for HCT. Adaptive platform trials, which evaluate multiple interventions simultaneously, offer a solution, but rely on a shared primary endpoint that can be used for all interventions/subgroups. No such short-term outcome currently exists in the HCT literature. We designed and evaluated a novel ordinal endpoint within the first 100 days post-transplant for use in an APT, 'BANDICOOT: AN adaptive platform trial Designed to Improve the Complications, cost-effectiveness and health Outcomes for children receiving a stem cell Transplant'.

Methods: A multi-disciplinary working group co-designed and validated a novel ordinal endpoint through literature review, focus groups, and blinded expert input. The endpoint was then evaluated using data from *n*=202 paediatric HCT recipients at The Royal Children's Hospital in Melbourne by (i) examining the distribution of patients across endpoint categories; (ii) assessing the association with long-term outcomes; (iii) evaluating if exposures with known efficacy had the expected associations with endpoints in a multivariate analysis adjusting for pre-transplant factors; and; (iv) assessing feasibility of collection from a clinician and consumer perspective.

Results: Through co-design with clinicians and individuals with lived experience, a primary ordinal endpoint that includes (i) CD4+ reconstitution; (ii) viral infection; CMV, EBV, HHV6 and adenovirus (at viral threshold and viraemia duration) and (iii) major and minor organ support was established (Table in Figure below). This novel endpoint utilises the combination of clinical outcomes; (viral reactivation, immune reconstitution (CD4 count) and organ support) to rank a patient from a good score (level 1) through to a poor score (level 5). The endpoint was evenly distributed across categories when applied to the HCT cohort of 202 patients. Associations with key exposures (e.g. donor type and cell source) were mostly in the expected direction e.g. patients who received a matched sibling donor transplant scored lower in the ordinal endpoint compared to patients who received haploidentical donor transplants. Importantly, the endpoint (censored at Day 100) correlated with traditional long-term HCT complications, including relapse, chronic-graft-versus-host disease, and death up to 5 years post HCT. These results, coupled with expert feedback from clinicians and family representatives identified that that the endpoint, was both feasible and relevant for use in BANDICOOT.

Novel Ordinal Endpoint

Worse outcome

Best outcome

Category	Criteria in the first 100 days post HCT
5	**Any of** (i) Death (ii) Graft loss requiring second HCT (iii) Relapse* (iv) Multi-organ support ≥ 14 days
4	**Any of:** (i) Persistent significant viraemia for any of adenovirus, CMV, EBV or HHV6 for ≥21 days and/or >1 viral reactivation for > 14 days# (ii) highest CD4+ T cells < 0.05 $CD4^+$ X 10^9/L (iii) Multi-organ support < 14 days.
3	**Any of** (i) Moderate duration of significant viraemia for any of adenovirus, CMV, EBV or HHV6 for 14- <21 days (inclusive) and/or >1 viral reactivation 14 days or less#. (ii) highest CD4+ T cells 0.05 - < 0.1 X 10^9/L (iii) Single organ support ≥ 10 days
2	**Any of:** (i) Short duration of significant viraemia for any of adenovirus, CMV, EBV or HHV6 for (ii) highest CD4+ T cells 0.1 - < 0.3 X 10^9/L (iii) Single organ support < 10 days
1	**All of:** (i) No significant viraemia (ii) highest CD4+ T cells ≥ 0.3 X 10^9/L (iii) No organ support.

Relapse defined as: minimal residual disease positivity > 10^{-4} or image confirmed extramedullary relapse. Significant viraemia defined as: HHV6 > 10^4, adenovirus positive on 2 occasions at least a week apart and/or EBV > 10^4 and/or CMV > 10^3

#>1 viral reactivation do not have to occur concurrently. All measures are counted from HCT admission.

Results

- Endpoint outcomes: day 100 post HCT for each patient
- This showed that 10% of patients had the worst outcome (category 5) and 12% of patients had the best outcome (category 1)

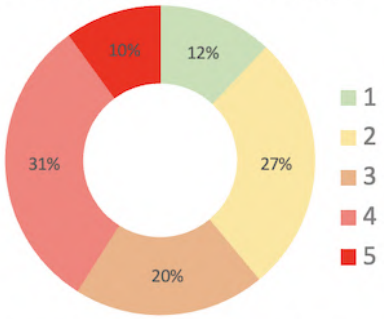


Figure 1: Distribution of patients across each category of the best performing ordinal endpoint (shown in Table 1)

Figure 2: Probability of developing cGVHD based on a patients score in the primary ordinal endpoint

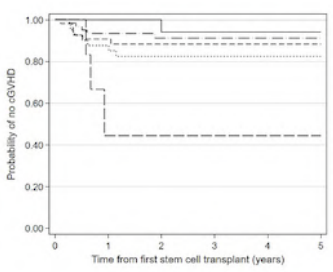
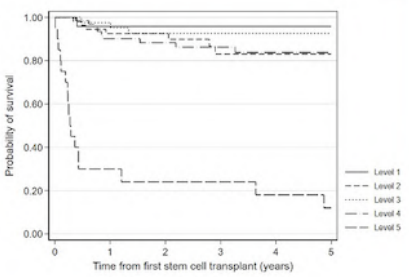


Figure 3: Probability of survival based on a patients score in the primary ordinal endpoint



- *Each endpoint category was associated with longer term HCT outcomes*
- *Category 5 patients had increased risk of adverse outcomes beyond day 100.*
- *The final endpoint was based on statistical performance and stakeholder feasibility.*

Conclusions: Our novel ordinal endpoint , measured at day 100 post HCT, is a paradigm shift away from traditional binary endpoints such as overall survival, graft versus host disease free survival and relapse free survival, which do not sufficiently incorporate the patient voice or accurately depict a patients worst outcome, often only the first. The BANDICOOT APT will transform paediatric HCT research, introducing a novel ordinal endpoint applicable across multiple outcomes. Future HCT advancements require global collaboration. The APT model accelerates progress, enabling rapid evaluation and refinement of interventions. BANDICOOT provides a scalable framework, ensuring faster access to optimal, evidence-based care for children.

Clinical Trial Registry: n/a

Disclosure: Nothing to declare.

B220

ORAL SUPPLEMENTATION VS ENTERAL VIA NASO-GASTRIC TUBE VS PARENTERAL NUTRITION AS NUTRITIONAL SUPPORT AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE STUDY

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Background: Deterioration of nutritional status in recipients of allogeneic hematopoietic stem cell transplantation (HSCT) is associated with increased morbidity. Although enteral nutrition (EN) has been favorably associated with improved outcomes compared with total parenteral nutrition (TPN), TPN remains first-line nutritional support in many pediatric transplant centers, mainly due to physician- and caregiver-related barriers. Oral nutritional supplementation (ON) may represent a feasible alternative capable of overcoming these limitations. However, evidence supporting the adequacy of ON in pediatric HSCT recipients remains limited.

Methods: We retrospectively evaluated the impact of three nutritional support modalities, oral nutrition (ON), enteral nutrition (EN), and total parenteral nutrition (TPN)—on nutritional status in children undergoing allogeneic HSCT. Nutritional status was assessed by body mass index (BMI) at ward admission and at day +30 post-transplant.
Patients were treated at two Italian pediatric centers: Santobono-Pausilipon Children's Hospital (Naples) between 2014 and 2023, and IRCCS Sant'Orsola (Bologna) between 2020 and 2023.
Secondary endpoints included associations between nutritional modality and HSCT outcomes: time to neutrophil and platelet engraftment (defined as the first of three

consecutive days with absolute neutrophil count >500/mm³ and platelet count >20,000/mm³ without transfusion support, respectively), length of hospitalization, and incidence of grade III–IV acute graft-versus-host disease (aGVHD) according to MAGIC criteria.

Results: Patient characteristics are summarized in Table 1. A decrease in BMI was observed across all groups after HSCT, with a median change of −0.6 kg/m² (range −9.86 to +12.29; IQR −1.34 to −0.04). BMI reduction was greater in males ($p<0.05$) and directly correlated with age ($p=0.0017$).
Patients receiving EN experienced a significantly smaller BMI decrease compared with other groups (median −0.45 kg/m²; range −2.18 to +3.95; IQR −0.67 to −0.15; $p<0.05$). In contrast, patients supported with TPN showed the greatest BMI reduction (median −1.1 kg/m²; range −9.86 to +0.58; IQR −1.78 to −0.36; $p<0.05$ vs all other groups). Notably, ON resulted in an intermediate outcome (median −0.91 kg/m²; range −4.09 to +12.29; IQR −1.66 to −0.06), neither significantly worse than EN ($p=0.0785$) nor better than TPN ($p=0.514$).
Median length of hospitalization was significantly associated with nutritional modality ($p<0.001$). EN was associated with the shortest hospital stay (median 35 days; range 25–193; IQR 30–44), while TPN resulted in the longest hospitalization (median 55 days; range 32–135; IQR 44–70). Patients receiving ON had a median hospitalization of 42 days (range 27–147; IQR 36–53), significantly shorter than TPN ($p<0.001$) and longer than EN ($p<0.05$).
Severe aGVHD (grade III–IV) occurred in 6/47 patients receiving ON, 5/41 receiving TPN, and 7/37 receiving EN. Nutritional modality was not significantly associated with severe aGVHD incidence ($p=0.691$).

	Overall (N=125)	Total Parenteral Nutrition (N=41)	Oral Nutrition (N=47)	Enteral Nutrition (NGT) (N=37)	P-value
Median age at HSCT [range, IQR], years	8.8 [0.3-20.7; 4.3-13.1]	10.1 [0.8-18.6; 4.5-13.7]	8.4 [0.3-18; 3.5-12.8]	8.5 [3.1-20.7; 4.7-12.5]	p = 0.67*
Sex:					
Male (%)	83 (66%)	23 (56%)	33 (70%)	27 (74%)	p = 0.234^
Female (%)	42 (34%)	18 (44%)	14(30%)	10 (26%)	
Disease:					
Malignant (%)	93 (74%)	31 (76%)	30 (64%)	31 (83%)	p = 0.12^
Not Malignant (%)	33 (26%)	10 (24%)	17 (36%)	6 (16%)	
Median weight before HSCT [range, IQR], kg	28 [5.5-85; 16-48.5]	27.3 [5.5-85; 16-54]	28 [5.52-76.7; 14.25-43.975]	30 [13-90; 19-58.4]	p = 0.485*
Median weight after HSCT [range, IQR], kg	25.5 [5.5-79.7; 16.1-45.4]	24.3 [5.45-79.7; 15.7-49]	26.3 [5.6-72.5; 14.4-41.1]	28 [12.8-77.5; 18.4-50.3]	p = 0.429*
Median BMI before HSCT [range, IQR]	17.1 [6-33.7; 15.3-20.4]	16.9 [6-33.7; 14.7- 21.1]	17.3 [8-27.1; 15.4-20]	17.6 [12.7-27; 15.7-20]	p = 0.912*
Median BMI after HSCT [range, IQR]	16.7 [6-32.6;14.6-19.1]	16.3 [5.6-32.6; 13.9-19.1]	17.2 [12.6-26.8; 15.3-18.9]	17 [13.2-27.2; 14.8-19.6]	p = 0.435*

Similarly, no significant differences were observed among groups in time to neutrophil or platelet engraftment.

Conclusions: ON supplementation showed intermediate outcomes, comparable to EN and superior to TPN in terms of length of stay, without negatively affecting engraftment or severe aGVHD. When supported by high-calorie supplements, ON may represent a feasible alternative to enteral feeding in selected patients when clinical conditions or compliance do not allow tube feeding.

Disclosure: NO COI

B221

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN PEDIATRIC PATIENTS RECEIVING LETERMOVIR AS CMV INFECTION PROPHYLAXIS

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Background: Among patients after allogeneic hematopoietic stem cell transplantation (HSCT), EBV can cause the development of a serious complication known as post-transplant lymphoproliferative disorder. (PTLD). In patients receiving letermovir prophylaxis, a higher risk of EBV reactivation is observed, including PTLD symptoms.The aim of this study is to assess the occurrence of EBV infection reactivation and its severity in children receiving letermovir for CMV prophylaxis after HSCT.

Methods: The population of children undergoing alloHSCT at the Department of Hematopoietic Stem Cell Transplantation, University Children's Hospital in Cracow, Poland, between 2023 and 2025 was analyzed. In total, 72 alloHSCT procedures were included in the analysis. Letermovir prophylaxis was administered to 34 children. EBV infection was identified in 6 children receiving letermovir. The analysis included patients who experienced EBV reactivation requiring preemptive therapy.

Results: The frequency of EBV reactivation was 18% (6/34). The time of EBV reactivation ranged from +39 to +123 days after HSCT, with a median of +79 days. Reactivation occurred in children aged 3-18 years, with a median age of 14. Only in 1 patient was the infection asymptomatic and detected solely during routine post-HSCT testing. In 83% (5/6) of patients, PTLD was diagnosed, presenting with massive painful lymphadenopathy, fever, and pancytopenia. All patients (100%, 6/6) were treated with Rituximab. In 2 patients, progression to non-Hodgkin lymphoma occurred in the course of PTLD, and R-CHOP chemotherapy was initiated. No deaths related to PTLD were observed in the study group.

Conclusions: CMV prophylaxis with letermovir may increase the risk of severe EBV reactivation. Intensive monitoring of patients receiving letermovir for EBV reactivation is recommended, particularly around 3 months after HSCT, especially in children over 14 years of age.

Disclosure: No conflict of interests.

B222

TREOSULFAN-BASED CONDITIONING REGIMENS ARE SAME EFFECTIVE, BUT LESS TOXIC IN COMPARISON WITH BUSULFAN-BASED IN PEDIATRIC SOLID TUMORS: RESULTS OF RETROSPECTIVE ANALYSIS FROM 148 PATIENTS

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Background: Autologous hematopoietic stem cell transplantation (aHSCT) is effective way of consolidation therapy in neuroblastoma (NB) and Ewing sarcoma (ES). Balance between toxicity and efficacy is important.
We aimed to present the data of retrospective analysis from 2 centres describing toxicity and efficacy of aHSCT for the patients with NB and ES.

Methods: Our retrospective study includes 148 patients with NB (n=116, 78%) and ES (n=32, 22%). M:F=62(46%):86(54%). All patients received aHSCT with treosulfan/melphalan or busulfan/melphalan conditioning in 2021-2023. Age median was 5.1 y.o. [8 months – 17 y.o.]. The majority of patients (73.6%) received aHSCT as a part of first-line therapy with complete response in 72.9% cases. HSCT with Treosulfan-based conditioning regimen received 89 patients (60.1%) and Busulfan-based – 59 (39.9%). Median infused dose of CD34+ cells was 7.1*10 6 /kg. Toxicity as well as overall survival and relapse-free survival estimated.

Results: All patients engrafted. Median day of engraftment was better in treosulfan group (11 vs 15). Toxicity rates were better in treosulfan group both mucositis and neutropenia: grade 3-4 – 12% in treosulfan group and 25% in busulfan group ($p<0.005$). Toxic deaths: treosulfan: n=2 (2.24%) and busulfan n=2 (3.4%). No differences were found in nutrition insufficiency, viral reactivations and hemorrhagic complications. At the median of FU of 2 years OS was higher in treosulfan group (78.1% vs 73.1%) as well as RFS (65.3% vs 59.8%), but no statistical difference found.

Conclusions: Treosulfan-based conditioning regimen is safe and effective for NB and ES. Less organ toxicity found in patients with treosulfan-based conditioning regimen in comparison with busulfan-based conditioning. Large multicenter studies required.

Disclosure: There are no conflicts of interest.

B223

COMPARATIVE STUDY OF CORD BLOOD TRANSPLANTATION FOR PEDIATRIC ACUTE LEUKEMIA: JOINT ANALYSIS BY EUROCORD AND JSTCT

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Background: Unrelated cord blood transplantation (CBT) is a well-established treatment approach for pediatric patients with acute leukemia. While both Europe and Japan have accumulated extensive CBT experience and have robust programs, differences in clinical practice and patient characteristics exist. However, studies directly comparing European and Japanese pediatric populations, side by side, are limited. This study uniquely evaluates CBT from both regions, allowing easy comparison of outcomes and prognostic factors of single-unit CBT for children with acute leukemia between these two distinct populations.

Methods: Retrospective analysis of patients aged <18 years who underwent first single-unit CBT for acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) between 2005 and 2020. Clinical data were retrieved from Eurocord/EBMT and JSTCT (Japan Society for Transplantation and Cellular Therapy) registries. Multivariate analyses (MVA) were performed separately for each registry, using Cox regression or Fine-Gray regression as appropriate.

Results: A total of: 1,645 from Europe and 1,131 from Japan were included in the analyses. The proportion of more advanced disease status at CBT was higher in Japan than in Europe (30% vs. 7%). The infused cell dose was significantly higher in Europe (median TNC 7.1 vs.

5.2 $\times 10^7$/kg; $CD34^+$ 2.6 vs. 1.7 $\times 10^5$/kg), while the use of total body irradiation (TBI) in conditioning regimens was more frequent in Japan (64% vs. 38%). Anti-thymocyte globulin (ATG) was used in 65% of European patients but only in 3% of Japanese patients.
Five-year OS was 62% (95% CI, 59-65%) in the Japanese cohort and 55% (52-57%) in the European cohort ($p<0.001$). In MVA, advanced disease status was associated with higher mortality in both cohorts. In Japan, lower CD34+ cell dose, multiple HLA mismatches, and earlier transplant year were also significant risk factors, whereas in Europe, ALL diagnosis and CMV positivity were significant predictors of higher mortality.
The cumulative incidence of aGVHD grades II-IV was 37% (95% CI, 34-40%) in Japan and 32% (95% CI, 29-34%) in Europe. In MVA, factors associated with higher aGVHD included higher TNC dose, MAC regimens, TBI use, and greater HLA mismatches in Japan, while male gender, younger age at CBT, and conditioning without ATG were significant in Europe. The CI of cGVHD was 22% (95% CI, 19-25%) in Japan and it was 14% (95% CI, 12-16%) in Europe.
The 5-year CI of relapse was slightly higher in Japan (31% vs 26% in Europe, $p=0.00121$). Conversely, 5-year NRM was higher in Europe than Japan (22% vs 11%, $p<0.001$).

Conclusions: This joint study of pediatric single-unit cord blood transplantation for acute leukemia reveals distinct transplant practices, as well as different outcome patterns and prognostic factors between Japanese and European cohorts. While OS was higher in Japan compared to Europe, relapse rates were lower for patients in the European cohort. Advanced disease status emerged as a consistent predictor of poor outcomes across both regions. However, other risk factors impacted the individual cohorts differently. These findings emphasize the importance of tailoring transplant strategies to regional practices to optimize outcomes in pediatric acute leukemia.

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ENTERAL VERSUS PARENTERAL NUTRITION IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE EVALUATION OF FEASIBILITY, CLINICAL OUTCOMES, AND RESOURCE UTILIZATION

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Background: Children undergoing hematopoietic stem cell transplantation (HSCT) are vulnerable to early post-transplant malnutrition due to impaired oral intake and treatment-related toxicities. Optimal nutritional support—enteral nutrition (EN) versus parenteral nutrition (PN)—remains a subject of debate in pediatric HSCT practice. EN is physiologic, maintains gut integrity, and may reduce infectious complications, whereas PN is often used when EN is assumed to be poorly tolerated. This study evaluates the tolerability of EN and compares its impact on clinical outcomes, early toxicities, and healthcare resource utilization during the first 100 days post-HSCT.

Methods: A retrospective cohort analysis was conducted following a shift prioritizing EN. Pediatric patients aged ≤14 years who underwent HSCT between 2015 and 2024 were included. The PN cohort comprised patients transplanted from 2015–2019, while the EN cohort included those transplanted from 2020–2024. Patients undergoing subsequent transplants were excluded. Clinical outcomes assessed included time to neutrophil and platelet engraftment, infectious complications, mucositis, graft-versus-host disease (GVHD), day-100 mortality, and length of stay. Data were extracted from institutional databases and analyzed using standard comparative statistics.

Results: A total of 1,246 pediatric HSCT patients met inclusion criteria, with a median age of 4.66 years (range 0.1–14.4). Females represented 56% (n=693), and males 44% (n=553). Most procedures were allogeneic HSCT (92%, n=1,150), with autologous HSCT accounting for 8% (n=96). Non-malignant disorders constituted 76% of indications, while malignant conditions comprised 24%. Among allogeneic recipients, 66% (n=757) received matched-related donor grafts, 23% (n=263) haploidentical grafts, and 11% (n=130) matched-unrelated donor grafts. Bone marrow was the predominant graft source (81%). Overall, 51% (n=632) received PN, and 49% (n=614) received EN, yielding a control-to-intervention ratio of 1.03:1. EN was associated with significantly faster neutrophil recovery (15.3 vs. 16.7 days; $p<0.001$) and platelet engraftment (28.5 vs. 33.4 days; $p<0.001$). EN recipients had lower rates of bacterial infections (190 vs. 262; $p<0.001$) and mucositis (157 vs. 214; $p<0.001$). Among allogeneic HSCT patients, the EN recipients showed a significantly lower incidence of Grade II – IV, GVHD compared to the PN (38 vs. 20; $p=0.044$. Overall day-100 mortality was 9%, with lower mortality in the EN group compared with PN (48 vs. 65 deaths; $p=0.535$). Resource utilization analysis demonstrated a significantly shorter average length of stay among EN recipients (29 vs. 49 days; $p=0.038$), reflecting reduced toxicities and improved recovery trajectories. Institutionally, this project was presented as a quality

improvement initiative and received the Performance Improvement Award for its measurable clinical and cost-saving impact.

Conclusions: Enteral nutrition was well tolerated in pediatric HSCT and associated with faster engraftment, reduced infectious and mucosal toxicities, and lower healthcare resource utilization compared with PN. Gut GVHD rates were lower in the EN group continues to decline with ongoing practice refinement as follow-up data demonstrates a further declining trend in acute GVHD during 2025. These findings support EN as a safe, feasible, and potentially superior nutritional strategy in pediatric HSCT. Future multi-center studies are needed to validate these results and guide standardized nutritional-support recommendations and its impact on healthcare resource utilization.

Clinical Trial Registry: Not Applicable.

Disclosure: Nothing to Declare.

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DAY +60 B LYMPHOCYTES POST-TRANSPLANT AS AN EARLY PREDICTOR OF CHRONIC GVHD

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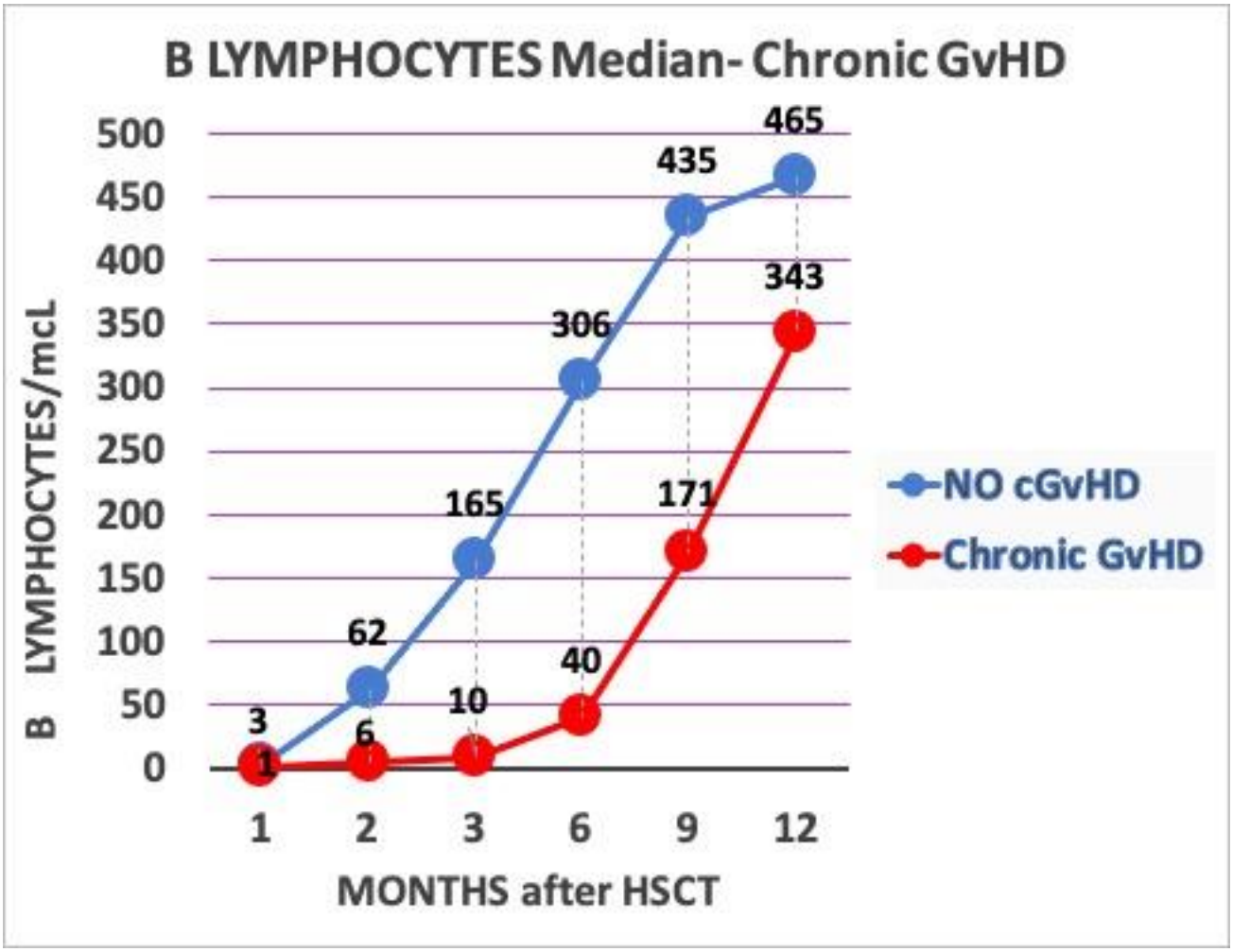
Background: Risk biomarker analyses for chronic GVHD (cGVHD) after HSCT in children are scarce. Recently, a 5-biomarker panel (IL1RL1, REG3α, MMP3, DKK3, and sCD163) measured 3 months post-HSCT was shown to predict susceptibility to cGVHD and was associated with TRM. However, these biomarkers are not routinely available in most centres. Therefore, we evaluated a more accessible approach based on post-transplant lymphocyte subset recovery.

Methods: We conducted a retrospective study of children with leukaemia who underwent haploidentical HSCT with T-cell depletion between 2005 and 2020. A total of 159 children were included, with a median age of 9 years (range, 1–19), diagnosed with ALL (n = 80) or AML (n = 79). One hundred and six were male (67%) and 53 were female (33%). Forty patients were in CR1 (25%), 66 in CR2 (42%), and 53 in ≥CR3 or had active disease (33%). The median donor age was 40 years (range, 2–54). Donors were parents in 143 cases and siblings in 16 cases. Most donors (84%) had a KIR-B genotype. Conditioning was mainly based on fludarabine, busulfan, and thiotepa. Patients received a T-cell–depleted peripheral blood graft containing a median CD34+ dose of 8 × 10^6/kg.
The primary objective was to identify risk factors for cGVHD. Secondary objectives included analysis of TRM and OS.

Results: The cumulative incidence (CI) of acute GVHD was 33 ± 6% at a median onset of 30 days, with 18% being grade III–IV. The CI of cGVHD was 27 ± 5% at a median onset of 120 days, with 7% being moderate or severe.

We evaluated lymphocyte subsets on day +60 as potential predictors of cGVHD.
In univariate analysis, both prior acute GVHD (55 ± 7% vs 15 ± 4%, p = 0.0001) and as early as day +60 B-cell counts (≤ median 15/µL: 59 ± 8% vs > median: 22 ± 6%, p = 0.00001, Figure 1) were associated with cGVHD risk.



In multivariate analysis, prior acute GVHD (yes vs no; HR 2.27, 95% CI 1.1–4.9, p = 0.042) and B-cell counts at day +60 (≤ median vs > median; HR 3.5, 95% CI 1.6–7.5, p = 0.001) independently predicted cGVHD development.
With a median follow-up of 6 years (range, 1–16), TRM and OS varied according to the day +60 B-cell count, below median it was TRM 35 ± 7%, OS 44 ± 7% vs above median: TRM 9 ± 4% and OS 70 ± 6%.
We developed a risk score for cGVHD based on Cox regression HR (0, 1, or 2 points), incorporating prior acute GVHD and day +60 B-cell count: 0 points: cGVHD 15 ± 6%, 1 point: cGVHD 32 ± 6% and 2 points: cGVHD 78 ± 10% (p = 0.001).

Conclusions: The incorporation of these readily accessible clinical and immunological risk factors enables early prediction of chronic GVHD and informs clinical management as early as day +60 post-transplant.

Disclosure: Nothing to declare.

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CURRENT USE OF BELUMOSUDIL FOR PEDIATRIC STEROID-REFRACTORY CHRONIC GVHD IN EUROPE: RESULTS OF RETROSPECTIVE SURVEY OF THE PEDIATRIC DISEASES WORKING PARTY (PDWP) OF THE EBMT

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Background: Chronic graft-versus-host disease (cGvHD) is a major cause of late morbidity and mortality following allogeneic hematopoietic stem cell transplantation (aHSCT) and remains a major focus within the European Society for Blood and Marrow Transplantation (EBMT). In pediatric and young adult patients, effective treatments beyond first-line corticosteroids is particularly challenging due to cumulative toxicity, and limited availability of evidence-based second-line options. Belumosudil, a selective ROCK2 inhibitor, has shown promising results in adult steroid-refractory (SR) cGvHD; however, pediatric data are scarce,

and European practices have not yet been systematically described. As EBMT updates its guidelines for GvHD management, real-world pediatric experiences are essential to shape consensus and address gaps in access and implementation.
Objective: To characterize current real-world use of belumosudil in children and young adults with SR cGvHD across European EBMT centres, including indications, dosing, timing of initiation, combination therapies, and observed safety signals.

Methods: The Pediatric Diseases Working Party (PDWP) conducted a retrospective survey to EBMT centres collecting information on belumosudil use in pediatric and young adult patients. The survey captures centre-level prescribing patterns and patient-level safety data.

Results: Twenty-seven centres reported their experience with 100 patients treated with belumosudil. Most patients (n=78) received belumosudil specifically for SR cGvHD. The majority of centres (65%) initiated belumosudil after inadequate response to two previous lines of therapy, and 61.5% reported use after two or more lines. Nine centres also reported organ-specific indications for belumosudil. Across centres, the number of treated patients ranged from 1 to 20. The most frequently used total daily dose was 200 mg (85% of centres), followed by 100 mg (three centres) and 400 mg (one centre). Therapy was started 6–12 months after cGvHD diagnosis in 46% of centres, 3–6 months in 32%, 1–3 months in 11%, and at SR cGvHD diagnosis in 11%. Most centres (94%) defined SR cGvHD as progression despite adequate steroid exposure, while 42% reported using multiple criteria, including incomplete response after 4–8 weeks of steroid treatment or steroid intolerance. Belumosudil was commonly used alongside ECP, ruxolitinib, sirolimus, or other immunomodulatory approaches. All experienced centres agreed to participate in a retrospective patient-level study. With reported use in children (0–12 years; 18 centres (72%)), adolescents (13–17 years; 10 centre (40%), and young adults (18–21 years; n=9 centres (33%)). These centres are in the process of being contacted, and detailed data will be made available at the meeting. Reported centre-level significant adverse events included nausea (48%), fatigue (37%), infections (30%), diarrhea (22%), liver toxicity (22%), renal impairment (15%), and headache, thrombocytopenia and visual disturbances one centre each.

Conclusions: This PDWP survey reveals widespread yet heterogeneous use of belumosudil for pediatric and young adult SR cGvHD across centres in Europe, with a generally manageable safety profile. These findings emphasize the need for harmonized EBMT guidance, highlight barriers such as limited drug availability in some countries, and serve as a vital foundation for upcoming EBMT recommendations and patient-level outcome studies.

Disclosure: J.B. has participated in advisory boards for Amgen, Novartis, Pfizer, Medac and Janssen (to the institution), has received speaker fees from Novartis, and is SSC/DMSB member for clinical trials sponsored by Novartis.
H.P. reports travel grants from Jazz Pharmaceuticals and Sanofi and speakers bureau fees from Vertex and Novartis.
C.D. has received speaker fees from Novartis and Therakos, has participated in Clinical Trial Steering Committees for Novartis and Autolus, has participated in a DSMB for a clinical trial sponsored by Orchard, has participated in advisory boards for Alexion, Sanofi and Vertex, and received travels grants from Jazz Pharmaceuticals.

A.L. COI: Neovii, Sanofi, Novartis, Therakos, Amgen, Medac, Vertex
Other authors - no COI

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THE DONOR'S FINGERPRINT: PEDIATRIC DONOR CELL LEUKEMIA

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Background: Most relapses of acute leukemia after allogeneic HSCT reflect re-emergence of the patient's original malignant clone. Donor Cell Leukemia (DCL) is a rare post-transplant relapse arising from donor-derived cells, identified by donor-specific mutations or cytogenetic markers (e.g., XX/XY in sex-mismatched transplants) present in donor and leukemic cells, but absent in the original leukemia. Proposed pathogenic mechanisms include transmission of a pre-malignant donor clone, host bone marrow microenvironment dysfunction, or multifactorial donor–host interactions. The incidence is 2–5% of relapses. The true incidence of pediatric DCL (pDCL) is presumed to be lower.

Methods: We describe a pDCL case occurring after allogeneic HSCT, including serial molecular analysis of recipient and donor samples. Retrospective testing of stored bone marrow specimens was performed to track clonal evolution over time. In addition, a literature review of previously reported pDCL cases was conducted.

Results: A 7-year-old boy was diagnosed in October 2020 with Ph-like pre–B- ALL. He achieved complete remission with chemotherapy and tyrosine kinase inhibitor therapy but experienced an early relapse with isolated CNS involvement and MRD-positive bone marrow. In December 2021, he underwent haploidentical HSCT from his apparently healthy father and achieved sustained molecular remission with full donor chimerism.
In April 2024, while maintaining complete donor chimerism, he developed a second leukemia- AML. Next-generation sequencing revealed mutations in DNMT3A R882C (41% variant allele frequency [VAF]) and two presumed biallelic RUNX1 (W106L and G199W; VAF 24% and 26%). Peripheral blood testing of the donor demonstrated the identical DNMT3A mutation (20% VAF), consistent with a pre-leukemic donor clone, while RUNX1 mutations were absent. The donor remains clinically healthy with normal blood counts.
Retrospective analysis of stored recipient bone marrow samples identified the DNMT3A mutation approximately 10 months prior to AML diagnosis, whereas RUNX1 mutations emerged only 2 months before diagnosis, supporting stepwise leukemic transformation of donor-derived cells. Following treatment with azacitidine and venetoclax, the patient achieved morphological remission but with persistent molecular disease. In July 2024, he underwent a second HSCT from a matched unrelated female donor. As of November 2025, he remains in molecular complete remission, with full second-donor chimerism and no detectable DNMT3A or RUNX1 mutations (NGS sensitivity 0.5%). Table presents a literature review of pDCL, including current case. Figure illustrates the clinical and molecular data of this patient.

Table: Pediatric Donor Cell Leukemia (DCL), Literature Review and Current Case

	Type of report	Patient age (years)	Primary diagnosis	Donor type and Graft source	Donor age (years)	Time to DCL (years)	Type of DCL	Genetics of DCL	Treatment of DCL	Outcome	Last follow up (years)	Reference
1	Cohort (31 pts.)	Median 8y	Malignant (ALL, AML)+ non-malignant (FA, SAA, CGD)	MSD / MUD / UCB	Varied (UCB + adults)	0.5 - 10 (median 3.5)	MDS/AML	Mostly monosomy 7, +8, del(5q), complex karyotype	Treatment generally included chemotherapy, with a minority of patients undergoing 2nd HSCT	Long-term survival was rare and mainly observed in patients who underwent a 2nd HSCT	0.5 - 10	Suárez-González. Biol Blood Marrow Transplant. 2018;24:1505-1513
2	Case	4	AML	MSD BM	NR	1	AML	NR	NR	NR	NR	Goh. Am J Hematol. 1977;2:283-290
3	Case	12	CML	MSD BM	NR	1.2	pre-B ALL	NR	NR	NR	NR	Smith. Br J Haematol. 1985;60:415-422
4	Case	Child	T-ALL	MSD	NR	NR	pre-B ALL	NR	NR	NR	NR	Feig. Bone Marrow Transplant. 1988;3:331-337
5	Case	16	AML	MSD BM	NR	1	pre-B ALL	NR	NR	NR	NR	Mouratidou. Bone Marrow Transplant.

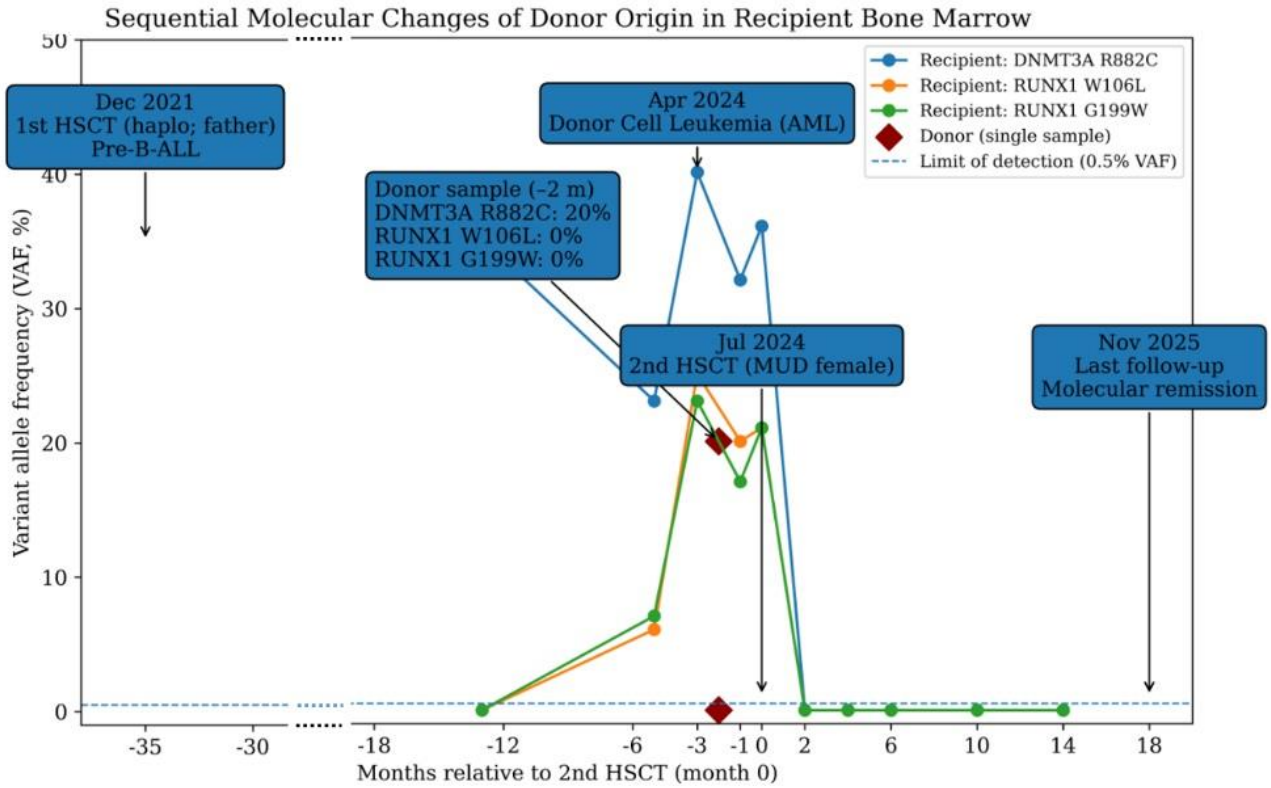
Table: Pediatric Donor Cell Leukemia (DCL), Literature Review and Current Case

												1993;12:77-80
6	Case	3	AML	MUD UCB	Newborn	1.2	AML	Monosomy 7	Chemotherapy	Death (DCL)	NR	Crow. J Mol Diagn. 2010;12:530-537
7	Case	16	AML	MSD BM	NR	2.8	AML	NR	Cytarabine, daunorrubicin	Death (Septic shock during induction for DCL)	0.16	Bobadilla-Morales. Mol Cytogenet. 2015;8:5
8	Case	1	LCH	MUD UCB	Newborn	1.6	AML	Chr22 abnormality	Chemotherapy	Death (Infection)	0.8	Fraser. Blood. 2005;106:4377-4380
9	Case	Child	Fanconi anemia	MUD UCB ×2	Newborn	2	AML	del 5q, t(9:11)	Cytarabine, FLA, Azacitidine à 2nd HSCT (haplo)	Death (GVHD)	1.3	Gustafsson. Pediatr Transplant. 2012:16;E241-E245
10	Case	5	SAA	MUD	NR	11	AML	del 9q, CEBPA mutations	Cytarabine, daunorubicin and Gentuzumab-Ozogamicin	Alive	NR	Testi. J Hematol Thrombo Dis. 2022;10:1000503
11	Case	10	CGD	MSD BM	NR	2	AML	t(9;11)	Chemotherapy --. 2nd, 3rd and 4th HSCTs	Death (sepsis after 3rd relapse of DCL)	10	Micheloni. Genes (Basel). 2023;14:2085
12	Case	4	GATA2 deficiency	MUD	34	2	pre-B ALL	monosomy 7 and t(9:22)	Daunorubicin, vincristine, pegaspargase,	NR	0.5	Scheuermann. J Pediatr Hematol Oncol.

Table: Pediatric Donor Cell Leukemia (DCL), Literature Review and Current Case

									dexamethasone, imatinib, blinatumomab à 2nd HSCT(haplo)			2022;44:268-270
13	Case	12	Ph-like pre-B ALL	Haplo BM	46	2.3	AML	DNMT3A R882C; RUNX1 (biallelic W106L, G199W)	Azacitidive and venetoclax à 2nd HSCT (MUD)	Alive	1.5	Current case

ALL: acute lymphoblastic leukemia, AML: acute myeloid leukemia, BM: bone marrow, CGD: chronic granulomatous disease, Chr: chromosome, DCL: donor cell leukemia, del: deletion, F: female, FA: Fanconi Anemia, Haplo: haploidentical, HSCT: hematopoietic stem cell transplantation, M: male, MSD: matched sibling donor, MUD: matched unrelated donor, NR: not reported, Ph: Philadelphia, SAA: severe aplastic anemia, t: translocation, UCB: unrelated cord blood



Conclusions: To date, only a limited number of pDCL cases have been reported. pDCL has been described following HSCT for both malignant and non-malignant disorders, with latency ranging from a few months to more than a decade. Reported cytogenetic abnormalities are heterogeneous and distinct from the original disease, including monosomy 7, del(9q), KMT2A rearrangements. Donor genetic data are largely unavailable in most published reports.
Our case uniquely demonstrates stepwise donor-derived clonal evolution preceding overt AML, providing direct molecular evidence of leukemic transformation originating from donor hematopoietic cells. These findings underscore the potential relevance of donor-related genetic factors and highlight the importance of careful donor selection, including pre-transplant donor molecular evaluation. Further studies are needed to better define the underlying biological mechanisms of pDCL.

Disclosure: Nothing to declare.

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REAL-WORLD EXPERIENCE WITH BELUMOSUDIL FOR STEROID-REFRACTORY CHRONIC GVHD IN CHILDREN: A MULTICENTER STUDY ON BEHALF OF RUSBMT PAEDIATRIC WORKING PARTY

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Background: Chronic GVHD (cGVHD) is a serious complication after allogeneic HCT in children. Belumosudil is one of the promising drug for treatment of advanced forms of cGVHD with an inhibitory mechanism of action ROCK-path. The drug is approved for the treatment of patients ≥12 yo after ≥2 prior lines of therapy. However, data on its effectiveness in pediatric patients is limited, especially in children under 12 yo.

Methods: We present a multicenter retrospective analysis of 43 children (<18 years) with steroid-refractory cGVHD treated with belumosudil across 9 HCT centers in Russia. Diagnosis, grading and response were assessed per NIH 2014 criteria.

Results:

Response rate	All pts	Age,12<yo	Age, 12>yo	Adverse events/Site toxicity	All pts	Age<12yo	Age>12yo
N of pts	N=43	N=24	N=19		N=43	N=24	N=19
Overall	28, 65%	17, 71%	11, 58%	Overall AE	30, 70%	16, 67%	14, 74%
Compele	2, 5%	2, 8%	0, 0%	Severe AE	16, 37%	11, 46%	5, 26%

Partial	26, 60%	15, 63%	11, 58%	Infections	24, 56%	13, 54%	11, 58%
No response	8, 19%	4, 17%	4, 21%	Kidney	7, 16%	2, 8%	5, 26%
Prigression	7, 16%	3, 12%	4, 21%	Neurological	9, 21%	6, 25%	3, 16%
				Liver	9, 21%	6, 25%	3, 16%
				GIT	8, 19%	4, 17%	4, 21%
				Hematological	16, 37%	9, 37.5%	7, 37%

Analysis included 30 boys (70%) and 13 girls (30%). Median age at belumosudil initiation was 12 yo (range 2-18), 24 patients (56%) < 12 yo. Median weight was 29 kg (5.5-80). Indications for allogeneic HCT were: acute leukemias (n=33, 77%), myelodysplastic syndrome (n=1, 2%), solid tumors (n=2, 5%), and non-malignant disorders (n=7, 16%). Donor types were: haploidentical (n=29, 67.5%), MUD (n=13, 30.5%), and MSD (n=1, 2%). A second allo-HCT performed in 13 patients (30.5%). Prior acute GVHD was documented in 25 patients (58%).
Median time to cGVHD onset was 180 days (54-1062); 13 patients (30.5%) had overlap syndrome. Patients were heavily cGVHD pre-treated: one prior line of systemic therapy received 5 (11.5%), two – 13 (30.5%), and three or more - 25 patients (58%), including corticosteroids (n=38, 88%), ruxolitinib (n=36, 84%), calcineurin inhibitors (n=22, 51%), mTOR inhibitors (n=17, 39.5%), extracorporeal photopheresis (n=19, 44%), rituximab (n=10, 23%), abatacept (n=9, 21%), etanercept (n=8, 19%), ibrutinib (n=6, 14%), and mycophenolate mofetil (n=4, 9%), and others (n=15, 35%).
At belumosudil initiation, NIH global severity was moderate in 5 patients (12%), severe in 38 (88%). Involved organ sites were: skin (n=35, 81%; sclerotic features in 24), oral mucosa (n=26, 60.5%), eyes (n=22, 51%), lungs (n=26, 60.5%), joints (n=15, 35%), gastrointestinal tract (n=11, 26%), liver (n=11, 26%), and genitalia (n=2, 5%).
Starting dose was weight-based: ≤15 kg received 50 mg/day, 15-40 kg received 100 mg/day, and >40 kg received 200 mg/day. The overall response rate (ORR=CR+PR) was 65% (28/43), including complete response in 2 (5%) and partial response in 26 patients (60%). No response was observed in 8 patients (19%), and 7 (16%) had progressive disease. Median time to response was 35 days (7-183). At data cutoff, 28 patients (65.1%) continued therapy with a median treatment duration of 148 days (14-1005). Adverse events occurred in 30 patients (70%), with serious adverse events in 16 (37%). Tabl.1 Dose reduction, temporary interruption, or permanent discontinuation due to an adverse event were required in 15 (35%), 9 (21%), and 8 patients (19%), respectively.

Conclusions: This is the large real-world series of belumosudil use in pediatric cGVHD. It demonstrates clinically meaningful efficacy in a heavily pre-treated population with predominantly severe, multi-organ disease, including children under 12 years. The safety profile was manageable. These findings support the therapeutic potential of belumosudil in pediatric cGVHD and highlight the need for prospective trials.

Disclosure: Nothing to declare.

B231

PLATFORM-SPECIFIC PATTERNS OF IMMUNE RECONSTITUTION AFTER PEDIATRIC ALLOGENEIC HSCT: COMPARATIVE ANALYSIS OF TCRAB/CD19⁺ DEPLETION AND POST-TRANSPLANT CYCLOPHOSPHAMIDE

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Background: Immune reconstitution is a critical determinant of post-transplant infectious risk and graft-versus-host disease (GVHD) in children undergoing allogeneic HSCT. Ex vivo TCRαβ/CD19⁺ depletion (TCR) and in vivo post-transplant cyclophosphamide (PTCY) represent two widely used approaches to alloreactivity control, yet comparative data on their immunological consequences in pediatric patients remain limited. Understanding platform-specific recovery patterns may support individualized GVHD prophylaxis and infection risk stratification.

Methods: We conducted a retrospective single-center analysis of 151 pediatric patients with acute lymphoblastic leukemia (ALL, n=93) and acute myeloid leukemia (AML, n=58) undergoing allogeneic HSCT between 2017 and 2024. Donor types included haploidentical (n=132), matched related (n=1) and matched unrelated (n=18). Conditioning regimens were MAC or RIC; ATG was used in 42 patients in the TCR group.
Patients were categorized into either TCRαβ/CD19⁺ depletion group (n=78) or PTCY — n=73 (50 mg/kg on days +3/+4). Gender, age, disease distribution were similar between these two groups ($p<0.05$ in each category).
Immune reconstitution of CD3⁺, CD4⁺, CD8⁺, CD19⁺ and NK cells was assessed at days +60, +100 and +180.Secondary endpoints included CMV reactivation, CD8⁺ dynamics in the context of viraemia, and associations between immune recovery and acute GVHD.

Results: At day +60, immune recovery profiles were comparable between groups ($p<0.05$ for parameter).
At day +100, distinct platform-specific patterns emerged: PTCY was associated with significantly higher CD3⁺ ($p=0.002$) and CD8⁺ ($p=0.003$) counts, while TCR led to significantly higher CD4⁺ recovery. By day +180, these trends persisted but lost statistical significance.
The overall incidence of CMV reactivation was comparable between the two groups. CMV reactivation was linked to a marked CD8⁺ expansion, most pronounced in the PTCY group (*$p=0.012$*), highlighting potential differences in antiviral T-cell responses across platforms.
The incidence of acute GVHD was significantly higher in the PTCY cohort (69.2% vs 30.6%,

p=0.0013). Within the TCR group, elevated $CD3^+$ levels at day +100 were associated with higher incidence of aGVHD (*p=0.047*), whereas no significant associations between T-cell subsets and aGVHD were identified in PTCY recipients. This divergence suggests distinct alloimmune dynamics between platforms.

Conclusions: Distinct patterns of immune reconstitution were observed between the two platforms. PTCY was associated with higher $CD3^+/CD8^+$ counts at day +100 and more pronounced $CD8^+$ expansion during CMV reactivation, whereas $TCR\alpha\beta/CD19^+$ depletion showed trends toward enhanced B-cell and NK-cell recovery. These findings indicate that immune recovery after pediatric HSCT is highly platform-dependent, with clinically relevant implications for infectious risk, alloimmune activation and GVHD. Our results support the need for platform-specific immune monitoring and may inform individualized selection of GVHD prophylaxis strategies in pediatric HSCT.

Disclosure: Nothing to declare.

B233

ROMIPLOSTIM IN PEDIATRIC PATIENTS POST HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR EARLY PLATELET ENGRAFTMENT- AN OPEN LABEL RANDOMISED CONTROLLED TRIAL

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Background: Delayed platelet engraftment following HSCT contributes substantially to post-transplant morbidity, transfusion dependence, and prolonged hospitalization in children. Thrombopoietin receptor agonists such as **romiplostim** have been used as rescue in delayed platelet engraftment and for secondary failure of platelet recovery. There is limited data, especially in the pediatric population, on its early use to enhance platelet engraftment. This study aimed to evaluate whether romiplostim administration accelerates platelet engraftment following HSCT in children.

Methods: A prospective, open-label, randomized controlled trial was conducted at the Department of Pediatric Oncology, All India Institute of Medical Sciences, New Delhi, between March 2024 and October 2025. Children aged 1–18 years undergoing autologous or allogeneic HSCT were randomized (1:1) to receive **romiplostim 5 µg/kg** subcutaneously on days +1 and +8 post-HSCT (day +5 and +12 for haploidentical PtCy transplants) or standard of care. The **primary endpoint** was days to platelet engraftment (first of three consecutive days with platelet count ≥20 × 10^9/L without transfusion). **Secondary endpoints** included platelet transfusion requirements, platelet count at day +28, platelet nadir, days to platelet ≥50 × 10^9/L, and safety. Exploratory analyses assessed neutrophil engraftment and multivariate predictors of engraftment.

Results: Thirty children (17 in the intervention arm, 13 controls) were enrolled, with a median age of 8 years (IQR 5–12); 57% underwent allogeneic HSCT and 77% had malignant indications. The median time to platelet engraftment was **12.0 (IQR 11–18.75) days** in the intervention group and **12.5 (IQR 11–18.5) days** in controls (p = 0.88), with **Kaplan–Meier analysis** confirming no significant difference (log-rank p = 0.66). Subgroup analyses across autologous, allogeneic, and malignant transplants similarly revealed no difference in engraftment times.
The **median platelet transfusion requirement** was comparable between groups (14 vs 17 mL/kg, p = 1.00). However, patients receiving romiplostim demonstrated a trend towards **higher platelet counts at day +28** [175,000 (94,000–365,000) vs 145,000 (56,500–175,000); p = 0.16], with a statistically **significant advantage in the allogeneic HSCT subgroup** [290,000 vs 165,000; p = 0.048]. The platelet nadir and days to platelet ≥50 × 10^9/L were similar between groups (p = 0.78 and p = 0.69, respectively). No grade ≥3 bleeding or thrombotic events occurred, confirming the **safety and tolerability of romiplostim** in this setting.
Exploratory analysis demonstrated no significant difference in median time to neutrophil engraftment [13 (10.75–16.75) vs 12 (11.75–14.5) days; p = 0.80]; however, **day +28 absolute neutrophil counts were significantly higher in the intervention group** within **autologous and malignant subgroups (p = 0.04)**.

Conclusions: Romiplostim was **safe and well tolerated** following pediatric HSCT. While it did **not significantly shorten platelet engraftment time**, the **intervention group demonstrated higher platelet and neutrophil counts by day +28**, particularly among **allogeneic and malignant subgroups**. These findings support the feasibility of romiplostim use post-HSCT and warrant larger multicenter trials to establish its efficacy in the pediatric population.

Clinical Trial Registry: Clinical trial registry- India: CTRI/2024/03/064716

Disclosure: Nothing to declare

B234

ACUTE GRAFT-VERSUS-HOST DISEASE REQUIRING SECOND-LINE THERAPY AFTER PEDIATRIC ALLOGENEIC HCT IN THE PRE-RUXOLITINIB ERA: A RETROSPECTIVE AIEOP ANALYSIS

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Background: The prognosis of children with severe acute graft-versus-host disease (aGVHD) who fail to respond to first-line systemic corticosteroids remains poor. However, the proportion of pediatric recipients requiring second-line therapy and the associated risk of non-relapse mortality (NRM) are not well defined. We performed a retrospective, registry-based analysis of children and adolescents undergoing allogeneic hematopoietic cell transplantation (allo-HCT) at AIEOP (Italian Association of Pediatric Hematology and Oncology) centers between 2010 and 2020, prior to the routine use of ruxolitinib in the pediatric setting, to estimate the frequency of steroid-refractory aGVHD requiring second-line treatment and to describe salvage therapies and clinical outcomes.

Methods: We analyzed 2,663 pediatric patients (41% female) who underwent allo-HCT between 2010 and 2020. Median age at transplant was 7.6 years (range, 0.1–18). Donor type was matched related donor (MRD) in 675 (25%), matched unrelated donor (MUD) in 1,315 (50%), and mismatched/haploidentical related donor in 673 (25%). Stem cell source was bone marrow in 64%, peripheral blood in 30%, and cord blood in 6%. *Ex vivo* T-cell depletion was used as GVHD prophylaxis/graft manipulation in 21% of cases.

Results: Overall, 756/2,663 patients (29%) developed grade II–IV aGVHD, with a cumulative incidence of 29% (95% CI, 28–31). Among these, 383/756 (51%) required second-line therapy (14% of the entire cohort). aGVHD requiring second-line therapy occurred more frequently after MUD transplantation compared with MRD or mismatched/haploidentical related transplantation (20% vs 8% vs 11%, respectively; $P<0.01$). It was also more frequent after cord blood transplantation compared with bone marrow or peripheral blood transplantation (25% vs 9% vs 10%, respectively; $P<0.001$). Second-line treatments included extracorporeal photopheresis (60%), mycophenolate mofetil (46%), mesenchymal stromal cells (12%), monoclonal antibodies (5%), and other therapies (28%); 32% of patients received ≥ 2 second-line treatments. The overall 1-year non-relapse mortality (NRM) in the study population was 10% (95% CI, 9–11). The 1-year NRM was 8% (95% CI, 7–10) in patients with grade 0–I aGVHD, 10% (95% CI, 7–14) in those with grade II–IV aGVHD responding to steroids, and 16% (95% CI, 13–20) in those with grade II–IV aGVHD requiring second-line therapy ($P = 0.005$). The overall cumulative incidence (CI) of chronic GVHD (cGVHD) was 13% (95% CI, 12–14). The CI of cGVHD was 5% (95% CI, 4–6) in patients with grade 0–I aGVHD, 21% (95% CI, 18–25) in those with grade II–IV aGVHD responding to steroids, and 36% (95% CI, 32–40) in those with grade II–IV aGVHD requiring second-line therapy ($P < 0.001$).

Conclusions: Children and adolescents with grade II–IV aGVHD requiring second-line therapy after failure of first-line corticosteroids experienced higher NRM and inferior outcomes compared with steroid responders. In this pre-ruxolitinib era cohort, available second-line approaches did not appear to mitigate the adverse prognostic impact of steroid refractoriness, supporting steroid-refractory aGVHD as a major determinant of transplant-

related mortality. This large, homogeneous registry-based dataset provides a benchmark against which contemporary and emerging therapeutic strategies can be compared.

Disclosure: No potential conflict of interest to disclose.

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POST-TRANSPLANT CYCLOPHOSPHAMIDE IN PEDIATRIC HEMOGLOBINOPATHIES: EXPANDING ACCESS TO ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Sickle cell disease (SCD) and thalassemia (TM) are two of the most prevalent genetic disorders globally. Despite the improvement in supportive medication, those affected nevertheless experience severe morbidity and early mortality. In addition to the recently approved gene therapy, haematopoietic stem cell transplantation (HSCT) remains the only curative treatment option. The overall survival rate following a HLA-identical related donor transplant (MRD) exceeds 97%, while the disease-free survival rate is 91%[MI1] (1-2). However, only a small proportion of patients have a suitable family donor, emphasizing the need for improvements in unrelated donor transplantations. HSCT from unrelated donors are accompanied with an elevated risk of graft-versus-host disease (GvHD) and rejection. To improve GvHD prophylaxis in (M)MUD transplantations, we changed our standard from CNI/MMF to CNI/Cy. Here, we report key outcome parameters of this cohort.

Methods: We retrospectively analyzed 70 patients who underwent allogeneic HSCT at our institution between 2018 and 2025. All patients received the same conditioning regimen consisting of treosulfan, fludarabine, thiotepa and ATLG.GvHD prophylaxis consisted of either calcineurin inhibitor (CNI) combined with mycophenolate mofetil (MMF) (n = 37) for the MRD group, or CNI with post-transplant cyclophosphamide (ptCy) in the UD cohort (n = 33).

Results: There was no significant difference in overall survival between the two groups (p = 0.17) with a Median follow up of 380 days (90-1105) for the ptCy group and 681 days (103-2310) for the CNI/MMF group. Grades II–IV acute GVHD occurred in 18.2% (95% CI, 7.0–35.5) versus 16.7% (95% CI, 6.4–32.8) (p = 1.00), and severe (grade III–IV) acute GVHD in 12.1% (95% CI, 3.4–28.2) versus 8.3% (95% CI, 1.8–22.5) (p = 0.70), respectively. The cumulative incidence of chronic GVHD was comparable between both groups (9.1% vs 8.3%, p = 1.00) (see Figure 1).
Hematopoietic recovery was rapid and comparable across groups and there was no difference in the usage of immunosuppressive agents. Immune reconstitution dynamics were comparable between groups across all lymphocyte subsets ($CD3^+$, $CD4^+$, $CD8^+$, $CD56^+/CD16^+$, and $CD19^+$). Infectious complications occurred in 57 patients overall, with comparable frequencies between the CNI/ptCy group (88%) and the CNI/MMF group (84%, p = 0.74). A total of 126 infections were documented (57 in CNI/ptCy and 69 in CNI/MMF

recipients, p= 0,88, 95% CI 0,67 – 1,36). The distribution by grade and timing was comparable between groups, with most infections occurring before day 30. The median number of infectious episodes per patient was two in both treatment arms.
GvHD prophylaxis using CNI/ptCy equilized the most important outcome parameters for hemoglobinopathy patients transplanted from a MRD versus MUD. The analysis revealed no significant difference in terms of overall survival (OS), event-free survival (EFS) and the proportion of patients who did not require transfusions (TFS). In addition, our data did not show a significant impairment of immune reconstitution or higher rates of viral reactivations in the ptCy group.

Conclusions: Overall, we conclude that CNI + ptCy as a GvHD prophylaxis could be a safe option for SCT and TM patients with no available family donor.

Disclosure: Nothing to declare.

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MULTIFACETED ROLE OF ELTROMBOPAG FOR POOR GRAFT FUNCTION IN PEDIATRIC ALLOGENEIC HSCT RECIPIENTS

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Background: Poor Graft Function (PGF) is a life-threatening complication of allogeneic hematopoietic stem cell transplantation (allo-HSCT) (5-27% incidence), and is defined by the development of two or three linear cytopenias with full donor chimerism and no disease relapse. Risk factors include low CD34+ cell dose in the graft, high donor-specific antibody titers, damaged bone marrow microenvironment, cytomegalovirus infection, graft-versus-host disease (GVHD), splenomegaly, and iron overload. Eltrombopag, a thrombopoietin receptor agonist, shows promise as a therapeutic option for PGF treatment due to its multilineage hematopoietic effects and ability to reduce inflammation and chelate intracellular iron with an affinity comparable to that of chelators such as deferoxamine.

Methods: We conducted a retrospective, single-centre, observational study at the pediatric Bone Marrow Transplant Centre of the Institute for Maternal and Child Health—IRCCS "Burlo Garofolo" in Trieste, Italy, from April 2018 to May 2025 (IRB approval: RC 44/24). This study involved 30 patients (mean age 8.76 years, IQR: 15.87, 73.3% males). The study evaluated the efficacy and safety of eltrombopag for PGF in pediatric allo-HSCT recipients, assessing clinical outcomes as transfusion independence, adverse events (infections and GVHD), and overall survival. Its ability to modify pro-inflammatory cytokine production and its chelating activity was evaluated either alone or in combined therapy with deferoxamine.

Results: The median duration of eltrombopag treatment is 136.5 days (IQR, 93.3 days). A complete hematological improvement was observed in 24 patients (80.0%), a partial response in 2 patients (6.7%), while 4 patients (13.3%) did not respond. Significant increases were seen in median neutrophil counts (from 636/mm³ to 2,675/mm³), platelets (from 113,500/mm³ to 218,500/mm³), and hemoglobin (from 9.35 g/dl to 11.35 g/dl).

Patients showed decreased transfusion dependence. Non-response was associated with significant viral infections (all 4 non-responders). Severe acute GVHD (grade 3–4) occurred in 4 patients (13.3%); moderate-to-severe chronic GVHD in 5 patient (16.7%). At the 1,281-day mean follow-up, 27 patient (90%) were alive.
Severe siderosis before eltrombopag treatment (15 patients, 50%) did not hinder hematologic response, and liver iron concentration was markedly reduced (median 298 mg Fe/g, IQR: 111.0 mg Fe/g to 88 mg Fe/g IQR: 44..0 mg Fe/g dry weight). Seven patients (23.3%) with severe siderosis received eltrombopag combined with deferoxamine. Double chelation therapy demonstrated a synergistic effect, significantly reducing treatment duration compared to deferoxamine (160 days, IQR: 17.5 vs. 355 days, IQR: 28.5; p=0.001) and Eltrombopag alone (160 days, IQR: 17.5 vs. 290 days, IQR: 153; p=0.010). Cytokine analysis suggested potential immunomodulatory effects: five cytokines (TNF-α, TNF-β, SDF1-α, SCGF-β, IL-9) showed a significant change after Eltrombopag treatment ($p<0.05$).

Conclusions: In conclusion, our finding supports the use of Eltrombopag as a safe and effective treatment option for managing PGF in the pediatric population, even when combined with other iron-chelating agents, potentially contributing to improved clinical outcomes. Cytokine profile suggests that Eltrombopag may exert immunomodulatory effects beyond megakaryopoiesis stimulation, potentially contributing to hematologic recovery by regulating the bone marrow niche. Further research is needed to validate these findings and to better define the optimal criteria for its use in the paediatric setting.

Disclosure: Nothing to declare

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HIGH VIRAL LOAD BK VIRURIA IS COMMON AFTER PAEDIATRIC HAEMATOPOIETIC STEM CELL TRANSPLANT AND DOES NOT PREDICT SYMPTOMATIC HAEMORRHAGIC CYSTITIS

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Background: BK virus is the most common cause for haemorrhagic cystitis (HC) in paediatric haematopoietic stem cell transplant (HSCT) patients. HC is associated with prolonged hospitalisation, poorer quality of life, and treatment related mortality, with an estimated incidence of 8-25% in paediatric HSCT recipients. HC typically develops 2-8 weeks post HSCT, and is associated with a triad of macroscopic haematuria, clinical signs and symptoms of cystitis, and demonstration of BKV viruria.
BK viruria alone is common, seen in up to 80% of paediatric transplant patients, but can occur in the absence of HC, and is not predictive of HC onset or severity. Risk factors associated with BK-associated HC include UCB source, BK viraemia, older age (>5 years), and use of ATG.

Methods: A retrospective review was performed of children undergoing HSCT at a single UK transplant centre between 1 January 2015 and 31 December 2024, who were identified to have BKV viruria detected by quantitative polymerase chain reaction (PCR) testing. Associated demographic data was collected, including donor, cell source, use of serotherapy in conditioning, and number of urine samples sent for BKV PCR. Patients were considered to have BKV-associated haemorrhagic cystitis if symptoms were reported and noted in the medical record on the day of the highest viral load detected by quantitative PCR, and documented by common terminology criteria for adverse events (CTCAE) cystitis grading.

Results: 502 transplants were performed during the 10-year period, and a total of 163 patients (2 of which had 2 transplants) developed BK viruria. The incidence of BKV viruria in this population was 33%. 126/165 (76%) were from unrelated donors 33/165 (20%) were matched family donors. Donor source was predominantly bone marrow (88/165, 53%), followed by cord (48/165, 29%), and PBSC (29/165 (17%). 84/165 (51%) received serotherapy as part of their conditioning regimen. There was no relationship between viral load and serotherapy received.
BKV in urine was measured either due to screening for BKV, or due to clinical symptoms such as haematuria, dysuria or urinary frequency. The median number of BKV PCR samples sent per patient was 4 (1-44). The median date post-transplant of peak BKV PCR result was day +26 (1-346). Median BKV copies/ml detected was $1.0x10^9$, ($9.2x10^1$ – $2.8x10^{11}$). Median BKV log was 9.06^{10} (1.96^{10} – 11.94^{10}).
Grade 1-2 haemorrhagic cystitis symptoms were reported in 7/45 patients transplanted between 2022 and 2025, with no significant difference in viral load between the patients who developed haemorrhagic cystitis and those who did not. Peak BKV log did not correlate with severity of haemorrhagic cystitis.

Conclusions: BK viruria is common in paediatric HSCT recipients, however peak BKV viruria does not predict the development HC. There is a poor relationship between urine BKV viral load and clinical symptoms, and peak BKV viruria is not predictive of the severity of cystitis.

Disclosure: Nothing to declare

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DONOR SELECTION STRATEGY IS CRITICAL IN DETERMINING OUTCOMES OF HIGH-RISK, PAEDIATRIC, RELAPSED, MRD POSITIVE T-ALL HSCT

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Background: Haematopoietic stem cell transplantation (HSCT) outcomes for T-cell acute lymphoblastic leukaemia (T-ALL) remain inferior to those for B-ALL due to the aggressive biology of T-ALL, higher relapse risk, limited options for targeted minimal residual disease

(MRD) control, and the lack of effective chimeric antigen receptor (CAR)-T programmes. Pre-transplant MRD is an independent predictor of poor relapse-free survival (RFS) and overall survival (OS) in T-ALL HSCT. We hypothesised that graft-versus-leukaemia (GVL) activity may play a particularly important role in T-ALL biology and could translate into improved outcomes with non-serotherapy–based HSCT. We examined the impact of transplant type and donor source on outcomes in a multicentre cohort.

Methods: We retrospectively reviewed children with T-ALL who underwent HSCT at two major UK paediatric transplant centres between 2014 and 2024. Clinical records were analysed for patient, donor, transplant characteristics, OS and relapse outcomes.Differences in RFS by donor type were assessed using the log-rank test, with multivariable Cox regression adjusting for MRD.

Results: Thirty-nine children (36 boys, 3 girls) aged 8–18 years (median 13) underwent HSCT. Nineteen had primary refractory T-ALL, of whom 10 were MRD-positive pre-transplant (10^{-4} to 10^{-6}). Twenty patients had relapsed T-ALL; 14 of these were MRD-positive at transplant. All except one received TBI-based myeloablative conditioning: approximately half received etoposide with 12 Gy TBI, and the remainder cyclophosphamide with 14.4 Gy TBI. Serotherapy was used only in matched unrelated donor (MUD) transplants using BM/PBSC as HSC source. Cord blood transplants were T-cell-replete (TRCBT) with ciclosporin ± mycophenolate mofetil as GVHD prophylaxis. Matched sibling donor (MSD) transplants used methotrexate plus ciclosporin as GVHD prophylaxis.
Of 39 patients, 11 received MSD bone-marrow grafts. The remaining 28 received unrelated donor grafts: 11 cord blood and 17 PBSC/BM. With a median follow-up of 6 years 5 months (range 1.5–11.2 years), 29 patients (74.3%) are alive. Relapse accounted for 9 of 10 deaths; one additional death occurred from transplant-related mortality (TRM) after TRCBT. All relapses occurred within one-year post-HSCT.
OS and RFS were 89.5% and 60% for transplants performed in CR1 and CR2, respectively. Pre-transplant MRD strongly influenced outcomes in CR2 patients: RFS was 50% in MRD-positive versus 83% in MRD-negative CR2 recipients. In contrast, MRD positivity appeared less impactful in CR1 transplants.
Outcomes varied markedly by donor type. MSD HSCT and TRCBT showed significantly superior post-transplant remission rates (90% and 80%, respectively) (log rank p=0.002) compared with a markedly lower RFS of 33% after MUD HSCT. Among MRD-negative recipients, differences were less pronounced: RFS was 100% for MSD (n=3) and TRCBT (n=1), and 81.8% for MUD (n=11).

Conclusions: Relapse remains the leading cause of HSCT failure in T-ALL, particularly in CR2 patients with persistent pre-transplant MRD. Where disease is chemo responsive, deeper pre-transplant cytoreduction—such as with nelarabine—may be beneficial. Our data suggest that in cases of refractory MRD, prioritising non-serotherapy platforms like MSD HSCT or TRCBT may better harness GVL and improve RFS and OS. Larger studies are warranted to validate these findings, inform donor-selection strategies, and improve outcomes in this high-risk population.

Disclosure: nil

B239

BORN TO HEAL? PSYCHOSOCIAL AND ETHICAL DIMENSIONS OF SAVIOR SIBLINGS AND RECIPIENT CHILDREN IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Hematopoietic stem cell transplantation (HSCT) remains a life-saving intervention for numerous malignant and non-malignant hematologic disorders in childhood. Advances in assisted reproductive technologies have enabled the intentional conception of HLA-matched "savior siblings," born with the potential to serve as stem cell donors for an affected child. While this practice has markedly improved transplant feasibility and outcomes, it simultaneously raises complex psychosocial and ethical questions concerning consent, identity formation, familial expectations, and moral responsibility. Existing literature has

largely emphasized clinical success and ethical debate, whereas qualitative studies capturing the lived experiences of both savior siblings and recipient children—within their familial and cultural contexts—remain scarce. This study aimed to explore these experiences in depth, focusing on psychosocial meanings and ethical perceptions across the HSCT trajectory.

Methods: A descriptive phenomenological qualitative design was employed. The study sample included savior siblings, transplanted children, and their parents. Data were collected through online semi-structured in-depth interviews guided by open-ended questions designed to elicit personal meanings and emotional experiences. Interviews were audio-recorded, transcribed verbatim, and analyzed using DataBeeg 1.0 qualitative analysis software. Colaizzi's seven-step method guided data analysis. Methodological rigor was ensured through participant validation, peer debriefing, and transparent documentation of analytic decisions, enhancing credibility and transferability of the findings. The study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the institutional ethics committee, and written informed consent was obtained from all parents. Only families in whom savior siblings and recipient children had received structured, age-appropriate information regarding the donation and transplantation process were included.

Results: Participants' narratives revealed a multidimensional experience shaped by four themes: (1) diagnosis and treatment journey, (2) meanings attributed to having a savior sibling, (3) coping strategies, and (4) reflections. The diagnosis and treatment phase involved urgency, long hospitalizations, and major emotional and physical strain on families, particularly mothers undergoing assisted reproduction, often disrupting family roles and social life. Savior siblings viewed donation as an act of healing and belonging, strengthening sibling bonds and family unity. Recipient children described transplantation as a turning point symbolizing survival and renewal. Parents voiced ethical concerns about informed consent at young ages and potential risks to the donor child. Coping relied on family and social support, trust in healthcare teams, continuous information, and maintaining hope, while some avoided recalling the experience as psychological self-protection.

Conclusions: This study demonstrates that savior siblings and recipient children experience HSCT not solely as a medical intervention but as a profound psychosocial and ethical life event. The findings highlight the need for longitudinal, family-centered psychosocial support embedded within pediatric transplant programs. Given the culturally sensitive and ethically complex nature of savior sibling practices, transplant physicians and nurses should proactively assess and address the evolving emotional and moral needs of both donor and recipient children. Although based on a single-center cohort, the depth and consistency of narratives suggest transferable insights relevant to pediatric HSCT programs across diverse cultural and religious contexts.

Clinical Trial Registry:

Disclosure: Nothing to declare.

B240

SECONDARY MALIGNANCIES IN SURVIVORS OF CHILDHOOD CANCER

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Background: Over the past 60 years, treatment and supportive care of children with cancer has improved, increasing the number of survivors living to adulthood. Treatment regimens have been modified to improve outcomes and reduce long-term sequelae. Secondary malignancies (SMN) contribute to high morbidity and mortality and the estimated 25-year cumulative incidence in one study of nearly 50,000 survivors was 5.4%. In haematopoietic stem cell transplant (HSCT) patients, the 30-year cumulative incidence of any SMN was 9.9%.

Methods: We performed a retrospective review of a database of patients treated by a single institution and followed up in the long term follow up clinic who self-reported SMNs following treatment with chemotherapy or radiation for malignant and non-malignant conditions. Patients included in the dataset include those treated as early as 1968 when the oncology unit was first opened, and were known to the LFTU service. Descriptive statistical analysis was used to describe characteristics of patients with SMNs.

Results: 95 patients had self-reported SMNs (59% female, 41% male). The majority were between the ages of 1-4 years when treated for their primary condition, with 28% patients having a primary diagnosis of acute lymphoblastic leukaemia. 81% were diagnosed before the year 2000. The most common reported SMN was thyroid cancer (18%), followed by sarcoma (11%) and meningioma (10%). 33% of patients had experienced multiple malignancies. 67% of patients had received radiation during their primary therapy.
41 patients who reported SMN had previously undergone HSCT for treatment of their primary condition (80% malignant disease, 20% non-malignant disease), of a total of ~1000 patients who had undergone HSCT at our institution (4%). 60% of patients had been transplanted before the year 2000, and 20% had died due to their SMN, with some SMN reported as late as 30 years post HSCT. Underlying germline cancer predisposition syndromes were reported in 1 patient.

Conclusions: SMNs contribute to significant health burden in survivors of childhood cancer, often contributing to early mortality. A challenge is the long latency period between the original diagnosis (often when the child is very young), and development of the SMN, often in early adulthood. The introduction of risk-adapted therapies has contributed to the changing nature of SMNs reported, as radiation has been removed from the majority of upfront ALL therapies.
The growing survivorship cohort requires specific and early SMN surveillance, and a patient-adapted approach is essential to consider underlying cancer predisposition syndromes, and use of more contemporary treatments such as targeted therapies.

Disclosure: Nothing to declare

B241

PERI-TRANSPLANT RUXOLITINIB FOR GRAFT-VS-HOST-DISEASE (GVHD) PREVENTION IN PEDIATRIC AND YOUNG ADULT PATIENTS UNDERGOING MYELOABLATIVE HEMATOPOIETIC CELL TRANSPLANTATION (HCT): INTERIM ANALYSIS

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Background: Ruxolitinib, a JAK 1/2 inhibitor, has been proven to be safe and effective in treating steroid refractory acute and chronic graft-versus-host disease (GVHD) in pediatric and adult patients after allogeneic hematopoietic cell transplant (HCT). However, it has not been studied upfront for GVHD prevention in pediatric patients. We previously reported peri-HCT ruxolitinib administration is safe and promotes engraftment in adults with myelofibrosis undergoing HCT. Similarly, our group showed that peri-HCT itacitinib, another JAK 1 inhibitor, is safe when added to tacrolimus/sirolimus as GVHD prophylaxis, with 100% engraftment and low rates of acute/chronic GVHD in adults. Peri-HCT ruxolitinib may be a strategy to reduce conditioning intensity. We are conducting a pilot study (NCT06128070) adding ruxolitinib to tacrolimus/methotrexate for GVHD prophylaxis in pediatric and young adult patients undergoing myeloablative HCT, with the primary objectives of evaluating safety, feasibility/tolerability and preliminary efficacy based on grades 3-4 acute GVHD-free survival.

Methods: This open-label study has a safety lead-in segment (n=6) with a modified rolling 6 phase 1 design, monitoring unacceptable toxicities (UT) until day 30 post-HCT. Upon confirming safety, the trial will proceed to the randomized segment (n=40), with patients randomized 1:1 to receive standard HCT care with or without ruxolitinib. UTs are defined as grade 3-4 non-hematologic toxicities per Bearman criteria, and grade 4 hematologic toxicities per CTCAE v5.0 at least possibly related to ruxolitinib. Patients ≤22-years-old, weight ≥25 kg, with a history of acute leukemia, myelodysplastic syndromes, or lymphomas receiving myeloablative HCT from an 8/8 matched donor are eligible. Ruxolitinib (5mg, twice a day) is administered from day -1 pre-HCT until day 100 post-HCT.

Results: To date, we have enrolled 6 patients. Median age was 15 years (range: 11-17). All patients received marrow stem cells; patient and transplant characteristics are shown in Table 1. All 6 patients achieved neutrophil engraftment (median 22 days, range: 14-26), 5 achieved platelet engraftment (median 24 days, range: 14-36). One patient passed on day 21 before platelet engraftment due to causes unrelated to ruxolitinib and was not evaluable for UTs. Of the 5 evaluable patients, none experienced UTs. Grade ≥3 adverse events (AEs) at least possibly related to ruxolitinib included anemia (n=1), elevated ALT and AST (n=1), and decreased lymphocyte count (n=1). By day 100 post-HCT, 3 patients had bacterial infections, 2 of which were disseminated, all resolved. Of the two with disseminated bacterial infections, one also had viral gastrointestinal infection and the other also had yeast infection (cause of death). Between days 100-130 post-HCT, 1 patient reported 2 episodes of viral

infections, both resolved. No patients experienced clinical CMV reactivation.
With a median follow-up duration of 120 days (range: 59-386), acute GVHD occurred in 2 patients (both Grade 2). One patient had NRM, and none have experienced relapse or chronic GVHD so far.

Table 1 Patient and Transplant Characteristics

	Total (N=6)
Gender	
Female	2 (33.3%)
Male	4 (66.7%)
Ethnicity	
Caucasian Hispanic or Latino	1 (16.7%)
Caucasian Non-Hispanic or Non-Latino	1 (16.7%)
Asian	4 (66.7%)
Diagnosis	
Acute myeloid leukemia	2 (33.3%)
Acute lymphoblastic leukemia	4 (66.6%)
KPS/Lansky Score	
60	1 (16.7%)
80-90	5 (83.3%)
Donor type	
Allogeneic, related	1 (16.7%)
Allogeneic, unrelated	5 (83.3%)
Conditioning Regimen	
BUSULFAN/CYCLOPHOSPHAMIDE	1 (16.7%)
FTBI/CYCLOPHOSPHAMIDE	5 (83.3%)

Conclusions: We show that peri-HCT ruxolitinib did not interfere with engraftment post-HCT. In addition, our data supports the safety and feasibility of adding ruxolitinib to tacrolimus/methotrexate as GVHD prophylaxis in young patients receiving HCT. Accrual is ongoing.

Clinical Trial Registry: NCT06128070

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B242

PROPHYLACTIC DLI IN PEDIATRIC PATIENTS WITH HIGH RISK HEMATOLOGICAL MALIGNANCIES – A SINGLE CENTER EXPERIENCE

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Background:

Allogeneic stem cell transplantation (allo-SCT) and donor lymphocyte infusions (DLI) can elicit a graft-versus-leukemia (GvL) effect in pediatric patients with hematological malignancies. We report our single-center experience with prophylactic DLI in high- risk pediatric patients with leukemia or lymphoma, focusing on feasibility, safety and efficacy.

Methods:

In total, 10 high-risk patients received prophylactic DLI following allo-SCT. Donors were either matched (n=5) or haploidentical (n=5). CD3+ T-cell doses of up to 1×107cells/kg body weight were administered, in some cases over extended periods exceeding three years.

Results:

The treatment was associated with a favourable toxicity profile. In our cohort, 40% of patients developed moderate acute (n=2) or chronic (n=2) graft-versus-host disease (GvHD), no cases of severe or high grade GvHD occurred. Given the high-risk profile of our cohort, outcomes were encouraging, with relapse-free survival (RFS) of 70% and overall survival (OS) of 80% at a median follow-up of 20.5 months. Especially the two subgroups of patients with acute myeloid leukemia (AML) after relapse and patients who were transplanted in first complete remission (CR1) showed outcomes superior to currently reported data. One AML-patient, who had experienced three relapses, received prophylactic DLI after a third allo-SCT and remains in complete remission (CR), more than three years after the last allo-SCT.

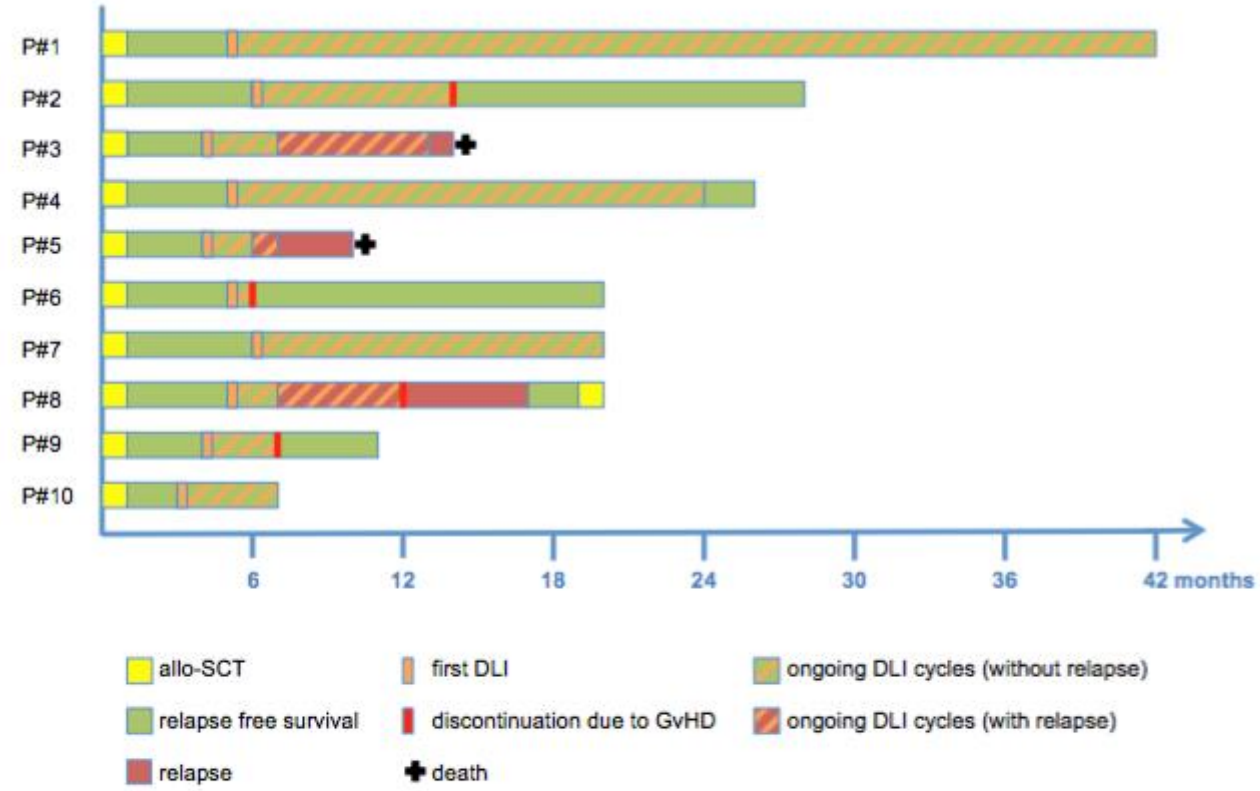

Figure 1 Clinical outcomes and survival of patients

Conclusions:

These data suggest that prophylactic DLI may represent a safe and effective treatment option for pediatric patients with hematological malignancies at high risk of post-transplant relapse.

Disclosure: The authors declare no potential conflicts of interests.

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B243

FEASIBILITY OF CADAVERIC DONOR-DERIVED HEMATOPOIETIC GRAFTS TO INDUCE MIXED CHIMERISM AS A STRATEGY TO ACHIEVE TOLERANCE IN MULTIVISCERAL TRANSPLANTATION

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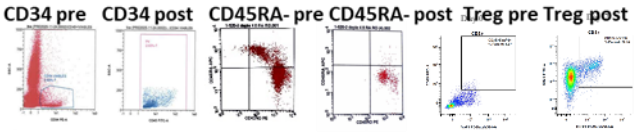
Background: Hematopoietic stem cell transplantation (HCT) has been investigated as a strategy to induce mixed chimerism in solid organ transplantation (SOT), aiming to promote tolerance and reduce long-term immunosuppression. Cadaveric donors represent a valuable source of hematopoietic progenitors and other immune cell populations. We hypothesize that grafts containing $CD34^+$ cells, $CD45RA^-$ T cells, and regulatory T cells (Tregs) from cadaveric donors can safely induce transient chimerism and improve graft acceptance. The addition of thymic tissue or Tregs may further reduce alloreactivity. We report our initial experience with four $CD34^+$ cell collections harvested from vertebral bodies of cadaveric donors (two brain-dead, two circulatory-dead). Additionally, we aimed to isolate $CD45RO^+/RA^-$ T cells from peripheral blood and generate Tregs from thymic tissue.

Methods: Harvest was done in vertebral corps and $CD34^+$ cells were isolated using CliniMACS Plus. $CD45RO^+/RA^-$ T cells were obtained from the $CD34^-$ fraction and peripheral blood. Tregs were generated by mechanical thymus disaggregation (GentleMACS), $CD25^+$ selection with magnetic beads, and one-week culture with cytokines. To model tolerance, we developed a rat small bowel transplant rejection model.

Results: $CD34^+$ cells were successfully obtained from all four donors. Median harvested volume was 96 mL (IQR, 65), yielding 1.25×10^8/kg total nucleated cells and 1.455×10^6/kg $CD34^+$ cells; after selection, 0.645×10^6/kg $CD34^+$ cells were recovered. $CD45RA^-$ T cells were isolated from the two older donors, while younger donors (1.6 years and 1 month)

had scarce memory T cells but provided thymic tissue for Treg isolation.
One patient (#1), with prior multivisceral transplant (MVT) rejections, received non-myeloablative conditioning followed by a graft containing naïve and memory T cells 88 days post-MVT from a mismatched deceased donor. No graft-versus-host disease or HCT-related toxicity occurred. The patient achieved transient mixed chimerism ($CD3^+$ cells 0.05–5.1% during the first year), a peak in Tregs at day 90, and remains stable >5 years on monotherapy without rejection. One patient (#2) died from surgical complications before HCT. Two patients (#3 and #4) are enrolled in the DUALGRAFT trial (NCT06997471) and awaiting HCT.
In rats, Brown Norway small bowel was transplanted into Lewis recipients under tacrolimus (Tac) alone or Tac plus delayed infusion of $CD90^+$ progenitors. Tac+$CD90^+$ animals showed increased chimerism and delayed lymphoid infiltration, but severe rejection persisted at day 21. We hypothesize that adding thymic tissue or Tregs to progenitor cells may improve outcomes.



	Dw	Da	Dt	Tim	BMV	TNC	CD34	CD34p	PBV	TNCp	RO	Thy	Treg0	Treg7
#1	25	14	BD	24	141	1.3	0.88	0.41	286	0.72	1	No	NA	NA
#2	4	0.1	CD	48	66	1.2	0.51	.,22	326	0.8	0.15	Yes	ND	ND
#3	16	1.6	BD	19	60	0.6	2.03	.,88	279	0.31	0.003	Yes	3.07	33.37
#4	3.2	0.07	CD	36	126	1.72	2.97	.,62	80	0	0	Yes	1.87	22.94

Dw: donor weight (Kg); Da: donor age (years); Dt: donor type; BD: brain dead; CD: circulatory dead; Tim: time to manufacturing (hours); BMV: Bone marrow volume (ml); TNC: total nucleated cells$x10^8$/kg; CD34: CD34$x10^6$/kg pre; CD34p: CD34$x10^6$/kg post; PBV: Peripheral blood volume (ml); TNCp: peripheral blood total nucleated cells$x10^8$/kg; RO: $CD45RO^+x10^6$/kg; Thy:Thymus; Treg0 (%):ThyTregs ($CD3^+CD4^+CD25^+FOXP3^+$) at D0; Treg7:ThyTregs ($CD3^+CD4^+CD25^+FOXP3^+$) at D7; NA:not applicable; ND: not done

Conclusions: We demonstrate the feasibility of obtaining non-alloreactive hematopoietic grafts from cadaveric donors, including $CD34^+$ cells, memory T cells, and Tregs, as a potential strategy to induce transient chimerism and tolerance in MVT. This approach is being implemented in the DUALGRAFT trial. Further preclinical work is needed to optimize protocols.

Clinical Trial Registry: https://clinicaltrials.gov/search?cond=NCT06997471

Disclosure: Nothing to declare

B244

IMPACT OF ANTI-THYMOCYTE GLOBULIN DOSE ON SURVIVAL, RELAPSE AND IMMUNE RECOVERY IN PEDIATRIC ALLOGENEIC HSCT FOR MYELOID MALIGNANCIES

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Background: Anti-thymocyte globulin (ATG) is widely used in pediatric allogeneic HSCT to prevent graft-versus-host disease (GvHD), but its optimal dose and impact on immune reconstitution remain uncertain. We evaluated dose-dependent effects of ATG on survival, relapse, viral complications and lymphocyte subset recovery in children transplanted for myeloid malignancies.

Methods: We retrospectively analysed 90 allogeneic HSCTs in children with AML (n=51), MDS (n=28) and JMML (n=11). Most procedures used matched unrelated donors (MD, 84.4%), and matched sibling donors (MSD) accounted for 15.6%. ATG was administered at 45 mg/kg (n=48) or 30 mg/kg (n=30) in MD transplants, while 12 MSD recipients received no ATG. Outcomes included overall survival (OS), relapse, viral infections, acute and chronic GvHD, and longitudinal recovery of cell subsets up to 36 months. Kaplan–Meier/log-rank and chi-square tests were used for univariable analyses.

Results: After a median follow-up of 62.0 months, 2- and 5-year OS were 87.8% and 79.7%, respectively. Relapse occurred in 20.0% and was the most significant adverse predictor of OS (5-year OS 90.2% without relapse vs 36.2% with relapse, $p<0.001$). ATG dose showed a modest association with early OS (2-year OS 91.7%, 96.7% and 81.2% for 0, 30 and 45 mg/kg, $p=0.024$), but differences diminished by 5 years ($p=0.487$). Relapse rates were not increased with higher ATG dosing (33.3%, 20.0% and 16.7% for 0, 30 and 45 mg/kg, $p=0.435$). EBV reactivation rose with ATG dose (0%, 13.3% and 37.5%, $p=0.006$), while other viral reactivations and GvHD rates showed no clear dose–response after adjusting for donor type. ATG demonstrated a significant, dose-dependent delay in early $CD4^+$ T-cell and B-cell reconstitution, with median counts at day +30 and +90 markedly lower in the 45 mg/kg group and only partial convergence by 12–24 months. Total and $CD8^+$ T-cell recovery was also delayed, although to a lesser extent, whereas NK-cell reconstitution was rapid and largely preserved across ATG dosing levels.

Conclusions: In pediatric HSCT for myeloid malignancies, higher ATG doses delay recovery of $CD4^+$ T cells and B cells, but do not clearly worsen long-term survival or increase relapse risk. These data highlight the need to individualise dosing to balance GvHD prophylaxis, infection and EBV risk, and timely immune reconstitution.

Disclosure: Nothing to declare.

B245

THE EFFECT OF ALLOGENEIC HSCT ON PEDIATRIC NON–DOWN SYNDROME AMKL: RESULTS FROM A MULTICENTER CALD-AMKL-18 TRIAL

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Background: Pediatric non–Down syndrome acute megakaryoblastic leukemia (non-DS AMKL) is a rare, high-risk AML subtype with poor outcomes. In this study we investigated the effect of allogeneic hematopoietic stem cell transplantation (HSCT) on the outcome of non-DS AMKL.

Methods: CALD-AMKL-18 is a prospective multicenter trial using a low-dose HAG induction backbone (low-dose of homoharringtonine and cytarabine, routine dose of G-CSF) for newly diagnosed pediatric non-DS AMKL at 9 Chinese centers. All patients received at least one HAG induction cycle followed by risk-adapted consolidation; those in first complete remission (CR1) either proceeded to HSCT or continued chemotherapy, and a minority underwent HSCT after relapse. Measurable residual disease (MRD) was monitored by multiparameter flow cytometry after each induction and, when applicable, immediately before HSCT. Survival was estimated by Kaplan–Meier; subgroup analyses by HSCT, fusion status and MRD were exploratory.

Results: From 2017 to 2022, 51 patients (median age 40 months) were enrolled. The most frequent lesions were *CBFA2T3::GLIS2*(15.7%), *NUP98::KDM5A* (15.7%), *KMT2A::MLLT3* (9.8%), *HOXr* (7.8%) and *RBM15::MRTFA* (7.8%). Eight patients (15.7%) carried infrequent or novel fusions (including *PICALM::MLLT10*, *TNIP1::CSF1R*, *ZEB2::RUNX1*, *MYB::GATA1*, *CCDC6::BCKDHB*, *ETV6::TLL2*, *EED::PRKAR1A*), and 14 (27.5%) were negative. After two HAG cycles, the CR/CRi rate was 76.5%; induction was very safe, with no early deaths and an overall treatment-related mortality of 2.0% (one fatal infection during consolidation). Overall, 27/51 patients (52.9%) underwent HSCT in CR1 or after consolidation, while 24/51 (47.1%) received chemotherapy alone. For the entire cohort, 5-year overall survival (OS) and event-free survival (EFS) were 42.7 ± 7.3% and 41.9 ± 7.6%. Relapse occurred in 16/51 (31.4%): 8/27 (29.6%) after CR1/early HSCT and 8/24 (33.3%) with chemotherapy alone, and was concentrated in patients with canonical adverse lesions (*CBFA2T3::GLIS2*, *NUP98::KDM5A*, *KMT2A::MLLT3*, monosomy 7/del(7q)). Many high-risk patients, particularly those with *NUP98::KDM5A* or *CBFA2T3::GLIS2*, had refractory or continuously progressive disease and died before they could proceed to HSCT. Fusion-stratified analyses showed that CR1 HSCT did not improve overall outcome in *CBFA2T3::GLIS2* patients (4/4 transplanted

relapsed and died), but appeared to convert a uniformly fatal course into long-term survival for half of *NUP98::KDM5A* cases (2/4 long-term survivors vs. 4/4 deaths with chemotherapy alone) and was associated with excellent disease control in *KMT2A::MLLT3* and monosomy 7/del(7q) disease (6/6 transplanted patients alive in first CR). Only two fusion-negative patients received salvage HSCT after relapse; one achieved durable second remission. MRD ≥0.1% after Induction II predicted markedly inferior OS/EFS, and pre-HSCT MRD negativity was associated with superior post-transplant survival.

Conclusions: CR1 HSCT appeared to improve survival for some adverse genotypes. These data support a risk-adapted HSCT strategy built on a low-toxicity HAG backbone, but also highlight the need for "low-dose chemotherapy (LDC) + X" approaches that integrate targeted agents and MRD-guided HSCT to overcome fusion-driven resistance in pediatric non-DS AMKL.

Clinical Trial Registry: ChiCTR1800015875; https://www.chictr.org.cn/showproj.html?proj=26027

Disclosure:

No conflicts of interest to disclose. Shengqin Cheng, Peifang Xiao and Yixin Hu drafted the manuscript and performed all the data analysis. Xiaowen zhai, Hua jiang, Ningling wang and Yong Zhuang are responsible for data collection. Xueju Xu, Ning Liao and Fang Xu helped interpret the results. Liangchun Yang and XiuLi Ju helped integrate all the clinical data. All authors read and approved the final manuscript for publication.

B246

PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN BRAZIL: A REGIONAL CHALLENGE

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Background: Hematopoietic stem cell transplantation (HSCT) is an advanced therapeutic modality that has revolutionized the treatment of several severe hematologic and immunologic diseases. In Brazil, HSCT has gained increasing relevance over recent years, consolidating its role as an effective and potentially curative option for multiple clinical conditions.
Nationwide, HSCT is performed in specialized centers supported by highly trained multidisciplinary teams. However, these centers are unevenly distributed, with a marked concentration in the South and Southeast regions, particularly in cities such as São Paulo and Curitiba. Although Brazil's Unified Health System (SUS) provides coverage for HSCT in several indications, the geographic distribution of services remains a significant barrier to equitable access.
We aim to demonstrate the disparity in the distribution of pediatric HSCT centers in Brazil, highlighting the disproportion between service availability and the incidence of diseases requiring transplantation.

Methods: This is a cross-sectional, retrospective, descriptive, and qualitative study based on data from the Brazilian Transplant Registry (ABTO). Pediatric HSCTs performed in 2023 across the different regions of Brazil were analyzed. Additionally, an attempt was made to collect data for the year 2024 from the Brazilian Transplant Registry; however, these data were not available or published at the time of analysis.

Results: In 2023, data from the Brazilian Transplant Registry revealed pronounced regional disparities in the performance of pediatric HSCT. The state of São Paulo accounted for 357 pediatric transplants, whereas the state of Ceará registered only one procedure during the same period. These findings stand in marked contrast to DATASUS data, which reported approximately 415 new cases of pediatric leukemia in the Northeast region in 2023—conditions that, when associated with poor prognosis, may indicate HSCT.
An even more critical situation was observed in the Northern region, where no pediatric HSCT centers were registered, despite the diagnosis of approximately 376 new cases of pediatric leukemia in the same year according to DATASUS.
The attempt to obtain data for 2024 from ABTO revealed the absence of published information, limiting more recent temporal analyses and suggesting weaknesses in transparency and prioritization of national monitoring of this therapy. Complementary data from the Summary Slides of the Brazilian Society of Cell Therapy and Bone Marrow Transplantation (SBTMO), published in 2025, report 42 HSCT centers in Brazil, of which 26 are located in the Southeast and 8 in the South, while only 3 centers are located in the Northeast and none in the North.

Conclusions: The distribution of pediatric HSCT centers in Brazil is markedly unequal, with a strong concentration in the South and Southeast regions, contrasting with the high incidence of pediatric hematologic diseases in other parts of the country. The lack of published ABTO data for 2024 limits updated analyses and highlights weaknesses in national HSCT monitoring. Data from the SBTMO further confirm that the North and Northeast regions remain extremely underserved in terms of pediatric transplant centers. Expanding and redistributing the HSCT network, along with improving transparency in national registries, is essential to ensure equitable access and improve clinical outcomes for Brazilian children.

Disclosure: No disclosures.

B247

DOSE REDUCTION IMPROVES THE OUTCOMES OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH WILMS TUMOR: DATA FROM RETROSPECTIVE TRIAL FROM TWO CENTRS

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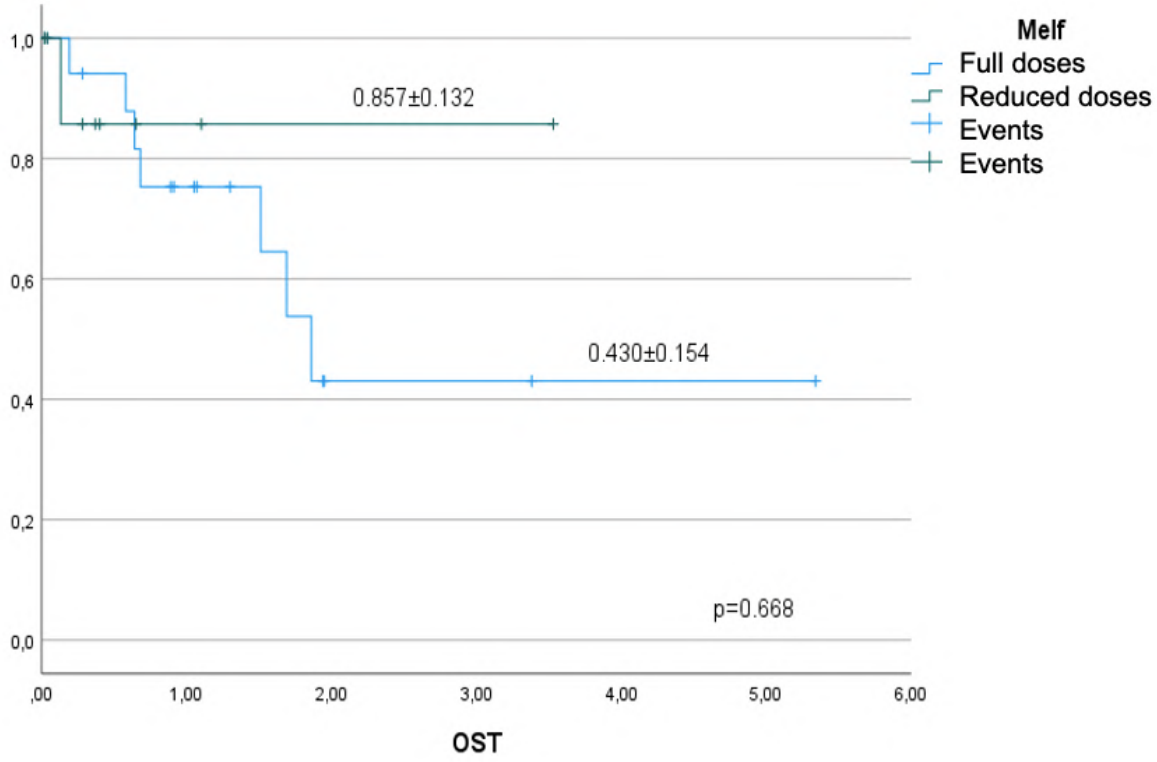
Background: High-risk Wilms tumor (WT) requires autologous hematopoietic stem cell transplantation (aHSCT) as a part of treatment plan. High-dose chemotherapy with melphalan is associated with high mortality and morbidity.
We presenting retrospective analysis of children with WT received aHSCT in different dosing regimen of melphalan.

Methods: A retrospective study analyzed the results of treatment of 27 children with WT (M/F ratio 15/12) belonging to the group of extremely high risk (group D, n = 3, 11.1%), disease progression/recurrence (n=24, 88.9%). Nineteen patients (70.4%) received two lines of induction, and 5 (18.5%) three or more lines of therapy (SIOP RTSG 2016 protocol). Median of age was 6 years 5 months. Peripheral blood stem cell apheresis (PBSC) was performed in all patients: 24 (89%) patients required one apheresis, 3 (11%) two or more. Full dose of Melphalan (single dose of 200 mg/sq.m.) was used in 17 (63.0%) cases (group 1), and reduced dose (140 mg/sq.m.) – in 10 (37.0%) cases (group 2). The median of infused CD34+ cells was 4.9 × 10 6/kg.

Results: All patients engrafted. Median of neutrophils recovery were faster in group 2 (7 days) in the contrast of group 2 (17 days). Toxicity rates were same in both groups, but no mucositis of gr. 3-4 was found in group 2. With a median follow-up of 1.5 years, 19/27 patients are alive in both groups. Overall survival: group 1 – 43.0%, group 2 – 85.7%. Disease-free survival: group 1 – 36%, group 2 – 78%. Causes of mortality in group 1: toxicity – 4, progression – 2; in group 2: toxicity – 1, progression – 1.



Conclusions: Autologous HSCT is an effective method of consolidation in case of WT of unfavorable prognosis in children. Our study showed that reduction of doses of Melphalan improves both overall and disease-free survival. Future large multicenter trials required.

Disclosure: There are no conflicts of interest.

B248

NEUROIMMUNOLOGICAL MORBIDITY AFTER PEDIATRIC ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A MULTICENTER ANALYSIS ON BEHALF OF THE PEDIATRIC SUBCOMMITTEE OF GETH (GRUPO ESPAÑOL DE TRASPLANTE HEMATOPOYÉTICO)

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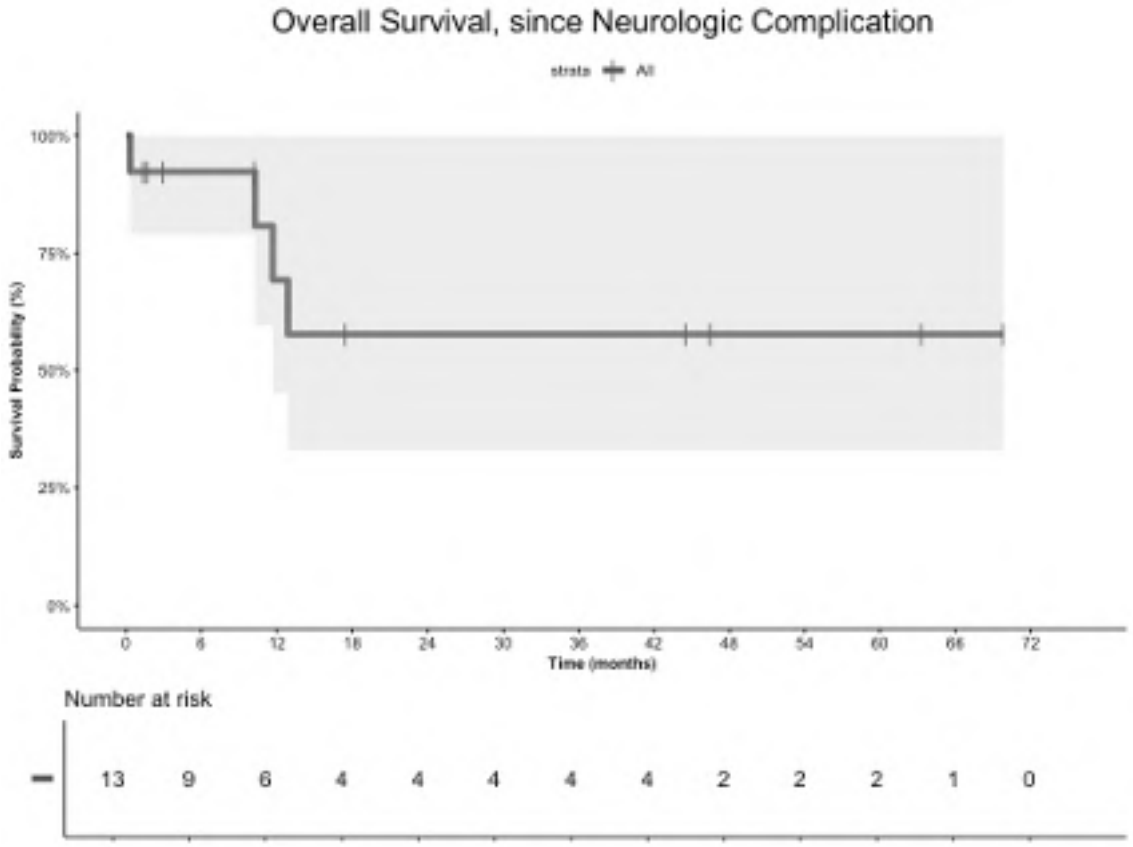
Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment for certain hematological malignancies and non-malignant disorders. Conditioning regimens and immunosuppressive therapies induce a profound transient immunodeficiency, which is associated with relapse of malignant diseases, infections, graft versus host disease (GvHD), and immune dysregulation. In recent years, neurological complications secondary to immune dysregulation induced by transplantation have been increasingly recognized. Nevertheless, their typification as atypical manifestations of GvHD remains challenging, and the available literature is limited and predominantly focused on adults.

Methods: The aim of this study was to describe immune-mediated neurological complications (INC) in pediatric HSCT recipients in Spain. We retrospectively analyzed patients under 18 years old who underwent HSCT and subsequently developed neurological complications not attributable to infectious, pharmacologic, or other non-immune causes, between January 2018 and September 2025.

Results: Thirteen patients were included. The majority were male (62%), transplanted because of a malignant disease (69%) from an unrelated (62%) or an haploidentical related donor (31%). The median age at INC diagnosis was 13.5 years (interquartile range [IQR] 10.3–16.4), at a median of 119 days post-HSCT (IQR 82–226). All but two patients (85%) had acute and 54% had chronic GvHD. Prior to the INC, patients were profoundly lymphopenic (median CD4+ 86/mcl [IQR 10-212]; median B cells 8/mcl [IQR 0-57]). INC affected mainly the central nervous system (8/13, 62%): 5/8 encephalitis, 1/8 neuromyelitis optica, 1/8 cerebellitis, and 1/8 transverse myelitis. Peripheral nervous system manifestations (38%) included 3/5 myositis and 2/5 peripheral neuropathies. Diagnostic workups excluded non-immune causes. Specific diagnostic tests (MRI, EEG, EMG, etc.) were tailored to the neurological presentation yielding heterogeneous findings. Half of the patients had no detectable autoantibodies in either serum or cerebrospinal fluid (CSF); in CSF were rarely detected (13% of tested patients), but 100% were anti-GAD. The majority of patients received at least two immunossupressant/immunomodulatory therapies (85%), including steroids (11/13, 85%), IVIg (10/13, 77%), rituximab (5/13, 38%), ruxolitinib (4/13, 31%), and plasmapheresis (4/11, 31%).
Ten patients (77%) developed long-term sequelae. Survival after INC was 69% at a median follow up of 12 months (IQR 3, 44) (figure 1). Death was attributed to NIC in one patient (refractory status epilepticus due to encephalitis). Other causes of death were sepsis in the context of status epilepticus (1/13), and relapse of malignant disease while remaining profoundly disabled (2/13).



Conclusions: Although uncommon, INC following pediatric allogeneic HSCT constitute a significant clinical entity with substantial implications for survival and long-term quality of life.

Disclosure: Nothing to declare.

B249

THE RESULTS OF ALLOGENIC HSCT IN PAEDIATRIC PATIENTS DIAGNOSED WITH MYELOID SARCOMA – A SINGLE CENTRE EXPERIENCE

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Background: Myeloid sarcoma (MS) is an extramedullary mass consisting of myeloid blasts and it may occur *de novo* or concurrently with acute myeloid leukemia, myelodysplastic

syndrome of myeloproliferative disease. There is no consensus on the treatment of MS, especially its isolated form. Systemic chemotherapy with consideration of allo-HSCT is usually used in paediatric patients.

Methods: We performed a retrospective analysis of 7 paediatric patients (age: 2,5-16,3 years old) with myeloid sarcoma who underwent allogenic HSCT between December 2010 and January 2024 in our institute. One patient had MS de novo, six patients developed MS in course of an underlying disease (AML, n=5; CML, n=1). The extramedullary disease was located in skin (n=2), orbit (n=2) and other organs (n=5). Patients were transplanted in CR1 (n=4; 57,1%), CR2 (n=2; 28,6%) or PR (n=1; 14,3%) and had Lansky or Karnofsky score >80% (n=7; 100%) at HSCT. Most children were transplanted from unrelated donor (n=5; 71,4%), one patient from sibling donor and one from haploidentical donor. The stem cell sources were peripheral blood stem cells (PBSC; n=4) and bone marrow (BM; n=3). The conditioning regimen was treosulfan-based (n=5) or busulfan-based (n=2), combined with different cytostatics, mostly fludarabine (n=6; 85,7%) and cyclophosphamide (n=1; 14,3%).

Results: All patients achieved engraftment (range: 12-23 days after HSCT; median 16 days). One SOS/VOD was diagnosed. Acute graft versus host disease (GvHD) grade II-IV occurred in 2/7 patients. There was no extensive chronic GvHD in our cohort. There was no non-relapse deaths. Relapse occurred in 3/7 patients: 2 months (relapse in skin and BM), 5 months (relapse in skin and BM), and 13 months after HSCT (relapse in BM), respectively. All relapsed patients finally died due to disease progression. Four patients remain in complete remission for 3-15 years after HSCT (median: 6 years).

Conclusions: Allogeneic hematopoietic stem cell transplantation is a feasible and well-tolerated treatment option for pediatric patients with myeloid sarcoma, providing long-term remission in a substantial proportion of cases. Despite acceptable transplant-related toxicity, relapse after HSCT remains common and is associated with dismal outcomes. These findings underscore the importance of careful patient selection and achieving optimal disease control before transplantation and further research to establish indications for allogenic HSCT and its optimal procedure, including optimal conditioning regimen.

Disclosure: Nothing to declare.

B250

POPULATION PHARMACOKINETIC EVALUATION OF EXTENDED INFUSION ACYCLOVIR IN PEDIATRIC HEMATOPOIETIC STEM CELL RECIPIENTS

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Background: Acyclovir represents the first-line prophylaxis and therapy for herpes virus infections. However, the pharmacokinetics (PK) of acyclovir in children highlights the risk of

achieving ineffective or toxic drug levels. Understanding its PK is crucial for optimizing antiviral therapy and reducing infectious complications in immunosuppressed patients. Understanding the PK profile is essential for tailoring dosing regimens to achieve optimal plasma concentrations. Adjusting infusion duration based on PK data offers a promising strategy to improve clinical outcomes in this population. Although acyclovir is typically administered as a 1-hour intravenous infusion, limited data exist on the effects of prolonged infusion times on drug PK. This study aimed to characterize and compare the PK parameters of acyclovir administered as a 2-hour intravenous infusion with those of the standard 1-hour regimen in pediatric HSCT recipients, evaluating potential benefits of infusion prolongation on drug exposure and plasma concentration profiles.

Methods: A population PK approach was employed using Monolix version 2024R1 according to standard methods. Individual estimates from the final POP/PK model for the 2-hour infusion group (n=35, 9 [1.2-12.5] years) were compared with those obtained from 99 children receiving 1-hour infusions (Maximova et al., Frontiers Pharmacol, 2022). Key PK metrics assessed included clearance (CL), volume of distribution (V), area under the concentration-time curve (AUC), and peak (Cmax) and trough (Cmin) plasma concentrations. Statistical comparisons were performed using t-tests.

Results: Results showed comparable systemic exposure and clearance between 1-hour and 2-hour infusion regimens, with mean AUC values of 26.0±13.2 and 26.3±17.8 h×mg/L, and CL values of 14.0±5.5 and 14.9±4.5 L/h, respectively ($p > 0.05$, Table 1). Volumes of distribution and Cmax were also comparable. Notably, the 2-hour infusion significantly increased trough concentrations (1.4±1.3 mg/L vs. 0.8±1.0 mg/L, $p=0.002$), which may enhance antiviral efficacy by maintaining higher minimum plasma drug levels.

TABLE 1	1-h infusion q6h			2-h infusion q6h	
	All patients (n=99)			All patients (n=35)	
	Mean±SD	Median	t-test, *p*	Mean±SD	Median
Dose (mg)	334.0±158.2	350.0	n.s.	352.2±195.6	300.0
CL (L/h)	14.0±5.5	14.6	n.s.	14.9±4.5	15.3
AUC (hxmg/L)	26.0±13.2	23.3	n.s.	26.3±17.8	21.5
V (L)	25.4±8.7	26.1	n.s.	31.1±4.4	31.3
Cmax (mg/L)	6.9±4.5	6.3	n.s.	7.4±3.8	7.3
Cmin (mg/L)	0.8±1.0	0.6	0.002	1.4±1.3	1.1

Conclusions: In conclusion, extending acyclovir infusion duration to 2 hours in pediatric transplant patients maintains overall drug exposure while increasing trough concentrations, potentially improving pharmacodynamic outcomes. These findings support considering infusion time extension as a viable approach to optimize antiviral therapy in this vulnerable population.

Disclosure: Nothing to declare

B251

EXCELLENT OUTCOMES OF UNMANIPULATED HLA-HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTS AFTER MINIMALLY INTENSIVE CONDITIONING FOR SALVAGE HSCT IN CHILDREN

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Background: For children with severe bone marrow (BM) hypoplasia due to graft failure (GF) or bone marrow failure disorders complicated by life-threatening infections, urgent rescue hematopoietic stem cell transplantation (HSCT) is required. If no HLA-matched sibling donor is available, haploidentical HSCT offers the quickest treatment option. Here we demonstrate excellent outcomes of HLA-haploidentical HSCT with unmanipulated grafts after a minimally intensive conditioning regimen, that was described by Rizzieri et al (Rizzieri et al, JCO, 2007) and so far has not been analyzed in children.

Methods: We conducted a retrospective investigation of 12 children with a median age of 11,1 years (range 1,7-17 years) who underwent a nonmyeloablative conditioning comprising fludarabine (120 mg/m2; d-5 to d-2), cyclophosphamide (90 mg/kg, d- 5 to d-2) and alemtuzumab (1.25 mg/kg; d-4 to d 0), followed by T-cell-replete haploidentical grafts from peripheral blood stem cells (PBSC). We analyzed overall survival (OS), event-free survival (EFS; events were defined as death, relapse, graft rejection or stem cell boost (SCB) administration), time to neutrophil and platelet engraftment, incidence of aGvHD ≥ grade 3 and cGvHD, viral complications and immune reconstitution.
Three patients suffered from severe aplastic anemia and life-threatening invasive infections. Two of these patients were transplanted in the intensive care unit (ICU). One patient with Cernunnos Syndrome suffered from intractable autoimmune hemolytic anemia. Nine patients were treated for GF and BM aplasia following their first allogeneic HSCT for various diseases.

Results: The median follow-up was 39 months (range 7-118 months). All 12 patients demonstrated excellent outcomes with 100% 2-year OS and 76.9% 2-year EFS. All patients engrafted, three patients needed unconditioned CD34+positive selected SCBs. The median time to neutrophil engraftment was 10.5 days (range 9-22) and the median time to platelet engraftment was 18 days (range 10-136). Acute GvHD grade 1-2 was observed in eight patients. There were no cases of aGvHD ≥ grade 3 and only one case of mild chronic skin GvHD. Two patients developed secondary autoimmune diseases (acquired hemophilia and immune thrombocytopenia ITP) which resolved after immunosuppressive treatment including rituximab. All patients could be completely weaned off immunosuppression.
Seven patients developed viral reactivations, which resolved following antiviral treatment and in two after additional donor lymphocyte infusions. All patients achieved a satisfactory immune reconstitution, however 2 patients remain on intravenous immunoglobulin replacement therapy. Ten patients demonstrate complete donor chimerism (DC) at last follow

up, one patient had a mixed chimerism with donor cells of >80% on CD14 and CD15 and complete DC on CD3 and CD19. One patient was transferred to his local hospital 7 months after HSCT for chronic granulomatous disease (CGD) with a DHR-test of 97%.

Conclusions: This non-myeloablative protocol for T-cell replete haploidentical salvage HSCT is here investigated for the first time in children. It shows promising outcome results in this extremely high-risk group of patients with stable engraftment and almost absent chemotherapy-associated toxicity. Although viral reactivations were frequent, the rapid neutrophil recovery was life-saving for children suffering from severe bacterial or fungal infections in severe aplasia. Further studies in larger patient cohorts are needed.

Disclosure: Nothing to disclose

B252

EFFICACY OF PROPHYLACTIC LEVOFLOXACIN IN PEDIATRIC AUTOLOGOUS HEMATOPOITIC CELL TRANSPLANTATION: A SINGLE CENTER, RETROSPECTIVE ANALYSIS

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Background: The practice of using prophylactic levofloxacin following hematopoietic cell transplantation remains variable among pediatric centers due to conflicting evidence and practice recommendations. Research is particularly limited in its utility in pediatric autologous hematopoietic cell transplantation (auto-HCT).

Methods: This was a retrospective single center study of pediatric patients who underwent auto-HCT at Mayo Clinic Children's (Rochester, MN) between 2018 to 2025. For patients with multiple transplants, each transplant was treated as a discrete episode. For eligible patients, collected data included: patient and transplant characteristics, antibiotic exposure (prophylaxis and treatment), hospital length of stay, and infectious outcomes. The primary objective was to quantify the impact of levofloxacin prophylaxis on duration of febrile neutropenia. Secondary objectives included evaluating the impact of levofloxacin prophylaxis on duration of empiric IV antibiotic usage, duration of hospital stay, frequency of bacteremia, and incidence of *Clostridioides difficile*-associated diarrhea and multidrug-resistant organisms (MDRO). Continuous variables were compared using two-tailed student's t-tests, and categorical variables were compared using Pearson's chi-squared tests.

Results: Data was analyzed from 67 discrete transplant episodes in 41 patients (median age at transplant of 8.3 years, range 1.4 - 21.7 years). Indications for transplant included CNS tumors (40.4%), neuroblastoma (29.9%), lymphoma (13.4%), germ cell tumors (12.0%), and rhabdoid tumors (3.0%). There was a similar distribution of tandem transplants and transplant indications between the two groups.
From day 0 through date of engraftment, the average days of febrile neutropenia were 2.9

for the prophylaxis group, and 4.3 for the non-prophylaxis group (p=0.036). Average days on empiric IV antibiotics through engraftment were 5.4 for the prophylaxis group, and 8.3 for the non-prophylaxis group (p=0.001). There was no significant difference in the proportion of patients who developed at least one MDRO or had at least one positive blood culture within 21 days of transplant (p=1.000 and 0.355 respectively).
Duration of hospital stay post day 0 approached statistical significance (p=0.063), with an average of 15.5 in the prophylaxis group and 20.3 in the no prophylaxis group. Proportion of patients to develop *C. difficile*-associated diarrhea within 21 days of transplant also neared significance (p=0.054) with 3/36 in the prophylaxis group and 8/31 in the no prophylaxis group.

Table 1. Short-term outcomes of pediatric auto-HCT based on use of prophylactic levofloxacin

	Prophylactic Levofloxacin (N=36)	No-Prophylactic Levofloxacin (N=31)	P-value
Mean days of febrile neutropenia through engraftment	2.9	4.3	0.036
Mean days on empiric IV antibiotics through engraftment	5.4	8.3	0.001
Proportion with a positive blood culture through engraftment	5/36	7/31	0.355
Mean days of hospitalization after transplant	15.1	20.3	0.063
Proportion with C. difficile-associated diarrhea within 21 days of transplant	3/36	8/31	0.054
Proportion with one or more MDRO on culture within 21 days of transplant	3/36	3/31	1.000

Conclusions: In this retrospective analysis, the use of prophylactic levofloxacin was associated with a significantly reduced number of days with febrile neutropenia and days requiring empiric IV broad spectrum antibiotic usage from day 0 through engraftment for pediatric patients undergoing auto-HCT. Length of hospitalization was numerically lower in the prophylaxis group, though this did not reach statistical significance. No statistically significant difference was seen in the proportion of patients who developed *C. difficile*-associated diarrhea or at least one MDRO within 3 weeks of transplant, though *C. difficile* rates were numerically lower in the prophylaxis group, nearing statistical significance. Additional prospective multicenter studies with a larger cohort are needed to confirm these findings.

Disclosure: Nothing to declare.

B254

POST-TRANSPLANT COMPLICATIONS AND MAINTENANCE THERAPY IN CHILDREN UNDERGOING AUTOHSCT DUE TO RELAPSE/PROGRESSION OF HODGKIN'S LYMPHOMA

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Background: Hodgkin's lymphoma (HL) accounts for 5-7% of malignancies in children and 30% of lymphomas in children. The use of hematopoietic stem cell transplantation (HSCT) in the treatment of HL in children remains controversial due to generally good outcomes. So far, there is no unified position regarding the selection of prognostic factors indicating the small group of patients (1–5%) who should undergo such an aggressive line of treatment. High doses of drugs and auto-HSCT are recommended for patients who experience HL progression during initial treatment, in cases of early relapse with inadequate response to therapy, and in subsequent relapses. Objective: To assess complications after auto-HSCT and the impact of maintenance therapy after HSCT in children treated for relapse/progression of HL.

Methods: The process of qualification and the course of the auto HSCT procedure in children hospitalized due to progression/relapse of Hodgkin's lymphoma treated at the Hematopoietic Stem Cell Transplantation Department of the University Children's Hospital in Krakow in the years 2022-2025 was analyzed.

Results: The auto HSCT procedure was performed on 5 children - 3 boys and 2 girls. The age of the patients was 14-18 years, median 17. All children were initially diagnosed with 4 clinical stage , nodular sclerosis type. 4 children were qualified due to progression of Hodgkin's lymphoma, and 1 due to early relapse. Second-line treatment - all children received 4 cycles of IGEV, and 1 girl additionally received 2 cycles of Brentuximab+Bendamustine. PET/CT before the auto HSCT showed the following treatment response levels: Deauville 3 in 4 children, and Deauville 4 in 1 child. Stem cells were collected from the peripheral blood of all children for autoHSCT, and all underwent BEAM megachemotherapy. No severe toxicities were observed in the peri-transplant period; all children experienced grade 2-3 mucositis according to WHO, and 2 children had mild grade 2 hepatotoxicity according to WHO. Conventional radiotherapy was administered to 4 children, and proton therapy to 1 child after autoHSCT. Maintenance therapy with 6 doses of brentuximab was given to 1 child. Early relapse after autoHSCT was observed in 2 patients, at 3 and 5 months post-autoHSCT, respectively. The first patient received 3 cycles of Brentuximab + Bendamustine and was qualified for alloHSCT; the second received Brentuximab + Bendamustine followed by Nivolumab—there was no response to the treatment, and the patient was referred to palliative care. The 4 children remain in remission, currently without late treatment complications.

Conclusions: Children treated for Hodgkin's lymphoma, due to a good response to the applied treatment, rarely require megachemotherapy and autoHSCT. In cases of relapse/progression, autoHSCT in most cases allows for achieving a lasting second remission. In patients with a poorer response to the applied treatment, maintenance therapy after autoHSCT should be considered.

Disclosure: No conflict of interests.

B255

LYMPHOMATOID GRANULOMATOSIS OF A CENTRAL NERVOUS SYSTEM AS THE ONLY MANIFESTATION OF POST- TRANSPLANT LYMPHOPROLIFERATIVE DISORDER AFTER HAPLOIDENTICAL STEM CELL TRANSPLANTATION: A PEDIATRIC CASE REPORT

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Background: Lymphomatoid granulomatosis is a rare Epstein-Barr virus (EBV)- associated B-cell lymphoproliferative disorder. It is characterized by angiocentric and angiodestructive infiltrates, leading to coagulative necrosis. This disease affects typically middle-aged adults. The most common sites of involvement are the lungs, skin, central nervous system (CNS), kidney and liver.

Methods: We present a six-year-old patient, who underwent a haploidentical hematopoietic stem cell transplantation (HSCT) due to relapse of stage 4 neuroblastoma. Conditioning included fludarabine, melphalan and thiotepa. Graft-versus-host-disease (GvHD) prophylaxis included antithymocyte globulin (ATG) and mycophenolate mofetil (MMF). Three months after HSCT she developed an acute GvHD of the skin (grade II) and gut (grade III), requiring systemic immunosuppressive therapy with high-dose steroids, ciclosporine and extracorporeal photopheresis. At day 260 post-transplant, she presented with fever without a clear focus of infection. EBV-PCR in peripheral blood was positive just above the detection limit of the assay. At this time, progressive neurological deterioration was observed, including pupillary difference, right-sided hemiballismus and altered mental status.

Results: MRI of the brain demonstrated involvement of the left basal ganglia and a rounded mass in the left frontal subcortical region with marked perifocal edema and central hemorrhage. Cerebrospinal fluid (CSF) analysis revealed a cell count of 7/µl, total protein of 410 mq/l; glucose of 2,4 mmol/l and a positive EBV-PCR (3 x10^3 copies/ml). Flow cytometry of CSF showed a small population of CD3-positive T-cells and a population of cells expressing CD20 and CD30. Brain biopsy was performed, which demonstrated a vascular lymphoid proliferation, with numerous small, mature- lymphoid cells, as well as blast-like-appearing

cells and areas of necrosis. Immunohistochemical staining confirmed a B-cell origin (PAX-5 positive) with expression of CD20 and CD30. Also, numerous EBV-positive blast cells were detected. A diagnosis of post-transplant lymphoproliferative disorder, specifically a CD30-positive, EBV-positive diffuse large B-cell lymphoma (DBCL) with morphological characteristics of lymphomatoid granulomatosis grade 3 was made. CT/PET scan showed no evidence of nodal or extranodal organ involvement. Immunosuppression with ciclosporine was discontinued. The patient was treated initially with Rituximab (375 mg/m^2) weekly for a total of 4 doses, systemic prednisolone and weekly intrathecal triple therapy with methotrexate, prednisolone and cytarabine. Due to the detection of CD30- positive cells, systemic Brentuximab Vedotine was also administered. Additionally, EBV-specific cytotoxic T lymphocytes were infused. Radiotherapy was not feasible due to previous radiation of the skull at relapse of the initial malignant disease, at this time in complete remission.

Conclusions: This case report describes a manifestation of lymphomatoid granulomatosis (LYG) of the central nervous system after haploidentical stem cell transplantation in a child. Primary CNS involvement is rare and the prognosis of LYG described in literature is poor. Different treatment modalities including steroids, rituximab, chemotherapy and radiotherapy have been reported in isolated CNS-LYG. With this therapy, remission of the disease was achieved, but only partial improvement of neurological symptoms could be observed after five months of therapy.

Disclosure: "Nothing to declare"

B256

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: A POLISH PEADIATRIC EXPERIENCE

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Background: Juvenile Idiopathic Arthritis (JIA) is the most common chronic rheumatologic condition in children, characterized by persistent joint inflammation, pain, and progressive functional impairment. Although substantial advances have been achieved with conventional disease-modifying antirheumatic drugs and biologic therapies, a subset of patients continues experience severe, treatment-refractory disease associated with long-term disability and reduced quality of life. For these patients, allogeneic hematopoietic stem cell transplantation (alloHSCT) may be considered as a rescue strategy due to its potential to reconstitute immune tolerance, supported by emerging evidence from recent studies.

Methods: Between 2022 and 2024, two adolescents with refractory juvenile arthritis underwent alloHSCT at our center in Wrocław, Poland. One patient had systemic JIA (without an identified underlying genetic defect), while the second presented with Blau syndrome (NOD2 mutation) with systemic arthritis manifestations. Both patients were transplanted from 10/10 HLA-matched sibling donors (MSD). Conditioning regimens included treosulfan, fludarabine, melphalan and alemtuzumab. Graft-versus-host disease (GvHD) prophylaxis consisted of methotrexate, tacrolimus or cyclosporine A.

Results: Both patients had prolonged, treatment-resistant disease with multi-joint involvement despite extensive therapy, including glucocorticosteroids, immunosuppressants, and multiple biologics. Early post-transplant complications included mucositis, viral infections, fever of unknown origin, and mild GvHD. Despite these complications, both patients recovered without sequelae. At a follow-up of one year in one patient and three years in the other, both achieved and remained in a complete clinical remission, with marked improvement in mobility, absence of morning stiffness, resolution of joint pain, and return to full physical activity.

Conclusions: AlloHSCT may represent a feasible and effective therapeutic option for selected pediatric patients with refractory arthritis syndromes who fail to respond to pharmacotherapy. In this small cohort, the procedure resulted in meaningful clinical improvement and enhanced quality of life. Nevertheless, the risks of transplant-related complications must be weighed against potential benefits, and long-term follow-up is essential to fully assess the durability of remission.

Disclosure: No

B257

MANAGEMENT OF TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY IN CHILDREN AFTER HSCT WITH RAVULIZUMAB: SINGLE CENTER EXPERIENCE

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Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is severe life-threatening complication of hematopoietic stem cell transplantation (HSCT). Diagnostics and treatment of TA-TMA in pediatric patients is challenging. Ravulizumab (a C5 complement inhibitor) could be used to treat severe refractory TA-TMA. Real-world data on Ravulizumab usage for TA-TMA in pediatric population required.

Methods: Seven children among 347 transplanted pediatric patients in Nikolay Blokhin National Medical Research Center of Oncology in 2023-2024 were diagnosed with TA-TMA according EBMT criterions. Three of these patients were diagnosed with severe refractory TA-TMA without adequate response on eculizumab. Patients received ravulizumab in recommended dose (by weight).

Results: Most of the patients were females (M/F=1/2), pt. 1 (F) was 17 y.o., pt. 2 (F) – 17 y.o. and pt. 3 (M) – 12 y.o. All patients suffered of leukemia (AML – 2 pts., ALL – 1 pt.) and received allogenic HSCT from matched unrelated donor (MUD). ALL patient received TBI-based conditioning regimen combined with VP and Flu and AML patients received Treo/Flu/Mel conditioning regimen. GvHD prophylaxis included ATG, rituximab, abatacept and tacrolimus or ruxolotinib in all cases. TA-TMA in pt. were found on day +77 with combination of renal bleeding. In pt. 2 and pt. 3 TA-TMA were found in the course of severe chronic GvHD with multiple therapy. TA-TMA was found in pt. 2 at day +280 and at pt. 3 at day 273 after HSCT. All patients received eculizumab (median no. of infusions – 4) before ravulizumab. Ravulizumab treatment started due to absence of clinical and laboratory effect of eculizmab. No severe side effects on ravulizamab infusion were found. All patients responded well in TA-TMA for Ravulizumab. Median number of infusions – 4.

Conclusions: TA-TMA is still challenging complication of HSCT. Use of Ravulizumab in refractory cases is promising strategy in pediatric patients. Future multicenter studies required for estimation of safety and efficacy of Ravulizumab in real-world practice.

Disclosure: Nothing to declare.

B258

OUTCOME OF SALVAGE SECOND HAPLOIDENTICAL STEM CELL TRANSPLANTATION FOR CHILDREN WITH HIGH-RISK HEMATOLOGICAL DISORDERS: A SINGLE CENTER EXPERIENCE FROM JORDAN

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) using post-transplant cyclophosphamide (PTCy) has become an important alternative for patients lacking a matched sibling donor. However, it remains associated with significant challenges, including graft failure (GF). Data on salvage second haplo-HSCT are limited.

Methods: This is a retrospective review of the medical files of all patients who underwent second haplo-HSCT at the Bone Marrow and Stem Cell Transplantation Center, Istishari Hospital, Jordan, between June 2016 and June 2025.

Results: Out of 27 patients who received T-replete Haplo-HSCT with PTCy, two required second transplant. The first patient was a 6-year-old female with severe aplastic anemia (SAA) who underwent upfront haplo-HSCT from the mother. The conditioning regimen

consisted of rATG 5 mg/kg, Fludarabine 150 mg/m^2, Cyclophosphamide 29 mg/kg, and 300 cGy TBI in a single fraction. GVHD prophylaxis was with PTCy at 100 mg/kg, mycophenolate Mofetil (MMF) and Tacrolimus. The graft was RBC depleted bone marrow (BM) due to major ABO incompatibility. The infused CD34$^+$ cell dose was 4.1 ×10^6/kg. The patient experienced non-engraftment and underwent a second haplo-HSCT from another donor (brother) 42 days later. The conditioning regimen consisted of Fludarabine 90 mg/m^2 and 300 cGy single fraction TBI. GVHD prophylaxis was with PTCy at 100 mg/kg, MMF and Tacrolimus. The graft was RBC depleted peripheral blood stem cell (PBSC) due to major ABO incompatibility with CD34$^+$ dose of 19.8 ×10^6/kg. Neutrophil and platelet engraftment were documented on day +14 and +16 post-HSCT respectively. The post-transplant course was uneventful. At last follow-up 76 months after second transplant, the patient is well and off immunosuppression. The second patient had high-risk infantile acute lymphoblastic leukemia, and underwent the first haplo-HSCT from the suitable donor (mother) following complete remission. He received myeloablative conditioning with targeted dose IV Busulfan 16 mg/kg and Cyclophosphamide 100 mg/kg. GVHD prophylaxis was with PTCy at 100 mg/kg, MMF and Tacrolimus. The graft was unmanipulated BM with CD34$^+$ dose of 3.5 ×10^6/kg. Neutrophil and platelet engraftment documented on days +14 and +17 respectively. The post-transplant course was complicated by CMV reactivation and grade 3 mucositis. The patient experienced early medullary disease relapse four months post-transplant. He received soft re-induction and consolidation chemotherapy followed by five blinatumomab cycles as bridging therapy. A second haplo-HSCT was performed 16 months after the first transplant from the same donor using PBSC. Conditioning regimen included rATG 5 mg/kg , Thiotepa 10 mg/kg, Fludarabine 150 mg/m^2, Cyclophosphamide 29 mg/kg, and 300 cGy TBI in a single fraction. GVHD prophylaxis was with PTCy at 100 mg/kg, MMF and Tacrolimus. CD34$^+$ cell dose was 10.2 ×10^6/kg. Neutrophil and platelet engraftment documented on days +14 and +15 respectively. Early post-transplant complications included grade 3 mucositis, CMV and HHV-6 reactivation, and grade 3 acute gut GVHD, all of which were successfully managed. The patient is currently doing well and disease-free at 8 months post 2nd transplant.

Conclusions: Saving lives with second Haplo-HSCT with PTCy is a feasible and effective option for complex pediatric cases. Multicenter studies are warranted to examine the best strategies for those patients.

Disclosure: Nothing to declare.

B259

CMV AND BK VIRUS REACTIVATION AFTER ALLOGENEIC HSCT ACCORDING TO DONOR TYPE: A SINGLE-CENTER PEDIATRIC EXPERIENCE

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Background: Viral reactivation remains a major cause of morbidity after allogeneic hematopoietic stem cell transplantation (allo-HSCT), particularly in pediatric patients. Cytomegalovirus (CMV) and BK virus (BKV) are among the most frequent viral complications, yet data regarding their incidence, clinical impact, and association with donor type in children are limited. We aimed to evaluate the incidence of CMV and BKV reactivation according to donor type and CMV serostatus in a large single-center pediatric allo-HSCT cohort.

Methods: We retrospectively analyzed pediatric patients undergoing allo-HSCT at the Fundeni Clinical Institute between January 2013 and July 2025. CMV reactivation was defined as CMV DNAemia requiring initiation of pre-emptive antiviral therapy. BKV reactivation was defined by detection of viruria and/or viremia, with clinically significant infection defined by the presence of hemorrhagic cystitis (HC) supported by clinical and imaging findings. Donor types included matched sibling donors (MSD), matched unrelated donors (MUD), and haploidentical donors (Haplo). Conditioning regimens were disease-specific. GVHD prophylaxis included methotrexate plus calcineurin inhibitor with or without ATG, post-transplant cyclophosphamide–based regimens, or MMF-based protocols. Associations between viral reactivation, donor type, and CMV serostatus were analyzed using chi-square tests.

Results: A total of 191 patients were included: 42 MSD, 103 MUD, and 46 Haplo transplants. CMV reactivation occurred in 83 patients (43.5%). The incidence was significantly lower in MSD recipients (26.2%) compared with MUD (47.6%) and Haplo (50%) transplants (overall p=0.037). Median time to CMV reactivation was day +25 for MSD, day +18.5 for MUD, and day +30 for Haplo recipients. Recipient CMV seropositivity was strongly associated with CMV reactivation (overall p=0.015), with the highest risk observed in D−/R+ patients (p=0.046). BKV reactivation was observed in 101 patients (52.9%) and showed comparable incidence across donor types (MSD 47.6%, MUD 54.3%, Haplo 54.3%). Clinically significant BKV-associated hemorrhagic cystitis developed in 20 patients (19.8% of BKV-positive cases), with similar proportions across donor groups. Imaging studies, when performed, revealed bladder wall thickening in all evaluated cases and intravesical clots in a subset. Concomitant CMV infection and acute GVHD were observed in a minority of patients with BKV-HC. Severe BKV-related complications, including graft loss, occurred in rare cases.

Conclusions: CMV and BKV reactivations remain frequent complications after pediatric allo-HSCT. CMV reactivation is significantly influenced by donor type and CMV serostatus, with MSD transplantation associated with a lower risk and D−/R+ status representing a major risk factor. In contrast, BKV reactivation is highly prevalent and occurs independently of donor type, while clinically significant hemorrhagic cystitis affects approximately one-fifth of BKV-positive patients. These findings support risk-adapted CMV monitoring strategies and highlight the need for improved preventive and therapeutic approaches for BKV-associated complications in pediatric allo-HSCT recipients.

CMV reactivation by donor type			
Donor type	No. patients	CMV reactivation n (%)	No CMV reactivation n (%)
MSD	42	11 (26.2)	31 (73.8)

MUD	103	49 (47.6)		54 (52.4)	
Haplo	46	23 (50.0)		23 (50.0)	
Total	191	83 (43.5)		108 (56.5)	
Overall comparison (χ^2 test): p = 0.037					
CMV serostatus in patients with CMV reactivation (n = 83)					
CMV serostatus	MSD n (%)	MUD n (%)	Haplo n (%)	Total n (%)	p-value
D+/R+	9 (81.9)	30 (61.2)	22 (95.6)	61 (73.5)	Reference
D+/R−	0	3 (6.1)	0	3 (3.6)	NS
D−/R+	2 (18.1)	16 (32.7)	1 (4.4)	19 (22.9)	0.046
D−/R−	0	0	0	0	—
Overall χ^2 test for serostatus: p = 0.015					
CMV serostatus in patients without CMV reactivation (n = 108)					
CMV serostatus	MSD n (%)	MUD n (%)	Haplo n (%)	Total n (%)	
D+/R+	27 (87.0)	40 (74.0)	22 (95.6)	89 (82.4)	
D+/R−	0	0	1 (4.4)	1 (0.9)	
D−/R+	3 (9.7)	9 (16.7)	0	12 (11.1)	
D−/R−	1 (3.3)	5 (9.3)	0	6 (5.6)	

MSD = matched sibling donor; MUD = matched unrelated donor; Haplo = haploidentical donor, p-values calculated using χ^2 test; NS = not significant

Disclosure: Nothing to disclose.

B260

THE CLINICAL COURSE OF HAPLOHSCT + DINUTUXIMAB BETA IMMUNOTHERAPY IN POLISH CHILDREN WITH RELAPSING NEUROBLASTOMA

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Background: Pediatric patients with relapsed neuroblastoma after autologous stem cell transplantation have an extremely poor prognosis. Especially after haploidentical stem cell transplantation anti tumor activity exerted by donor derived NK cells could be demonstrated. Thus, the donor derived immune system post-transplant may be a basis for further immunotherapeutic approaches and anti tumor effects of antibody and cytokine administration are likely. Those effects may help to reduce the relapse rate and to improve the outcome of those patients.

Methods: The aim of the study was to analyse the qualification, toxicity and response to treatment in children with relapsed neuroblastoma undergoing haploHSCT with immunotherapy with dinutuximab beta afer HSCT.

Results: In years 2024-2025 6 children with relapsing neuroblastoma were transplanted from haploidentical donors with 5-8/10 HLA matching. The inclusion criteria were: relapse after autoHSCT, no severe organ toxicities (e.g.nephrotoxicity), no features of progression in MIBG/MRI/PET-CT and agreement of the parents. The procedure included FluMelTT (Fludarabin 4 x 40 mg/m2 BSA, Thiotepa 10 mg/kg body weight, melphalan 2 x 70 mg/m2 BSA) conditioning + ATG Grafalon in dose 30mg/kg with immunosuppresion – mycophenolate of mofetil depending of the T cell level in transplant (600-1200 mg/ kg body weight) and G-CSF support from +4 day after HSCT. The transplantation material was PBSC donated by one of the parents (1-mother, 5-fathers), with alphabetaTdepletion. The material after depletion included 8-24 mln CD 34/ body weight of the recipient. 5 boys and 1 girl were qualificated to haplo HSCT, with number od relapses 1-3. The age of patients was between 3-14 years, median 6,5. 3 patients received 131I MIBG therapy 2-3 weeks before transplantation. The tolerance of chemotherapy was good, with no severe toxicities. Deeper pancytopenia was observed in patients undergoing MIBG therapy. In peri-transplant period all patients demonstrated mild stomatitis 1-2 stage WHO. Severe infection with septic shock was observed in one patient, with no necessity of ICU hospitalization. Engraftement of WBC ctiteria were fulfilled in +10 to + 15 day, median +12. 1The MMF immunosupression was driven from 30 to 60 days depending of the level of T cell in transplant. 1 patient presented the features of acute GvHD with skin and intestine involvement, with good response to methylprednisolone id dose 2 mg/kg/day. 1 patient developed reactivation of CMV and HHV 6 neuroinfection with mild course. Only 1 patient started dinutuximab beta therapy with delay-4 weeks. All these patients completed the dinutuximab beta therapy and remain in remission.

Conclusions: HaploHSCT with dinutuximab beta therapy seems to be encouraging method of treatment for children with relapsing neuroblastoma, connecting chemotherapy and

immunotherapy. This method seems to be well tolerated with no serious toxicities. Although due to posiible toxicities of the method, the patients should be carefully selected to this method of theatment. Also well conducted alphabetaTcell depletion helps to protect patients against GvHD, enables fast withdrawal from immunosupression and continuation of therapy with dinutuximab with no delays.

Disclosure: no conflict of interests

B261

ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHILDREN WITH DIAMOND-BLACKFAN ANAEMIA: A SINGLE-CENTER EXPERIENCE

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Background: Diamond-Blackfan anaemia (DBA) is a rare congenital pure red cell aplasia characterised by macrocytic anaemia, reticulocytopenia, constitutional abnormalities and cancer predispositions, typically diagnosed in the first year of life. Most cases are caused by heterozygous loss-of-function mutations or deletions affecting genes encoding ribosomal proteins (RPs). Standard therapy includes regular red blood cell (RBC) transfusions with iron chelation and corticosteroids from ≥ 1 year of age. Although initial steroid response reaches 80%, long-term efficacy is limited, and only 20% of children become treatment-independent. Allogeneic haematopoietic stem cell transplantation (HSCT) remains the only curative option.

Methods: Between January 1998 and June 2025, a total of 9 patients (2 males, 7 females) with DBA underwent allogeneic HSCT in the Czech Republic. The diagnosis of DBA was established at 1.3-3 months of age based on clinical and laboratory criteria. Among six children born after 2000, pathogenic RP mutations were identified: RPS26 (n=2), RPS19 (n=2), RPL5 (n=1), RPL35A (n=1). Congenital skeletal or craniophacial malformations were present in 4/9 patients. Corticosteroid therapy was initiated in all patients, with transient response in one child and no response in eight. The indication for HSCT was transfusion dependence in all 9 children. All patients received long-term iron chelation (deferoxamine, deferasirox). Before HSCT, 6/9 patients had serum ferritin level >1000 ug/l, and 8/9 showed organ iron overload confirmed by liver biopsy or MRI. Median age at HSCT was 9 years (range 4.4–19.1); the first three patients transplanted before 2000 were > 10 years old. Donors were HLA-identical siblings (n=5), 10/10 HLA-matched unrelated donor (n=3), and 9/10-HLA matched unrelated donor (n=1). Stem cell source was bone marrow in 3 patients, peripheral blood stem cells in 5 patients, and a combined graft in 1 patient. All conditioning regimens were busulfan-based. Before 2000, busulfan was combined with cyclophosphamide; later, the BuFluTT was used. ATG serotherapy was administered in all unrelated donor transplants. Rituximab was included in the conditioning of the last four patients.

Results: Engraftment was achieved in all patients; acute graft-versus-host disease (GVHD) was documented in 6/9 children, with complete response to immunosuppressive therapy in 5/6. One patient transplanted in 1998 at the age of 19 years died from grade IV acute GVHD and infection 3 months post-HSCT. Mild hepatic veno-occlusive disease occured in three patiens without need for therapeutic intervention (defibrotide). One patient developed severe transplant-associated thrombotic microangiopathy managed successfully with eculizumab. Eight of nine children are alive and well, RBC transfusion-independent, with full donor chimerism and no evidence of chronic GVHD, at a median follow-up of 4.9 years (range 0.5–27 years) post-HSCT.

Conclusions: Allogeneic HSCT from matched related or unrelated donors is currently indicated for steroid-non-responsive or transfusion-dependent children with DBA. Our experience confirms high efficacy and acceptable safety, particularly in childern < 10 years, while the decision must be individualised and carefully weighed in older patiens.
Supported by MHCZ for conceptual development 0064203

Disclosure: Nothing to declare

B262

CHRONIC GRAFT VERSUS HOST DISEASE DURING 20-YEAR OF MONOCENTRIC EXPERIENCE

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Background: Chronic Graft-versus-Host Disease (cGvHD) is one of the most common causes of morbidity and mortality affecting survivors of allogeneic hematopoietic cell transplantation (HCT). The incidence is lower in children (6-33%) than adults. Risk factors are mismatched donor, PBSCs as source, older age, and female donor/male recipient combination. The therapeutic approach of cGvHD is still challenging although new therapeutic approaches has improved the outcome of these patients.

Methods: This single-center retrospective study includes 396 pediatric patients who underwent allogeneic HSCT at IRCCS Giannina Gaslini Institute between 2004 and 2024. The median follow-up is 11.5 years (range 0-21 years). Second transplants performed for relapse of malignant disease were included, while primary and secondary graft failure were excluded. We retrospectively collected data about underlying disease, source of HSC, conditioning regimens, GvHD prophylaxis, onset and grading of acute and cGvHD, organ involvement (according to the 2014 National Institutes of Health consensus criteria), treatments and response to therapies.

Results: We examined 402 transplants (396 first transplants and 6 second transplants for disease relapse) in a cohort of 396 patients with malignant and non-malignant diseases: 85 patients (21.4%) developed cGvHD. The characteristics of the examined population are reported in Table 1.

83.5% (71/85) of patients had cGvHD after a previous acute GvHD and in 69% of them aGvHD was grade 1-2, while in 31% grade 3-4. The 77.5% of patients with aGvHD reached a complete response after a first line therapy with steroid.
Among patients with cGvHD, 15/85 (17.6%) developed grade 1, 40/85 grade 2, and 30/85 grade 3 disease. The most involved organ was the skin which was affected in 76.4 % of patients, followed by GI tract (45.8%), lung (25.8%), liver (22%), eye and oral mucosae (16.4%) and two patients had sierositis as main clinical manifestation of cGvHD. 61.1% of patients showed multiorgan involvement.
Most patients received steroids as first-line treatment (73/85, 85.9%), but it was often necessary to combine other treatments as Extracorporeal Photopheresis (14/85) and JAK inhibitors (imatinib or ruxolitinib) (38/85) to achieve a clinical response. A complete treatment response was reached from the 53% patients, 40% obtained a partial response, while 6 (7%) patients did not respond to any line of treatment.
Of 85 patients 19 died (22.3%) and transplant related mortality was cause of death in 14.%, and cGvHD in 8 patients.

Characteristics	**Patients with cGVHD (n =85)**
Male	51 (60%)
Female	34 (40%)
Malignant	46 (54.1%)
Benign	39 (45.9%)
MSD	22 (25.8%)
Haplo	24 (28.2 %)
MUD	39 (46 %)
Myeloablative	39 (45.8 %)
RIC	46 (54.2%)
BM	60 (70.6%)
PBSC	24 (28.2%)
CORD BLOOD	1 (1.2%)
GVHD prophylaxis	
MTX	39 (45.9%)
ATG	56 (65.9%)
Alemtuzumab	5 (5.9%)

Characteristics	Patients with cGVHD (n =85)
Engraftment	
PMN	85 (100%)
PLT	81 (95.2%)

Conclusions: Chronic GvHD represent as one of the major late complications of allogeneic HSCT, with an incidence comparable to that described in literature. Retrospective analysis of cGvHD is essential to identify the incidence in our population in particular in pediatric patient and it is complex yet extremely useful for guiding the clinical practice; the application of the NIH classification allows us to objectify this complication. The treatment of cGvHD is challenging, requiring the use of steroid therapy as first-line treatment, often in combination with other methods as steroids-sparing strategy.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

B263

THE ACHILLES HEEL OF KMT2A-REARRANGED ACUTE LYMPHOBLASTIC LEUKEMIA IN INFANTS

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Background: Infant˙s KMT2A-rearranged acute lymphoblastic leukemia (I-KMT2A-r ALL) is characterized by unique biology: multiple KMT2A partners genes engagement, early B-lineage phenotype predominance; agressive clinical course: initial hyperleukocytosis, central nervous system involvement (CNS pos); high rate of relapses refractory (r/r) to the standard programs of chemotherapy with or without hematopoietic stem cells transplantation (HSCT) Targeting immunotherapy implementation into the infant˙s ALL treatment programs demonstrates very convincing results, but until now, little is known about its effectiveness for the r/r CNS positive KMT2A-r ALL in this age group.

Methods: From 2014 to 2025, 21 uncelected patient (pts) with r/r I-KMT2A-r ALL, who were treated initially by MLL-Baby programm, with median of age 5 months (range: 4 days-10.5 mo) at the time of primary ALL diagnostic , underwent 25 HSCT after complete CSF clearance and hematological remission (CR) achievement in one Pediatric Oncology and

Hematology Center. Depending on CD19 and/or CD22 expression, 28-days blinatumomab (blina) course (5mcg/15mkg/sq.m/day by IV continuous infusion) or inotuzumab ozogamicin (ino) 3 times once a week (0.8-0.5-0.5 mg/sq.m/1 hours IV infusion were applied prior to HSCT in all minimal residual disease positive (MRD(+)) cases (range 0.011-0.4% by flow cytometry). 17 of 21(86.5%) were CNS+, all of them with B-lineage immunophenotype and BI- ALL predominance (62%); KMT2A::AFF1/t(4;11) in 57%, KMT2A::MLLT3/t(9;11) in 24%, KMT2A::MLLT1/t(11;19) and KMT2A::MLLT10/t(10;11) both at 9.5%. 19(76%) pts received haplo HSCT, 5MSD and 1MUD. Treo/Flu/Mel(or Thio) MAC regimens have been applied in all cases, except one with Bu/Flu/Mel with various regimens of immunosupression, TCRαβ /CD19 depletion in 15 and PTCy in 10 cases.

Results: All the transplanted pts achieved MRD(-) CR at the Day(D)+28. 3 pts with MRD reappearance at the D+62, D+83,D+93 have been salvaged by one or two 28D blina courses with 4 DLI each, one of them progressed and died , another 2 pts are survived in MRD(-) CR for 4 and 7 years respectively. One more patient developed graft rejection after first HSCT and died from engraftment failure, despite of the second haplo HSCT. Another one patient died after first HSCT due to the acute GvHD Grade 4.
9(53%) out of 17 CNS positive pts relepsed: 6 developed very early, 1 - early and 2 late BM BM+CNS relapses . It is important to note: all 4 CNS negative pts are alived in MRD(-)CR since its time of achievement
3 patients who were relapsed despite of the bridge immunotherapy and MRD(-) status after first HSCT, underwent secondary HSCT, succsessfully achieved MRD(-)status and alive in CR. EFS in our group of patients with multiple unfavorable factors is 0.47 ±0.2; OS – 0.69± 0.15; RFS – 0.56± 0.19 and CIR 0.43 ±0.1.

Conclusions: Although the combination of immunotherapy and HSCT together with chemotherapy for infant's KMT2A-r demonstrates promising results, treatment of pts with CNS positive KMT2A-r infants R/R ALL still a challenging problem. New CNS-directed curative strategy for this group of patients must be evaluated in the nearest future.

Disclosure: Nothing to declare.

B264

EXTRACORPOREAL PHOTOPHERESIS INWITH DIFFERENT SYSTEMS PERFOREMD; A REAL WORLD SINGLE CENTER REPORT

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Background: Extracorporeal photopheresis (ECP) is still an accepted second line treatment in acute and chronic GVHD. In the adult setting the use of commercial available systems is mostly easy and vascular access is feasable with an experienced team. In pediatric setting this is more challenging. Therefore especially in pediatric centers different systems could be used for treating extrem small children or children in difficult situations. In our centre we

have MINI ECP (manual treatment of 200 ml peripheral blood in under GMP conditions processed), offline Systems (AMICUS™+PIT™, OPTIA™+PIT™) inline systems (UVARXTS™, CELLEX™(historically, AMICUS BLUE™) available. One major impact in using differnet systems might be the cell dose treated (smallest in MINI ECP).We ask our self, if the use of different systems has an impact on outcome of acute or chronic GVHD. Therefore we retrospectively analysed in our patients the use of different systems and the overall outcome, especially when we used MINI ECP, due to different cell doses been treated (the sammlest amount in MINI ECP and the highest in offline ECP).

Methods: We retrospectvely collected data from patients charts used for the documentation of the treatment of acute and chronic GVHD. ECP was used as second line treatment in corticoid refractory situations, or in cirtical situations to avoid massive immunosppressive agents. MINI ECP was performed form 200 ml peripheral blood harvested by either isovolemic hemodilation or exchange. In offline methods the leukapheresis was performed by processing 1000 to 2000 ml peripheral blood, and Reinfusion once or twice on consecutive days. Inline methods were performed in Cellex bei processing 100 to 1500 ml blood, and the same for the AMICUS BLUE inline system. For statistical analysis WinSTAT™ add in for xcel was used. The internal policy to choose the method of ECP was 1.) available vascular access, 2.) absence of critical illness, 3.) willingness of accept a longterm vascular access, if not MINI ECP was preferred, and also for tappering strategies.

Results: We treated from 2011 to 2025 81 patients with episodes of acute (n=50) and chronic GVHD (n=38), median age 9.79 y (min 0.32 to max 25.3) and in median 25 ECP per episode (min 2, max 141) corresponding to n=2228 procedures (MINI ECP 703, AMICUS BLUE 617, offline 679, CELLEX/UVARXTS 206). The five years survival rate for the whole group was 78% (Kaplan-Meier), for the patients with acute GVHD group 78.4% and chronic GVHD 75.4%. Only deaths were directly related to untreatable GVHD (BOOP, GVHD after DLI). A subgroup of patients recieves only MINI ECP (n=23, median age 4.6y) versus patients with combination of MINI ECP with offline or inline systems (n=58, median age 11.7y). ECP was in every case part of an multimodular therapy. This subgroup has not significant dfferent outcome versus the mixed group (87% overall survival versus 74%). Reductions of corticoid and/or immunosuppressive therapy was one of the main results.

Conclusions: Especially in young patients the combination or the only use of MINI ECP instead of standard treatment (offline and inline) can result in faivorable overall outcome.

Disclosure: Nothing to declare.

B265

TACKLING MIXED CHIMERISM WITH WHOLE BLOOD DONOR LYMPHOCYTE INFUSION IN RESOURCE LIMITED SETTING – CASE SERIES

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Background: Mixed donor chimerism is increasingly common in the pediatric hematopoietic stem cell transplantation (HSCT) setting because of the increased use of reduced-toxicity preparative regimens for nonmalignant diseases. Mixed chimerism poses a threat to disease relapse and transplant failure. Donor lymphocyte infusion (DLI) is a well established strategy to mitigate the mixed chimerism, however in the resource limited settings and in Low middle income countries which adds the extra financial burden to the family and donors consent for the DLI procedure become difficult, Here in our study we used whole blood DLI for mixed chimerism in 7 pediatric patient and retrospectively analyzed the data and presented.

Methods: This is the retrospective case series data collected from the EMR, our series includes total 7 children we have undergone allogenic stem cell transplantations for the various benign conditions. Chimerism was done by using the VNTR PCR analysis. Whole blood DLI was considered, after the failure of immunosuppression boost, to the children who had mixed and dropping chimerism along with cytopenias. Before whole blood DLI donor peripheral blood CD3 count was enumerated by using flow cytometry and each time before DLI donor Complete blood counts and Differential counts perfomred and Whole blood DLI [W DLI] volume was calculated as per dose required. Following W-DLI, chimerism was performed once every 2weeks and W-DLI was planned until complete donor chimerism.

Results:

	Case-1	Case-2	Case-3	Case-4	Case-5	Case-6	Case-7
Diagnosis	Griscelli syndrome	SCID T-B-NK+ (RAG27+)	Thal Major-class II	Thal Major-Class II	IBMFS-ERCC6L2+	Hyper IgE syndrome-DOCK8+	MPS-type IH & II
Age at HSCT	18mon	5mon	4yrs	5yr	10yr	6yr	15mon
Type of HSCT	MSD	MSD	Haplo/PtCY	Haplo/PTCY	MRD(Father)	Haplo / PtCY	MSD
Conditioning	FTT	FTT	FTTA	FTTA	FTTA	Flu-CTx-TBI	FTTA
GVHD prophylaxis	MTX+CSA	MTX+CSA	PtCY + Tac+MMF	PtCY + Tac +MMF	MTX + Tac	PtCY + Tac+MMF	MTX+Tac

Engraftment [N/P]	10 /17	14/21	18/24	17/22	12/18	14/18	16/20
Day+30 chimerism	98%	97.6%	99%	97.9%	99.25%	99%	86%
Reason for DLI	Cytopenias	Cytopenias	Cytopenia - Transfusion	Cytopenia	Cytopenia	Cytopenia-symptoms	Cytopenia
Strategies before DLI	Withdrwal of immunosuppression	Immunoboost/ Withdrwal	Immunoboost/ Withdrwal	Immunoboost/ Withdrwal	Immunoboost/ Withdrwal	Immunoboost/ Withdrwal	Immunoboost/ Withdrwal
Number of DLI dose	3	7	4 – Secondary GR	8	2	6	2
Post DLI chemirism	FDC	Stable mixed Chimerism -86%; no cytopenia	Secondary graft rejection	FDC	FDC	FDC	FDC
Outcome	Alive -CR	Alive-CR	Alive – Auto recovery	Alive-CR	Alive -CR	Alive-CR	Alive-CR

In our series out of 7children who received W-DLI, 6 were responded and cytopenias and symptoms were controlled, one child had stable mixed chimerism but cytopenias recovered. We have seen 85% success with W-DLI in our series.

Conclusions: Mixed chimerism in benign condition stem cell transplantation poses a threat for disease relapse, DLI has success rate in between 60-85% in the literature, however which as extra financial burden on the families and for repeated doses patient will be exposed to DMSO and storage related challenges. In W- DLI in our series we have seen 85% success rate and easy to use and DLI product is free from DMSO. Therefore in resource limited settings Whole blood DLI is a good alternative for DLI and with at least similar results as conventional DLI.

Clinical Trial Registry: No.

Disclosure: No conflict of interest.

B266

DEVELOPMENT OF A NOVEL SCORING INDEX TO QUANTIFY THE NEED FOR NUTRITIONAL SUPPORT INTERVENTIONS DURING STEM CELL TRANSPLANT AND GENE THERAPY IN CHILDREN

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Background: Children undergoing haematopoietic stem cell transplant (HSCT), chimeric antigen receptor (CAR-T) therapy, or autologous gene therapy require intensive dietetic input and nutrition support due to treatment-related toxicities to optimise patient outcome. There is no scoring index to quantify the intensity and duration of such dietetic interventions in children despite nutritional status being known to correlate with outcomes. We developed a quantitative score to capture the cumulative intensity and duration of dietetic support delivered over the first 100 days to cell therapy recipients.

Methods: We performed a single-centre retrospective study of 131 children. Nutritional interventions were categorised into five levels: dietetic review (1 point), oral nutritional support (2 points), enteral nutritional support (4 points), parenteral nutritional (PN) support (6 points), and bespoke PN support (7 points). The cumulative nutritional intensity score was calculated by multiplying the intervention points by the duration (in days) and summing across all interventions. The primary endpoint was the cumulative score at day +100. Secondary analyses assessed predictors of ≥PN requirement at day +100 with multivariable logistic regression.

Results: The cohort included allogeneic HSCT (n=109, 83.2%), CAR-T (n=16, 12.2%), and gene therapy (n=6, 4.6%). CAR-T patients showed notably lower median nutritional intensity score (53.0, 95%CI: 30-117) relative to allogeneic (326.0, 95%CI: 282-404) or stem cell gene therapy (124.5, 95%CI: 56-182, $p < 0.05$) recipients. Within allogeneic patients, malignant disease was associated with higher scores than non-malignant disease (444.0 vs 261.5, $p<0.01$). Conditioning with total body irradiation (TBI) had higher scores than non-TBI (476.0 vs 302.0, $p<0.01$). On multivariable analysis, higher nutritional intensity and malignant disease independently predicted ≥PN at day +100 (OR = 2.43 per 100-unit increase). Model discrimination was strong (AUC-ROC: 0.87).

Demographic	**N=131**
Age	
Median Age (IQR)	7 (3-12)
Gender	

Male	86 (65.6%)
Female	45 (34.4%)
Transplant Type	
Allogeneic	109 (83.2%)
CAR-T	16 (12.2%)
Gene therapy	6 (4.6%)
Of those undergoing allogeneic transplant	***N =109***
Allogeneic Cell Source	
Cord Blood	31 (28.4%)
Others	78 (72.6%)
Disease	
Malignant	45 (41.3%)
Non-malignant	64 (59.7%)
Conditioning	
Total body irradiation	14 (12.8%)
Not irradiated	95 (87.2%)

Conclusions: Our nutritional intensity score captures the cumulative burden of dietetic support. Higher scores identify patients at risk of prolonged PN. This tool may enable early risk stratification and inform resource planning. Prospective validation is warranted.

Disclosure: Nothing to declare

B267

POOR OUTCOMES FOR CHILDREN WITH REFRACTORY POST TRANSPLANT LYMPHOPROLIFERATIVE DISORDER

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a rare but serious complication of paediatric haematopoietic stem cell transplant (HCT) and solid organ

transplant (SOT). Although most PTLD arises in the setting of Epstein Barr virus (EBV) driven B-cell proliferation, disease biology spans a clinicopathological spectrum from benign hyperplasia to aggressive monomorphic lymphoma. Survival has improved with rituximab based therapies however, refractory or relapsed PTLD remains challenging, with poor survival outcomes and limited paediatric-specific evidence to guide management. This study aimed to describe the natural history, treatment approaches and outcomes of paediatric PTLD according to transplant type, with particular emphasis on relapsed and refractory disease.

Methods: We conducted a retrospective single centre review of paediatric patients (<18 years) diagnosed with PTLD following HCT and SOT at the Royal Children's Hospital (Melbourne, Victoria) from 2016-2024. Clinical, histological and transplant-related variables were extracted from electronic medical records. Overall survival (OS) and event-free survival (EFS) were estimated using Kaplan–Meier methods.

Results: Twenty-five children developed PTLD, eighteen following SOT and seven following HCT. Histological subtypes included hyperplasia (36%), polymorphic PTLD (24%), and monomorphic lymphoma (40%). Advanced (Ann Arbor Stage III/IV) disease was common (69%), including three cases with CNS involvement and four with marrow infiltration. Rituximab and/or reduction in immunosuppression (RIS) was first-line therapy in 64% of patients with a complete response rate of 56%. EBV-specific cytotoxic T lymphocytes (CTLs) were used in 32% of patients with an overall response rate of 87%. Chemotherapy was typically reserved for monomorphic lymphoma or failure of rituximab-based therapy. Refractory disease occurred in 28% of patients (n=7), predominantly in those post HCT (57%) and with monomorphic lymphoma (86%). All deaths (n=5) occurred in this group, all within 12 months of diagnosis. In contrast, relapsed cases (20%), exclusively in SOT recipients, were all successfully salvaged with further therapy. Five-year overall survival was 80% and event-free survival was 52%. Refractory disease, monomorphic lymphoma, and stage IV disease were associated with inferior survival.

Conclusions: Refractory monomorphic PTLD accounted for all deaths in this cohort, highlighting a critical unmet need in paediatric transplant care. These findings highlight a need for clinical trials evaluating earlier risk stratification, integration of CTLs and optimising management strategies for this high-risk population.

Disclosure: Nothing to declare

P214

ULTRA-RAPID CD3/CD45RA-DEPLETED HAPLOIDENTICAL HSCT FOR PEDIATRIC CEREBRAL ALD: FEASIBILITY, ENGRAFTMENT KINETICS, CHIMERISM BEHAVIOR, AND EARLY NEUROLOGIC OUTCOMES IN THREE CASES

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Background: Cerebral X-linked adrenoleukodystrophy (cALD) is a progressive neuroinflammatory demyelination in boys. Allogeneic HSCT can arrest MRI activity and preserve function when performed early (low Loes scores, minimal neurologic impairment), but donor acquisition delays can be critical in a disease where "time is brain." Haploidentical HSCT offers immediacy; however, ALD-specific data—particularly using ex vivo T-cell–depleted platforms—are sparse and often embedded within broader inherited metabolic disorder cohorts. In parallel, lentiviral gene therapy (elivaldogene autotemcel) is an option for select early-stage patients, but eligibility, access, and time-to-treatment constraints frequently limit real-world use relative to the pace of inflammatory progression. We present an ALD-focused pediatric series using a standardized CD3/CD45RA-depleted haploidentical platform, emphasizing operational timelines, engraftment/chimerism kinetics, safety, and early neurologic outcomes.

Methods: We analyzed three boys with cALD (ages at HSCT 6.7–9.0 years) who underwent paternal haploidentical peripheral blood stem cell transplantation. All grafts were ex vivo CD3/CD45RA-depleted. Conditioning comprised ALC-based Thymoglobuline, model-based Fludarabine and Busulfan, Rituximab, and IVIG; GVHD prophylaxis included Tacrolimus. Pre-HSCT staging captured MRI Loes scores, gadolinium enhancement, and clinical status. Outcomes included timeliness (referral-to-admission and referral-to-transplant), engraftment (ANC and platelets), donor chimerism at predefined timepoints, immune reconstitution (IgG), GVHD, infections, hospital length of stay, and serial clinical neurologic assessments.

Results: Disease spectrum: One symptomatic patient had a Loes score of 7 with extensive enhancement; two were presymptomatic with low Loes scores (1–1.5) and focal enhancement on screening MRI. Operational timeliness: Referral-to-transplant was 23–34 days; referral-to-admission was 9–21 days. Graft/platform: CD34+ doses were high (10.66–25.06 × 10^6/kg) with ultralow CD3 contamination (0.039–0.050 × 10^6/kg). Engraftment: Myeloid recovery occurred on day +8 or +9 in all patients; platelets exceeded 100,000/μL on days +12, +13, and +69. Early chimerism: All achieved ≥95% donor chimerism by day +8–9. Chimerism dynamics: The symptomatic patient maintained 100% donor chimerism through year 2. Both presymptomatic patients developed mixed/declining chimerism, prompting pre-emptive donor lymphocyte infusion (DLI) at day +157 with 7 doses and day +54 with 4 doses, respectively; latest available chimerism stabilized at 0.91 in both. Safety: No grade ≥2 acute GVHD or chronic GVHD occurred; one suspected upper GI aGVHD episode (vomiting) resolved. Infections/toxicity: One CMV DNAemia episode was managed successfully with anti-virals. Regimen-related toxicities were predictable and manageable (nausea/vomiting, mucositis, tacrolimus-related hypomagnesemia; one busulfan-associated

rash; one case of engraftment fevers/rash). Length of stay was 28–37 days. Immune reconstitution: IgG at day +100 was 8.9, 11.3, and 12.6 g/L. Neurologic outcomes: The symptomatic patient showed stabilization with functional gains by year 2. Presymptomatic patients remained clinically stable at early follow-up.

Conclusions: A standardized CD3/CD45RA-depleted haploidentical platform enabled rapid time-to-transplant, ultra-fast engraftment, and low GVHD in pediatric cALD. The recurrent observation of mixed/declining chimerism in early-stage patients—despite robust initial engraftment—highlights a potentially stage- and platform-specific behavior that may benefit from protocolized monitoring and timely DLI. These data support haploidentical HSCT as a timely, feasible option for cALD for multicenter evaluation to refine conditioning intensity, graft composition, and DLI strategies to optimize durable chimerism and neurologic preservation.

Disclosure: Nothing to declare

P215

TORQUE TENO VIRUS IN PEDIATRIC CAR-T RECIPIENTS

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Background: CART therapy has improved outcomes in relapsed/refractory (R/R) B-acute lymphoblastic leukemia (B-ALL) and diffuse large B-cell lymphoma (DLBCL), although immune-mediated toxicities remain a concern. Torque Teno Virus (TTV) is the main component of human virome. A recent study in adults suggests that plasma TTV viral load (TTV-VL) in CART patients may correlate with immune effector cell-associated neurotoxicity syndrome (ICANS) severity and progression-free survival (Benzaquén, 2024). We aimed to analyze plasma TTV-VL kinetics in pediatric CART recipients, its association with complications, outcome, lymphocytes and CART subsets, and its predictive value.

Methods: Retrospective single center study including <18 years treated with CART CD19 or CD19/22 (2019-2023) for R/R B-cell malignancies. Blood samples were collected pre-lymphodepletion (pre-LD), at CART infusion (0d), +7, +14, +21, +28, +35, +42, +60 and + 90 days (d), and at the onset of immunotoxicities. Immune cell typing was performed by flow cytometry. CART was monitored via HIV qPCR and flow cytometry. TTV in plasma was measured with TTV
R-GENE® (Biomérieux, France).

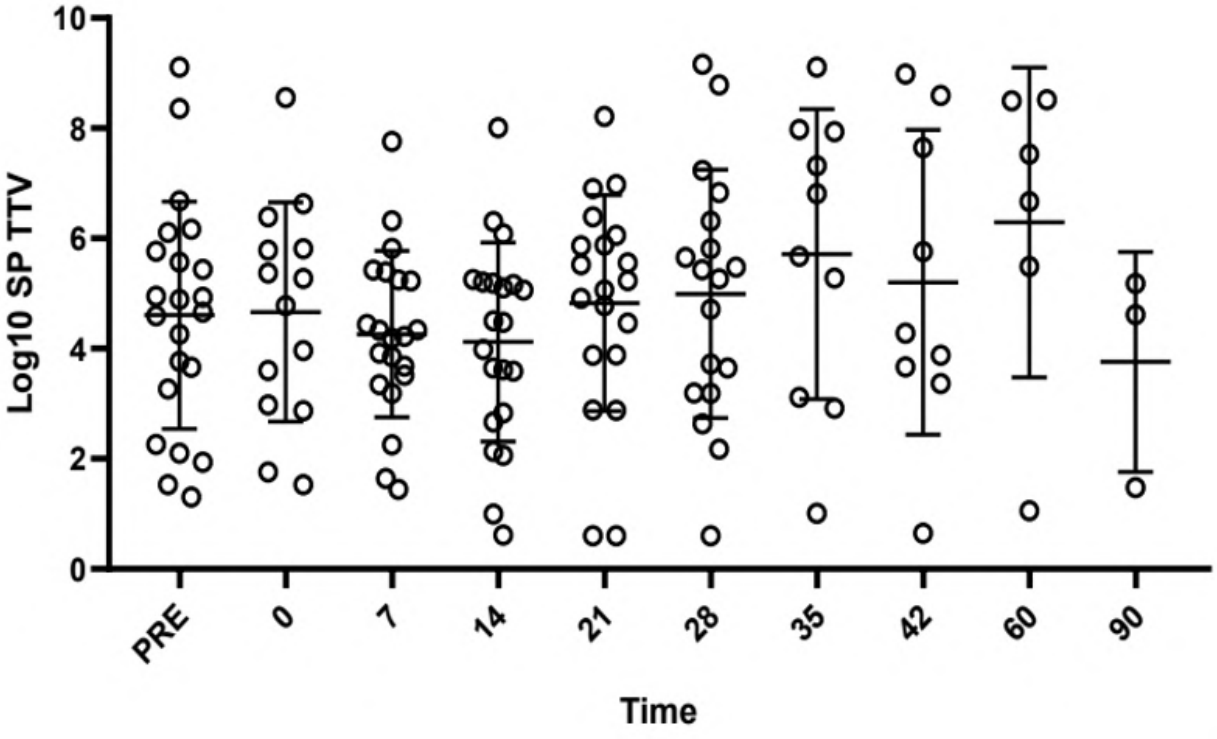
Results: Twenty-seven patients were included, treated with CD19 (70.4%) or CD19/22 (29.6%) CART because of B-ALL (81.5%) or DLBCL (18.5%). Most were male (59.3%),

caucasian (55.6%), mean age 12.5 years (SD 5.6); 18.5% Down Syndrome. Immune-mediated toxicities and other complications are detailed in table 1.

IMMUNOTOXICITIES	n=27
CRS, n (%)	23 (85.2)
Onset day, median [Q1, Q3]	3 [1, 6.5]
Grade 3-4, n (%)	9 (33.3)
ICANS, n (%)	8 (29.6)
Onset day, mean (SD)	8.1 (2.6)
Grade 3-4, n (%)	5 (18.5)
HLH, n (%)	10 (37)
Onset day, mean (SD)	8.1 (2.6)
Treatments, n (%)	
Steroids	13 (48.1)
Tocilizumab	11 (40.7)
Siltuximab	8 (29.6)
Anakinra	9 (33.3)
COMPLICATIONS AT 30 DAYS	n=27
Pancytopenia, n (%)	6 (22.2)
Infections, n (%)	7 (25.9)
PICU admission, n (%)	14 (51.9)

B-cell recovery occurred in 29.6% (mean 92 days, SD 61.4), 40.7% relapsed (mean 139 days, SD 105), and 11.1% had progressive disease (PD). Twenty patients (74.1%) received treatment after CART, 48.1% HSCT. Survival was 55.6% (median follow up 752 days, [134.5,1421]). Main causes of death were PD (64.3%) and HSCT complications (14.3%). TTV was analyzed in 173 samples (figure 1). Pre-LD, it was detectable in 81.5%, with no differences regarding patient characteristics. Receiver Operating Characteristics curve analysis (ROC) at Pre-LD revealed a TTV-VL threshold of 4.91 log copies/ml predicted PICU

admission (AUC 0.77; Sp 70%, Se 75%). Each increase in pre-LD TTV-VL diminished the probability of receiving tocilizumab by 45.1% (p=0.0496).
At 0d, TTV-VL inversely correlated with CRS grade (p=0.0165). ROC showed 6.51 log copies/ml predicted CRS (AUC 0.82; Sp 66.7%, Se 100%) and 2.93 grades 3-4 (AUC 0.96; Sp 91.7%, Se 100%); 3.29 HLH (AUC 0.85; Sp 90%, Se 75%), PICU admission (AUC 0.77; Sp 90%, Se 75%), and steroid treatment (AUC 0.85; Sp 90%, Se 75%). Treatment with tocilizumab was predicted by 3.78 (AUC 1; Sp 100%, Se 100%) and siltuximab by 1.64 log copies/ml (AUC 0.75; Sp 100%, Se 50%).
TTV-VL could predict mortality with 0.75 AUC: 4.99 log copies/ml at +28d (Sp 80%, Se 75%), 4.2 at +35d (Sp 100%, Se 75%), and 3.77 at +42d (Sp 100%, Se 75%).
TTV-VL directly correlated with absolute NK cells count at +7 (p=0.0371), double negative at +21 (p=0.0356), and Treg lymphocytes at +42d (p=0.0386). The correlation resulted inverse with total T lymphocytes at +21d (p=0.0064).
TTV-VL at 0d inversely correlated with HIV qPCR at +28d (p=0.0231). We found no associations with CART flow subsets.



Conclusions: In pediatric CART recipients, TTV-VL does not correlate with CART monitoring methods, but could predict toxicity and outcomes.

Disclosure: Nothing to declare.

P217

A PILOT RANDOMIZED STUDY OF SMOFLIPID VERSUS INTRALIPID IN PEDIATRIC ACUTE LEUKEMIA UNDERGOING HSCT: EARLY ANTHROPOMETRIC, METABOLIC, INFLAMMATORY, AND CLINICAL EFFECTS

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Background: Nutritional management of children undergoing allogeneic hematopoietic stem cell transplantation (HSCT) for acute leukemia remains a challenge and unresolved aspect of care. Although enteral feeding is increasingly advocated, many pediatric patients cannot meet requirements enterally, necessitating parenteral nutrition (PN). The optimal formulation and dosing of PN in this population remain uncertain, as clear evidence or HSCT-specific guidelines are lacking. SMOFlipid has been suggested to offer metabolic benefits over conventional Intralipid; however, it is not FDA-approved for pediatric use, despite adoption clinical practice. To address these uncertainties, we performed a double-blind pilot randomized trial in pediatric HSCT recipients comparing SMOFlipid with Intralipid.

Methods: This double-blind randomized pilot trial enrolled pediatric acute leukemia patients undergoing allogeneic HSCT and assigned them to high-protein PN using either SMOFlipid or Intralipid for a standardized 10-day post-transplant regimen. Oral intakes were concurrently recorded to quantify total energy delivery. Anthropometric, biochemical, inflammatory, and hematological markers were assessed at baseline and predefined follow-up points, and early clinical outcomes were prospectively monitored.

Results: Thirty-one patients were included (13 SMOFlipid, 18 Intralipid; mean age 9.26±3.62 years). Baseline characteristics, estimated energy targets, initial PN composition, oral intake, and appetite scores were comparable. During the first 10 post-transplant days, patients achieved on average 47.35±7.84 % of estimated energy needs parenterally, 33.97±12.20 % orally, and 81.32±11.55 % in total. ANCOVA adjusting for baseline values and key covariates, showed no significant differences between groups on day +15 in the means of 10-day oral energy and protein intakes, appetite, anthropometric indices, lipid profile, glucose, electrolytes, inflammatory markers (IL-6, CRP), engraftment, or other clinical outcomes. Paired t-test analyses showed declines in anthropometric indices in both groups, which were statistically significant only for weight (SL, P=0.003; IL, P=0.01) and BMI (SL, P=0.001; IL, P=0.04). Total cholesterol decreased in both groups (SL, 173.57±23.81 vs, 156.71±23.64; IL, 150.83±52.93 vs, 142.17±27.64), reaching statistical significance only with SMOFlipid (P=0.032). Triglycerides increased significantly in both groups, with a notably larger rise in the Intralipid group (SL, 140.42±55.36 vs,

296.71±82.18, *P*=0.008; IL, 102.50±59.48 vs, 420.0±191.76, *P*=0.006). Fasting glucose increased in both groups (SL: 100.85 ± 9.65 vs. 111.42 ± 52.51; IL: 82.83 ± 5.81 vs. 98.67 ± 18.69), reaching marginal statistical significance only in the Intralipid group (P = 0.07). Electrolytes trended downward, with magnesium showing a significant reduction (P = 0.024) and phosphorus a marginally significant reduction (P = 0.08). Notably, inflammatory markers increased in both groups: IL-6 (SL: 10.41 ± 14.29 vs. 38.92 ± 47.25; IL: 10.85 ± 13.36 vs. 18.64 ± 18.89) and CRP (SL: 12.08 ± 10.10 vs. 58.65 ± 52.42; IL: 14.04 ± 15.09 vs. 40.14 ± 41.26), with marginal significance observed in the SMOFlipid group (P = 0.055).

Conclusions: In this pilot randomized study, SMOFlipid provided no short-term advantage over Intralipid and, unexpectedly, was associated with greater increases in inflammatory markers by day +15. Given the metabolic vulnerability of pediatric HSCT recipients, cautious use of SMOFlipid and careful selection of lipids overall appear warranted. Larger, adequately powered studies are necessary to clarify the safety and clinical implications in this population.

Disclosure: Nothing to declare.

P219

ETOPOSIDE OR FLUDARABINE MAY BE COMBINED WITH 1.200CGY TOTAL BODY IRRADIATION FOR PEDIATRIC HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION TO TREAT ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Acute lymphoblastic leukemia (ALL), is the most common indication for allogeneic pediatric hematopoietic cell transplant (HCT). The superiority of 1,200 cGy Total Body Irradiation-Etoposide (TBI-VP) conditioning was demonstrated by the FORUM trial, but optimal conditioning therapy for Haploidentical HCT (Haplo) with post-transplant cyclophosphamide (PT-Cy) to prevent GVHD is still unknown. We have initiated the Haplo program 25 years ago using TBI-Fludarabine (Flu) (*Solomon et al,* 2012) but in the past three years have adopted TBI-VP based on the FORUM experience (*Peters et al, 2020*). Since a direct comparison of both conditioning regimens has not been performed yet, our objective

is to compare overall survival (OS) and event-free survival (EFS) of consecutive pediatric patients with ALL undergoing Haplo-HCT with TBI-Flu and TBI-VP.

Methods: Retrospective analysis of all consecutive pediatric ALL patients undergoing Haplo with Flu 90 mg/m2 -TBI 1,200cGy or TBI-VP 60 mg/kg. All used GvHD prophylaxis with post-transplant Cyclophosphamide (PTCy) 50 mg/kg and MMF 15 mg/kg TID. TBI-Flu also used Tacro and TBI-VP, Cyclosporine.

Results: Between February 2020 and June 2025, we performed 58 Haplo for ALL with a median follow-up of 2.4 years (3.6 for TBI-Flu and 1.7 for TBI-VP). 88% of cases were B-cell ALL; 35/58 (60%) received Flu-TBI, and 23 (40%), TBI-VP. VP had a 2-day delay to neutrophil engraftment: median 15 days with Flu (13-21) and 17 days with VP (12-24), (p=0.003). Peripheral blood grafts were used in 63% of the patients with Flu-TBI and in 2 TBI-VP (9%). With Flu-TBI, 69% had GvHD: 22/35 aGvHD and 14/35 cGvHD; 34% relapsed and 23% died of TRM. Four underwent a second HCT and all unfortunately died. With Flu-TBI, the EFS was 43% and OS 65% at 2.4 years p-NS). The 23 patients receiving TBI-VP, had 57% GvHD — 9/23 cGvHD and 8/23 cGvHD. Four patients relapsed and four died of TRM (17%). Therefore, after TBI-VP, the EFS was 65% and OS 74%. Compared to Flu-TBI, TBI-VP had a Hazard Ratio (HR) of relapse of 0.77 (95%CI 0.26-2.24), and TRM of 0.96 (95%CI 0.8-4.9), OS of 1.94 (95% CI 0.29-3.18) although with the small numbers none of the outcomes has reached statistical significance.

Conclusions: TBI-VP marrow and TBI-Flu PBSC may have comparable outcomes in Haplo HCT for ALL.

Disclosure: Nothing to declare.

P220

REDUCTION OF TOTAL BODY IRRADIATION DOSE IN THE CONDITIONING OF CHILDREN WITH ALL AND ITS IMPACT ON SURVIVAL AND TOXICITY

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Background: Hematopoietic stem cell transplantation (HSCT) remains a curative strategy for children with acute lymphoblastic leukemia (ALL) who present high-risk features at diagnosis or relapse. Total body irradiation (TBI) is a critical component of conditioning regimens, contributing significantly to both treatment efficacy and long-term toxicity. The conventional TBI dose of 1200 cGy has shown strong anti-leukemic efficacy but is associated with substantial adverse effects. This study evaluates whether reduced TBI doses maintain comparable overall survival (OS) and event-free survival (EFS) while reducing toxicity

Methods: To determine whether reduced TBI doses (600 cGy and 200 cGy) preserve OS and EFS comparable to the standard 1200 cGy regimen and to assess whether lower TBI doses correlate with reduced late toxicities.
A retrospective, longitudinal, observational analytical study was conducted in pediatric ALL patients who underwent HSCT between 2013 and 2023 and received TBI-based conditioning. Patients were stratified into three dose groups: 1200 cGy, 600 cGy, and 200 cGy. OS and EFS were analyzed using Kaplan–Meier methods. Toxicity was evaluated in patients with at least 24 months of follow-up.

Results: Seventy-six patients were included: 81.6% received 600 cGy, 10 received 200 cGy, and 4 received 1200 cGy. OS in the 600 cGy group was 74% at 1 year and 72% at 5 years. In the 200 cGy group, OS was 88% at 1 year and 64% at 5 years. The 1200 cGy group showed 50% OS at 1 year. Differences showed a trend toward significance (p = 0.086). EFS in the 600 cGy group was 83% at 1 year and 71% at 5 years. The 200 cGy group showed 75% for both time points, and the 1200 cGy group showed 66% at 1 year (p = 0.8). Among 46 patients evaluable for toxicity, endocrine dysfunction occurred in 56.5%, pulmonary toxicity in 19.6%, and secondary neoplasms in 3 patients (all thyroid cancer). No statistically significant association was found between TBI dose and toxicity.

Conclusions: Patients receiving 600 cGy achieved OS and EFS comparable to historical outcomes with 1200 cGy, with similar or slightly lower toxicity rates. Although limited by sample size and group heterogeneity, findings suggest that 600 cGy may offer adequate disease control with a potentially more favorable toxicity profile. Larger studies are required to confirm these observations.

Disclosure: The authors declare no conflict of interest.

P221

CLINICAL EFFICACY OF HEMATOPOIETIC STEM CELL TRANSPLANTATION IN 20 JMML CASES: A SINGLE-CENTER STUDY

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Background: JMML is a rare clonal hematopoietic neoplasm occurring predominantly in infants and young children, with an incidence of 1.2 per million and constituting 2% to 3% of childhood leukemias. Based on the 2016 World Health Organization (WHO) classification of myeloid neoplasms, JMML is categorized as a myelodysplastic/myeloproliferative neoplasm. HSCT currently remains the only potentially curative therapy for JMML. Although transplant strategies are continuously evolving and improving, the OS rate post-HSCT is only 50% to 73%, with high relapse rates due to frequent disease recurrence and severe treatment-related complications. Therefore, this study retrospectively analyzed 20 pediatric JMML patients who underwent HSCT at our institution. Univariate analysis was conducted on factors including whether the patients received intensive chemotherapy(IC) prior to

transplantation, conditioning regimen, transplant type, and occurrence of aGVHD, to identify determinants of prognosis in pediatric patients.

Methods: A retrospective analysis was conducted on 20 pediatric patients diagnosed with JMML who received treatment at Hebei Yanda Lu Daopei Hospital between February 2013 and February 2025. All patients underwent comprehensive diagnostic evaluations, including complete blood count (CBC) with peripheral blood smear review, bone marrow morphology examination, immunophenotyping, molecular biological testing, and cytogenetic analysis. The diagnosis of JMML was confirmed for all patients according to the 2016 WHO diagnostic criteria.
Treatment response was evaluated using the six clinical characteristics and three genetic features outlined in the 2015 consensus as criteria for efficacy assessment. Additionally, minimal residual disease and molecular-cytogenetic monitoring were performed on patient bone marrow samples.
As of December 2025, the primary endpoints were 3-year OS, LFS, and CIR. Secondary endpoints included acute and chronic GVHD,as well as other transplantation-related complications.

Results: Among the 20 patients who underwent HSCT, the 3-year OS, LFS and CIR were 85% ± 7.98%, 84.4% ± 8.32%, and 10.6%. For the 15 Haplo-HSCT, the corresponding 3-year OS, LFS, and CIR were 86.7% ± 8.78%, 86.7% ± 8.78%, and 6.7%(Fig.1).

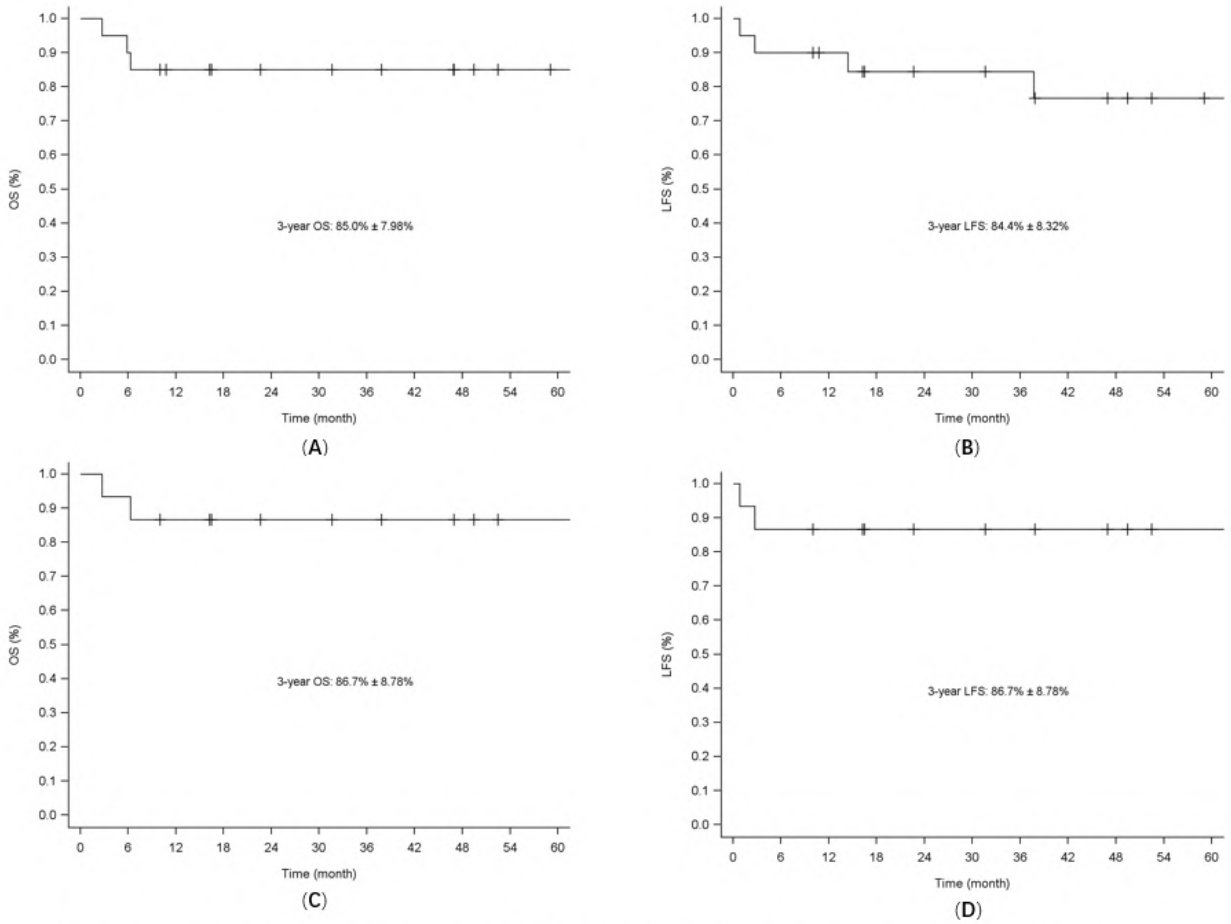

Fig.1 Outcomes of 20 JMML Patients Undergoing HSCT:(**A**) overall survival (OS), (**B**) leukemia-free survival (LFS) Outcomes of 15 JMML Patients Undergoing Haplo-HSCT:(**C**) overall survival (OS), (**D**) leukemia-free survival (LFS)

Factors associated with OS, LFS, and CIR were analyzed using the log-rank test. The results showed no significant correlation with patient age, platelet count at diagnosis, hemoglobin level at diagnosis, genetic subtype, pre-transplant chromosomal karyotype, or conditioning chemotherapy agents. However, OS and CIR were significantly associated with the occurrence of aGVHD after transplantation (Table 1).

Table1 Analysis of factors influencing OS, LFS, and CIR based on log-rank test

Items	**N**	**3-year-OS (95% CI)**	**P**	**3-year-LFS (95% CI)**	**P**	**3-year-CIR (95% CI)**	**P**
Received IC			0.188		0.525	0.199	

Yes	7	0.714 (0.258 - 0.920)		0.686 (0.213 - 0.912)		0.286 (0.031 - 0.636)	
No	13	0.923 (0.566 - 0.989)		0.923 (0.566 - 0.989)		0.077 (0.004 - 0.303)	
Transplant type			0.886		0.643		0.886
Total	20	0.850 (0.604 - 0.949)		0.844 (0.589 - 0.947)		0.150 (0.036 - 0.340)	
Haplo-HSCT	15	0.867 (0.564 - 0.965)		0.867 (0.564 - 0.965)		0.133 (0.020 - 0.354)	
aGVHD			0.023		0.151		0.025
Yes	8	0.625 (0.229 - 0.861)		0.625 (0.229 - 0.861)		0.375 (0.072 - 0.694)	
No	12	1.000		1.000		0	

Transplantation-related complications:The incidence of grade II or higher aGVHD was 35% (n=7), with 6 cases being severe, two of which occurred following donor lymphocyte infusion administered after relapse. cGVHD was 40% (N=8). Three patients died: two due to relapse and one due to severe GVHD. One patient progressed to acute myeloid leukemia.

Conclusions: Whether JMML patients received intensive chemotherapy before transplantation showed no significant difference in OS, LFS, or CIR. Patients with JMML undergoing Haplo-HSCT achieved higher OS and reduced CIR, thereby improving clinical outcomes. This study is limited by its small sample size, and further validation with larger cohorts is required.

Disclosure: Nothing to declare

P222

THRASSA, A MULTICENTER, OPEN-LABEL STUDY EVALUATING THE SAFETY, TOLERABILITY AND EFFICACY OF MAAT013 IN RUXOLITINIB-REFRACTORY OR INTOLERANT PAEDIATRIC/ADOLESCENT PARTICIPANTS WITH GASTROINTESTINAL ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: Acute graft-versus-host disease (aGvHD) is a serious complication following allogeneic haematopoietic stem cell transplantation (allo-HSCT). aGvHD impacts many children (Vincent et al. 2025). The incidence of Grade II–IV aGvHD in children receiving allo-HSCT from unrelated donors varies from 40 to 85% (Andolina et al. 2022; MacMillan et al. 2020). Standard first-line therapy involves corticosteroids (CS), however fewer than half of paediatric patients have durable complete responses and require second-line therapy (Gottardi et al. 2023; MacMillan et al. 2020). In Europe, ruxolitinib was granted approval for the treatment of Steroid-refractory (SR) aGvHD patients aged 28 days and older based on the REACH 2&4 (NCT02913261, NCT03491215) studies. Despite a high response rates for paediatric patients, ORR at any time varies from 45% to 100% (Baccelli et al. 2024), 27% of REACH 4 participants discontinued treatment due to lack of efficacy and 22% due to AEs resulting in almost half of the participants with limited therapeutic options (Locatelli et al. 2024), poor clinical outcomes and a heightened risk of morbidity and mortality.
MaaT013 is an allogeneic, full-ecosystem pooled biotherapeutic intestinal microbiota, drug candidate tested in a completed phase III in adult patients with Gastrointestinal (GI)-aGVHD (NCT04769895) and available on a compassionate use program for patients with aGvHD. MaaT013's promising efficacy and acceptable safety profile suggest a favorable benefit–risk profile as a third-line therapy, warranting evaluation in children. THRASSA is a phase II study designed to evaluate the safety, tolerability and efficacy of MaaT013 as a 3rd line therapy after systemic corticosteroids and ruxolitinib failure in paediatric and adolescent participants with GI-aGvHD (EU-CT#: 2025-524302-15-00).

Methods: It is an open-label, single arm, two-cohort (Cohort 1: ≥ 6 - < 12 years; Cohort 2: ≥ 12 - < 18 years) study involving up to 18 participants (up to 9 per cohort) followed-up for 12-mo. Allo-HSCT recipients diagnosed with Grade II to IV (MAGIC criteria) GI-aGvHD and identified as refractory to steroids and either refractory or intolerant to ruxolitinib, with a Karnofsky/Lansky performance status ≥ 40, and a minimum weight of 15 kg are eligible.

Main exclusion criteria include: previous lines of systemic aGvHD treatment other than CS and ruxolitinib, presence of uncontrolled infection or requiring antibiotics, any other diseases that in the opinion of the investigator would contraindicate study treatment, cGvHD, active cytomegalovirus colitis, relapsed/persistent malignancy requiring rapid immune suppression withdrawal, severe organ dysfunction or other uncontrolled complication. After a 2-day oral vancomycin pre-treatment, patients will receive 3 doses of MaaT013 over 10 days.
The primary endpoint, safety and tolerability, includes incidence of (Serious) adverse events (AEs), assessment of all safety parameters (clinical, laboratory) until M6 and, from M6 to M12 incidence of SAEs and AE of special interest. Main secondary endpoints include: feasibility of MaaT013 administration in paediatric population, GI and all-organ overall response rate, duration of response, overall survival, progression-free survival of the underlying disease and time to progression.

Results: The study is expected to start in May 2026 in France, Italy, Netherlands and Spain.

Conclusions: THRASSA

Disclosure: Laura Alonso declares no competing interests.
Virginie Gandemer declares no competing interests.
Marta Gonzalez Vicent declares no competing interests.
Caroline Lindemans declares no competing interests.
Riccardo Masetti declares no competing interests.
Pietro Merli : received honoraria from AMGEN and SOBI and is part of MEDAC advisory board.
Luisa Sisinni declares no competing interests.
Francesco Paolo Tambaro declares no competing interests.
Marco Zecca declares no competing interests.
Marion Bruelle is employee and stockholder of MaaT Pharma.
Juliette Jouve is employee and stockholder of MaaT Pharma.
Behzad Kharabi Masouleh received consulting fees and travel support from Maat Pharma.
Emilie Plantamura is employee and stockholder of MaaT Pharma.
Karima Yakouben declares no competing interests.

P223

ONE SIZE DOESN'T FIT ALL: MODIFICATION OF CONDITIONING REGIMEN IN METABOLIC DISEASE HSCT IN PEDIATRIC TRANSPLANTS

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Background: Conditioning regimen in Allogenic stem cell transplantation is a crucial determining factor for long-term outcome in benign conditions. Modification of conditioning regimen, based on underlying pathophysiology consideration will have great impact for smooth and successful transplant outcomes. Mevalonate kinase deficiency (MKD) is a rare

auto inflammatory syndrome, Allogenic stem cell transplantation has promising results however during the transplantation in view of hyper inflammatory nature of background condition, higher risk of severe cytokine release syndrome and graft rejections and higher Graft versus host disease is a potential threat. Here we are reporting two cases of severe MKD refractory to conventional therapies, undergone haploidentical stem cell transplantation with successful outcome.

Methods: This is a retrospective case study of two MKD with hyper immunoglobulin D phenotype, both were refractory to conventional therapies like steroids, TNF inhibitors and presented with significant crippling joint pains and swelling along with recurrent fever. Both children undergone haploidentical stem cell transplantation, with very high pre-transplantation IL-6 levels, Conditioning regimen was Fluderabine, Treosulfan, Thiotepa and Rabbit ATG as serotherapy [FTTA] ;conditioning regimen was supplemented with addition of Tocilizumab 2weeks prior to conditioning and IL-1 inhibitor Anakinra weekly twice from the conditioning regimen to until the engraftment was continued. Descriptive Data were retrieved from the EMR and tabulated.

Results:

	Case-1	Case-2
Age /Sex	4yrs2month /Male	5yr 8monts/Female
Phenotype	Hyper IgD phenotype	Hyper IgD phenotype
NGS	MVK gene mutation+	MVK gene Mutation+
Prior therapies	NSAIDs, Steroids, Methotrexate	NSAIDs, Steroids, Methotrexate , TNF inhibitors
Type of Transplant	Haploidentical - Father 6/12	Haploidentical – Mother 8/12
Pre-transplant IL-6 level [<7pg/ml]	560pg/ml	316.30pg/ml
Conditioning	FTTA Tocilizumab 2weeks prior at 8mg/kg single dose	FTTA Tocilizumab 2weeks prior at 8mg/kg single dose Inj. Anakinra 100mg S/c weekly twice from conditioning regimen to engraftment.
Stem cell source CD 34 dose	PBSC $7x10^6$/kg	BM + PBSC $4.8x10^8$ MNC + $4x10^6$/kg
Date of HSCT	May-2023	August-2025
GVHD prophylaxis	Pt/CY 40mg/kg Day +3 and +4 Tac + MMF from Day +5	Pt/CY 40mg/kg Day +3 and +4 Tac + MMF from Day +5

Post Transplant events	1. Severe CRS on day +1, 3inotropes / Ventilator support. 2. Mucositis grade 3 3. Delayed engraftment [N-Day+28;P-Day+56 4. CMV reactivation	1. Serum sickness [rATG] 2. CRS-grade -1 3. Mucositis-grade-2 4. Pseudomonas CLABSI
Outcome	Alive	Alive

Conclusions: MVK deficiency related auto-inflammatory condition is difficult to treat, stem sell transplantation though a curative treatment option,we need to modify our conditioning protocol to reduces the hyper-inflammatory response and related complications. Ours is probably first presentation in literature about usage of Anakinra and Tocilizumab even before conditioning chemotherapy to reduces the inflammatory response,CRS,GVHD and Graft rejection in this condition.

Clinical Trial Registry: No.

Disclosure: No conflict of interst.

P224

NON HAEMATOLOGICAL AUTOIMMUNE MANIFESTATIONS FOLLOWING PAEDIATRIC HAEMATOPOIETIC STEM CELL TRANSPLANT

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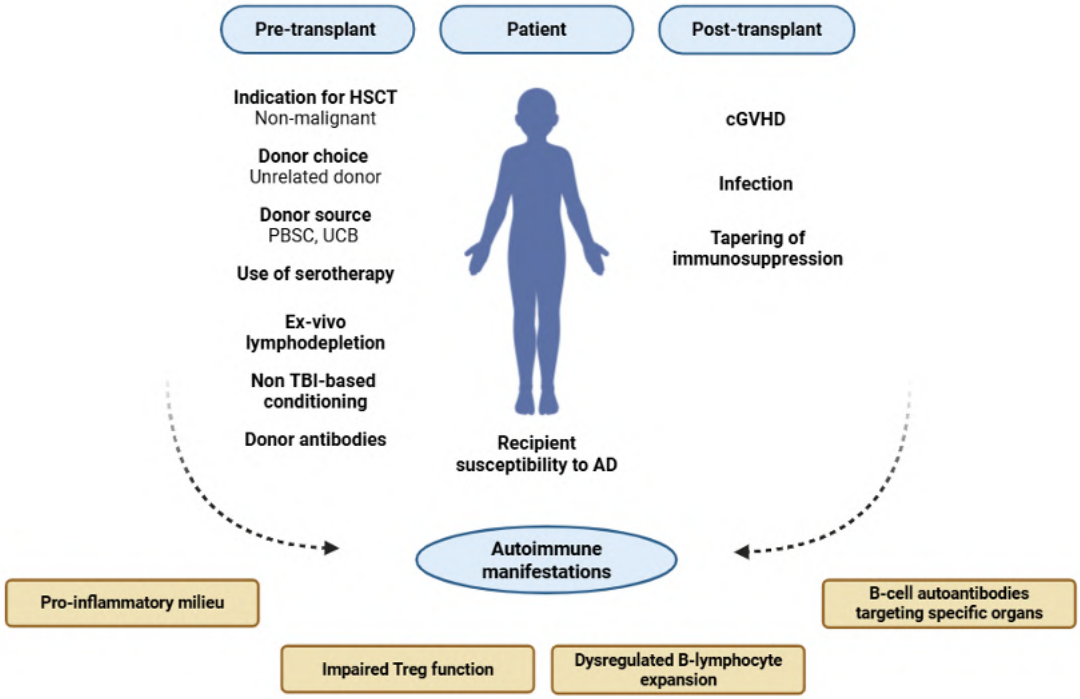
Background: Autoimmune manifestations following haematopoietic stem cell transplant (HSCT) are increasingly recognised as a contributor to morbidity and mortality in paediatric HSCT recipients, and are under-recognised. Most reported autoimmune manifestations are haematological, with autoimmune cytopenias accounting for 22% of all paediatric HSCT complications(1). However, less commonly, single organ or multi-system involvement may manifest, distinct from the more widely recognised immune-mediated graft-vs-host disease (GVHD). The literature is sparse and limited to case reports in paediatric patients. The pathophysiology is poorly understood and is thought to be due to the interaction between the dysregulation of a recovering immune system, and inflammatory factors (see Figure 1). Non-haematological autoimmune manifestations are presumed to be driver by donor immunity against host organs and tissues(2).
We describe three interesting cases from a single UK paediatric transplant centre, who developed non-haematological autoimmune manifestations post HSCT.

Methods: We conducted a retrospective analysis of three patients with non-haematologic autoimmune manifestations post HSCT in a single UK centre, and subsequently analysed

known risk factors and pathophysiology associated with the development of such autoimmune manifestations.

Results: Patient 1 underwent a fully matched unrelated (MUD) donor bone marrow transplant (BMT) with total body irradiation (TBI) and etoposide conditioning with alemtuzumab serotherapy for refractory acute lymphoblastic leukaemia (ALL). She developed grade 1 gut GVHD and HHV6 infection in her post HSCT course, and asymptomatic SARS-Cov-2 infection. Three months post HSCT she developed a rapidly ascending sensorimotor neuropathy consistent with Guillain-Barre syndrome (GBS) treated with IVIG and pulse steroids.
Patient 2 had refractory acute myeloid leukaemia (AML) and underwent a mismatched unrelated umbilical cord blood transplant with busulfan and fludarabine conditioning. Two months post HSCT he developed acute onset hypoalbuminaemia with secondary peripheral oedema. Kidney biopsy was consistent with membranous nephropathy, which responded to increased immunosuppression.
Patient 3 underwent a MUD transplant with busulfan and cyclophosphamide conditioning with anti-thymocyte globulin serotherapy for AML in 2nd remission. He experienced asymptomatic primary Epstein Barr virus reactivation 1 month post HSCT, and went on to develop significant haematological and non-haematological autoimmune manifestations including refractory autoimmune cytopenias, GBS and autoimmune hepatitis. His complications were refractory to a number of lines of therapy. He required a second reduced intensity HSCT for life threatening multi-system autoimmunity however died on day +5 due to severe veno-occlusive disease.

Conclusions: Whilst rare, non-haematologic autoimmune manifestations following transplant are clinically significant and often refractory to treatment. Diagnosis can be challenging due to similar clinical features seen in other more common HSCT complications. Further understanding of the pathophysiology of such conditions is essential to identify patient-specific risk factors and allow for early diagnosis and initiation of targeted therapies to improve patient outcomes. Our reported experience adds to the range of systemic autoimmunity documented in literature, giving insightful consideration for early recognition and treatment.



Disclosure: Nothing to declare

P225

CHALLENGES AND ACHIEVEMENTS OF BUILDING PEDIATRIC BONE MARROW TRANSPLANT PROGRAM IN A DEVELOPING COUNTRY; SINGLE CENTER EXPERIENCE IN IRAQ

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Background: Hematopoietic stem cell transplantation (HSCT)) is now one of the integral treatment modalities for many malignant and non-malignant conditions in pediatric population and considered the only curative option for many diseases. Establishment of a HSCT program in developing countries can face significant challenges, due to lack of infrastructure and resources, lack of well-trained health professionals and expertise, and lack of knowledge about the safety and costs of procedures. The study objective was to assess the feasibility and challenges of building pediatric BMT program in Iraq and to highlight the strategies and interventions that were associated with the successful outcome.

Methods: Initiation of the program started in March 2024 through infrastructure modification to fit for the standard requirement, infection control precautions, cell separation, processing and cryopreservation policies and guidelines, stem cell lab preparations and continuous training and awareness for all the included staff. G-CSF mobilized peripheral blood as 1st line therapy and pre-emptive plerixafor were used for stem cell collection. All Allogenic HCT patients received peripheral blood grafts from fully matched related donors and were given Pt Cy in addition to Cy CSA/ MTX as GVHD prophylaxis

Parameter	**Total (n=36)**	**Autologous NB (n=25)**	**Autologous HL (n=4)**	**Allogeneic (n=**
Age at transplant (years)	Median (range) 6.9 (2.5-16)	5.8 (3-12)	10.75 (5-16)	7.5 (2.5 -14)
Conditioning regimen		BuMel	BeEAM	BU/CY- TBI/CY
CD34⁺ cell dose (×10⁶/kg)	Median (range)	4.03 x 10^6 /kg	3.6 x 10^6 /kg	5.4 x 10^6 /kg
Median ANC engraftment (day)		13.28 (12-19)	13 (12-14)	21.6 (14-31)
Median platelet engraftment (day)		19.4 (12-26)	21.5(20-23)	16.4(14-19)
Patient status Survival in CR Relapse and alive Relapse and death		 21(84%) 2 (8%) 2 (8%)	 4(100%) 0 0	 6(85.7%) 1(14.3%) 0

Results: A total of 36 patients ≤ 15 years were transplanted from March 2024 till November 2025 and included 29 auto transplants (25 cases with high risk neuroblastoma and 4 cases with relapsed Hodgkin lymphoma), and 7 allogenic transplants (5 cases with AML, one with CML blastic crises and one with relapsed Ph positive ALL). Of the neuroblastoma patients, 4/25 (16%) relapsed and 0% non-relapse mortality (NRM) at d+100 with one-year disease free survival and overall survival probabilities of 78% and 88% respectively, while no reported relapses or NRM among the 4 cases of HL. Regarding the allotransplant patients, all of them showed complete chimera and negative MRD post HSC, while one patient with HR AML in CR1 relapsed at d+160. Also, NRM at d+100 was 0% and one patient developed grade I (stage 1 skin) acute GvHD.

Conclusions: Despite the challenges, building a successful pediatric bone marrow program in limited resources countries is feasible through following well planned systematic steps. Following standardized approaches, efficient pre operation staff training and effective infection control precautions and supportive care guidelines are key component for transplant success. Autologous HCT was associated with survival advantages in high-risk neuroblastoma patients in our center.

Disclosure: Nothing to declare.

P226

TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY DRIVES MORTALITY IN PEDIATRIC HSCT: INSIGHTS FROM A SINGLE-CENTER COHORT

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Background: Transplant-associated thrombotic microangiopathy (TA-TMA) is a severe and under-recognized complication of hematopoietic stem cell transplantation (HSCT).

Methods: We retrospectively analyzed 205 HSCT from 191 pediatric allogenic HSCT recipients from our center for the accomplishment of diagnostic criteria according to the recently published EBMT-TA-TMA consensus criteria.

Results: Eleven patients met criteria for severe TA-TMA (overall incidence 5.4%) although routine sC5b-9 measurement was frequently unavailable. Nine cases occured after first HSCT (4.8%) and two after second HSCT (12.5%). Nine patients were diagnosed during the clinical course and treated with eculizumab. 5 out of 9 treated patients (56 %) survived. Two patients were diagnosed retrospectively as probable TA-TMA, both had fulminant disease with acute respiratory distress syndrome (ARDS), were not treated with a complement inhibitor and subsequently died. Overall transplant-related mortality (TRM) in our cohort was 15/191 (7.9%), 6 out of these 15 patients (40%) succumbed to TA-TMA, identifying TA-TMA as a major contributor to TRM.
IN TA-TMA patients we observed three clinical manifestation patterns:

1. Six patients (55%) showed prolonged renal involvement in the context of graft-versus-host disease (GvHD) and/or poor graft function.
2. Three patients (27 %) presented with early, fulminant deterioration characterized by a rapidly progressive ARDS.
3. Two patients (18 %) had neurological involvement presenting initially with seizures due to posterior reversible encephalopathy syndrome (PRES).

Out of 6 TA-TMA associated deaths, two presented with ARDS and four with renal involvement. Patients with bone marrow failure syndromes were disproportionately represented in the TA-TMA group (6/11, 55%).

Conclusions: TA-TMA significantly contributes to TRM in pediatric HSCT recipients. Its heterogeneous and sometimes fulminant presentations highlight the need for heightened clinical awareness. In response, we implemented a structured screening protocol for TA-TMA. Development of more precise treatment algorithms is essential to improve outcomes in this otherwise dismal condition.

Disclosure: Nothing to declare

P228

LINEAGE SWITCH FROM B-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA TO T-CELL ACUTE LYMPHOBLASTIC LEUKAEMIA IN A PAEDIATRIC PATIENT WITH *HOX11* EXPRESSION AFTER 11 YEARS：A CASE REPORT

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Background: Lineage switch, defined as the phenomenon where leukaemia cells of the same clonal origin transform from one lineage to another at relapse, is a rare and challenging event in haematological oncology.We report a unique case of a paediatric patient initially diagnosed with *HOX11*-positive B-cell acute lymphoblastic leukaemia (B-ALL) who, after 11 years of remission, relapsed with T-cell acute lymphoblastic leukaemia (T-ALL). This represents the first reported instance of such a late lineage switch. Furthermore, we identified the rare *KMT2A::BCL9L* fusion gene and a complex mutational landscape potentially driving this transformation.

Methods: In October 2013, a 2-year-old boy presented with fatigue and petechiae. Laboratory tests revealed leucocytosis, anaemia, and thrombocytopenia. Bone marrow (BM) examination confirmed ALL(Figure 1A), with immunophenotyping showing B-lineage markers (Table 1) and positivity for HOX11 by multiplex PCR. Chromosomal analysis showed no dividing cells after two rounds of banding; all FISH tests were negative. The patient was enrolled in the CCCG-2008 intermediate-risk protocol, achieving remission and completing therapy in July 2016.
In January 2025, the patient presented with fever.BM examination revealed relapse(Figure 1B). Strikingly, immunophenotyping now demonstrated a T-lineage phenotype (Table 1). The results of multiplex PCR and karyotyping were consistent with those at initial diagnosis, and FISH demonstrated trisomy of cen4 and cen10. However, transcriptome sequencing identified a rare III-type fusion gene,KMT2A::BCL9L (Figure 1C), along with class I (NRAS p.G13D), class II (WT1 p.R374fs,WT1 p.V268fs,BCL11B p.E34fs,CTCF p.L98*,NOTCH1 p.R1598P), and metabolic (CPT2 p.F383Y) and motility (CCDC40 p.R301*) mutations. T-cell receptor (TCR) clonality assays were positive.
Following the lineage switch diagnosis, the patient received re-induction regimens, achieving morphological remission with negative flow cytometry minimal residual disease (FC-MRD). However, the KMT2A::BCL9L fusion transcript and TCR clonality remained positive. After consolidation, the patient underwent allogeneic haematopoietic stem cell transplantation (HSCT) in May 2025, using a dual graft (umbilical cord blood and peripheral blood stem cells from a haploidentical father).The time to neutrophil and platelet engraftment was achieved on day +14 and +15.

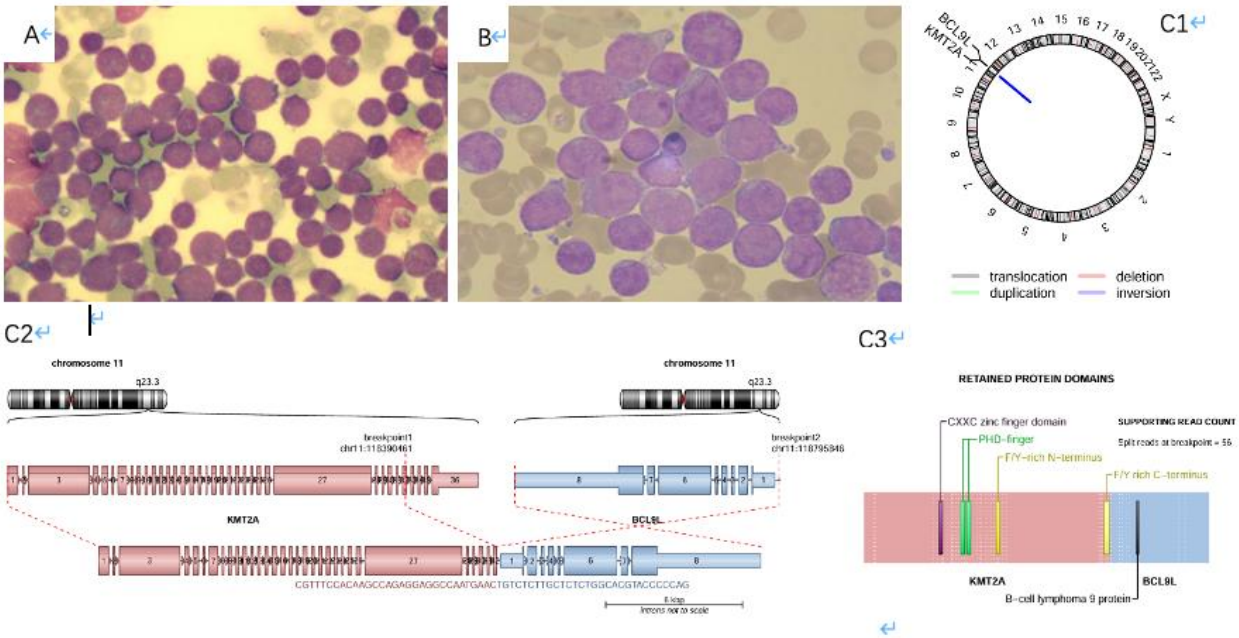

Figure1: Morphological and molecular characteristics of the patient.(A) Bone marrow smear at initial diagnosis (Oil immersion, 100×).(B) Bone marrow smear at relapse (Oil immersion, 100×).(C1-C3) Genomic breakpoint and domain structure of the KMT2A::BCL9L fusion gene.

Results: The patient remained in remission until August 2025, when BM examination revealed a second relapse (blasts: 65%, FC-MRD: 37.1%,KMT2A::BCL9L: 5.02%). Salvage therapies, including the Menin inhibitor Revumenib combined with Venetoclax and Azacitidine, Daratumumab, and the HDAC inhibitor Chidamide, failed to induce remission. Palliative care has been continued for the patient to date.

Conclusions: This case underscores the aggressive nature of lineage-switched leukaemia.Achieving molecular-level MRD negativity prior to HSCT may reduce relapse risk. Administering palliative targeted agents, particularly menin inhibitors, pre-transplant to achieve molecular remission could potentially be superior to post-transplant palliative therapy.

Disclosure: Nothing to declare.

P229

BEYOND NUMBERS: SUPERIOR PEDIATRIC BONE MARROW TRANSPLANT OUTCOMES THROUGH STANDARDIZED, RISK-ADAPTIVE CARE AND PROACTIVE COMPLICATION MANAGEMENT

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Background: Pediatric hematopoietic stem cell transplantation (HSCT) is a complex, high-risk intervention with significant morbidity and mortality. Our center aimed to evaluate survival and quality-of-life outcomes in all pediatric patients transplanted since inception, emphasizing that superior outcomes can be achieved through strict adherence to standardized, risk-adaptive protocols and proactive complication management, even in limited cohorts.

Methods: We retrospectively analyzed all pediatric HSCT procedures performed between January 2020 and January 2025. Thirty patients underwent 31 HSCT procedures. Patient demographics, underlying diagnoses, donor type, stem cell source, and transplant characteristics were collected. Survival was estimated using Kaplan-Meier analysis. Quality of life was assessed using Lansky/Karnofsky and ECOG performance scores. All procedures followed a standardized, risk-adaptive transplant protocol, implemented consistently by the multidisciplinary team. Proactive complication management included daily risk assessments, early intervention protocols, and structured team communication.

Results: Thirty patients underwent 31 transplants. Median age at HSCT was 104 months (range, 8–233); 65.3% were male. Diagnoses included acute lymphoblastic leukemia (ALL, 42.3%), acute myeloid leukemia (AML, 15.4%), Wilms tumor (7.7%), thalassemia major (7.7%), juvenile myelomonocytic leukemia (JMML), Hodgkin and non-Hodgkin lymphoma, Fanconi aplastic anemia, acquired severe aplastic anemia, MHC class II deficiency, and Wiskott-Aldrich syndrome (each 3.85%).
Allogeneic HSCT was performed in 27 cases (87.1%), autologous in 4 (12.9%). Related donors accounted for 66.3% (all 10/10 HLA-matched); unrelated donors 33.7% (50% 10/10, 50% 9/10). Stem cell sources included peripheral blood (48.2%), bone marrow (25.9%), and combined sources (25.9%). Median follow-up was 20 months (range 1–51).
Overall survival was 92.3%, with 100-day survival of 100%. Disease-free survival reached 95% for malignant and 83.3% for non-malignant cases. One JMML patient relapsed after the first transplant but remains in remission four years post-second transplant. Complications were minimal: only one patient developed bronchiolitis obliterans; all others (88.4%) maintained Lansky/Karnofsky ≥90 and ECOG ≤1. Two patients (7.7%) died >100 days post-transplant due to thrombotic microangiopathy and adenovirus-related complications.

Conclusions: Our outcomes exceed published benchmarks (ALL: 91% vs 85–90%; AML: 100% vs 65–75%; JMML post-second transplant: 100% vs 50–60%). These results highlight the effectiveness of standardized, risk-adaptive protocols implemented consistently across the multidisciplinary team, combined with proactive complication management. Early recognition and intervention for complications, structured nursing and physician

collaboration, and evidence-based decision-making were pivotal.
This study demonstrates that exceptional pediatric HSCT outcomes can be achieved "beyond numbers," even in a small cohort, offering a model for centers aiming to maximize survival and quality of life through meticulous protocol adherence and proactive clinical management.

Disclosure: Nothing to declare

P230

PEDIATRIC ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHRONIC GRANULOMATOUS DISEASE: A CASE SERIES OF SINGLE CENTER EXPERIENCE

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Background: Chronic granulomatous disease (CGD) is a rare primary immunodeficiency, and is associated with phagocyte dysfunction resulting from genetic defects in some of the different subunits of the NADPH oxidase complex. Depending on the protein subunit affected, the pattern of inheritance is autosomal recessive (AR) or X-linked. Hematopoietic stem cell transplantation (HSCT) can cure CGD. We aimed to present our transplant experiences in pediatric patients with CGD at Acibadem Adana Hospital, Pediatric Bone Marrow Transplantation Unit.

Methods: A total of 650 allogeneic hematopoietic stem cell transplantations were performed at Acıbadem Adana Hospital Pediatric Bone Marrow Transplantation Unit in Turkey from 2013 to 2025. 7 of 650 pediatric patients were CGD. In this retrospective analysis of medical records and treatment modalities were evaluated.

Results: In this retrospective analyses, 7 patients were evaluated, age ranging from 2 to 17 years with an average of 10.5 years. Five patients were males, two were female. Five patients had HSCT from an unrelated donor. We included all patients except one patient conditioning with ATG, fludarabine and treosulfan. One patients experienced secondary graft failure and this patients underwent a second transplant. Four CMV reactivation developed in our patients. Acute GVHD ≥ Grade III was observed in only one patient. Chronic GVHD was seen in three patients. Two patients died. One of them died on day 25 due to sepsis. Another patient, who underwent second transplant due to primary graft failure, died on the 277th post-transplant day due to COVİD19 pneumonia. One patient developed VOD despite receiving defibrotide prophylaxis. No serious toxicity was observed in other patients. 5 patients are alive and still following up GVHD free.

Conclusions: HSCT is the only potentially curative treatment option in patients with CGD with significant morbidity and mortality, especially in patients who receive grafts from unrelated donors. These factors need to be considered in the decision-making process and when discussing conditioning and GVHD prophylaxis. In this retrospective study, we showed the results of our reduced toxicity myeloablative conditioning regimen is excellent overall

survival, negligible GVHD, and low toxicity among in pediatric patients with CGD even in those with high-risk pre-HSCT clinical features or those with no HLA-identical family donor who transplanted match unrelated donor.

Disclosure: No disclosure.

P231

CONCENTRATION OF TOTAL NUCLEATED CELLS IN HARVESTED BONE MARROW FROM PEDIATRIC DONORS

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Background: Bone marrow (BM) has traditionally been the preferred source of hematopoietic stem cells (HSC) in matched sibling donors for pediatric patients. However, data on expected total nucleated cell (TNC) and CD34⁺ cell yields from healthy pediatric donors remain limited.

Methods: We conducted a retrospective analysis of TNC and CD34⁺ cell counts obtained from BM harvests performed in donors aged ≤18 years between January 2015 and October 2025 at two pediatric HSC transplant and collection centers. Demographic characteristics of donors and recipients were recorded. Kendall's tau-b coefficient was used to assess the association between donor age and TNC and CD34⁺ cell concentrations.

Results: During the study period, 81 BM harvests were performed. Fifteen were excluded due to donor age >18 years (n = 4) or insufficient data (n = 11). A total of 66 harvests were included. The median donor age was 11 years (range: 2–17). Median harvested concentrations were 22.06 × 10^6 TNC/mL (range: 8.34–52.12) and 0.39 × 10^6 CD34⁺ cells/mL (range: 0.04–9.48), both measured with additives. No significant correlation was observed between donor age and TNC concentration ($\tau = -0.078$; $p = 0.37$) or CD34⁺ cell concentration ($\tau = -0.026$; $p = 0.76$). The median recipient age and weight were 6 years (range: 0.1–22) and 27 kg (range: 5–97), respectively. The median infused cell dose was 2.00 × 10^9 TNC/kg (range: 1.02–13.20) and 4.8 × 10^6 CD34⁺ cells/kg (range: 0.43–26.75).

Conclusions: Concentrations of TNC and CD34⁺ cells harvested from BM were within the expected numbers and similar to those of high activity adult registries. BM allows the achievement of satisfactory cell doses from pediatric donors to pediatric receptors.

Disclosure: Nothing to declare

P232

TRANSFUSION PRACTICES AND COMPLICATIONS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CUBAN EXPERIENCE

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Background: Hematopoietic stem cell transplantation in pediatric patients requires intensive transfusion support, which can be challenging in resource-limited settings. Understanding transfusion patterns and associated complications is essential to optimize care.

Methods: A retrospective analysis was conducted on pediatric hematopoietic stem cell transplantation recipients treated between March 2000 to December 2023 at Institute of Hematology and Immunology, Cuba. Transfusion data were collected for red blood cells, platelets, and plasma, along with clinical variables including graft source (bone marrow vs. peripheral blood), ABO compatibility, and transfusion reactions.

Results: The mean age was 10.2 ± 4.9 years old and 66 % were male. Acute non-lymphoid leukemia was the most common transplanted disease. In peripheral blood transplants the mean number of units of blood cells and platelets transfused was 3.9±2.13 and 23.2±18.74 and with the use of bone marrow it was 4.8±2.44 and 41.8±39.8, respectively. ABO incompatibility was present in 35% of cases, associated with delayed engraftment and increased transfusion needs. Transfusion reactions occurred in 12% of patients, predominantly febrile non-hemolytic events.

Conclusions: Peripheral blood grafts were associated with lower transfusion requirements and fewer complications, suggesting a potential advantage in pediatric hematopoietic stem cell transplantation settings. These findings support tailored transfusion strategies and highlight the importance of ABO compatibility in transplant planning.

Disclosure: Nothing to declare

P233

HAPLOIDENTICAL HEMATOPOEITIC STEM CELL TRANSPLANT (HSCT) – MY EXPERIENCE OVER 2 YEARS FOR VARIED HEMATOLOGICAL ONCOLOGICAL CONDITIONS

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Background: The problem faced in our Country is lack of awareness and lack of willingness to register as donors.Not having a matched donor in the family or the registry compels us to use a family member as a haploidentical donor.
Aim: To evaluate the outcome of Haploidentical HSCT in children aged 0-18 years of age

across different hematological conditions.The evaluation incudes the cell dose, engraftment, chimerism, immune reconstitution as well as complications encountered such as Graft vs host disease, viral reactivations, duration of follow up and costs incurred.

Methods: A retrospective analysis of Haploidentical transplants done by me over a 2 year period from October 2023 to December 2025 at a tertiary Pediatric hospital in Mumbai.12 children had undergone a haploidentical transplant,3T cell deplete and 9T replete.

Results: 12 children underwent Haploidentical HSCT, 3 each with Acute myeloid leukemia(AML) and Acute lymphoblastic leukemia(ALL) ,2 with thalassemia major and 1 each with severe aplastic anemia, CML with AML blast crisis in remission,homozygous sickler and with Primary hemophagocytic lymphohistiocyosis. Out of these 12,3 underwent T deplete HSCT, the child with AML blast crisis in CML, one child with Thalassemia major and one child with primary HLH. The median CD34 stem cell dose was 8 x10^6/kg and the median CD3 dose was 3.5x10^8/kg in the T replete cohort and median CD34 of 20x10^6/kg in the T deplete cohort.The median time to neutrophil engraftment was14 days and the median time to platelet engraftment was 18 days of the entire cohort.2 children succumbed to complications of transplant, child with B ALL heavily pretreated prior to transplant with chemotherapy and immunotherapy developed septicemia and venoocclusive disease and succumbed on DAY +43 post transplant to enterococcus septicemia.The child with Thalassemia major developed secondary graft failure secondary to HHV6, cytokine storm and could not be revived. One more child with ALL having undergone nonTBI based conditioning relapsed 4 months post transplant.The rest all are alive at a median follow up of 265 days(range day+29 to +561).Chimerism was 100% at day +30 in 11/12 children except one child with ALL who succumbed to complications.The chimerism persisted to be 100% in those who have completed 365 days post HSCT. Apart from CMV viremia and grade I–II gut GVHD none of the 10/12 children faced any major complications like chronic GVHD.The immune reconstitution was robust with all children having a CD4 of more than 50 cells/ul at day +100.The cost of transplant on average was 16,500-17,000 pounds for T replete and around 33,000-35,000 pounds for T deplete HSCT.

Conclusions: Haploidentical HSCT is a boon for the resource limited countries with meagre donor registries,good outcomes with very few complications post HSCT and not very expensive even in a private tertiary care hospital.Adequate CD34 dose ensures robust engraftment. The maximum CD3 dose in the T replete cohort was 7.8x10^8/kg, range being 1.88 to 7.8x10^8/kg, not inciting severe GVHD in any child.

Disclosure: Nothing to declare

P234

BUSULFAN ASSOCIATED PULMONARY TOXICITY AND INFECTIOUS COMPLICATIONS FOLLOWING AUTOLOGOUS SCT IN A 3-YEAR-OLD CHILD WITH NEUROBLASTOMA

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Background: High-dose busulfan/melphalan (Bu/Mel) remains a standard conditioning regimen for autologous stem cell transplantation in high-risk neuroblastoma but is associated with significant organ toxicity, particularly hepatic and pulmonary injury. Pulmonary toxicities present with nonspecific clinical symptoms and radiological features and have been linked to the development of pulmonary hypertension and acute respiratory distress syndrome (ARDS).

Methods: Here, we report the case of a 3-year-old girl with stage IV neuroblastoma who developed severe, multifactorial pulmonary complications after Bu/Mel conditioning and autologous stem cell transplantation (SCT).

Results:

Early post-transplant complications included a left-sided diaphragmatic hernia on d +9 after previous surgical intervention (abdominal neuroblastoma surgery), hepatic veno-occlusive

disease (VOD) d +26 and respiratory deterioration with need for mechanical ventilation due to concomitant CMV infection and Legionella pneumoniae infection on d +27. A treatment with Defibrotide, Ganciclovir and Azithromycin was initiated. Extubation to High-Flow was possible by d +37; however, a persistently high oxygen requirement and progressive right-sided pulmonary opacification was noted. On d +61, the patient experienced acute deterioration with a cardiopulmonary resuscitation event in the setting of ARDS and methicillin-resistant staphylococcus aureus (MRSA) sepsis, confirmed by MRSA in blood cultures and bronchial secretions. CT imaging demonstrated bilateral pneumonia with necrotizing changes in the right lower lobe and diffuse ground-glass opacities. Management included broad-spectrum antibiotics, inhaled nitric oxide (iNO) and mechanical ventilation with high pressure levels (PEEP and peak pressure). We saw a clinical response with iNO, while echocardiography showed only moderate pulmonary hypertension. We started a treatment with Sildenafil, Macitentan, Epoprostenol in addition to Methylprednisolone pulse therapy and antifibrotic treatment with Nintedanib, Hydroxychloroquin and Azithromycin. While infectious complications and hepatic VOD completely resolved, the patient's respiratory function remained critically impaired. CT scans showed progressive interstitial lung disease with coarse-cystic fibrosis in the right lower lobe, subpleural honeycombing and diffuse ground-glass opacities.In response to recurrent pulmonary bleeding and pneumothorax, a therapeutic attempt was made to functionally exclude the most damaged lung segment, using an occluder device. The procedure was technically successful. However, despite maximal intensive care support the patient's course was ultimately fatal due to persistent severe hypoxemia and refractory ventilation failure.

Conclusions: This case illustrates the complex interplay between infectious complications, post-transplant inflammation and busulfan-induced pulmonary toxicity in a young neuroblastoma patient undergoing Bu/Mel conditioning and autologous SCT. Consideration of busulfan toxicities, especially when presenting with nonspecific early symptoms is important even when alternative explanations such as severe infection may appear equally plausible after autologous SCT. Early recognition, close monitoring of busulfan exposure, and multidisciplinary management are critical to mitigating the risk of life-threatening pulmonary toxicity in children undergoing Busulfan conditioning.

Disclosure: Nothing to declare.

Paediatrics – Basic and translational

Paed4-03

ENDOTHELIAL BIOMARKER DYNAMICS IN SINUSOIDAL OBSTRUCTION SYNDROME FOLLOWING PEDIATRIC ALLOGENEIC HSCT

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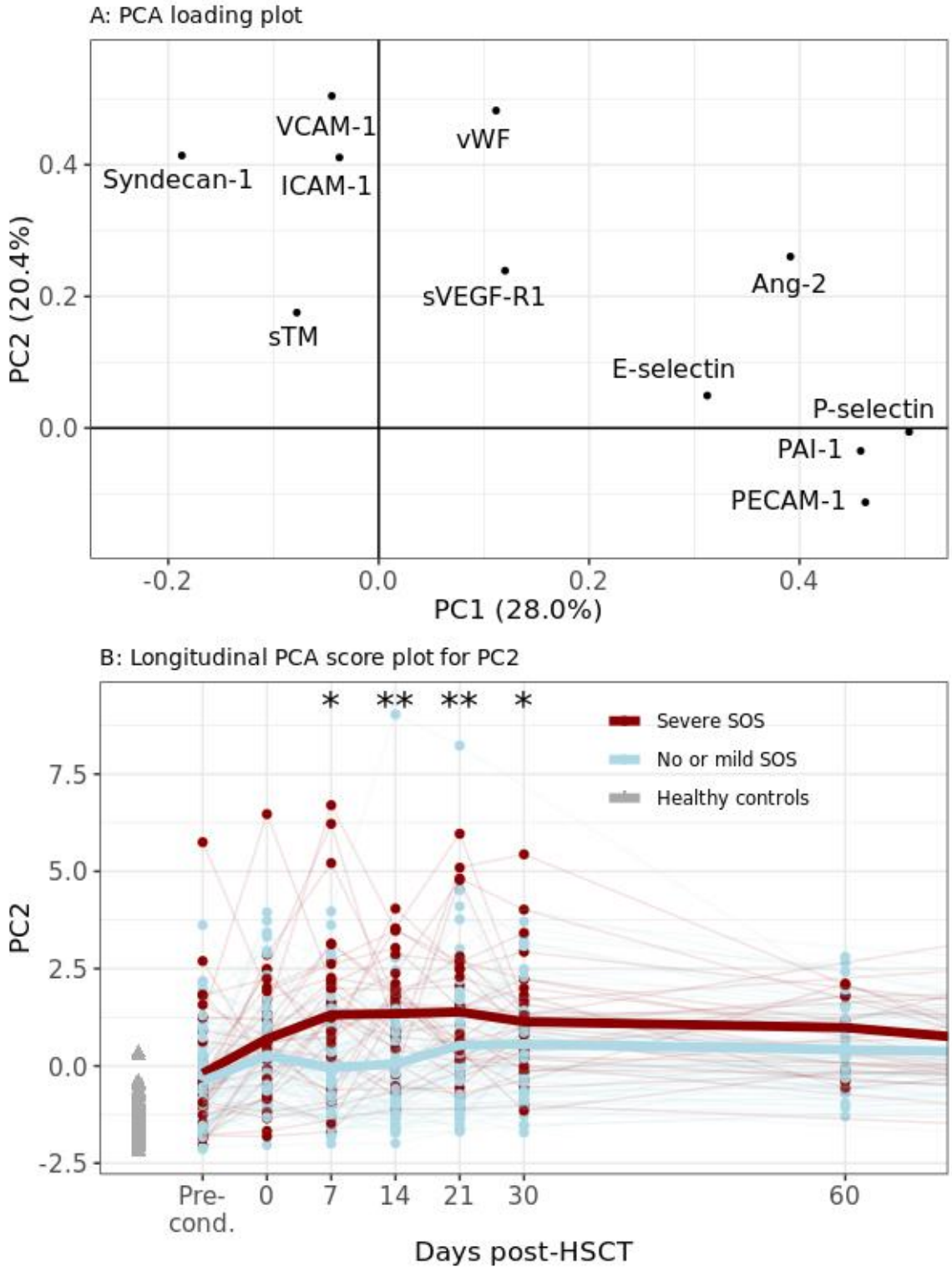
Background: Allogeneic HSCT is limited by toxicities related to endothelial dysfunction, including sinusoidal obstruction syndrome (SOS), which can be life-threatening. Early diagnosis of SOS is difficult due to non-specific symptoms and insufficient diagnostic tools, highlighting the need for a biomarker-guided approach. This study investigates longitudinal patterns of endothelial activation and damage biomarkers before conditioning and during the first 2 months after pediatric HSCT.

Methods: We prospectively included 113 children (median age: 8.8 years) undergoing standard HSCT at Rigshospitalet in Denmark from 2010-2019 (Table 1). Two hundred children aged 6-19 years served as controls.
Endothelial biomarkers (ICAM-1, VCAM-1, P-selectin, E-selectin, sVEGF-R1, PECAM-1, sTM, vWF, PAI-1, syndecan-1, and angiopoietin-2) were measured by Luminex and ELISA before conditioning and on days 0, +7, +14, +21, +30, and +60 post-HSCT. Severe SOS was diagnosed retrospectively according to the pediatric EBMT criteria based on medical records. Statistical analyses included principal component analysis (PCA) to identify biomarker patterns and random forest machine-learning models with cross-validated ROC-AUCs to evaluate predictive performance of SOS from biomarkers and demographic baseline information.

TABLE 1 Patient and transplant characteristics		HSCT patients (n=113)		Controls (n=200)	
Sex, male, n (%)		66	(58.4%)	97	(48.5%)
Age (years), median (range)		8.8	(1.1-17.6)	11.7	(6-18.8)
Malignant disease at transplantation, n (%)		68	(60.2)		
Donor type, n (%)					
	Matched sibling donor (10/10)	33	(29.2%)		
	Matched unrelated donor (≥9/10)	80	(70.8%)		

Stem cell source, n (%)					
	Bone marrow	108	(95.6%)		
	Peripheral blood stem cells	5	(4.4%)		
Conditioning regime, n (%)					
	BU-based	49	(43.4%)		
	TBI-based	27	(23.9%)		
	Other chemotherapy-based regimens	37	(32.7%)		
ATG as part of conditioning, n (%)		85	(75.2%)		
GvHD-prophylaxis, n (%)					
	CyA	19	(18.8%)		
	CyA/TA + MTX	94	(83.2%)		
Prophylactic defibrotide, n (%)		7	(6.2%)		

Results: Fifty-one patients developed SOS, including 32 with severe SOS. Median diagnosis was day +5 (range +2-+58).
All selected biomarkers were detectable and included in a PCA analysis to identify patterns associated with severe SOS. The leading principal component (PC1) was mainly characterized by PECAM-1, P-selectin and PAI-1 (figure 1A) with a similar temporal trajectory for patients with mild/no SOS (n=81) and severe SOS (n=32), reflecting general post-transplant changes. PC2 (driven by VCAM-1, ICAM-1, vWF, and syndecan-1, 1figure A) distinguished severe SOS (from mild/no SOS) with the largest differences observed from day +7 to +30 (all $p<0.05$, 1figure B). This indicates that PC2 patterns may identify high-risk patients around the time of severe SOS diagnosis.
Among controls (n=200), PCA revealed distinct differences in biomarkers variability compared with HSCT-patients. PC1 showed greater variability compared to HSCT-patients across day 0, +7, +14, and +21 (all $p<0.001$), while PC2 demonstrated tighter clustering at all time points (all $p<0.00001$). These patterns could indicate that HCST induces a characteristic shift in biomarker patterns, while both controls and HSCT patients show variation within their own groups.
Machine-learning models combining biomarker patterns with baseline characteristics (age, malignant diagnosis, and busulfan-based conditioning) showed high diagnostic accuracy for predicting severe SOS (AUC: 0.75 pre-conditioning, 0.74 day 0, and 0.79 day +7). These combined models outperformed both biomarker-only models (AUC: 0.67, 0.67, and 0.78, respectively) and baseline characteristics-only models (AUC: 0.70), demonstrating that integrating clinical and biological information enables earlier risk identification. Overall, sensitivity was modest while specificity was high for predicting/diagnosing severe SOS in the combined models (16.2% and 92.8% before conditioning, 28.5% and 93.8% on day 0, and 36.5% and 90.1% on day +7, respectively).


A: PCA loading plot
VCAM-1
vWF
Syndecan-1
ICAM-1
sVEGF-R1
Ang-2
sTM
E-selectin
P-selectin
PAI-1
PECAM-1
PC2 (20.4%)
PC1 (28.0%)
0.4
0.2
0.0
-0.2
0.0
0.2
0.4
B: Longitudinal PCA score plot for PC2
* ** ** *
Severe SOS
No or mild SOS
Healthy controls
PC2
7.5
5.0
2.5
0.0
-2.5
Pre-cond.
0
7
14
21
30
60
Days post-HSCT

Conclusions: Pediatric HSCT patients show significant and early biomarker changes compared to controls. Patterns involving VCAM-1, ICAM-1, vWF, and syndecan-1 may distinguish severe SOS around the time of diagnosis. Combining biomarkers with baseline characteristics may lead to a restriction of the SOS criteria for prediction of high-risk pediatric SOS, supporting targeted monitoring and risk-stratified care.

Disclosure: Nothing to declare.

B268

PRE-TRANSPLANT RESISTOME DISRUPTION PREDICTS ESBL GENE ACCUMULATION IN PEDIATRIC TRANSPLANT RECIPIENTS: A PROSPECTIVE MULTI-CENTER STUDY

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Background: Extended-spectrum β-lactamase (ESBL)–producing organisms are an important cause of post-transplant infections in children undergoing allogeneic hematopoietic cell transplantation (HCT). Whether ESBL gene accumulation during early transplant is primarily driven by peri-transplant antibiotic exposure or by pre-existing resistome disruption remains unclear.

Methods: We conducted a prospective multi-center study including pediatric patients (<18 years) receiving HCT from 4 European centers (Bologna, Genova, Verona, Wroclaw) and one American center (St. Jude Children's Research Hospital, Memphis). Stool samples were collected before HCT, at neutrophil engraftment, and on day +30 after HCT. Metagenomic sequencing was used to quantify antibiotic resistance genes (ARGs), with ESBL genes annotated via MEGARes 3.0. Associations between antibiotic exposure and ESBL gene accumulation before engraftment were assessed using linear regression models weighted by covariate balancing propensity scores. To account for differences in transplant practices between countries, analyses were performed comparing European and American centers.

Results: A total of 133 pediatric HCT recipients were included, 39 from European centers and 94 from St. Jude. Full patients' characteristics are reported in the Table. The cohorts presented some significant differences. As transplant indications, acute myeloid leukemia predominated in the St. Jude cohort (54.3% vs 17.9%), and nonmalignant diseases occurred exclusively in European patients (35.9% vs 0%) ($p<0.001$). Myeloablative regimens used in

79.5% of European patients compared with 34.0% at St. Jude (p<0.001). T-cell depletion strategies, as ATG was used routinely in Europe (71.8%) and not at all at St. Jude (p<0.001). Analysis of ESBL gene dynamics revealed distinct temporal patterns between cohorts. European patients showed a pronounced rise in ESBL gene abundance between HCT and engraftment that persisted through day +30, whereas St. Jude patients demonstrated increases primarily after engraftment. When antibiotic classes were examined, only aminoglycoside exposure before engraftment was associated with ESBL gene accumulation, and this was limited to the European cohort (est: 0.93; 95% CI 0.66–1.20; p=0.002). No associations were observed for exposure to total β-lactams (Europe p=0.685; St. Jude p=0.353), ESBL-cleavable β-lactams (St. Jude p=0.933), antibiotics with anaerobic activity (Europe p=0.893; St. Jude p=0.073), or total daily antibiotic exposure (Europe p=0.643; St. Jude p=0.815). In contrast, pre-HCT resistome disruption emerged as a strong predictor of subsequent ESBL expansion. A higher Bray–Curtis distance from the healthy resistome centroid at baseline was associated with increased ESBL gene abundance both before engraftment (Europe est: 7.48, SE 3.65, p=0.052; St. Jude est: 15.85, SE 6.19, p=0.024) and during the first 30 days post-HCT (Europe est: 15.12, SE 5.51, p=0.013; St. Jude est: 9.58, SE 4.99, p=0.079). Notably, only minimal additional resistome perturbation occurred during neutropenia, despite intensive antibiotic exposure.

Characteristic	European (N = 39)	St. Jude (N = 94)	P-value
Age at Transplant	8.1	8.4	0.865
Gender- Female	17 (43.6%)	42 (44.7%)	0.908
Diagnosis			<0.001
Acute myeloid leukemia	7 (17.9%)	51 (54.3%)	
Acute lymphoblastic leukemia	12 (30.8%)	33 (35.1%)	
Other malignancy	6 (15.4%)	10 (10.7%)	
Nonmalignant disease	14 (35.9%)	0 (0.0%)	
Donor			<0.001
Haploidentical	7 (17.9%)	54 (57.4%)	
Related	5 (12.8%)	14 (14.9%)	
Unrelated	27 (69.2%)	26 (27.7%)	
Graft Source			0.417
Bone Marrow	15 (38.5%)	37 (39.4%)	
Peripheral Blood Mononuclear Cells	23 (59.0%)	57 (60.6%)	

T Cell Depletion			0.006
Yes	28 (71.8%)	43 (45.7%)	
Type of T Cell Depletion			<0.001
Antithymocyte Globulin	28 (71.8%)	0 (0.0%)	
CD3 Depletion and/or CD34 Enrichment	0 (0.0%)	42 (44.7%)	

Conclusions: In pediatric HCT recipients, ESBL gene accumulation is more strongly driven by pre-existing resistome disruption than by early post-transplant antibiotic exposure. Aminoglycosides may contribute to ESBL gene expansion, whereas β-lactam exposure alone does not appear to be a major driver. These findings highlight the importance of pre-HCT microbiome and resistome preservation strategies as potential avenues to reduce ESBL colonization and infection risk in vulnerable transplant populations.

Disclosure: Nothing to declare.

B269

REGULATORY T CELL RECONSTITUTION IS ASSOCIATED WITH ONSET AND SEVERITY OF ACUTE GRAFT-VERSUS-HOST DISEASE IN PEDIATRIC AND YOUNG ADULT HCT RECIPIENTS

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Background: Regulatory T cells (Tregs), a small subset of circulating $CD4^+$ T cells, play a crucial role in immune tolerance by suppressing auto- and alloreactive immune responses and are essential for establishing and maintaining immune tolerance after allogeneic hematopoietic cell transplantation (alloHCT). A reduction in Treg frequency or numbers has been associated with the onset of acute Graft-versus-Host Disease (aGvHD), a potentially life-threatening complication following alloHCT. The dynamics of Treg reconstitution and differentiation after alloHCT may modulate development of aGVHD. Here, we examined the potential association between Treg frequencies (% Tregs of $CD4^+$ T-cells) and the 90-day onset of aGvHD in pediatric and young adult HCT recipients.

Methods: Patients transplanted between 2020-2025, who had provided consent for ancillary immune reconstitution studies within our TCT program were included. We used our CLIA-approved Treg panel which includes CD4+ regulatory T-cell (CD3+CD4+CD25+CD127low), naïve (CD45RO-HLA-DR-), activated (HLA-DR+) and memory (CD45RO+) Treg subsets. Primary outcome of interest was studying the association between Treg reconstitution and

the development of aGvHD in the first 90 days after alloHCT. We also examined post-HCT Treg patterns in relation to GvHD severity. Uni- and multivariate logistic regression analyses were performed.

Results: 117 patients were enrolled with median age of 12 years, range 0-26. Early Treg data before the onset of aGvHD were available for 79 out of 117 patients; 24 (30%) received cord blood, 14 (18%) T-cell deplete peripheral blood stem cells and 41 (52%) unmodified grafts. 38 (48%) patients developed aGvHD (grade 2-4).
Higher Treg frequencies (>3% of $CD4^+$ T-cells) before day 90 or onset of aGVHD were associated with decreased odds of developing aGVHD (p=0.027). Also age (<12 yrs; p=0.038) and cord blood; p=0.027) were found to be predictors for aGvHD 2-4. Treg frequencies rapidly declined after HCT in patients who went on to develop aGvHD (Figure 1). This decrease was not observed in patient who did not develop aGvHD or in patients treated for aGvHD. The Treg differentiation trajectory indicated that memory and activated Treg subsets, but not naïve Tregs, declined prior to GvHD onset. After development of aGvHD Tregs remained decreased (about 20%) in Grade 3-4 GvHD compared to Grade 0-2 GvHD untill 12-18 months after HCT (n=117; Figure 2).

Figure 1 I Treg frequencies decline prior to aGvHD onset.

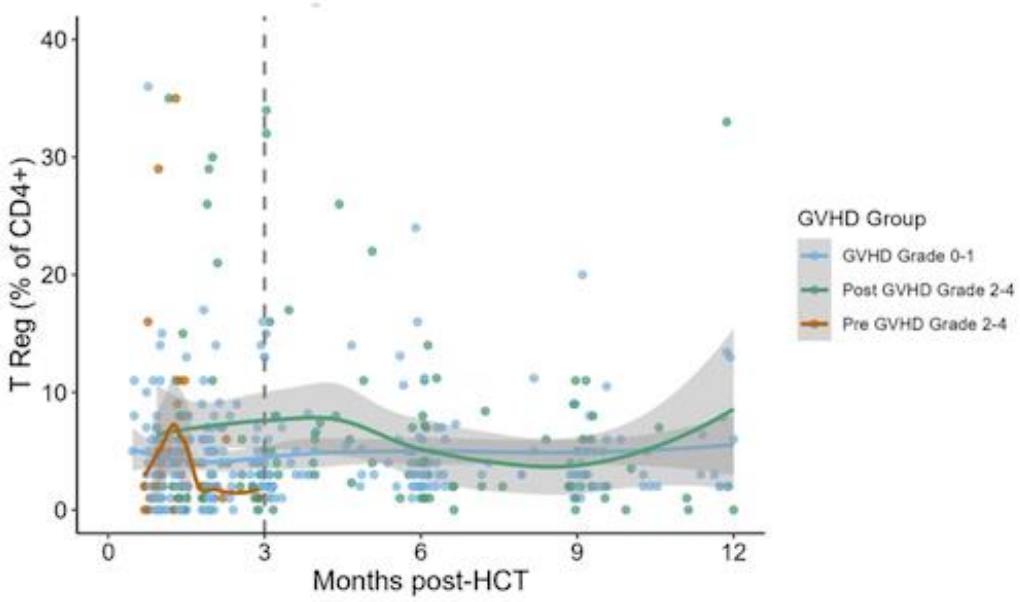
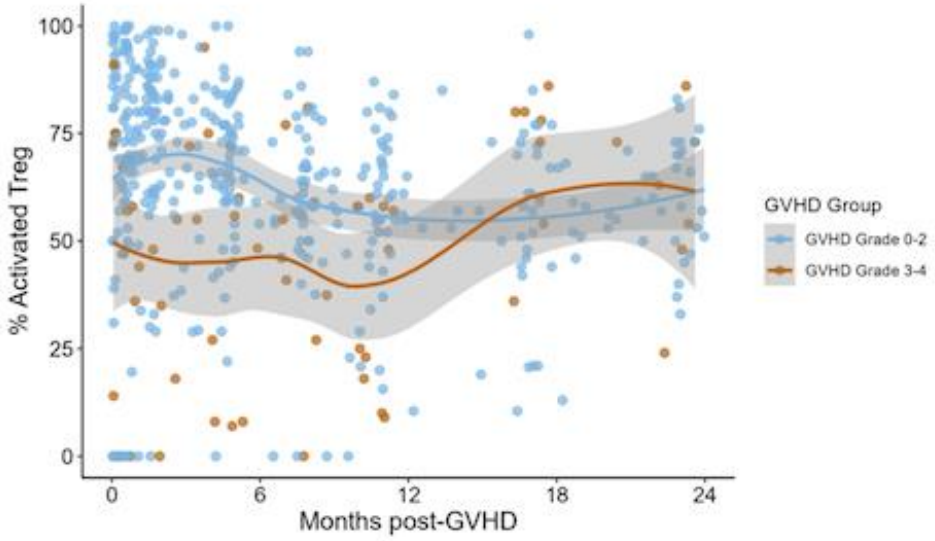


Figure 2 I Activated Tregs decrease with GvHD severity.



Conclusions: In this large pediatric and young adult cohort, early robust Treg reconstitution (>3% of CD4+ T-cells) was associated with a lower risk of aGvHD. The observed decline in Treg frequencies prior to aGvHD onset appeared to reflect a shift toward a less active Treg profile, with decreasing activated Tregs correlating with GvHD severity. The association between early loss of Treg subsets and aGvHD onset and severity must be confirmed in a larger, multicenter cohort but could be implemented for risk stratification and clinical decision-making.

Disclosure: Nothing to declare.

B272

ROLE OF PHARMACOGENETICS IN THE EFFICACY OF LOW-DOSE METHOTREXATE ADMINISTERED AS GVHD PROPHYLAXIS IN PEDIATRIC ALL PATIENTS: A FORUM STUDY

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Background: Methotrexate (MTX) is commonly used as acute graft versus host disease (aGvHD) prophylaxis in combination with cyclosporine A (CsA) following hematopoietic stem cell transplantation (HSCT) in pediatric acute lymphoblastic leukemia (ALL) patients. It inhibits folate metabolism, thus blocking T-cell proliferation and decreasing inflammation. While the pharmacogenetic (PGx) of MTX has already been broadly investigated in the context of high-dose administration for cancer treatment, less is known about its role in GvHD prevention. Here, we investigated whether some of the previously identified polymorphisms impacting MTX pharmacodynamics or pharmacokinetics are playing a role in its anti-aGvHD efficacy.

Methods: The genetic association analysis was performed using data collected from 370 MTX-treated children among 485 participants in the PGx add-on (NCT02670564) of the ALL SCTped 2012 FORUM (NCT01949129) study. We included patients who received bone marrow (BM) or peripheral blood (PB) stem cell transplantation from an HLA-identical sibling (MSD) or a 9-10/10 HLA-matched related or unrelated donor (MD). According to protocol, all analyzed patients received additional CsA prophylaxis and, for non-sibling donors ATG. As most patients who underwent MSD-BM transplantation received CsA prophylaxis alone, this group is underrepresented in the current subset. Patients with cord-blood and missmatched donors HSCT were excluded.
We tested the association between single genetic determinants and grade II-IV aGvHD using Fine-Gray regression models adjusting for donor type, stem cell source, conditioning regimen, disease phenotype, and sex as covariates. Death and relapse were considered competing events for aGvHD and p-values <0.05 after adjustment for multiple testing using Benjamini-Hochberg FDR, were statistically significant.
We selected 24 genetic variants involved in MTX transport or the folate pathway with previous interactions described in the literature.

Results: Of 370 patients aged 0.5-20 years (median=9.4 years), 108 (29.2%) developed grade II-IV aGvHD. In this FORUM subset, PB grafts (N=107, 5 MSD, 102 MD) were associated with a higher risk of aGvHD than BM grafts (N=263, 30 MSD, 233 MD; HR 1.9, 95% CI 1.3-2.8, p=0.001). Acute, but not chronic, GvHD correlated with a lower cumulative incidence of relapse (aGvHD grade II-IV: HR 0.61, 95% CI 0.37-0.98, p=0.042, grade III-IV: HR 0.23, 95% CI 0.06-0.95, p=0.021).
From the 24 selected variants, we identified one significant association between ***MTHFR* rs1801131** (MAF = 0.31) and the cumulative incidence of aGvHD (HR 0.60, 95% CI 0.44-0.82, adjusted p-value=0.024). This single nucleotide polymorphism, also known as **A1298C**, encodes a non-synonymous **E429A** mutation in methylenetetrahydrofolate reductase protein catalyzing a rate limiting step in the one-carbon cycle.

Conclusions: Our candidate gene approach validated the recipient ***MTHFR* A1298C** variant as a significant determinant of MTX prophylaxis efficacy against aGvHD in a homogenous cohort of children with ALL undergoing HSCT from HLA 9-10/10 matched donors. Elucidating the regulatory mechanism of the folate pathway may help personalize MTX administration for post HSCT GvHD prophylaxis.

Clinical Trial Registry: NCT01949129, NCT02670564

Disclosure: Fanny Gonzales: advisory board for MSD.
Jochen Buechner: advisory boards for Amgen, Novartis, Pfizer, Medac and Janssen (to institution); speaker fees from Novartis; SSC/DMSB member for clinical trials sponsored by Novartis.
Tayfun Güngör: advisory board for Vertex.
Herbert Pichler: travel grants from Jazz Pharmaceuticals and Sanofi; speakers bureau fees from Vertex and Novartis.
Tony H. Truong: Consultancy & honorarium from Sanofi, Vertex, Jazz Pharma, Medexus.
Franco Locatelli advisory board for Vertex, Sanofi, Novartis and Amgen; speakers bureau fees from Miltenyi, Amgen, Novartis, BMS, Medac, Gilead, SOBI.
Peter Bader research grants from Neovii, Riemser, Medac GmbH (to Institution); advisory

board for Novartis, Amgen, Medac GmbH, (personal and to institution); Speakers Bureau of Medac, Novartis, Vertex and Amgen (to institution).
Christina Peters: Amgen, Medac, Jazz, Neovii, Novartis, Pfizer, Riemser, Vertex.
Marc Ansari: advisory board for Jazz Vertex Swiss; travel grants from Novo Nordisk.
Other authors have no COI to declare.

B273

POTENTIAL FOR PHARMACOGENOMICS TO IMPROVE MEDICATION SAFETY AND EFFICACY IN AUSTRALIAN HAEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Background: Children undergoing a haematopoietic stem cell transplant (HSCT) often receive intensive conditioning regimens prior to receiving stem cells. In addition, HSCT patients are prescribed multiple supportive care medications including anti-emetics and anti-infectives, increasing their risk of adverse drug reactions (ADRs). Treatment toxicities can be severe and even life-threatening for these patients. Using pharmacogenomic (PGx) guided prescribing could result in safer and more effective therapy, with established guidelines for many commonly prescribed supportive care medications. Here we describe the frequency of high-risk PGx phenotypes identified in a diverse Australian paediatric oncology cohort, and estimate the prevalence of PGx medications prescribed in paediatric HSCT patients.

Methods: 14 pharmacogenes affecting medications commonly prescribed in paediatric oncology were selected for analysis from the Clinical Pharmacogenetics Implementation Consortium (CPIC) and Dutch Pharmacogenetics Working Group (DPWG) databases. Whole Genome Sequencing (WGS) data was obtained from 180 patients, and a custom PGx bioinformatic pipeline used to genotype and call consensus diplotypes. CPIC diplotype-to-phenotype tables were used to infer predicted phenotypes for the 14 pharmacogenes, including CYP2C19, CYP2D6, CYP3A5, G6PD, HLA-A, HLA-B, MT-RNR1, ABCG2, NUDT15 and TPMT. Paired supportive care medications included allopurinol, sertraline, omeprazole, pantoprazole, voriconazole, ondansetron, tramadol, tacrolimus, flucloxacillin, carbamazepine and amikacin. Electronic medical records were accessed to estimate prescribing rates of PGx medications in a paediatric oncology cohort, and specifically in paediatric HSCT patients.

Results: More than 90% of patients had at least one high-risk PGx phenotype, 58% for CYP2C19 phenotype and 49% for CYP2D6. 30% had high-risk phenotypes for both CYP2C19 and CYP2D6. Most patients (89%) were prescribed ondansetron and a significant number prescribed omeprazole (38%), pantoprazole (19%) and voriconazole (15%). PGx actionability rates were highest amongst patients taking omeprazole, voriconazole and sertraline when analysed as a proportion of patients prescribed the medication. In a cohort of

44 paediatric HSCT patients, ondansetron was prescribed in 71%, voriconazole in 39%, pantoprazole in 41%, omeprazole in 14%, tacrolimus in 9% and tramadol in 9%.

Conclusions: We have demonstrated the prevalence of clinically relevant high-risk PGx phenotypes in a diverse paediatric oncology cohort. Many supportive care medications prescribed for paediatric HSCT patients are likely to be affected, with high prescribing rates observed for some medications with available PGx prescribing guidelines. These results highlight the potential for PGx guided prescribing to improve medication efficacy and reduce toxicity in a paediatric HSCT setting.

Disclosure: Nothing to declare.

B274

HEMATOPOIETIC STEM CELL TRANSPLANTATION AND GUT MICROBIOME DIVERSITY IN CHILDREN

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Background: The gut microbiome (GM) is increasingly recognized as a key modulator of immune homeostasis and post-HSCT recovery. In adult HSCT recipients reduced microbial diversity – driven by conditioning, antimicrobial treatment, and mucosal injury – has been linked to infection risk, delayed immune reconstitution, aGvHD, and overall survival (OS). In children GM diversity pre-conditioning has been associated with aGvHD and OS. Because the pediatric gut microbiome is still developing, longitudinal responses to HSCT may differ substantially from adults, underlining the importance for high-resolution studies of GM in larger pediatric cohorts.

Methods: We prospectively enrolled children aged 1-18 years undergoing allo-HSCT at the national pediatric HSCT center in Copenhagen, Denmark (2015-2024). Patient characteristics are summarized in Table 1. Participants provided stool samples at up to 11 predefined timepoints from pre-conditioning through 52 weeks post-HSCT, yielding 825 samples from 134 patients. Shotgun metagenomic sequencing was performed and species-level community profiles were generated using MetaPhlAn.
Alpha diversity (within-sample diversity) was quantified using Shannon Index.
Longitudinal changes in alpha diversity were evaluated using linear mixed-effects models with fixed effects for time, age, sex, malignant disease, TBI ≥12 Gy, and GVHD grade.
Beta diversity (between-sample diversity) was assessed using Bray–Curtis dissimilarities, visualized by principal coordinates analysis (PCoA), and tested by PERMANOVA (999 permutations).

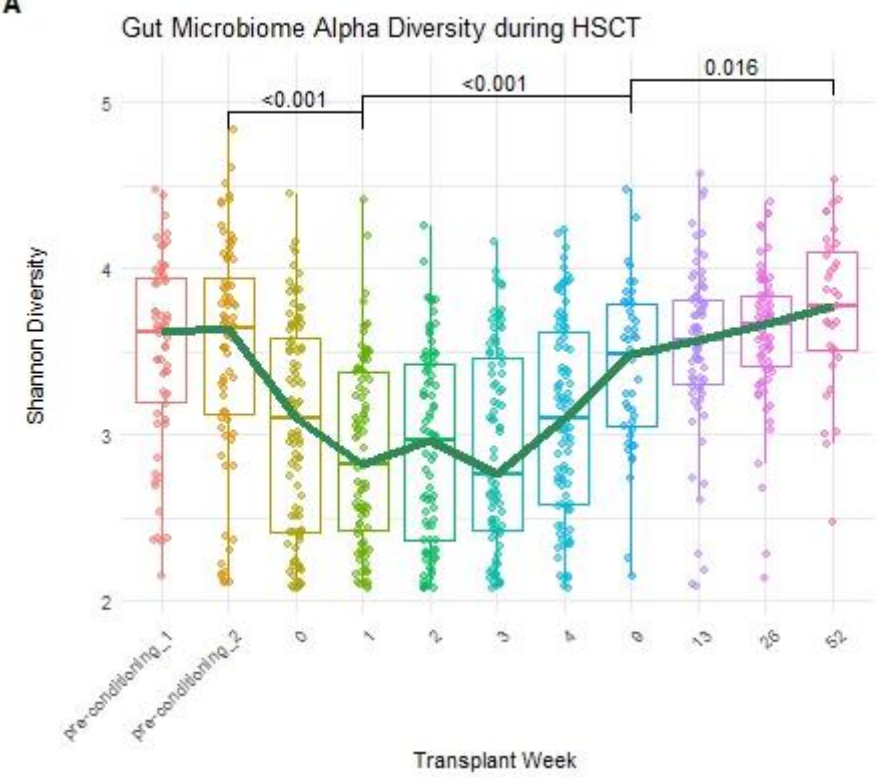
Results: GM alpha diversity declined markedly from pre-conditioning through Day 0 and weeks 1 to 3, followed by steady increase beginning at week 4. Diversity returned to pre-transplant levels by week 9 and remained stable through week 52 (Figure 1A).

In a multivariate linear mixed-effects model accounting for repeated measurements and clinical variables, mean alpha diversity decreased significantly immediately after conditioning and remained low post stem cell infusion (day 0: $\beta = -0.45$, $p < 0.001$; week 1: $\beta = -0.68$, $p < 0.001$) but increased above the pre-conditioning baseline by 52 weeks ($\beta = 0.23$, $p = 0.029$). Older age was associated with higher diversity ($\beta = 0.021$ per year, $p = 0.006$), whereas sex, malignancy status, TBI ≥12 Gy, and aGvHD grade were not significantly associated with alpha diversity.
Beta diversity analyses showed strong temporal restructuring of the GM, with sampling timepoint explaining 11.9% of community variation ($p = 0.001$). Samples taken the first few weeks after graft infusion (day 0 to week 4) formed a distinct cluster, separate from both pre-conditioning and late timepoint samples, and showed greater within group dispersion, indicating high inter-individual variability during the early transplant phase. In contrast, late timepoints (week 9 – 52) had lower dispersion than early timepoint (Day 0 to week 4) (Tukey's HSD test, $p < 0.001$) and clustered closely with pre-conditioning samples indicating greater compositional similarity between late post-HSCT and pre-conditioning GM (Figure 1B).

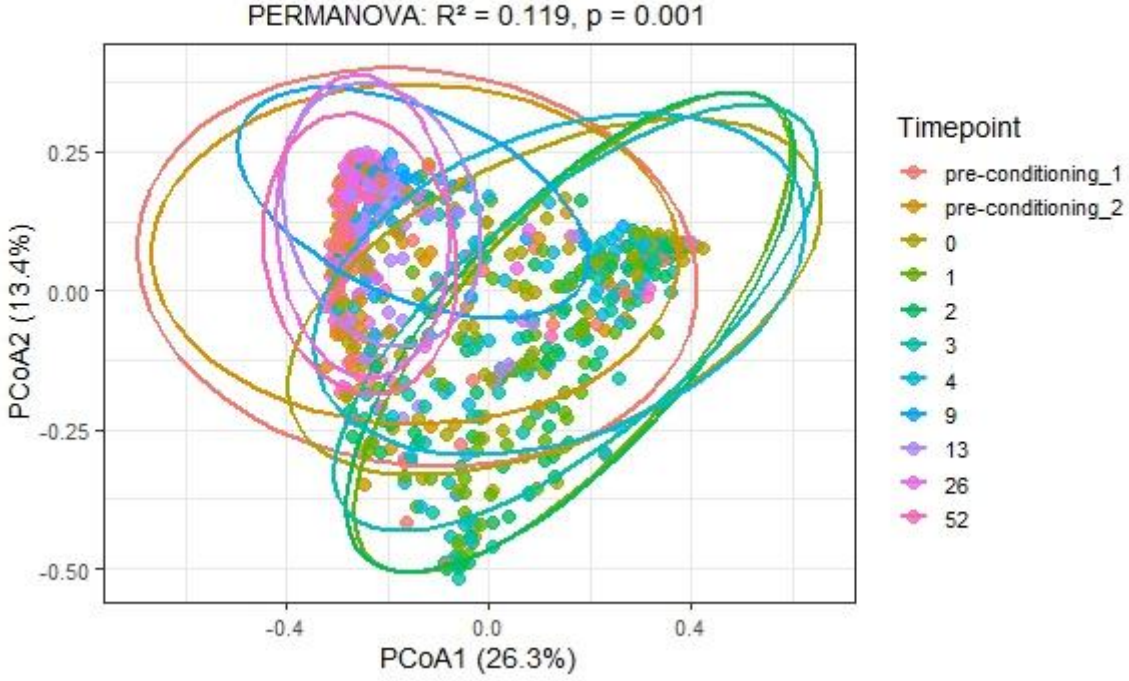
	Overall (N=134)
Sex	
Female	55 (41.0%)
Age at HSCT (Years)	
Median [Min, Max]	8.81 [1.18, 17.9]
Diagnosis	
Benign Disease	58 (43.3%)
Leukemia	60 (44.8%)
Other Hematologic Malignancy	16 (11.9%)
GVHD Grade	
0	74 (55.2%)
I	20 (14.9%)
II	28 (20.9%)
III - IV	12 (8.9%)
Graft Source	
Bone Marrow	108 (80.6%)

	Overall (N=134)
Peripheral Blood	23 (17.2%)
Umbilical Cord	3 (2.2%)
TBI-based Conditioning	
12 Gy	22 (16.4%)

A


Gut Microbiome Alpha Diversity during HSCT
<0.001
<0.001
0.016
Shannon Diversity
5
4
3
2
pre-conditioning_1
pre-conditioning_2
0
1
2
3
4
9
13
26
52
Transplant Week

B


Bray-Curtis PCoA
PERMANOVA: R² = 0.119, p = 0.001
PCoA2 (13.4%)
0.25
0.00
-0.25
-0.50
-0.4
0.0
0.4
PCoA1 (26.3%)
Timepoint
pre-conditioning_1
pre-conditioning_2
0
1
2
3
4
9
13
26
52

Conclusions: This study provides the first large-scale, year-long cohort study with high-resolution characterization of GM dynamics in pediatric HSCT. GM diversity follows a collapse-and-recovery trajectory with GM diversity restored by late follow-up. These findings lay essential groundwork for future studies linking GM dynamics to clinical outcomes and immune reconstitution.

Disclosure: Nothing to declare

Late complications, quality of life, fertility and survivorship

A414

CARDIOVASCULAR HEALTH OF HAEMATOPOIETIC STEM CELL TRANSPLANT SURVIVORS IN THE UK BIOBANK

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Background: Haematopoietic cell transplantation (HSCT) is often the only curative option for patients with malignant and non-malignant disorders. Advances in transplant care have improved survival, resulting in an expanding cohort of long-term HSCT survivors in whom cardiovascular sequelae are increasingly recognised. However, comprehensive population-level data on these risks remain limited. We evaluated cardiovascular event incidence in HSCT survivors and identified key risk factors in the UK Biobank.

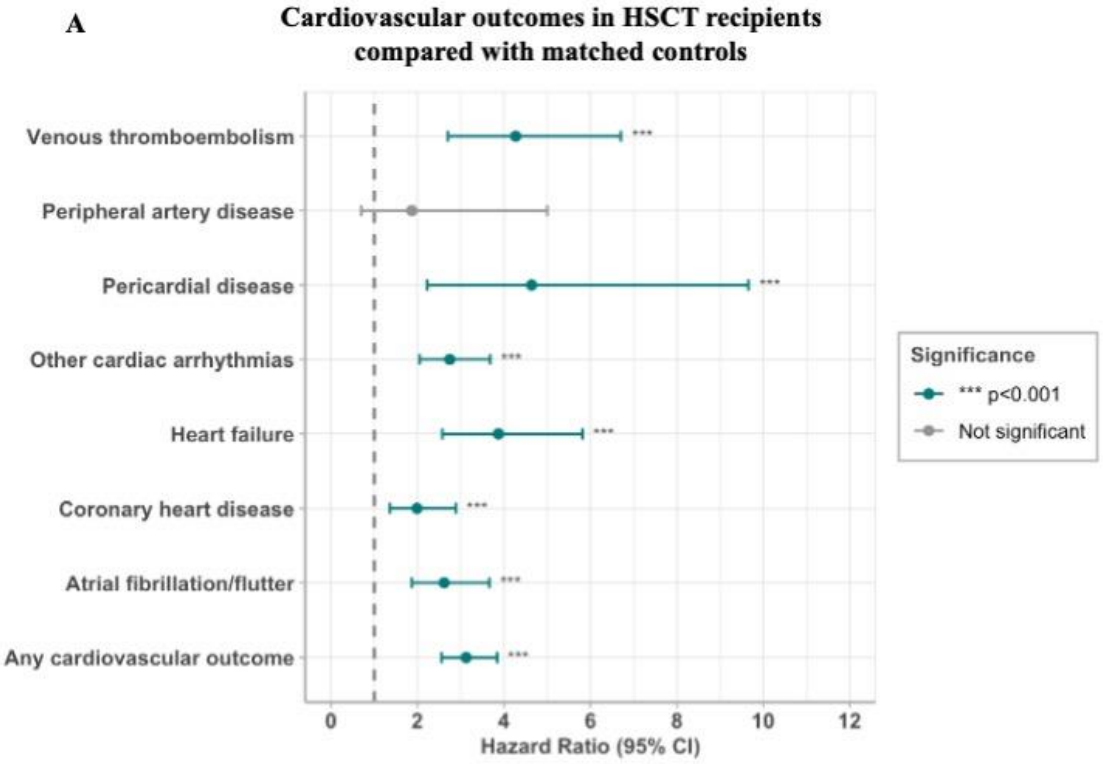
Methods: UK Biobank is a population-based cohort of 500,000 adults recruited between 2006 and 2010, with detailed baseline profiling and prospective follow-up. We identified participants who underwent their first HSCT after recruitment and matched each to up to four non-transplanted controls using propensity-score nearest-neighbour matching. The

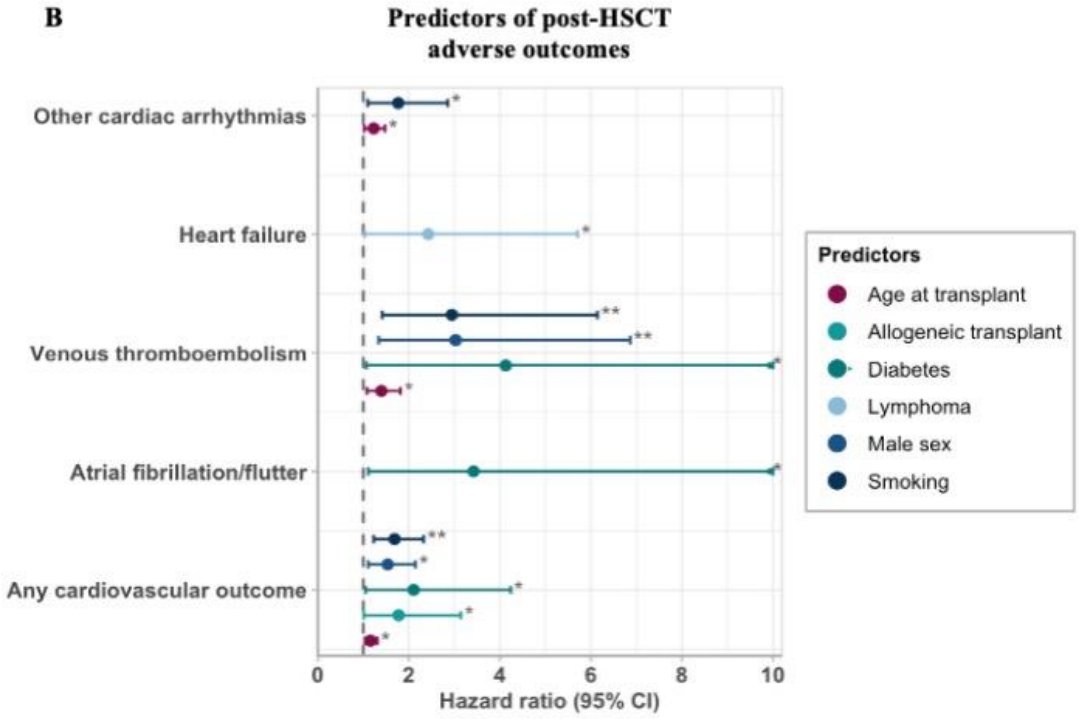
model included baseline sociodemographic factors (age, sex, ethnicity, education level, and deprivation index), lifestyle behaviours (smoking status, alcohol intake, and physical activity), and pre-existing comorbidities (hypertension, diabetes, and hyperlipidaemia). The HSCT date was defined as the index date, with matched controls assigned the same index date as their corresponding case. We identified seven incident cardiovascular diseases using linked hospital and mortality records. Cause-specific Cox proportional hazards models (stratified by matched set) were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). In secondary analyses restricted to HSCT recipients, we fitted multivariable Cox proportional hazards models to evaluate how pre-transplant patient factors influence risk of adverse outcomes. We additionally assessed effect modification by age through interaction terms with transplant type. The HCT-specific comorbidity index (HCT-CI) was replicated using linked hospital records, based on published definitions and used for descriptive purposes.

Results: The study cohort included 757 HSCT recipients (59% men; mean age at transplant, 63.1 years) and 3,028 matched controls (60% men; mean age at recruitment, 56 years) (**Table 1**). The cohort was predominantly White (≥94%). Among HSCT recipients, 72.1% underwent autologous transplants, with peripheral blood stem cells being the predominant graft source (93.3%, n = 706). Common transplant indications included multiple myeloma/plasma cell dyscrasia (49.5%), lymphoma (19.0%), and leukaemia (18.9%). In HSCT recipients, the median HCT-CI was 1 (IQR 0–3). Over a median follow-up of 4.25 years, HSCT survivors had more than a threefold increased risk of cardiovascular disease (HR 3.13; 95% CI 2.56–3.84), with the greatest excess risks observed for pericardial disease (HR 4.64; 95% CI 2.23-9.66), venous thromboembolism (HR 4.27; 95% CI 2.71-6.71), and heart failure (HR 3.87; 95% CI 2.58-5.82) (**Figure 1, panel A**). Within the HSCT cohort, older age at transplant, allogeneic grafts, male sex, pre-transplant smoking, and diabetes were associated with higher post-transplant cardiovascular risk (**Figure 1, panel B**). In interaction analyses, age significantly modified the effect of transplant type, with older allogeneic recipients showing the highest excess cardiovascular risk.

Characteristic	HSCT	General population
N	757	3,028
Age at transplant, years	63.1 (± 7.1)	-
Male	446 (58.9%)	1,808 (59.7%)
White ethnicity	715 (94.5%)	2,893 (95.5%)
Townsend Deprivation Index	-2.4 (-3.8, -0.1)	-2.4 (-3.8, 0.1)
Post-secondary education	410 (54.1%)	1,534 (50.7%)
Alcohol intake daily	143 (18.9%)	592 (19.6%)

Smoking	335 (44.3%)	1,342 (44.3%)
Body mass index, kg/m2	27.5 ± 4.6	27.5 ± 4.7
Hypertension	209 (27.6%)	812 (26.8%)
High cholesterol	147 (19.4%)	535 (17.7%)
Diabetes	43 (5.7%)	170 (5.6%)
Autologous transplant	548 (72.4%)	-
Peripheral blood haematopoietic cell source	706 (93.3%)	-
Transplant indication		
Multiple myeloma/plasma cell dyscrasia	375 (49.5%)	-
Lymphoma	144 (19.0%)	-
Leukaemia	143 (18.9%)	-
Other	95 (12.6%)	-


A
Cardiovascular outcomes in HSCT recipients compared with matched controls
Venous thromboembolism
Peripheral artery disease
Pericardial disease
Other cardiac arrhythmias
Heart failure
Coronary heart disease
Atrial fibrillation/flutter
Any cardiovascular outcome
***
0
2
4
6
8
10
12
Hazard Ratio (95% CI)
Significance
*** p<0.001
Not significant


B
Predictors of post-HSCT adverse outcomes
Other cardiac arrhythmias
Heart failure
Venous thromboembolism
Atrial fibrillation/flutter
Any cardiovascular outcome
*
**
0
2
4
6
8
10
Hazard ratio (95% CI)
Predictors
Age at transplant
Allogeneic transplant
Diabetes
Lymphoma
Male sex
Smoking

Conclusions: HSCT survivors experience a substantially elevated cardiovascular morbidity compared to matched controls. These findings highlight the importance of evaluating cardiovascular risk before transplant and the need for ongoing monitoring for cardiovascular complications in the long term post-transplant, especially given the shifting demographics toward an older eligible transplant population with greater age-related comorbidities.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

A415

SOCIAL IMPACT AND PATIENT–CAREGIVER EXPERIENCE IN CHRONIC GVHD: RESULTS FROM A NATIONAL SURVEY IN SPAIN

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Background: Chronic Graft-versus-Host Disease (cGVHD) is a complex, multisystemic complication following allogeneic hematopoietic cell transplantation, with profound and lasting effects on patients and caregivers. Despite advances in donor selection, prophylaxis, and treatment, many patients still develop cGVHD remaining a major cause of long-term morbidity, reduced quality of life, and significant social and emotional burden. the objetive of the estudy was to evaluate the social, emotional, physical, and functional impact of cGVHD on patients and caregivers in Spain, identifying unmet needs and areas for improvement in care and support.

Methods: A mixed-methods design combined qualitative data from focus groups with young patients, minors, and caregivers, and quantitative results from an anonymous survey conducted between May and July 2025. The study assessed clinical manifestations, daily life, family, work and studies, economic impact, social and emotional well-being, psychological support, and access to information. The survey was reviewed by a medical board and distributed via the Josep Carreras Foundation. All participants gave informed consent. The study was approval by the CEIM HCB/2025/0626.

Results: A total of 278 participants (207 patients, 71 caregivers) Most patients were women aged 36–60 (55%), living in Catalonia or Madrid, and transplanted for leukaemia more than five years ago (49%). Caregivers were predominantly women (82%), aged 26–45 (70%), and close relatives in 40% of cases.
Symptoms of cGVHD emerged within the first six months post-transplant in **66%** of patients, with **44%** reporting diagnostic delays. Almost all participants (**96%**) required immunosuppressive therapy: **33%** received one line, **33%** received two lines, and **20%** required more than three lines. In **14%**, the number of treatment lines could not be recalled.
Skin (72%), eyes (64%), joints (47%), and oral mucosa (46%) were the most affected areas, with many patients reporting multiple symptoms. Multidisciplinary care was lacking in

almost 40% of cases, and communication between specialists was considered poor.
Family dynamics were notably impacted, with 70% reporting consequences for mental health.
Employment was severely affected: before transplantation, 88% of patients were working, but only 22% remained employed at the time of the survey. 92% of those who have been able to continue working report limitations in their work activity. The care of a patient with cGVHD has a work-related impact on most caregivers (82%).
Social relationships changed for 82% of patients, mainly due to misunderstanding and lack of awareness in their environment. Sexual life was affected for 82%, particularly among women, who also reported a lack of information and support.
Psychological support is considered necessary by 96% of patients; however, only 59% of patients and 46% of caregivers had accessed it. Peer support groups were valued by 88% of respondents.
Information about cGVHD was often perceived as insufficient or overwhelming, with 56% of participants feeling they lacked adequate information, especially regarding symptoms (77%), severity (73%), and treatment (70%).

Conclusions: cGVHD is a transformative and invisible disease that disrupts every aspect of life for patients and families. Greater recognition, multidisciplinary care, and improved information and support systems are urgently needed to address the complex challenges posed by cGVHD.

Disclosure: no conflict of interest. Nothing to declare.

A416

SURVEY ON FERTILITY MANAGEMENT AND OUTCOMES AFTER CAR T, ON BEHALF OF THE EBMT CELLULAR THERAPY AND IMMUNOBIOLOGY WORKING PARTY

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Background: CAR T-cell therapy has become a highly effective treatment for haematological malignancies, and emerging evidence indicates promising benefits for non oncohematological conditions. As its clinical use broadens, understanding long-term outcomes and late complications is increasingly crucial. One critical yet understudied area is fertility, for which current evidence remains limited and no formal guidelines provide direction for patients undergoing CAR T-cell therapy.

Methods: To address this gap, we conducted a cross-sectional survey on behalf of the Cellular Therapy and Immunobiology Working Party (CTIWP) of the EBMT, distributed from January to April 2025 to 341 centers, assessing current fertility-related practices around CAR T-cell therapy. A second, complementary questionnaire was then circulated to gather detailed information on reported pregnancies following CAR T treatment.

Results: In total, 93 centers (27%) answered and were included in the analysis. While most centers reported offering fertility counselling before CAR T-cell infusion, 11 centers (17%) indicated that they do not routinely inform patients of the potential reproductive risks; Indeed, the majority of centers (79%) offered fertility preservation procedures to male and female patients. Additionally, 41 % of the reporting centers do not routinely provide psychological support during CAR T-cell therapy. The most common barriers to fertility preservation referral were the urgency of initiating CAR T-cell therapy in aggressive disease (38%) and extensive prior chemotherapy exposure, defined as more than three previous treatment lines (36%). Among male patients, semen collection and cryopreservation were the most frequently used methods (63%). For female patients, the predominant approaches were oocyte cryopreservation (43%) and ovarian tissue cryopreservation (40%). Endocrinologic follow-up practices after CAR T-cell therapy varied substantially across centers.
A total of 22 pregnancies were reported in 20 patients, resulting in 17 live births, 1 ongoing pregnancy, and 4 miscarriages at the time of data censoring. Fourteen pregnancies occurred in female CAR T-cell recipients, and seven were reported by male recipients through their partners. Notably, pregnancies occurred naturally in 70% of cases. Among 8 patients with

available information, the median time between CAR T-cell infusion and delivery or miscarriage was 2.8 years, (range 2 months to 6 years). Although both low- and high-grade Cytokine Release Syndrome (CRS) and Immune Effector Cell–Associated Neurotoxicity Syndrome (ICANS) were reported among these patients, these events did not appear to influence pregnancy outcomes, acknowledging the small sample size (Table 1).

Center	Female Patient Reporting Pregnancy	Male Patient Reporting Pregnancy With The Partner	Natural or assisted	Live Births	Miscarriages	Time from CAR-T	CRS	ICANS
#1	1	-	Natural	1	-	6 years	G4	G3
#2	1(1 Patient Twice)	-	Natural (Twice)	1	1	1 year 2 months (miscarriage); 2 years 9 months (delivery)	G0	G0
#3	1	-	Assisted	Currently Pregnant	-	1 year	G1	G1
#4	1	1	Natural (Both patients)	2	-	Female: 15 months; Male: 36 months	Female: G1 Male: G0	Female: G2 Male: G0
#5	-	1	Natural	1	-	NA	NA	NA
#6	-	1	Assisted	1	-	3 years	NA	NA
#7	-	1	Natural	1	-	1 year 4 months	NA	NA
#8	-	3	2 Assisted, 1	3	-	NA	NA	NA

			donor semen					
#9	3	-	2 Natural, 1 Assisted	2	1	na	P1: G1 P2: G2 P3 (Miscarriage + Live birth): G1	P1: G1 P2: G4 P3 (Miscarriage + Live birth): G0
#10	3(1 Patient Twice)	-	3 Natural, 1 Assisted	3	1	NA	NA	NA
#11	1	-	Natural	1	-	3 years	G2	G4
#12	1	-	Natural	-	1	2 months	G0	G0
#13	1	-	Natural	1	0	NA	NA	NA

Conclusions: These findings underscore significant heterogeneity in fertility related practices worldwide. As CAR T-cell therapy is increasingly administered earlier in the treatment algorithms and to younger populations, integrating standardized fertility counselling and preservation strategies into routine care will be essential. The pregnancies and live births reported here represent some of the earliest evidence of post–CAR T reproductive success and highlight the urgent need for robust research and formalized guidelines in this evolving field.

Clinical Trial Registry: na

Disclosure: na

A417

SECOND PRIMARY MALIGNANCIES AFTER T-CELL ENGAGING BISPECIFIC ANTIBODY THERAPY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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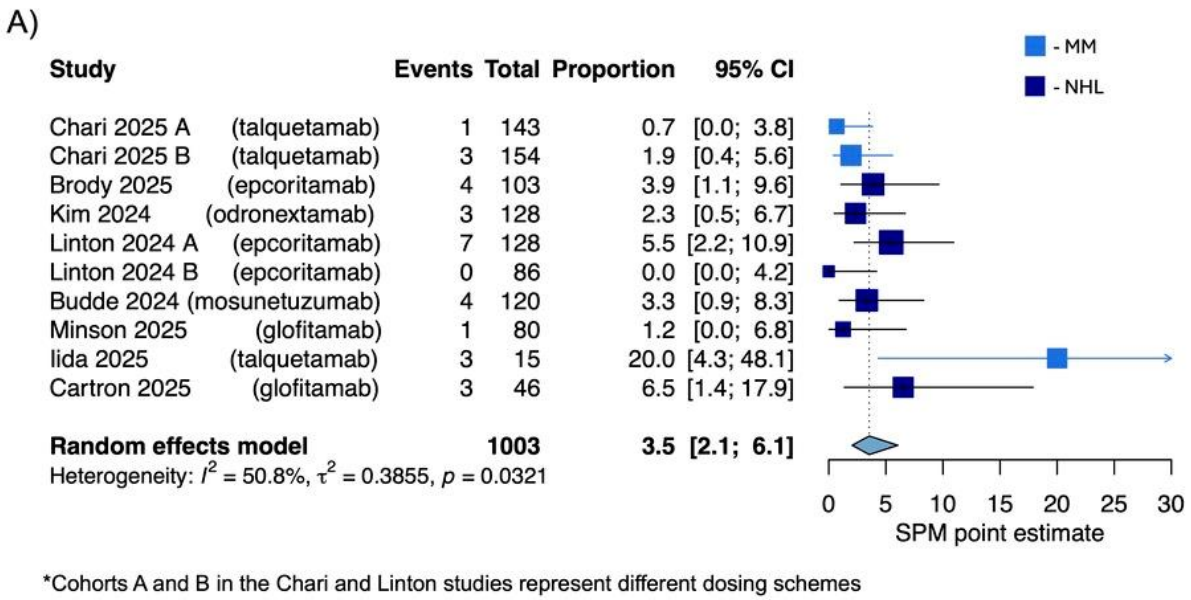
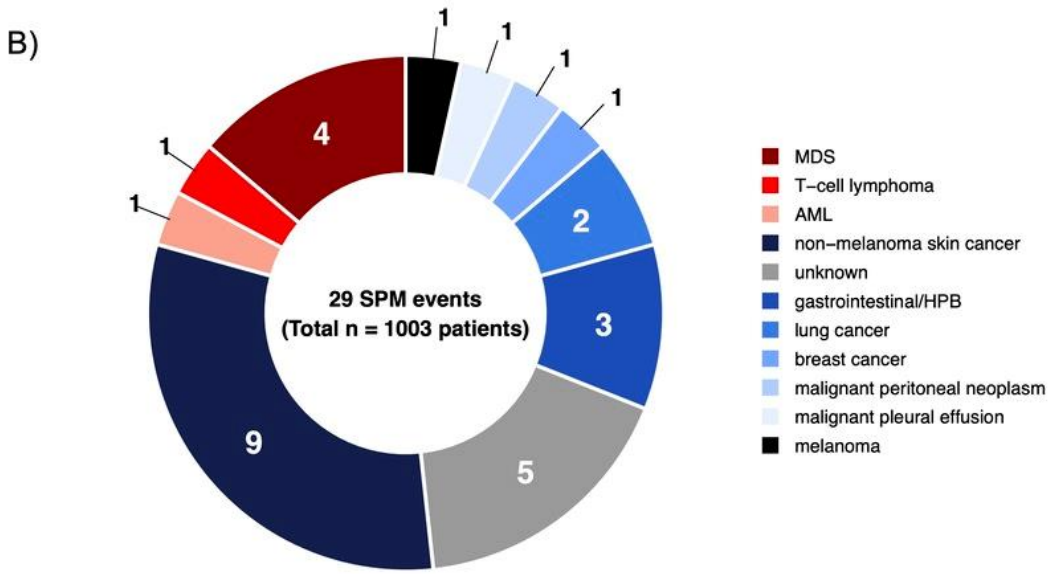
Background: T-cell–redirecting therapies, including CAR T-cell therapy and bispecific antibodies (BsAbs), have transformed the treatment landscape of B-cell lymphoma and multiple myeloma. While second primary malignancies (SPMs) have been reported after CAR-T therapy, it remains unclear whether similar long-term risks accompany T-cell engaging (TCE) bispecific antibody treatment. To address this gap, we conducted a systematic review and meta-analysis to quantify SPM occurrence following TCE BsAb therapy.

Methods: We performed a systematic review and meta-analysis following PRISMA guidelines and a prespecified PROSPERO-registered protocol (CRD420251039203). PubMed/MEDLINE and Embase were searched through October 1, 2025. Clinical trials and real-world studies reporting SPM outcomes in adults treated with TCE BsAbs targeting CD20 for B-cell lymphoma or BCMA/GPRC5D for multiple myeloma were included. Pooled SPM point estimates were calculated using random-effects meta-analysis of single proportions. Meta-regression analyses examined associations between observed SPM rates and study-level features, including follow-up duration, disease type, number of prior therapy lines, prior CAR-T exposure, and completeness of SPM reporting.

Results: Twenty studies met the inclusion criteria. Eight studies (10 cohorts; 1,003 patients) reported all SPMs observed during follow-up and were included in the primary analysis. With a median follow-up of 15.3 months, the pooled SPM point estimate was 3.5% (95% CI, 2.1–6.1) (Figure 1.A). Across these cohorts, 29 SPMs were reported, most commonly non-melanoma skin cancers (n=9), followed by hematologic malignancies (n=6); no single solid tumor subtype predominated (Figure 1.B). Among the hematologic malignancies, myelodysplastic neoplasms were the most common (n=4), while one case of each acute myeloid leukemia and T-cell lymphoma were reported. The SPM point estimate for hematologic malignancies was 1.1% % (95% CI, 0.6–2.1). No study-level clinical or treatment characteristics were significantly associated with SPM occurrence among cohorts with complete reporting.
For sixteen additional cohorts (1548 patients) only SPMs were reported that led to treatment discontinuation or death and demonstrated a lower pooled SPM estimate of 2.1% (95% CI, 1.5 to 3.0). Two MDS cases were identified in this subgroup; for five cohorts (768 patients) no differentiation of SPM was reported.
In a multivariable meta-regression spanning all cohorts, complete SPM reporting was independently associated with higher observed SPM incidence compared with selective

reporting (p=0.02), indicating that reporting practices significantly influence risk estimates.





Conclusions: This study delivers the first quantitative benchmark of SPM risk following TCE BsAb therapy, identifying a point estimate of approximately 3.5% after a median follow-up of 15.3 months, including 1.1% specifically for hematologic malignancies. The strong dependence of observed risk on reporting practices indicates that SPMs are systematically underrecognized, highlighting an urgent need for standardized long-term safety surveillance as TCE BsAbs move earlier in treatment.

[+] co-first authors, J.T. and T.T. contributed equally to this work
[x] co-last authors, K.R. and R.S. contributed equally to this work

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Competing Interests
Samuel Yamshon
Consulting: Kite Pharma, Bristol Myers Squibb, Ipsen
Advisory Board: Abbvie, ADC Therapeutics, Bristol Myers Squibb, Genmab, Incyte, Ipsen, Kite Pharma, Pfizer
Research: Bristol Myers Squibb, Ipsen, Kite Pharma, Marker Therapeutics
Gloria Iacoboni
Consulting: Autolus, Bristol-Myers Squibb, Kite/Gilead, Janssen, Miltenyi, Abbvie, MSD, Regeneron. Honoraria: Abbvie, AstraZeneca, BMS, Kite/Gilead, Miltenyi, Sobi, Roche, Lilly. Travel support: Abbvie, AstraZeneca, Kite/Gilead, Miltenyi, Roche
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A418

QUALITY OF LIFE RECOVERY FOLLOWING CHRONIC GRAFT-VERSUS-HOST DISEASE RESOLUTION IN LONG-TERM ALLOGENEIC TRANSPLANT SURVIVORS

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Background: Chronic graft-versus-host disease (cGVHD) is a major cause of impaired quality-of-life (QoL) following allogeneic haematopoietic stem cell transplantation (alloHSCT). Whilst cGVHD can resolve in long-term survivors, it remains unclear whether QoL deficits persist after systemic immunosuppression (SI) is no longer required. We aimed to determine whether QoL improves in long-term survivors who have discontinued SI for cGVHD.

Methods: We conducted a single-centre retrospective analysis of QoL in alloHSCT recipients ≥16 years with haematologic malignancies transplanted at the Royal Melbourne Hospital (2009-2020), Melbourne, Australia. Patients evaluated 2-5 years post-transplant completed QoL surveys including the FACT-BMT, EORTC-QLQ-C30, FACIT-F, and the Hospital Anxiety and Depression Scale(HADS). Significant active cGVHD was defined as requiring SI at assessment. Patients were categorized as either never requiring SI for cGVHD(cohort A), having discontinued SI for cGVHD(cohort B), or having active cGVHD on SI(cohort C). HRQoL scores were compared using the Kruskal-Wallis test (significance $p<0.05$), with post-hoc Dunn's comparisons. K-means cluster analysis evaluated whether cGVHD status could predict QoL cluster membership. Statistics were performed using SPSS v29 (IBM Corp, 2024).

Results: Among 511 participants (median 3 years post-transplant), cohort A comprised 210(41%), cohort B 179(35%), and cohort C 122(24%) participants. Mean total FACT-BMT scores were similar for cohorts A and B (117, SD±20.0 vs 114, SD±21.0; $p=0.92$) but significantly improved compared to cohort C (106, SD±22.0; $p=0.001$) (Table 1). Differences were driven by worse physical ($p<0.001$) and functional wellbeing ($p=0.007$), and the bone marrow transplant-specific subscale($p<0.001$) among cohort C patients.
Fatigue, measured by FACIT-F, was similar in cohort A and B (mean 41, SD±10 vs 39, SD±10.5; $p=0.212$), but worse for cohort C (mean 35, SD±11.9, $p<0.001$). Global EORTC-QLQ-C30 was similar between cohort A and B (mean 74, SD±18.0 vs 75, SD±18.9; $p=1.0$), but significantly worse for cohort C (mean 63, SD±20.4, $p<0.001$). EORTC-QLQ-C30 functioning subscales were similar for cohorts A and B but significantly worse for cohort C in physical ($p<0.001$), role ($p<0.001$), emotional ($p<0.001$), cognitive ($p=0.006$), and social functioning ($p<0.001$). Whilst cohort B reported similar symptom burden to cohort A, worse fatigue ($p<0.001$), pain ($p=0.031$), and dyspnoea ($p<0.001$) were reported for cohort C. Financial difficulty showed a different pattern – similar between cohort B and C ($p=0.496$), but both significantly worse than cohort A ($p=0.047$). No differences in HADS anxiety

(p=0.699) or depression symptoms (p=0.083) were observed.
Cluster analysis (Figure 1) identified two statistically distinct QoL clusters: C1(more adverse) and C2(better). Patients with resolved cGVHD were distributed between clusters, comprising 32% of C1 and 34% of C2. In contrast, active cGVHD patients comprised 35% of those in C1 compared to 19% in C2(p<0.001).

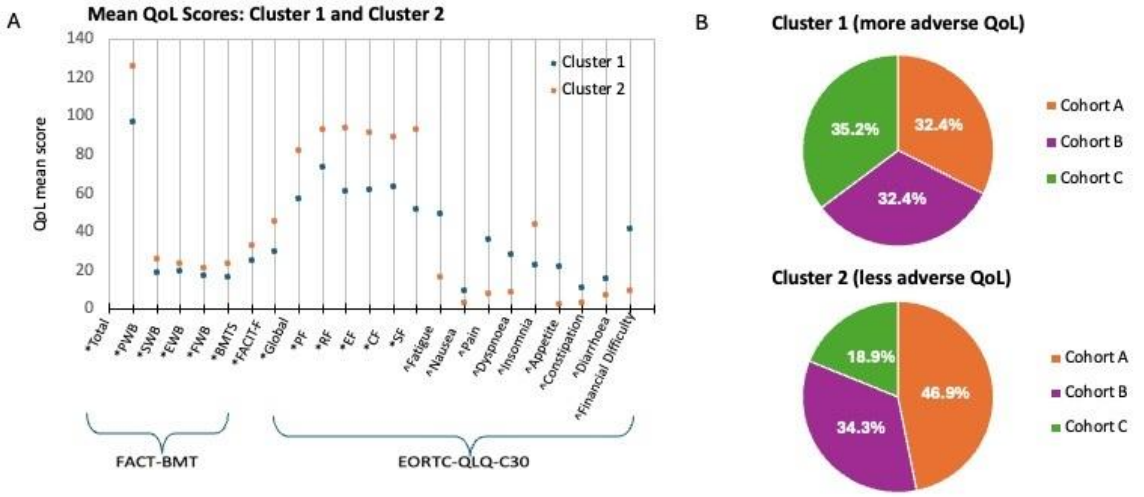
Table 1: Mean quality of life survey scores with comparison for Cohorts A, B and C

Quality of life survey	Cohort A mean score (range)	Cohort B mean score (range)	Cohort C mean score (range)	p-value
FACT-BMT Total*	117.0 (50-147)	115.1 (54-144)	108.7 (55-144)	**0.001**
PWB*	24.0 (9-28)	22.9 (1-28)	21.1 (2-28)	**<0.001**
FWB*	21.4 (8-28)	20.9 (7-28)	19.1 (4-28)	**0.007**
BMTS*	30.1 (11-40)	30.1 (13-39)	28.0 (14-39)	**<0.001**
FACIT-F *	41.0 (14-52)	39.5 (5-52)	35.8 (5-52)	**<0.001**
EORTC-QLQ-C30 Global*	74.6 (17-100)	75.2 (25-100)	66.6 (33-100)	**<0.001**
PF*	88.1 (33-100)	85.5 (33-100)	80.1 (40-100)	**<0.001**
RF*	87.2 (17-100)	82.1 (0-100)	70.9 (17-100)	**<0.001**
EF*	84.3 (17-100)	80.3 (8-100)	74.7 (25-100)	**<0.001**
CF*	81.9 (17-100)	77.5 (0-100)	76.2 (17-100)	**0.006**
SF*	83.5 (0-100)	75.6 (0-100)	70.4 (0-100)	**<0.001**
Fatigue^	24.1 (0-100)	29.8 (0-100)	34.8 (0-100)	**<0.001**
Pain^	14.7 (0-83)	18.7 (0-100)	25.5 (0-100)	**0.031**

Dyspnoea^	10.2 (0-67)	15.5 (0-100)	26.8 (0-100)	**<0.001**
Diarrhoea^	6.0 (0-67)	13.7 (0-100)	12.2 (0-100)	**0.023**
Financial difficulty^	19.6 (0-100)	22.0 (0-100)	23.0 (0-100)	**0.047**

PWB=physical wellbeing, SWB=social wellbeing, EWB=emotional wellbeing, FWB=functional wellbeing, BMTS=bone marrow transplant subscale, HADS=Hospital anxiety and depression score, PF=physical functioning, RF=role functioning, EF=Emotional functioning, CF=Cognitive functioning, SF=social functioning
*The higher the score, the better the QoL
^ The higher the score, the worse the symptom is rated

Figure 1: Quality-of-life cluster analysis
A: Mean QoL survey scores for clusters 1 (more adverse) and 2 (less adverse)
B: Pie-chart demonstrating proportion of patients within cohorts A, B and C, for each QoL cluster



PWB=physical wellbeing, SWB=social wellbeing, EWB=emotional wellbeing, FWB=functional wellbeing, BMTS=bone marrow transplant subscale, HADS=Hospital anxiety and depression score, PF=physical functioning, RF=role functioning, EF=Emotional functioning, CF=Cognitive functioning, SF=social functioning *The higher the score, the better the QoL ^ The higher the score, the worse the symptom is rated

Conclusions: Long-term survivors with resolved cGVHD can achieve QoL comparable to those without prior significant cGVHD, while those with active cGVHD show persistent impairment across multiple domains. Financial difficulty appears problematic for those who experience significant cGVHD, regardless of resolution. These findings demonstrate that QoL recovery is possible following cGVHD resolution and underscore the limitations of single-timepoint assessments for evaluating long-term outcomes after alloHSCT.

Disclosure: Nothing to declare

A419

LONGITUDINAL ASSESSMENT OF FRAILTY AND FUNCTIONAL RECOVERY AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE PROPHYLAXIS

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Background: Post-transplant cyclophosphamide (PTCy) is widely used for GVHD prophylaxis, but its early post-transplant course is associated with increased toxicity, delayed engraftment, and higher infectious burden, factors that may hinder functional recovery. Frailty is an established predictor of survival in allo-HCT, but its evolution after transplantation remains insufficiently characterized. In 2021, our institution implemented a structured multidisciplinary frailty assessment program to determine the incidence and trajectory of frailty before and after PTCy-based allo-HCT.

Methods: From 2021 to 2025, all consecutive adults undergoing PTCy-based allo-HCT were systematically assessed for frailty and prospectively enrolled after informed consent. Patients were evaluated by trained nursing staff in 10–15 minutes without additional resources and categorized as fit, pre-frail, or frail. Assessments were performed at admission, day +100, 6 months, and 1 year, limited to patients in remission. Quality of life (QoL) was monitored at admission, day +100, and 1 year using the EQ-5D-3L.

Results: A total of 166 patients were evaluated at baseline: 21.3% were fit, 61.3% pre-frail, and 17.8% frail. Frail patients had a higher comorbidity burden (HCT-CI >3: 29% vs. 11% in fit; P=0.023), lower performance status (KPS <90%: 43% vs. 14%; P=0.048), higher prevalence of mobility impairment, self-care limitations, and greater symptom burden (Table 1). Frailty at admission did not predict specific complications but was associated with longer hospitalization (median 32 vs. 26 days; P<0.001). Frail patients had lower 1-year OS (42.9% vs. 82.1% and 80.0%; P<0.001), mainly due to increased NRM (21.4% vs. 8.2% and 5.9%; P=0.127) compared with fit and pre-frail individuals (Figure 1A).
At day +100 (n=119), frailty prevalence was unchanged (fit 21.8%, pre-frail 59.1%, frail 19.1%) and was more frequent in patients experiencing early toxicities such as sinusoidal obstruction syndrome, invasive fungal infections, or grade II–IV acute GVHD requiring corticosteroids (Table 1). Frailty at day +100 landmark was associated with inferior outcomes (1-year OS: 63.6% vs. 87.5% and 91.3%; P=0.003; 1-year NRM: 19.5% vs. 0 and 2.5%; P=0.017) (Figure 1A) and poorer QoL.
Among 6-month survivors (n=84), frailty prevalence declined (fit 24.4%, pre-frail 68.6%, frail 4.7%), suggesting progressive functional recovery (Figure 1B). Persistent frailty was mainly associated with prolonged complications, especially steroid-dependent chronic GVHD. At 1 year (n=67 evaluated), recovery was more pronounced: 41.3% were fit, 52.3% pre-frail, and only 6.4% frail (Figure 1B). With a median follow-up of 15 months, only 6

additional deaths occurred after 6 months, all due to relapse. Among survivors, QoL improved over the first year, with fit patients increasing to 41% and reporting better mobility, self-care, activities of daily living, and higher EQ-VAS scores.

Table. Characteristics according to frailty assessment and post–trasplantation complications.

	HCT Admission				Day +100				+ 6 months				+ 1 year		
Baseline Characteristics	**Fit N=70**	**Pre-Frail N=82**	**Frail N=14**	**P value**	**Fit N=16**	**Pre-Frail N=92**	**Frail N=11**	**P value**	**Fit N=21**	**Pre-Frail N=59**	**Frail N=4**	**P value**	**Fit N=22**	**Pre-Frail N=43**	**Frail N=2**
Median age (range) Older 65 years (%)	52(37-63) 20	56(44-66) 26	62(52-66) 29	0.123 0.644	52(32-61) 19	59(43-66) 28	51(34-65) 18	0.50 0.558	51(39-60) 4	58(44-65) 24	60(48-66) 25	0.40 0.653	56(39-65) 23	60(49-64) 21	62(57-68) 50
Sex: Male/ Female (%)	64/36	57/43	64/36	0.655	62/38	60/40	55/45	0.917	76/24	59/41	75/25	0.345	82/18	60/40	50/50
Baseline diagnosis (%) AML+MDS+ MPN ALL NHL+CLL Others	55 22 10 13	55 25 13 7	79 14 7 0	0.082	69 19 6 6	61 20 11 8	37 36 18 9	0.803	58 33 0 9	61 17 10 2	50 0 50 0	0.231	68 18 0 14	56 23 12 9	0 50 0 50
HCT-CI >3 (%)	11	29	29	0.023	13	25	18	0.508	10	25	25	0.308	14	28	0
KPS <90% (%)	14	22	43	0.048	13	15	45	0.038	5	9	50	0.064	18	21	50
Intensity:	53/47	43/57	21/79	0.088	50/50	40/60	55/45	0.546	52/48	41/59	50/50	0.631	50/50	40/60	0/100

MAC/RIC (%)															
HCT Hospitalization	26(22-30)	31(24-37)	32(24-28)	<0.001	22(18-27)	27(22-33)	39(30-37)	<0.001	24(21-28)	24(21-28)	39(29-83)	0.016	22(21-29)	28(23-36)	39(29-39)
Infections(%) Bloodstream infection CMV Reactivation Fungal Infections	43 6 13	38 13 11	50 36 14	0.788 0.004 0.971	38 6 0	37 6 7	36 9 27	0.803 0.946 0.036	31 0 14	42 0 8	75 0 0	0.280 0.404 0.630	32 18 14	40 17 14	0 0 50
SOS (%) TA-TMA (%)	4 4	2 4	7 7	0.606 0.835	6 6	2 0	18 9	0.027 0.023	5 0	3 3	25 0	0.145 0.648	0 0	2 2	0 0
GVHD (%) Acute Grade II-IV Chronic moderate-severe	16 14	28 15	14 14	0.170 0.490	0 N/A	21 N/A	9 N/A	0.097	5 0	17 5	50 25	0.061 0.097	5 9	19 21	100 0
	N=37	**N=39**	**N=3**		**N=13**	**N=65**	**N=6**						**N=16**	**N=38**	**N=2**
Mobility 1/2/3 (%)	97/3/0	92/8/0	67/33/0	0.099	92/8/0	86/14/0	17/83/0	0.001					100/0/0	89/11/0	50/50/0
Self Care 1/2/3 (%)	97/0/3	95/5/0	67/33/0	0.042	100/0/0	97/3/0	50/50/0	<0.001					100/0/0	100/0/0	50/50/0
Daily Activitie	95/5/0	79/21/0	67/33/0	0.597	100/0/0	78/22/0	33/50/17	0.001					100/0/0	89/11/0	50/50/0

s 1/2/3(%)															

Figure 1A. OS and NRM according to frailty categories

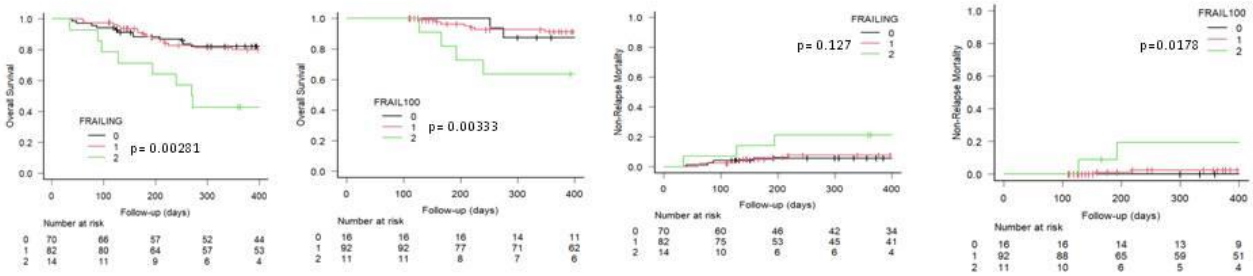
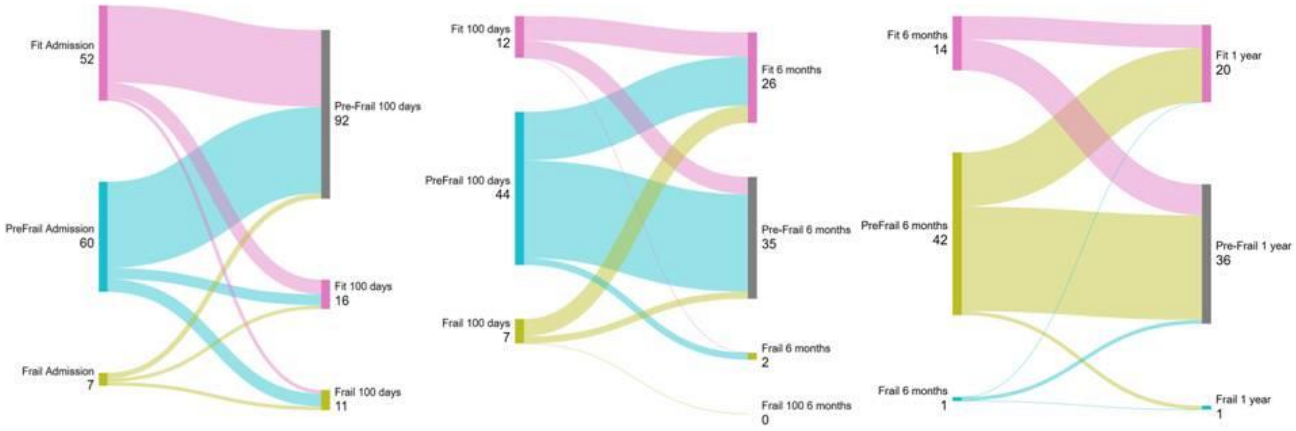


Figure 1B. Frailty dynamics towards post-transplant evolution



Conclusions: Frailty in the context of PTCy-based allo-HCT is dynamic, with clear functional improvement over the first post-transplant year among survivors. Nonetheless, when present, frailty is associated with inferior survival and poorer QoL. Early complications—particularly prolonged hospitalization, GVHD, and infections—appear to limit functional recovery and contribute to persistent frailty. Routine frailty monitoring may help identify patients who could benefit from multidisciplinary interventions aimed at enhancing recovery and QoL.

Disclosure: Nothing to declare.

A420

EXTENSIVE OR SEVERE CHRONIC GVHD IS ASSOCIATED WITH SUSTAINED AND WORSENING IMPAIRMENTS IN SYMPTOMS AND WELL-BEING UP TO 5 YEARS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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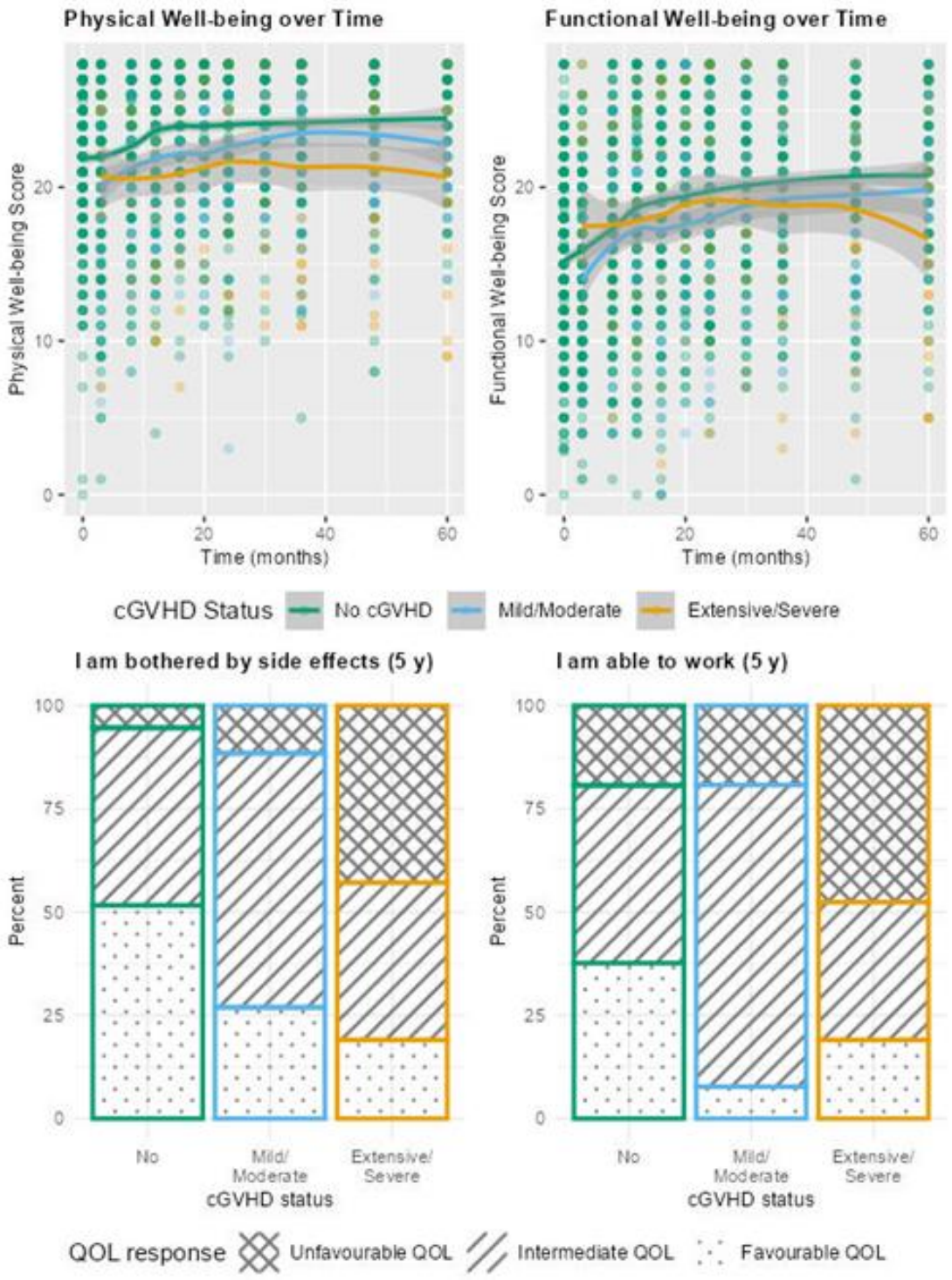
Background: While allogeneic haematopoietic stem cell transplantation (allo-HSCT) can be curative, chronic GVHD (cGVHD) remains a debilitating complication, despite novel transplantation techniques. We investigated how cGVHD affects health-related quality of life (HRQOL) long-term after allo-HSCT.

Methods: Adult patients undergoing an allo-HSCT at UMCU were invited from 2013 to complete HRQOL questionnaires from pre-transplant (2017) through 10 years post-transplant. Analyses included first allo-HSCTs with follow-up up to five years. HRQOL data were collected through PROFILES, a registry for collecting data on impact of cancer developed by the Netherlands Comprehensive Cancer Organization(IKNL) and Tilburg University. HRQOL was assessed using the Functional Assessment of Cancer Therapy-General(FACT-G), with items scored on a 5-point Likert scale. Clinical data were extracted from EBMT and UMCU databases.
To assess symptom prevalence, single HRQOL item outcomes were grouped into unfavourable, intermediate, and favourable responses. For being bothered by side effects of treatment, unfavourable comprised "Quite a bit"/"Very much"; for being able to work, "Not at all"/"A little bit". cGVHD groups were compared cross-sectionally using Kruskal-Wallis and post-hoc Wilcoxon tests. HRQOL-subscales (scores for physical, social, emotional, and functional well-being) were analysed longitudinally using mixed-effects models with random intercepts and cGVHD-time interactions. Models adjusted for sex, age, indication, HCT-CI, graft engineering, donor type/match, donor age, and sex match.

Results: This study included 525 patients. Median age at transplant was 58 years (IQR 45-65), 60% were female, and 73% of patients received an αβT cell-depleted allograft. Up to five years post-transplant, 406 patients (77%) did not develop cGVHD, 74 (14%) developed mild/moderate, and 45 (9%) developed extensive/severe cGVHD. Median cGVHD onset was 259 days (IQR 170-457) post-transplant. The Table shows numbers of individuals at each time point.
Three months to five years post-transplant, patients without cGVHD showed significant improvements in physical (21.3-24.1), functional (17.3-22.4), and emotional well-being (19.2-20.6; all $p<0.001$) (Figure). In contrast, patients with extensive/severe cGVHD showed different trajectories: physical (19.6-19.8) and functional well-being (17.9-18.0) remained stable, while emotional well-being declined slightly (19.2-18.6, all $p\leq0.002$). Patients with mild/moderate cGVHD had similar trajectories to those without cGVHD. Social well-being remained stable over time.

At one year post-transplant, 32% of extensive/severe cGVHD patients reported being bothered by side effects "Quite a bit"/"Very much", compared to 17% (mild/moderate) and 9% (no cGVHD, $p<0.001$) (Figure). At five years, these were 43%, 12% and 5% respectively ($p<0.001$). Similarly, at one year, 43% of extensive/severe cGVHD patients reported to be able to work "Not at all"/"A little bit", compared to 37% (mild/moderate) and 29% (no cGVHD, $p=0.041$). At five years, these were 48%, 19% and 19% ($p=0.011$).


Physical Well-being over Time
Physical Well-being Score
Time (months)
Functional Well-being over Time
Functional Well-being Score
Time (months)
cGVHD Status
No cGVHD
Mild/Moderate
Extensive/Severe
I am bothered by side effects (5 y)
I am able to work (5 y)
Percent
No
Mild/ Moderate
Extensive/ Severe
cGVHD status
QOL response
Unfavourable QOL
Intermediate QOL
Favourable QOL

Number of individuals with available QOL data by cGVHD status at each time point after allo-HSCT											
Time point (months after allo-HSCT)	0	3	8	12	16	20	24	30	36	48	60
No cGVHD	324	256	204	255	175	141	175	129	148	118	93
Mild/moderate cGVHD	0	46	40	60	41	37	56	34	45	35	26
Extensive/severe cGVHD	0	20	17	32	20	11	24	16	26	22	21

Conclusions: We present one of the largest HRQOL datasets in allo-HSCT to our knowledge and demonstrate that cGVHD, particularly extensive/severe forms, associates with persistent symptom burden and impairments in physical, functional, and emotional well-being. Almost half of extensive/severe cGVHD patients are unable or barely able to work five years post-transplant. Instead, patients without cGVHD show sustained recovery. These findings highlight the long-term impact of cGVHD and the need for improved prevention.

Disclosure: We have no conflicts of interest to disclose.

A421

SIGNIFICANT IMPROVEMENT OF SURVIVAL AND GVHD- AND RELAPSE-FREE SURVIVAL AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKEMIA OVER TIME

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Background: Currently, AML is one of the main indications for allogeneic HSCT. Although survival after allogeneic HSCT has improved, relapse of the underlying disease and transplant-associated complications have remained to be a challenge negatively impacting outcome.

Methods: We conducted a retrospective single-center cohort analysis of all patients undergoing allogeneic HSCT for AML at our institution between 01/2010 and 12/2024. This analysis aims to show changes in patient characteristics and outcome after allogeneic HSCT for AML over the last 15 years. Patients were grouped into two cohorts based on transplant year.

Results: A total of 546 patients (median age: 53 [IQR: 43-61] years, 47% female) received an allogeneic HSCT, 248 (45%) in group 1 (2010-2017) and 298 (55%) in group 2 (2018-2024). Patients in group 2 were older (median 51 [IQR: 39-59] vs. 55 [IQR: 45-62] years, p<0.001), had more frequently ELN 2022 adverse risk AML (44% vs. 25%, p<0.001) and were more often in first complete remission at HSCT (74% vs. 65%, p<0.001). Also, more patients received reduced intensity or reduced toxicity conditioning in group 2 (73% vs. 52%, p<0.001). Haploidentical donors (19%) and posttransplant cyclophosphamide (25%) were used exclusively after 2018. For better comparability between the two groups patients who received haploidentical HSCT or cord blood were excluded, leaving 469 patients for further analyses. At 2 years after HSCT a lower cumulative incidence of acute GvHD (21% vs. 32%, p=0.0018), chronic GvHD (16% vs. 27%, p=0.0019) and CMV reactivation (26% vs. 38%, p=0.0019), was observed in group 2. Relapse rates were comparable between both groups (cumulative incidence at 2 years of 22% vs. 27%, p=0.5262), but 2-year cumulative incidence of NRM was lower in group 2 (13% vs. 18%, p=0.0582). Survival was significantly improved in group 2 compared to group 1 with a 5-year overall survival (OS) of 63% vs. 48% (p=0.0113) and a 5-year GvHD- and relapse-free survival (GRFS) of 56% vs. 42% (p<0.001), with a median follow-up of 34 and 102 months, respectively. In the univariate Cox regression model, ELN 2022 risk (HR 2.914 for intermediate risk AML and HR 3.716 for adverse risk AML, p<0.001), disease status at HSCT (HR 2.293 for patients with active disease, p<0.001) and transplant year showed a significant impact on survival, with a mortality risk reduction of 4.3% per year (HR 0.957, p=0.0261). A time-dependent mortality risk could be identified for patients with active disease at transplant (HR 4.072 2 months after HSCT, HR 1.633 1 year and HR 0.720 5 years after HSCT). These results were confirmed in the multivariable model with an even greater mortality risk reduction of 6.5% per year.

Conclusions: We observed an improvement in OS and GRFS, and a reduction of acute and chronic GvHD in AML patients given HSCT in more recent years even though patients' pretransplant risks including age were increasing. These promising findings can be explained by the use of lower intensity conditioning regimens, improved GvHD prophylaxis and treatment and expanded infectious prophylaxis. Unfortunately, relapse risk remains an area for improvement.

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A422

POST-HCT EMPLOYMENT AND ASSOCIATED FACTORS AMONG CHILDHOOD, ADOLESCENT, AND YOUNG ADULT PATIENTS AT THE TIME OF TRANSPLANTATION

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Background: Employment after hematopoietic cell transplantation (HCT) is an important indicator of social reintegration and long-term survivorship. However, data on younger HCT recipients who had no work experience before diagnosis remain limited. This study aimed to clarify post-HCT employment outcomes and identify associated factors.

Methods: Eligible participants were survivors aged ≤39 years at the time of allogeneic or autologous HCT, aged ≥20 years at the time of the survey, relapse-free for at least two years after transplantation, and without continuous employment experience before diagnosis. A nationwide anonymous web-based questionnaire was conducted from November 2023 to October 2024. Participants were recruited from 135 HCT centers (94 adult and 41 pediatric). The questionnaire assessed employment outcomes (employment status, timing of first employment, employment type, leave of absence, and resignation) and potential associated factors (age, sex, educational background, donor source, disease disclosure, availability of an occupational physician, and use of employment support systems). Multivariate analyses were performed to identify independent factors associated with employment and job stability.

Results: Among 694 survivors recruited from 135 centers, 275 responded (40%). After excluding two non-consenting and 33 previously employed respondents, 240 responses were analyzed. Median ages at diagnosis, transplantation, and survey were 16 (range, 0–39), 17 (0–39), and 26 (20–54) years, respectively. Transplant types included unrelated bone marrow (29%), related bone marrow (21%), cord blood (19%), related/unrelated peripheral blood stem cell (15%), and autologous transplantation (13%). The median post-transplant duration was 11 (3–36) years. Overall, 78% (n = 186) had work experience after HCT, with a median time to first employment of 5 years post-HCT (range, 0–21 years). At their first employment, 39% held regular positions, 26% had fixed-term or part-time contracts, and

12% were self-employed or in temporary positions. Among employed survivors, 16% had taken leave, and 37% had resigned. In a multivariate analysis of pre-transplant factors (sex, age, underlying disease, donor type, number of transplants, education, and post-HCT duration), only educational attainment was independently associated with post-HCT employment (reference: junior high/high school; vocational/junior college: HR 1.7, 95% CI 1.1–2.6; university/graduate school: HR 1.0, 95% CI 0.7–1.5). In analyses limited to employed survivors (n = 186), female sex was associated with a higher risk of taking leave (HR 2.3, 95% CI 1.0–5.2). The availability of an occupational physician was independently associated with higher leave rates (HR 3.4, 95% CI 1.4–8.1) and lower resignation rates (HR 0.5, 95% CI 0.2–0.9), suggesting that their involvement may help facilitate leave rather than resignation.

Conclusions: Many CAYA survivors without prior work experience eventually achieved employment after HCT. Clinical factors had minimal impact on post-HCT employment, whereas educational attainment was the only independent pre-transplant predictor. The presence of an occupational physician was associated with higher leave but lower resignation rates, suggesting that good communication between workplaces and healthcare providers—for example, sharing information on health status and feasible working conditions—may promote sustainable employment among CAYA HCT survivors.

Disclosure: Nothing to declare

A423

GONADAL FUNCTION OF CHILDREN AND ADOLESCENTS AFTER ALLOGENEIC HSCT WITH TREOSULFAN- AND TBI-BASED CONDITIONING

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is the only curative treatment for many orphan diseases. HSCT significantly improves prognosis and survival. Conditioning regimens include gonadotoxic alkylating agents and/or body irradiation. Here we present the function of gonads in children after HSCT with treosulfan- and total body irradiation (TBI)-based conditioning.

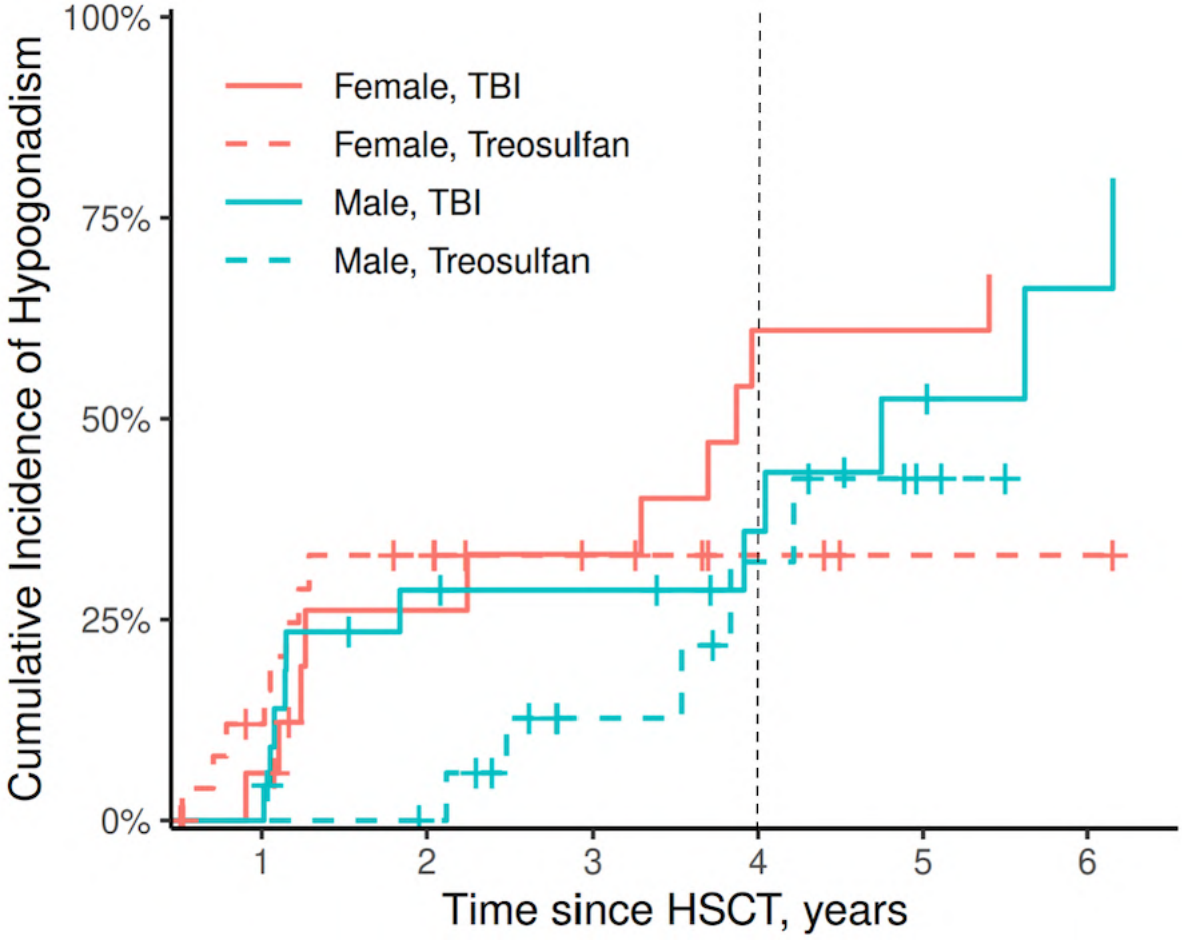
Methods:

Diagnosis	Overall, N=185	Treosulfan, N=88	TBI, N=97
B-/T- acute lymphoblastic	108 (58.4%)	16 (18.2%)	92 (94.8%)

leukemia, acute bilineal leukemia, lymphoma			
Acute myeloid leukemia, myelodysplastic syndrome	50 (27%)	45 (51.1%)	5 (5.2%)
Non-malignant disorders (aplasia, thalassemia, primary immunodeficiencies)	27 (14.6%)	27 (30.7%)	0

From September 2018 to December 2023, 747 paediatric patients with various diagnoses underwent allogeneic HSCT at our centre (Table). The study included 73 girls (=>8 years) and 112 boys (=>10 years at HSCT), aged >13 and >14 years, respectively, on the day of data analysis. First group received treosulfan 36-42mg/m^2 (N=88, f/m=40/48), second - TBI 12Gr (N=97, f/m=33/64) as part of conditioning regimen.
Levels of gonadotropins, sex hormones, menstrual cycle and pubertal development were assessed dynamically. Total gonadotoxicity of alkylating agents was calculated using Cyclophosphamide Equivalent Dose (CED) (threshold - 4000mg/m^2).
Median age at HSCT was 13.5 years (range, 8.2-18.3). Additional conditioning agents were fludarabine 150mg/m^2 (in all), thiotepa 10mg/kg(51.9%)/ melphalan 80-140mg/m^2(7.6%)/ etoposide 40-60mg/kg(32.4%), cyclophosphamide 50-100mg/kg(8.1%). 15.1% patients received post-transplant cyclophosphamide as GVHD prophylaxis, 73.5% got transplants with TCRab depletion. Incidence of acute and chronic GVHD did not differ between the groups.

Results:



Median follow-up was 31.4 months (0–76.9 months). The rates of graft rejection (5.7/6.2%) and relapses (26.1/29.9%) were similar in both groups. In boys of group1, level of gonadotropins was slightly lower than in group2; median follicle-stimulating hormone (FSH) levels returned to normal after 3 years of follow-up. In girls, median FSH level after treosulfan and TBI was similar and higher than in boys and did not decrease throughout the follow-up period. Median testosterone levels in boys remained within the normal range and median estradiol levels in girls were decreased in both groups over the follow-up.
Overall hypogonadism (HG) cumulative incidence (CI) in boys by 3 years after HSCT was 21%, by 4 years – 34%, while in girls the rates were higher – 34 and 54%, respectively. Differences depending on conditioning regimen are presented on figure: the 4-year HG CI in boys in group1 – 36% vs 32% in group2 while in girls the 3-year HG CI was the same in both groups (33%), but the 4-year HG CI doubled after TBI (61%), while in treosulfan group the figures did not change.
HG CI in boys at 4 years after HSCT with low CED ranged from 0% in group1 to 24% in group2, in girls - 14% and 75%, respectively. In girls receiving treosulfan the difference between low and high CED was 14% versus 39% (p=0.4). There were no cases of HG in

boys receiving treosulfan in combination with CED<4000mg/m², the addition of alkylators with high CED led to toxicity comparable to the effect of TBI (p=0.2).

Conclusions: The effect of treosulfan on gonadal function in children was less significant than TBI, but the final gonadotoxicity depends on the combination of treosulfan with other alkylating agents and is directly proportional to the increase in their CED. Further monitoring and analysis is needed to fully understand the fertility prognosis of patients.

Disclosure: Nothing to declare

A424

LONG-TERM SURVIVAL AND QUALITY OF LIFE IN OLDER ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AFTER ALLOGENIC STEM CELL TRANSPLANT

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Background: Allogeneic stem cell transplantation (alloSCT) can be considered as consolidation therapy for Acute lymphoblastic leukemia (ALL) patients over 40 years old in first complete remission (CR1). A Dutch cohort study from 2001-2015 indicated a 5-year survival for this group of 39-54%, depending on the conditioning intensity used (Sijs-Szabo et al. 2023). Modern transplant strategies incorporating fractionated total body irradiation and post-transplant cyclophosphamide potentially lead to better outcomes. Impact of alloSCT on the long-term quality of life (QoL) in this vulnerable patient group is unknown.

Methods: In July 2025, a nationwide study started, including all patients ≥ 40 years with ALL in CR1 who underwent an alloSCT between January 1 2018, and June 30 2023. The study consists of two parts. First, we investigated overall survival (OS), non-relapse mortality (NRM) and relapse rate in this cohort. Second, we evaluated prospectively changes in QoL of surviving patients. OS was estimated using Kaplan–Meier methods. NRM and relapse rate were analyzed using competing-risks methods, with NRM and relapse rate treated as mutually competing events. Point estimates at the cohort's median follow-up were reported with 95% confidence intervals. QoL is evaluated using two validated questionnaires: PROMIS Global Health (PROMIS-GH) and Functional Assessment of Cancer Therapy - Bone Marrow Transplantation (FACT-BMT). The PROMIS-GH is a general health questionnaire providing mental and physical health scores, classifying into 5 categories: poor, fair, good, very good,

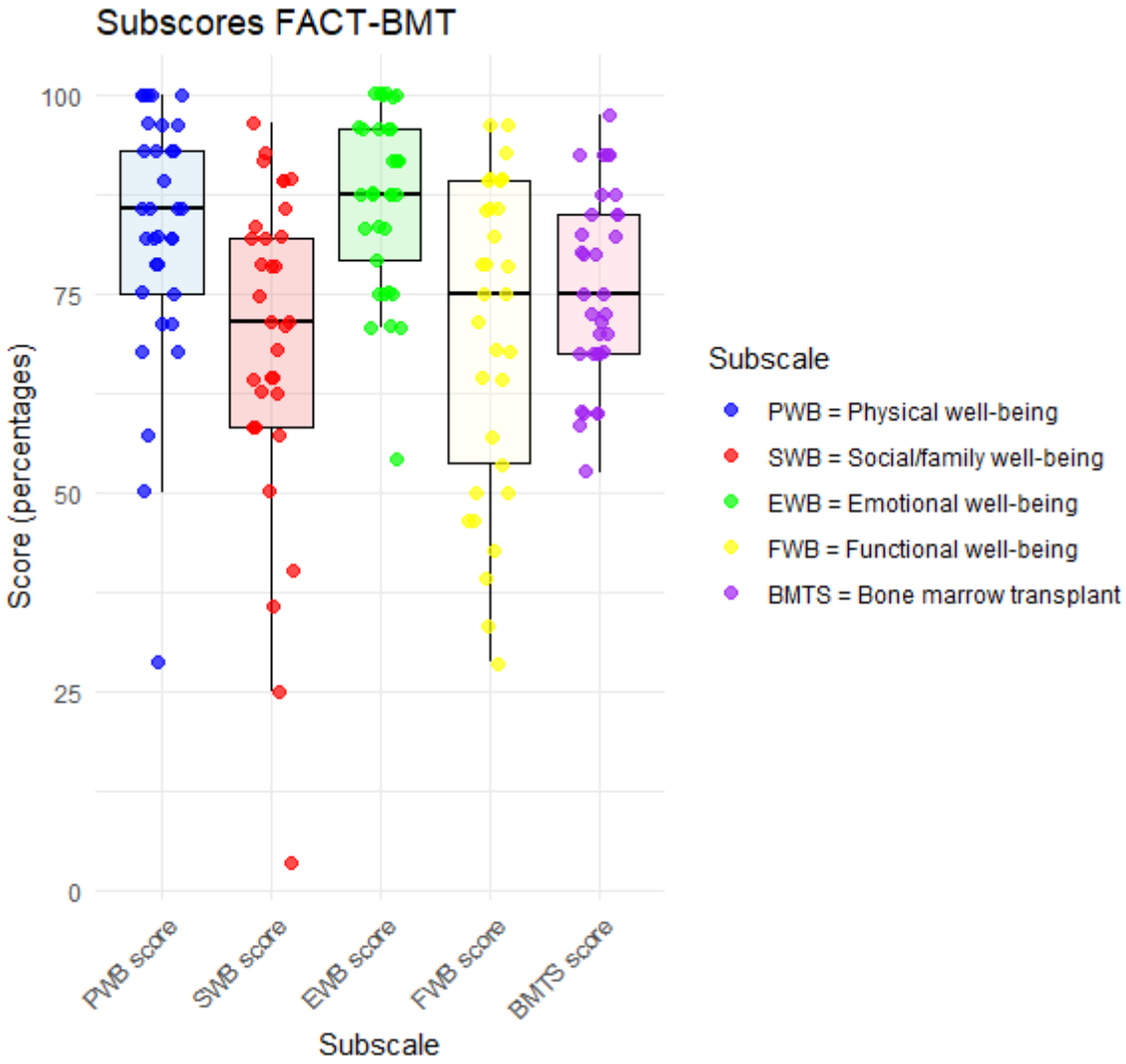
and excellent. The FACT-BMT is a cancer- and transplant-specific questionnaire with 5 subscales: Physical, Social/Family, Emotional and Functional Well-Being and a transplant subscale. QoL data are collected at start of the study and 1, 3, and 5 years thereafter. This abstract presents the first analysis assessing the feasibility of the study and results from 5 of the 7 participating centers.

Results: To date, the cohort consists of 99 patients. The 76 surviving patients were invited to participate in the QoL assessment; 45 provided consent, 11 declined and 20 have not yet responded. Baseline characteristics for both the total group and QoL group are shown in Table 1.
Median follow-up time of surviving patients was 4 years. The 4-years OS was 77% (95% confidence interval 69%-86%), NRM 14% (95% CI 8%-22%) and relapse rate 13% (95% CI 7%-21%).
In the PROMIS-GH questionnaire, Physical Health scores were distributed as follows: 6% poor, 27% fair, 27% good, 18% very good, and 21% excellent. For Mental Health: 24% poor, 15% fair, 18% good, 24% very good, and 18% excellent. FACT-BMT scores are shown in Figure 1, indicating relatively high scores for Emotional and Physical Well-Being, while Social/Family and Functional Well-Being have lower scores.

Baseline characteristics	**Total cohort (n=99)**	**QoL cohort (n=45)**
Gender		
Male	55 (56%)	28 (62%)
Female	44 (44%)	17 (38%)
Age (median, range)	56 (41 - 73)	58 (41-72)
Type of ALL		
B-ALL	83 (84%)	37 (82%)
B-ALL with BCR::ABL1 fusion	*27 (31%)*	*11 (30%)*
T-ALL	16 (16%)	8 (18%)

Baseline characteristics	Total cohort (n=99)	QoL cohort (n=45)
Donor		
MSD 10/10	25 (25%)	9 (20%)
MUD 10/10	67 (68%)	32 (71%)
MUD 9/10 (GvH)	7 (7%)	4 (9%)
HCT-CI score		
0	17 (17%)	6 (13%)
1-2	40 (40%)	19 (42%)
3+	36 (36%)	19 (42%)
Unknown	6 (6%)	1 (2%)
Median follow-up time of patients alive (years)	4.1	3.9

Tabel 1. Baseline characteristics. MSD: matched sibling donor, MUD: matched unrelated donor, GvH: graft versus host, HCT-CI-score: Hematopoietic Cell Transplantation-specific Comorbidity Index



Conclusions: This analysis of the first data from a nationwide study showed a promising 4-year OS of 77% compared to earlier cohorts. With a median follow-up of 4 years, patients reported generally good physical QoL, whereas mental health outcomes are still insufficient. In the future, this study will show how QoL evolves over time, aiming to identify factors associated with QoL with the goal of developing interventions that may improve (mental) QoL in this patient group.

Disclosure: **Remco J. Molenaar (consultancy and speakers fee Servier)**

A425

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GONADAL TOXICITY AND PREMATURE OVARIAN INSUFFICIENCY AFTER HEMATOPOIETIC STEM CELL GENE-THERAPY IN FEMALE PATIENTS WITH METACHROMATIC LEUKODYSTROPHY

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Background: Metachromatic leukodystrophy (MLD) is a severe demyelinating lysosomal storage disorder caused by arylsulfatase A (ARSA) deficiency. Atidarsagene autotemcel (arsa-cel) is an ex vivo autologous hematopoietic stem-cell gene therapy and it is infused intravenously following single agent busulfan conditioning. Arsa-cel is currently the only disease-modifying treatment for pre-symptomatic late-infantile (LI) or early-juvenile (EJ) MLD, or early-symptomatic EJ MLD. Premature ovarian insufficiency (POI) is one of the most relevant long-term sequelae after chemotherapy because of its gonadotoxicity. We investigated the incidence, determinants and characteristics of POI in pediatric females with MLD treated with arsa-cel.

Methods: To identify cases of POI we retrospectively reviewed endocrine clinical, hormonal and instrumental assessments after arsa-cel treatment, performed according to local standard of care.

Results: As of October 2025 at our institution 51 early-onset pediatric patients with MLD (M 32, F 19) received arsa-cel across several clinical trials and in the commercial setting. In 13 (7 LI, 6 EJ) of 19 female patients, baseline and post-treatment endocrine data were consistently available and they were included in this analysis. Median follow up post arsa-cel was 8.8 years (range 3-12.6). Five (38.5%) of 13 patients received sub-myeloablative busulfan conditioning (median total predicted area-under-the-curve [AUC] 68 µg*h/mL), and the remaining 8 (61.5%) received myeloablative regimen (median total predicted AUC 82.5 µg*h/mL).
In the sub-myeloablative group, median age at last follow-up was 12 years (range 9.4–14.6). Four patients reached pubertal age. Among these, 3 patients showed POI (hypergonadotropic hypogonadism, absence of menarche) and started hormone replacement therapy (HRT) at median age of 13 years (range 10.5–15.4), with median menarche at 15.4 years (range 13.3–17.5). One patient experienced normal puberty, with menarche at 11.8 years. One patient (8.2 years of age at last follow-up) remained prepubertal without hormonal alterations.
In the myeloablative group, median age at last follow-up was 8.1 years (range 3.7–16.6). Three patients reached pubertal age. Among these, POI was identified in 2, who started HRT at 13 and 14.6 years, and menarche occurred at 15.5 and 17.9 years respectively. One patient exhibited spontaneous puberty with menarche at 12.8 years despite initial hypergonadotropic hypogonadism (FSH peak 169 IU/mL; undetectable estradiol), which normalized without treatment. Among the 5 pre-pubertal patients (median age 5.8 years, range 3.7–10.2), 3 showed severe persistent biochemical hypergonadotropic hypogonadism. Anti-Müllerian hormone (AMH), a biomarker of ovarian reserve, was undetectable in 84.6%

(11/13) of patients during follow-up.
Overall, most patients in both groups showed evidence of severe gonadal dysfunction. However, longer follow-up is needed to correlate this aspect with other clinical parameters, such as bone mineralization.

Conclusions: In our analysis POI is a frequent adverse effect associated with busulfan, consistent with previous reports. Sub-myeloablative exposure does not appear reducing the incidence of gonadal dysfunction compared with myeloablative regimen. Longitudinal hormonal assessments demonstrate early impairment of ovarian reserve, and the need to offer fertility preservation before arsa-cel and to initiate HRT when indicated. Finally, further long-term analyses are also needed to assess the unclear potential contribution of sulfatide accumulation in the gonadal tissue of patients with MLD.

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- Francesca Fumagalli: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd
- Valeria Calbi: Received fees for consulting and research activities from Orchard Therapeutics Ltd. Received reimbursement for travel costs and participation fees for attending scientific conferences from Orchard Therapeutics Ltd
- Alessandro Aiuti: Orchard Therapeutics is funding gene therapy clinical trials carried out at San Raffaele Hospital for lysosomal genetic diseases (MLD and MPSI), of which he is principal investigator or investigator. Telethon Foundation is funding gene therapy studies at San Raffaele Hospital for genetic diseases of the immune system (ADA-SCID, Wiskott-Aldrich Syndrome), of which he is principal investigator or investigator

A426

MAPPING QUALITY OF LIFE OVER TIME: INSIGHTS FROM THE ACCESS TRIAL USING MISMATCHED UNRELATED DONORS

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Background: Allogeneic hematopoietic cell transplantation (HCT) is curative for hematologic malignancies, yet access remains inequitable. To address these challenges, the NMDP-sponsored, CIBMTR-led ACCESS trial (NCT04904588) evaluated safety and efficacy of peripheral blood stem cells (PBSC) from mismatched unrelated donors (MMUD) in adults with high-risk hematologic malignancies receiving myeloablative (MAC) or reduced-intensity/non-myeloablative conditioning (RIC/NMA) and PTCy as GVHD prophylaxis. Primary results demonstrated excellent one-year overall survival and acceptable rates of GVHD and other complications, irrespective of conditioning intensity and HLA mismatch. This study examines 1-year post-treatment quality of life (QOL) trajectories, particularly by age.

Methods: Patients who completed at least a baseline and 1-year patient-reported outcome (PRO) surveys were included. QOL surveys were collected at baseline, day (D)100, D180, and 1-year post-HCT using the Lee Symptom Scale (LSS) and PROMIS domains (physical, cognitive, social, sexual function, anxiety, depression, fatigue, sleep disturbance, and pain interference). Mixed models for repeated measures (MMRM) assessed QOL trajectories over time for each PRO measure, adjusting for baseline clinical characteristics and QOL. ANCOVA models assessed adjusted mean differences at 1-year between patients who developed moderate/severe chronic GVHD (cGVHD) versus no/mild cGVHD. Clinically meaningful differences were defined as >5 points for LSS and PROMIS; published norms interpreted symptom burden.

Results: Among 268 ACCESS participants, 113 (42%) patients submitted baseline and 1-year PRO surveys; 18 (15.9%) developed moderate/severe cGVHD. 66 (58%) of patients were <65; 47 (42%) were 65+.
Impact of cGVHD at 1-year. Patients with moderate/severe cGVHD at 1-year had significantly higher LSS scores (Figure 1) and lower PROMIS physical function (PF) compared to those with no/mild cGVHD. LSS scores were 5.21 points higher for moderate/severe cGVHD, a clinically and statistically significant difference. Higher HCT-CI (≥3) was the only other factor tested associated with higher 1-year LSS (4.07 vs. HCT-CI 0). PF was 4.82 points lower for patients with moderate/severe cGVHD; age and educational level were also significantly different. No other QOL domains differed by cGVHD status, however several factors were significantly associated with differences in other QOL domains at 1-year (Table 1).
Trajectory Analyses. Sex and KPS significantly impacted LSS scores over time. Female patients reported an average of 3.5 points lower LSS scores at 1 year than male patients (9.0 vs. 12.5, p<.05). Patients with KPS 90–100 reported 12.4 versus 9.0 for <90 KPS. Age significantly impacted PROMIS cognitive function trajectories, with the largest difference at D100 (patients ≥65 scored 3.1 points lower than <65), though 1-year cognitive was not different by age. PROMIS fatigue trajectories were also age-affected (older patients reported

less fatigue after D100).

Figure 1. Lee Symptom Scale Scores at each timepoint, by cGVHD status

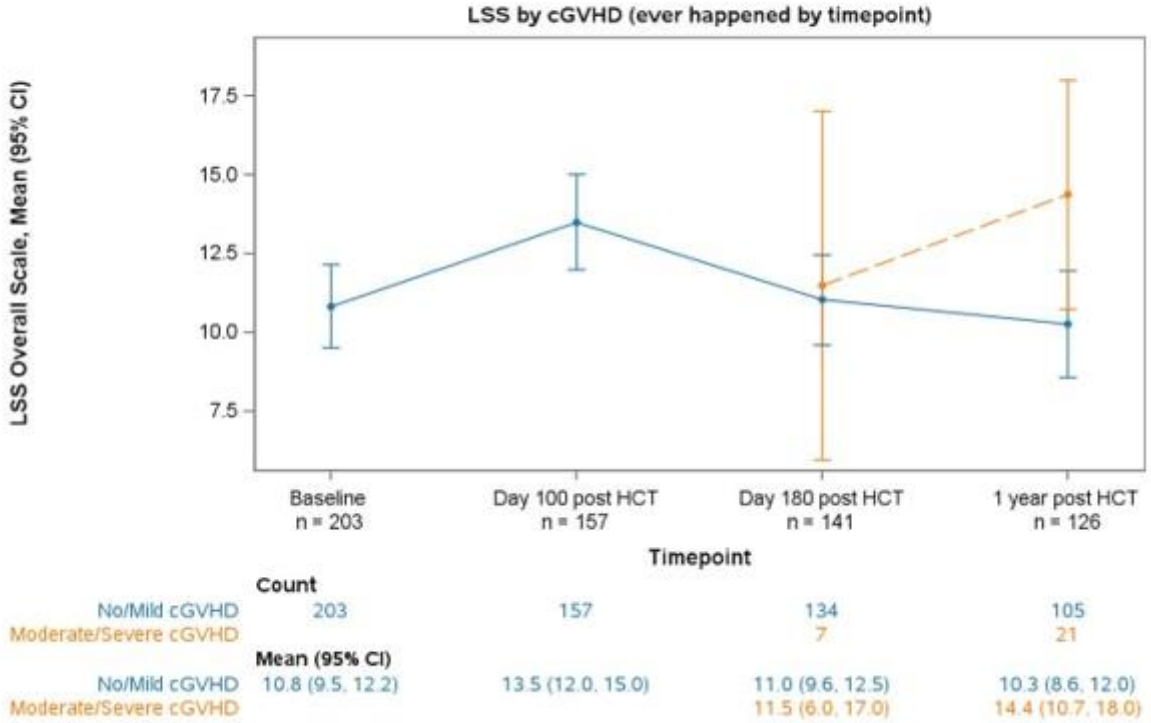

Table 1. ANCOVA Results for each Quality of Live (QOL) domain, significant cGVHD or other covariates		
QOL Outcome	**1-year score differe by cGVHD (95% CI)**	**Other Significant Covariates associated with <u>better</u> QOL scores**
LSS	5.21 (1.43, 8.99)**	Lower HCT-CI
PROMIS Cognitive Function	--	--
PROMIS Physical Function	-4.88 (-8.67, -.96)*	Younger Age Higher Education

PROMIS Social Function	--	--
PROMIS Anxiety	--	Female Job status: Currently employed (vs. Retired or Unable to work due to illness or disability)
PROMIS Depression	--	--
PROMIS Fatigue	--	--
PROMIS Sleep Disturbance	--	Higher Education
PROMIS Pain Interference	--	--
PROMIS SexFS Interest	--	Male
PROMIS SexFS Satisfaction	--	Job status: Currently employed (vs. all other job statuses)
Note: *=p<.05; **=p<.01		

Conclusions: The incidence of moderate/severe cGVHD in this study was relatively low. We found the overall LSS and PF were worse at 1-year for patients with moderate/severe cGVHD, but no other QOL domains were impacted. Older patients typically had less fatigue after D100 and higher cognitive scores over the first-year post HCT, but had significantly worse PF at 1-year. Similar QOL data are being collected in current accruing trials to allow further validation of these findings.

Clinical Trial Registry: NCT04904588
ClinicalTrials.gov

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EVALUATING THE POTENTIAL OF E-HEALTH TO IMPROVE POST-TRANSPLANT CARE: PRELIMINARY RESULTS OF THE MY-MEDULA RANDOMIZED TRIAL

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Background: eHealth-based integrated care models have shown benefits in the management of chronic diseases; however, evidence supporting their implementation in the allogeneic hematopoietic cell transplantation (alloHCT) setting remains limited. "MyMedula" is a mobile application and web platform developed by a multidisciplinary HCT team to provide individualized, behavior-based support aimed at mitigating post-HCT complications. A prior pilot study confirmed the tool's feasibility and high patient acceptance (Redondo et al., TCT 2021). The present analysis reports preliminary findings from a randomized clinical trial evaluating whether complementing standard care with "MyMedula" can enhance patient experience and clinical outcomes following alloHCT.

Methods: Single-center randomized-controlled trial (IIBSP-EME-2019-44) conducted at a tertiary university hospital by an interdisciplinary team. Adult alloHCT recipients were randomized 1:1 to standard care (control group, CG) or to the "MyMedula" strategy (intervention group, IG). The intervention comprised multifaceted, patient-tailored actions triggered by patient-reported data captured through the mobile application. Primary endpoints were major post-HCT complications and healthcare resource utilization during the first-year post-transplant.

Results: Between August 2022 and August 2024, 105 alloHCT recipients were invited to participate within one month after discharge; 6 (5.7%) declined due to technological barriers. A total of 99 patients were finally enrolled: 54 (54.5%) in the CG and 45 (45.4%) in the IG. Median follow-up was 19.6 months (95% CI: 17.5–23.5) in the CG and 20.2 months (95% CI: 15.6–23.9) in the IG. Baseline demographic and clinical characteristics were comparable between groups (Table 1), and no differences in baseline technological proficiency were observed according to the CAMBADOS questionnaire.
At last follow-up, no significant differences were observed between groups in the incidence of major post-HCT complications, including infections and graft-versus-host disease. Rates of unplanned visits to the day care clinic or emergency department, hospital readmissions, and other healthcare utilization indicators were also comparable between the CG and IG.

However, when all visit types were aggregated, the IG presented a higher total number of visits than the CG (median [IQR]: 8 [5–12] vs. 6 [3–11]; p = 0.04974).
Survival outcomes—including relapse incidence, transplant-related mortality, and overall survival—also showed no meaningful differences between groups (Table 2). Analyses of patient satisfaction, app usability, and quality-of-life measures are ongoing.

Variable	Control group (n=54)	Intervention group (n=45)	p-value
Age, Median [IQR]	54 [41–62]	55 [45–62]	0.459
Age ≥ 65, n (%)	9 (16.7)	7 (15.6)	1.000
Sex, female	28 (51.9)	22 (48.9)	0.927
Underlying disease AML ALL NHL MDS	31 (57.4) 8 (14.8) 2 (3.7) 7 (13.0)	14 (31.1) 10 (22.2) 4 (8.9) 9 (20)	0.169
Conditioning regimen MAC RIC	28 (51.9) 26 (48.1)	21 (46.7) 24 (53.3)	0.755
GVHD prophylaxis PTCy–tacrolimus Siro–Tacro Others	51 (94.4) 1 (1.9) 2 (3.7)	40 (88.9) 2 (4.4) 3 (6.7)	0.624
Donor type Identical sibling Haploidentical MUD MMUD	13 (24.1) 11 (20.4) 20 (37.0) 10 (18.5)	9 (20) 6 (13.3) 26 (57.8) 4 (8.9)	0.189
Female to male	48 (88.9)	39 (86.7)	0.978
Prophylactic letermovir	29 (53.7)	21 (46.7)	0.700

	Control group (n=54)	Intervention group (n=45)	p-value
Complications			
Acute grade II-IV GVHD	14 (25.9%)	14 (31.1%)	0.729
Chronic moderate-severe GVHD	11 (20.4%)	7 (15.6%)	1.000
Thrombotic microangiopathy / acute renal failure	1 (1.9%)	1 (2.2%)	1.000
CMV reactivation	10 (18.5%)	5 (11.1%)	0.402
Viral respiratory tract infection	31 (57.4%)	29 (64.4%)	0.612
Invasive fungal infection	2 (3.7%)	0 (0%)	0.499
Relapse	9 (16.7%)	8 (17.8%)	1.000
Causes of death:			1.000
- Relapse	6 (11.1%)	3 (6.7%)	
- Infection	1 (1.9%)	0 (0%)	
Healthcare utilization			
Total number of day-care clinic visits *median [IQR]*	2 [1-4]	1 [0-3]	0.457
Total number of hospital admissions *median [IQR]*	0 [0-1]	1 [0-2]	0.272
Total number of primary care visits *median [IQR]*	2 [0-5]	4 [2-7]	0.064
Total number of emergency department visits *median [IQR]*	1 [0-2]	1 [0-3]	0.173

Conclusions: Integrating a mobile health tool into post-alloHCT follow-up is feasible and well accepted for most patients across age groups. In this preliminary analysis, the "MyMedula" strategy did not reduce post-transplant complications and was associated—perhaps paradoxically—with a modest increase in healthcare interactions compared with standard care. Ongoing analyses will further clarify its impact on patient-reported outcomes and help identify strategies to optimize its clinical utility.

Disclosure: Nothing to declare

A429

IMPACT OF REDUCED-INTENSITY CONDITIONING REGIMENS ON FEMALE GONADAL FUNCTION IN SICKLE CELL DISEASE

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Background: Reduced-intensity conditioning (RIC) regimens are increasingly employed in allogeneic hematopoietic stem cell transplantation (HSCT) for young adults with sickle cell disease (SCD). These strategies aim to reduce treatment-related toxicity while maintaining curative potential. Among the potential toxicities of HSCT, impairment of ovarian function is a major concern for young women, given the impact on fertility and long-term quality of life.
Objective: This study evaluated the impact of three RIC regimens on ovarian function and fertility outcomes among female SCD patients undergoing HSCT, with the goal of improving fertility preservation counselling.

Methods: We conducted a retrospective analysis of 30 consecutive women with severe SS genotype SCD who underwent HSCT between November 2013 and March 2022 for cerebral vasculopathy, recurrent vaso-occlusive crises, or refractory acute chest syndrome. Patients received one of three transplant modalities

- **R1 (n=11):** RIC haploidentical HSCT (Antithymoglobulin (ATG), thiotepa, fludarabine, cyclophosphamide, 2Gray TBI followed by post cyclophosphamide).
- **R2 (n=4):** RIC matched related HSCT (ATG, fludarabine, cyclophosphamide, 2 Gy Total Body irradiation (TBI)).
- **R3 (n=15):** Non myeloablative matched related HSCT: Alemtuzumab, 3Gy TBI.

All patients attended fertility preservation (FP) consultations prior to HSCT. Logistic regression analysis was performed to identify potential risk factors for premature ovarian insufficiency (POI). POI was defined as cessation of menstruations more than 4 months before the age of 40 and FSH levels >25IU/L.

Results: The median age at HSCT was 21.4 years (range 15.8–37.9), highest in R2 group (31.3 years). FP was undertaken in 66.7% overall, most frequently in R1 (90.9%) and R2 (100%) compared with 40% in R3. Pre-HSCT median Anti-Müllerian Hormone (AMH) levels were highest in R2 group (3.5 ng/mL). The medium cumulative Cyclophosphamide exposure was greater in R1 (6.9 g; 129 mg/kg) than R2 (2.9 g; 50 mg/kg). Median follow-up was longest in R2 (6.8 years vs. 4.0 in R1 and 3.0 in R3). Menstrual recovery occurred in 67.9% overall, with rates of 100% (R2), 78.6 % (R3) and 45.5% (R1). Despite clinical recovery of ovarian function, post-HSCT AMH levels remained low in all three groups (median 0.1 ng/mL, range 0.01 – 0.87). Four natural pregnancies (13.3%) occurred post-transplant: two in R1 and two in R2. The highest incidence of POI (21.4%) occurred in the R3 group. Logistic regression did not identify significant predictors of POI.

Table 1. Patients characteristics

Patients characteristics	**Overall** N = 30	**R1** N = 11	**R2** N = 4	**R3** N = 15
Age at HSCT (years)				
Median [Min, Max]	21.4 [15.8, 37.9]	20.4 [16.7, 32.4]	31.3 [18.5, 37.9]	21.1 [15.8, 37.7]
Cumulative dose of cyclophosphamide (g)				
Median [Min, Max]	6.8 [2.4, 8,2]	6.9 [2.4, 8.2]	2.9 [2.8, 3.1]	NA
AMH pre HSCT(ng/mL)				
Median [Q1, Q3]	1.3 [0.7, 3.0]	1.6 [0.4, 2.4]	3.5 [0.4, 6.5]	1.3 [0.7, 3.5]
(Min, Max)	(0.2, 19.0)	(0.2, 3.0)	(0.4, 6.5)	(0.3, 19.0)
Fertility preservation, n (%)	20 (66.7)	10 (90.9)	4 (100.0)	6 (40.0)
Age at last follow-up (years)				
Median [Min, Max]	27.1 [17.6,40.9]	29.1 [17.9, 36.9]	38.3 [25.6, 40.7]	24.5 [17.6, 40.9]
Duration of follow-up at study (years)				
Median [Min, Max]	3.3 [0.9, 8.7]	4.0 [0.9, 8.7]	6.8 [2.7, 7.5]	3.0 [1.2, 6.1]
Menstrual recovery after HSCT, n (%)	19 (67.9)	5 (45.5)	3 (100.0)	11 (78.6)

(Missing)	2	0	1	1
POI n(%)	9 (32.1)	6 (54.5)	0 (0)	3 (21.4)
AMH post HSCT (ng/mL)				
Median [Q1, Q3]	0.10 [0.03, 0.15]	0.04 [0.02, 0.13]	0.07 [0.07, 0.07]	0.10 [0.05, 0.30]
(Min, Max)	(0.01, 0.87)	(0.01, 0.30)	(0.07, 0.07)	(0.01, 0.87)
Natural pregnancies, n (%)			4 (13.3)	2 (18.2)

NA: non adapted; HSCT: hematopoietic stem cell transplantation; AMH: Anti-Müllerian Hormone

Conclusions: RIC regimens can preserve ovarian function in some women with SCD undergoing HSCT. Nonetheless, persistently low AMH levels indicate diminished ovarian reserve and highlight the risk of future POI. These findings emphasize the importance of early fertility counseling, pre-transplant preservation strategies, and long-term reproductive monitoring to optimize fertility outcomes in this population.

Disclosure: Nothing to declare

A430

NOT JUST SURVIVING BUT THRIVING – A PEDSQL-MEASURED QUALITY OF LIFE IN LONG TERM SURVIVORS WHO UNDERWENT HSCT FOR IBMFS

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Background: Inherited bone marrow failure syndromes (IBMFS) constitute a diverse group of genetic disorders requiring hematopoietic stem cell transplantation (HSCT) for cure. We report a twenty-year experience with emphasis on graft outcomes, transplant-related complications, survival, and long-term health-related quality of life (HRQoL) using the PedsQL 4.0 system in survivors over two years post-HSCT.

Methods: This retrospective analysis included all children ≤18 years undergoing HSCT for genetically or clinically confirmed IBMFS between January 2005 and December 2023. Conditioning was diagnosis-adapted, with reduced-intensity conditioning (RIC) used for Fanconi anemia (FA) and myeloablative conditioning (MAC) applied in non-FA disorders. HRQoL was assessed in children surviving over two years post-HSCT using the PedsQL 4.0 Generic Core Scales. Total Transform scoring categorized QoL as good (score=1), moderate

(score=2), or poor (score=3). Statistical comparisons between FA and non-FA survivors used Fisher Exact testing, Mann-Whitney U test, and ordinal logistic regression.

Results: A total of 96 HSCTs were performed for 91 children (median age 8 years; male: female ratio 1.5:1). FA constituted the largest subgroup (n=72, followed by pure red cell aplasia (n=8), congenital amegakaryocytic thrombocytopenia (n=5), congenital neutropenia (n=2), Shwachman–Diamond syndrome (n=2), and other IBMFS (n=5). The overall survival at last follow-up was 53.8% (49/91)**.**
We performed the long-term follow-up HRQoL in 48 survivors as one child's family refused participation in the survey due to a language barrier. As graft versus host disease had an impact on the quality of life, we documented the impact of chronic GVHD. 19.7 % children had chronic GVHD and 3/48(6.2%) had extensive chronic GVHD impacting on all domains of quality of life.
The majority demonstrated reassuring functional recovery: 39 children (81.2%) achieved a "good" quality-of-life score, while 14 (18.8%) fell within the moderate-to-poor range and there was no difference was observed in outcome distribution using either dichotomized or ordinal scoring methods (Fisher exact p=0.74; Mann–Whitney U p=0.68; ordinal logistic regression p=0.67), indicating that underlying diagnosis did not independently predict quality-of-life status among survivors.
Domain-specific analysis revealed variability in recovery patterns. Emotional functioning demonstrated the highest mean score (86.46%), followed by physical health (84.88%), while Social (83.13%) and School Functioning (82.71%) were the lowest scoring domains. School functioning was identified as the most affected area, suggesting sustained challenges with academic reintegration, fatigue, absenteeism, and psychosocial impact following prolonged treatment and immune isolation. Despite these limitations, the majority of surviving children reported relatively high HRQoL scores, indicating meaningful functional recovery following transplant.

Conclusions: The majority of long-term pediatric IBMFS survivors demonstrated encouraging post-HSCT HRQoL outcomes, with emotional well-being and physical functioning largely preserved.

Clinical Trial Registry: None

Disclosure: Nothing to declare

A431

INCIDENCE, RISK FACTORS AND OUTCOMES OF AVASCULAR NECROSIS IN ALLOGENEIC STEM CELL TRANSPLANT RECIPIENTS DEVELOPING GRAFT-VERSUS-HOST DISEASE

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Background: Avascular necrosis(AVN) is an important late complication of allogeneic stem cell transplant(ASCT), impacting mobility in survivors. Prior studies report AVN post-ASCT at rates of 3.7% to 24%, with up to 80% of patients needing joint replacement within five years. However, data on risk factors beyond graft-versus-host disease (GVHD) remains inconsistent, and there is no published data from India.

Methods: This single-centre retrospective analysis included ASCT recipients between January 2008 and December 2022 who survived at least 180 days post-transplant and developed either acute or chronic GVHD. AVN was assessed in symptomatic patients; diagnosis was based on MRI, and the ARCO (Association Research Circulation Osseous) stage was recorded for involved hip joints. Serum vitamin D levels were assessed pretransplant and at the diagnosis of AVN and supplemented if deficient(<20ng/ml). Use of steroids pre- and post-transplant was recorded, and steroid doses were standardized to prednisolone equivalents for analysis. Data on demographics, transplant parameters, and other risk factors were compared between AVN and non-AVN patients using the Mann-Whitney U test.

Results: Of 411 transplanted patients, 192 were excluded for early mortality(n=92), pre-existing AVN(n=5), or absence of GVHD(n=95), leaving 219 eligible patients(median age 28 years, 72% male). Primary indications for ASCT in the eligible cohort were AML(n=62), ALL(n=68), MPAL(n=6), CML(n=46), Hodgkin lymphoma(n=9), MDS(n=13), and other(n=15). Transplants in thse patients were MRD(n=176,81%), MUD(n=11,5%), and haploidentical(n=32,15%) with median post-ASCT follow-up of 60 months.
Fourteen of 219 patients(6.4%) developed AVN symptoms at a median of 641 days post-ASCT(range: 21-1299), confirmed by MRI at a median of 644 days(range: 40-1330). All patients had hip involvement with median ARCO stage II; 4 had shoulder and 1 had wrist involvement(median number of joints involved: 2,range:1-4).
Twelve AVN patients required vitamin D supplementation at diagnosis of AVN, and 13 received bisphosphonates(alendronate:11, zoledronate:2). Five were managed conservatively; surgery was advised in 9 of whom 8(57.1%) underwent at least one procedure(hip decompression:2, joint replacement:7, both:1). Median time to first surgery was 1,046 days(range: 576-1,547).
No significant differences were noted in age, anthropometric measurements, ASCT type, conditioning intensity, TBI use, comorbidities, or CD34+ cell dose between both groups. AVN patients received higher median CD3+ cell dose (184.6 vs 135.5 ×10^6 cells/kg, p=0.048) and had higher rates of pre-ASCT vitamin D deficiency(12/14, 85.7% vs 117/205, 57.1%; p=0.036). Pre-ASCT steroid exposure was more common(13/14, 92.8% vs 133/205, 65.2%; p=0.035), and median pre-ASCT steroid dose was higher in the AVN group(2,643 vs 202.7 mg/m^2, p=0.006). AVN cases received higher starting dose of systemic steroids for acute GVHD(median:2.19 vs 1.19 mg/kg prednisolone equivalents, p=0.016), but there were no differences in steroid therapy duration, steroid-refractoriness, or use of maintenance prednisolone and oral budesonide. Chronic GVHD occurred in 11/14(78.5%) AVN patients and 127/205(61.9%) non-AVN patients, with a higher proportion of AVN patients requiring systemic steroids(7/11, 63.6% vs 42/127, 33.1%; p=0.043).

Conclusions: Symptomatic AVN incidence among ASCT recipients who developed GVHD was 6.4%, with 57% requiring surgery. Higher pre-ASCT steroid exposure, higher initial steroid dose for acute GVHD, higher CD3+ cell dose, and pre-ASCT vitamin D deficiency were potentially modifiable risk factors for AVN.

Disclosure: Nothing to declare

A432

SECOND PRIMARY MALIGNANCY AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION – LONG-TERM FOLLOW-UP AT A SINGLE INSTITUTE EXPERIENCE

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Background: Hematopoietic stem cell transplantation is a curative treatment for various hematologic malignancies and some benign hematologic diseases. Besides chronic GVHD, the second primary malignancy is also a long-term adverse effect.

Methods: We retrospectively searched our post-transplant patients' long-term follow-up data between 2001 and 2021, and analyzed the incidence, types, and outcomes of second malignancies and excluded EBV-related post-transplant lymphoproliferative disorders at a single institution over 20 years.

Results: Twelve patients of second primary malignancy, including 5 of head and neck squamous cell carcinoma, 3 of MDS/AML, 1 of ALL, 1 of esophageal squamous cell carcinoma, 1 of breast cancer, and 1 of papillary thyroid cancer in 380 patients of our cohort (autologous in 184 and allogeneic in 196 patients). Eight patients who underwent allogeneic hematopoietic stem cell transplants had five head and neck, one esophageal, one breast, and one papillary thyroid cancer. Four who underwent autologous transplants were three MDS/AML and one ALL. All six patients with five head and neck cancers and one esophageal cancer had extensive chronic GVHD. Of these six squamous cell carcinoma patients, four were disease-free after surgery, but one died after the vaccination for COVID-19. The other two died of a second cancer in progression. In four of the MDS/AML and ALL patients, two were persistent leukemia-free after intensive chemotherapy and salvage allogeneic hematopoietic stem cell transplantation, one low-risk MDS on watchful observation without treatment, and one AML patient died of leukemia relapse even after allogeneic transplant. The other two patients with breast cancer and papillary thyroid cancer were disease-free after surgery and adjuvant therapy. Nine of our patients were disease- or progression-free; three died of second cancers (hypopharyngeal, esophageal, and AML).
The cumulative incidence was 6% at 10 years and 16% at 19 years, including 5% versus 7% at 10 years and 15% versus 17% at 19 years after autologous and allogeneic HCT, respectively, which is higher than reported in a previous large-scale study of the CIBMTR database, the cumulative incidence of new solid cancers was 1% at 10 years, 2.2% at 15

years, and 3.3% at 20 years after transplantation. A single-institution review of 4905 survivors of allogeneic hematopoietic cell transplant from Seattle reported 581 secondary cancers in 499 individuals after a median follow-up of over 12 years. The cumulativeincidence of secondary malignant neoplasms at 30 years after HCT for the entire cohort was 22.0%. At 20 years post-HCT, the cumulative incidence rates were 8.1%, 13.5%, and 23.6% for patients younger than 20 years of age, 20–50 years, and older than 50 years, respectively, which is similar to our cohort.

Conclusions: The cumulative incidence of second malignancy was 6% in 10 years and 16% in 19 years, and post-autologous and post-allogeneic transplants were 5% vs. 7% and 15% vs. 17% in 10 years and 19 years, respectively. Extensive chronic GVHD is a risk factor for upper aerodigestive tract squamous cell carcinoma. Most patients can be salvaged after local or systemic treatment.

Clinical Trial Registry: KFSYSCC-IRB No./Protocol No.: 20221110A (Interim report 3).

Disclosure: No disclosure.

A433

NON-INFECTIOUS COMPLICATIONS AFTER CAR-T CELL THERAPY

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Background: CAR-T has demonstrated remarkable efficacy in treating R/R B-cell neoplasms, such as diffuse large B-cell lymphoma (DLBCL) and multiple myeloma (MM). Despite its success, long-term effects and sequelae of CAR-T on the immune system remain underestimated.

Methods: In the present retrospective study, we aim to analyze non-infectious complications after CAR-T cell therapy.

Results: Sixty patients were infused between august-2022 and November-2025. 50% were males, 32% had an auto previous and 12% had tandem auto. Median lines of therapy were 1.9 (range 1-5) and median age was 64-yo (range 37-79). Twenty-three patients (38%) had DLBCL, 5 (8%) other B cell lymphomas and 32 (53%) had MM. Previous to CAR-T, 6 patients (10%) were in CR, 19 patients (32%) in PR, 7 (12%) in VGPR, 4 (7%) with stable disease and 23 (38%) with RR.Forty-six patients had CRS grade 1 or 2 (27 [39%] and 20 [29]). Twenty-one patients had ICANS grade 1 (7 [10%]), grade 2 (3 [4%]), grade 3 (7 [10%]),

grade 4 2 (3%) or grade 5 (1 [1%]). In our series, 13 patients (22%) needed to be admitted in the ICU after CAR-T infusion, the causes of ICU admission were: severe CRS (2), severe ICANS (9) and other (1). At 28 days post-infusion, 37 patients (54%) had ICAHT requiring treatment in 22 (59%). G-CSF, Eritropoyetin or Eltrombopag were used in 20 (29%), 16 (23%) and 14 (20%) of the patients.

In terms of non-infectious complications (NIC), we observed late onset neurotoxicity in 6 patients, cardiovascular in 4 , immunomediated fenomena in 4 , pulmonary complications in 3 and secondary malignancies y other 3. See Table1. Cumulative incidence (CI) of (NIC) at 1y for the whole series was 22% (CI 95% 11-38) and for lymphoma and MM was 31% (CI 95% 16-54) and 11% (CI 95% 3-40).

With a median follow up of 5 months, at last follow up 50 patients were alive. Ten patients died after the infusion, in 5 cases due to relapse and in the other 5 cases due to non-relapse mortality (NRM) (1 ICANS, 4 infections). For the whole population, 1-year overall survival (OS), relapse free survival (RFS) and NRM was 83% (CI 95%: 68-91), 76% (CI 95%: 60-86) and 10% (CI 95%: 4-21), for lymphoma patients was 73% (CI 95% 51-86), 62% (95% CI 40-77) and 15% (CI 95% 5-31) respectively and for MM patients was 96% (CI 95% 75-99), 96% (CI 95% 75-99) and 4% (CI 95% 1-17), respectively.

Univariable analysis showed that a diagnosis of MM vs lymphoma (p=0.03) and 1 vs >1 treatment lines prior to CAR-T (p=0.02) were associated with an inferior CI of NIC. Multivariable analysis showed that only lines of therapy pre-CAR-T was associate with an inferior CI of NIC (HR 0.1: CI 95% 0.02-0.9; p-value=0.02).

Patient	Non-infectious complication	Age	Sex	Disease	Lines of therapy	CAR-T product	Response pre/post	CRS	ICANS	D10 lymphocytosis	Last status	Cause of death
1	- Fronto-subcortical cognitive impairment - Warthin's tumor/Oncocytoma	63	Male	Lymphpoma	3	Tisacel	RR/CR	Grade2	No	Yes ALC7400/uL	Alive	
2	- Mild cognitive impairment - Pneumonitis on CT scan - Transaminitis	58	Female	MM	1	Ciltacel	PR/CR	Grade1	No	Yes ALC3500/uL	Alive	
3	- Trigeminism	76	Male	Lymphoma	2	Tisacel	RR/CR	Grade2	Grade1	Yes ALC3600/uL	Alive	
4	- Unclassified Interstitial Lung Disease (ILD)	69	Female	MM	1	Ciltacel	CR/CR	Grade1	No	No	Alive	
5	- Movement and neurocognitive treatment-emergent adverse event (MNTs)	73	Male	Lymphoma	2	Tisacel	PR/CR	Grade1	Grade2	Yes ALC4800/uL	Alive	
6	- Pulmonary hypertension and hypertensive arteriopathy	76	Female	Lymphoma	2	Axicel	RR/RR	Grade1	No	No	Death	Disease
7	- Self-limiting ICANS, no treatment	48	Female	Lymphoma	2	Axicel	RR/CR	Grade1	Grade3	No	Alive	
8	- Hypovolemic shock	71	Female	Lymphoma	2	Axicel	CR/CR	Grade2	Grade2	No	Alive	
9	- Septapical dyssynchrony with LVEF 45%	66	Male	Lymphoma	2	Axicel	RR/CR	Grade2	Grade3	No	Alive	
10	- Pituitary macroadenoma	77	Male	Lymphoma	1	Axicel	RR/CR	Grade1	Grade1	No	Alive	
11	- Late onset ICANS - IEC-HS	71	Female	Lymphomoa	2	Axicel	CR/CR	Grade2	Grade3	No	Death	Infection
12	- Enteritis	72	Male	MM	4	Ciltacel	VGPR/CR	Grade1	No	Yes ALC3000/uL Prophylactic dexametasone	Alive	
13	- AML	72	Male	Lymphoma	3	Tisacel	RR/CR	Grade1	No	No	Alive	
14	- IEC-HS	58	Female	Lymphoma	2	Axicel	RR/PR	No	Grade4	No	Death	Infection
15	- Cranial nerve palsy	67	Female	MM	1	Tisacel	PR/Pending	Grade2	No	No but later needed prophylactic dexametasone for ALC>3000/uL	Alive	

ILD: Interstitial Lung Disease, MNTs: Movement and neurocognitive treatment-emergent adverse event, ICANS: Immune-effector-cell associated neurotoxicity syndrome, LVEF: Left ventricular ejection fraction, IEC-HS: Immune Effector Cell-associated Hemophagocytic Lymphohistiocytosis-like Syndrome, AML: Acute myeloid leukemia, RR: Relapse/refractory, CR: Complete remission, PR: Partial remission, VGPR: Very good partial remission, ALC: Absolute lymphocyte count

Conclusions: Non-infectious complications after CAR-T are underestimated in many of the guidelines. In our study more than 1 line of therapy was associated with higher NIC development. In terms of mortality, NRM was 10% and mostly due to infectious complications.

Disclosure: No COI.

A434

FROM CHILDHOOD TO ADOLESCENCE: LONG-TERM RISKS AND RECOVERY MORE THAN FIVE YEARS AFTER NON-TBI HSCT

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Background: Hematopoietic stem cell transplantation (HSCT) remains a cornerstone of curative therapy for children with life-threatening hematologic, oncologic, immunologic disorders and inborn errors of metabolism. Conventional conditioning regimens incorporating total body irradiation (TBI) are associated with substantial long-term toxicities, including endocrine dysfunction, infertility, and increased risk of secondary malignancies. Consequently, non-TBI conditioning approaches have gained wider adoption in pediatric HSCT. However, data on the late effects associated with these regimens remain limited. As survival improves, understanding long-term complications and quality-of-life outcomes in survivors is increasingly important. This study aimed to evaluate late effects among pediatric patients who underwent non-TBI HSCT.

Methods: We conducted a cross-sectional analysis of patients who underwent HSCT at <18 years of age, had at least 5 years of post-transplant survival, and were attending routine follow-up visits at the HSCT clinic of Children's Medical Center, the country's leading pediatric HSCT center. Transplant indications included both malignant and non-malignant disorders. All patients received non-TBI conditioning regimens, categorized as myeloablative (MAC), non-myeloablative (non-MAC), or reduced-intensity conditioning (RIC), according to disease-specific protocols.

Results: A total of 67 patients were enrolled. The mean follow-up duration was 8.62 ±2.64 years , with 30% of patients having undergone HSCT more than 10 years prior. The most common indications for transplantation were malignant hematologic disorders (29.9%) and primary immunodeficiencies (22.4%). Most patients received fully matched donor grafts (80.6%), and 59.7% were transplanted from sibling donors; all grafts were peripheral blood stem cells. Only one patient required a second transplant. At last follow-up, 9 patients (13.4%) demonstrated mixed chimerism and had received donor lymphocyte infusion. 27 (40.3%) patient had a bone mineral density Z-score < −2 indicating below the expected range for age.Cardiac function remained normal (EF >55%) in all but one patient. Endocrine complications included hypoparathyroidism in 4 patients (6%) and hypothyroidism in 11 patients (16.4%). Metabolic abnormalities were observed in 10 patients (14.9%) with dyslipidemia, 8 patients (11.9%) with pre-diabetes, and 1 patient with diabetes mellitus. Gonadal dysfunction was present in 36 patients (40.7%); among 10 male patients who underwent semen analysis, 6 (60%) showed evidence of infertility.No cases of disease recurrence or secondary malignancy were identified.

Conclusions: In this cohort of long-term survivors of pediatric HSCT conditioned without TBI, late effects remained common but were largely manageable, with a notably low burden

of cardiotoxicity, secondary malignancies, and disease recurrence. Endocrine, metabolic, and gonadal complications represented the predominant long-term morbidities, underscoring that non-TBI regimen, while mitigating many classic radiation-associated toxicities, do not fully eliminate the risk of late organ dysfunction. The high prevalence of reduced bone mineral density and gonadal impairment highlights the need for structured survivorship care, proactive screening, and early intervention. As non-TBI conditioning strategies continue to expand in pediatric transplantation, comprehensive long-term follow-up is essential to refine risk-adapted conditioning, optimize supportive care, and ultimately improve the quality of survival for this growing population of HSCT survivors.

Clinical Trial Registry: N/A

Disclosure: The authors declare no conflict of interest

A435

BRONCHIOLITIS OBLITERANS SYNDROME AFTER PAEDIATRIC ALLOGENEIC HSCT: A SYSTEMATIC REVIEW OF THERAPEUTIC STRATEGIES

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Background: Bronchiolitis obliterans syndrome (BOS) is a rare but severe complication following allogeneic haematopoietic stem cell transplantation (HCT). Management strategies for paediatric BOS are largely extrapolated from adult data, and no prior systematic review has synthesised the evidence base specific to the paediatric population. This review aimed to evaluate all available data on therapeutic interventions for paediatric BOS and to assess the quality of the available evidence.

Methods: A systematic search of MEDLINE, EMBASE, PubMed, and the Cochrane Library was performed. The search strategy was adapted, with permission, from the strategy used in the European Respiratory Society (ERS)/European Society for Blood and Marrow Transplantation (EBMT) clinical practice guidelines on the treatment of pulmonary cGvHD in adults. Eight PICO questions were explored. Eligible studies reported therapeutic interventions for BOS or lung cGvHD in patients <18 years, including mixed-age cohorts where paediatric data were extractable. Screening, data extraction and risk-of-bias assessment were performed independently by two reviewers. Observational studies were assessed using a modified Newcastle–Ottawa Scale, prospective interventional studies using ROBINS-I-V2, and the included systematic review using ROBIS. A complementary search of major clinical trial registries identified ongoing or unpublished trials relevant to paediatric BOS.

Results: Only sixteen studies met inclusion criteria, encompassing fewer than 205 children worldwide. The majority of studies were single-centre, retrospective case series with heterogeneous diagnostic and response criteria. Evidence for treatment effectiveness

remained limited. Ruxolitinib demonstrated the most consistent therapeutic benefit, with clinical and functional improvements and notable steroid sparing effects. Risk of bias was high or critical in most studies due to small sample sizes, retrospective design and inconsistent outcome measurement.

Conclusions: The current evidence base for the management of paediatric BOS following HCT is sparse, heterogeneous and of generally of low methodological quality. Although ruxolitinib showed some promise, the evidence remains low and no therapy has been validated in a prospective paediatric clinical trial. There is an urgent need for paediatric specific diagnostic and response criteria and for prospective, multicentre studies to define optimal treatment strategies and improve outcomes for children affected by this rare but devastating complication.

Disclosure: Nothing to declare

A436

LATE MORTALITY IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION SURVIVORS

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Background: Hematopoietic stem cell transplantation (HSCT) is curative for various pediatric malignant and nonmalignant disorders. As post-transplant survival improves, late mortality, defining as death occurring more than 2 years after HSCT, has become an important health issue in survivorship care. However, data on Asian pediatric populations remain limited.

Methods: We conducted a single-center, retrospective cohort study of pediatric patients who underwent HSCT between 2005 and 2022 at Taipei Veterans General Hospital, and survived more than 2 years post-transplant. Clinical records were reviewed.

Results: Eighty-four long-term survivors (85 HSCTs) were analyzed, with a median follow-up of 8.5 years. Hematologic malignancies were the most common underlying diseases (38.8%), followed by brain tumors (23.5%), solid tumors (23.5%), and benign diseases (14.1%). The 10-year overall survival and relapse-free survival were 83.5% and 70.7%, respectively. Fifteen patients (17.6%) died within a median of 6.2 years post-HSCT; relapse accounted for 54% of deaths, followed by secondary malignancies (20%), chronic graft-versus-host disease (13%), and pulmonary fibrosis (13%). In multivariate analyses, disease type was the only independent predictor of late mortality, with higher risk in brain and solid tumors compared with hematologic malignancies or benign diseases (HR = 0.208, p =

0.009). Relapse related mortality (RRM) plateaued at 12 years, while non-relapse related mortality (NRM) continued to rise and exceeded RRM after 18 years after HSCT. Secondary malignancies occurred in 9.5% of patients, mostly diagnosed within 5–10 years post-transplant.

Conclusions: In this Asian pediatric HSCT cohort, late mortality is strongly related to the underlying disease, with poorer outcomes in patients of brain and solid tumors. While relapse was the leading cause of late death, NRM, particularly secondary malignancies and pulmonary fibrosis, became more prominent over time. Transplant strategies to maintain treatment efficacy while avoiding unnecessary long-term NRM are urgently required. In addition, long-term risk-adapted surveillance is essential for early identification and prompt intervention for transplant survivors.

Disclosure: Nothing to declare.

P235

SEXUAL ACTIVITY DURING NEUTROPENIA AND IMMUNOSUPPRESSION: WHAT DO YOU TELL YOUR PATIENT?

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Background: Patients undergoing intensive chemotherapy or hematopoietic stem cell transplantation frequently develop neutropenia and immunosuppression, increasing vulnerability to infections. Sexual health guidance is traditionally highly restrictive, with some sources recommending abstinence or consistent condom use even within long-term monogamous relationships. However, these recommendations are based largely on theoretical risks rather than clinical evidence. The situation parallels the historical "neutropenic diet," which persisted for decades without proven benefit and negatively affected quality of life. Given the importance of sexual well-being and intimacy during cancer treatment, there is a critical need to reassess current practices.

Methods: We performed a narrative synthesis of published transplant and infection-prevention guidelines, patient education materials, psychosocial studies, and clinical evidence related to infection risks during neutropenia. Risk factors were categorized according to partner type, mucosal integrity, sexual practices, and exposure routes. Hygiene recommendations, contraceptive considerations, and chemotherapy-related excretion risks were reviewed to distinguish infection-related advice from other valid indications for barrier protection.

Results: Direct evidence linking sexual activity to increased infection rates during neutropenia is limited. Infection risk varies substantially depending on context:
• **Lower-risk situations:** monogamous, stable partnerships where partners share household flora; routine condom use adds minimal infection-prevention benefit if the partner is healthy.

• **Higher-risk situations:** sexual practices involving fecal exposure, significant mucositis or genital ulceration, or involvement of new or multiple partners.
• **Hygiene:** gentle routine hygiene is sufficient; excessive washing may disrupt mucosal barriers and microbiome integrity.
• **Other indications for condoms:** prevention of drug exposure after chemotherapy and contraception should not be conflated with infection prevention.
Restrictive, non-evidence-based advice may reduce intimacy and worsen psychological distress.

Conclusions: Current sexual activity recommendations for neutropenic and immunosuppressed patients often exceed available evidence and may negatively impact quality of life. Counseling should be individualized, balancing genuine infection risks with patient values and relationship context. Further research—including behavioral-infection correlation studies, qualitative partner-focused research, and trials comparing counseling strategies—is needed to inform evidence-based guidelines.

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P236

LONG-TERM RESULTS OF AUTOLOGOUS AND ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (AUTO-HCT AND ALLO-HCT) – REAL-LIFE DATA FROM A SINGLE CENTER ANALYSIS OF 15- AND 20-YEAR SURVIVALS

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Background: Despite the well-documented efficacy of both auto-HCT and allo-HCT in treating malignancies of the hematopoietic system, survival analyses in the literature are mostly limited to 5-year or 10-year survival following transplantation. Further observations are lacking, despite the potential occurrence of relapses even 10 years following HCT. The study aimed to evaluate 15- and 20-year overall and progression-free survival (OS and PFS) rates of auto-HCT and allo-HCT, and discuss these results in the context of available data on 5-year and 10-year survival rates.

Methods: We identified 468 auto-HCT recipients and 272 allo-HCT recipients treated in a single center from 1999 to 2014. If available, survival analyses were performed using Kaplan-Meier curves, the Cox proportional hazards model, and the log-rank test. Survival analyses were valid for auto-HCT recipients with multiple myeloma (MM), Hodgkin lymphoma (HL), non-Hodgkin lymphomas (NHLs), AL amyloidosis, acute myeloid leukemia (AML), and

immunodeficiencies, and for allo-HCT recipients with AML, acute lymphoblastic leukemia (ALL), chronic myeloid leukemia (CML), myelodysplastic neoplasms (MDS), NHLs, and severe aplastic anemia (SAA).

Results: In most cases, both 15-year and 20-year OS and PFS rates were obtained. Crucial findings for selected diseases were summarized in the attached Table.

OS rates	**5-year**	**10-year**	**15-year**	**20-year**	**median OS**	**last death**
auto-HCT in MM	50.5%	27.3%	17.1%	8.9%	62 months	month 236
auto-HCT in HL	74.2%	65.9%	62.3%	62.3%	N/A	month 154
auto-HCT in NHL	58.7%	54.3%	45.2%	45.2%	125 months	month 157
PFS rates	**5-year**	**10-year**	**15-year**	**20-year**	**median PFS**	**last relapse**
auto-HCT in MM	43.0%	22.7%	19.2%	19.2%	45 months	month 179
auto-HCT in HL	65.4%	58.1%	54.8%	54.8%	N/A	month 108
auto-HCT in NHL	54.7%	52.7%	43.8%	43.8%	125 months	month 59
OS rates	**5-year**	**10-year**	**15-year**	**20-year**	**median OS**	**last death**
allo-HCT in AML	45.2%	42.6%	39.3%	39.3%	31 months	month 176
allo-HCT in ALL	63.6%	60.6%	60.6%	60.6%	N/A	month 102
allo-HCT in CML	42.1%	42.1%	42.1%	31.6%	41 months	month 202
PFS rates	**5-year**	**10-year**	**15-year**	**20-year**	**median PFS**	**last relapse**
allo-HCT in AML	42.7%	38.6%	36.6%	36.6%	24 months	month 128
allo-HCT in ALL	59.5%	56.7%	56.7%	56.7%	N/A	month 12
allo-HCT in CML	38.9%	34.0%	34.0%	25.5%	22 months	month 67

In auto-HCT recipients with MM, both 5-year and 10-year survival rates were consistent with other studies performed in similar years. Plateau effect was obtained in PFS after 10 years of analysis. In patients with HL, 5-year survival rates were consistent with other studies, while 10-year survival rates were ~15% higher than in another study performed in the 1990's. It implies that these findings were reasonable for our inclusion period. Plateau effects in both OS and PFS were obtained after 12 years of analysis. In patients with NHLs, our results were consistent with other studies, with the exception of 10-year PFS, which was ~15% higher in our analysis. However, the reference study included only patients with relapsed/refractory NHLs, while our study included all auto-HCT recipients with NHLs.
In allo-HCT recipients with AML, both 5-year and 10-year survival rates were consistent with other studies. Plateau effects for both OS and PFS were obtained after 5 years of analysis.

While in patients with ALL, 5-year survival rates were ~15% higher than in other studies, 10-year survival rates were consistent with other studies. Notably, ALL is a disease with heterogeneous clinical manifestations and genetic background, and complex indications of transplantation, which frequently cause discrepancies in survival analyses. Plateau effects for both OS and PFS were obtained after 8 years of analysis. In patients with CML, our findings were consistent with another study from the 1980s up to 20 years of follow-up, implying a similar prognosis in individuals who cannot be treated with alternative therapies throughout the years.

Conclusions: HCT is a group of therapeutic methods with unprecedented efficacy in treating malignancies of the hematopoietic system. Its therapeutic effect is often maintained for over 15, or 20 years following transplantation. It implies the possibility to cure patients with these diseases, or, in other words, achieve a prognosis comparable to the general population.

Disclosure: Nothing to declare.

P237

MORBIDITY BURDEN, SOCIAL REHABILITATION AND QUALITY OF LIFE IN LONG-TERM SURVIVORS OF HAEMATOPOIETIC CELL TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE FROM INDIA

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Background: The combined impact of conditioning regimens and transplant-related complications can lead to chronic health conditions (CHCs) and quality of life (QoL) impairment post hematopoietic cell transplant (HCT). To our knowledge there is no data from India. We conducted this study to assess the burden of morbidity, functional status, fertility and QoL in long-term survivors post-HCT from a tertiary cancer centre in India.

Methods: Patients who underwent autologous or allogeneic HCT between 1st July 2007 and 30th June 2013 and had completed at least 10 years of follow-up were eligible. Autologous HCT for multiple myeloma was excluded. Data were collected between 1st January 2024 and 4th June 2025. CHCs were captured using a structured interview and record review against a pre-specified list of 36 cardiovascular, neurological, respiratory, renal, musculoskeletal, mucocutaneous, hematological, ocular, gastrointestinal, endocrine, ear, psychiatric and malignant disorders. Patients with pre-transplant comorbidities were excluded. Functional status, social rehabilitation and fertility outcomes were assessed using investigator-developed questionnaires, while QoL was measured using the validated FACT-BMT instrument, which includes physical, social, emotional, functional and BMT-specific subscales, with higher scores reflecting better QoL.

Results: Sixty patients consented and were included, 43 allogeneic and 17 autologous recipients. The median age at transplant was 24 years (range 4–51), and 78% were male. Indications of allogeneic transplant were acute leukemia (n=26; 43 %), CML(n=5; 8 %), aplastic anemia (n=7; 11 %), MDS/MPN (n=3, 5 %), thalassemia (n=1, 2 %),lymphoma (n=1, 2 %) and for autologous transplant were HL (n=12, 20 %), NHL (n=4,7%) and neuroblastoma(n=1,2%). Forty-five patients (75%) developed at least one CHC (median 2, range 1-5). The most frequent CHCs were diabetes mellitus (30%), hypertension (20%), dyslipidemia (13%), obesity (12%) and cataract (10%). Incidence of CHCs was higher post-allogeneic HCT in comparison to autologous HCT (diabetes in 14/43 (32%) vs 4/17 (23%); p=0.55) and hypertension in 10/43 (23%) vs 2/17 (12%);p=0.47). All 23 patients employed pre-HCT returned to work, and 26 of 28 (93%) who were pursuing education at transplant completed their education post-HCT. Regular menstrual cycles resumed in 9/22 (40%) female patients. Of 15 patients or partners desiring conception, 9 (60%) achieved pregnancy, indicating partial preservation of fertility. Median Composite FACT-BMT score was 127 (score range 0-148) suggesting good QoL in majority of the patients. Importantly, there was no difference in QoL between autologous and allogeneic HCT survivors.

Conclusions: In patients who have survived a decade after their HSCT; three-fourth of our long-term survivors have at-least one CHC. The commonest chronic health conditions in our cohort were diabetes mellitus, hypertension, dyslipidemia and obesity. Most patients were able to have gainful employment and those pursuing education were able to complete their education post-HCT. Fertility was preserved in at least half of the patients who desired conception. Majority of patients had good QoL post-HCT. This is the first study to our knowledge from India that highlights comprehensively the chronic health conditions including fertility and QoL of patients who are long term survivors and emphasizes the importance of long-term monitoring and follow up of patients post-HCT.

Disclosure: Authors have no conflict of interest to disclose.

P238

DE NOVO DONOR-DERIVED PDGFRA-REARRANGED EOSINOPHILIA AFTER HAPLOIDENTICAL HSCT IN A PATIENT WITH PRIOR AML AND T-LBL: A CASE OF SEQUENTIAL MULTILINEAGE MALIGNANCIES

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Background: Donor-derived hematologic neoplasms are rare complications after allogeneic hematopoietic stem cell transplantation (HSCT) and are distinct from recipient relapse. While myeloid/lymphoid neoplasms with eosinophilia (MLN-Eo) associated with PDGFRA rearrangements are well described, donor-derived PDGFRA-positive disease is uncommon. We report a unique case of sequential hematologic malignancies—AML followed by T-cell lymphoblastic lymphoma (T-LBL)—in a patient who subsequently developed de novo donor-derived PDGFRA-rearranged eosinophilia more than 600 days after haploidentical HSCT.

Methods: Clinical data, histopathology, cytogenetics, fluorescence in situ hybridization (FISH), and short tandem repeat (STR) chimerism analyses were reviewed in a patient presenting with late post-transplant hypereosinophilia. The timeline of engraftment and onset of eosinophilia was assessed to distinguish between relapse, secondary recipient neoplasm, and donor-derived disease.

Results: A 58-year-old male was diagnosed with FLT3-negative AML in 2014 and achieved complete remission following 7+3 induction and HiDAC consolidation. Nine years later, in 2023, he developed T-LBL presenting as large bilateral mediastinal masses, confirmed by biopsy with expression of CD3, TdT, CD5, CD7, CD99, and Ki-67 >95%. After two cycles of hyper-CVAD with marked radiographic response, he underwent haploidentical HSCT from his son in January 2024. Pre-transplant CBCs from both donor and recipient showed no eosinophilia. Post-transplant recovery was uneventful, and routine CBC monitoring through 2024–2025 demonstrated stable engraftment and no eosinophilia (eosinophils 0–7%).
The patient remained in remission until September 2025, when new-onset hypereosinophilia was observed with eosinophils rising to 40% and 23% (absolute eosinophil count ~4.1 × 10^9/L) despite stable hemoglobin, platelets, and no clinical signs of leukemic relapse. FISH for HES-associated abnormalities demonstrated a PDGFRA rearrangement in 32.67% of cells. STR chimerism at day +634 showed 100% donor alleles across all informative loci, establishing complete donor chimerism and indicating a donor-derived myeloid neoplasm rather than recurrence of the patient's previous AML or a lineage switch from T-LBL.
The donor remains hematologically normal, supporting a de novo acquisition of the mutation in the recipient. Imatinib therapy was initiated, with clinical stabilization and declining eosinophil counts.

Conclusions: This case highlights a rare instance of de novo donor-derived *PDGFRA*-rearranged eosinophilia arising more than 1.5 years post–haploidentical HSCT. It demonstrated the sequential occurrence of three distinct clonal hematologic disorders—AML, T-LBL, and donor-derived eosinophilia—representing a unique pattern of multilineage malignancies spanning both recipient and donor hematopoiesis. The absence of hematologic abnormalities in the donor strongly supports a de novo origin of the PDGFRA clone within the recipient's post-transplant milieu. This case emphasizes the need for early molecular workup and chimerism studies in post-transplant eosinophilia, as PDGFRA-positive disease is highly responsive to imatinib.

Disclosure: Nothing to declare

P239

KIDNEY TRANSPLANTATION FOLLOWING HSCT, COMPLICATED BY TA-TMA WITH PROGRESSION TO END-STAGE RENAL DISEASE

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Background: Chronic kidney disease (CKD) is a significant long-term complication affecting survivors of allogeneic hematopoietic stem cell transplantation (HSCT), with 5-20% progressing to end-stage renal disease (ESRD). The principal etiologies include nephrotoxic drug exposure, Graft-Versus-Host Disease (GVHD), recurrent viral infections (notably BK virus and cytomegalovirus), and Transplant-Associated Thrombotic Microangiopathy (TA-TMA). Kidney transplantation following related-donor hematopoietic stem cell transplantation (HSCT) raises the question of using the same individual as the kidney donor. This consideration is important due to the potential for reducing immune-mediated risks and fostering immune tolerance.

Methods: We report the case of a 7-year-old girl with severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID) who developed ESRD following haploidentical HSCT. Four years prior, she received a TCRab-depleted graft from a haploidentical donor (mother). Engraftment was achieved by day +18, with sustained full donor chimerism. Post-transplant complications included late acute GVHD grade 3 progressed to chronic GVHD of the skin and lungs, persistent viral infections with organ involvement (HHV6, CMV, BK-viruses), invasive pulmonary aspergillosis. Graft failure led to the introduction of CD34-selected boost and combined with freshly isolated donor-derived regulatory T-cell (Treg) infusion to control GVHD and improve immune reconstitution. Finally progressive CKD attributed to BK virus-associated nephritis, nephrotoxic therapy and secondary TA-TMA developed. Following last 2-year period she required renal replacement therapy and was maintained on peritoneal dialysis for 12 months.

Results: One year after the initiation of peritoneal dialysis, a kidney transplant (KT) from the same related donor (mother) was successfully performed. A personalized regimen for induction and maintenance immunosuppression was tailored based on the patient's complex history: high-dose methylprednisolone and eculizumab. Eculizumab was selected for dual rationale: 1) prophylaxis against TA-TMA recurrence, taking into account the patient's history and pro-thrombotic risk of KT; and 2) immunomodulation without inducing profound lymphodepletion. On post-operative day +4, the same donor-derived Treg cells were infused to promote tolerance and prevent immune complications. Current therapy consisted of abatacept and continued eculizumab.
Pathological examination of the removed kidney revealed diffuse global glomerulosclerosis, severe interstitial fibrosis, and C3d deposition in the glomeruli, consistent with advanced CKD caused by a combination of TA-TMA and viral nephritis.
At the two-month follow-up, the patient remains off systemic immunosuppressive therapy with excellent kidney graft function.

Conclusions: Kidney transplantation from a hematopoietic stem cell donor became a necessary step in the therapy of a patient with ESRD following HSCT. The presence of full donor chimerism prior to kidney transplantation allowed to minimize the volume of induction therapy before the solid organ transplant. The use of regulatory T-cells was considered as an additional option, aimed both at controlling GVHD and preventing kidney allograft rejection

while promoting immune tolerance. Thus, the potential to forego prolonged immunosuppression emerges as a major advantage of this approach, directly contributing to an improved long-term quality of life.

Disclosure: Nothing to declare.

P240

COST EFFECTIVENESS EVALUATION OF THE IMPLEMENTATION OF AN ON-LINE EXTRACORPOREAL PHOTOCHEMOTHERAPY TECHNOLOGY FOR POST BMT C-GVHD PREVIOUSLY TREATED WITH AN OFF-LINE TECHNOLOGY IN ANOTHER HOSPITAL

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Background: Extracorporeal photopheresis (ECP) is an immunomodulatory therapy to treat patients with graft-versus-host disease (GVHD), solid organ transplant rejection, cutaneous T-cell lymphoma and various autoimmune disease. ECP can be performed using two technologies: Off-line ECP with leukapheresis and photoactivation performed on separate devices and On-line ECP with all phases of the procedure collection, photosensitization, irradiation, and reinfusion performed within a single closed and automated system. Until July 2025 haematological patients with c-GVHD followed in our hospital were treated with an off-line ECP technology in the nearest ECP center 150 Km far from our area because our department was not equipped with a device for ECP treatments.

Methods: In July 2025 our center in Cuneo implemented a new technology (*Amicus Blue, Fresenius Kabi AG*) to perform on-line ECP in house. Four patients, affected by c-GVHD, previously treated in the other center started treatments in our center. In this paper we retrospectively evaluate our experience comparing procedures data, timing, cost and the patient perception of effectiveness and quality of life through individual Patient questionnaire.

Results: 40 ECP procedures were performed on four patients from July 2025 to December 2025 using the on-line system with a single procedure average time of ~ 120 minute using single needle procedures because of patient's choice; all ECP products were compliant with our quality controls (MNC harvest efficiency, T-cell apoptosis, microbiological evaluation). All products were reinfused to patients with no side effect. Response was comparable to previous treatments. Time related to the single procedure was reduced in all cases from 8 to 2-3 hours with a time saving of 65-75%. Cost analysis of the two different procedures showed a higher cost of 26% for the on-line one that was completely covered by patient's transportation cost for the off-line one. Evaluation of time saving cost of the on-line procedure was -390€ so that the real cost for the on-line ECP was 870€ compared to 1280 of the off-line performed in the other hospital with a cost saving of 32% (Table 1). Patient's perception of effectiveness was only slightly higher with the on-line procedure while quality

of life was clearly globally improved (mean +65%) mainly due the opportunity to perform ECP in their city with a mean time saving of ~5 hours for each "ECP procedure day".

Off-line ECP external hospital	Time (h)	Cost (€)	On-line ECP internal hospital	Time (h)	Cost (€)
Patient transportation time/cost*	~ 4 h	~ 280 €	Patient transportation time/cost*	-	-
ECP Off-line time/cost**	~ 4 h	~ 1.000 €	ECP On-line time/cost**	2 h	~ 1.260 €
Total ECP external Time/Cost	~ 8 h	~ 1.280 €	Total ECP internal Time/Cost	3 h	~ 1.260 €
			Time/cost saving On-line Procedure***	2	- 390€
			Real ECP on-Line cost		870€

*cost for patient transportation to external Hospital (RT); no transportation needed for internal on-line ECP
**calculation of all disposable and timing (converted in €) for each methodology
***calculation of time saving (converted in €) generated by the on-line technology

Table 1. Cost analysis comparison of the off-line and on-line ECP procedures in our context.

Conclusions: Our experience showed that our strategy to implement a local on-line ECP service, clearly increased the patient quality of life maintaining a high standard of ECP treatment quality with no impact on financial hospital resources.

Disclosure: Nothing to declare.

P241

ERYTHROCYTOSIS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A SINGLE-CENTRE EXPERIENCE

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Background: Post-transplant erythrocytosis is a rare complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). Its underlying mechanisms and clinical course remain poorly understood. In the literature, most reported cases involve young male

patients, frequently with aplastic anemia (AA). Here, we present our single-centre experience with post-transplant erythrocytosis in long-term survivors of allo-HSCT.

Methods: We conducted a retrospective analysis of our institutional database, including a total of 315 adult allogeneic HSCTs performed at the Ege University Adult Bone Marrow Transplantation Unit between January 2014 and November 2025. All patients were aged ≥18 years.Erythrocytosis was defined as: (a) hemoglobin/hematocrit (Hb/Hct) levels exceeding 16.5 g/dL/49% in men and 16 g/dL/48% in women, extrapolated from the WHO fifth edition polycythemia vera criteria, and (b) persistent elevation confirmed by at least two measurements obtained ≥3 months apart. Patients with conditions commonly associated with secondary erythrocytosis were excluded.

Results: A total of 11 patients who developed erythrocytosis after allo-HSCT were included. With a median follow-up of 6.1 years (range, 0.4–12.3 years), long-term outcomes could be adequately assessed. The cohort was predominantly male (10/11, 91%), with a median age of 32 years (range, 23–52 years).Underlying diagnoses included aplastic anemia (AA, n=4), acute myeloid leukemia (AML, n=3), primary myelofibrosis (PMF, n=1), pure red cell aplasia (PRCA, n=1), myelodysplastic syndrome (MDS, n=1), and paroxysmal nocturnal hemoglobinuria (PNH, n=1). Five patients (45%) received grafts from matched sibling donors and six (55%) from matched unrelated donors; 10 patients (91%) had fully matched (10/10) donors. Two patients required immunosuppressive therapy for chronic GVHD. Erythrocytosis developed at a median of 32 months (range, 23–52 months) following allo-HSCT. The median duration after the onset of erythrocytosis was 14.3 months (range, 2.7–56.9 months). At the time of erythrocytosis, the median LDH level was 222 U/L (range, 171–311 U/L), with mild LDH elevation observed in 5 patients (45%). Median leukocyte and platelet counts were within normal ranges, and no patient had splenomegaly. Among evaluable patients, serum erythropoietin levels were within normal limits, and no patient demonstrated elevated EPO levels. JAK2 V617F mutation analysis, performed in 5 patients, was negative in all cases. All patients received low-dose aspirin as antithrombotic prophylaxis. Therapeutic phlebotomy was required in 3 patients (27%), while the remaining patients were managed conservatively without additional cytoreductive interventions. A single thrombotic event occurred, with one patient experiencing myocardial infarction requiring coronary stent implantation during the sixth year of follow-up. All patients were alive at the last follow-up. Patient characteristics are summarized in Table 1.

Table 1. Patient Characteristics

Patients, n	11
Male sex, n (%)	10 (91)
Age, years	32 (23–52)
Underlying diagnosis, n Aplastic anemia AML Other*	 4 3 4

Follow-up duration, years	6.1 (0.4–12.3)
Time from HSCT to erythrocytosis, months	32 (23–52)
Normal EPO, n / tested	4/4
JAK2 mutation detected, n / tested	5/0
Low-dose aspirin, n (%)	11 (100)
Therapeutic phlebotomy, n (%)	3 (27)

* MDS, PRCA, PMF, PNH

Conclusions: Post-transplant erythrocytosis is an uncommon complication. In our single-centre cohort, predominantly affecting young male long-term survivors, it followed a generally benign clinical course and was not associated with clonal myeloproliferative disease, as evidenced by normal erythropoietin levels and the absence of JAK2 mutations among evaluable patients. Patients were successfully managed with low-dose aspirin, with or without therapeutic phlebotomy. However, long-term surveillance remains warranted to monitor potential vascular complications.

Disclosure: Nothing to declare.

P242

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH SEVERE CARDIOVASCULAR COMORBIDITY

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Background: Allogeneic hematopoietic stem cell transplantation (alloHSCT) is a key therapeutic option for patients with hematologic malignancies. However, the prevalence of cardiovascular disease (CVD) among alloHSCT recipients is higher than in general population. Prior exposure to cardiotoxic antineoplastic therapy, advanced age, and a history of coronary interventions further increase cardiovascular risk. Patients with ischemic heart disease, previous myocardial infarction, or myocardial revascularization are frequently considered at very high CVD risk, and evidence regarding the safety of alloHSCT in this population remains limited. Real-world data addressing post-transplant cardiovascular outcomes in such patients are particularly scarce.

Methods: Seven patients with hematologic malignancies and confirmed cardiovascular disease who underwent alloHSCT were included to the analysis. Median age was 63 years

(range 48–67); four patients were male and three female. The median duration of hematologic disease prior to transplantation was 17 months, and the median overall duration of hematologic disease follow-up was 50 months. All patients had documented CVD, including ischemic heart disease, prior atherothrombotic myocardial infarction or myocardial infarction with non-obstructive coronary arteries (MINOCA), coronary stenting, coronary artery bypass grafting, cerebrovascular disease, valvular heart disease. Due to CVD anamnesis, all patients were stratified to the very high cardiovascular risk category according to European Society of Cardiology stratification.
Pre-transplant assessment included cardiovascular history, electrocardiography, echocardiography, and laboratory markers of myocardial dysfunction and atherosclerosis. Data on prior antineoplastic therapy, conditioning regimens, graft-versus-host disease (GVHD) prophylaxis, cardioprotective treatment, and cardiovascular events in early (<100 days) and late post-transplant period were collected.
Cardiovascular risk of new or worsening pre-existing CVD at 1 and 5 years was estimated using the CARE-BMT Risk Score.

Results: Patients' characteristic and the details of alloHCT are presented in Table. All patients successfully proceeded to alloHSCT. Median follow-up after alloHSCT in all 7 patients was 14 months, while in survivors after alloHST it was 40,5 months. No acute or chronic GVHD ³ grade 2 was observed.
Four patients remain alive after alloHSCT, and no deterioration of CVD was observed in the post-transplant period. Of these, two patients (with diffuse large B-cell lymphoma and chronic myeloid leukemia, respectively) had a history of unstable angina and prior coronary artery bypass grafting; one patient with acute myeloid leukemia had stable coronary artery disease, a history of cerebrovascular accident, and arterial thrombosis; and one patient with peripheral T-cell lymphoma had a history of MINOCA).
Three patients with a history of myocardial infarction and coronary artery stenting (underlying hematologic malignancies: hepatosplenic T-cell lymphoma, blast transformation of essential thrombocythemia, and acute myeloid leukemia) had a stable cardiovascular status; however, they died in the post-transplant period due to relapse of the underlying disease.

Patient	Hematologic Malignancy	Cardiovascular History	Time from CV Event to HSCT (mon)	CARE-BMT Score	Cardioprotective therapy	Conditioning Regimen / GVHD Prophylaxis	Date of allo-HSCT	Follow-up after HSCT (mon)	Outcome
F / 53y	Essential thrombocythemia, blast transformation	MI with RCA stenting	11	5	Antiplatelet, β-blocker, statin	FluBu8 / PtCy + Rux	09 Apr 2024	8	Relapse, death

		(June 2024)							(Dec 2024)
M / 67y	Hepatosplenic T-cell lymphoma	MI, LAD stenting (June 2023); aortic and mitral valve stenosis; AH	12	7	Antiplatelet, β-blocker, statin	FluBend / PtCy + Rux + abatacept	19 June 2024	14	Relapse, death (Aug 2025)
M / 48y	Hodgkin lymphoma → DLBCL in 13 years	IHD, unstable angina; LCx stenting (Feb 2018)	60	4	Antiplatelet, β-blocker, Ca-channel blocker, statin	FluBu8 / PtCy	20 Feb 2023	33	Alive, no CV events
M / 52y	Chronic myeloid leukemia	Stable IHD; CABG (Nov 2017)	48	6	Antiplatelet, β-blocker, statin	FluBu8 / PtCy + tacrolimus + MMF	02 Nov 2021	48	Alive, no CV events
F / 65y	Peripheral T-cell lymphoma	MINOCA (2008)	192	5	Not required	FluBu8 / PtCy + tacrolimus + MMF	11 Sep 2024	14	Alive, no CV events
M / 64y	Acute myeloid leukemia	Stable angina; CHF; AH; stroke (2010)	84	11	Antiplatelet, β-blocker, ACE inhibitor, statin	FluBu8 / PtCy + tacrolimus + MMF	30 Mar 2017	104	Alive, no CV events
F / 63y	Acute myeloid leukemia	IHD; MI (2016); multiple coronary stents (2016–2024)	91	5	Antiplatelet, statin, diuretic	FluBu8 / PtCy + tacrolimus + MMF	20 June 2024	7	Relapse, death (Feb 2025)

Abbbeviations and acronyms: M – male, F – female, CV – cardiovascular; HSCT – hematopoetic stem cell transplantation; CARE-BMT – Cardiovascular Registry in Bone Marrow Transplantation; GVHD – graft-versus-host-disease; MI – myocardial infarction;

RCA – right coronary artery; left anterior descending artery; IHD – ischemic heart disease; LCx – circumflex artery; AH – arterial hypertension; CABG – coronary artery bypass grafting; MINOCA – myocardial infarction with non-obstructive coronary arteries; CHF – congestive heart failure; ACE-inhibitor – angiotensin-converting enzyme inhibitor; FluBu8 – fludarabine150 mg/m2 + busulfan 8 mg/kg; PtCy – posttransplant cyclophosphamide; Rux – ruxolitinib; FluBend – fludarabine 90 mg/m2 + bendamustine 130 mg/m2; Tx – tacrolimus; MMF – mycophenolate mofetil.

Conclusions: The presence of severe cardiovascular comorbidity, including prior myocardial infarction and coronary revascularization, should not be considered as an absolute contraindication to alloHSCT. In patients with stable cardiovascular disease, careful pre-transplant cardiovascular assessment and continuation of cardioprotective therapy allow alloHSCT to be performed safely without cardiovascular comorbidity exacerbation.

Disclosure: Nothing to declare.

P244

SUCCESSFUL TREATMENT OF SECONDARY HISTIOCYTIC SARCOMA AFTER B-ALL TRANSPLANTATION WITH TARGETED THERAPY COMBINED WITH RADIOTHERAPY: A CASE REPORT

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Background: This article reports a case of secondary histiocytic sarcoma (HS) following transplantation for B-cell acute lymphoblastic leukemia (B-ALL), in which the patient achieved long-term survival after receiving targeted therapy with a MEK1/2 inhibitor combined with a bispecific antibody (BsAb) and radiotherapy.

Methods: A patient, 17-year-old male, was diagnosed B-ALL in August 2020.
Bone marrow morphology evaluation confirmed the second completed remission (CR), the patient subsequently underwent unrelated allogeneic hematopoietic stem cell transplantation on 26th Aug 2021. Consecutive bone marrow morphology revealed maintained CR and chimerism analysis demonstrated persistent mixed chimerism after transplantation. The decitabine and a single reinfusion of the donor's cryopreserved peripheral blood stem cells were administered.
In June 2022, the patient presented fever without responding to anti-infective treatment. CT-scan revealed rib bone destruction. Whole-body PET-CT showed multiple focal areas of increased metabolic activity throughout the skeletal system. Bone marrow morphology revealed CR. On 28th July 2022, Ultrasound-guided biopsy of a lower rib lesion confirmed histiocytic sarcoma on pathological examination, and genetic testing identified FANCC, BRCA2, ARAF and NF1 mutations.
The patient initiated MEK1/2 inhibitor Trametinib on 19th August 2022. The osteolytic destruction was improved. In May 2024, multiple abnormal changes observed in the liver and

pancreatic tail by abdominal ultrasound. CT-guided liver biopsy indicated involvement by histiocytic sarcoma. Genetic testing identified new PTPN11, SH2B3, LUC7L2, SF3A1 mutation. Consideration of Disease progression, trametinib was discontinued due to presumed drug resistance.
On 21st June 2024, the patient started on oral MEK1/2 inhibitor tunlametinib at a dose of 12 mg twice daily which induced severe Skin and soft tissue infection after 4 weeks, necessitating a dose reduction to 6 mg twice daily without interruption of therapy. The Skin and soft tissue infection occurred intermittently with symptomatic treatment. After 6th August 2025, the dose of trametinib was reduced to 9 mg once daily which has been continued to the present. The Skin and soft tissue infection was completely recovery. After six months, PET/CT indicated nodular metabolic activity in the pancreatic tail, suspected to represent residual HS and slightly increased metabolic activity in liver segment 7 (S7). Tunlametinib was combined with one dose of ipilimumab. After ten months, proton therapy was administered targeting the lesions in the pancreatic tail (GTV60GyE/30F, CTV54GyE/30F) and liver S7 (57GyE/19F). Ipilimumab was given twice during radiotherapy and followed by an additional once after radiotherapy.

Results: Bone destruction showed a significant reduction in pre and post trametinib (Image 1-A). The nodules in the pancreatic tail and liver S7 decreased in size before and after tunlametinib (Image 1-B).
The patient is recovering well at home and able to perform activities of living independently by follow-up visit.

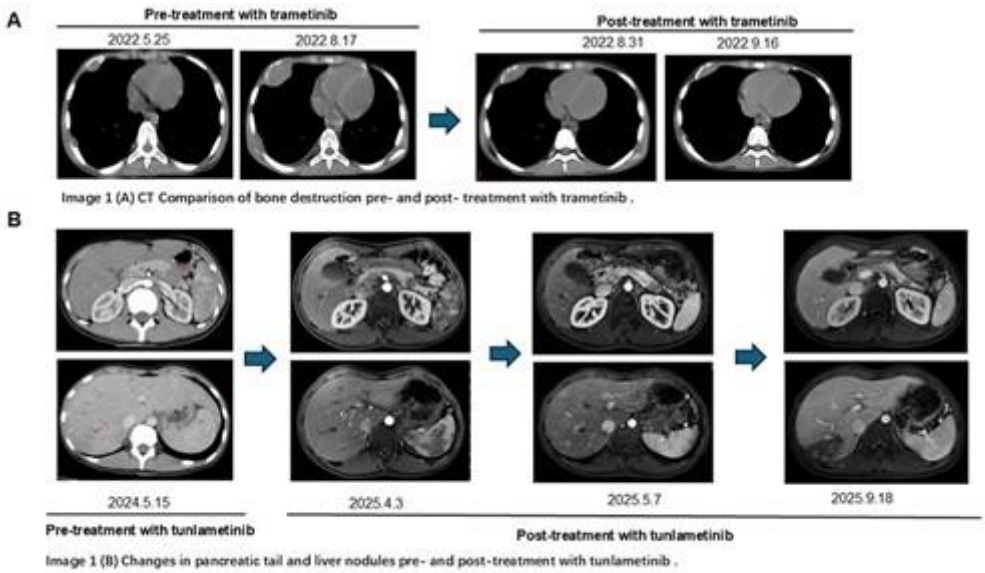

Image 1 (A) CT Comparison of bone destruction pre- and post- treatment with trametinib .
Image 1 (B) Changes in pancreatic tail and liver nodules pre- and post-treatment with tunlametinib .

Conclusions: This patient presents with a rare secondary HS following B-ALL transplant. There is no standardized or consistently effective treatments. Patients who are gene test positive, targeted therapies can be considered. However, genetic evolution may occur during treatment and frequently lead to resistance. The combination of MEK1/2 inhibition with BsAb and radiotherapy may offer potential survival benefits for patients with HS.

Disclosure: Nothing to declare.

Artificial Intelligence and Computational Approaches

GS2-2

HIGH-THROUGHPUT DEEP LEARNING-BASED PROFILING OF CAR-T IMMUNE DYNAMICS FROM ROUTINE PERIPHERAL BLOOD SMEARS

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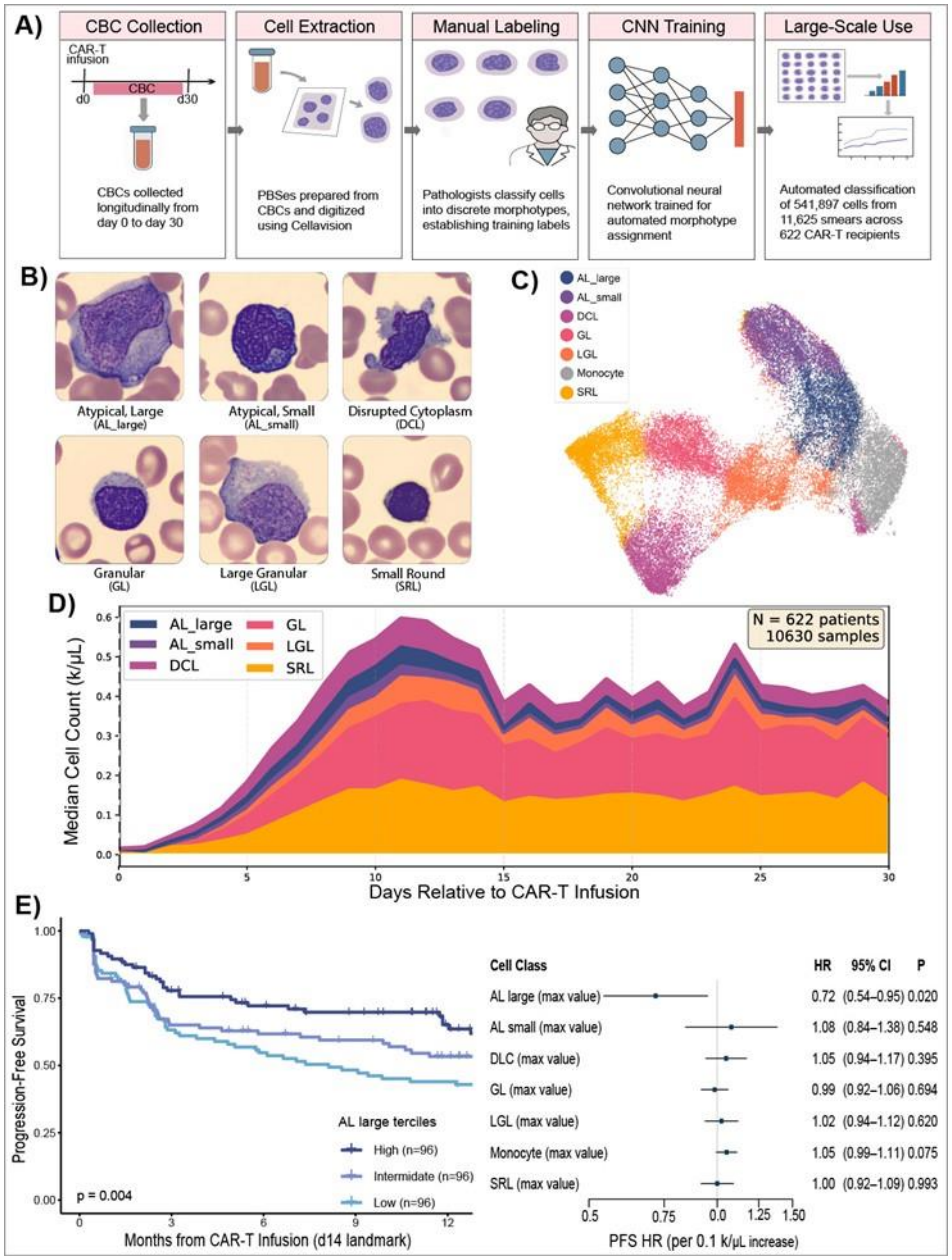
Background: Real-time assessment of CAR T-cell activity remains challenging in routine clinical practice, as available assays are resource-intensive and poorly suited for longitudinal monitoring at scale. Peripheral blood smears (PBS) are inexpensive, ubiquitous, and serially collected, yet remain largely unexplored as an immune-monitoring modality. We developed a deep learning–based framework to transform standard PBS into scalable and quantitative markers of post–CAR-T immune dynamics.

Methods: We assembled a large repository of digitized PBS obtained between days 0–30 after infusion from patients treated with commercial CAR-T products for non-Hodgkin lymphoma, B-cell acute lymphoblastic leukemia, and multiple myeloma (2018–2025). Expert hematopathologists reviewed early post-infusion smears and defined recurrent lymphocyte morphologies ("morphotypes"). A convolutional neural network was trained to classify single-cell images into these morphotypes (**Fig. 1A**). Longitudinal morphotype distributions were quantified and associated with clinical outcomes. Correlations between morphotype abundance and CAR-T transgene levels measured by digital droplet PCR (ddPCR) were assessed using Spearman's coefficient.

Results: Hematopathologist curation of 1,600 lymphocyte-like cells from days 0–14 post-infusion defined six reproducible lymphocyte morphotypes based on cell size, nuclear contour, cytoplasmic texture, and granularity, with monocytes add as a distinct class (**Fig. 1B).** Using this framework, we trained MorphoCAR, a convolutional neural network that

achieved strong performance on patient-separated test data (macro-accuracy 83%, AUROC 0.98).
MorphoCAR was applied to 541,897 single-cell images derived from 11,625 peripheral blood smears obtained between days 0 and 30 following CAR-T infusion in a cohort of 622 patients. UMAP projection of learned embeddings revealed a coherent morphologic landscape with clear clustering by morphotype (**Fig. 1C**). Longitudinal analyses demonstrated dynamic morphotype trajectories (**Fig. 1D**), with variations by CAR-T product. For instance, large and small atypical lymphocytes (ALs) expanded early post-infusion, typically peaking on days 6–14 before contracting, whereas small round lymphocytes (SRLs) showed early expansion followed by stabilization. Large AL expansion was highest with liso-cel and cilta-cel and lowest with tisa-cel.
Among patients with large B-cell lymphoma (n=322) treated with axi-cel, liso-cel, or tisa-cel, higher peak abundance of large AL morphotypes during the early expansion window was independently associated with improved progression-free survival in multivariable Cox models landmarked at day 14 (**Fig. 1E**). No prognostic association was observed for other morphotypes or for absolute lymphocyte count, underscoring the added value of morphology-resolved immune profiling.
In a subset of patients with paired PBS and ddPCR measurements, CAR transgene levels correlated positively with both large AL ($\rho = 0.534$, $p = 0.023$) and small AL ($\rho = 0.479$, $p = 0.044$) morphotypes. Finally, CAR-T cells expressing activation marker CD69 sorted from infusion products consistently exhibited morphologic features closely resembling the large AL phenotype.



Conclusions: Artificial intelligence applied to routine peripheral blood smears reveals quantitative and qualitative immune signals that enhance assessment of CAR-T activity and treatment risk. This study delivers the first scalable morphology-based monitoring tool for CAR-T therapy and create the basis for real-time immune analytics grounded in routine clinical data.

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OS07-06

MULTIMODAL PREDICTION OF EARLY CARDIOVASCULAR TOXICITY AFTER CAR-T THERAPY

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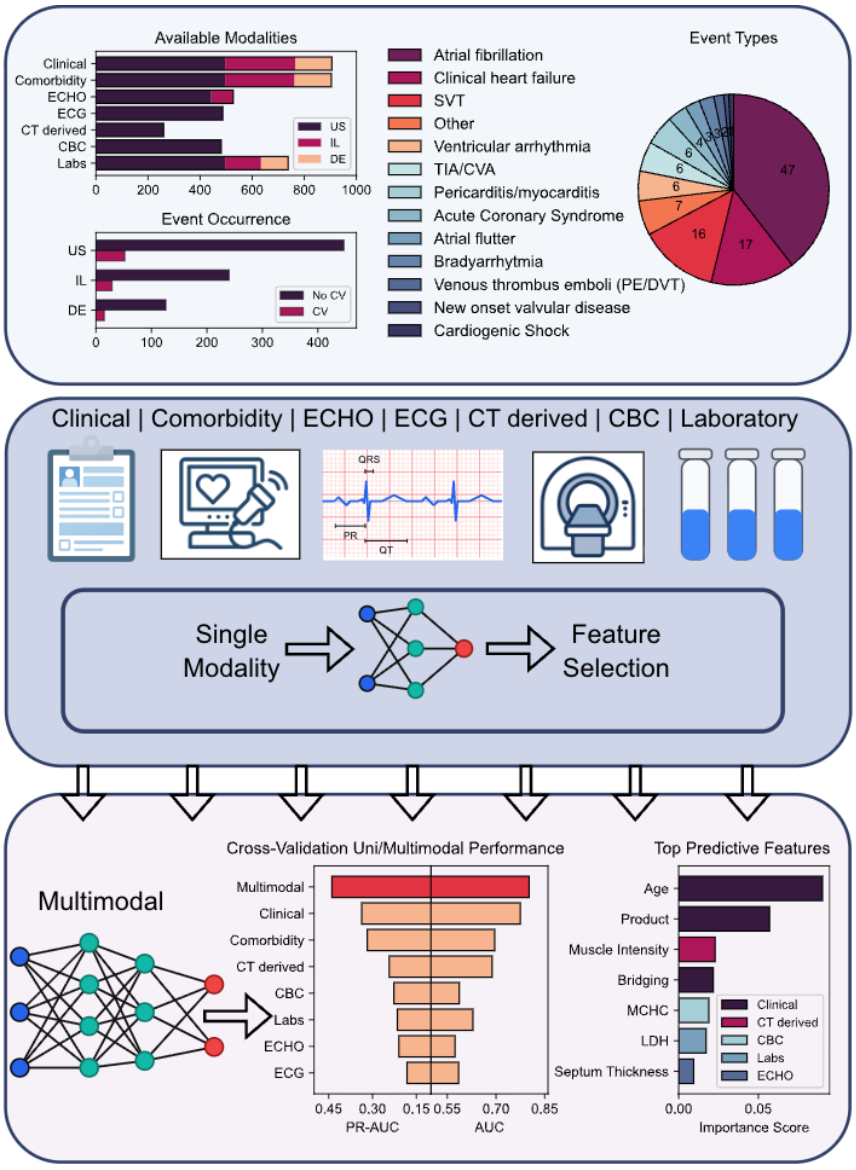
Background: Cardiovascular toxicity is an increasingly recognized complication of chimeric antigen receptor T-cell (CAR-T) therapy, yet remains difficult to anticipate at the individual patient level. Although comprehensive cardiovascular assessments are routinely performed prior to CAR-T, these heterogeneous data are not systematically integrated for risk stratification. We developed a multimodal machine-learning framework that integrates clinical, laboratory, imaging, and electrophysiologic data to predict early cardiovascular toxicity after CAR-T therapy.

Methods: We conducted a multicenter international study of adult patients treated with commercial CAR-T therapy for large B-cell lymphoma, mantle cell lymphoma, or indolent B-cell lymphoma across tertiary centers in the United States (US), Germany (DE), and Israel (IL). The primary endpoint was composite cardiovascular toxicity within 30 days of CAR-T infusion, including clinically significant arrhythmias, heart failure, ischemic and cerebrovascular events, and other major cardiovascular complications.
Pre-treatment data included clinical characteristics (demographics-, disease-, and treatment-

related factors) and comorbidities, laboratory testing and complete blood counts, electrocardiography (ECG), echocardiography, and CT-derived body composition features, with variable availability across centers (**Fig. 1**). Data were analyzed using a multimodal machine-learning framework with modality-specific encoders that integrate heterogeneous inputs and accommodate missing modalities. Model performance was assessed using internal cross-validation in the US development cohort and external validation across international cohorts, using area under the receiver operating characteristic curve (AUC) and precision–recall area under the curve (PR-AUC).



Results: The study included 906 patients across five centers (development cohort n=496; validation cohort n=410). Most patients had large B-cell lymphoma (development 83%, validation 86%), followed by mantle cell lymphoma (11%, 9%) and indolent B-cell

lymphoma (6%, 5%). CAR-T products included axi-cel (41%, 62%), tisa-cel (16%, 25%), liso-cel (37%, 4%), and brexu-cel (6%, 9%).
Approximately 10% of patients in the development cohort experienced cardiovascular toxicity within 30 days, most commonly arrhythmias. Event rates in external validation cohorts ranged from 7% to 15%.
In unimodal analyses, clinical characteristics, comorbidity profiles, and CT-derived body composition measures demonstrated the strongest predictive contribution, while laboratory parameters, complete blood counts, ECG, and echocardiography provided complementary information. Given the low event rate, PR-AUC was particularly informative (higher value corresponds with better performance). The multimodal model outperformed all unimodal approaches, achieving an AUC of 0.81 and PR-AUC of 0.43 in internal cross-validation (Fig. 1).
Feature-importance analyses (Fig. 1) for prediction of 30-day cardiovascular toxicity identified established clinical determinants, including age, CAR-T product, and bridging therapy, alongside modality-specific predictors such as CT-derived skeletal muscle radiodensity and CBC-derived hematologic indices, including mean corpuscular hemoglobin concentration.
External validation of the multimodal model demonstrated comparable discrimination despite heterogeneous data availability. In Israeli cohorts, performance was AUC 0.70; PR-AUC 0.26, and in the German cohort AUC 0.69; PR-AUC 0.30, indicating stable performance across independent healthcare settings.

Conclusions: This international multicenter study establishes an artificial intelligence–based multimodal framework for predicting early cardiovascular toxicity after CAR-T therapy. By integrating routinely collected pre-treatment data across clinical, imaging, and laboratory domains, this approach enables robust, generalizable risk stratification and supports a shift toward AI-informed, risk-adapted cardiovascular assessment and management in CAR-T recipients.

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Miguel-Angel Perales- Reports honoraria from Allogene, Celgene, Bristol-Myers Squibb, Exevir, ImmPACT Bio, Incyte, Kite/Gilead, Merck, Miltenyi Biotec, Nektar Therapeutics, Novartis, Omeros, OrcaBio, Pierre Fabre, Sanofi, Syncopation, Takeda, VectivBio AG, and Vor Biopharma. He serves on DSMBs for Cidara Therapeutics and Sellas Life Sciences. He has ownership interests in Omeros and OrcaBio. He has received institutional research support for clinical trials from Allogene, Genmab, Incyte, Kite/Gilead, Miltenyi Biotec, Novartis, and Tr1x.

B275

HLA STRUCTURAL PROFILES IDENTIFIED BY PROTEIN LANGUAGE MODELS PREDICT GRAFT FAILURE IN HAPLOIDENTICAL TRANSPLANTATION

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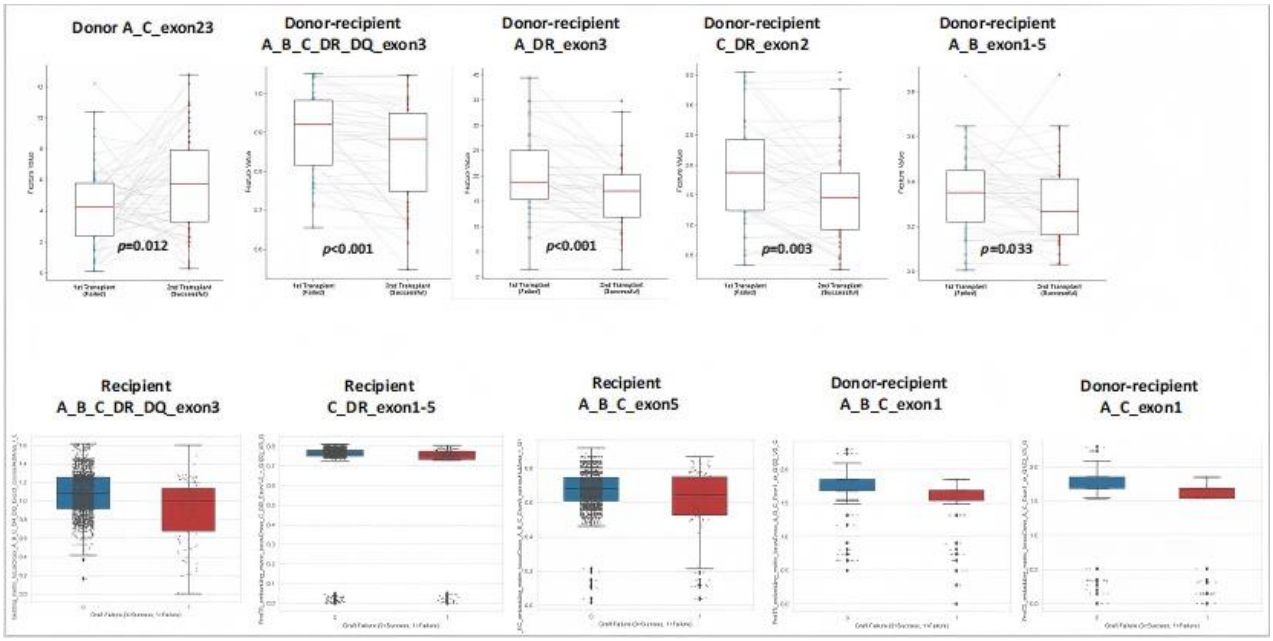
Background: Graft failure (GF) remains a fatal complication after haploidentical stem cell transplantation (haplo-SCT). While our previous multicenter, retrospective study suggested that changing donors improves outcomes in second transplantation (*Haematologica, 2025*), the underlying immunological mechanisms, particularly those involving donor-specific or donor–recipient paired factors remain unclear. In haplo-SCT, conventional HLA matching based on allelic identity often fails to capture subtle physicochemical and structural incompatibilities that drive immunogenicity. With recent advances in protein language models (PLMs), we employed a machine learning approach to explore the association between HLA structural features in donors or donor–recipient pairs and GF, aiming to identify HLA structural biomarkers for GF prediction.

Methods: 127 patients who experienced GF after haplo-SCT and subsequently underwent a second transplantation from the same (n=53) or a different donor (n=74) were analyzed. Using protein embedding models (ESM, ProtT5, and protV), functional embedding vectors from the amino acid sequences encoded by HLA alleles were extracted. Specifically, a novel PLM-based HLA functional diversity metric (the joint convex hull area) representing the total breadth of the HLA physicochemical landscape was defined. Metrics were calculated for donors and donor-recipient pairs in the GF cohort. Successful second donors from the same patients, as well as donors from a historical haplo-SCT cohort without GF (n=1,699), were used as control groups for comparative analysis.

Results: From an initial pool of 8,718 features, five structural features were identified to be significantly associated with GF ($p < 0.05$). Spatial mapping demonstrated that all five features involved cross-class interactions between HLA class I and class II loci, rather than single-locus effects, highlighting the importance of overall structural topology. Feature importance analysis revealed that one of the five features was donor-intrinsic, while the other four reflected interactions between donors and recipients. Compared with the successful second donors, the failed first donors exhibited a smaller hull area spanning HLA-A to HLA-C loci (A_C_exon23, p=0.012, HR=0.4987). Failed first donor–recipient pairs displayed larger hull areas across several multi-locus regions (A_B_C_DR_DQ_exon3, p<0.001; A_DR_exon3, p<0.001; C_DR_exon2, p=0.003; A_B_exon1-5, p=0.033;) relative to successful second-transplant pairs (Figure 1, top panels). Compared with the non-GF control cohort (n=1699), five structural features were established, including three recipient-intrinsic features (A_B_C_DR_DQ_exon3, C_DR_exon1-5, A_B_C_exon5) and two donor-recipient interaction features (A_B_C_exon1, A_C_exon1) (Figure 1, bottom panels). A composite risk score based on these five features showed robust predictive performance (AUC=0.656).



Conclusions: To our knowledge, this is the first study to interrogate GF mechanisms in haplo-SCT through an HLA immunogenicity lens using protein language models. Our findings suggest that, beyond conventional HLA matching, structural and spatial features of HLA molecules may identify “bad donors” or “bad pairs” that are at high risk for GF. This approach could refine donor selection and risk stratification regarding GF for haploidentical transplantation.

Clinical Trial Registry: NA.

Disclosure:

All authors declare no conflict of interest.

B276

MINOR HISTOCOMPATIBILITY ANTIGEN BURDEN AS A RISK FACTOR FOR ACUTE GVHD AFTER HLA-IDENTICAL UNRELATED DONOR TRANSPLANT

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Background: GvHD remains a major cause of morbidity and mortality after allogeneic hematopoietic cell transplantation (alloHCT). Beyond HLA mismatch, GvHD occurrence in HLA-identical transplants suggests the relevance of minor histocompatibility antigens (mHAg), donor-recipient (D/R) differing peptides arising from genetic variation and expected to be highly immunogenic due to lack of donor tolerance. Recent collaborative studies in which a computational framework for exome-wide mHAg discovery was developed associated mHAg load with increased risk of acute GvHD (aGvHD) in AML/MDS patients treated with HLA-identical sibling-donor alloHCT (Cieri *et al.*, Nat Biotechnol. 2025). Since mHAgs as GvHD biomarkers beyond HLA-identical sibling-donor HCT remain unexplored, we herein aimed to assess such mHAg-GvHD association in the HLA-identical unrelated-donor HCT setting.

Methods: We recruited 52 AML/MDS patients receiving their first HLA-matched unrelated-donor HCT between 2013-2021 and analyzed D/R pairs through whole-exome sequencing and an adaptation of our previous pipeline. For mHAg load quantification, we filtered D/R identified variants to retain non-synonymous polymorphisms absent in the donor and occurring on genes expressed on GvHD target organs. We retrieved organ-specific expression profiles from single-cell RNAseq datasets (liver, lung, skin, vaginal wall, eye, gastrointestinal tract, oral mucosa and hematopoietic tissue), selecting all genes with pseudobulk expression above 20 counts per million in at least one cell cluster. Finally, we computed all variant-encompassing 8-11-mer peptides and kept those which could not arise from any other loci (blasting them against D/R exome-inferred proteomes) and which would be presented on patient-specific HLA-I molecules, relying on NetMHCpan-4.2 for binding assessment (predicted rank below 0.5%). We compared GvHD cumulative incidence (CI) between groups using Gray's test and Fine-Gray model for hazard ratio (HR) calculation, considering non-GvHD death and relapse as competing events.

Results: Median mHAg load was 1208 peptides, which we used to stratify patients into low or high mHAg groups. Although we did not find differences regarding chronic GvHD, our results showed greater grades II-IV aGvHD CI in patients with high mHAg load, *P*=0.049 (Gray's test) and HR [95% confidence interval] = 2.99 [0.98–9.15], *P*=0.055 (univariable Fine-Gray model) (Figure 1). Subsequent multivariable Fine-Gray analysis adjusting for D/R ages, female-to-male transplant, graft source, conditioning regimen and GvHD prophylaxis suggested mHAg load as independent predictor of grades II–IV aGvHD (Table 1).

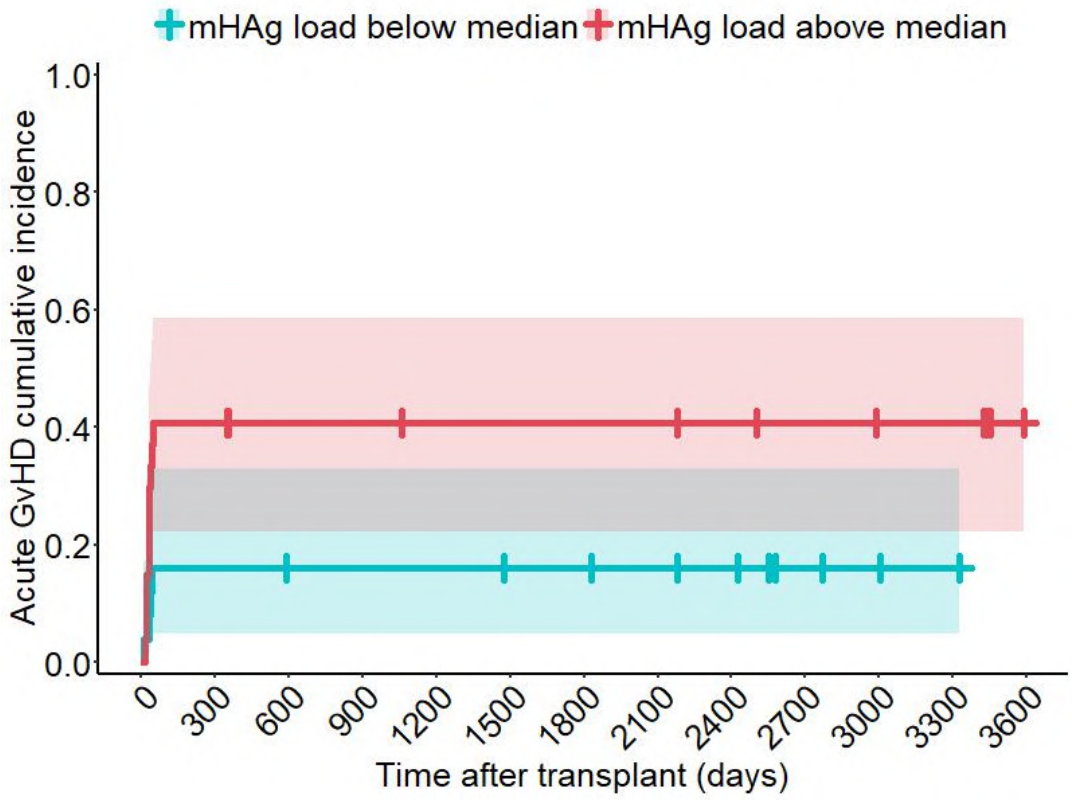

Figure 1: High mHAg load patients display greater aGvHD incidence after unrelated-donor HCT. Grades II-IV aGvHD CI of patients below (blue) or above (red) median mHAg number of 1208. One-year aGvHD CI [95% confidence interval] was 16% [4.9%–33%] and 41% [22%–59%] for low and high groups, respectively. Two-sided *P*=0.04919 (Gray's test); HR = 2.99 [0.98–9.15], *P*=0.055 (Fine-Gray model); n=52.

Variable	n (%) / median (IQR)	HR	95% confidence interval	P
mHAg load				
Below median	25 (48.1)	-	-	-

Variable	n (%) / median (IQR)	HR	95% confidence interval	P
Above median	27 (51.9)	3.93	0.90, 17.1	0.068
Donor age	29 (24.5, 36.5)	0.99	0.94, 1.04	0.6
Patient age	53 (40, 62)	1.00	0.94, 1.05	0.9
Female to male transplant				
No	46 (88.5)	-	-	-
Yes	6 (11.5)	0.27	0.04, 1.84	0.2
Graft source				
Peripheral blood	49 (94.2)	-	-	-
Bone marrow	3 (5.8)	2.09	0.33, 13.2	0.4
Conditioning regimen				
Reduced intensity	24 (46.2)	-	-	-
Myeloablative	28 (53.8)	1.20	0.28, 5.08	0.8
GvHD prophylaxis				
CNI based	35 (67.3)	-	-	-
PTCy/ATG based	17 (32.7)	0.37	0.10, 1.42	0.2

Table 1: Multivariable Fine-Gray model for aGvHD risk assessment. mHAg: minor histocompatibility antigens; CNI: calcineurin inhibitor; PTCy: post-transplant cyclophosphamide; ATG: anti-thymocyte globulin; IQR: interquartile range; HR: hazard ratio.

Conclusions: Our results suggest mHAg as useful aGvHD biomarkers in HLA-identical unrelated-donor transplants. This supports the potential of mHAg-based donor selection and post-transplant risk stratification and therapeutic intervention to reduce aGvHD incidence and thus decrease healthcare costs and improve patients' quality of life.

Disclosure: Nothing to declare.

B277

STACKED MACHINE-LEARNING SURVIVAL MODELING FOR MYELODYSPLASTIC SYNDROMES UNDERGOING ALLOGENEIC TRANSPLANTATION: AN EBMT REGISTRY STUDY

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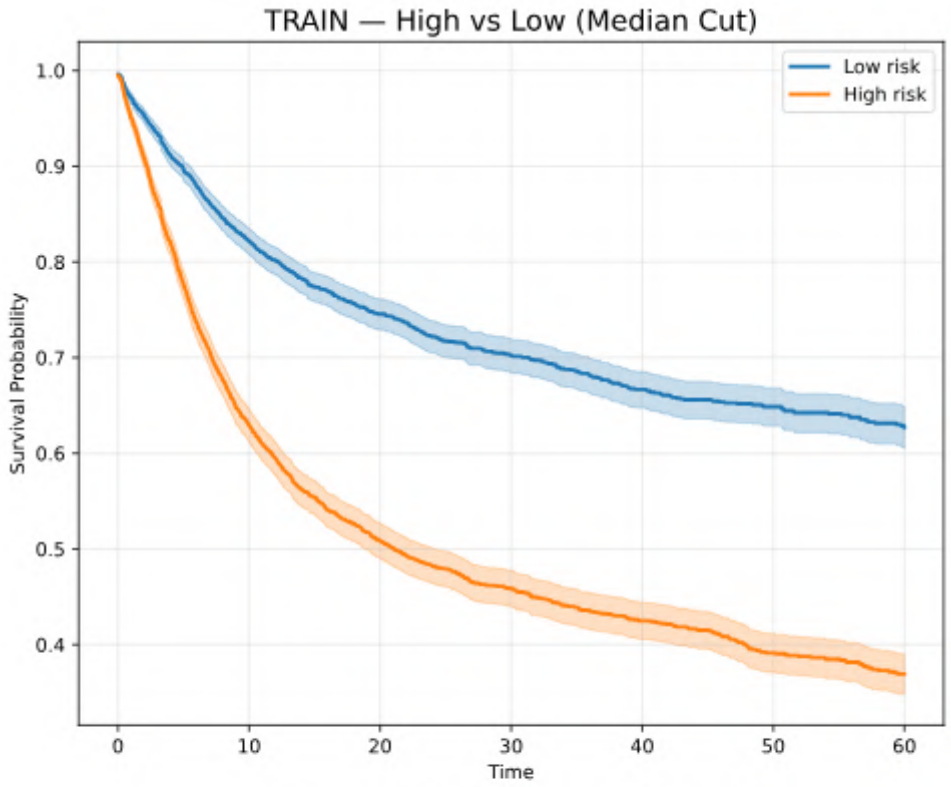
Background: Allogeneic hematopoietic cell transplantation (allo-HCT) is the only potentially curative option for patients with myelodysplastic syndromes (MDS). However, only 10-15% access to this procedure, post-transplant outcomes remain highly heterogeneous, and widely used scores such as IPSS-R, developed outside the transplant setting, show only modest discrimination. Using the EBMT registry, we aimed to develop and validate a stacked machine-learning (ML) survival model for MDS patients undergoing allo-HCT and to benchmark it against other clinical scores (IPSS-R, HCT-CI) to assess its incremental prognostic value.

Methods: We analyzed 10,129 patients with MDS undergoing allo-HCT, partitioning the EBMT dataset by country into a ~70% training and ~30% test cohort. Missing baseline data were handled using Multiple Imputation by Chained Equations, incorporating 34 available pre-transplant variables into the models. Four survival analysis algorithms (L2-penalized Cox, elastic-net Cox, Random Survival Forest, and Gradient Boosting) were trained via cross-validation, and risk estimates were used to train a stacked survival model with penalized Cox and Random Survival Forest metalearners. Performance was evaluated in the geographically

independent test cohort using the concordance index and benchmarked against IPSS-R and HCT-CI.

Results: Thirty-four baseline variables were used for model development, including demographic characteristics (patient and donor age, sex), disease-related factors at diagnosis (blast percentage, cytogenetic risk, MDS subtype), performance status, donor–recipient compatibility measures (HLA matching, specific locus mismatches, donor relationship), transplant-related features (conditioning regimen, stem-cell source, type of GvHD prophylaxis), and established clinical indices (HCT-CI and IPSS-R). Four types of survival models were trained. In the training set, their performance was broadly comparable (CoxNet: 0.618, CoxPen: 0.620, RSF: 0.624, Gradient Boosting: 0.625). In the external test cohort, performance remained stable (CoxNet: 0.620, RSF: 0.616, Gradient Boosting: 0.620, CoxPen: 0.622). To improve predictive accuracy, out-of-fold risk estimates from all four models were combined into a stacked survival model. Among the two metalearners evaluated, the Random Survival Forest metalearner achieved the best internal performance (C-index 0.629 vs 0.628 for penalized Cox). In the external test cohort, the stacked model showed a C-index of 0.625, very similar to the penalized Cox metalearner (0.623). Compared with the stacked model, conventional clinical scores showed markedly weaker prognostic performance in patients with complete data (IPSS-R: n=2,489; HCT-CI: n=8,991). For IPSS-R, the C-index was 0.523 in train and 0.578 in test, while the stacked model reached 0.650 and 0.647, respectively. HCT-CI achieved 0.535 in train and 0.547 in test, compared with 0.642 and 0.629 for the stacked model.


TRAIN — High vs Low (Median Cut)
Low risk
High risk
Survival Probability
Time
1.0
0.9
0.8
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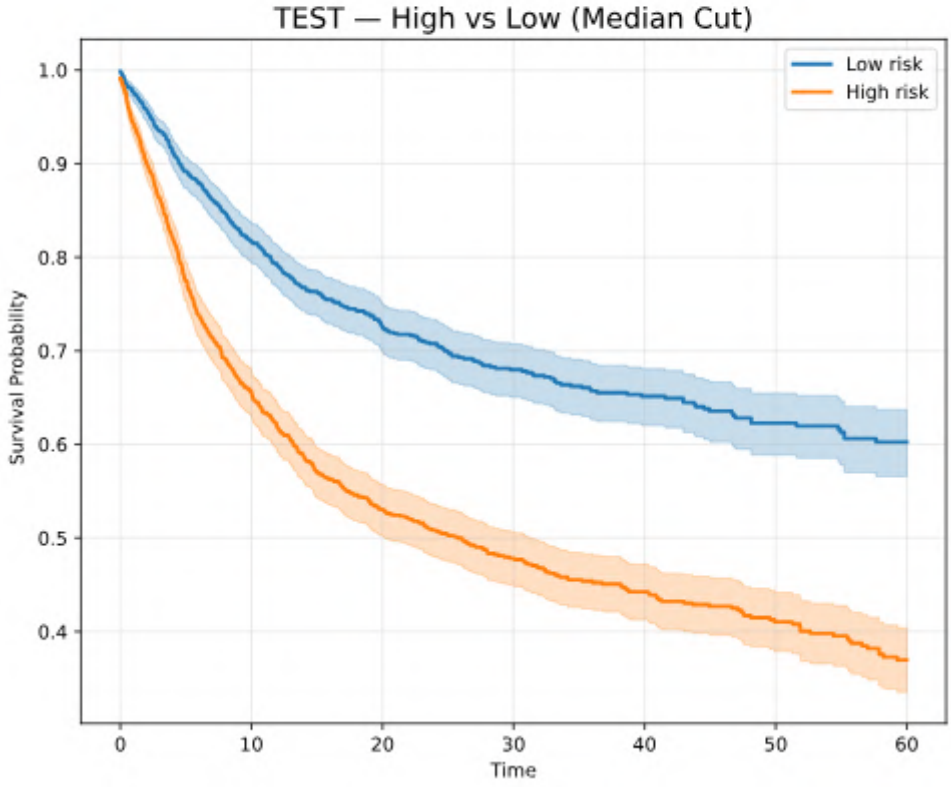
TEST — High vs Low (Median Cut)
Low risk
High risk
Survival Probability
Time
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0
10
20
30
40
50
60

Conclusions: We present a stacked ML survival model that outperforms established clinical risk scores, including IPSS-R and HCT-CI, while maintaining discrimination in an external, geographically independent test cohort. This integrative ML approach captures prognostic information beyond traditional scoring systems and substantially improves risk stratification for patients with MDS undergoing allo-HCT.

Disclosure: Nothing to disclosure

B278

PROTEIN LANGUAGE MODEL-DERIVED FUNCTIONAL DIVERSITY METRIC OF HLA ALLELES BETWEEN DONOR AND RECIPIENT PREDICTS GRAFT FAILURE IN SALVAGE SECOND HAPLO-HSCT USING THE SAME DONORS

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Background: Graft failure (GF) is a severe and life-threatening complication of haploidentical hematopoietic stem cell transplantation (haplo-HSCT), and salvage second transplantation serves as a critical therapeutic strategy for patients with primary GF. Notably, from our previous study, recurrent GF remains highly prevalent in second transplantations when using the same donor (*Haematologica, 2025*), while the underlying immunogenetic mechanisms remain poorly elucidated. We hypothesized that functional diversity of HLA alleles between donor and recipient, extracted via protein language models (PLMs), might serve as a computational tool to dissect HLA-associated contributors to recurrent GF in salvage haplo-HSCT with the original donor.

Methods: We analyzed a cohort of 39 patients undergoing salvage haplo-HSCT with the original donor following primary GF. We utilized ProtV, a published PLM fine-tuned on Gene Ontology-Biological Process (GO-BP) annotations; this fine-tuning specifically aligns high-dimensional embeddings with immune regulation-related biological objectives (Fig.1a), thereby enhancing the capture of HLA molecules' functional relevance to immune recognition and antigen presentation. Principal Component Analysis (PCA) was applied to project HLA allele embedding vectors into a 2D functional space (Fig.1c), on which we introduced a novel PLM-based HLA functional diversity metric (defined by the joint convex hull area, Fig.1b) representing the total breadth of the HLA physicochemical landscape. Associations of this metric with GF post second transplantation were assessed using the Mann-Whitney U test, with false discovery rate (FDR) correction applied to adjust for multiple testing errors. The critical threshold of the convex hull area (0.2) was determined via receiver operating characteristic (ROC) curve analysis to maximize diagnostic accuracy for engraftment outcome.

Results: Among the 39 cases of original-donor retransplantation, 15 developed recurrent GF while 24 achieved successful engraftment, corresponding to an overall engraftment success

rate of 61.5%. Despite identical donor-recipient pairings across the two transplantations, biologically aware embeddings from the ProtV-GO-BP model revealed distinct functional profiles between the engraftment success and recurrent failure groups. Specifically, the functional convex hull area formed by donor-recipient HLA-A and HLA-B alleles differed significantly between groups (Fig.1d): the median area was substantially higher in the successful engraftment group (0.19; interquantile range [IQR]: 0.12–0.37) than in the recurrent failure group (0.06; IQR: 0.04–0.15) (p=0.0069). For cases with a convex hull area > 0.2, the engraftment success rate reached 91.7% (11/12), whereas the rate dropped to 48.1% (13/27) for cases with an area ≤ 0.2. This finding indicates that broader functional diversity of donor-recipient HLA-A and HLA-B alleles is associated with a higher likelihood of successful salvage engraftment.

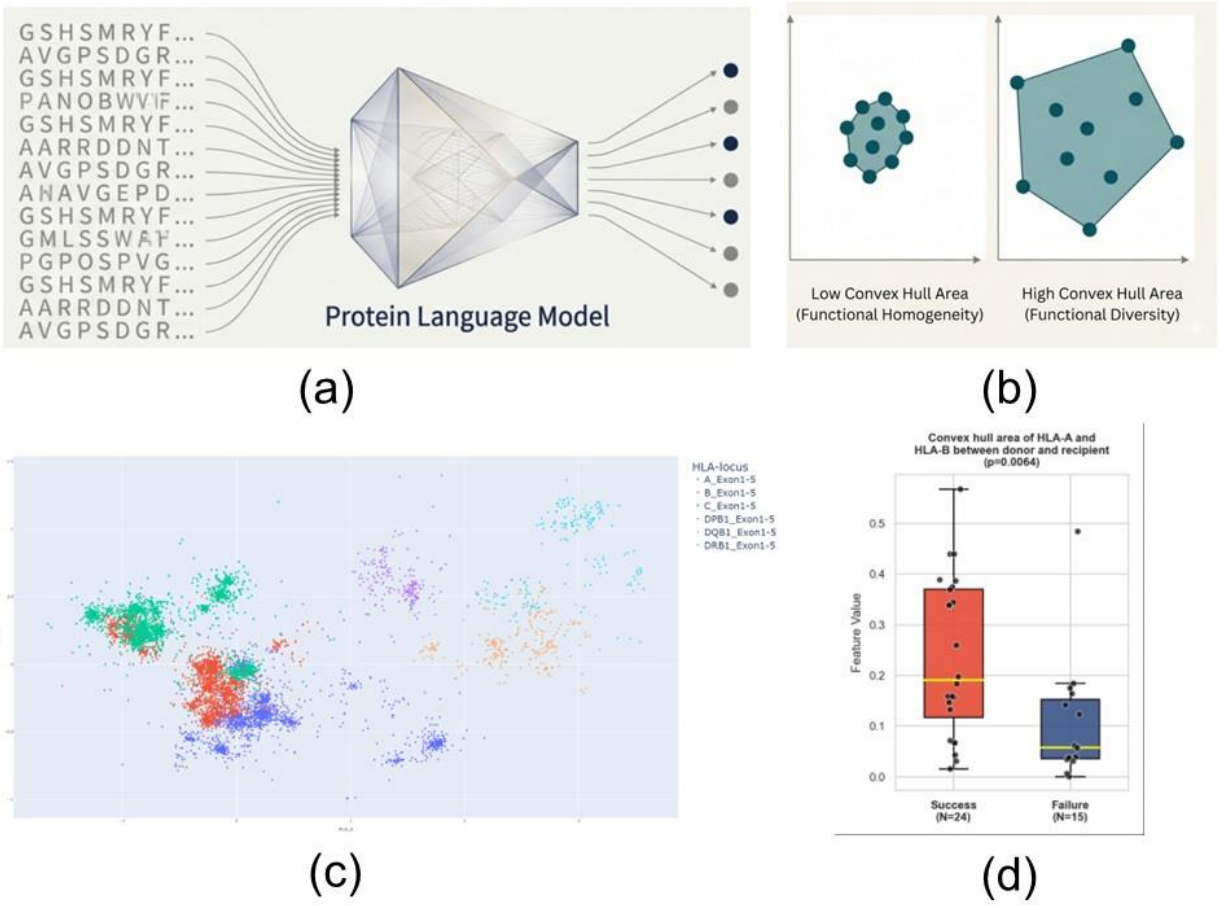

Figure 1. PLM-based HLA functional analysis workflow and clinical validation. (a) Schematic of transforming HLA amino acid sequences into high-dimensional functional embeddings using the **ProtV** protein language model. **(b)** Definition of the **Joint Convex Hull Area**, quantifying the physicochemical breadth of the combined donor-patient allele repertoire projected in 2D space. **(c)** Dimensionality reduction strategy using **ProtV fine-tuned on GO-BP** annotations to capture biologically relevant immune features via PCA. **(d)** Comparison of the **Joint HLA-A/B Convex Hull Area** in the second haplo-HSCT cohort (unchanged donors). The metric is significantly higher in the successful engraftment group (**n=24**) compared to the recurrent failure group (**n=15**) (**P=0.0069**, Mann-Whitney U test).

Conclusions: This study introduces a PLM-integrated geometric convex hull analysis as a novel approach to evaluating donor suitability in salvage haplo-HSCT using the original donor. While our findings are limited by the small sample size, this metric holds promise as a potential biomarker to aid clinical decision in donor selection for salvage second transplantations. Further validation in multicenter, large-scale cohorts is warranted to confirm its clinical utility.

Clinical Trial Registry: NA.

Disclosure:

All authors declare no conflict of interest.

B279

AUTOMATED EXTRACTION AND VISUALIZATION OF PEDIATRIC BMT CLINICAL NOTES USING A COST-EFFICIENT GPT-4.1-MINI PIPELINE

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Background: Physician documentation in patient records is the ultimate source for data extraction for research purposes. Hematopoietic Stem Cell Transplant (HSCT) clinical notes carry a large load of information that need to be accurately detailed and organized, given the complicated variables and prolonged hospitalizations. However, free-text notes bring a major challenge in this realm, since they have a high rate of human errors and are add labor to the data extraction process.

Methods: We included 100 discharge summaries from records of patients admitted to receive HSCT. We used pydantic_ai (GPT-4.1-mini; mean 37 s/note, <$0.01) for data extraction, to fill 23 predefined fields relating to patient and transplant details and inpatient early post-transplant course. Three blinded human evaluators reviewed the discharge summaries and data extraction to score each extracted field. A two-review design produced 4,363 field-level decisions and 1,297 evaluator pairs. A 10% error threshold was set for non-approval of data extraction.

Results: Global approval of data extraction reached 96.8 % (4,223/4,363 fields). Fifteen fields achieved ≥99 % approval; a further six exceeded 90 %. Only two fields breached the 10 % non-approval threshold over 139 instances: pre-transplant morbidity (38.1 %) and engraftment kinetics (11.3 %). The non-approved instances spanned 97 notes and were dominated by "section extracted" (22 %) and missing conditioning-intensity keywords (10 %). Inter-observer raw agreement was 95.5 % across 1,297 pairs ($\kappa = 0.10$, reflecting class imbalance). Field-specific agreement ranged 78–100 %; conditioning intensity showed the most discordance ($\kappa \approx 0.42$). Independent evaluator-level approval rates were 95.2 %, 97.2 % and 97.6 %, respectively. The resulting dashboard successfully aggregated 723 pediatric HSCT episodes, allowing interactive queries on clinical data such as engraftment timing, GvHD prophylaxis and post-HSCT complications in under 2 seconds.

Conclusions: GPT-4.1-mini provided near-real-time, high-fidelity extraction of complex HSCT notes at negligible cost. Error clustering in pre-transplant morbidity and engraftment data fields prompts future engineering refinements for the platform. This interactive pipeline offers an opportunity for rapid and accurate data extraction of free-text clinical notes, tailored to BMT-related variables. Our future plan is to further enhance its performance so it serves in research data extraction and building quality dashboards for the department.

Disclosure: Nothing to Declare

B280

CREATING A POOL OF READY-TO-USE CORD BLOOD UNITS BY SELECTING DONORS USING HLA-INFORMED ALGORITHMS

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Background: Cord blood (CB) represents a readily available source of stem cell for hematopoietic stem cell transplantation, associated with a shorter time required for search and procurement compared to an adult donor. However, most CB units still require final release testing once they are reserved, a process which usually takes at least two weeks. CB units could be pre-qualified in advance to shorten this time, although at a non-negligible cost if applied to the entire CB bank.
In this study, we compared three different strategies for the selection of CB units with the objective to maximise the proportion of patients having access to a suitable graft in a small pool of selected CB units.

Methods: Two different HLA-informed selection algorithms were compared: (1) ECTmatch which optimizes donor selection based on HLA-typing data only, and (2) HQmatch which optimizes donor selection based on HLA-typing data and CD34 cell content and which selects a portion of donors specifically for ethnic minorities. These two algorithms are then compared to the selection of the same number of CB units based on their CD34 cell content (largest CB units). CB selection was done within the Hema-Quebec CB bank for CB units that contained a minimum of $7x10^6$ CD34 cells (n=2260).
Population coverage was assessed using two datasets: (1) donors registered in the Hema-Quebec registry (n=39 828), and (2) patients for whom a donor search has been performed at Hema-Quebec between January 2013 and October 2025 (n=6463). For the second dataset, patients were also analyzed in sub-groups according to age, ethnicity, country of residence and type of donor search. Patient weight was also used to assess whether the selected CB units contained enough total nucleated cells (TNC) and CD34 cells for a single CB transplant.

Results: ECTmatch and HQmatch significantly increased population coverage compared to the largest units. When only considering HLA-match, a small pool of 100 CB units selected using HLA-informed algorithms achieved a 55-60% population coverage for a 5/8 HLA match, compared to 30% with the 100 largest CB units.
When considering TNC, CD34 cell contents and HLA-matching, HQmatch outperformed ECTmatch for adult patients, who require larger CB units to achieve the targeted TNC and CD34 cell dose. When considering both cell dose and HLA-match, a small pool of 100 CB units selected using HQmatch achieved a 31% population coverage for a 5/8 HLA match, compared to 26% coverage with ECTmatch or 24% with the largest CB units.

In contrast, ECTmatch achieved slightly higher population coverage for pediatric patients (47%) compared to HQmatch (44%) and the largest units (23%), suggesting that ECTmatch selects a pool of donor with a slightly broader genetic diversity than HQmatch. When evaluating the algorithms performance for different ethnic groups, HQmatch achieved a higher population coverage than other selection strategies, especially for adult patients of Asian and Hispanics descents.

Conclusions: Using HLA-informed selection algorithm allows the selection of a small number of donors that significantly increases the percentage of patients having access to an adequately HLA-matched CB donor.

Disclosure: MDL and DF are employed at Hema-Quebec. GT is employed by ExCellThera Inc. SC is a consultant for the clinical program of ExCellThera and will receive royalties from the sales of UM171. GS is the founding scientist and major shareholder of ExCellThera which owns an exclusive license to use UM171 for stem cell expansion.

P245

DEVELOPMENT OF A MACHINE LEARNING MODEL TO PREDICT PROGRESSION FREE SURVIVAL IN PATIENTS WITH MULTIPLE MYELOMA AFTER CAR-T CELL THERAPY

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Background: In multiple myeloma (MM), accurate post–CAR-T progression-free survival (PFS) estimation is challenging in contemporary real-world cohorts because outcomes are evolving and follow-up is immature. Post–CAR-T PFS is important for patient selection and post–CAR-T maintenance and disease management. Machine-learning (ML) survival models may integrate high-dimensional clinical and biological data to support individualized risk estimation. Leveraging institutional experience with ML in hematologic malignancies, we developed an ML model for PFS prediction using patient-related, clinical, and laboratory data collected before and after CAR-T therapy in a real-world cohort.

Methods:

We identified 49 patients with MM treated with ciltacabtagene autoleucel (anti-BCMA CAR-T) at our institution between 9/2023 and 3/2025; data were obtained by manual chart review and modeled in Python. PFS was defined as time from CAR-T infusion to progression or death, censored at last follow-up.

Two approaches were evaluated: a Random Survival Forest and a ridge-penalized Cox model as a benchmark, each using demographic, disease, and treatment variables. Model

performance was assessed on a 20% held-out validation set using 6- and 12-month concordance indices, Brier scores, and comparison with a Kaplan–Meier model, with diagnostics examining follow-up maturity, censoring, event sparsity, and stability of risk rankings.

Results:

Forty-nine patients with relapsed triple-class-refractory MM were included, with median follow-up of ~13 months. The cohort had immature follow-up (76% censoring) with sparse events (12 PFS events). In the validation cohort, only two progression events occurred, and all samples had follow-up exceeding 314 days.

Global concordance for the RSF model was low (C-index = 0.23), reflecting metric instability with sparse events. Directional concordance was higher when risk rankings were inverted (C-index = 0.77), suggesting meaningful prognostic structure despite heavy censoring. Horizon-specific concordance at 6 months could not be estimated due to the absence of early progression events, indicating that early relapse risk cannot yet be reliably determined in this cohort. 12-month concordance estimates were less stable and highly sensitive to individual events because of limited event accrual within that time window.

Brier score analysis showed comparable calibration between the RSF and Kaplan–Meier models. The penalized Cox model yielded similar results, with no improvement in 12-month prediction error. Across both modeling approaches, diagnostic and resampling analyses consistently suggested underlying prognostic signal, with predictive performance constrained primarily by limited event accrual rather than model specification.

Conclusions:

In small, heavily censored real-world myeloma CAR-T cohorts, ML-based and penalized survival models identified biologically meaningful risk patterns, but individualized prediction was constrained by rare events. Calibration-based metrics and horizon-specific evaluation were more appropriate at this stage. Evaluation of 18-month concordance is planned as follow-up matures and additional progression events accrue. This study represents a methodological proof of concept for post–CAR-T PFS modeling. As follow-up matures, these models may support population-level risk stratification and inform post–CAR-T management strategies. Ongoing multi-institutional validation is planned.

Disclosure: Nothing to declare.

P246

AN EXPLORATORY STUDY EVALUATING *T*UMOUR *R*ADIOMICS *A*S A *M*OLECULAR *A*DJUNCT IN *D*IFFUSE *L*ARGE *B*-CELL *L*YMPHOMA (TRAMADOL STUDY)

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Background: Diffuse large B-cell lymphoma (DLBL) has been classified into two distinct molecular subtypes based on their cell of origin- namely germinal center B-cell-like (GCB) and activated B-cell-subtype (non-GCB) based on Han's algorithm. These two entities are also prognostically distinct. We assessed CT based tumour radiomic features using machine learning classifiers to distinguish the two molecular subtypes.

Methods: One hundred one patients of DLBL were accrued in the study after institutional ethics committee approval. GCB subtype was diagnosed in 59 while 42 patients were non-GCB subtype. Lesion with maximum SUV was delineated using a semi-automated segmentation method (3D slicer) and radiomic features were extracted using Pyradiomics. A total of 1030 features were extracted including Shape features, first, second, third, higher order and wavelet-based features. Recursive feature elimination was used for feature selection and optimal 10 features were selected. Five machine learning (ML) tools were used to build a model to sub- classify the two molecular subtypes. Model performance was assessed using Accuracy, Precision, Recall, F1 score and Area under curve of receiver operating characteristic curve. The models were constructed by two methods.1) using a 10-fold internal cross validations strategy and 2) by splitting the data set into training set (70%) and a validation set (30%).

Results: Recursive feature elimination using a random forest algorithm method was used to select 10 radiomic features. These features were then used to build the model using the 5 ML classifiers. Of the five classifiers, Random Forest Classifier (RFC) using a 70:30 training: test strategy was the best performer among all the ML models, with the highest accuracy of 80%, AUC of 0.87, recall(sensitivity), f1score(specificity) & precision (Positive Predictive value; PPV) or precision of 82% respectively. When an internal 5-fold cross validation strategy was used, RFC again performed better than other ML classifiers with an accuracy of 75%, AUC of 0.80, recall of 79%, PPV of 77% and specificity of 79%.

	Validation	Model	Accuracy	Classification report			AUC
				Precision	Recall	f1-score	
Random Forest Classifier (RFC)	10-folds cross-validation	RFC	0.75±0.10	0.79±0.12	0.79±0.14	0.77±0.12	0.80±0.1
	Train-Test(7:3)	RFC	0.80	0.82	0.82	0.82	0.87
Support vector classifier (SVC)	10-folds cross-validation	SVC	0.61±0.15	0.63±0.12	0.76±0.16	0.69±0.13	0.70±0.1
	Train-Test(7:3)	SVC	0.73	0.75	0.78	.81	0.75
Gradient Boosting Classifier (GBC)	10-folds cross-validation	GBC	0.65±0.12	0.72±0.14	0.68±0.13	0.69±0.10	0.70±0.1
	Train-Test(7:3)	GBC	0.63	0.65	0.76	0.70	0.81
Naive Bayes Classifier	10-folds cross-validation	NBC	0.64±0.16	0.67±0.13	0.77±0.13	0.71±0.12	0.63±0.2
	Train-Test(7:3)	NBC	0.67	0.83	0.87	0.85	0.68
AdaBoost Classifier (ABC)	10-folds cross-validation	ABC	0.73±0.13	0.76±0.14	0.79±0.13	0.77±0.11	0.76±0.1
	Train-Test(7:3)	ABC	0.68	0.75	0.78	0.75	0.74

Conclusions: Models using machine-learning based radiomics features extracted from pre-treatment CT images can provide a simple and non-invasive method for the prediction of DLBL molecular subtypes with favourable predictive accuracy. The Random Forest Classifier was the most accurate in distinguishing GCB subtype from the ABC subtype.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

DISEASE-SPECIFIC TOPICS

Acute Leukaemia

GS2-7

NANOBODY-DERIVED CD19/CD22 TANDEM CAR-T THERAPY AS SALVAGE TREATMENT FOR IMMUNOTHERAPY-REFRACTORY B-ALL AFTER BLINATUMOMAB, INOTUZUMAB, OR PRIOR SINGLE-TARGET CAR-T: PHASE 1A DOSE FINDING AND RP2D EVALUATION

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Background: Emerging data from single-target CAR-T trials (e.g., ZUMA-3) indicate that prior exposure to immune-based therapies significantly compromises CAR-T efficacy in R/R B-ALL. As immunotherapies such as Blinatumomab, inotuzumab, and prior CAR-T are increasingly used, effective salvage strategies for immunotherapy-refractory disease remain an unmet clinical need. Nanobody-derived CD19/CD22 tandem CAR-T therapy represents a promising high-activity salvage approach for this population.

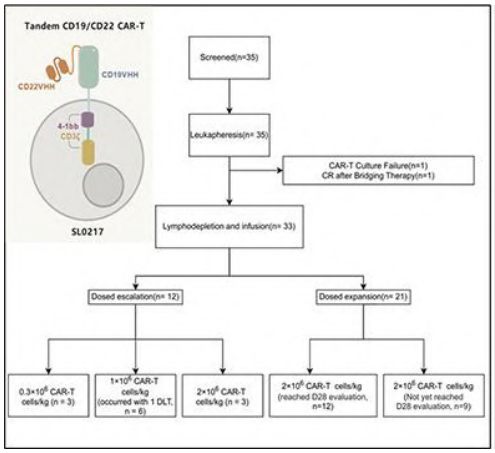
Methods: Unique alpaca-derived nanobodies (VHHs) targeting CD19 and CD22 were screened and engineered into a tandem dual-target CAR construct (SL0217). In the phase I study (NCT06880913), a standard 3+3 dose-escalation design is being used to evaluate the safety and tolerability of autologous nanobody-based CD19/CD22 CAR-T cells and to determine the recommended phase 2 dose (RP2D). Three dose levels are tested: 0.3×10^6, 1.0×10^6, and 2.0×10^6 CAR-T cells/kg. Following dose escalation, a single-dose expansion cohort at the RP2D is conducted to further evaluate efficacy.

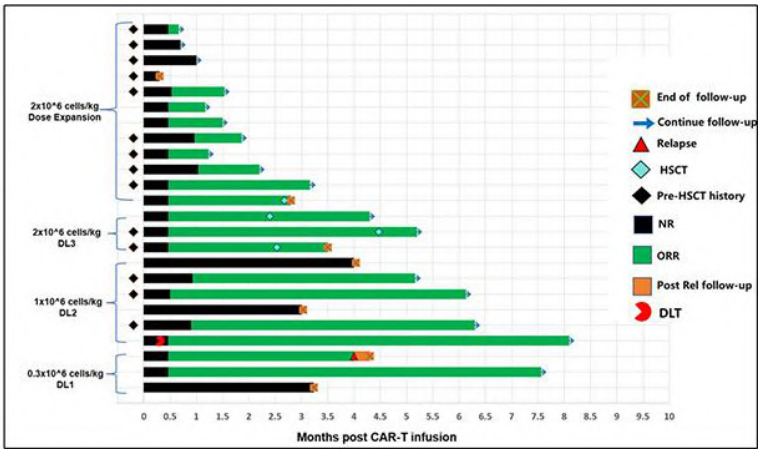
Results: As of Dec 2025, 35 patients with R/R B-ALL were enrolled; one patient with high tumor burden (PB blasts >90%) failed CAR-T manufacturing, and one withdrew after achieving remission with bridging therapy. Thirty-three patients received standard FC lymphodepletion followed by CAR-T infusion. During 3+3 dose escalation, one dose-limiting toxicity (DLT, grade 3 CRS resolving after 7 days) occurred at dose level 2, prompting cohort expansion without additional DLTs and allowing escalation to dose level 3, which was selected as the RP2D (2.0×10^6 cells/kg). Overall analyses were performed in 12 patients in dose-escalation and 12 patients in RP2D with completed M1 evaluation.
Bone marrow MRD was monitored by FCM, fusion gene qPCR, and NGS-IgH monthly for the

first 6 months and every 3 months thereafter, while extramedullary disease(EMD) was assessed by PET–CT at baseline, M1, and M3. Among the 24 evaluable patients, the median age was 34.5 years, and 62.5% were male. All patients were heavily pretreated, with **prior exposure to blinatumomab (41.6%), inotuzumab (41.6%), prior CD19 CAR-T (37.5%), or CD22 CAR-T (8.3%); 58.3% had prior allogeneic HSCT.** Dual CD19/CD22 expression was observed in 87.5% of patients. Disease involvement included isolated bone marrow (37.5%), extramedullary diseases (29.1%), or both (33.3%), with a median pre-lymphodepletion marrow blast of 12.0% (Interquartile range 0.5-79.5%).
CAR-T cells reached peak expansion at a median of 14 days after infusion. Grade 1–2 CRS occurred in 58.4% of patients, while CRS ≥3 was observed in two patients (8.3%), including one RP2D patient who died from progressive leukemia with pericardial infiltration. No ICANS was observed; one patient developed tumor inflammation–associated neurotoxicity (TIAN). Grade 3–4 early neutrophil Immune effector cell–associated hematotoxicity(N-ICAHT) occurred in 29.1%. **The ORR (CR/CRi/MLFS) was 83.3% (20/24), including 82.4%(14/17) in bone marrow disease and 93.3%(14/15) in extramedullary disease.** Among patients achieving bone marrow response, **100% attained MRD negativity across all available assessment methods**. Median PFS and OS were not reached, with 6-month PFS and OS of 58.8% (95% CI, 37.6–91.9%) and 89.0% (95% CI, 75–100%), respectively.

Characteristics		**Characteristics**		**Characteristics**		**Safety**	
Age, M (Interquartile range, IQR)	34.5 (24.5, 43.8)	**Antigens by FCM, n (%)**		**Morphology Pre-FC, M (Interquartile range, IQR)**	12.00 % (0.5, 79.5%)	**CRS 1, n (%)**	10 (41.7%)
Male, n (%)	15 (62.5%)	CD19 and CD22	21 (87.5%)	**Genetics, n(%)**		**CRS2, n(%)**	4 (16.7%)
Prior therapies n (%)		Isolated CD22	3 (12.5%)	BCR::ABL	7 (29.1%)	**CRS3+, n(%)**	2 (8.3%)
Blinatumomab	10 (41.6%)	**Sites of Lesion, n(%)**		IKZF1 del or plus	3 (12.5%)	**ICANS, n(%)**	0 （0%）
Inotuzumab	10 (41.6%)	BM+EMDs	8 (33.3%)	TP53	2 (8.3%)	**TIAN, n (%)**	1 (4.2%)

CD19 CAR-T	9 (37.5%)	Isolated BM	9 (37.5%)	KMT2A rearrange	1 (4.2%)	**Early N-ICAHTG1, n(%)**	12 (50%)
CD22 CAR-T	2 (8.3%)	Isolated EMDs	7 (29.1%)	Ph-Like	3 (12.5%)	**Early N-ICAHTG2, n(%)**	5 (20.8%)
Pre-HSCT history, n(%)	14 (58.3%)			UBTF::ATXN7L3	2 (8.3%)	**Early N-ICAHTG3, n(%)**	2 (8.3%)
				HLF::E2A	1 (4.2%)	**Early N-ICAHTG4, n(%)**	5 (20.8%)





Conclusions: Nanobody-derived CD19/CD22 tandem CAR-T demonstrated promising efficacy and manageable toxicity as salvage therapy for immunotherapy-refractory B-ALL following prior immunotherapies.

Clinical Trial Registry: NCT06880913

Disclosure: ML received grants from Beijing Research Ward Excellence Program(BRWEP2024W134080103) and National key research and development plan of China (2021YFA1100902)

OS03-01

PHASE 1 EVALUATION OF THE SAFETY AND EFFICACY OF RAPCABTAGENE AUTOLEUCEL (YTB323) IN ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (R/R B-ALL)

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Background: Most adult patients with r/r B-ALL suffer disease progression, indicating a need for more effective therapies. Rapcabtagene autoleucel is an innovative autologous next-generation CD19-directed chimeric antigen receptor (CAR)-T cell therapy, rapidly manufactured using the T-Charge™ platform. Here we present safety and efficacy data for

rapcabtagene autoleucel in adults with r/r B-ALL in a phase 1, multicenter study (EUCT number: 2023-507062-34-00).

Methods: Eligible patients were ≥18 years of age, had CD19-positive r/r B-ALL, morphologic disease in the bone marrow, ECOG 0-1, and ≥1 of the following: prior allogeneic hematopoietic stem-cell transplantation (alloHSCT), ≥2 prior therapeutic lines, primary refractory disease, relapse within 12 mo of first remission, or Philadelphia chromosome-positive B-ALL with failure/intolerance of ≥2 different tyrosine kinase inhibitors. Patients received single-infusion rapcabtagene autoleucel at targeted dose level (DL) DL1 (2.5×10^6 CAR+ cells), DL2 (5×10^6 CAR+ cells), DL3 (7.5×10^6 CAR+ cells), or DL4 (12.5×10^6 CAR+ cells). Primary endpoints characterized safety and dose-limiting toxicities (DLTs) to identify a recommended dose. Secondary endpoints include best overall response (BOR) of complete remission (CR)/CR with incomplete blood count recovery (CRi) by month 3, and duration of response (DOR).

Results: At data cutoff (February 20, 2025; median follow-up from infusion: 27.7 [18.9-49.5] months), 35 (85%) of 41 enrolled adult patients with r/r B-ALL received rapcabtagene autoleucel: DL1 (n=10), DL2 (n=6), DL3 (n=12), DL4 (n=6), and 1 patient, assigned to DL3 received 18.9×10^6 CAR+ cells. Median age was 41 years, 91% received ≥2 prior lines (range 1-10), and 66% had prior alloHSCT. Sixteen (46%) patients were previously treated with blinatumomab and 13 (37%) patients with inotuzumab. Median (range) time from most recent relapse/progression to infusion was 2.3 (1.0-7.6) months. Reported adverse events are summarized in **Table 1**. DLTs were experienced by 2/10 patients at DL1 (1 patient: Grade 5 cytokine release syndrome [CRS]; 1 patient: Grade 4 neurotoxicity, Grade 3 CRS, Grade 4 bone marrow failure), 1/6 patients at DL2 (Grade 4 CRS, Grade 4 ICANS), 1/12 patients at DL3 (Grade 4 neutropenia) and 0/6 patients at DL4. BOR (CR/CRi) by 3-month was achieved in 70% (40% / 30%), 100% (50% / 50%), 92% (50% / 42%), and 83% (67% / 17%) patients at DL1, DL2, DL3 and DL4 respectively. Median DOR was 5.3 months for DL1 and 10.8 months for DL2 and not reached for DL3 or DL4. Cellular expansion was higher at DL2 (139,000 copies/µg DNA), DL3 (55,300 copies/µg), and DL4 (68,300 copies/µg) compared with DL1 (20,900 copies/µg). Median time to last detectable CAR19 transgene concentration was 91, 226, 57, and 181 days for DL1, DL2, DL3, and DL4, respectively.

Table 1: Summary of the reported AEs

AEs	**N=35**			
AE, % Any grade Grade ≥3	 100 94			
AE by DL, n (%)	**DL1 (n=10)**	**DL2 (n=6)**	**DL3 (n=12)**	**DL4 (n=6)**
Grade ≥CRS Grade ≥ICANS	3 (30) 1 (10)	3 (50) 1 (17)	2 (17) 2 (17)	0 1 (17)

Table 1: Summary of the reported AEs				
Grade ≥3 cytopenia Grade ≥3 infections	9 (90) 4 (40)	5 (83) 4 (67)	9 (75) 4 (33)	6 (100) 2 (33)
CRS Any grade, n (%) Grade ≥3, n (%) Median time to onset, days (range) Median time to resolution, days (range)	 30 (86) 8 (23) 8 (2-15) 6 (4-8)			
CRS management, % Tocilizumab Siltuximab Corticosteroids Tocilizumab + corticosteroids Anakinra	 70 10 40 37 7			
ICANS Any grade, n (%) Grade ≥3, n (%) Median time to onset, days (range) Median time to resolution, days (range)	 9 (26) 5 (14) 13 (4-35) 5 (1-NE)			
ICANS management, % Dexamethasone Anakinra	 71 43			
AE, adverse event; CRS, cytokine release syndrome; DL, dose level; DLT, dose-limiting toxicity; ICANS, immune effector cell-associated neurotoxicity syndrome; NE, not estimable.				

Conclusions: Data from this phase 1 study suggest high cellular expansion, durable efficacy for DL2–DL4, and a manageable safety profile of rapcabtagene autoleucel in adult patients with r/r B-ALL. DL3—at which 92% of patients achieved BOR of CR/CRi by 3 months, with median DOR not reached after 22 months median follow-up— exhibited a favorable risk-benefit based on safety, cellular expansion, and encouraging efficacy.
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Clinical Trial Registry: 2023-507062-34-00 (https://euclinicaltrials.eu/?lang=en)

Disclosure: ***Pere Barba***: Pierre Fabre, Miltenyi Biomedicine, Novartis, Jazz Pharmaceuticals, Allogene, Pfizer, Nektar, Bristol Myers Squibb/Celgene: Consultancy (Includes expert testimony); Pierre Fabre, Miltenyi Biomedicine, Novartis, Amgen, Gilead Sciences, Jazz Pharmaceuticals, Allogene, InCyte, Pfizer, Nektar, Bristol Myers Squibb: Research Funding. ***Alessandro Rambaldi***: Amgen, Otsuka, Sanofi, Italfarmaco, Incyte, Menarini Stemline, Omeros, Kite-Gilead: Consultancy (Includes expert testimony); Italfarmaco: Patents & Royalties. ***Nicolas Boissel:*** Amgen, Novartis, Jazz Pharamaceuticals,

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OS03-02

OPTIMIZING TRANSPLANT OUTCOMES IN PHILADELPHIA CHROMOSOME–POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA WITH PRE-TRANSPLANT SECOND- AND THIRD-GENERATION TKIS AND POST-TRANSPLANT PROPHYLACTIC MAINTENANCE: A STUDY FROM THE EBMT ALWP

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) remains a key component in the management of Philadelphia chromosome-positive acute lymphoblastic leukemia (Ph+ ALL), particularly in patients with high-risk genetics and delayed measurable residual disease (MRD) clearance. Multiple TKIs are used in frontline therapy, including imatinib and more potent second- and third-generation TKIs. Early molecular remission is more frequently achieved with newer generation TKIs, and predicts better long-term outcomes. However, the impact of different TKIs used before and after allo-HCT on long-term clinical outcomes in Ph+ ALL remains to be explored.

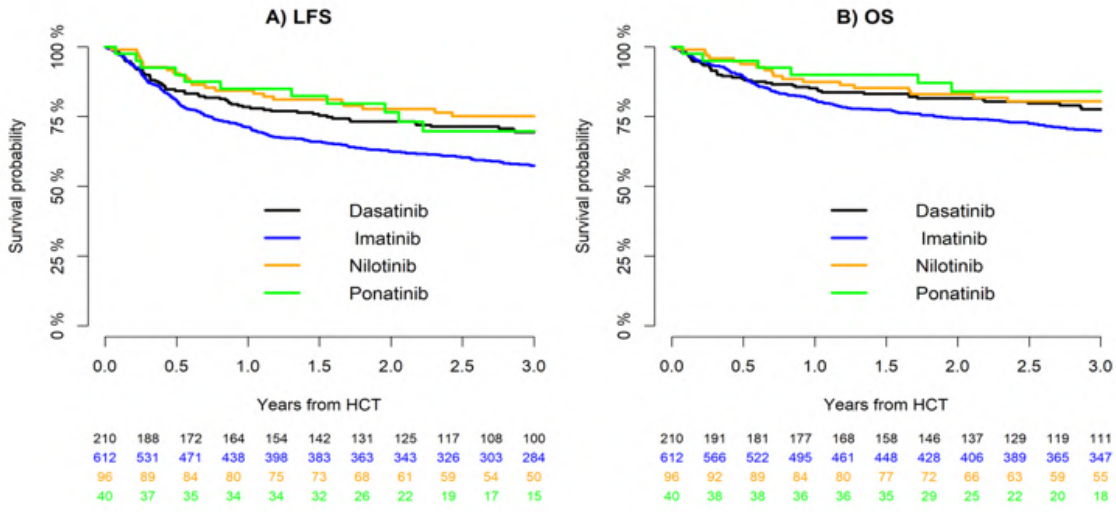
Methods: This retrospective registry-based analysis used data from the European Society for Blood and Marrow Transplantation. Adult patients (≥18 years) diagnosed with Ph+ ALL, treated with TKI-based induction therapy, and who underwent allo-HCT in CR1 regardless of MRD between 2010 and 2022 were included. The use of a prophylactic TKI was evaluated as a time dependent covariate in an adjusted Cox model.

Results: A total of 958 patients were analyzed (median age: 44 years [range 18–76]; 54% male). The median time from diagnosis to transplant was 5.5 months. At the time of allo-HCT, 61% were MRD-undetectable, assessed by PCR (75%) or flow cytometry (21%). Donors included matched related (37%), haploidentical (21%), and matched unrelated (26%). Peripheral blood stem cells were used in 84% of cases, with 79% receiving myeloablative conditioning, and 51% receiving total body irradiation.
TKI use prior to transplant included imatinib (N=612, 64%), dasatinib (N=210, 22%), nilotinib (N= 96, 10%), and ponatinib (N=40, 4%). Ponatinib was more frequently used in recent years and in older patients. Baseline characteristics, including MRD status at transplantation, were otherwise balanced across TKI groups.
The 3-year post-allo-HCT prophylactic TKI incidence was 31% including imatinib (51%), dasatinib (28%), nilotinib (16%) and ponatinib (3%). After a median follow-up of 5.2 years (95% CI: 4.9-5.7), 3-year overall survival (OS) was 73% (95% CI: 70–76) and leukemia-

free survival (LFS) was 62% (95% CI, 59–65). Three-year OS was 70% with imatinib, 78% with dasatinib, 81% with nilotinib, and 84% with ponatinib. Corresponding 3-year LFS rates were 57%, 69%, 75%, and 70%, respectively. The 3-year cumulative incidence of relapse was 21%, and graft-versus-host disease–free, relapse-free survival was 47%.
Multivariable analysis showed that use of pre-transplant TKIs other than imatinib was independently associated with improved LFS (hazard ratio [HR]: 0.75; 95% CI: 0.58–0.97; p=0.03). Increasing age negatively affected both LFS and OS. Use of a prophylactic post-allo-HCT TKI was associated with significantly improved LFS (HR: 0.62) and OS (HR: 0.50), both p<0.001. Donor type, TBI use, and pre-transplant MRD status were not significant predictors of survival outcomes.

Variables	**Modalities**	**N=958**	**Imatinib (N=612)**	**Dasatinib (N=210)**	**Nilotinib (N=96)**	**Ponatinib (N=40)**	**Test**
Patient sex	Female	441 (46)	294 (48)	92 (44)	39 (41)	16 (40)	0.37
	Male	517 (54)	318 (52)	118 (56)	57 (59)	24 (60)	
Year at allo-HCT	median	2017 (2010-2022)	2016 (2010-2022)	2018 (2010-2022)	2018 (2010-2022)	2020 (2015-2022)	< 0.001
Age at allo-HCT	median (range)	44 (18-76)	45 (18-76)	38 (18-67)	44 (19-69)	51 (23-68)	< 0.001
Time from first to last TKI (months)	Median (range)	4 (0-11)	4 (0-11)	4 (0-10)	5 (0.5-8)	4 (0.9-9)	0.2
Months from diagnosis to CR1	median (range)	1.4 (0-11)	1.5 (0-10)	1.4 (0-11)	1.3 (0.4-6)	1.3 (0.6-6)	0.008
Months from diagnosis to allo-HCT	median (range)	6 (2-12)	5.5 (2-12)	5 (2-12)	6 (3.6-11)	6 (3-10)	0.06
MRD	Positive	378 (40)	247 (40)	82 (39)	37 (39)	12 (30)	0.62
Source of cells	BM BM+PB PB	91 (10) 66 (7) 801 (84)	61 (10) 27 (4) 524 (86)	18 (9) 30 (14) 162 (77)	8 (8) 9 (9) 79 (82)	4 (10) 0 (0) 36 (90)	Not done
Donor type	Matched related Haplo-identical Matched unrelated Mismatched	354 (37) 205 (21) 253 (26) 118 (12) 28 (3)	241 (39) 92 (15) 170 (28) 87 (14) 22 (4)	65 (31) 84 (40) 35 (17) 60 (10) 3 (3)	32 (33) 19 (20) 38 (40) 7 (7) 0 (0)	16 (39) 10 (25) 10 (25) 4 (10) 0 (0)	Not done

	unrelated Others						
Female to male	Yes	159 (16.6)	99 (16.2)	35 (16.7)	23 (24)	2 (5)	0.053
Patient CMV	Positive	579 (68.4)	379 (68.4)	126 (74.1)	49 (57.6)	25 (65.8)	0.06
TBI use	Yes	488 (51)	323 (53)	77 (37)	67 (70)	21 (53)	< 0.001
MAC regimen	Yes	751 (79)	454 (74)	180 (86)	87 (91)	30 (75)	< 0.001
Use of PTCy	Yes	141 (15)	97 (16)	20 (10)	5 (5)	19 (48)	< 0.001
In vivo TCD	Yes	535 (57)	329 (55)	127 (63)	63 (68)	16 (40)	0.005



Conclusions: In this large, multicenter cohort of patients with Ph+ ALL undergoing allo-HCT in CR1, the use of second- and third-generation TKIs during induction was associated with superior survival outcomes compared to imatinib. Post-transplant TKI prophylaxis significantly improved survival regardless of pre-transplant MRD status. These findings support the incorporation of newer TKIs and prophylactic strategies in the transplant setting to optimize long-term outcomes in Ph+ ALL.

Clinical Trial Registry: Not applicable.

Disclosure: The authors declare no conflict of interest.

OS03-03

CLINICAL OUTCOMES IN ADULT PATIENTS WITH RELAPSED/REFRACTORY ACUTE LYMPHOBLASTIC LEUKAEMIA (R/R B-ALL) WHO ACHIEVED REMISSION FOLLOWING TREATMENT WITH OBECABTAGENE AUTOLEUCEL (OBE-CEL) IN THE FELIX STUDY

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Background: Obe-cel is an autologous fast off-rate 41BB-ζ CD19-directed chimeric antigen receptor (CAR) T-cell therapy, with demonstrated efficacy and low, single-digit incidence of severe immunotoxicity in adult patients with R/R B-ALL, based on data from the Phase Ib/II FELIX study (NCT04404660). Here, we report long-term clinical outcomes in patients who achieved remission in FELIX, presented by best overall response (BOR). These data provide beneficial information for evaluating treatment efficacy and guiding clinical decision making.

Methods: In FELIX, overall remission was defined as a BOR of complete remission (CR) or CR with incomplete haematological recovery (CRi). CR criteria were <5% blasts in the bone marrow, no extramedullary disease, no circulating lymphoblasts in peripheral blood, absolute neutrophil count (ANC) >1000/μL, platelet count >100,000/μL, no platelet transfusions in the last seven days and no administration of short-acting granulocyte colony-stimulating factor (G-CSF) and long-acting G-CSF in the last three and 14 days, respectively. CRi was defined as CR criteria with recovery of platelets to ≤100,000/μL and/or recovery of ANC to

<1000/µL. Duration of remission, EFS and OS were summarised using Kaplan-Meier methodology.

Results: In FELIX, 78.0% (99/127) of infused patients achieved remission following treatment with obe-cel (responders); 73.7% (73/99) achieved CR (CR group) and 26.3% (26/99) achieved CRi (CRi group) anytime following obe-cel infusion. The CRi group were more likely to have received ≥3 lines of prior therapy (42.3% vs 30.1%; prior blinatumomab or inotuzumab ozogamicin: 65.4% vs 43.8%) and had higher median bone marrow blasts at screening (78.5% vs 30.0%) vs the CR group. The median study follow-up was 32.8 months (range: 19.9–52.8). Long-term outcomes in responders and by BOR are summarised in the **Table**. Of the responders, 38.4% (38/99) were in ongoing remission without receiving other anti-cancer therapy, excluding tyrosine kinase inhibitors: 42.5% (31/73) of the CR group and 26.9% (7/26) of the CRi group. Whilst in remission, 18.2% (18/99) of responders received consolidative stem cell transplant at the investigators' discretion: 16.4% (12/73) of the CR group and 23.1% (6/26) of the CRi group. Median EFS (95% confidence interval [CI]) was 44.6 months (14.3–not estimable [NE]) in responders, 44.6 months (15.1–NE) in the CR group and 6.1 months (2.9–NE) in the CRi group. Median OS (95% CI) was 28.8 months (21.0–NE) in responders, 44.6 months (23.8–NE) in the CR group and 11.9 months (6.7–28.8) in the CRi group.

Conclusions: Most patients with R/R B-ALL who achieved remission following obe-cel achieved CR. Interpretation of long-term outcomes among the CRi group remains limited due to the small number of individuals in this subgroup. A substantial number of patients who responded to obe-cel treatment had a sustained survival benefit, regardless of BOR, with the most pronounced long-term benefit observed in patients who achieved CR.

Table. Long-term outcomes in responders and by best overall response.

Clinical outcome	**Responders (n=99)**	**Patients who achieved CR (n=73)**	**Patients who achieved CRi (n=26)**
Median DoR, months (95% CI)*	42.5 (12.5–NE)	42.5 (14.2–NE)	5.2 (1.4–NE)
12-month rate, % (95% CI)	61.8 (50.1–71.5)	68.3 (54.8–78.5)	40.9 (19.5–61.4)
24-month rate, % (95% CI)	54.1 (42.1–64.6)	58.0 (43.9–69.8)	40.9 (19.5–61.4)
Median EFS, months (95% CI)*	44.6 (14.3–NE)	44.6 (15.1–NE)	6.1 (2.9–NE)
12-month rate, % (95% CI)	63.2 (51.5–72.7)	68.1 (54.6–78.4)	47.4 (24.8–67.1)
24-month rate, % (95% CI)	54.1 (42.1–64.6)	57.9 (43.8–69.7)	41.5 (19.8–62.0)
Median OS, months (95% CI)‡	28.8 (21.0–NE)	44.6 (23.8–NE)	11.9 (6.7–28.8)

12-month rate, % (95% CI)	73.7 (63.9–81.3)	82.2 (71.3–89.2)	50.0 (29.9–67.2)
24-month rate, % (95% CI)	56.0 (45.6–65.2)	62.1 (49.7–72.3)	38.5 (20.4–56.3)

*DoR/EFS censoring for non-protocol anti-cancer therapies, including consolidative SCT.
‡OS without censoring for consolidative SCT.
Disease assessment was completed by an independent response review committee.
CI, confidence interval; CR, complete response, CRi, CR with incomplete haematological recovery; DoR, duration of remission; EFS, event-free survival; NE, not estimable; OS, overall survival;
SCT, stem cell transplant.

Clinical Trial Registry: NCT04404660; https://clinicaltrials.gov/study/NCT04404660

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OS03-05

CHANGING LANDSCAPE OF HAPLOIDENTICAL TRANSPLANTATION IN ACUTE MYELOID LEUKEMIA: A TEN-YEAR ANALYSIS OF PRACTICES AND OUTCOMES - A STUDY FROM THE ALWP/EBMT

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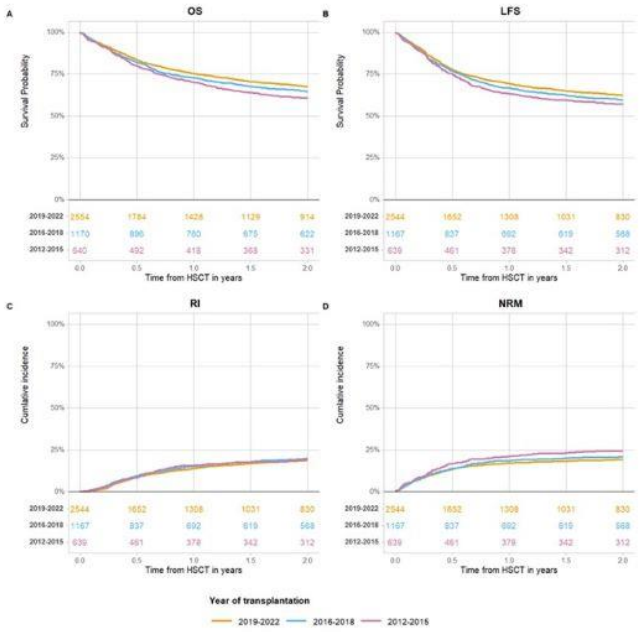
Background: Over the past decade, haploidentical stem cell transplantation (haplo-SCT) has evolved from an experimental approach to a standard option in many centers. This progress has been driven by the introduction of post-transplant cyclophosphamide (PTCy), the use of anti-thymocyte globulin (ATG), advances in HLA typing, and developments in immunology. However, limited data exist on longitudinal changes in haplo-SCT practices and associated outcomes. This study aimed to evaluate trends in graft source, GVHD prophylaxis strategies, and outcomes over time in patients with AML undergoing haplo-SCT.

Methods: Adult patients (≥18 years) receiving a first haplo-SCT for AML between 2012 and 2022 were identified in the EBMT registry. Three time periods were predefined for comparison: 2019–2022, 2016–2018, and 2012–2015. Patient-, disease-, and transplant-related characteristics were compared between groups using the Pearson's Chi-squared test for categorical data and the Kruskal-Wallis rank sum test for continuous data. All outcomes were measured from the time of transplant. NRM was calculated using cumulative incidence curves in a competing risk setting. LFS and OS were evaluated using the Kaplan-Meier

method. Univariate analyses were performed using the log-rank test for LFS and OS. A Cox regression multivariate analysis was used for all endpoints.

Results: A total of 6,818 patients were included: 1,207 (2012–2015), 1,914 (2016–2018), and 3,697 (2019–2022). PBSC became the dominant graft source, rising from 53.4% to 83.4% across the study periods (p<0.001). The proportion of patients transplanted in CR1 increased from 53% to 69.1%, while those with active AML decreased from 26.2% to 18.8% (p<0.001). Median age at transplant rose from 49.6 to 55 years (p<0.001), and the use of RIC increased from 36.2% to 43.3% (p<0.001). Donors were significantly younger in the most recent cohort, and there were also more male donors. GVHD prophylaxis practices evolved markedly: ATG without PTCy decreased from 21.8% to 11.8%, PTCy alone increased from 58.7% to 68.8%, and PTCy+ATG from 4.6% to 7.9% (p<0.001).
Among patients transplanted in CR1, 2-year outcomes improved over time. OS increased from 60.4% to 67.3%; LFS from 56.8% to 62.2%; and NRM decreased from 24.1% to 19.2%, however relapse incidence (RI) remained stable (19.1% vs. 18.6%).
In multivariate analysis using 2019–2022 as the reference, outcomes were significantly worse in earlier periods: OS: HR 1.42 (95% CI 1.17–1.73), p<0.001 ; LFS: HR 1.36 (95% CI 1.13–1.64), p=0.001 ; NRM: HR 1.61 (95% CI 1.25–2.08), p<0.001. No significant changes were observed in RI.

Outcomes in AML patients transplanted in CR1 : overall survival (OS), Leukemia-free survival (LFS), Relapse incidence (RI), Non-relapse mortality (NRM)



Conclusions: Since 2012, haplo-SCT for AML has expanded significantly, accompanied by major shifts in clinical practice: transplantation in older patients, increased use of RIC, greater proportion of transplants performed in CR1, widespread adoption of PBSC as the preferred graft source, and changing patterns of PTCy utilization. These evolutions were associated with significantly improved OS, LFS, and NRM. Relapse remains the main challenge, which underscores the importance of developing new conditioning regimens,

exploring the value of post-transplant maintenance therapy, and above all integrating targeted therapies and immunotherapy in order to improve patient outcomes.

Disclosure: Nothing to declare

OS08-01

DISTINCT PROGNOSIS AND TRANSPLANT TIMING IN CORE-BINDING FACTOR ACUTE MYELOID LEUKEMIA

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Background: Core binding factor acute myeloid leukemia (CBF-AML), defined by t(8;21)/*RUNX1::RUNX1T1* or inv (16)/*CBFβ::MYH11*, is categorized as favorable-risk. We aimed to delineate the clinical similarities and differences between these two subsets.

Methods: 779 de novo CBF-AML patients (511 *RUNX1::RUNX1T1*, 225 *CBFβ::MYH11*) were enrolled (Figure 1A). Measurable residual disease (MRD) was assessed via multi-parameter flow cytometry (MFC-MRD) and quantitative polymerase chain reaction (Mol-MRD) during/after treatment. Responders are defined as achieving MRD negativity (MFC-MRD 0.01% aberrant cells and Mol-MRD > 3-log reduction) after the second consolidation cycle (C2). Otherwise, it is considered positive. Survival analyses employed Kaplan-Meier and landmark methods (3-month cutoff [corresponding to the median time of C2 completion] for immortal time bias). Treatment response comparisons used time-dependent Cox models, while relapse risks were evaluated via the Prentice, Williams and Peterson (total times) (PWP-TT) modeling.

Results: With a median follow-up of 34.6 months (range: 3.9-106.2), early mortality by C2 was lower in *RUNX1::RUNX1T1* (4.7%, n=25) versus *CBFβ::MYH11* (7.1%, n=18, P = 0.042) patients. The 3-year overall survival (OS) was significantly better in patients with

CBFβ::MYH11 compared to *RUNX1::RUNX1T1* (90.2% vs 80.6%, P = 0.011) .
695 patients were evaluable for C2 assessment, with 42.5% with *RUNX1::RUNX1T1*(n = 206) and 33.2% with *CBFβ::MYH11* fusions (n = 74) as responders (Figure 1A). Landmark analysis showed superior 3-year OS for *RUNX1::RUNX1T1* responders vs. non-responders (86.3% vs. 76.5%, P = 0.008) (Figure 1B), however, responders and non-responders have comparable survival outcomes in patients with *CBFβ::MYH11* (95.1% vs. 88.1%, P = 0.49) (Figure 1C). Multivariable Cox model and the PWP-TT model further identified non-responders at C2 as significant risk factors for *RUNX1::RUNX1T1* survival and relapse, respectively, with no associations in *CBFβ::MYH11*.
For *RUNX1::RUNX1T1* non-responders, Allogeneic hematopoietic stem cell transplantation (allo-HCT) provided a superior 3-year OS than chemotherapy (81.9% vs. 56.4%, P < 0.001) (Figure 1D), which was different from non-responders with *CBFβ::MYH11*(Figure 1E). Responders with *RUNX1::RUNX1T1* or *CBFβ::MYH11* had comparable outcomes when consolidated with allo-HCT or chemotherapy. Transplant in first CR provided better outcomes for *RUNX1::RUNX1T1* (CR1 vs. non-CR1: 3-year OS: 85.8% vs. 71.4%, P < 0.001; relapses: 8.3% vs. 18.9%, P = 0.024) (Figure 1F-G). Consolidation therapies did not show significant impacts on long-term outcomes in *CBFβ::MYH11* patients (Figure 1H-I).
At last, we developed a comprehensive predictive model by Logistics regression models for C2 response incorporating clinical factors: (age < 50y [1 score], initial white blood count [<10 × 109/L: 10 score; 10 -50: 1 score; 50-100: 2 score; ≥ 100: 3 scores]; hemoglobin < 100 g/L [1 score]), mutational profiling (KIT D816/D822 variants [3 scores], other KIT mutations [1 score], FLT3-ITD [1 score]), as well as initial RUNX1::RUNX1T1/ABL value (<500%[4 scores], 500-1000%[3 scores], 1000-1500%[2 scores], ≥1500%[1 score]). A score ≥8 predicted non-response with 78.3% specificity and 57.4% sensitivity, effectively identifying high-risk *RUNX1::RUNX1T1* AML cases needing transplant evaluation (Table 1).

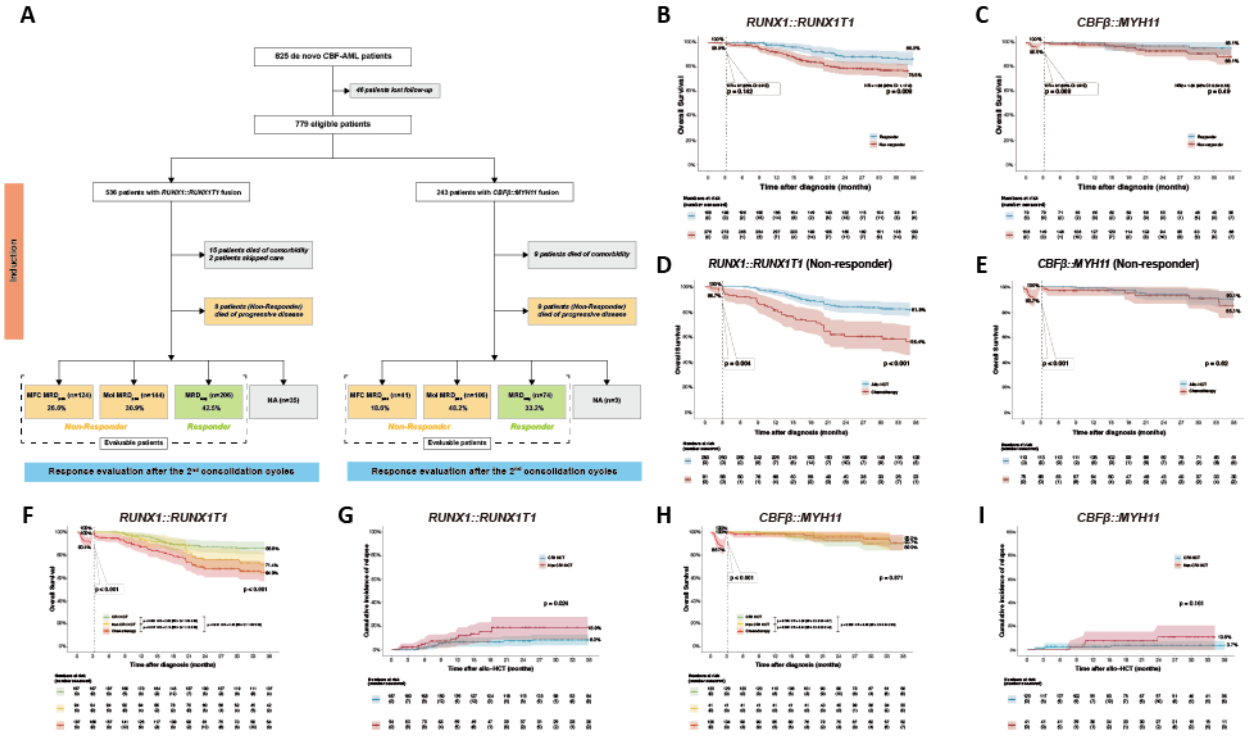

Figure 1. The diversity of CBF-AML. (A). Flow chart. Comparison of 3-year OS according to MRD status at PC2 among patients with RUNX1::RUNX1T1 **(B)**, patients with CBFβ::MYH11 fusions**(C).** Comparison of 3-year OS al between chemotherapy and allo-HCT in MRD non-responders at PC2 among RUNX1::RUNX1T1 **(D)** and CBFβ::MYH11 **(E)** patients. Comparison of 3-year OS or cumulative incidence of relapse (CIR) among patients with RUNX1::RUNX1T1 **(F-G)** or CBFβ::MYH11 **(H-I)** who underwent allo-HCT at different times or chemotherapy alone.

Table 1. Predictive scoring system for treatment response at PC2 in *RUNX1::RUNX1T1* patients.

Predictive variable	0	1	2	3	4
Age	≥50y	<50y	—	—	—
WBC count (× 10^9/L) at diagnosis	<10	10-50	50-100	≥ 100	—
Hemoglobin (g/L) at diagnosis	≥ 100	< 100	—	—	—
FLT3 mutations	WT or other FLT3 mutation	—	*FLT3-ITD*	—	—
KIT mutations	WT	Other KIT mutations	—	KIT D816/D822 mutations	—

Predictive variable	0	1	2	3	4
Initial RUNX1::RUNX1T1/ABL value at diagnosis	—	≥1500%	1000-1500%	500-1000%	<500%

— indicates not applicable.
Abbreviations: WBC, white blood cell; WT, Wild type.

Conclusions: For *CBFβ::MYH11* AML, C2 assessment offers minimal clinical significance, with allo-HCT reserved for CR2. In contrast, *RUNX1::RUNX1T1* patients with post-C2 MRD positivity should receive allo-HCT at CR1.

Disclosure: Nothing to declare.

OS08-02

A COMPARISON OF FLUDARABINE MELPHALAN AND FLUDARABINE TREOSULFAN FOR ADULT ACUTE LYMPHOBLASTIC LEUKAEMIA.A STUDY ON BEHALF OF THE ACUTE LEUKEMIA WORKING PARTY OF THE EBMT

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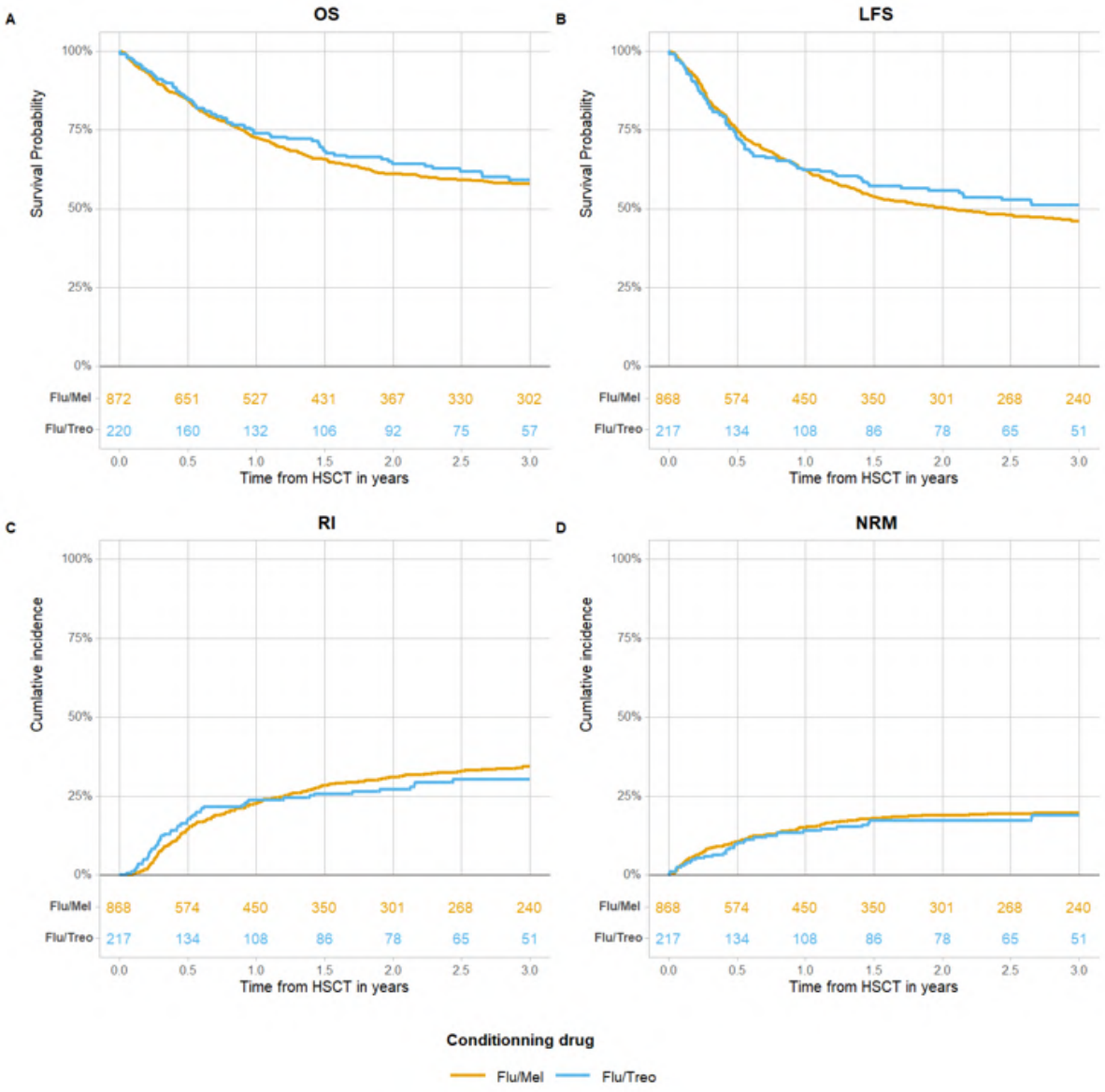
Background: Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is a potentially curative option for adult patients with high-risk acute lymphoblastic leukaemia (ALL), but outcomes are influenced by conditioning-related toxicity and disease control. Many patients are older or have comorbidities limiting the use of myeloablative regimens, leading to increased use of reduced- or intermediate-intensity approaches. Treosulfan offers a favourable toxicity profile while preserving myeloablative and anti-leukaemic activity, although evidence in adult ALL remains limited. This study evaluated whether fludarabine–treosulfan (Flu/Treo) provides survival and disease control comparable to fludarabine–melphalan(Flu/Mel) in adult ALL undergoing allo-HSCT.

Methods: This retrospective study included adult patients(≥18 years) with ALL undergoing first allo-HSCT between 2012 and 2024. Patients receiving Flu/Mel or Flu/Treo conditioning were analysed. Patients transplanted in CR1, CR2+ or with active disease were eligible, and all donor types were allowed. GVHD prophylaxis was administered according to centre practice.
The primary endpoint was 2-year leukaemia-free survival(LFS). Secondary endpoints included overall survival (OS), relapse incidence(RI), non-relapse mortality (NRM) and GVHD. Survival was analysed using Kaplan–Meier estimates, while competing risks methodology was applied for RI and NRM. Multivariable Cox models adjusted for relevant covariates. Subgroup analyses were performed in B-lineage and T-lineage ALL, with propensity score matching applied in T-ALL.

Results: A total of 1,097 adult patients were included, of whom 876 received Flu/Mel and 221 Flu/Treo conditioning. Median follow-up was 3.8 years overall and differed between groups, being longer in the Flu/Mel cohort (4.1 years) than in the Flu/Treo cohort (2.9 years), reflecting more recent adoption of treosulfan-based regimens. Patients treated with Flu/Treo were older at transplantation and more frequently received myeloablative-intensity conditioning, whereas Flu/Mel was predominantly administered as reduced-intensity conditioning.
Despite these differences, transplant outcomes were comparable. At 2 years, OS was 64.2% after Flu/Treo and 60.9% after Flu/Mel, while LFS was 55.7% and 50.3%, respectively. The cumulative incidence of relapse was numerically lower in the Flu/Treo group (27.1% vs 30.9%), whereas NRM was similar (17.1% vs 18.8%). In multivariable analysis adjusting for year of transplantation, disease status at transplant, performance status, patient and donor age, CMV serostatus and centre effect, Flu/Treo conditioning was independently associated with improved LFS (HR 0.70, 95% CI 0.52–0.94; p=0.018) and reduced relapse risk (HR 0.62, 95% CI 0.42–0.91; p=0.014), without increasing NRM. No significant difference in OS was observed.
Results were consistent in B-lineage ALL. In T-lineage ALL, a propensity score–matched analysis generated well-balanced cohorts (94 Flu/Mel and 36 Flu/Treo). In the matched population, 2-year OS (72.9% vs 65.7%), LFS (68.8% vs 59.5%), RI (21.9% vs 31.3%) and NRM (9.3% vs 9.1%) were comparable between regimens. Cox regression confirmed no significant association between conditioning type and outcomes.



Conclusions: In adult patients with ALL undergoing first allo-HSCT, Flu/Treo conditioning provides survival and disease control outcomes comparable to Flu/Mel. Flu/Treo was associated with similar overall survival and non-relapse mortality, and with improved leukaemia-free survival and reduced relapse risk in multivariable analysis. These findings, support Flu/Treo as an effective and safe intermediate-intensity conditioning alternative to Flu/Mel in adult ALL.

Disclosure: DA received travel grant, study grant from MEDAC.

OS08-03

ADULT ACUTE MYELOID LEUKEMIA WITH *FUS::ERG* FUSION: A NATIONAL, RETROSPECTIVE, MULTI-CENTER STUDY

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Background: Acute myeloid leukemia (AML) patients with t(16;21)(p11;q22)/*FUS::ERG* demonstrate poor outcomes even after allogeneic hematopoietic cell transplantation (allo-HCT). Therefore, it is necessary to investigate the clinicopathological features, genomic and transcriptomic landscape, as well as treatment outcomes in a larger cohort to gain an in-depth understanding of this specific subtype.

Methods: We initiated a retrospective study of adult patients in Chinese TROPHY group. Patients with t(16;21)(p11;q22)/*FUS::ERG* were identified by reviewing karyotypes, polymerase chain reaction or RNA sequencing (RNA-seq) results. The survival data were estimated using Kaplan–Meier curves and log-rank test. Prentice, Williams and Peterson total time (PWP-TT) model was used for analysis of recurrent time-to-event data, with results presented as hazard ratios (HR) and corresponding 95% confidence intervals (CI) for risk factors (age, gender, ELN risk stratification, and allo-HCT) regarding disease relapse. Data of 899 patients with transcriptome results were provided as a reference cohort.

Results: A total of 104 adult AML patients with *FUS::ERG* were identified, and RNA-seq were available in 25 patients. The median age was 35 (range: 14-73) years old, 13 patients aged older than 60. Patients showed high WBC (median: 12.9×10^9/L) and BM blast counts (median: 72.0%), M5 (51.0%) was the predominant FAB subtype. Complex karyotypes were found in 41.3% of patients. *PTPN11*, *RUNX1*, and *NRAS* are the most prevalent somatic

mutations. Ninety-two patients were stratified according to 2022 ELN with 56 (60.9%) cases in adverse-risk group. Ninety-one patients were eligible for intensive chemotherapy, 8 patients received low intensity induction. After two courses of induction, 83.8% patients achieved morphology complete remission (CR).

Characteristics	***FUS::ERG* fusion· (N=104)**
Male, *n* (%)	60 (57.7)
Age (median [IQR])	35.0 [22.5, 51.0]
White blood cell count (x10^9/L, median [IQR])	12.9 [4.0, 30.8]
Bone marrow blast% (median [IQR])	72.0 [55.0, 84.0]
Induction treatment, *n* (%) Intensive Lower-intensity Frail	 91 (87.5) 8 (7.7) 5 (4.8)
CR after 1st course, *n* (%)	61/99 (61.6)
MFC-MRD negativity after 1st course, *n* (%)	20/52 (38.5)
CR after 2nd course, *n* (%)	83/99 (83.8)
MFC-MRD negativity after 2nd course, *n* (%)	33/71 (46.5)
Allo-HCT in CR1, *n* (%)	55/83 (66.3)

The estimated 2-year probability of relapse, EFS, and OS of 77.2%, 18.7%, and 38.1%, respectively. Fifty-five patients underwent allo-HCT in CR1, 3 in CR2, and 7 in active disease. In CR1 cohort, both 2-year OS (allo-HCT: 59.1%, 95% *CI*: 46.2-75.5%; chemotherapy: 5.1%, 95% CI: 0.8-33.7%, *P*<0.0001) and EFS (allo-HCT: 34.1%, 95% *CI*: 22.7-51.2%; chemotherapy: 0%, *P*<0.0001) were improved significantly with allo-HCT. The PWP-TT model revealed higher risk of relapse in patients aged ≥60 (HR: 8.1, 95% CI: 2.7–23.7, *P*<0.001), and allo-HCT can significantly reduce recurrence (HR: 6.5; 95% CI, 3.8–11.4, *P*<0.001). Compared to reference cohort, *FUS::ERG* AML demonstrated similar long-term survival to the ELN adverse-risk group.

Transcriptome-based analysis clustered all 25 cases together and classified into the myelodysplasia-related/-like subtype.Differential expression gene (DEG) analysis revealed that insulin-like growth factor-2 mRNA-binding protein 1 (*IGF2BP1*) expression was significantly upregulated in *FUS::ERG* fusion AML comparing to reference cohort. Gene Ontology (GO) analysis indicated that immune function-related pathways were significantly down-regulated, including immune system process, immune response, regulation of immune system, MHC protein complex binding, antigen binding and immune receptor activity.

Elevated levels of *IGF2BP1* correlated with loss of MHC class II expression (HLA-DR, -DQ, -DP, -DM, -DO) alongside suppression of most immune stimulators (CD28, CD80, CD86, KLRK1 and TNFSF/TNFRSF).

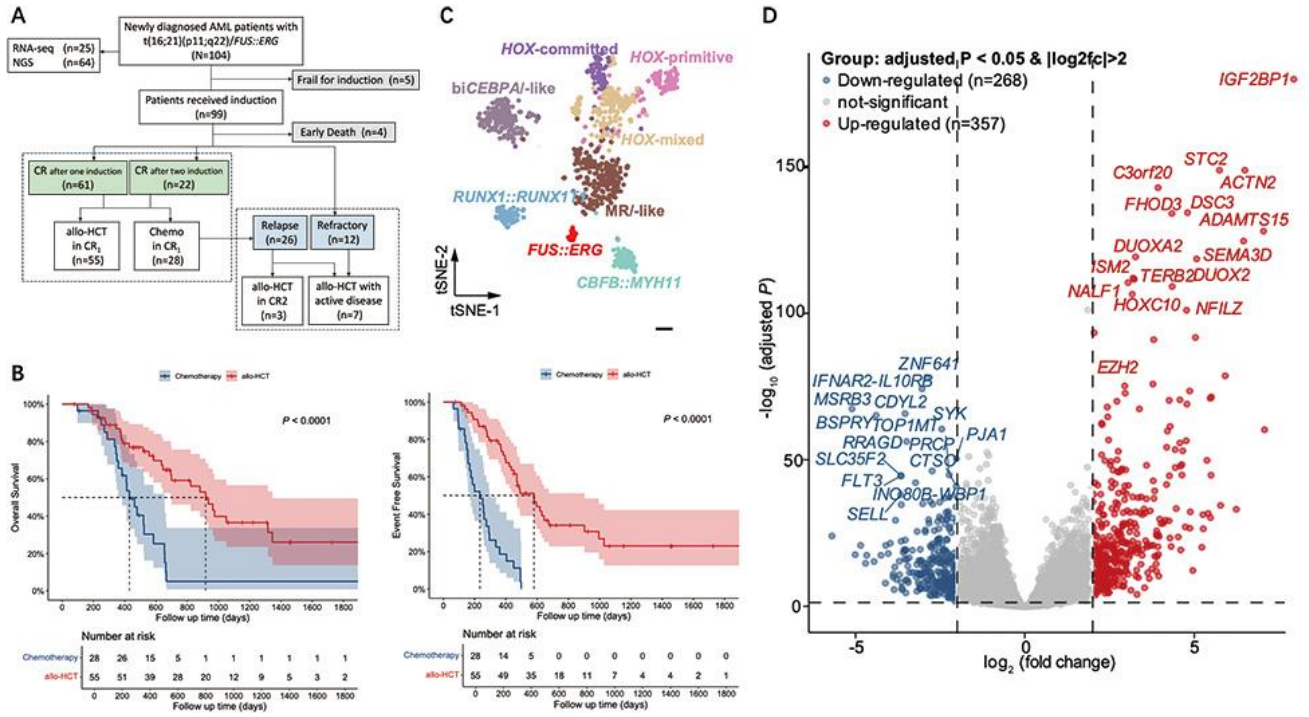

Figure 1. (A) Flow Chart. (B) Long-term survival of *FUS::ERG* AML. OS and EFS between patients treated with allo-HCT or chemotherapy for consolidation in CR1. (C) Transcriptome-based analysis clustered all 25 cases together. (D) Volcano plots show the positive and negative correlation of gene expression patterns.

Conclusions: We presented the largest comprehensive evidence to characterize adult AML with *FUS::ERG* fusion which demonstrate poor outcomes with high relapse even after allo-HCT. Immune-evasion phenotype driven by *IGF2BP1* overexpression may be the key factor contributing to the poor prognosis.

Disclosure: Nothing to declare.

OS17-01

VENETOCLAX PLUS HYPOMETHYLATING AGENTS IN ACUTE MYELOID LEUKEMIA RELAPSING POST ALLOGENEIC STEM CELL TRANSPLANT: EBMT ALWP REAL-WORLD EVIDENCE

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Background: Relapsed acute myeloid leukemia (AML) post allogeneic stem cell transplant (HSCT) remains a major challenge. Hypomethylating agents (HMA) alone or combined with venetoclax (VEN) are effective and well tolerated in newly diagnosed and relapsed AML. While the former have been used as maintenance, preemptive and salvage therapy to enhance graft-versus-leukemia effects; nonetheless, optimal combinations-particularly with VEN remain undefined.

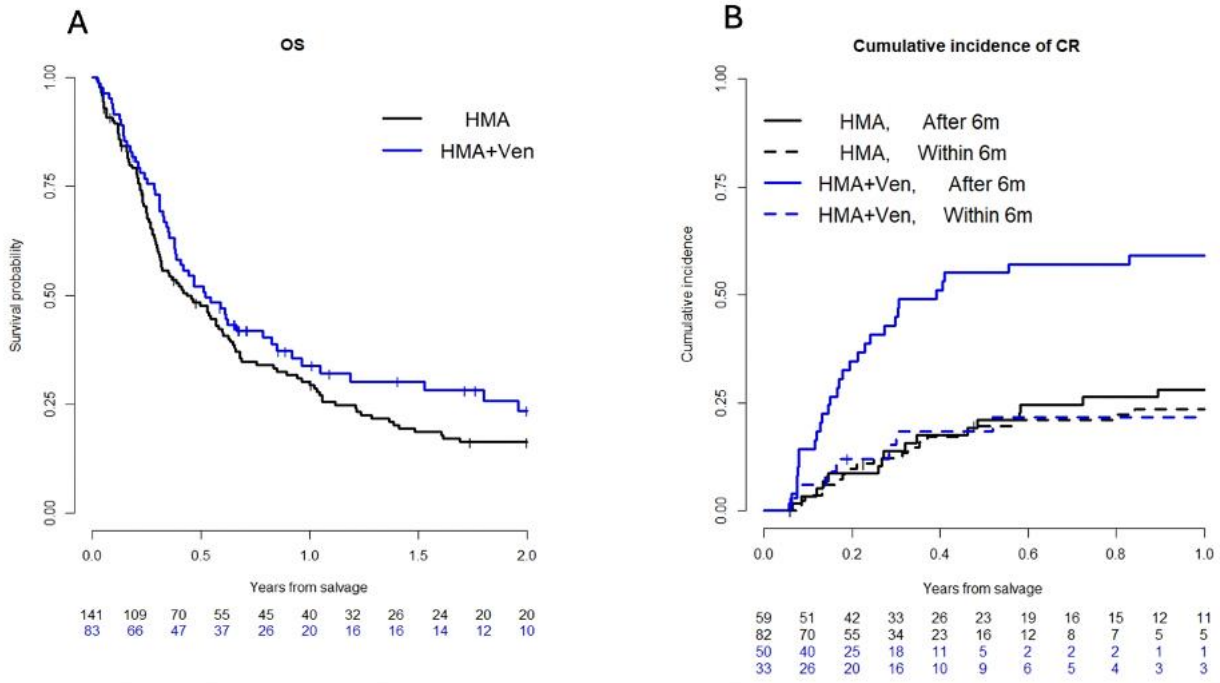
Methods: EBMT registry-based multicenter analysis approved by the ALWP, including adults who underwent first HSCT in first complete remission between 2010-2022 with subsequent relapse comparing outcomes with treatment with HMA alone or with venetoclax (started within 2 months of relapse).

Results: A total of 224 patients (NPM1 mutation in 17% and FLT3-ITD in 18%) with relapse post HSCT. Of the total cohort, 83 received HMA/VEN (75 azacitidine/VEN), while 141 patients received HMA alone (128 azacitidine). Most received peripheral blood stem cells (97%). Table 1 shows baseline characteristics for both groups. Pre-transplant azacitidine (21% vs. 8%; p=0.006) or VEN (11% vs. 2%; p=0.01) were more commonly used in the combination group. There was no significant difference with respect to gender or female donor to male recipient. HMA/VEN resulted in improved 1-year cumulative incidence of complete remission (CR) post salvage [44% (95% CI 33-55) vs. 26% (95% CI 19-33); p=0.003], and higher likelihood of second HSCT [27% (95% CI 17-38) vs. 12% (7-18)], with however no difference in 2-year overall survival (OS) from salvage [24% (IQR 14-35) in the HMA/VEN group vs.16% (IQR 11-23); p=0.18]. Relapse beyond 6 months post HSCT and the absence of adverse risk cytogenetics positively affected the 1-year cumulative incidence of CR post-salvage and 2-year OS, while female gender improved 2-year OS. In multivariable analysis, the absence of adverse cytogenetics (hazard ratio [HR] 0.68, 95% CI 0.5-0.9; p=0.01) and late relapse were predictive of better OS [HR for early relapse 1.64, (95% CI 1.2-2.2); p=0.002]. For those with late relapse, HMA/VEN treatment was associated with improved cumulative incidence of CR (HR 3.52, 95% CI 1.9-6.7; p<0.001), while in the early relapse group there was no difference between the salvage groups (HR 0.49, 95% CI 0.3-1.9; p=0.61). 73 patients achieved CR following post-HSCT relapse (2-year OS from CR was 47%); including 36 who received combination therapy having shorter median time from

salvage to CR compared to those who received HMA alone (62 vs. 115 d; p=0.008), higher likelihood to receive a 2nd HSCT within 2-year from CR (46% vs. 8%), and lower likelihood to receive donor lymphocyte infusion (6% vs. 22%).

Patient Characteristics		HMA N=141	HMA/VEN N=83	P-value
Year of HSCT	Median [IQR]	2016 [2014-2018]	2020 [2019-2021]	<0.001
Age at HSCT	Median [IQR]	57 [47-63]	55 [40-62]	0.25
AML type (%)	De novo Secondary	100 (72) 39 (28)	61 (75) 20 (25)	0.59
Adverse risk cytogenetics (%)	Yes	76 (56)	32 (43)	0.13
Pre-HSCT Treatment (%)	Azacitidine VEN	11 (8) 3 (2)	17 (21) 9 (11)	**0.006** **0.01**
Time to HSCT (months)	Median [IQR]	4.4 [4-6]	4.6 [4-6]	**0.47**
Donor type (%)	Matched sibling Haploidentical Unrelated	42 (30) 15 (11) 82 (57)	20 (24) 14 (17) 47 (57)	NA
Conditioning (%)	Myeloablative	58 (41)	49 (59)	**0.01**
PTCy (%)	Yes	30 (21)	28 (34)	**0.03**
Time to relapse post HSCT (days)	Median [IQR]	157 [97-356]	269 [142-528]	**0.002**
Time relapse to salvage (days)	Median [IQR]	12 [4-19]	13 [6-21]	0.39
Follow up (years)	Median [IQR]	6.8 [4.4-7.5]	2.6 [1-3.3]	NA

Table 1. Baseline Characteristics for patients receiving HMA and those receiving combination HMA/VEN
Abbreviations: AML: acute myeloid leukemia; HMA: hypomethylating agents; PTCY: post-transplant cyclophosphamide; VEN: venetoclax.



Graph 1. A Overall survival (OS) for both groups; B: cumulative incidence of complete remission (CR) with treatment and time to relapse.

Conclusions: HMA±VEN are viable salvage treatment options for AML relapsing post HSCT, with long-term survival in a select group of patients, particularly those with late relapse and no adverse risk cytogenetics. HMA/VEN combination results in increased CR rates and likelihood of a second HSCT.

Disclosure: Nothing to declare.

B281

A NOVEL RISK STRATIFICATION FRAMEWORK FOR CEBPA MUTANT AML BASED ON CEBPA BZIP IN-FRAME INSERTION/DELETION AND NRAS/CSF3R CO-MUTATIONS

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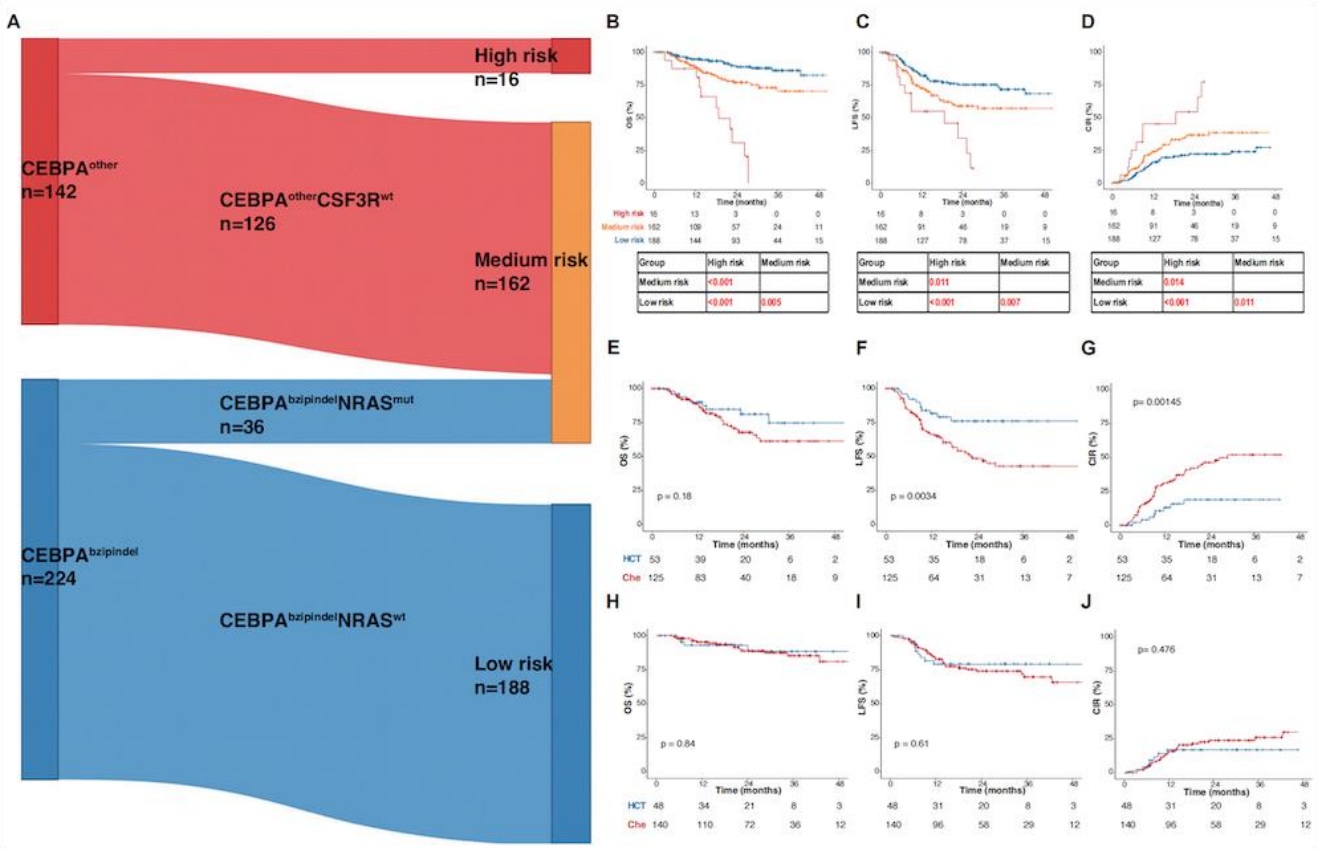
Background: CEBPA mutation occurs in 10% to 15% of AML patients. CEBPA bZIP in-frame insertions/deletions (CEBPA^{bzipindel}) have been identified as a distinct entity associated with favorable outcomes. However, co-occurrence of other mutations significantly impacts prognosis of CEBPA mutant AML. A refined framework for CEBPA-mutant AML is needed for risk stratification and clinical decision-making.

Methods: Data from 366 consecutive de novo CEBPA mutant adult AML patients diagnosed between 2015 and 2024 from three centers across China were analyzed. Based on CEBPA mutation subtype, patients were classified into CEBPA^{bzipindel} (n=224) and CEBPA^{other} (n=142) cohorts. Multivariate survival analyses were conducted using Cox proportional hazards regression models.

Results: The median follow-up were 21.87 months (interquartile range [IQR], 12.47-33.64) for the CEBPA^{bzipindel} cohort and 17.35 months (IQR, 10.24-28.12) for the CEBPA^{other} cohort. Following two cycle of induction chemotherapy, the composite complete remission rate (CRc) rate was 99.5% in the CEBPA^{bzipindel} and 94.5% in the CEBPA^{other} cohort, respectively.
An exploration of the co-mutation landscape identified WT1, TET2, GATA2, NRAS, and CSF3R as the most recurrent mutations in the entire population. The top 5 co-mutations in the The CEBPA^{bzipindel} cohort were WT1, GATA2, NRAS, TET2, and CSF3R, respectively. The top 5 co-mutations in the CEBPA^{other} cohorts was TET2, WT1, NPM1, STAG2 and IDH2, respectively.
In multivariate analysis, CSF3R mutation emerged as an independent factor for poorer overall survival (OS), both in the entire cohort (aHR = 2.02 [95%CI, 1.07-3.81]) and the CEBPA^{other} cohort (aHR = 3.51 [95%CI, 1.68-7.30]). NRAS mutations was independently correlated with poorer leukemia-free survival (LFS) in the entire cohort (aHR = 1.65 [95%CI, 1.01-2.69]) as well as the CEBPA^{bzipindel} cohort (aHR = 1.95 [95%CI, 1.03-3.47]).
Within the *CEBPA*^{bzipindel} cohort, patients harboring concurrent *NRAS* mutations (*CEBPA*^{bzipindel}*NRAS*^{mut}) had significantly inferior 2-year LFS and higher 2-year cumulative incidence of relapse (CIR) than *CEBPA*^{bzipindel}*NRAS*^{wt}. Within the *CEBPA*^{other} cohort, the presence of *CSF3R* mutations (*CEBPA*^{other}*CSF3R*^{mut}) was associated with significantly inferior 2-year OS, LFS and higher 2-year CIR compared with *CEBPA*^{other}*CSF3R*^{wt} cohort.
Furthermore, all major transplant outcomes were comparable between the *CEBPA*^{bzipindel}*NRAS*^{mut} and *CEBPA*^{other}*CSF3R*^{wt} cohorts.
Accordingly, the four cohorts were further re-defined into a three-tier risk model: low risk (*CEBPA*^{bzipindel}*NRAS*^{wt}), intermediate risk (*CEBPA*^{bzipindel}*NRAS*^{mut} and *CEBPA*^{other}*CSF3R*^{wt} combined), and high risk (*CEBPA*^{other}*CSF3R*^{mut})
. This proposed risk model demonstrated robust discriminatory capacity for key survival endpoints, including 2-year OS, LFS, and CIR.To further evaluate the utility of this risk model in guiding allogeneic hematopoietic stem cell transplantation (allo-HCT) decision making, we compared outcomes between patients receiving allo-HCT and those treated with chemotherapy only within each risk category. In the intermediate/high risk cohort, allo-HCT conferred a clear survival advantage over chemotherapy alone (OS: HR = 0.60 [95%CI, 0.29-1.26]; LFS: HR = 0.39 [95%CI, 0.21-0.75]; CIR: HR = 0.33 [95%CI, 0.16-0.71]). In the low risk cohort, allo-HCT was associated with similar outcomes compared with chemotherapy.



Conclusions: Integrating *CEBPA* bZIP insertion/deletion, *NRAS* and *CSF3R* status into the stratification of *CEBPA* mutant AML allow for a more precise risk stratification and assist in clinical decision making especially allo-HCT.

Disclosure: Nothing to declare.

B282

ALLOGENEIC TRANSPLANTATION OUTCOMES OF PHILADELPHIA-POSITIVE ACUTE LYMPHOBLASTIC LEUKEMIA WITH OR WITHOUT ADDITIONAL CYTOGENETIC ABNORMALITIES AND COMPLEX KARYOTYPE: A STUDY FROM THE ALWP/EBMT

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Background: Ph+ is the most common cytogenetic abnormality in adults with ALL. 60%-70% of the Ph+ ALL patients (pts) harbor additional chromosomal abnormalities (ACA) and complex karyotype (CK). The impact of ACA and CK on outcomes of Ph+ ALL pts undergoing allogeneic transplantation (HSCT) while in first complete remission (CR1) in the tyrosine kinase inhibitors (TKIs) era is controversial.

Methods: 514 Ph+ pts that received TKI (Imatinib-62%, Dasatinib-17.7%, Nilotinib-13.3%, other-7%) followed by HSCT while CR1 between 2010-2022 were included.

Results: 345 pts harbor ACA (109 had 1 ACA, 100 had 2-3 ACA, and 136 had $\geq$ 4 ACA) and 169 did not (noACA). 210 pts had at least one monosomy, most frequently monosomy 7 (n=63). 101 pts had at least one trisomy. Twelve pts had 11q23 translocations. IKZF1 mutations were observed in 8.7% and 7.7% of pts with and without ACA, respectively. The presence of ACA was associated with a higher rate of MRD-negativity pre HSCT (56.2% vs. 46.5%, p=0.04). Median follow-up was 4.2 years. Median year of transplant was 2018. Median age was 42.6 years, and 54.5% were male. The groups (ACA vs. noACA) did not differ significantly in terms of age, gender, and interval from diagnosis to HSCT. Donors were matched siblings in 32.5% vs. 28.4%, unrelated in 37.1% vs. 27.2%, or haploidentical in 28.7% vs. 40.2%, respectively. More pts with ACA received PB grafts compared to the noACA group (86.4% vs. 78.1%, p=0.03). CMV seropositivity was higher in the ACA group (70.5% vs. 57.2%, p=0.009). Myeloablative conditioning was used more frequent in the noACA group (87% vs. 75.9%, p=0.003), with TBI-based in 51.9% vs. 40.2%, respectively. Day 30 ANC $\geq 10^9$/L was 97.9 % vs. 98.2 % and day 60 platelet count $\geq 20x10^9$/L was 93.9 % vs. 95.5%, for the ACA and noACA groups. Day 100 acute (a) GVHD grades II-IV was 26.4% vs. 31% and of grades; III-IV was 8.6% vs. 9.7%, respectively. 4-year chronic (c) GVHD was 40.5 % vs. 39.9 % and of extensive cGVHD was 19.3% vs. 20.1 %. 4-year NRM was 13.1 %

vs. 13. 5%, and 4-year RI was 19.2 % vs. 21.1 %, respectively. The 4-year LFS and OS rates were 67.7% vs. 65.4 % and 76.3% vs. 78.5%, respectively. 4-year GRFS was 48.5% vs. 45%, respectively (Figure). In multivariate analysis, having ACA and the number of ACAs did not affect transplant outcomes significantly. Compared to noACA, HR for LFS were 0.93, 0.90, and 1.06 for 1 ACA, 2-3 ACA, and ≥4 ACA, respectively. MRD-positivity pre-HSCT was a poor prognostic factor for LFS, OS, and NRM. A mismatched related donor was associated with lower RI and higher NRM.

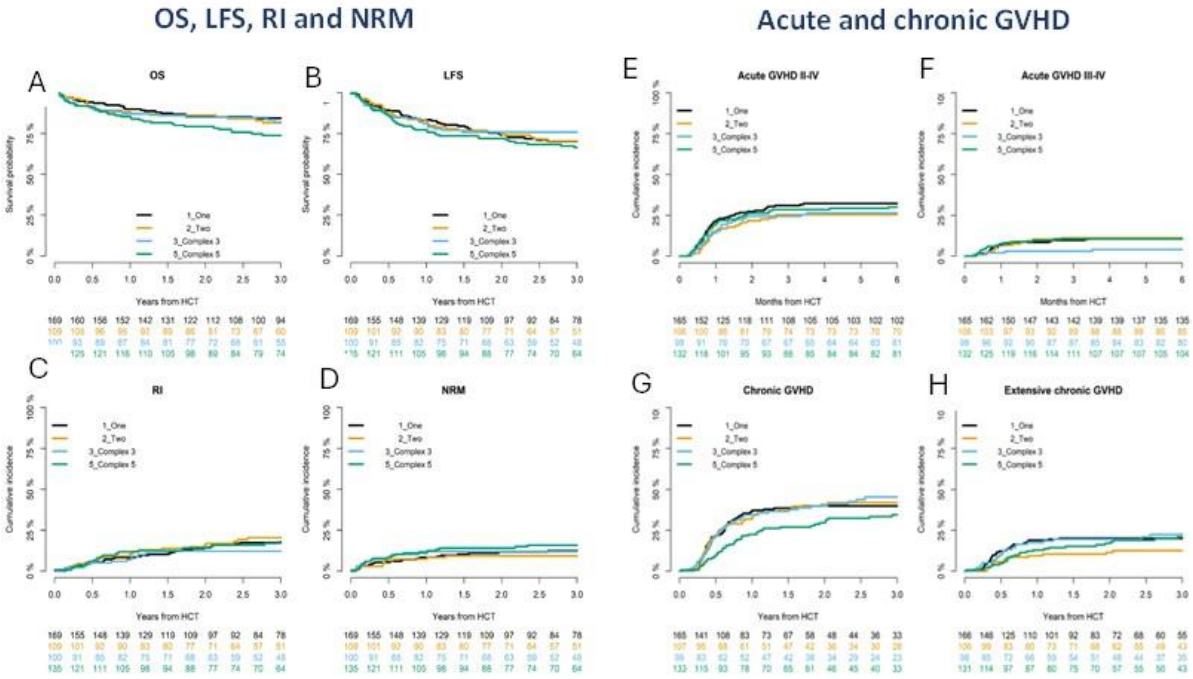

Figure legend: Outcomes of allogeneic HSCT in patients with Ph+ ALL in CR1 with or without additional cytogenetic abnormalities and complex karyotype: A. overall survival (OS); B. leukemia-free survival (LFS); C. relapse incidence (RI); D. non-relapse mortality (NRM); E. acute graft versus host disease (GVHD) II-IV; F. acute GVHD III-IV; G. chronic GVHD; H. extensive chronic GVHD.

Arnon Nagler[1*] and Jordi Esteve[2*] contribute equally to the study

Conclusions: Harboring ACA and CK did not affect outcomes of Ph+ ALL pts receiving a TKI and subsequent HSCT. Notably, achieving MRD-negativity pre HSCT was significantly higher in pts with ACA. These data may indicate that the administration of a TKI upfront, followed by HSCT, may overcome the poor prognosis influence of the ACA, including CK in Ph+ ALL.

Disclosure: Nothing to declare

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SURVIVAL BENEFIT OF ALLOGENEIC TRANSPLANT IN TP53-MUTATED AML ACROSS SINGLE- AND DOUBLE-HIT DISEASE

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Background: Outcomes in TP53-mutated AML remain poor, while the role of allogeneic hematopoietic stem cell transplant(allo-HSCT) in this group is increasingly debated. TP53 mutations can be categorized as single-hit(SH) or double-hit(DH), however, its impact on transplant outcomes is not well defined. We assessed the use allo-HSCT and outcomes across TP53-mutated AML subgroups.

Methods: We retrospectively reviewed TP53-mutated AML patients, defined by a TP53 mutation (VAF ≥2%), 17p cytogenetic abnormality, or both. Allelic status was classified per Grob et al., 2022: DH was defined as ≥2 TP53 mutations, a TP53 mutation with 17p abnormality, or a single mutation with VAF >55%. Post-transplant outcomes were analyzed from day 0, whereas survival comparisons between transplanted and non-transplanted groups were measured from morphological leukemia-free state (MLFS). To reduce immortal-time bias inherent to the transplant group, comparisons of transplant versus non-transplant were restricted to patients who achieved MLFS with survival ≥4 months, the median time to transplant. Overall survival (OS) and relapse-free survival (RFS) were estimated with Kaplan–Meier methods and estimated cumulative incidences (ECI) with Gray's competing risk model.

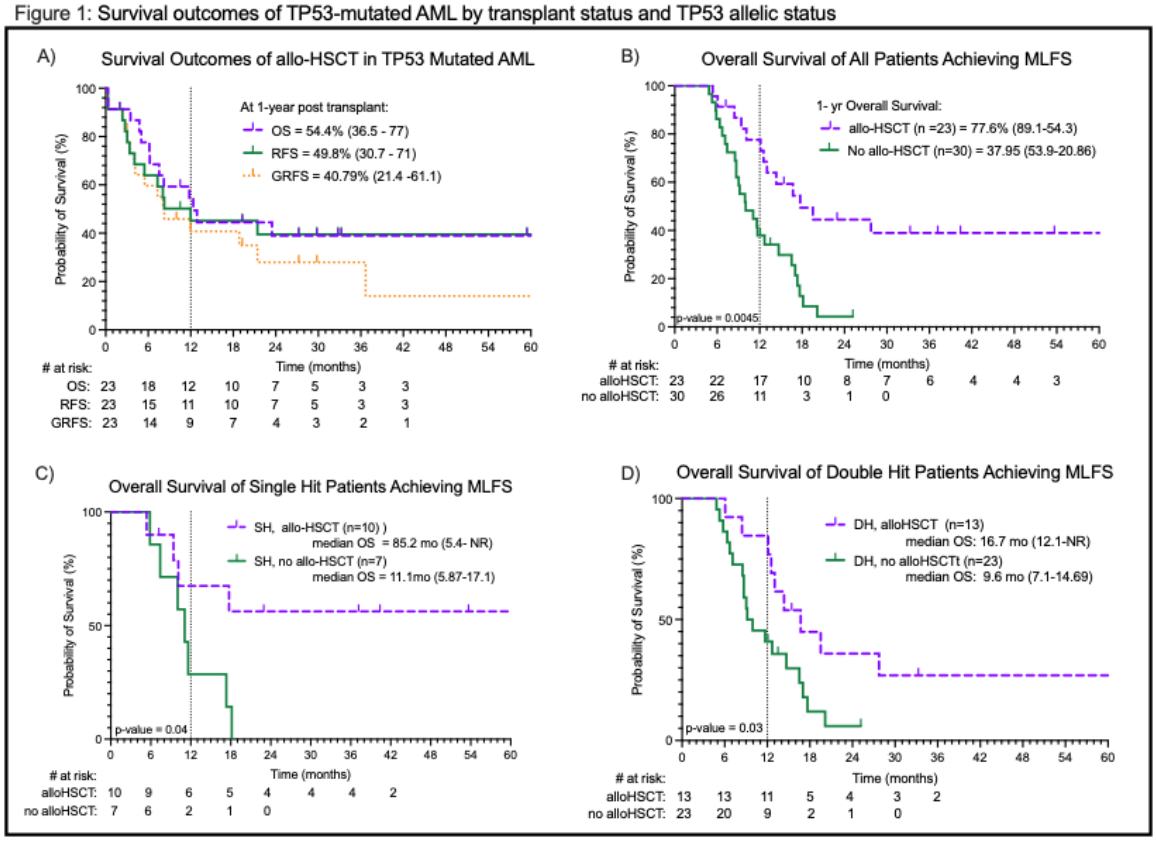
Results: Between 2019 and July 2025, 113 TP53-mutated AML patients were identified (median age 71.3years); 26.5% had SH, 61.9% had DH, and 11.5% were unclassifiable due to missing data. Most had de novo AML(56.6%) and received HMA +/- Venetoclax induction regimens(63.7%). Of classifiable patients, 53 achieved MLFS with 23 whom underwent allo-HSCT in first remission(Table 1). In the allo-HSCT cohort, median OS, RFS, and GVHD- and relapse-free survival (GRFS) from transplant were 12.4 mo(6.16–NR), 12 mo(3.4–NR), and 8.3 mo(4–21.4), respectively(Figure 1A). The 1-year ECI of grade II–IV acute GVHD was 27.1%(10.6-46.7%), with no grade III–IV events; the 2-year ECI of moderate/severe chronic GVHD was 9.1%(1.4–26%). Patients who developed GVHD(n=9) had improved 2-year OS (76.2% vs 25.4%; p=0.006) and RFS(76.2% vs 23.4%; p=0.004). One-year ECI of relapse and NRM were 27%(10-46%) and 8.7%(1.4-24.6%). Likely due to a small cohort, conditioning intensity, donor type, and GVHD prophylaxis did not significantly affect OS, RFS, or GRFS.
In the MLFS-eligible group, allo-HSCT was associated with improved mOS (17.7 vs 10.0mo; p=0.0045) and mRFS (19.2 vs 9.2mo; p=0.0005) compared with non-transplanted patients (Figure 1B). This benefit was observed in both SH and DH patients with improved OS and RFS(Figures 1C–1D). Within the allo-HSCT cohort, SH patients had longer OS (81.2 vs 12.3mo; p =0.29) and RFS (81.2 vs 8.3mo, p=0.43) compared to DH patients though did

not reach statistical significance. ECIs of relapse, NRM, and acute or chronic GVHD were similar between SH and DH. Of note, three DH patients with day +60 MRD positivity received HMA maintenance.

Table 1: Baseline Characteristics of TP53-mutated AML cohort		All TP53 mutated (n=113)	No Allo-HSCT (n=90)	Allo-HSCT (n=23)
Sex (%)	Female	50 (44.2)	43 (47.8)	7 (30.4)
AML subtype:	Denovo	64	54	10
	AML with myelodysplastic changes	24	15	9
	Secondary AML	25	21	4
TP53 Allelic Status:	Single Hit	30	20	10
	Double Hit	70	57	13
	Unknown	13	13	0
Induction Treatment:	HMA +/-Ven	72	55	17
	Intensive	20	14	6
	Other/None	4/17	4/17	0
Donor:	MRD/MUD	-	-	4/9
	MMUD	-	-	2
	Haplo	-	-	8
Conditioning Regimen:	Myeloablative	-	-	3
	Reduced intensity	-	-	14
	Non-myeloablative	-	-	6
GVHD Prophylaxis:	MTX based	-	-	6
	PTCy based	-	-	13

	Clinical trial/Unknown	-	-	2/2

Figure 1: Survival outcomes of TP53-mutated AML by transplant status and TP53 allelic status



Conclusions: Allo-HSCT conferred a significant OS and RFS advantage for TP53-mutated AML patients who achieved MLFS, with benefit observed in both SH and DH disease. As modern transplant strategies continue to reduce toxicity, our findings support offering allo-HSCT to eligible TP53-mutated AML patients, although it remains unlikely to be curative for most. Larger studies are needed to define optimal conditioning and GVHD prevention regimens in this high-risk population.

Disclosure: Nothing to declare

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INOTUZUMAB OZOGAMICIN AS A BRIDGE TO ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN RELAPSED/REFRACTORY B-ALL: A STUDY ON BEHALF OF GETH-TC

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Background: Inotuzumab ozogamicin (InO) is an anti-CD22 antibody-drug conjugate that achieves high rates of remission and measurable residual disease (MRD) clearance in relapsed or refractory (R/R) B-ALL, and is increasingly used as a bridge to allogeneic hematopoietic cell transplantation (alloHCT). Its use may increase the risk of sinusoidal obstruction syndrome (SOS) and affect transplant outcomes, but real-world data remain limited.

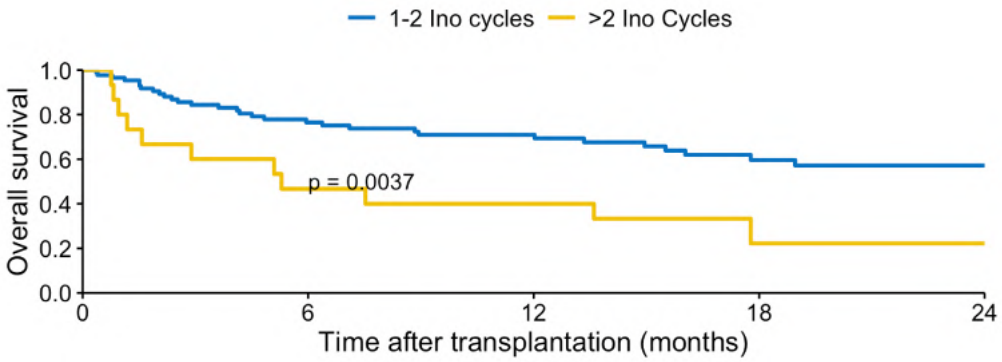
Methods: We conducted a retrospective multicenter analysis of adolescent and adult patients (³15 years old) with R/R B-ALL treated with InO who subsequently underwent alloHCT at 19 Spanish centers to evaluate its impact on transplant outcomes and SOS. Cases refractory to InO were excluded.

Results: A total of 101 patients were analyzed, 53 were male, with a median age of 38 years (range, 15-70). B-ALL NOS was the most frequent subtype (65%). InO was given for relapsed (55%) or refractory (43%) disease, with a median of 2 cycles (range, 1-6) and a median interval of 49 days (range, 16-189) from last InO to alloHCT. CR prior to transplant was 97%, with 71 MRD-negative patients. Donors included MSD (n=31), MUD (n=27), MMUD (n=19) and haploidentical (n=24). Myeloablative conditioning was used in 65 patients; overall, 57 received TBI-based and 31 double-alkylator regimens. PTCY-based GVHD prophylaxis was used in 73 patients.
Main transplant outcomes and risk factors are summarized in Table 1. SOS occurred in 33 patients at a median of 13 days (range, 4-90), mostly early-onset (88%) Cumulative incidence of SOS was 32% at 100 days. According to EBMT severity criteria, 3% were mild, 15% moderate, 41% severe and 41% very severe. Defibrotide was used in all but one patient, with SOS resolution in 22 patients (67%). Eleven patients died (30%) directly due to SOS (n=7) or from other causes with active SOS (n=4). SOS had a negative impact on NRM (HR 3.57, 95% CI: 1.6-8.3, P=0.002). Risk factors for SOS in multivariate analysis were: male gender, 2 or more lines prior to InO, <50 days interval between InO and alloHCT and TBI-based conditioning whereas type of donor and double-alkylator showed no impact.

Median follow-up of survivors was 16 months. Cumulative incidence of grades 2-4 acute GVHD and moderate-severe chronic GVHD were 27% and 16%, respectively.
Twenty-three patients died without prior relapse at a median of 101 days, most commonly due to infections (48%) or SOS (30%). One-year NRM was 21%. Thirty-three patients relapsed a median of 159 days; 1-year relapse incidence was 27%.
OS, LFS and GRFS at one year were 66%, 50% and 41%, respectively. Multivariate analysis showed worse OS and LFS for patients receiving 2 or more lines prior to InO and > 2 cycles of InO (Figure 1) as well as those with positive MRD prior to alloHCT.

Outcomes	Overall, % (95% CI)	Multivariate analysis Variables	HR	95% CI per HR	P value
SOS, at 100 days	32 (24-42)	Male Gender Lines prior InO >1 Interval InO-HCT ≥ 50d TBI-based	3.2 2.22 3.57 2.56	1.45-7.05 1.06-4.65 1.6-7.7 1.2-5.2	0.004 0.034 0.002 0.015
NRM, at 1 year	21 (14-30)	Lines prior InO >1 Interval InO-HCT ≥ 50d InO cycles >2	2.61 2.86 2.84	1.2-6.1 1.06-7.7 1.16-6.96	0.028 0.037 0.022
Relapse, at 1 year	27 (18-37)	Negative MRD	0.45	0.22-0.93	0.031
LFS, at 1 year	50 (41-62)	Negative MRD Lines prior InO >1 InO cycles >2	0.30 2.01 2.47	0.17-0.55 1.15-3.62 1.21-5.05	<0.001 0.015 0.013
OS, at 1 year	66 (57-76)	Negative MRD Lines prior InO >1 InO cycles >2	0.50 2.34 3	0.25-0.99 1.21-4.53 1.4-6.44	0.047 0.011 0.005
GRFS, at 1 year	41 (32-53)	Negative MRD Lines prior InO >1	2.44 2	1.39-4.17 1.17-3.46	0.002 0.012

Figure 1.



Conclusions: InO is an effective bridge to alloHCT for responsive R/R B-ALL patients. However, relapse and SOS remain major challenges, with InO exposure (>2 cycles or <50-day interval), number of prior treatment lines, and MRD status emerging as key risk factors influencing transplant outcomes.

Clinical Trial Registry: No.

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All other authors: Nothing to declare.

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"LESS IS MORE"? PTCY+CNI WITH VS WITHOUT MMF IN 10/10 MUD HCT FOR AML IN CR1. FROM THE GLOBAL COMMITTEE AND ALWP OF EBMT

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Background: Post-transplant cyclophosphamide (PTCy) is increasingly adopted in matched unrelated donor (MUD) hematopoietic cell transplantation (HCT) to decrease the risk of graft-versus-host disease (GVHD). While its efficacy is recognized, the optimal companion agents

for PTCy in the MUD setting remain debated. Clinical practice currently varies between a two-drug regimen (PTCy plus a calcineurin inhibitor [CNI]) and a three-drug regimen that adds mycophenolate mofetil (MMF). With limited data directly comparing these two approaches, the necessity of including MMF remains unproven. Therefore, a direct comparison is urgently needed to define the optimal GVHD prophylaxis strategy for patients undergoing MUD HCT in the PTCy era.

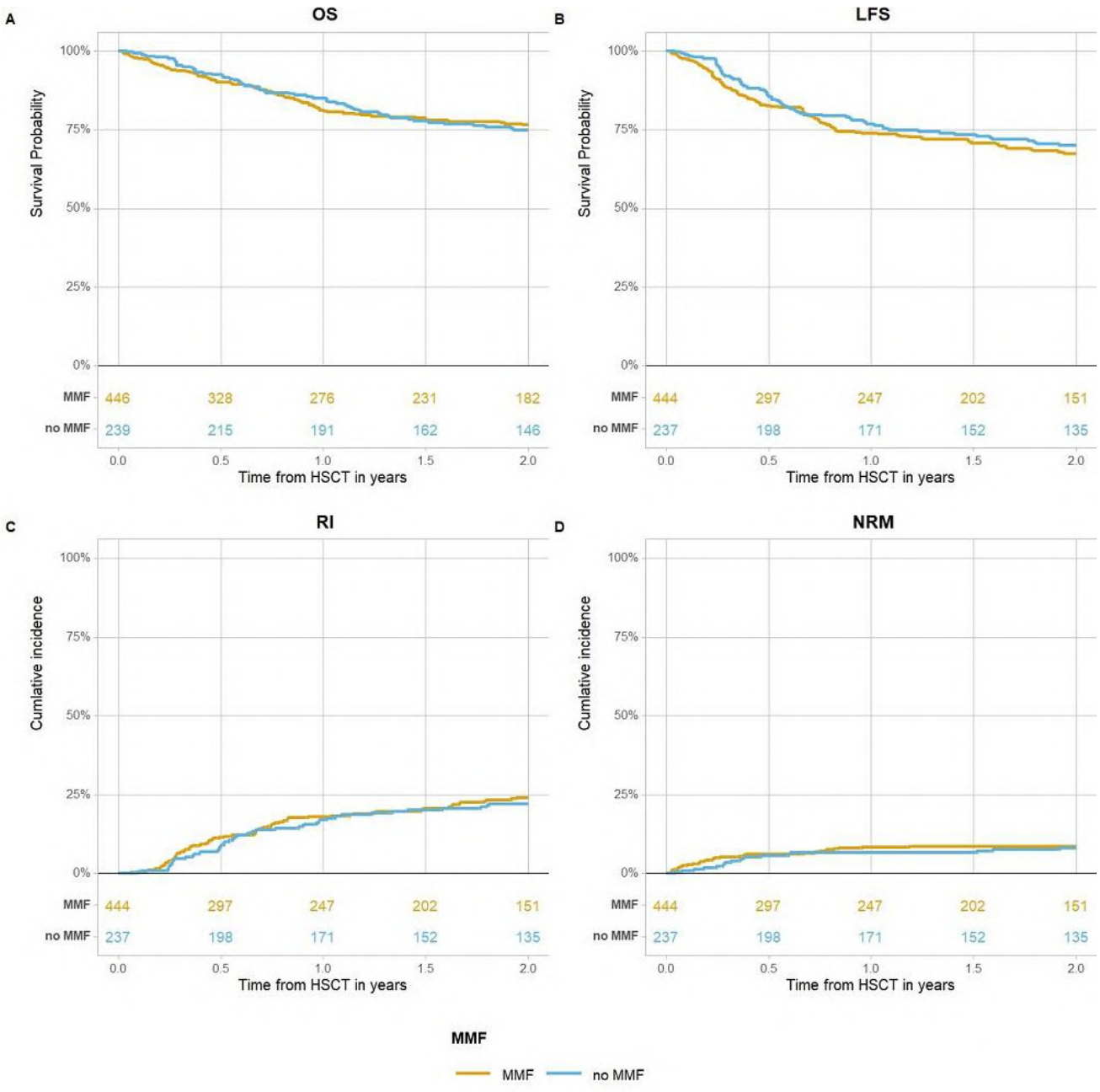
Methods: We retrospectively analyzed adult patients (≥18 years) with acute myeloid leukemia (AML) in first complete remission (CR1) who underwent their first allo-HCT between 2010 and 2022 from a 10/10 MUD using peripheral blood (PB) stem cells. Patients received PTCy+CNI with or without MMF for GVHD prophylaxis. Data were reported to the European Society for Blood and Marrow Transplantation (EBMT).

Results: The analysis included 687 patients: 448 received PTCy+CNI+MMF and 239 received the PTCy+CNI regimen. The median follow-up was 2.1 and 3.2 years, respectively. In the PTCy+CNI+MMF and PTCy+CNI groups, 52.8% and 66.1% of patients were male (P<0.001), respectively. Patients in the PTCy+CNI+MMF group were younger (median age: 52.8 vs. 58.1 years, P<0.001), transplanted more recently (median year: 2020 vs. 2019, P<0.001), and had better Karnofsky Performance Score (KPS ≥90: 84.8% vs. 60.3%, P<0.001). The PTCy+CNI+MMF group had a higher rate of patient Cytomegalovirus (CMV) seropositivity (79.4% vs. 61.2%, P<0.001) and a lower rate of donor-/recipient- CMV seronegative pairs (14.7% vs. 33.9%, P<0.001). More patients in the PTCy+CNI+MMF group received reduced-intensity conditioning (RIC) (39.4% vs. 30.5%, P=0.022). Cyclosporine was used as the associated CNI in 37% and 56.7% of the PTCy+CNI+MMF and PTCy+CNI groups, respectively (P<0.001). Patients in the PTCy+CNI+MMF group received grafts from older donors (median donor age: 29.6 vs. 27.0, P<0.001). The two patient cohorts did not differ regarding European LeukemiaNet (ELN) 2022 risk, donor sex, donor/recipient sex mismatch, and donor CMV status.
Outcomes at 2 years for the PTCy+CNI+MMF vs. PTCy+CNI groups were: overall survival (OS) 76.4% vs. 74.8%; leukemia-free survival (LFS) 67.3% vs. 70%; relapse incidence (RI) 24.1% vs. 22.1%; and non-relapse mortality (NRM) 8.6% vs. 7.9% (Figure 1). In multivariate analysis, no significant differences were observed in OS (HR=0.8, P=0.269), LFS (HR=0.89, P=0.583), or RI (HR=1.11, P=0.681). However, the omission of MMF (PTCy+CNI group) was significantly associated with lower NRM (HR=0.41, P=0.02). Additionally, older patient age (per 10 years) was associated with higher NRM (HR=1.47, P=0.007). Myeloablative conditioning (MAC) was associated with superior OS (HR=0.66, P=0.023) compared to RIC. More recent transplantation (per 5 years) was associated with better OS (HR=0.62, P=0.014) and lower NRM (HR=0.29, P=0.001).

Table 1. Patient characteristics

	Overall N = 687	PTCy+CNI+MMF N = 448	PTCy+CNI N = 239	P-value
Year of transplantation				<0.001

Median (IQR)	2020 (2018, 2022)	2020 (2018, 2022)	2019 (2017, 2021)	
KPS				<0.001
≥90	507 (76.2%)	367 (84.8%)	140 (60.3%)	
< 90	158 (23.8%)	66 (15.2%)	92 (39.7%)	
Missing	22	15	7	
Age of the Patient				<0.001
Median (IQR)	55.4 (41.4, 64.2)	52.8 (38.8, 63.4)	58.1 (47.2, 66.3)	
Sex of the Patient				<0.001
Female	292 (42.6%)	211 (47.2%)	81 (33.9%)	
Male	394 (57.4%)	236 (52.8%)	158 (66.1%)	
Missing	1	1	0	
RIC or MAC regimen				0.022
RIC	249 (36.3%)	176 (39.4%)	73 (30.5%)	
MAC	437 (63.7%)	271 (60.6%)	166 (69.5%)	
Missing	1	1	0	



Conclusions: Addition of MMF to PTCy+CNI resulted in comparable survival and relapse outcomes but significantly higher NRM compared to PTCy+CNI alone. The two-drug regimen (PTCy+CNI) may be a sufficient and potentially safer GVHD prophylaxis strategy for AML patients in CR1 undergoing 10/10 MUD transplantation.

Disclosure: Nothing to declare.

B286

IMPACT OF INDUCTION RESPONSE AND CO-MUTATIONS ON TRANSPLANT OUTCOMES IN AML WITH MYELODYSPLASIA-RELATED GENE MUTATIONS: A MULTICENTER RETROSPECTIVE STUDY

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Background: Acute myeloid leukemia (AML) is a genetically heterogeneous hematologic malignancy. According to the International Consensus Classification (ICC) 2022, AML with mutations in ASXL1, BCOR, EZH2, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2, or RUNX1 is defined as AML with myelodysplasia-related gene mutations (AML-MR) and categorized as adverse risk by ELN-2022. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a potentially curative treatment; however, the prognostic impact of AML-MR co-mutations in the transplant setting remains unclear.

Methods: This is a multicenter, retrospective designed study, based on the transplant database of the TROPHY group. AML patients receiving allo-HSCT between February 2016 and December 2023 were screened. Inclusion criteria were AML diagnosis, ELN-2022 adverse-risk classification, and presence of ≥1 AML-MR mutation. Induction therapy followed NCCN guidelines. Complete remission (CR) was defined as <5% bone marrow blasts with hematologic recovery. Patients failing first induction received a second cytarabine-based regimen. Consolidation strategies were determined by MRD status, donor availability, and patient fitness. Endpoints included relapse-free survival (RFS), overall survival (OS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM).

Results: A total of 341 patients were included. The most frequent AML-MR mutations were ASXL1 (32%), RUNX1 (29%), and BCOR (22%). Common co-mutations included TP53 (7%) and epigenetic regulator genes (IDH1/2, DNMT3A, TET2; each 6%). Overall, 193 patients (56.6%) achieved CR after first induction. Hypomethylating agent- or venetoclax-based regimens resulted in higher CR rates than conventional IA regimens (61.8% vs. 45.0%, p=0.007). Prior to allo-HSCT, 322 patients (94.4%) achieved CR. The 2-year OS and RFS for the entire cohort were 77.4% and 70.0%, respectively.
Patients achieving CR before transplantation had superior RFS (2y-RFS: 71.1% vs. 49.3%,

p=0.026) and a trend toward lower CIR. Achieving CR after first induction was associated with significantly improved RFS (81.8% vs. 55.5%), OS (85.6% vs. 66.3%), lower CIR (9.5% vs. 18.8%), and reduced NRM (all *p*<0.05). Multivariate analysis identified post-remission consolidation as an independent predictor of improved OS (HR=0.56, *p*=0.015). Grade III–IV acute GvHD and TET2 co-mutation were associated with inferior OS, while Grade III–IV acute GvHD and pre-transplant MRD positivity predicted inferior RFS. TP53 and NPM1 co-mutations showed no significant impact on survival. Patients with epigenetic regulator mutations had reduced OS (2y-OS: 73.0% vs. 83.1%, *p*=0.044).

Conclusions: In patients with AML-MR, Induction regimens incorporating hypomethylating agents or Venetoclax were associated with improved CR rates. Achieving CR after first induction significantly improves post-transplant RFS and OS along with reduced CIR and NRM. Co-mutations in TP53 and NPM1 did not significantly impact survival. Notably, epigenetic regulator mutations were linked to reduced OS, highlighting the prognostic relevance of specific co-mutations in AML-MR.

Disclosure: Nothing to declare.

B287

TREOSULFAN-BASED CONDITIONING WITH PTCY IN AML: A COMPARISON BETWEEN HAPLOIDENTICAL AND 9/10 MUD TRANSPLANTS. A STUDY FROM THE ACUTE LEUKEMIA WORKING PARTY OF THE EBMT

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Background: The availability of reduced-toxicity conditioning regimens and modern graft-versus-host disease (GVHD) prophylaxis has expanded access to allogeneic haematopoietic stem cell transplantation (allo-HSCT). Treosulfan-based conditioning reduces transplant-related mortality while preserving antileukaemic efficacy, and post-transplant cyclophosphamide (PTCy) effectively limits acute and chronic GVHD across donor platforms. The combination of reduced toxicity and selective elimination of alloreactive T cells may mitigate the historical impact of donor HLA disparity. This study compared outcomes after 9/10 HLA-mismatched unrelated donor and haploidentical transplantation in adult AML patients in first complete remission (CR1), testing whether reduced toxicity conditioning may outweigh donor HLA matching.

Methods: This retrospective EBMT registry study included adult patients with acute myeloid leukaemia (non-APL) in first complete remission (CR1) undergoing allo-HSCT between 2012 and 2023. All patients received treosulfan-based conditioning and PTCy-based GVHD prophylaxis, and were transplanted from either a 9/10 mismatched unrelated donor or a haploidentical related donor. The primary endpoint was 1-year event free survival. Secondary endpoints included survival outcomes, non-relapse mortality, relapse incidence, GVHD, GVHD-free/relapse-free survival, and engraftment. Survival analyses used Kaplan–Meier estimates, while competing risks and multivariable Cox and Fine–Gray models were applied as appropriate.

Results: Overall, 275 adult AML patients in first complete remission were included, of whom 206 underwent haploidentical transplantation and 69 received a 9/10 HLA-mismatched unrelated donor transplant. Median follow-up was 2.5 years and was comparable between donor groups. Median age at transplantation was similar (62.3 vs 60.3 years, p=0.39), as were performance status and time from diagnosis to transplantation. The primary endpoint, 1-year event-free survival(EFS - 66.3% vs 65.2%, HR 1.12 p =0.66), was comparable between haploidentical and 9/10 MMUD transplants, with overlapping survival curves and no statistically significant difference between donor types. This finding remained consistent despite differences in conditioning intensity and stem cell source. Secondary outcomes supported the primary analysis. At 2 years, overall survival was similar between haploidentical and MMUD transplants(73.1% vs 71.6%, p=0.96). The cumulative incidence of relapse did not differ between donor groups (17.1% vs 18.7%, p=0.84), nor did non-relapse mortality (16.6% vs 16.1%, p=0.86). The cumulative incidence of acute GVHD grade II–IV by day 100 was 28.1% (17.1–40.1) in the MMUD group and 24.7%(18.7–31.2) in the haploidentical group (p=0.70), while acute GVHD grade III–IV occurred in 8.9%(3.2–18.2) and 9.5% (5.8–14.3) of patients, respectively (p=0.99). At 2 years, the cumulative incidence of chronic GVHD was significantly lower after MMUD transplantation compared with haploidentical transplantation (12.7% vs 36.4% HR 2.14 p =0.048). However, the incidence of extensive chronic GVHD remained low and similar between groups (6.0%, 1.5–14.9 vs 5.0%, 2.3–9.1; HR 1.18 p=0.81).

Fig. 1A

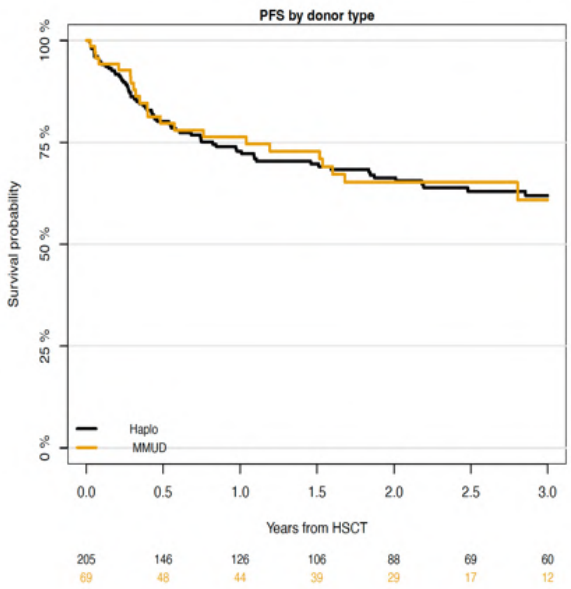
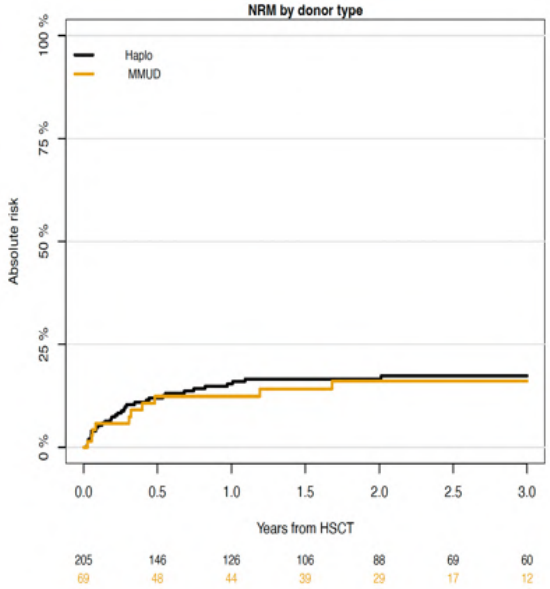


Fig. 1B



Conclusions: In AML patients in CR1 undergoing allo-HSCT with treosulfan-based conditioning and PTCy, transplant outcomes are comparable between 9/10 mismatched unrelated and haploidentical donors. These data indicate that effective control of toxicity and alloreactivity largely mitigates the historical impact of HLA mismatch, supporting donor availability and rapid access to transplantation as key determinants of outcome within a treosulfan–PTCy platform.

Disclosure: DA rececеived travel, speaking and research grant by MEDAC.

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RESULTS OF ALLOGENEIC HSCT IN CR1 FOR PEDIATRIC PATIENTS WITH *DE NOVO*, HIGH-RISK, ACUTE MYELOID LEUKEMIA (AML): A REPORT FROM AIEOP

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Background: Allogeneic HSCT (alloHSCT) is commonly used as consolidation therapy in children with high-risk (HR) *de novo* AML in first complete remission (CR1). According to AIEOP (Associazione Italiana OncoEmatologia Pediatrica) guidelines, HR patients (defined on the basis of the presence of specific, recurrent genetic lesions and response to induction therapy) have an indication to allogeneic HSCT in CR1.

Methods: HR patients were defined as: i) those carrying high-risk clinical/cytogenetic feature [including monosomal/complex karyotype, most of KMT2A-rearrangments, FLT3-ITD, CBFA2T3-GLIS2, NUP98-rearrangements, FAB M0, M6, M7, and infants without FABM7/t(1;22,)] or ii) showing poor response to induction therapy, defined as no CR at end of first of the 2 induction (EOI1) or measurable residual disease by flow-cytometry (fMRD) >1% at EOI1 or >0.1% at EOI2. The recommended conditioning regimen was busulfan+cyclophosphamide+melphalan in case of transplant from an HLA-matched donor, while for mMUD or PMFD conditioning was chosen by the treating physician. GvHD prophylaxis consisted of short-course methotrexate and cyclosporine-A; serotherapy (Grafalon 5 mg/kg/day for 3 days) was added in patients transplanted from an unrelated donor. For transplant from haploidentical donors, either TCRαβ/CD19-depletion or post-transplant cyclophosphamide (PT/Cy) were applicable, depending on center choice/expertise.

Results: 152 patients (52.6% males) consecutive HR patients were enrolled in 13 AIEOP centers and underwent alloHSCT in CR1 between 2014 and 2021. Median age at diagnosis and HSCT were 7.1 (range 0-18) and 7.7 years (range 0.4-18.6), respectively. The donor was a matched family donor for 36 patients (23.7%), an unrelated donor for 65 (42.7%; 48 fully-matched, MUD, and 27 mismatched, mMUD), and a PMFD for 51 (33.6%); of these haploidentical HSCT 38 were performed after *ex-vivo* TCRαβ/CD19-depletion, while 13 patients were given a PT/Cy HSCT. Stem cell source was bone marrow in 91 cases (59.9%), peripheral blood in 52 (34.2%) and cord blood in 9 (5.9%). Median total nucleated and CD34+ cells infused with the graft (excluding cord transplants) were 5.7 x 10^8/kg (range 0.9-13.7) and 6.9 x 10^6/kg (range 1.9-38.7), respectively. Cumulative incidence of grade II-IV and grade III-IV acute GvHD were 23.7% (95% CI 17.6-31.4) and 8.2% (95% CI 4.7-14.0), while that of chronic GvHD was 9.5% (95% CI 5.4-16.3). Non-relapse mortality and cumulative incidence of relapse were 7.2% (95% CI 3.9-12.2) and 21.7% (95% CI 15.4-28.7); patients transplanted from PMFD experienced the lowest NRM (3.9%,95% CI 0.7-11.9), while those receiving an allograft from a mMUD the highest (14.8%, 95% CI 4.7-30.4). With a median follow-up of 6.6 years for surviving patients, 10-year projected overall survival and event-free survival were 77.4% (95% CI 68.9-83.9) and 71.0% (95% CI 62.9-77.6), respectively.
Seven patients (4.6%) developed a severe VOD at a median of 13 days after HSCT; two of these patients died of transplant-related causes (both because of sepsis). Additional seven

patients developed thrombotic microangiopathy, 2 of them dying later because of this complication.

Conclusions: These data confirm improvement in transplant technique in recent years, as supported by the low incidence of NRM, and indicate that allo-HSCT is an efficacious option for consolidation of pediatric patients with HR AML.

Disclosure: P.M. reports personal fees from Sobi, Miltenyi, and Amgen, outside the submitted work. F.L. reports personal fees from Amgen, personal fees from Novartis, other from Bellicum Pharmaceutical, other from Neovii, personal fees from Miltenyi, Medac, Jazz Pharmaceutical, and Takeda, outside the submitted work.

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MAINTENANCE THERAPY POST HEMATOPOIETIC STEM CELL TRANSPLANT IN ACUTE MYELOID LEUKEMIA WITH FLT3 INHIBITORS AND HYPOMETHYLATING AGENTS: INSIGHTS FROM THE EBMT ACUTE LEUKEMIA WORKING PARTY

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Background: Relapse post allogeneic stem cell transplantation (HSCT) for acute myeloid leukemia (AML) remains a major challenge. Post-HSCT prophylaxis, primarily with FLT3 inhibitors (FLT3i) has shown promising efficacy with acceptable safety, while the role of hypomethylating agents (HMA) remains controversial. Key questions persist regarding patient selection, optimal agent, timing and duration of treatment.

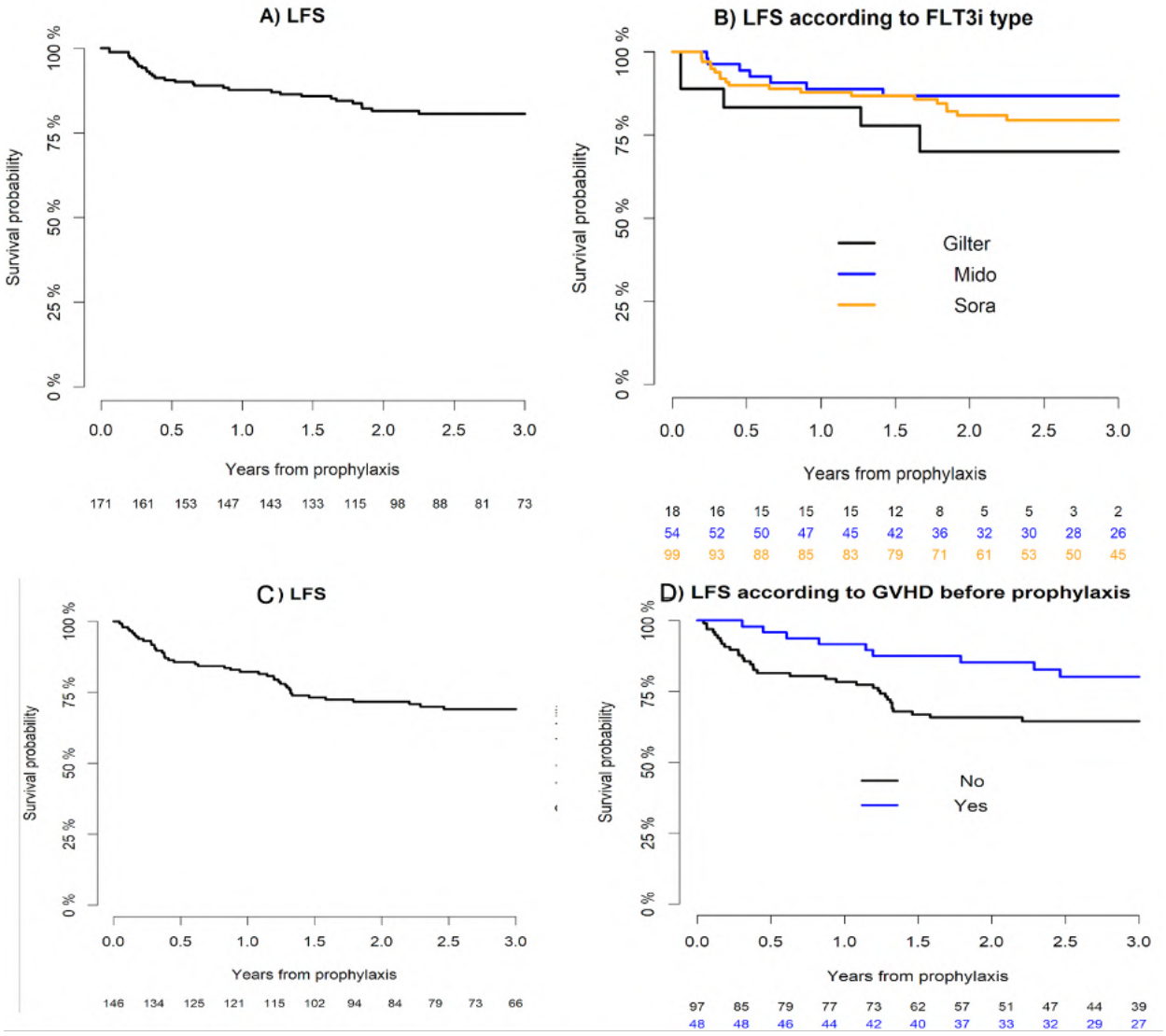
Methods: EBMT registry-based multicenter analysis, approved by the ALWP, including adult AML patients (> 18 years) in first complete remission who underwent first HSCT between 2010-2022, then received FLT3i or HMA prophylaxis within 180 days post-HSCT.

Results: 317 patients identified, 171 received prophylaxis with FLT3i (58% Sorafenib, 30% midostaurin, 11% gilteritinib; 3 patients received sorafenib and midostaurin); while 146 patients received HMA (135 azacitidine/11 decitabine). Table 1 shows the characteristics for each group (not intended to compare the groups due to significant differences). Overall, 63% received myeloablative conditioning, and 97% peripheral blood stem cells. The median time to initiation of post HSCT FLT3i was 74 days [Interquartile range(IQR) 50-111], while the median duration of FLT3i prophylaxis was 364 days(IQR 98-675). At a median follow up of 3 years, the 2-year overall survival (OS) and leukemia free survival (LFS) from time of initiation of prophylaxis were 87% (95% CI 81-91) and 82% (95% CI 75-87) respectively; and were not significantly affected by age, measurable residual disease (MRD) status at HSCT, use of FLT3i before HSCT, prior graft-versus-host-disease (GVHD), or type of FLT3i (2-year OS and LFS: 88% and 81% for sorafenib; 91% and 87% for midostaurin; 70% and 70% for gilteritinib; p=0.13 and 0.28-figure 1). Conversely, the 2-year relapse incidence was higher for those with MRD positivity at transplant (21% versus 8%; p=0.03). For the HMA group, maintenance was initiated at a median of 69 days(IQR 52-97) and given for a median duration of 172 days(IQR 86-343); with 2-year OS and LFS of 77% (95% CI 69-83) and 72% (64-78) respectively. GVHD prior to initiation of maintenance improved OS and LFS [2-year OS 91% (95% CI 78-97) versus (vs) 71% (95% CI 60-79); p=0.03, 2-year LFS 85% (95% CI 72-93) vs 66 (95% CI 55-74); p=0.02], while age, type of AML, cytogenetics and pre-transplant MRD status had no significant impact on these outcomes. Adverse risk cytogenetics was associated with worse 2-year molecular LFS (56% vs 73%; p=0.047) which was conversely improved by presence of GVHD before maintenance (83% vs 61%; p=0.007).

Patient Characteristics		FLT3i (N=171)	HMA (N=146)
Age at HSCT	Median (IQR)	51 (41-61)	55 (38-63)
Year of HSCT	Median (IQR)	2020 (2019-2022)	2018 (2016-2021)
Type of AML (%)	Secondary	28 (17)	57 (39)
Mutations (%)	NPM1 FLT3 ITD FLT3 TKD alone/other FLT3 absent/missing	85 (51) 154 (90) 8 (5)/4 (2) 4 (2)/1 (1)	9 (7) 10 (8) 4 (3)/0 (0) 112 (89)/20 (14)
Cytogenetics (%)	Adverse risk (ELN 2022)	15 (9)	41 (30)
Treatment before HSCT	Sorafenib Midostaurin Giltertinib Azacitidine Decitabine	19 (11) 106 (62) 25 (15) 16 (9) 0 (0)	0 (0) 3 (2) 0 (0) 22 (15) 1 (1)
MRD status at HSCT (%)	Positive	39 (25)	44 (34)

Conditioning (%)	Myeloablative	108 (63)	66 (46)
Donor type (%)	Matched sibling Unrelated Haploidentical Other	51 (30) 79 (46) 38 (22) 3 (2)	49 (34) 63 (43) 32 (22) 2 (1)
GVHD prior to prophylaxis (%)	Yes	60 (35)	48 (33)
Agent used as prophylaxis (%)	Sorafenib Midostaurin Giltertinib Azacitidine Decitabine	99 (58) 54 (31) 18 (11) NA NA	NA NA NA 135 (92) 11 (8)

Table 1. Patient characteristics for both groups (FLT3i and HMA)
Abbreviations: AML: acute myeloid leukemia; ELN: European LeukemiaNet; GVHD: graft versus host disease; HSCT: allogeneic hematopoietic stem cell transplant; IQR: interquartile range; MRD: minimal residual disease



Graph 1. Leukemia free survival for FLT3 inhibitor group (A: total cohort; and B by FLT3i type) and for patients receiving hypomethylating agents (C: total cohort and D: by prior graft-versus-host disease)

Conclusions: This real-world data reinforces FLT3i, especially sorafenib, as standard post-HSCT maintenance in AML patients, with 2-year LFS exceeding 80% regardless of MRD status or prior FLT3i exposure. Additionally, HMA showed encouraging results with 2-year LFS >70% particularly among those with prior GVHD.

Disclosure: Nothing to declare.

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Advancing the Art of Patient Care

SUCCESSFUL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR NEWLY DIAGNOSED AND RELAPSED/REFRACTORY ACUTE MYELOBLASTIC LEUKEMIA FOLLOWING A HIGHLY EFFICIENT REGIMEN, FLAG-MITOXANTRONE WITH LOW-DOSE 7 DAYS VENETOCLAX

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Background: FLAG (G-CSF, Fludarabine, Cytarabine) combined with either Idarubicin (Ida) or Mitoxantrone (Mitox) are effective and well tolerated in newly diagnosed (ND) or relapsed/refractory (R/R) Acute Myeloblastic Leukemia (AML)(Burnett et al. 2018 – Muhlneck et al. 2022). FLAG-Ida with Venetoclax (Ven) induced deep remissions and high rates of transition to allogeneic hematopoietic stem cell transplantation (AHSCT) in patients (pts) with ND or R/R AML (DiNardo 2022). Lowering the Cytarabine dose (to 1.5mg/m2/d for 5d) and shortening the duration of Ven administration in FLAG-Ida+Ven led to lower hematological and infectious toxicities (DiNardo 2025 – Shahswar 2024). We report the outcomes of a pilot study on FLAG-Mitox+Ven (given for 7d) in ND and first R/R AML pts.

Methods: Between 6/2020 and 6/2025, pts from 18 to 60 yo fit for intensive chemotherapy were included. FLAG-Mitox +Ven combined G-CSF (5µg/kg/d) on d1-7, Fludarabine (30mg/m2/d IV), and Cytarabine (1.5g/m2/d IV) on d2-5, Mitox (12mg/m2/d IV) d2,4 and Ven (100mg PO daily) given with voriconazole d2-8. Responding pts planned for AHSCT received 1 to 2 cycles of consolidation, while responding pts non planned for AHSCT received 3 cycles of consolidation. Fludarabine and Cytarabine were given on d2-4 and G- CSF d1-5, while Mitox and Ven were given at the same schedule in consolidation. Anti FLT3 was given to pts with FLT3 mutations. Measurable residual disease (MRD) was assessed by flow cytometry.
Endpoints included rate of composite CR (CRc: CR, CRh, CRi), OS, EFS and toxicity.

Results: Hundred and five pts were included with 55 ND and 50 R/R pts. There were 55 females and 50 males. Median age was 43yo (18–60). Among the ND pts, 11 (20%), 18 (33%), and 26 (47%) were ELN 2022 favorable, intermediate, and adverse, respectively. Sixty percent of the ND pts transitioned to AHSCT in CR1. The CRc rate after the first induction therapy was 91%, with a flow MRD-negativity of 86%. The 3-y OS and 3-y EFS rates were 68% and 64%, respectively. Outcomes were not significantly different across ELN 2022 risk groups. Among the 50 R/R pts, first induction therapy consisted of 7+3 regimen in 32 pts (64%), FLAG-Ida in 15 pts (30%) and 5-Azacytidine+Ven in 3 pts (6%). AHSCT was included in first line therapy of 15 pts. The CRc rate after FLAG-Mito+Ven was 78% with a flow MRD- negativity of 74%. Sixty percent of these R/R pts transitioned to AHSCT. The 3-y OS and 3-y EFS rates were 66% and 62%, respectively, for the pts who underwent AHSCT.

However, non-transplanted pts had a significantly lower 3-y OS (22%, p=0.025) and 3-y EFS (18%, p=0.002), respectively. The most frequent adverse events (grade ≥3) were hematologic, infectious (pneumonia), and gastrointestinal. The mortality rates at 30 and 60 days of FLAG-Mitox+Ven were 0% and 2.8%, respectively.

Conclusions: FLAG–Mitox+Ven (7d) is a highly-effective and well-tolerated for remission induction and MRD negativity in ND and R/R AML pts. High survival outcomes were demonstrated across ELN 2022 risk groups in ND AML pts. This regimen is also an effective bridge to AHSCT.

Disclosure: No

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POST-TRANSPLANT OUTCOMES IN ACUTE MYELOID LEUKEMIA HARBORING NRAS AND/OR KRAS MUTATIONS: A STUDY ON BEHALF OF EBMT-ALWP

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Background: *NRAS*, and/or *KRAS* mutations are identified in 10–15% of patients diagnosed with acute myeloid leukemia (AML). While their prognostic value in non-transplant settings remains inconsistent and treatment-dependent, their impact in the context of allogeneic hematopoietic cell transplantation (allo-HCT) is underexplored.

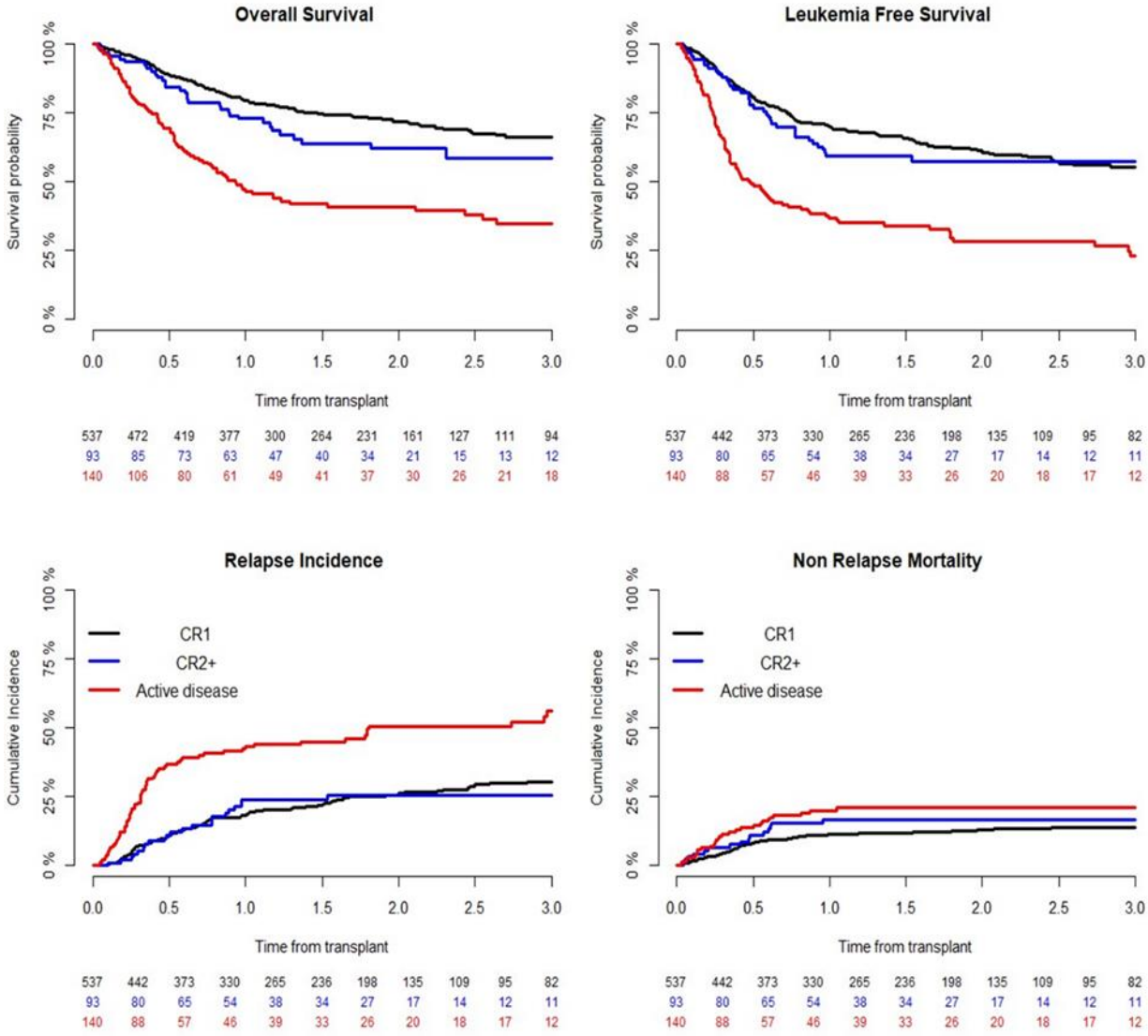
Methods: This retrospective registry-based study was conducted following approval by the Acute Leukemia Working Party (ALWP) of the EBMT. Adult AML patients who underwent allo-HCT between 2016 and 2021 with known *NRAS* and/or *KRAS* mutation status at diagnosis

were included, regardless of the disease status at transplant. The primary endpoints were overall survival (OS), leukemia-free survival (LFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM).

Results: A total of 770 patients were identified, with a median age at allo-HCT of 53 years (range: 18–79); 53% were male. Median time from diagnosis to allo-HCT was 5 months (interquartile range: 4–8) for patients in first complete remission (CR1). Most had *de novo* AML (77%) and intermediate-risk ELN2022 cytogenetics (64%, with normal karyotype in 43%); 25% had adverse-risk cytogenetics. *NPM1* and *FLT3*-ITD mutations were present in 42% and 30% of patients, respectively. Myeloablative conditioning was used in 56% of cases. Donors included matched sibling (19%), haploidentical (25%), and matched unrelated (33%).
At transplant, 537 patients were in CR1, 93 in second or third CR (CR2+), and 140 had active disease. Compared to CR1 and active disease patients, those in CR2+ were more often female (59% vs. 46% vs. 43%, p=0.03), had *de novo* AML (91% vs. 80% vs. 57%), and were enriched for favorable cytogenetics (mainly inversion 16; 26% vs. 10% vs. 5%, p<0.001) and *NPM1* mutations (67% vs. 37% vs. 38%, p<0.001).
After a median follow-up of 2 years (95% confidence interval [CI]: 1.9–2.1), 2-year OS and LFS for the entire cohort were 65% (95% CI: 61-69) and 54% (95% CI: 50-58), respectively; 2-year CIR was 31% (95% CI: 27-35), and NRM 15% (95% CI: 12-18). In CR1 patients, 2-year OS, LFS and CIR were 72%, 61% and 26%, respectively; for CR2+ patients, 2-year OS was 62%, LFS 57%, and CIR 26%; for active disease, 2-year OS was 41%, LFS 28%, and CIR 51%. According to ELN2022 cytogenetic risk, 2-year LFS among CR1 patients was 77%, 61%, and 55% (p=0.04) for favorable, intermediate, and adverse risk, respectively.
Multivariable analysis for CR1 patients showed inferior LFS in secondary AML (hazard ratio [HR]: 1.57; 95% CI: 1.11–2.22; p=0.01), while haplo-identical transplant (HR: 0.54; 95% CI: 0.34–0.86; p=0.009), and recipient cytomegalovirus seropositivity (HR: 0.71; 95% CI: 0.5-0.96; p=0.03) were associated with improved LFS. Increasing age adversely affected OS.

Variables	Modalities	N=770	CR1 (N=537)	CR2+ (N=93)	Active (N=140)	Test
Age at allo-HCT	median (range)	53 (18-79)	53 (18-79)	49 (18-76)	57 (19-76)	< 0.001
Patient sex	Female	359 (47)	244 (46)	55 (59)	60 (43)	0.03
Months diagnosis-allo-HCT	median (range)	5 (0.3-97)	4.8 (1-22)	15 (3-97)	4 (0.3-59)	Not tested
Year of HCT	median (range)	2020 (2016-2021)	2020 (2016-2021)	2020 (2017-2021)	2020 (2016-2021)	0.11

AML type	de novo	594 (77)	429 (80)	85 (91)	80 (57)	< 0.001
	Sec AML	176 (23)	108 (20)	8 (9)	60 (43)	
MRD	Positive		125 (39)	26 (40)		Not tested
ELN 2022 Cytogenetic risk	Favorable Intermediate Adverse	79 (11) 468 (64) 183 (25)	50 (10) 332 (65) 127 (25)	23 (25) 59 (66) 8 (9)	6 (5) 77 (59) 48 (36)	< 0.001
NPM1	Mutant	168 (42)	108 (37)	43 (67)	17 (38)	< 0.001
FLT3ITD	Mutant	126 (30)	91 (30)	19 (37)	16 (29)	0.58
Myeloablative regimen	No	330 (43.9)	205 (39.3)	42 (46.2)	83 (59.3)	< 0.001
PTCY	Yes	151 (19.9)	98 (18.5)	26 (28.3)	27 (19.6)	0.09
Invivo TCD	Yes	522 (67.9)	366 (68.3)	64 (68.8)	92 (65.7)	0.83
Patient CMV	Positive	404 (53.9)	277 (53.3)	52 (58.4)	75 (53.6)	0.66
KPS	< 90	292 (40.6)	196 (38.8)	32 (37.6)	64 (49.2)	0.08
Source of cells	PB BM	635 (82) 43 (6)	434 (81) 26 (5)	77 (83) 4 (4)	124 (89) 13 (9)	Not done
Donor type	Matched related donor Haplo-identical Matched Unrelated Mismatched Unrelated	157 (20) 191 (25) 253 (33) 31 (10)	119 (22) 143 (27) 165 (31) 45 (8)	11 (1) 27 (29) 28 (30) 12 (13)	27 (20) 21 (15) 60 (43) 14 (9)	Not done



Conclusions: In this large EBMT registry analysis, outcomes of AML patients harboring *NRAS* and/or *KRAS* mutations were encouraging, with 2-year LFS exceeding 60%. Notably, patients in CR2+ had predominantly favorable features, and achieved survival outcomes not different to those in CR1. In addition, haploidentical transplant appeared to confer a better LFS in this cohort, suggesting a potential role for graft-versus-leukemia effects.

Clinical Trial Registry: Not applicable.

Disclosure: The authors declare no conflict of interest.

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"STICK TO THE STANDARD": ADDITION OF THIOTEPA TO FLU/BU INCREASES NRM IN MSD/URD TRANSPLANTS FOR MRD+CR1 AML. FROM THE GLOBAL COMMITTEE AND ALWP OF EBMT

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Background: The thiotepa-busulfan-fludarabine (TBF) protocol has shown promising outcomes in haploidentical and cord blood hematopoietic cell transplantation (HCT), but evidence remains limited for matched sibling donor (MSD) and unrelated donor (URD) transplants in acute myeloid leukemia (AML) patients in first complete remission (CR1) with measurable residual disease positivity (MRD+).

Methods: We retrospectively analyzed adult AML patients in CR1 with MRD+ undergoing first allogeneic HCT (allo-HCT) between 2010–2023 using 10/10 MSD or 10/10 or 9/10 URD. Conditioning was TBF or fludarabine/busulfan (Flu/Bu).

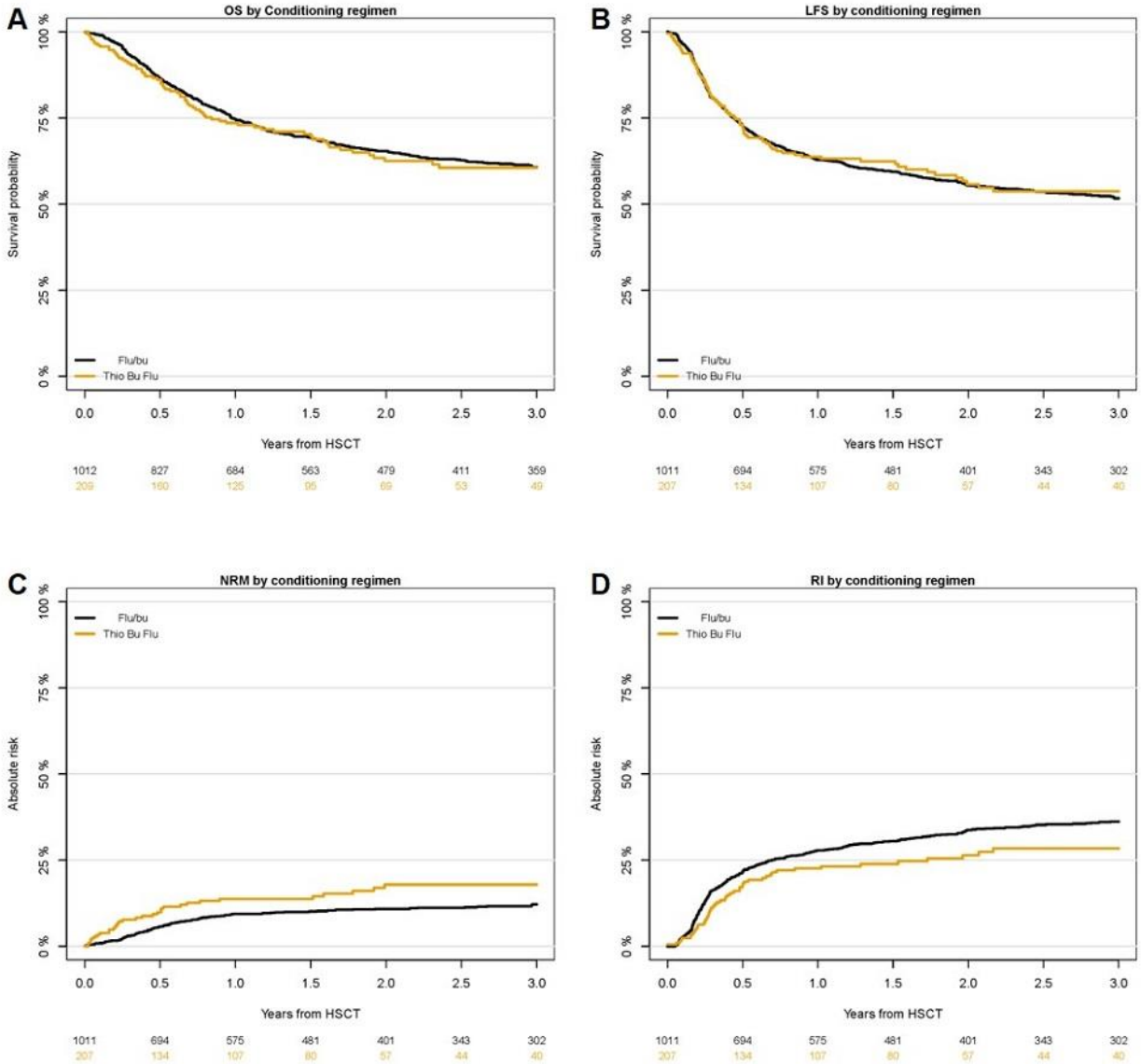
Results: The analysis comprised 1221 patients, with 209 in the TBF group and 1012 in the Flu/Bu group. The median follow-up was 2.2 and 3.8 years, respectively. Compared to the Flu/Bu group, patients in the TBF group were younger (50.4 vs. 55.1 years, P<0.0001), transplanted more recently (2020 vs. 2018, P<0.0001), had longer diagnosis-to-transplant intervals (5.9 vs. 5.3 months, P=0.0036), had higher Karnofsky Performance Scores (KPS ≥90: 88.3% vs. 77.8%, P=0.0007), received more 9/10 URD grafts (28.2% vs. 12.1%, P<0.0001), and received post-transplant cyclophosphamide (PTCy) more frequently (32.5% vs. 10.7%, P<0.0001). Other baseline characteristics were comparable between groups (Table 1).
In univariate analysis, 100-day acute graft-versus-host disease (aGVHD) grades II–IV and III–IV were similar between the TBF and Flu/Bu groups (26.5% vs. 24.6%, P=0.76; 12% vs. 8.9%, P=0.53). However, the TBF group exhibited lower 2-year chronic GVHD (cGVHD; 21.3% vs. 34.8%, P=0.0006) and extensive cGVHD (0.6% vs. 8.3%, P=0.0005). Two-year overall survival (OS; 62.5% vs. 65.4%, P=0.8) and leukemia-free survival (LFS; 55.7% vs. 55.4%, P=0.77) did not differ between groups. Notably, the TBF group experienced higher non-relapse mortality (NRM; 17.9% vs. 10.9%, P=0.04) and potentially lower relapse incidence (RI; 26.4% vs. 33.7%, P=0.06) (Figure 1).
In multivariate analysis, the incidence of aGVHD grade II–IV and grade III–IV was comparable between groups. However, TBF conditioning was associated with a marginally lower risk of cGVHD (HR=0.66; P=0.05) and a significantly lower risk of extensive cGVHD (HR=0.07; P=0.01) compared to the Flu/Bu group. Additionally, female donor to male

patient combination was a risk factor for extensive cGVHD (HR=2.41; P=0.01).
No significant difference was observed in OS, LFS, or RI between groups, but TBF conditioning was associated with a higher risk of NRM (HR=1.81; P=0.01). Earlier year of transplantation was associated with lower OS (HR=0.83; P=0.046). Older patient age was a prognostic factor for higher NRM (HR=1.06; P=0.002). Patient CMV seropositivity was a risk factor for OS (HR=1.48; P<0.001) and LFS (HR=1.33; P=0.008). Favorable and intermediate risk cytogenetics were prognostic factors for improved OS, LFS, and lower RI. Reduced intensity conditioning (RIC) was associated with lower OS (HR=1.39; P=0.004) and LFS (HR=1.4, P=0.007), as well as a higher risk of RI (HR=1.57; P<0.001).

Table 1. Patients characteristics

	Total N=1221	TBF N=209	Flu/Bu N=1012	P-value
Patient age				< 0.0001
median [IQR]	54.49 [46.2-62.2]	50.4 [42.9-58.9]	55.1 [47.1-62.7]	
Year of HCT				< 0.0001
median [IQR]	2019 [2016-2021]	2020 [2018-2022]	2018 [2016-2021]	
KPS				0.0007
< 90	240 (20.4)	24 (11.7)	216 (22.2)	
≥90	936 (79.6)	181 (88.3)	755 (77.8)	
missing	45	4	41	
Donor type				< 0.0001
MSD	463 (37.9)	66 (31.6)	397 (39.2)	

10/10 URD	577 (47.3)	84 (40.2)	493 (48.7)	
9/10 URD	181 (14.8)	59 (28.2)	122 (12.1)	
Use of PTCY				< 0.0001
No PTCY	1045 (85.6)	141 (67.5)	904 (89.3)	
PTCY	176 (14.4)	68 (32.5)	108 (10.7)	



Conclusions: The addition of Thiotepa to Flu/Bu significantly increased NRM without improving survival or relapse outcomes, outweighing the benefit of reduced cGVHD. Consequently, the standard Flu/Bu regimen remains a safer and sufficient strategy for AML patients undergoing MSD/URD transplantation in CR1 with MRD+. Further studies are needed in other settings such as haploidentical transplants.

Disclosure: Nothing to declare.

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COMBINED PRE-TRANSPLANT MRD DETECTION BY FACS AND NGS MAY ENHANCE RELAPSE PREDICTION IN AML PATIENTS RECEIVING ALLO-SCT IN COMPLETE REMISSION

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Background: Accurate assessment of measurable residual disease (MRD) before allogeneic hematopoietic stem cell transplantation (allo-HSCT) is critical for risk stratification and personalised treatment in acute myeloid leukaemia (AML). Flow cytometry (FACS-MRD) and error-free next-generation sequencing (NGS-MRD) are complementary techniques that differ in analytical principles, target specificity, and sensitivity. Their integration in the pre-transplant setting may improve prediction of relapse risk and post-transplant outcomes and guide post-transplant interventions.

Methods: Adult AML patients (n = 107) undergoing first allo-HSCT in first CR at the University Medical Centre Hamburg-Eppendorf (2020–2023) were evaluated for MRD in bone marrow aspirates obtained within 14 days before conditioning. Two approaches were used: (i) multiparameter flow cytometry (FACS-MRD) with sensitivity 10^{-4}–10^{-5}, and a cut-off of 0.1% for MRD positivity; (ii) error-corrected NGS-MRD (non-DTA) using the Oncomine Myeloid MRD (RUO)Assay (Thermofisher) (limit of detection ≈ 0.1 % of variant allele frequency). MRD results were dichotomised (positive/negative) and correlated with post-transplant outcomes (CIR, LFS, OS).

Results: Pre-transplant MRD was detected in 37% by FACS and in 45% by NGS. Concordance between both modalities was moderate to substantial (Cohen's κ = 0.60). NGS identified additional subclonal variants (e.g. *TP53*, *RUNX1*, *FLT3-ITD*) in 26% of FACS-MRD negative patients.
Patients who were MRD-positive in either single modality showed significantly higher relapse incidences (FACS: 5-year CIR 53% [95% CI, 37–69] vs 14% [95% CI, 8–24], p < 0.01; NGS: 5-year CIR 45% [95% CI, 31–60] vs 14% [95% CI, 7–25], p < 0.01) and inferior overall survival (FACS: 5-year OS 39% [95% CI, 25–55] vs 79% [95% CI, 68–87], p < 0.001; NGS: 49% [95% CI, 39–63] vs 76% [95% CI, 64–85], p = 0.006).
Patients with discordant MRD results had an intermediate risk profile, with a 5-year CIR of 20% (95% CI, 9–39) and OS of 60% (95% CI, 41–77). In contrast, patients positive in both MRD modalities had higher relapse risk (5-year CIR 62% [95% CI, 43–78] vs 15% [95% CI, 9–24], p < 0.01) and inferior survival (5-year OS 33% [95% CI, 18–50] vs 76% [95% CI, 65–84], p < 0.001).
In multivariate analysis, dual MRD positivity remained the strongest independent predictor of relapse (HR 6.8, 95% CI, 3.0–15.0; p < 0.001) and overall survival (HR 3.2, 95% CI, 1.6–6.1; p = 0.001).
With otherwise comparable predictive performance, the dual-modality MRD approach

demonstrated higher specificity (84%) and a higher positive predictive value (60%) than either single-modality strategy.

Conclusions: The dual-modality MRD approach (FACS + NGS) lowers the frequency of false positives and yields approximately 10% greater accuracy in relapse prediction, though without a marked improvement in prediction of overall survival. This combined strategy may enable more refined selection of patients who are appropriate candidates for early post-transplant interventions.

Disclosure: Nothing to declare.

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ALLOGENEIC TRANSPLANTATION IN SECONDARY COMPARED TO DE NOVO ACUTE MYELOID LEUKEMIA- THE IMPACT OF NEXT-GENERATION SEQUENCING BASED MUTATION PROFILE: A STUDY FROM THE ALWP/EBMT

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Background: Secondary AML (sAML) is characterized by a unique cytogenetic and mutational profile that dictates inferior outcomes. NGS allows identification of secondary-type signatures, even in patients (pts) presenting with *de novo* disease (Lindsley C, *et al*.

Blood 2015). The specific role of allogeneic transplantation (HSCT) among pts harboring secondary-type gene mutations needs further investigation.

Methods: We aimed to compare NGS mutation profile (by multiple correspondence analysis and circle plot interaction schemes) and assess its prognostic impact in sAML *vs de novo* AML (dnAML) pts undergoing HSCT (92.8% in CR1) between 2010-2023. Donors were unrelated - 39.4%, matched related – 34.6%, haploidentical - 19.8% (other - 6.5%).

Results: 746 pts were included, sAML -63, dnAML -683. Follow-up was 2 years. Median year of transplant was 2019. Pts with sAML were older, 61.1 vs. 53.8 years (p<0.001). The two groups did not differ in gender, performance status, CMV seropositivity, gender combination, or time from diagnosis to transplant. Cytogenetic risk was intermediate in 67.2% vs 69.3% and adverse in 32.8% vs 25.5%, respectively (p=0.1). Pts with sAML received BM grafts (9.5% vs. 4%; p=0.051) and RIC (61.9% vs. 44.2%; p=0.007) more frequently. The 2-year LFS and OS rates were 47.5% vs. 59% (HR=0.88, p=0.557) and 55.5% vs. 68.9% (HR=0.74, p=0.2), in sAML vs. dnAML, respectively. 2-year RI was 35.4% vs. 27.7% (HR=1, p=0.996) and 2-year NRM was 17.1% vs. 13.2% (HR=0.71, p=0.342), for sAML vs dnAML (Figure 1A). The leukemia was the main cause of death, 58.3% vs. 57.2% of those who died. The incidence of day 180 acute GVHD grades II-IV was 25.1% vs. 24.2%, and grades III-IV was 5.5% vs. 7.9%, while 2-year total chronic GVHD was 36.6% vs. 38.8%, and of extensive chronic GVHD was 11.1% vs. 13.5%, respectively (Figure 1A). GRFS was 43% vs. 48.4 % (HR=0.86, p=0.448) in sAML vs. dnAML. Day 30 ANC $\geq$ 10^9/L was 89.8% vs. 95.7 % and day 60 platelet count $\geq$ 20x10^9/L was 91.4% vs. 92.5%. Mutations in JAK2 (11.5% vs. 1.7%, p<0.001); splicing factors SF3B1 (11.5% vs. 4.9%, p=0.04), SRSF2 (29% vs. 8.7%, p<0.001), U2AF1 (10% vs. 2.7%, p=0.011), ZRSR2 (11.6% vs. 1.5%, p=0.002), and TP53 (16.7% vs. 5.9%, p=0.004) were more prevalent among sAML pts. NPM1 (21.2% vs. 7.9%, p=0.012) and FLT3-ITD mutations (24.8% vs. 9.8%, p=0.008) were more frequent in dnAML (Figure 1B). On MVA, cytogenetic risk showed a negative impact on OS, LFS, RI, and GRFS. The number of mutated genes (0 vs 1 vs$\geq$2) did not affect outcome parameters. The association of mutations in TP53, RUNX1, ASXL1, and the splicing factors (SF3B1, SRSF2, U2AF1, and ZRSR2) is depicted in Figure 1C. Due to the small number of patients, the data should be interpreted with caution, and no definitive conclusions can be drawn.

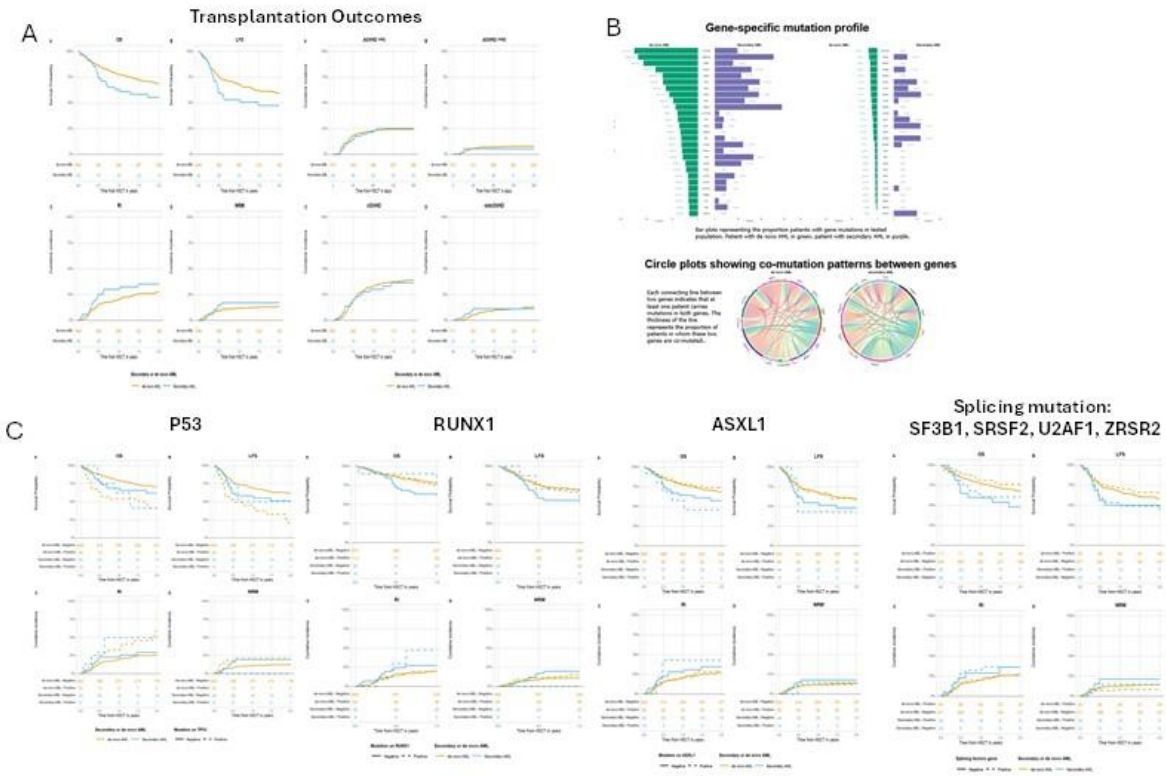

Figure legend: A. Outcomes of allogeneic HSCT in patients with secondary vs de novo AML: overall survival (OS); leukemia-free survival (LFS); relapse incidence (RI); non-relapse mortality (NRM); acute GVHD grade II-IV (>=II) and III-IV (>=III); chronic GVHD total(cGVHD) and extensive (extcGVHD). B. NGS mutation profile by multiple correspondence analysis and circle plot interaction schemes; C. Association between specific mutations in secondary vs de novo AML-TP53; RUNX1; ASXL1 and splicing factors (SF3B1, SRSF2, U2AF1 and ZRSR2) and transplantation outcomes: overall survival (OS); leukemia-free survival (LFS); relapse incidence (RI); non-relapse mortality (NRM) .

Arnon Nagler[1*] and Jordi Esteve[2*] contribute equally to the study

Conclusions: This study confirmed differences in the mutational landscape between sAML *and* dnAML. Nonetheless, AML presentation type did not show a prognostic impact, whereas the presence of TP53 mutation and adverse risk cytogenetics were the only genetic disease factors showing prognostic impact.

Disclosure: Nothing to disclose

B296

ICT01-AZACITIDINE-VENETOCLAX INDUCES HIGH REMISSION RATE IN PATIENTS WITH NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA: RESULTS FROM THE PHASE 1/2 STUDY EVICTION

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Gassart[9], Emmanuel Valentin[9], Maelle Mairesse[9], George Saad[9], Patrick Brune[9], Katrien Lemmens[9], Noemi Angelosanto[9], Norbert Vey[1], Daniel Olive[10], Stephan Braun[9], Naval Daver[11], Abhishek Maiti[11]
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Background: γ9δ2TCs drive *Graft Versus Leukemia* in the post-transplant and intra-tumor presence of γ9δ2TCs is prognostic. ICT01 is a first-in-class anti-butyrophilin 3A mAb who activates γ9δ2TC determining anti-leukemic cytotoxicity and NK/CD8 T cell activation. ICT01-Aza-Ven showed synergistic efficacy in a mouse model with adoptive γδTC transfer. From the dose-optimization phase 1/2 study investigating 10 mg ($ICT01^{LOW}$) and 75 mg ICT01 ($ICT01^{HIGH}$) with Aza-Ven, $ICT01^{LOW}$ was chosen as the RP2D (Maiti et al. Cancer Res. 2025) and that cohort expanded to 41 patients. Here, we report safety and efficacy results as of 6 Oct 25 DCO, including a preliminary analysis for OS from fully enrolled population in EVICTION.

Methods: ND-AML patients ≥ 75 years or unfit for intensive chemotherapy were randomized 1:1 to standard dosing of Aza-Ven plus ICT01 at either 10 mg ($ICT01^{LOW}$) or 75 mg ICT01 ($ICT01^{HIGH}$) on day 1 of each cycle. The primary objective was CR and CRc by ELN 2022; secondary endpoints were safety per NCI-CTCAE 5.0, ICT01 pharmacodynamics (PD) in peripheral blood (PB) and bone marrow (BM).

Results: 54 patients, 38 $ICT01^{LOW}$ and 16 $ICT01^{HIGH}$, were evaluable for efficacy. Median age was 75 yrs (range 51–87). Median baseline BM blasts was 40% (range 7–98%). Per refined ELN 2024 classification, 30%, 28% and 42% patients had favorable, intermediate and adverse risk disease. Median days (IQR) of venetoclax dosing in cycles 1, 2, 3,4 were 22 (20, 27), 20 (13, 21), 13 (6, 16), 12 (6, 20), respectively. Median duration (IQR) of cycles 1, 2, 3 was 31 (28, 38), 31 (28, 47), and 29 (28, 42) days. Patients who had $ICT01^{LOW}$ achieved 71% CR (95% CI, 54–85%) and 84% CRc (69–94%) vs 44% CR (95% CI, 20–70%) and 69% CRc (41–89%) from the $ICT01^{HIGH}$ (p=0.0715 and p=0.269 for CR and CRc respectively; χ2 test). For favorable, intermediate and adverse-risk patients who had $ICT01^{LOW}$, CRc was 100%, 83% and 67% and CR was 86%, 67% and 58%, with a time to first CRc response of 0.9 months (range, 0.7–2.9). After a median follow-up time of 10.8 months (95% CI, 8.9–12.8), 9-months OS was 67% (54–81%) in the $ICT01^{LOW}$ cohort and 56% (39–81%) in the $ICT01^{HIGH}$ (HR 0.4 [0.2–0.9] for OS [p=0.07; log rank]). Patients CRc or MLFS vs NR, had significantly higher baseline γ9δ2TC counts (p=0.001) and a greater increase in serum IFNγ 4h post first ICT01 dose (p=0.0001 vs. p=0.38; Wilcoxon test). Higher trough PB γ9δ2TC levels with $ICT01^{LOW}$ vs $ICT01^{HIGH}$ in subsequent cycles were

associated with higher efficacy. No DLT reported; 30-day mortality was 4%. No new safety signal detected for ICT01. Grade 3/4 febrile neutropenia occurred in 51% of the patients. No ICT01-related deaths or treatment discontinuations reported.

Conclusions: ICT01 was safe, well tolerated, and associated with high CR and CRc rates in older/unfit ND-AML patients. The high response rate and promising early OS signal, warrant further clinical investigation. Consistent PD effects suggest an individual contribution of ICT01 to the efficacy of the novel triplet regimen ICT01-Aza-Ven.

Clinical Trial Registry: Clinical trial.gov: NCT04243499

Disclosure: Sylvain Garciaz: consultancy at: Servier, Imcheck, Sanofi, Abbvie, Janssen
Pierre Peterlin:consultancy at: Servier , Abbvie Astellas
Daniel Morillo Giles:consultancy at: BMS, Daiichi Sankyo, Takeda, Roche, Ascentage
Matthew Ulrickson: consultancy at: ADC Therapeutics, Genentech, Stemline Therapeutics, Immunogen, Autolus, BMS/Celgene/Juno, Kura Oncology, Kite
Emmanuel Valentin: Imcheck Therapeutics employee
Maelle Marisse: Imcheck Therapeutics employee
George Saad: Imcheck Therapeutics employee
Patrick Brune: Imcheck Therapeutics employee
Katrien Lemmens: Imcheck Therapeutics employee
Noemi Angelosanto: Imcheck Therapeutics employee
Daniel Olive: consultancy at Stealth Therapeutics Alderaan, Imcheck therapeutics
Stephan Braun: Imcheck Therapeutics employee
Naval Daver: consultancy at : Astellas, Stemline Therapeutics/Menarini, Jazz Pharmaceuticals, Agios, BMS, Hanmi, Immunogen, Syndax, Shattuck Labs, Trillium Therapeutics, Genentech, Amgen, Trovagene, Novimmune, FATE Therapeutics , Abbvie, Gilead, Daiichi Sankyo, GlycoMimetics, Servier, Celgene, Kite, Arog,Pfizer, Servier, Rigel
Abhishek Maiti: consultancy at: Ferring Ventures, Takeda Pharmaceuticals, BMS, Sanofi Aventis, Astex Pharmaceuticals, Galecto biotech, IGM Biosciences,Caribou Biosciences, Electra Therapeutics, Chimeric Therapeutics, Cytomed Therapeutics, Lin Biosciences, Cera bio, Qurient Inc, BioSight, Orum Therapeutics, Imcheck Therapeutics, Ingenium, Inspirna Therapeutics

B299

FLAMSA-BASED CONDITIONING IS ASSOCIATED WITH LOWER NRM AND HIGHER SURVIVAL IN PATIENTS WITH RELAPSED/REFRACTORY AML

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Background: Allogeneic stem cell transplantation (allo-SCT) remains the only potentially curative option for patients with relapsed/refractory acute myeloid leukemia (rrAML). The

optimal conditioning regimen for these patients is still unclear. Studies investigating FLAMSA-based sequential conditioning protocols have reported lower non-relapse mortality (NRM), better disease control, and higher overall survival compared to classical myeloablative conditioning (MAC) or reduced-intensity conditioning (RIC) regimens. However, prospective randomized studies are lacking, and comparative real-world data on FLAMSA versus other conditioning strategies for rrAML remain limited.

Methods: This retrospective single-center study includes 245 patients with rrAML (59% male, median age 60 years, range 6-76) who underwent allo-SCT at the Department for Stem Cell Transplantation, University Medical Centre Hamburg Eppendorf, between 1995 and 2025. Ninety percent of the patients received their first allo-SCT. Most patients received grafts from unrelated donors (MUD, 47%; MMUD, 27%; MRD, 19%; haploidentical, 7%) after MAC (42%) or RIC (58%). FLAMSA-based conditioning was used in 132 patients (FLAMSA/Bu, n=68; FLAMSA/TBI, n=50; FLAMSA/Treo, n=14). Other regimens included TBF (n=29), Bu/Flu or Bu/Cy (n=21), TBI-based conditioning (n=34), and other regimens (n=29). Anti-thymocyte globulin (ATG) was used in 80% of patients.

Results: Median age did not differ between the FLAMSA and non-FLAMSA groups. FLAMSA-based regimens were more frequently used before 2020 (83% vs. 56%, p<0.001), with RIC regimens being significantly more common in the FLAMSA group (71% vs. 42%, p<0.001). Total body irradiation was more frequently applied in younger patients (<60 years) in both groups.
The cumulative incidence of relapse at 3 years was comparable between the FLAMSA and non-FLAMSA groups (47% [38-56%] vs. 45% [36-55%], p=0.73). However, the cumulative incidence of NRM at day 100 and 1 year was significantly lower in the FLAMSA group (day 100: 14% [9-21%] vs. 24% [17-33%]; 1 year: 19% [13-27%] vs. 36% [27-46%], p=0.003). The 3-year overall survival (OS) and leukaemia-free survival (LFS) were significantly higher in the FLAMSA group: 34% [26-42%] vs. 21% [14-30%], p=0.002 and 28% [21-36%] vs. 16% [10-25%], p=0.005, respectively. Within the FLAMSA group, the highest 3-year OS of 36% [22-50%] was observed after FLAMSA/TBI. Among other conditioning regimens, the highest 3-year OS of 27% [13-47%] was seen with thiotepa-based conditioning (TBF).
In multivariate analysis, FLAMSA-based conditioning and younger age were independently associated with reduced NRM (HR 0.42, 0.24-0.77, p=0.004 and HR 0.31, 0.29-0.99, p=0.045). FLAMSA-based conditioning also showed a favourable association with LFS (HR 0.66, 0.48-0.90, p=0.008) and OS (HR 0.66, 0.48-0.90, p=0.01).

Conclusions: In this large single-center cohort of rrAML patients undergoing allo-SCT, FLAMSA-based sequential conditioning was associated with significantly lower non-relapse mortality and improved survival compared to non-FLAMSA regimens, without increasing the risk of relapse. Among the FLAMSA variants, FLAMSA/TBI showed the most favourable long-term survival.

Disclosure: Nothing to disclose.

B300

OUTCOMES OF MORPHOLOGICAL VERSUS MINIMAL RESIDUAL DISEASE (MRD) RELAPSE AFTER ALLOGENEIC TRANSPLANTATION (ALLO-HCT) FOR ACUTE MYELOID LEUKEMIA (AML)

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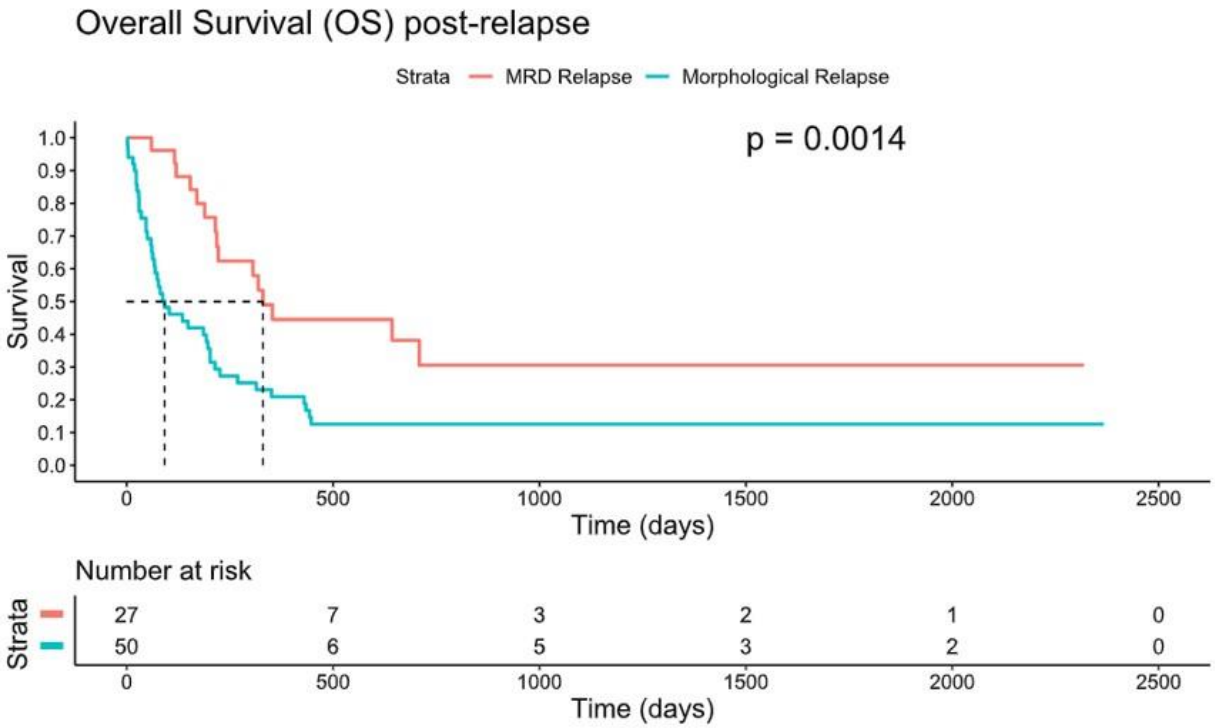
Background: Relapse remains the leading cause of mortality following allo-HCT for AML. With increasing use of sensitive methods to detect MRD, the prognostic impact of type of relapse detected morphologically versus at MRD level remains unclear. We evaluated treatment-patterns and outcomes of post-transplant morphological versus MRD-relapse.

Methods: We retrospectively reviewed all adult AML patients undergoing allo-HCT at Mayo Clinic Rochester between 2018–2025. Morphological relapse was defined as ≥5% marrow blasts and/or extramedullary disease (EMD). MRD relapse was defined by multiparametric flow cytometry (MRD^{F}), molecular testing by digital droplet polymerase chain reaction (MRD^{M}), or cytogenetic abnormalities (MRD^{C}).

Results: Among 272 consecutive AML allo-HCT recipients, 77(28%) relapsed at a median of 128 days (range 28–741). Median age was 57 years (IQR 43-64), 51% were male, and 64% had ELN-2022-adverse-risk disease. Most received myeloablative conditioning (51%) and matched-unrelated-donor-grafts (58%).
Fifty patients (65%) experienced morphological-relapse without preceding-MRD-detection, while 27 (35%) presented with MRD-relapse. Morphological-relapse was associated with a higher rates of ELN-adverse-risk (77.5% vs 22.4%; p=0.006) and adverse-cytogenetics (58% vs 14.8%; p<0.001). Conditioning-intensity and donor-source were similar; however, PTCy use was more frequent in the MRD-relapse-group (74% vs 34%; p=0.042).
Time-to-relapse did not differ between morphologic and MRD-relapse (119 vs 128 days; p=0.83). Morphologic-relapse was associated with inferior 1-&-2-yr OS compared with MRD-relapse (21% vs 44.5% and 12.6% vs 30.5%; p=0.0014)(Figure-1).



Among morphologic-relapse (n=50), median marrow-blast % at relapse was 26 (range 3-97%), with EMD in only 3 (6%) patients. First-line-therapy included hypomethylating agents (HMA) in 28 (56%) patients (frequently combined with-venetoclax/targeted agents), intensive chemotherapy in 5 (10%), single-agent-FLT3i in 3 (6%), immunosuppression-taper/withdrawal alone in 7 (14%) patients, radiation in 2 (4%); five (10%) received no therapy due to clinical decline. DLI was used in 4 (8%) patients, and 5 (10%) proceeded to 2nd allo-HCT. Eighteen patients (36%) achieved remission (13-MLFS, 4-CRi, 1-CR), with median-time-to-response of 73 days (range 14–296) and a median-duration-of-response being 146 days, after which 10(20%) subsequently relapsed.

Among MRD-relapse (n=27), pretransplant-MRD was negative in 11(41%), positive in 10 (37%), unknown in 5(19%), while 1(3%) patient had active-disease. Post-transplant-MRD-relapse presented as MRD^{M} in 8(30%), MRD^{F} 11(41%), MRD^{C} 6(22%), and mixed-MRD in 2(7%) patients (1-MRD^{M+F},1-MRD^{M+C}). First-line-therapy included HMA-based-therapy in 9(33%) patients (frequently combined with-venetoclax), low-dose HMA in 8(30%) patients, targeted therapy alone (6-FLT3i, 1-IDH2i) in 7(26%), a 2nd allo-HCT in 2(7%), immunosuppression taper/withdrawal alone in 1(4%). Later, DLI was used in 3 patients, and a 2nd allo-HCT in one. During a median 447-day follow-up, 18(67%) patients developed morphological relapse, while 9 (33%) remained morphological-relapse-free, of whom 8 achieved MRD negativity with a median of 69.5 days. MRD^{M} had numerically superior 1-yr morphological-relapse-free-survival (MRFS) and overall-survival (OS)(Table-1).

	MRD (n=27)	MRD^{M} (n=9 including 1 1-MRD^{M+F})	MRD^{F} (n=11)	MRD^{C} (n=7, including 1 MRD^{M+C})
1-yr MRFS	47.8% (95%CI, 30.9-73.9%)	77.8% (95%CI, 54.9-100%)	25.9% (95%CI, 5.75-100%)	28.57% (95%CI, 8.86-92.18%)
1-yr OS post MRD relapse	44.5% (95%CI, 28.2-70.3%)	55.6% (95%CI, 31-99.7%)	46.7% (95%CI, 21-100%)	28.6% (95%CI, 8.86-92.2%)

Conclusions: Post-transplant-relapse in AML continues to have dismal prognosis despite novel therapies. Morphological relapse-more frequently observed in ELN adverse-risk disease-confers significantly inferior survival compared with MRD relapse, likely reflection of aggressive disease biology. Among MRD-relapses, molecular-relapse appears to have more favorable-outcomes. These findings highlight the importance of standardized MRD surveillance following transplant to enable earlier therapeutic intervention prior to an overt morphological relapse.

Disclosure: Nothing to declare.

B301

PATIENTS WITH HIGH-RISK ACUTE MYELOID LEUKAEMIA UNDERGOING UNMANIPULATED G-CSF–PRIMED HAPLOIDENTICAL BONE MARROW TRANSPLANTATION: FAVOURABLE LONG-TERM OUTCOME IN FIRST REMISSION WITH POSITIVE MEASURABLE RESIDUAL DISEASE

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) has become an increasingly feasible curative strategy for patients with high-risk acute myeloid leukaemia (AML). Moreover, positive measurable residual disease (MRD+) at transplant has been associated with poorer survival. Advances in graft-versus-host disease (GVHD) prophylaxis have markedly improved safety—particularly through ATG-based and post–cyclophosphamide platforms—broadening access to transplantation for patients lacking an

HLA-identical donor. Despite these developments, comparative analyses remain limited by heterogeneous cohorts and variable transplant approaches.

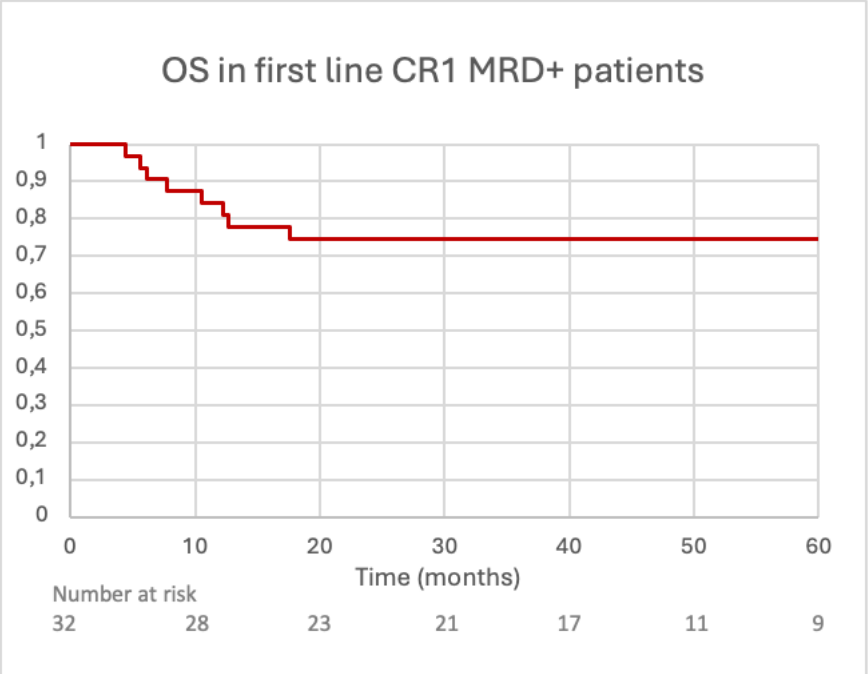
Methods: We conducted a retrospective single-center study including a population of 110 consecutive adult patients with high-risk AML who underwent unmanipulated G-CSF–primed bone marrow haplo-HSCT with intensified ATG and Basiliximab based GVHD prophylaxis between 2008 and 2023. The policy of donor selection, conditioning regimen including thiotepa-busulfan-fludarabine, graft source, supportive care, and infections prophylaxis were uniform across the cohort. Primary endpoints were overall survival (OS) and non-relapse mortality (NRM); secondary endpoints included GVHD and relapse incidence. MRD was assessed using multiparametric flow cytometry or molecular assay.

Results: The main characteristics of the patients are reported in the table. In the overall population, OS was 60% at 12 months and 46% at 5 years, with a 10-year OS of 44%. Cumulative incidence of acute GvHD grade II-IV and 5-yrs extensive chronic GvHD were 48% and 18% respectively. NRM was 24% at 12 months and 27% at 24 months. Disease status at transplant was the only independent predictor of NRM (p = 0.008), with significantly lower NRM among patients transplanted in complete remission.
Within the 72 patients transplanted in first complete remission (CR1), outcomes were markedly superior. NRM was 18% at 2 years, and relapse incidence was 22% and 28% at 12 and 24 months, respectively. These translated into a 5-year OS of 58% for the full CR1 cohort, reaching 74% among those 32 patients transplanted after first-line therapy with MRD+ (Graph).

Descriptive characteristics of the overall population (N=110)

Median patient age, years (range)	54 (14–70)
Median donor age, years (range)	36 (18–70)
Patient sex, male/female	54/56 (49%/51%)
Donor sex, male/female	68/42 (62%/38%)
Recipient/Donor sex combination	
Male/Male	34 (31%)
Female/Female	22 (20%)
Male/Female	34 (31%)
Female/Male	20 (18%)
Disease status at transplant	
CR1	72 (66%)
CR2	21 (19%)

≥ CR3 or active disease	17 (15%)
Conditioning regimen	
Myeloablative (TBF-MAC)	64 (58%)
Reduced-intensity (TBF-RIC)	46 (42%)



Conclusions: In this homogeneously treated population of adults with high-risk AML, unmanipulated G-CSF–primed haploidentical bone marrow transplantation with ATG and Basiliximab based prophylaxis yielded excellent long-term outcomes despite the moderately high NRM and the unfavorable disease-risk features. These results indicate that, while NRM remains a significant limitation, this strategy represents a *valuable therapeutic option* for appropriately selected high-risk AML patients—particularly when applied in first remission, even in patients with MRD+.

Disclosure: Nothing to declare.

B302

SYSTEMIC EVALUATION FOR EXTRAMEDULLARY DISEASE AND TREATMENT OUTCOMES IN ADULT PATIENTS WITH RELAPSED/REFRACTORY B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: In leukemia, the extramedullary disease (EMD) is typically assessed by CT, MRI, or ultrasound when patients exhibit relevant symptoms, whereas 18F-FDG PET/CT is rarely used. The systemic evaluation for EMD is unavailable in B-cell acute lymphoblastic leukemia (B-ALL), and the prognosis of relapsed/refractory (r/r) B-ALL with non-central nervous system (non-CNS) remained poor even after treatment with CD19 chimeric antigen receptor-T (CAR-T).

Methods: In this cohort of patients with r/r B-ALL, EMDs were assessed in each patient regardless of whether the patient had EMD symptoms or not. EMDs were evaluated either using CT/MRI/ultrasound or using 18F-FDG PET/CT. CD19 and CD22 CARs were lentiviral vectors carrying the second generation CAR with 4-1BB and CD3ζ. The overall survival (OS) and progression-free survival (PFS) were calculated from the date of first CAR-T cell infusion. Data of patients were collected from October 2021 through March 2025.

Results: A total of 91 adult patients were included, 42 were male and 49 were female, with a median age of 34 years (range, 18 to 61). Of them, 48 (52.7%) patients underwent allogeneic hematopoietic cell transplant (allo-HCT), 28 (30.8%) received antibodies blinatumomab/inotuzumab ozogamicin and 17 (18.7%) had a history of CAR-T therapy.
For EMDs, 50 patients were assessed by PET/CT and 41 were assessed by CT/MRI/ultrasound. Of all 91 patients, 47 presented with EMD and most of them (85.1%, 40/47) had combined bone marrow involvement (seven cases with isolated EMD). The overall incidence of EMD including CNS leukemia was 51.6% (47/91), while the non-CNS EMD was 42.9% (39/91). Further analysis revealed that the frequency of non-CNS EMD was 60.0% (30/50) in PET/CT group and it was 22.0% (9/41) in non-PET/CT group (p=0.0003), Importantly, among patients with MRD-positivity, five who did not exhibit any EMD symptoms had concurrent non-CNS EMDs determined by PET/CT; whereas none of patients showed EMDs in non-PET/CT group.
Treatment outcomes of patients with non-CNS EMD were observed in PET/CT group. Twenty-five patients received CD19 (n=19) or CD22 (n=6) CAR-T therapy as the initial treatment, additional consolidations following CAR-T were administered to 23 patients, which included allo-HCT (n=13, 10 were second allo-HCT), reinfusion of CAR-T cells (CD22 CAR-T, n=11; CD19 CAR-T, n=2), and others. Long-term outcomes were assessed in the 23 patients who received initial CAR-T and subsequent consolidations. As of the last follow-up, four patients died, 12 maintained in progression-free survival, five relapsed again, one failed CAR-T but survived with disease, and one lost follow-up. Kaplan-Meier survival analysis showed that the estimated 12-month OS and PFS rates were 89.5% and 69.4%; and the 24-month OS and PFS rates were 70.3% and 45.8%, respectively.

Conclusions: Among heavily treated adult patients with r/r B-ALL, 18F-FDG PET/CT identified a higher incidence of non-CNS EMD and hidden EMDs in MRD-positive patients, suggesting that PET/CT scan could be as a routine approach for EMD evaluation in r/r B-ALL. CAR-T followed by consolidation treatments improved long-term survival of patients with non-CNS EMD, providing a promising option for these patients with poor prognosis.

Disclosure: We have nothing to declare.

B303

SUPERIOR GVHD-FREE/RELAPSE-FREE SURVIVAL WITH HAPLOIDENTICAL TRANSPLANTATION USING TCRAB/CD45RA-DEPLETED GRAFTS IN AML: A COMPARATIVE ANALYSIS WITH MATCHED DONORS

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Background: For patients with acute myeloid leukaemia (AML) lacking a matched donor, haploidentical hematopoietic cell transplantation (Haplo-HCT) with ex vivo T-cell depletion is an emerging option. We have previously reported favourable GVHD-free/relapse-free survival (GRFS) with this approach (Ref: *Koh LP et al. BMT 2025*).

Methods: We conducted a single-centre retrospective analysis of 64 consecutive adult patients (median age 55 years) in National University Cancer Institute, Singapore with AML who received Haplo-HCT with TCRαβ-depleted graft with CD45RA-depleted memory T-cell add-back (αβTCD+TMDLI) between 2017 and 2025. Most patients (77%) were measurable residual disease (MRD)-positive pre-HCT, and 42% had adverse-risk molecular-genetics per ELN 2022. Conditioning regimen comprised of fludarabine, thiotepa, melphalan, with either total lymphoid irradiation (TLI; n=12) or low-dose total body irradiation (TBI; 2 Gy; n=52). GVHD prophylaxis (tacrolimus, n=57/sirolimus, n=1/MMF, n=3) was given for 30 days. Outcomes were compared with contemporaneous cohorts receiving matched sibling donor (MSD; n=43) or matched unrelated donor (MUD; n=35) transplants.

Results: The Haplo-HCT cohort showed promising 2-year overall survival (OS, 70%), event-free survival (EFS, 66%), GRFS (59%), with low 2-year cumulative incidence (CI) of relapse (15%) and severe GVHD (grade III–IV acute GVHD: 8%; moderate/severe chronic GVHD: 5%). Pre-HCT MRD negativity predicted excellent outcomes (2-year OS: 93 %; relapse: 0%). In multivariable analysis, high/very high disease risk index predicted inferior OS, EFS, GRFS, and higher relapse, whereas TBI 2Gy was associated with favourable survival and lower non-relapse mortality.

Comparative analysis showed no significant difference in 3-year OS (Haplo: 70% vs. MSD: 71% vs. MUD 51%; p=0.278) or EFS (66% vs. 59% vs. 37%; p=0.168). Notably, 3-year GRFS was significantly superior in the Haplo cohort (59%) compared to MSD (21%) and MUD (27%) (p=0.0025). Among MRD-positive patients, Haplo-HCT was associated with significantly lower relapse (p=0.006) and the most favourable GRFS (p=0.008).

Conclusions: Haplo-HCT with αβTCD+TMDLI achieves survival rates comparable to matched-donor transplants while offering significantly better GRFS, underscoring a major advantage in quality of survival. For MRD-positive patients, this approach confers the lowest relapse risk and the best GRFS. It represents a highly effective and preferable alternative donor strategy, particularly for AML patients with detectable MRD pre-HCT.

Disclosure: Nothing to declare

B304

SECOND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM DIFFERENT DONOR FOR PATIENTS WITH ACUTE LEUKEMIA RELAPSED AFTER FIRST TRANSPLANTATION：A SINGLE CENTER REAL WORLD STUDY

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Background: Allo-HSCT2 may be one possible and effectively way to treatment acute leukemia relapse after transplantation. but prognostic factors impact on survival have not been determined.

Methods: We analyzed the patients with acute leukemia who undergoing allo-HSCT2 relapsed post-HSCT1 from April 2012 to February 2024. The criteria for including patients were: second donors with allo-HSCT2 were different from the first transplant donors,HSCT1 donor are all derived from allogeneic.

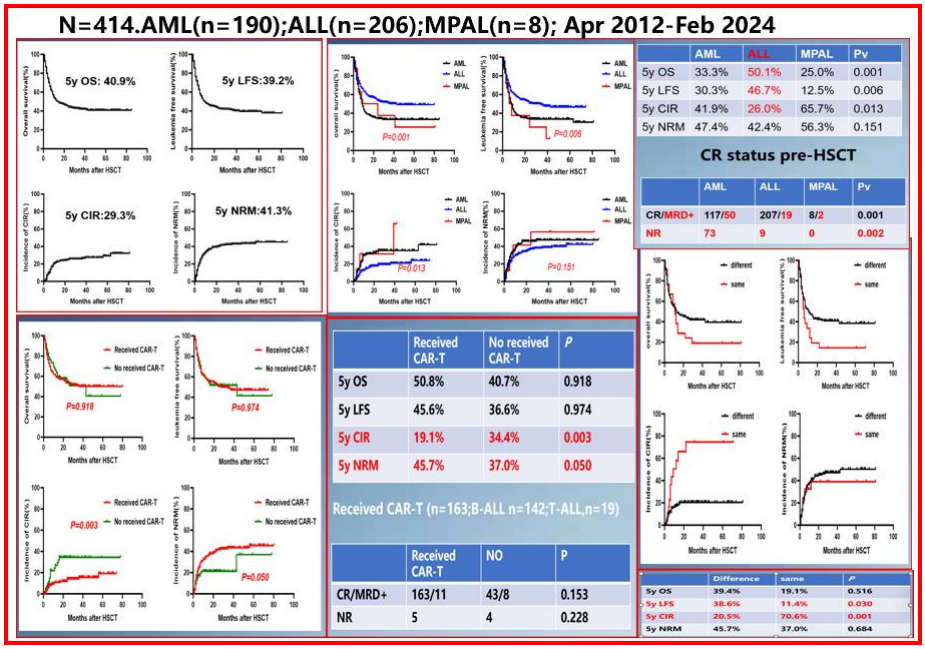
Table1 .Patients Characteristics

	Allo-HSCT1（n=414）	Allo-HSCT2（n=414）
Male/Female		231/183
Median age at HSCT,years	23(0.5-63) yrs	26(2-65) yrs
Age ≤18 year	172(41.5%)	144(34.7%)

Allo-HSCT1 versus allo-HSCT2 donor, difference		414(100%)
Donor type		
HID	241(58.2%)	327(78.9%)
MUD	40(9.6%)	78(18.8%)
MSD	119(28.7%)	5(1.2%)
UCBD	14(3.3%)	4(0.9%)
CR Status before HSCT(CR)	360(86.9%)	332(80.1%)
HCT-CI pre-allo-HSCT2(score 0)		232(56.0%)
With Extramendullary before HSCT	125(30.1%)	117(28.2%)
Received CAR-T before HSCT	125(30.1%)	117(28.2%)
Conditioning regimen(Intensified)		153(36.9%)
The median time to relapse after HSCT1(mon.) (range)		11（1-137）
Median time between HSCT1 and HSCT2 (mon.) (range)		18（2-159）
Median time from diagnosis to HSCT2 (mon.) (range)		26（8-162）
Developed of aGVHD post-HSCT1	119(28.7%)	
Developed of cGVHD post-HSCT1	350(84.5%)	

Results: Donor types for Allo-HSCT2: Haploidentical donor(HID) were 327(78.9%),matched unrelated donor(MUD) were 78(18.8%),matched sibling donor(MSD) were 5(1.2%) ,unrelated cord blood donor(UCBD) were 4(0.9%). The median age at Allo-HSCT2 was 26(range 2 to 65) years . The types of underlying diseases were Acute myeloid leukemia (AML)(n=190;); Acute lymphoblastic leukemia (ALL)(n=206), Mixed-phenotype acute leukemia(MPAL) (n=8). Disease status before Allo-HSCT2, 332(80.1%) patients at complete

remission(CR), and 82(19.8%) at non remission(NR). The median time to relapse after HSCT1 were 11(1-137）months, median time between HSCT1 and HSCT2 were 18（2-159）months. 119(28.7%) patients developed acute graft verse host disease(aGVHD) and 350(84.5%) cases developed chronic GVHD(cGVHD) post-HSCT1 respectively. In term of hematopoietic cell transplantation-specifc comorbidity index(HCT-CI) pre-allo-HSCT2, 47(11.3%) patients score more than 2. All patients received Myeloablative conditioning regimens(MAC) for allo-HSCT2,and 153(36.9%) received intensified MAC. the median follow-up time was 38(16-85) months.The 5-years overall survival(OS) and leukemia free survival(LFS) for the whole cohorts was 40.9% and 39.2% respectively,and 5-years cumulative incidence of relapsed(CIR) and non-relapsed mortality(NRM) were 29.3% and 41.3% respectively. Multivariate analysis for the whole cohorts showed that: Disease status pre-HSCT2 at CR status compared to NR status had higher 5-yrs OS[HR1.761,CI(1.305-2.378),P=0.001] and LFS [HR1.761,CI(1.305-2.378).P=0.001] due to lower CIR [HR3.184,CI(2.045-4.958),P=0.001]. HCT-CI score 0 compared to those ≥1 had higher 5-yrs OS[HR1.549,CI(1.202-1.872),P=0.001] and LFS [HR1.517,CI(1.257-1.829).P=0.001] due to lower NRM [HR1.638(1.312-2.045),P=0.001].the patient with intensified MAC compared to standard had higher NRM [HR1.536 ,CI(1.022-2.308),P=0.039],lower 5-yrs OS[HR1.511,CI(1.149-1.988),P=0.003] and LFS [HR1.673,CI(1.244-2.250).P=0.050].Occurrence of aGVHD post-HSCT1 had higher NRM [HR 1.579,CI(1.144-2.181),P=0.005],lower 5-yrs OS[HR 1.440,CI (1.040-1.994),P=0.048] and LFS [HR 1.459,CI(1.111-1.915).P=0.007].In term of three different primary disease subtype, in the ALL subgroup, more patients were MRD-negative before HSCT2 compared to the AML and MPAL subgroup(85.9% vs 35.2% vs 75.0,P=0.001),so had lower CIR (20.6% vs 41.9% vs 65.7%,P=0.013) ,therefore translates into higher 5-yrs OS(50.1% vs 33.3% vs 25.0%,P=0.001) and LFS(46.7% vs 30.3% vs 12.5%,P=0.006).For the ALL subgroup, the patients who received CAR-T pre-HSCT2 had lower (19.1%vs 34.4%,P=0.003),but had higher NRM(45.7% vs 37.0%,P=0.050), so did not translates into better OS and LFS finally. For subgroups both donors were from HID, the donor with new mismatched haplotype had lower CIR (20.5% vs 70.6%,P=0.001) therefore this translates into higher 5-years LFS(38.6% vs 11.4%,P=0.030). Survival was not associated with other factors.



Conclusions: Patients with HCT-CI 0, no GVHD developed post-HSCT1, and CR before HSCT2 are suitable factor candidates for Allo-HSCT2. The conditioning regimen is not recommended for intensification. Switching to a HID with a new mismatch haplotype can reduces CIR and improves survival when both donors are HID.

Clinical Trial Registry: No

Disclosure: No relevant conflicts of interest to declare

B305

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION MAY OVERCOME THE ADVERSE PROGNOSTIC IMPACT OF *IKZF1* ALTERATIONS IN ADULT PRECURSOR B-ALL

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Background: B-cell acute lymphoblastic leukemia (B-ALL) is a genetically heterogeneous disease in which recurrent genomic alterations significantly influence prognosis. Alterations of *IKZF1*, a key regulator of lymphoid differentiation, are associated with aggressive disease biology and inferior outcomes in conventionally treated patients. Allogeneic hematopoietic

cell transplantation (allo-HCT) is an established therapeutic option for high-risk B-ALL; however, the prognostic impact of *IKZF1* alterations in the post-transplant setting remains insufficiently defined. We therefore analyzed transplant outcomes in adult patients with precursor B-ALL according to *IKZF1* status.

Methods: Between January 2007 and September 2024, adult patients undergoing allo-HCT for precursor B-ALL were retrospectively evaluated. *IKZF1* status was assessed using multiplex ligation-dependent probe amplification (MLPA). A total of 91 patients were included: 46 patients harbored *IKZF1* alterations (*IKZF1* deletion only, n=20; *IKZF1* plus, n=26), while 45 patients had other or no detectable aberrations. Median age was higher in the *IKZF1* group (46 vs. 40 years). No significant differences were observed between groups with respect to disease status at transplantation (CR1 75%, CR2 20%, active disease 5%), donor type (matched related 23%, matched unrelated 48%, mismatched unrelated 19%, haploidentical 10%), conditioning intensity (myeloablative conditioning [MAC] 85%, non-myeloablative [NMA] 15%), or use of TBI-based conditioning (87%). Prior to allo-HCT, 52% of patients were MRD-negative. The incidence of Ph-positive B-ALL was significantly higher in the *IKZF1* group (72% vs. 24%, p<0.0001).

Results: For the entire cohort, 3-year overall survival (OS), event-free survival (EFS), relapse incidence (RI), non-relapse mortality (NRM), and GVHD-free/relapse-free survival (GRFS) were 72%, 67%, 21%, 15%, and 59%, respectively. The 3-year cumulative incidence of acute and chronic GVHD was 14% and 38%. No significant differences were observed between patients with and without *IKZF1* alterations in terms of OS, EFS, or RI (3-year OS 65% vs. 79%, p=0.06; EFS 60% vs. 73%, p=ns; RI 20% vs. 21%, p=ns). However, NRM was significantly higher in the *IKZF1* group (25% vs. 2% at 3 years, p=0.01).
MRD-negative patients demonstrated superior OS compared with MRD-positive patients (84% vs. 67% at 3 years, p=0.05). Comparable OS was observed in MRD-negative patients transplanted in CR1 and CR2 (85% vs. 80% at 3 years, p=ns).
In multivariate analysis, MRD positivity was independently associated with inferior EFS (HR 2.15, p=0.046) and showed a trend toward worse OS (HR 2.2, p=0.059). Disease status at transplantation (CR2 vs. CR1) was associated with higher RI (HR 3.5, p=0.02). The presence of *IKZF1* alterations was independently associated with increased NRM (HR 3.8, p=0.023), potentially reflecting differences in patient-related characteristics, including the higher median age observed in this subgroup. Age itself was a strong predictor of OS (HR 0.96, p=0.01).

Conclusions: Allo-HCT appears to mitigate the adverse prognostic impact of *IKZF1* alterations in adult patients with precursor B-ALL. Achievement of MRD negativity prior to transplantation remains a key determinant of outcome. Importantly, selected patients transplanted in second complete remission may achieve outcomes comparable to those transplanted in first remission, particularly when MRD negativity is achieved.

Disclosure: Nothing to declare

B306

DEPTH OF REMISSION PREDICTS OUTCOME AFTER ALLOGENEIC HSCT FOR AML: A SINGLE-CENTER STUDY OF 263 PATIENTS

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Background: The prognostic impact of measurable residual disease (MRD) at the time of allogeneic hematopoietic stem cell transplantation (allo-HSCT) for acute myeloid leukemia (AML) is well established. However, confirmation in contemporary real-world cohorts remains clinically relevant.

Methods: We retrospectively analyzed 263 consecutive AML patients undergoing a first allo-HSCT at the Hematology and Cellular Therapies Unit, IRCCS San Martino Hospital, Genoa, Italy, between January 2018 and June 2025. Disease status at transplant was categorized as MRD-negative complete morphological remission (MRD− CR, *n* = 152), MRD-positive complete morphological remission (MRD+ CR, *n* = 46), or active AML (*n* = 65).
MRD assessment was performed by multiparametric flow cytometry in patients with a leukemia-associated aberrant immunophenotype or by polymerase chain reaction (PCR) when a leukemia-specific molecular marker was available. The primary endpoint was event-free survival (EFS); secondary endpoints included overall survival (OS), relapse incidence, and transplant-related mortality (TRM).

Results: The median age was 59 years (range, 20–75), and 46% of patients had an HCT-Comorbidity Index score ≥3. According to the European LeukemiaNet (ELN) 2022 risk stratification, 12% of patients were favorable, 58% intermediate, and 30% adverse risk. Donor type distribution was as follows: haploidentical in 50%, MUD in 28%, MMUD in 12%, and HLA-identical related donors in 10% of patients. Median follow-up was 31.5 months (range, 3–91.1). In the overall cohort, the 48-month EFS was 49%. According to disease status at transplant, 48-month EFS was 63% in MRD− CR patients, compared with 32% in MRD+ CR and 29% in patients with active AML. EFS was significantly better in MRD− CR compared with both MRD+ CR ($p < 0.001$) and active AML ($p < 0.001$), whereas MRD+ CR and active AML showed comparable outcomes. The estimated 48-month OS in the overall cohort was 57.6% and OS showed the same pattern observed for EFS, being significantly superior in MRD- CR patients compared with both MRD+ CR and active AML. The cumulative incidence of relapse at 24 months was 31.6% in the overall cohort. According to disease status at transplant 24 -month relapse incidence was 19.1% in MRD- CR patients, 45.7% in MRD+ CR and 46.2% in patients with active AML ($p < 0.001$). The 24-month TRM was 13.1% overall, being 11.8%, 10.9%, and 23.1% in MRD− CR, MRD+ CR, and active AML patients, respectively, but these differences did not reach statistical significance. In multivariable analysis, ELN 2022 risk category, donor type, stem cell source, conditioning platform and intensity did not significantly affect EFS, OS, relapse and TRM incidence. MRD status at transplant remained the only independent predictor of post-transplant outcomes.

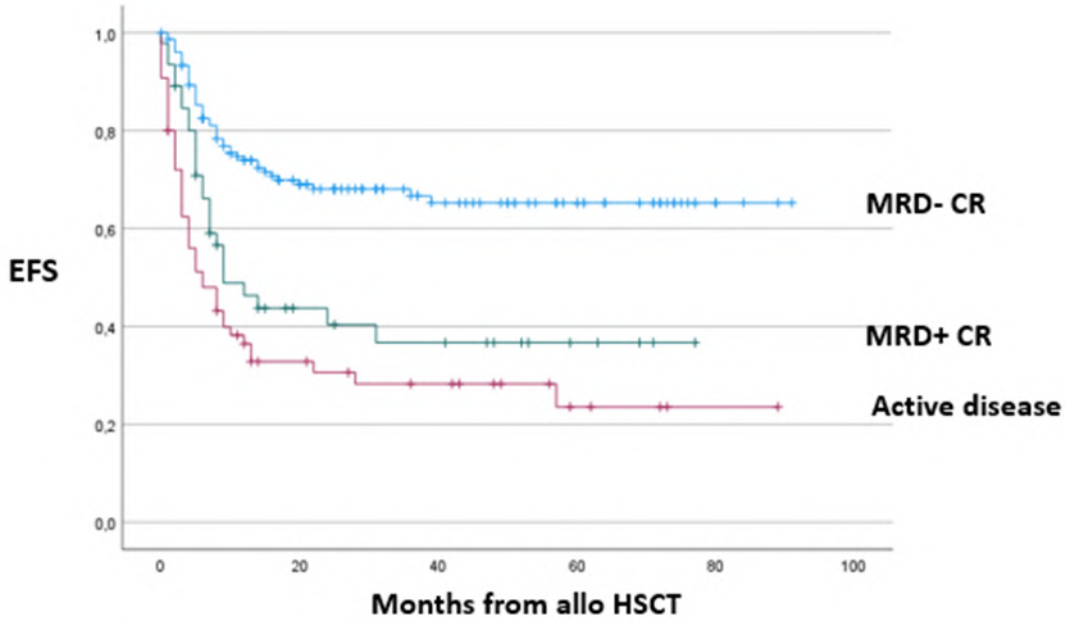

Figure 1

Conclusions: In this contemporary single-center cohort, MRD negativity at the time of allo-HSCT was the strongest determinant of post-transplant outcomes. Patients in MRD-positive complete morphological remission experienced relapse risk and EFS comparable to those transplanted with active AML. This finding indicates that MRD positivity neutralizes the effectiveness of morphological remission and confirms the need for new therapeutic strategies for these patients.

Disclosure: Nothing to declare.

B307

REAL-WORLD EXPERIENCE WITH GILTERITINIB MAINTENANCE FOLLOWING ALLOGENEIC TRANSPLANTATION IN RELAPSED/REFRACTORY AML PATIENTS HARBORING *FLT3* MUTATIONS

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Background: *FLT3* mutations, especially *FLT3*-ITD, are associated with a high risk of relapse after allogeneic transplantation in patients with acute myeloid leukemia. Gilteritinib is an established treatment for relapsed or refractory *FLT3*-mutated disease and has been used as maintenance therapy after transplantation in patients who enter transplant in remission.

Evidence, however, is still scarce for patients who receive gilteritinib as salvage therapy during active relapsed or refractory disease, proceed to transplantation, and then continue gilteritinib as maintenance. This clinical sequence is not well represented in prior trials, and data from Asian populations remain limited. To describe the real world outcomes of patients with relapsed or refractory *FLT3*-mutated acute myeloid leukemia who received gilteritinib before transplantation and again as maintenance. The study also aimed to identify patient groups, based on measurable residual disease, that may derive the greatest benefit.

Methods: This was a prospective observational study conducted at a single medical center in Taiwan between 2017 and 2023. Forty two patients with relapsed or refractory *FLT3*-mutated acute myeloid leukemia received gilteritinib as salvage therapy and then underwent allogeneic transplantation. Maintenance therapy with gilteritinib was offered between day 30 and day 90 after transplantation for patients with stable engraftment and no significant acute graft versus host disease. Measurable residual disease was evaluated using multiparameter flow cytometry or quantitative polymerase chain reaction. The primary outcomes were relapse free survival and overall survival. Safety events and transplantation related complications were recorded.

Results: The median age was 48 years and most patients carried *FLT3*-ITD. Salvage treatment with gilteritinib produced a complete response rate of 76 percent. With a median follow up of more than 46 months, patients who received gilteritinib maintenance had longer relapse free and overall survival compared with those who did not receive maintenance. Relapse at one year was less common in the maintenance group. In multivariable analyses that included measurable residual disease and the presence of chronic graft versus host disease, gilteritinib maintenance remained an independent predictor of improved survival. The effect of measurable residual disease was clear. Patients who were negative for measurable residual disease before or after transplantation had the most pronounced benefit from maintenance therapy. In contrast, patients with persistent measurable residual disease had less evident benefit, in part because many received other post transplantation interventions such as venetoclax based therapy or donor lymphocyte infusion. Gilteritinib was well tolerated. No excess in clinically significant cytomegalovirus infection was observed. No patient developed severe graft versus host disease related to the drug. Adverse effects were limited to mild liver enzyme elevation or creatine kinase increase in a few patients.

Conclusions: This study provides real world evidence that gilteritinib used both before and after transplantation can offer meaningful clinical benefit in relapsed or refractory *FLT3*-mutated acute myeloid leukemia. Patients who are negative for measurable residual disease appear to benefit most. The findings support the use of targeted maintenance therapy in this clinical setting and help fill an important knowledge gap for Asian populations and for patients who undergo transplantation during active disease.

Disclosure: Research funding and honorarium from Astellas: Xavier Cheng-Hong Tsai

B309

REAL-WORLD OUTCOMES OF DONOR LYMPHOCYTE INFUSIONS AFTER ALLOGENEIC HCT FOR ACUTE LEUKEMIA: A 20-YEAR MULTICENTER STUDY

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Background: Relapse of acute leukemia after HCT remains a major clinical challenge, and growing efforts are directed toward its prevention through pre-emptive strategies. DLIs are widely used both for relapse treatment and for disease control in the presence of residual disease (MRD) or mixed chimerism; however, their use remains heterogeneous due to the absence of prospective studies and standardized guidelines. Real-world data are essential to better define their efficacy, safety, and optimal timing, and to support a more uniform clinical practice.

Methods: We conducted a multicenter retrospective study of 79 adults with acute leukemia who received DLI between 2005 and 2025 across four centers in Rome. The primary endpoint was overall survival (OS), while secondary endpoints included treatment response, disease-free survival (DFS), graft-versus-host disease (GVHD), infection rates, and non-relapse mortality (NRM). Collected variables included demographic, biological, and transplant-related data such as diagnosis, disease status at HCT, donor type, conditioning regimen, leukemia subtype, number and timing of DLI infusions, pre-DLI therapies, concomitant treatments, and post-infusion complications. Statistical analyses were performed using SPSS 26.0. OS and DFS were estimated using the Kaplan–Meier method, and NRM was assessed using cumulative incidence analysis. Group comparisons were made using the Mann–Whitney U test and chi-square test. Prognostic factors were assessed through univariate and multivariate Cox regression models.

Results: Among the 79 patients, 72% had AML and 28% ALL; 38% received pre-emptive DLI and 62% therapeutic DLI, while 64% received concomitant treatments with DLI. At a median follow-up of 12 months, 45.5% were alive, and the 4-year OS was 37%. Older age, ALL, active disease at transplant, therapeutic DLI, and combination therapy were associated with poorer outcomes. In contrast, post-DLI GVHD and achievement of complete remission correlated with improved survival. CR was achieved in 41.8% of patients and was sustained in 70% of responders. The 4-year DFS was 44%, and was lower among patients receiving therapeutic DLI, those transplanted with active disease, and those treated with combination therapy. Sibling donors were associated with inferior CR rates and DFS compared with MUD donors. The apparent negative effect of combination therapy likely reflected selection bias and was not observed in the pre-emptive setting. GVHD occurred in 39% of patients, with five GVHD-related deaths. NRM reached 22.7%, while disease progression remained the leading cause of mortality.

CHARACTERISTICS	NUMBER OF PATIENTS (%)
PATOLOGIA AL TRAPIANTO • CR1 • CR ≥ 2 • Active disease	 45 (57) 24 (30) 10 (13)
INDICATION • Pre-emptive • treatment	 30 (38) 49 (61)
THERAPEUTIC ASSOCIATIONS • Chemotherapy • iFLT3 • HMA • TKI +/- CHT or Blinatumomab • Blinatumomab • Inotuzumab +/- Chemotherapy • Azacitidine - Venetoclax • Chemotherapy - Venetoclax	**51 (64)** 17 (33) 9 (18) 6 (12) 8 (16) 3 (6) 2 (4) 5 (9) 1 (2)
DONOR • Sibiling • Matched Unrelated Donor (MUD) • Mismatched Unrelated Donor (MMUD) • Haploidentical	 26 (33) 26 (33) 6 (7.5) 21 (26.5)
NUMBER OF ADMINISTRATIONS • 1 • 2 • 3 • ≥ 4	 21 (26.5) 22 (28) 15 (19) 21 (26.5)
GVHD AFTER DLI	**31 (39)**

Acute GVHD	**19 (24)**
G1-2	11 (14)
G3-4	8 (10)
Chronic GVHD	**12 (15)**
Mild	4 (5)
Moderate/Severe	8 (10)
INFECTIOUS COMPLICATIONS	**14 (24)**
ACHIEVEMENT OF CR	**33 (41.8)**
RELAPSE AFTER DLI	**30 (38)**
Median (months)	16
Range (months)	1 - 103
DEATHS	**43 (54.4)**
	27 (63)
• Disease relapse/progression	7 (16)
• Infectious disease	7 (16)
• TRD	2 (5)
• Other causes	

Conclusions: This represents one of the longest real-world cohorts, demonstrating that pre-emptive DLI was associated with superior outcomes compared with DLI for overt relapse, highlighting the critical role of timing and the need for systematic MRD and chimerism monitoring. Post-DLI GVHD correlated with improved survival, reflecting an effective GVL effect, while NRM underscores the importance of optimizing infusion strategies. Active disease at transplant remained a major adverse prognostic factor, and combination therapy did not overcome the negative impact of aggressive **disease**. In this setting, the role of DLI remains incompletely defined, warranting further investigation. Future prospective, risk-adapted strategies are warranted to harmonize DLI use across centers and fully harness its curative potential, while minimizing GVHD risk and optimally integrating combination therapies.

Disclosure: Nothing to declare

B310

AGE OVER SIBLING: YOUNGER UNRELATED DONORS PROVIDE SUPERIOR OUTCOMES COMPARED TO SIBLING DONORS IN FULLY MATCHED HCT IN OLDER AML/MDS PATIENTS

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Background: Fully matched sibling donors (MSDs) have traditionally been the preferred graft source for allogeneic hematopoietic cell transplantation (HCT) in patients with acute myeloid leukemia (AML) or myelodysplastic syndromes (MDS). As patient age increases, sibling donor age also rises. Emerging evidence suggests that donor age may influence outcomes more than donor relatedness. To verify this hypothesis, we examined in the multicenter cohort study whether younger matched unrelated donors (MUDs) provide superior outcomes compared to MSDs in older patients with AML/MDS.

Methods: This retrospective study included patients aged ≥60 years with AML/MDS who underwent HCT at centers at the Polish Adult Leukemia Group and the University of Rostock between 2014 and 2024. Overall survival (OS), non-relapse mortality (NRM), and relapse incidence (RI) at 2 and 5 years post-HCT were estimated using the Kaplan–Meier method. Associations between risk factors and OS, NRM, and RI were assessed using Cox proportional hazards models.

Results: Of the 293 patients included in the study, the median age at HCT was 64 years (range: 60–76), and 44% were over 65 years old. The median follow-up was 21 months (range: 0–146). MSD and MUD groups differences are summarized in Table 1. The donor age of MSDs was higher, with a median of 60 years (range: 41–79), compared to 31 years (range: 19–57) for MUDs.
The estimated 2- and 5-year OS rates were 61% and 48% for MUD and 47% and 42% for MSD, respectively (Figure 1A). Relapses occurred in 27 MSD patients (38%) and 70 MUD patients (32%), with the highest incidence within the first 24 months. In multivariable analysis, 5-year OS was affected only by disease status prior-HCT (not in complete remission (CR): adjusted hazard ratio (aHR) 1.78, 95% CI 1.2–2.5, p<0.05). Neither ATG nor type of conditioning affected OS; however, there was a trend toward better outcomes in the MUD group (aHR 0.74, 0.5–1.08, p=0.12).
When OS, NRM, and RI were analyzed in the cohort with available donor age data (n = 221), the best outcomes were observed in patients who received transplants from MUDs younger than 30 years (Figure 1B). In this group, 5-year OS was 53% (p < 0.05), with the lowest NRM (Figure 1C). Causes of NRM were similar between groups, with infection-related deaths accounting for 50% of cases.
In the multivariate model, NRM was affected by recipient age over 65 years (aHR 1.9, 1.0–3.6, p=0.04) and donor age over 50 years (aHR 3.01, 95% CI 1.29–7.82, p<0.05). Relapse incidence was increased when HCT was done not in CR (aHR 1.77, 1.01- 3.0, p<0.05), with the lowest risk in the MUD group (aHR 0.28, 0.09 to 0.8, p<0.05), and showed a decreasing trend with an increasing donor age (aHR 0.96, 0.93–0.98, p<0.05).

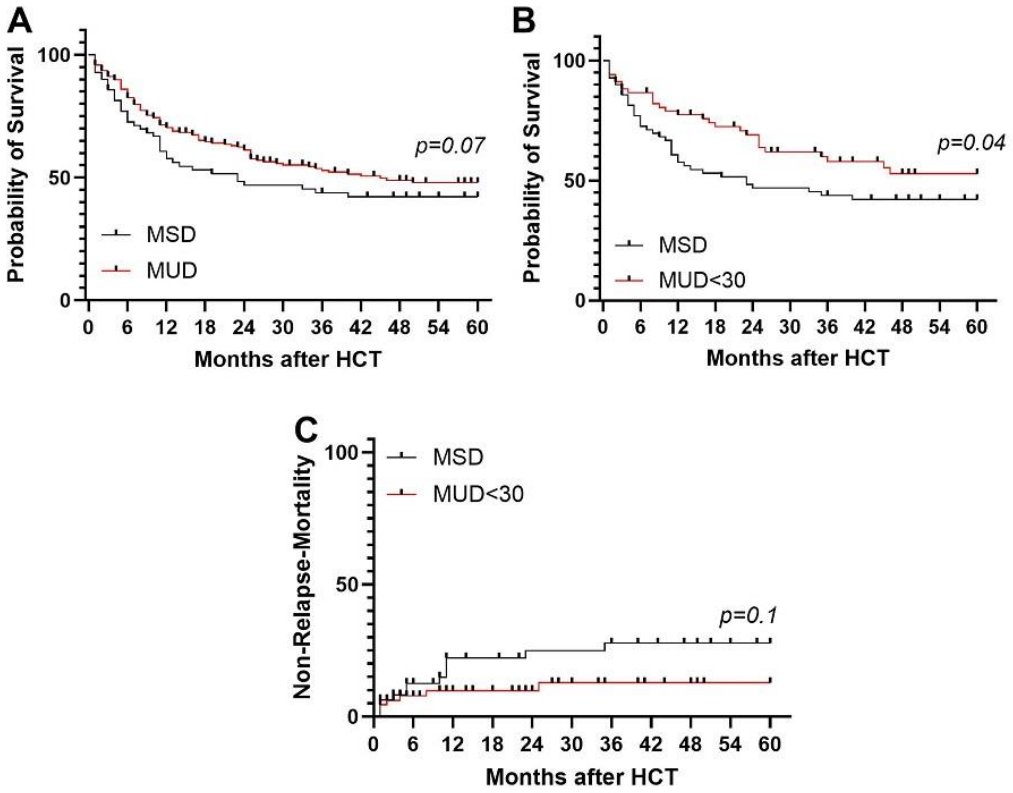

Figure 1. Kaplan–Meier plot of overall mortality within 5 years after transplantation, comparing matched sibling donor (MSD) and matched unrelated donor (MUD) in the overall cohort (A) and in the subset with available donor age data (B). Cumulative incidence of non-relapse mortality within 5 years after transplantation in the subset with available donor age data (C).

*Table1 : Baseline characteristics*of patients included in the study

		Matched sibling donor n=72	Matched unrelated donor =221	p
Age	Age ≥65	25 (34%)	104 (47%)	0.07
Sex	Female / Male	34 (47%) /38 (53%)	89 (40%) /132(60%)	
Uderlying disease	Acute myeloid leukemia	61 (85%)	187 (85%)	ns
	Myelodysplastic syndrome	11 (15%)	34 (15%)	

Disease status	Complete remission	51 (71%)	172 (78%)	ns
	Not-complete remission	18 (29%)	49 (22%)	
Conditioning intensity	TCI 1.5-3	52 (72%)	182 (82%)	0.03
	TCI 3.5-4	20 (28%)	35 (18%)	
ATG or PT-Cy	No	50 (69%)	4 (2%)	<0.001
	Yes	22 (31%)	217 (98%)	
Donor Age years	<30	0	68 (31%)	<0.001
	>30	72	81 (37%)	
	No Data	0	72 (32%)	
Engraftment	Yes	60 (83%)	189 (86%)	0.07
	No	7 (10%)	14 (6%)	
	No Data	5 (7%)	18 (8%)	
Graft-versus-host disease	Any aGvHD	18 (25%)	60 (27%)	ns
	Grade 3-4 aGvHD	10 (14%)	13 (6%)	0.04
	cGvHD	22 (31%)	52 (23%)	ns

Conclusions: MUD transplantation was associated with more favorable outcomes than MSD procedures, primarily due to lower NRM when donors were younger than 30 years, suggesting that younger unrelated donors may be preferable to older siblings.

Disclosure: Nothing to declare.

B311

CHARACTERISTICS AND OUTCOMES OF ALLOGENEIC STEM CELL TRANSPLANTATION FOR ADULTS WITH PHILADELPHIA-LIKE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE-CENTER ANALYSIS

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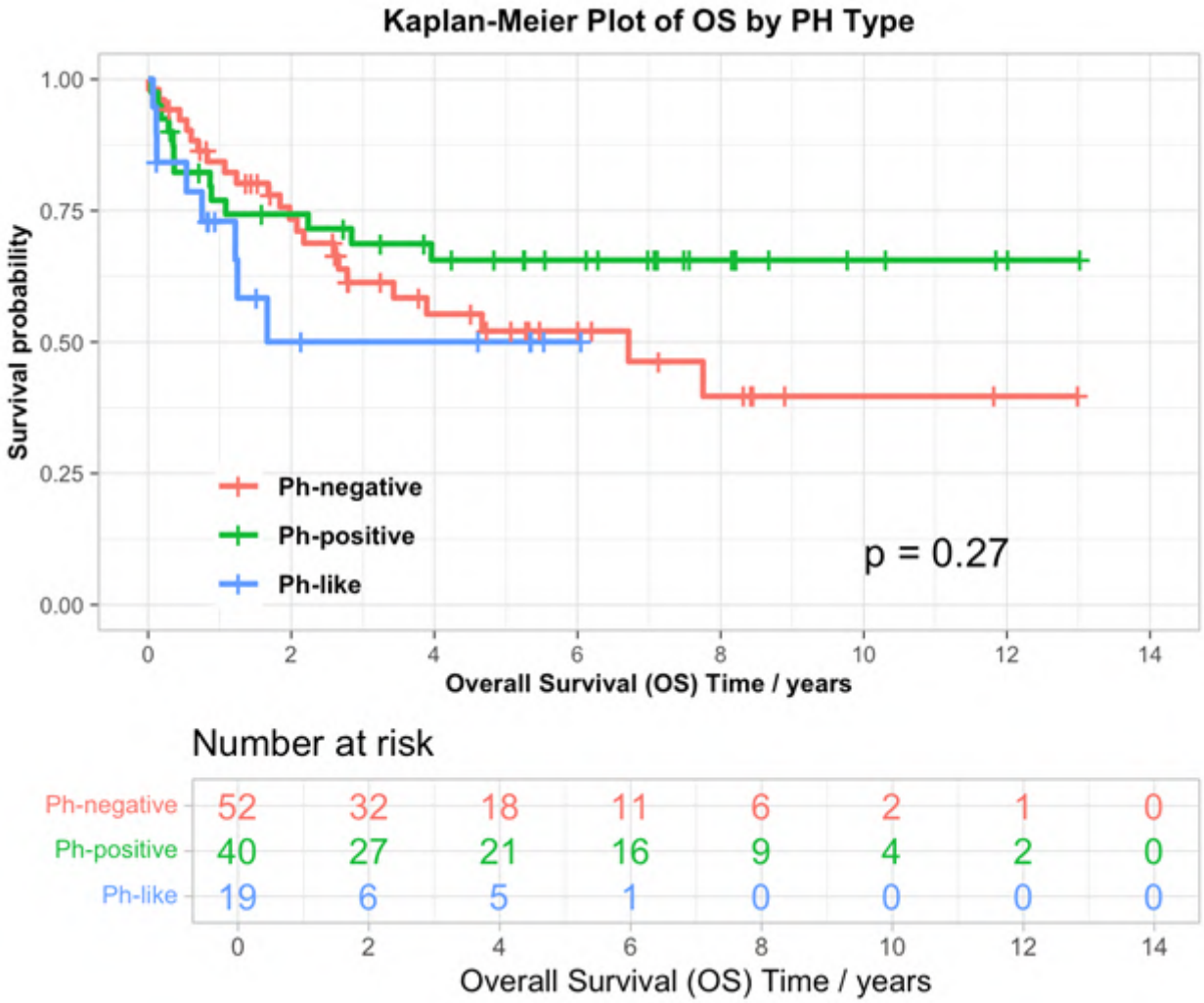
Background: Philadelphia-like (Ph-like) B-cell acute lymphoblastic leukemia (B-ALL) is a genomically defined, high-risk subset that is associated with treatment resistance, increased relapse, and poor outcomes. Given its novelty as a disease subtype and related diagnostic challenges, more data is needed to delineate outcomes after allogeneic hematopoietic stem cell transplantation (HSCT).

Methods: We performed a retrospective cohort analysis of 111 adults with B-ALL undergoing first allogeneic HSCT between 2011-2025, grouped as Ph-negative (n=52), Ph-positive (n=40), and Ph-like (n=19). Baseline characteristics were summarized by group and compared using Fisher's exact tests for categorical variables and Kruskal-Wallis tests for continuous variables. Overall survival (OS) and relapse-free survival (RFS) were estimated by Kaplan-Meier from HSCT date and compared using log-rank tests (exploratory univariate log-rank screening for selected covariates). In the Ph-like subgroup, exploratory competing-risk analyses were summarized using cumulative incidence functions for relapse-related mortality (RRM) with non-relapse mortality (NRM) as the competing event, and for NRM with relapse as the competing event.

Results: Among 111 HSCT recipients, 46.8% were Ph-negative, 36.0% Ph-positive, and 17.1% Ph-like. Median age was 43 years (range 19-75), 50.5% were male, and 65.8% Hispanic; 78.4% received myeloablative conditioning and 65.8% received TBI. Baseline characteristics were broadly similar across groups, except time from diagnosis to HSCT was longer in Ph-negative patients (median 12.5 months vs 8.0 and 7.39 months, p=0.007) with a trend toward more ≥CR3 disease status at HSCT in Ph-negative/Ph-like (p=0.077).OS and RFS did not significantly differ by Ph subtype (log-rank p=0.27 and p=0.28), though curves suggested inferior early outcomes for Ph-like. Relapse occurred in 36.8% of Ph-like vs 34.6% of Ph-negative and 20.0% of Ph-positive patients. Day-100 TRM was highest in Ph-like (15.8%) vs 5.8% (Ph-negative) and 7.5% (Ph-positive). In univariate log-rank screening, donor type and TBI were associated with OS and RFS (both p≤0.014), and conditioning intensity showed a nominal association (p=0.03).
Among the Ph-like cohort, the most common genomic alterations involved CRLF2 in 53% (n=10), JAK2 in 26% (n=5), EPOR in 11% (n=2), PDGFR in 11% (n=2), and ABL in 5% (n=1). Exploratory competing-risk curves in the Ph-like subgroup suggested heterogeneity in the balance of relapse vs non-relapse events across transplant characteristics, but small numbers precluded formal comparisons.



Conclusions: Ph-like B-ALL patients are a high-risk cohort with higher relapse and mortality after HSCT. Alterations involving CRLF2 were the most common, introducing potential for post-HSCT targeted therapeutics. Given this rare subtype and small cohort, larger scale validation studies are warranted.

Disclosure: Nothing to declare.

B312

ALLOGENEIC STEM CELL TRANSPLANTATION DURING FIRST REMISSION IMPROVES SURVIVAL IN CORE-BINDING FACTOR ACUTE MYELOID LEUKEMIA

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Background: Core-binding factor acute myeloid leukemia (CBF-AML) represents a prognostically favorable AML subtype. However, while allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a standard therapy for relapse, its definitive role in first complete remission (CR1)—particularly for patients with high-risk features such as poor measurable residual disease (MRD) response—remains uncertain.

Methods: In this study, we retrospectively analyzed 165 consecutive CBF-AML patients who underwent allo-HSCT at our center between May 2016 and January 2024. We evaluated the impact of pre-transplant disease status and measurable residual disease (MRD) levels, assessed by both multiparameter flow cytometry (MFC) and RT-PCR, on survival and relapse outcomes.

Results: A total of 165 CBF-AML patients (median age 38.4 years; range 4-67) were enrolled. The cohort comprised 102 patients with AML1-ETO and 63 with CBFβ-MYH11 fusion gene. Based on pre-transplant disease status, patients were categorized as follows: first complete remission (CR1, n=108), second complete remission (CR2, n=38), beyond second remission (>CR2, n=6), primary refractory disease (NR, n=3), and relapsed disease (Relapse, n=10).
Survival outcomes were analyzed according to pre-transplant status. Patients transplanted in CR1 demonstrated the most favorable prognosis, with significantly superior outcomes compared to those in CR2 (3-year RFS: 93.1% vs. 78.4%, P = 0.028; 3-year OS: 92.5% vs. 77.5%, P = 0.011). Among the six patients transplanted beyond CR2, one experienced early relapse-related mortality. For patients transplanted in relapse, the 3-year OS and RFS were 58.3% and 50.0%, respectively.
We further stratified patients in pre-transplant CR1 and CR2 based on remission depth using flow cytometry and RT-PCT. Of the evaluable patients, 95 in CR1 and 27 in CR2 were MFC-MRD-negative, compared to 6 and 5 positive cases, respectively. Given the small number of positive patients, we pooled the two negative groups for comparison. This analysis yielded that CR1 patients with negative MFC-MRD had better overall survival and a lower trend towards relapse than their CR2 counterparts (CR1 vs. CR2, 3-year CIR: 5.6% vs. 16.4%, *P* = 0.1; 3-year OS: 92.6% vs. 71.0%, *P* = 0.007).
Stratification by molecular MRD yielded 14 PCR-MRD-negative and 58 PCR-MRD-positive cases in CR1, compared with 6 negative and 13 positive cases in CR2, respectively. Among CR1 patients, MRD status did not significantly affect outcomes (PCR-MRD- vs. PCR-MRD+, 3-year OS: 85.7% vs. 94.7%, P=0.223). In contrast, PCR-MRD+ patients in CR1 had better survival and a lower trend towards relapse than their PCR-MRD+ counterparts in CR2 (CR1

vs. CR2, 3-year CIR: 9.30% vs. 24.78%, P=0.16; 3-year OS: 94.7% vs. 74.0%, P=0.025). The interpretation of comparisons involving the CR2 PCR-MRD-negative group is cautioned due to its limited patient numbers.

Conclusions: We found that allo-HSCT in CR1 provided a survival benefit for CBF-AML patients. MRD monitoring is particularly important for the selection of transplantation timing.

Disclosure: Nothing to declare.

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FACTORS PREDICTING OUTCOME OF PATIENTS WITH ACUTE MYELOID LEUKEMIA WITH ACTIVE DISEASE UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Up to 30% of adult patients with Acute Myeloid Leukemia (AML) experience a Primary Refractory Leukemia as they fail to achieve a Complete Remission (CR) after one or two courses of chemotherapy and almost 50% of those obtaining CR will eventually relapse. Despite salvage therapies, most patients do not achieve CR and their prognosis is dismal. However, hematopoietic stem cell transplantation (HSCT) remains a therapeutic option in this very high-risk category of patients and the identification of predictive prognostic factors could improve the selection of those who could most benefit from HSCT.

Methods: From March 2010 to October 2025, at the Department of Stem Cell Transplantation of Tor Vergata University in Rome, 35 patients affected by AML underwent HSCT with active disease, defined by the presence of ≥5% of blasts in bone marrow or extramedullary disease (EMD). The median age at transplant was 51 years (range 28-68); patients received a reduced intensity (RIC; n=16) or a myeloablative (MAC; n=19) conditioning regimen. All patients received chemotherapy-based conditioning consisting of Thiotepa, Busulfan and Fludarabine combination and a graft versus host disease (GvHD) prophylaxis according to the type of donor. 65% of patients received HSCT from a relative donors. Statistical analysis was performed using XLSTAT (Version 25.02.1414.0).

Results: With a median follow up of 48.3 months (9-133) for living patients, the 5-year Overall Survival (OS) and Disease-Free Survival (DFS) were 28.1% (95% confidence interval (CI), 12.3-43.8) and 27.7% (95% CI,12.6-42.8), respectively.
5-year cumulative incidence of relapse and transplant related mortality were 57.5% (95% CI,41.8-79.1) and 31.2% (95% CI,16-60.6), respectively. The cumulative incidence of aGvHD was 34.5% (95% CI,21.3-55.8).

In univariate analysis, 2-year OS and DFS were not significantly affected by intensity of conditioning regimen (RIC vs MAC), patient age (≤50 vs >50 years) and cytogenetic risk (low vs intermediate-high risk). The 2-year OS by the "interval time between diagnosis and transplantation" of <9 months vs >9 months was 40.8% and 7.7% (p=0.02) respectively, and by "disease burden" with ≤20% of blasts and absence of EMD vs >20% of blasts or with EMD was 41.1% and 8% (p=0.01), respectively. For the same variables, the 2-year DFS was 39.4% and 7.7% (p=0.05) by interval time and 38% and 8.3% by tumor burden, respectively (p=0.02).

Conclusions: This single-center retrospective study found that about 30% of the AML patients uniformly transplanted for active disease survive and supports the role of HSCT in such very high-risk category of patients. Post-transplant relapse remains the main reason for failure. In univariate analysis, patients transplanted earlier with low blast count and without EMD had a significantly better outcome. However, the small sample size of our population doesn't allow to draw solid conclusions or establish a prognostic scoring system. Our results emphasize the need for larger studies to identify predictive factors useful to select patients with overt AML that may benefit from HSCT. Furthermore, they underline the importance of developing post-transplant strategies such as maintenance therapies, Donor Lymphocyte Infusion, and modulation of immunosuppressive agents to reduce the risk of post-transplant relapse.

Disclosure: Nothing to declare.

B314

AN EARLY MYELOID STEM CELLS-BASED IMMUNOPHENOTYPIC PANEL CAN RAPIDLY AND EFFICIENTLY DISTINGUISH APL FROM APL-LIKE

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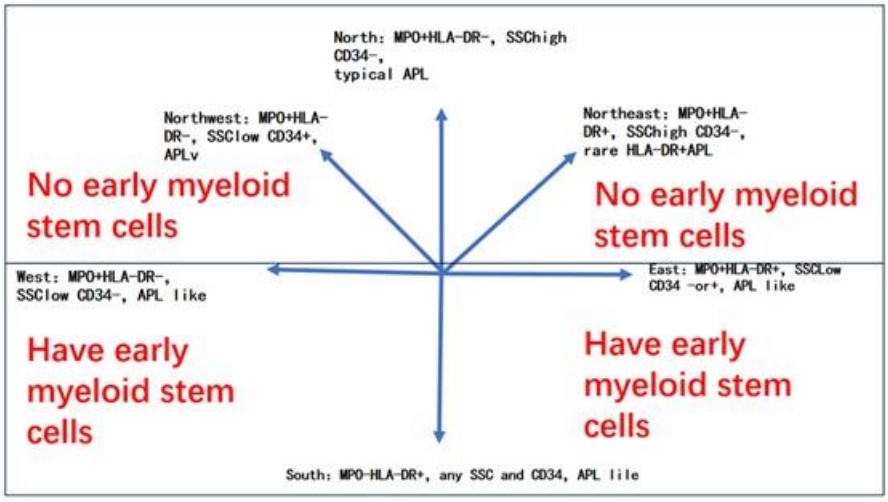
Background: Acute promyelocytic leukemia (APL) has unique morphology and immunophenotype in typical cases. However, 10-20% of cases show atypical changes, and some non-APL AML (especially NPM1-mutated or KMT2A-rearranged AML) can also present with APL-like morphology and immunophenotype, known as APL-like. Therefore, the clinical differentiation between APL and APL-like poses a significant challenge for flow cytometry detection.

Methods: A total of 313 cases of APL (165 males and 148 females) were treated at Hebei Yanda Lu Daopei Hospital from Jan. 1, 2016 to Dec. 20, 2024, including 236 cases of classic APL (124 males and 112 females) and 77 cases of APLv (41 males and 36 females). APL-like cases were 426 (311 cases of NPM1-mutated AML and 115 cases of other genetically abnormal AML), including 219 males and 207 females. Morphology, genetics, and clinical manifestations were used for simultaneous verification. The 2-tube 8-color panel was as follows: CD16 FITC/CD117 PE/CD34 PerCP-Cy5.5/CD13 PE-CY7/CD33 APC/HLA-DR APC-

CY7/CD11b BV421/CD45 V500; MPO FITC/CD64 PE/CD34 PerCP-Cy5.5/CD117 PE-CY7/CD14 APC/CD36 APC-CY7/CD38 BV421/CD45 V500. EMSC were defined as CD34+/SSCdim/CD117dim/CD33dim/HLA-DRdim/CD13+/CD11b-/CD38dim.



Results:

1. The detection rate of EMSC. The positive rate of EMSC in APL was 2/313 (0.64%), including 1/236 (0.42%) in classic APL and 1/77 (1.30%) in APLv. The positive rate in APL-like was 423/426 (99.30%). The sensitivity of using the presence of EMSC to distinguish APL from APL-like was 99.36%, and the specificity was 99.30%. The positive predictive value of the absence of EMSC for APL was 99.04%, and the negative predictive value was 99.53%. Combined with classic MPO, CD34, and HLA-DR, APL and APL-like can be easily, efficiently, and rapidly distinguished. 2. Other immunophenotypes. The immunophenotype of the APL group was relatively consistent, with typical cases expressing CD64 and MPO and not expressing HLA-DR and CD34. The expression rate of CD34 in APLv was the highest, exceeding APL-like. HLA-DR had significant predictive value for APL, with a very low positive rate. However, a considerable number of cases in the APL-like group presented with immunophenotypes extremely similar to APL. Due to the heterogeneity of APL-like, there were statistical differences in CD64, MPO, CD34, and HLA-DR.
3. A positioning map was designed based on EMSC and immunophenotypes (Figure 1). With MPO as the boundary, MPO and HLA-DR form one group, and CD34/SSC form another. South (MPO-HLA-DR+, SSC and CD34 positive or negative), East (MPO+HLA-DR+, small SSC, CD34 positive or negative), and West (MPO+HLA-DR-, small SSC, CD34-) are all non-APL, among which West is APL-like. North (MPO+HLA-DR-, large SSC, CD34-) is typical APL, Northwest (MPO+HLA-DR-, small SSC, CD34+) is APLv, and Northeast (MPO+HLA-DR+, large SSC, CD34-) is the rare HLA-DR+ APL. Most of the Northward ones lack EMSC, while most of the Southward ones have them. This can serve as a prototype for artificial intelligence diagnosis.

Conclusions: A multi-parameter immunophenotypic panel based on the detection of EMSC was discovered. By combining immunophenotypes and creating a four-quadrant orientation map, it can rapidly and efficiently distinguish APL from phenotypically similar leukemias, and is expected to serve as the foundation for artificial intelligence.

Disclosure: Nothing to declare

B315

STUDY OF BONE MARROW-INFILTRATING NK CELLS (BINK) AND PERIPHERAL BLOOD NK CELL (PBNK) IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Leukaemia is the most common childhood cancer. While treatments cure 70-90% of children with acute lymphoblastic leukaemia (ALL), relapsed cases have poor survival rates (<40%). Immunotherapy has introduced innovative therapeutic strategies aimed at improving outcomes. The use of natural killer (NK) cells with anti-tumor activity has been proposed as a promising adjuvant or alternative treatment for leukemic patients. Our study analyzed bone marrow (BM) infiltrating NK (BiNK) and NK cells on peripheral blood (PbNK) of pediatric ALL patients at various stages of disease to understand the immunosurveillance, immunoscape and phenotype related to BiNK cells.

Methods: BM and PB samples were collected from pediatric patients with B-ALL at La Paz University Hospital in Madrid and HUMS/IIS Aragón in Zaragoza, Spain, between March 2019 and May 2023. Samples were obtained at diagnosis (n=48), the end of induction A (IA) phase (n=47), the end of induction B (IB) phase (n=45)and relapse (n=12). The percentages of BiNK and PbNK cells, and the expression of activating and inhibitory receptors and NK ligands in the blast cells, were monitored and analyzed using multiparametric flow cytometry. Additionally, the degranulatory capacity was assessed following co-culture with the K562 cell line at an effector-to-target ratio of 1:2. Furthermore, single-cell RNA sequencing (scRNAseq), cytokine profile and unsupervised analysis (tSNE-CUDA) was performed on a BM samples at both diagnosis and IB to evaluate transcriptomic and clustering changes over time.

Results: Regarding percentages of BiNK/PbNK cells, we observed a significant increase in BiNK cells at IA compared to diagnosis. Similarly, NK cells showed a significant increased at IA and IB phases compared to diagnosis. In contrast, both BiNK and NK cells exhibited a significantly lower percentage at relapse compared to rest time points. BiNK cells showed a

significant decrease in CD56dim, CD16, activating receptors (NKG2D, DNAM-1, and CD57), and inhibitory receptors (TIGIT, TIM-3, PVRIG, and KIRs) while NKG2A expression significantly increased at IA/IB phases compared to diagnosis. At relapse, BiNK cells demonstrated a significant decrease in activating receptors (NKG2D and CD7) and inhibitory receptors (NKG2A, TIM-3, andKIR3DL1), but an increase in CD57 and NKG2C receptors compared to both diagnosis and induction phases. PbNK cells showed a significantly higher percentage of activating receptors (NKG2D, CD7, CD57, CD16, and DNAM-1) and a lower percentage of immune checkpoint receptors (LAG-3, TIGIT, PD-1, and PVRIG) compared to BiNK cells. Furthermore, PbNK cells demonstrated a significant increase degranulation at IB phase compared to diagnosis. ScRNAseq revealed that BiNK cells at IB phase exhibit significant transcriptional changes, suggesting a shift toward a pro-inflammatory state accompanied by reduced functional capacity. Additionally, when comparing cytokine levels at different time points, IL-15, a pro-inflammatory cytokine, showed increased levels during treatment. Unsupervised analysis reveals treatment-dependent BiNK-cell clusters and subclusters. Finally, leukemia blasts showed a higher PD-L1 SFI and a lower HLA-II SFI at relapse compared to diagnosis in pediatric patients with B-ALL.

Conclusions: Our findings indicate that the biological characteristics of BiNK cells are shaped by the specific microenvironment in which they reside, whether within the leukemic niche or during the different phases of treatment.

Disclosure: Nothing to declare.

B316

EARLY TRANSPLANTATION FOLLOWING INDUCTION CHEMOTHERAPY IN ADULT AML PATIENTS WITH A *NUP98* REARRANGEMENTS LEADS TO MRD-NEGATIVE REMISSION

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Background: NUP98 rearrangements (NUP98r) are seen in 5-10% paediatric and 2-4% adult AML and confer a poor response to induction chemotherapy and poor overall survival (OS). Outcomes can be improved with progression to HSCT, however evidence on the optimal timing of HSCT and role of Minimal residual disease (MRD) is lacking. We report on our single centre experience of HSCT in NUP98r AML at University College London Hospitals (UCLH), a UK tertiary referral centre, incorporating MRD data pre- and post-HSCT to determine optimal HSCT timing.

Methods: Ten patients with NUP98r AML were treated with intent-to-transplant at UCLH between 2022-2025.

Results: Median age was 30 years (20-65). 80% were standard risk by ELN 2022, 20% were adverse risk. 70% had a NUP98::NSD1 fusion and 80% had a co-existing FLT3-ITD mutation. The median number of chemotherapy cycles pre-HSCT was 3 (2-8). 90% received intensive induction chemotherapy first-line. 80% received venetoclax containing regimes in induction or consolidation (VEN/AZA, GAV, or FLAV-IDA). 60% received FLT3i. 80% achieved cCR with chemotherapy, within a median of 114 days. Two patients (20%) did not achieve cCR; one died of infection during induction, the other was transplanted with refractory disease. Eight patients (80%) achieved HSCT, within a median of 174 days [130-297]. Of these, three died of relapsed AML post-HSCT, whilst five (62.5%) were alive at last follow up. The median OS in transplanted patients is 29 months from diagnosis and median PFS post-transplant is 13.5 months. Patients who received 1-3 lines chemotherapy pre-HSCT had an improved OS compared to those who received 4+ lines pre-HSCT (15 months vs 5 months, p=0.01).

Patient outcomes were stratified according to disease state pre-HSCT. Two were transplanted with refractory disease, three in MRD positive MLFS, two in MRD positive cCR, and one patient in MRD negative cCR. Both patients transplanted with refractory disease died of relapsed disease post-HSCT, with a median LFS of 48 days post HSCT. However, there was no difference in outcomes between patients who were in MLFS vs those in cCR pre-HSCT. 87.5% patients who were MRD positive at the time of HSCT became MRD negative post-HSCT (MLFS n=3/3; cCR n=4/5). Median time to MRD negativity post HSCT was 104 days (21-182).

Figure 1A: Survival stratified on number of chemotherapy cycles pre-transplant

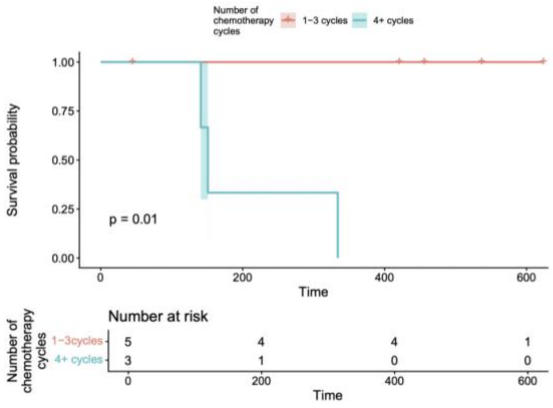
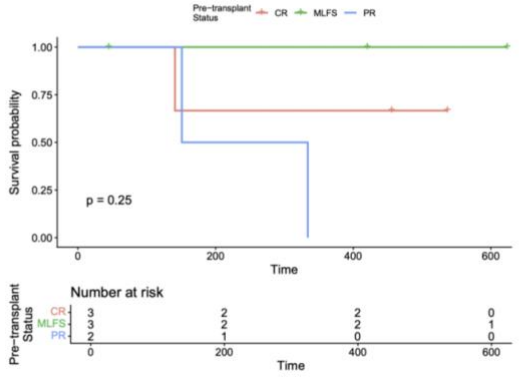


Figure 1B: Survival based on disease status pre-transplant



Conclusions: This cohort had a poor response to standard induction chemotherapy with prolonged time to first cCR and low levels of MRD negativity. We identify a trend towards improved response following targeted therapy and venetoclax; only two patients achieved cCR with standard chemotherapy alone, whilst the remainder required either targeted therapy with FLT3i (n=2), venetoclax (n=2) or GAV (n=2). Although patients transplanted with residual leukaemia had poor outcomes, those in MRD positive cCR or MLFS at the time of HSCT had improved outcomes, with no difference observed between MLFS and cCR. We recommend early transplantation following induction chemotherapy in MLFS or CR to offer potential molecular remission and long-term disease-free-survival in adult patients with NUP98r AML.

Clinical Trial Registry: NA

Disclosure: Nothing to declare

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B317

OUTCOMES OF SECOND ALLOGENEIC STEM CELL TRANSPLANTATION FOR ACUTE MYELOID LEUKAEMIA AT THE IRISH NATIONAL ADULT STEM CELL TRANSPLANT UNIT

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Background: Allogeneic stem cell transplantation (AlloSCT) is the only curative treatment for high-risk AML. However, 30% of patients suffer relapse with dismal subsequent survival. While salvage treatment may re-capture disease response, re-harnessing a graft-versus-leukaemia (GVL) effect through the use of donor lymphocyte infusions (DLI) or a second transplant (AlloSCT2) is usually the only avenue to secure long-term survival. Patient candidacy for AlloSCT2 is challenged by the cumulative toxicity of prior therapies.

Methods: We conducted a 10-year retrospective review of patients who underwent AlloSCT2 (2016-2025) at the Irish National Adult Stem Cell Transplant Unit. Total AlloSCT2 numbers were extracted from our EBMT dataset. The electronic patient record was interrogated for patients who had an initial diagnosis of AML as well as patients relapsing post-AlloSCT1 as a high-grade myeloid malignancy (>10% blasts). Overall survival (OS) and progression free survival (PFS) were estimated using Kaplan-Meier methodology.

Results: Our cohort comprised 20 patients: 13(65%) male and 7(35%) female. Seven (35%) of AlloSCT2s were performed from 2016-2020, and 13 (65%) from 2021-2025.
AlloSCT1: The median age was 37.5 years (IQR 28.5-42y). Original diagnoses were AML (75%), MPAL (5%), MDS (5%) and MDS/MPN (15%). Sixteen patients (80%) received myeloablative conditioning (MAC) and 4(20%) patients reduced intensity conditioning (RIC). Twelve patients (60%) received cells from matched siblings (SIB), 6(30%) from fully-matched unrelated donors (MUD) and 2(10%) from single antigen-mismatched unrelated donors (MMUD). The median time to relapse after AlloSCT1 was 4.1 years (IQR 2.0-8.2y). Only 3 patients had relapsed <1y from AlloSCT1.
AlloSCT2: The median age was 43.8 year (IQR 41-49y). Nineteen (95%) were re-transplanted due to relapse and 1 for primary graft failure (n=1). Nineteen patients. (95%) received RIC or non-myeloablative conditioning; 1 was myeloablated. Of the RIC transplants, 12 (60%) received melphalan, 4 (20%) received sequential regimens. Four patients (20%) were re-transplanted using the same donor. There was an increase in alternative donor sources compared to AlloSCT1: 3 (15%) haplo-identical and 1 (5%) cord blood.
With a median follow-up of survivors of 1.8y, median OS was 5.25y. One and two-year OS were estimated at 66% and 52% respectively. Median PFS was 2.7y, with one and two-year PFS estimated at 60% and 52%. Variable analyses were limited by sample size, but no significant association was observed between survival outcomes and duration of remission after AlloSCT1, choice of donor for AlloSCT2 or conditioning regimen employed for AlloSCT2. At the time of this review 9 patients had died post-AlloSCT2. Causes of death were relapse (n=5), sepsis (n=3) and GVHD (n=1). All non-relapse mortalities (23%) occurred within 1 year of AlloSCT2.

Conclusions: Acknowledging limited numbers, we demonstrate the potential for long-term survival after AlloSCT2 in patients with AML relapsing after AlloSCT1. Room for improvement remains and our cohort is biased against patients relapsing <1yr from AlloSCT1, who are often considered poor AlloSCT2 candidates and suffer dismal outcomes. Further research into the mechanisms of post-transplant relapse in AML may allow a precision approach to treatment, refining our use of targeted therapy, AlloSCT2 and DLI, in order to maximize survival while sparing unnecessary toxicity.

Disclosure: Nothing to disclose

B318

EFFICACY AND SAFETY OF BLINATUMOMAB AS COMBINATION OF INDUCTION OR EARLY CONSOLIDATION THERAPY IN NEWLY DIAGNOSED B CELL ACUTE LEUKEMIA

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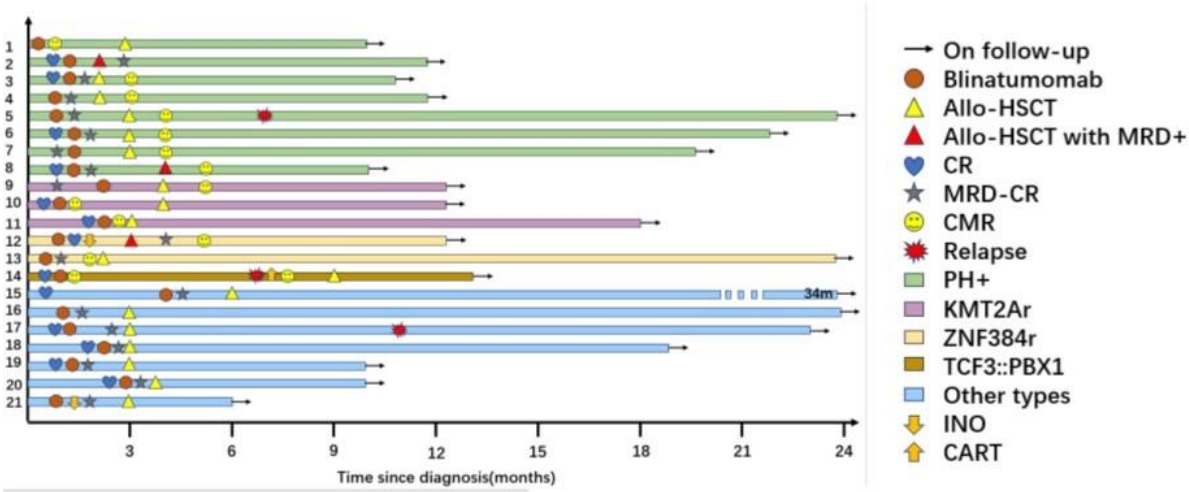
Background: For patients with newly diagnosed acute B-lymphoblastic leukemia (B-ALL), intensive chemotherapy is frequently associated with significant toxicity and a high risk of infection. In contrast, blinatumomab, a novel immunotherapy, has demonstrated favorable efficacy and a promising safety profile.

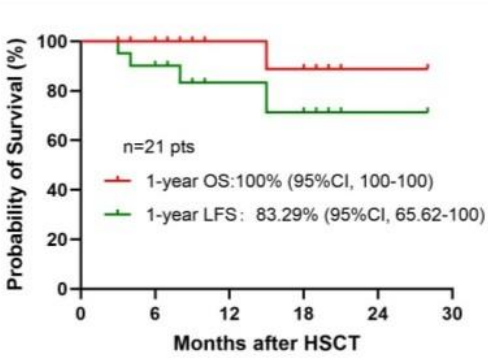
Methods: This study was conducted at Hebei Yanda Lu Daopei Hospital and included all consecutive pediatric and adult patients with newly diagnosed acute leukemia who received blinatumomab as induction or early consolidation therapy between January 1, 2023 and June 30, 2025. Indications for blinatumomab were: intolerance to intensive chemotherapy, minimal residual disease (MRD) positivity, or failure to achieve remission after chemotherapy.

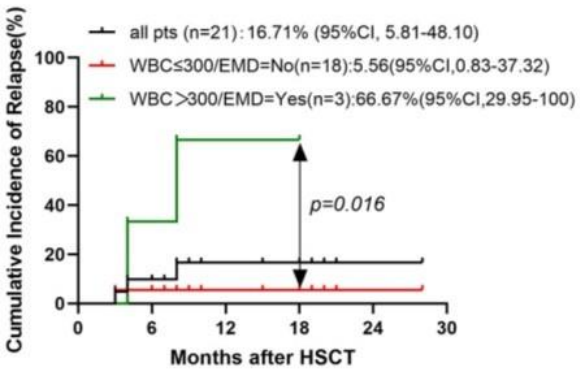
Results: A total of 21 newly diagnosed acute leukemia patients were enrolled, comprising 2 cases of mixed-phenotype acute leukemia (MPAL, B/myeloid) and 19 cases of B-ALL, among whom 2 had a history of antecedent chronic myeloid leukemia (CML) （Table 1）. The median age was 35 years (range 6–57), 11 (52.4%) were male, and 6 (28.6%) were pediatric. Blinatumomab was used as induction therapy in 13 patients and as consolidation in 8. Prior to blinatumomab, 7 patients had no remission (NR), 14 were in first complete remission (CR1), 12 were MRD-positive, and 2 were MRD-negative. After blinatumomab treatment (median duration 2 weeks), 6 of the 7 NR patients achieved CR1 (CR rate 85.7%), with 5 attaining MRD-negative CR. One NR patient received only 3 days of blinatumomab due to severe cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) and remained MRD-positive. Another NR patient discontinued blinatumomab after 2 days due to ICANS and remained NR. Among the 12 MRD-positive patients, 10 became MRD-negative (MRD-negative rate 83.33%), and 2 showed reduced MRD levels. Adverse events included CRS in 2 patients (grade 3 and grade 1, respectively)

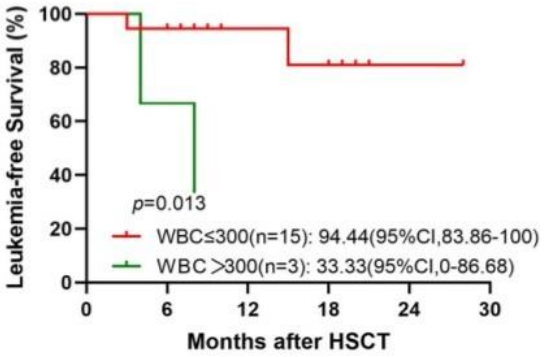
and ICANS in 2 patients. All patients proceeded to allogeneic hematopoietic stem cell transplantation (allo-HSCT, Figure 1). After a median follow-up of 10 months (range 3–28), the estimated 1-year overall survival was 100% and 1-year leukemia-free survival (LFS) was 83.29% (95% CI: 63.47–100). Univariate analysis showed that patients with a presenting WBC $>300 \times 10^9$/L had significantly lower LFS (P=0.013; 94.44% [95% CI: 83.86–100] vs. 33.33% [95% CI: 0–86.68]) and higher relapse rates (P=0.016; 66.67% [95% CI: 29.95–100] vs. 5.56% [95% CI: 10–44.28]). Similarly, extramedullary disease (EMD) before transplant was associated with lower LFS (P=0.049; 93.33% [95% CI: 80.71–100] vs. 33.33% [95% CI: 0–86.68]) and higher relapse (P=0.016; 66.67% [95% CI: 29.95–100] vs. 5.56% [95% CI: 10–44.28]). Two relapses occurred at a median of 6 months, involving one CNS infiltration and one ocular relapse .

Figure 1.Newly diagnosed acute leukemia patients;MPAL(N=2),B-ALL(n=19)









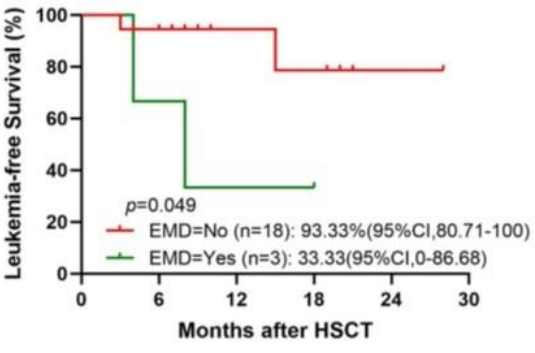


Table1,patient and transplant characteristics

characteristics	N=21
Median age，years(range)	35（6~57）
Children(＜18y) n.(%)	6（28.6）

Males n.(%)	11（52.4）
WBC at diagnosis n.(%) ＞300×10^9/L	 3（16.7）
Genetics n.(%) BCR::ABL P190 BCR::ABL P210 ZNF384 rearrangement KMT2A rearrangement IKZF1 deletion	 5(23.8) 3(14.3) 2(9.5) 3(14.3) 4(19)
chemotherapy before blinatumomab (cycles) ≤1 2	 17 4
MRD status on starting blinatumomab NR CR MRD- CR MRD+	 7 2 12
MRD status after blinatumomab CR1 MRD- CR1 MRD+ NR	 17 3 1
days of blinatumomab to HSCT ≤30 ＞30	 8 13
EMD before HSCT n.(%) CNSL	 3（14.3）
Indication for HSCT high risk MRD+ after chemotherapy Primary induction failure	 13 5 3
MRD status at HSCT MRD+ MRD-	 3 18
Donor type HID MSD	 20 1

Conditioning regimen TBI based BU based	 17 4
ABO compatibility Major/bidirectional mismatch Other	 7 14
Graft source PB BM+PB	 16 5
CD34 + cells count, $\times 10^6$/kg, median(range)	8.2（3.6~15）
Nucleated cells count, $\times 10^8$/kg, median (range)	7.7（3.4~17.3）
Maintenance treatment after HSCT Y N	 13 8

Conclusions: Blinatumomab demonstrated favorable efficacy and safety in patients with newly diagnosed acute leukemia. However, extramedullary relapse warrants close monitoring, particularly in patients with high presenting WBC counts or EMD before transplantation.

Disclosure: Nothing to declare.

B319

PROGNOSTIC FACTORS FOR EARLY LEUKEMIA-FREE SURVIVAL IN NPM1-MUTATED AML UNDERGOING ALLOGENEIC TRANSPLANTATION WITH ACTIVE DISEASE

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents the only potentially curative treatment option for patients with relapsed or refractory NPM1-mutated acute myeloid leukemia (AML). Although this entity is generally considered chemosensitive, a substantial proportion of patients proceed to transplantation with active disease, a clinical scenario associated with inferior outcomes. Up to now, there is limited evidence to guide risk stratification in the transplant setting.

Methods: We analyzed 49 patients with NPM1-positive AML transplanted with active disease. Leukemia-free survival (LFS) was dichotomized as ≤6 versus >6 months. Logistic regression with backward selection based on the Akaike Information Criterion was used to identify factors associated with LFS > 6 months.

Results: Extramedullary disease was the only variable independently associated with inferior LFS > 6 months ($\beta = -1.43$; $p = 0.03$; odds ratio ≈ 0.24). Age, sex, secondary AML, ECOG performance status, donor type, conditioning intensity, CMV matching and acute graft-versus-host disease did not significantly contribute to the final model. Reduction to the final model resulted in a moderate improvement in model fit ($\Delta AIC \approx 5$). Molecular risk factors such as FLT3 status and ELN risk could not be analyzed due to insufficient variance within this selected cohort.

Conclusions: In *NPM1*-mutated AML patients undergoing allo-HSCT with active disease, extramedullary manifestation is a strong adverse prognostic factor for early leukemia-free survival. These findings emphasize the high-risk nature of transplantation in active disease and support the incorporation of extramedullary involvement into transplant-specific risk stratification and decision-making.

Disclosure: Nothing to declare.

P247

REDUCED RELAPSE RATES IN LEUKEMIA PATIENTS UNDERGOING HAPLOIDENTICAL VERSUS MATCHED RELATED ALLOGENIC BONE MARROW TRANSPLANT: RESULTS FROM A COLOMBIAN BONE MARROW TRANSPLANTATION UNIT

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Background: Some studies have shown enhanced anti leukemic activity of transplants from haploidentical donors versus identical related donors in leukemia patients (1); most patients lack an identical related donor available and access to unrelated donors in Colombia is significantly limited. Haploidentical transplant with post-transplant high dose Cyclophosphamide (PTCy) is associated with similar overall survival compared with identical

related donor or matched unrelated donors with less graft versus host disease in Acute Lymphoblastic Leukemia patients (2).

Methods: We retrospectively reviewed clinical records of leukemia patients who had undergone a bone marrow transplantation in our unit between January 1st 2017 and July 30th 2025.

Results: 143 allogenic bone marrow transplants were performed, the most frequent transplant was from haploidentical donor (n=101, 70.6 %) versus allogenic related identical sibling (n=42, 29.4%). The median age was 36 years (11-66 years), and most were male (89, 62.2 %). The most frequent diagnosis were Acute Lymphoblastic Leukemia (82, 57.3 %) followed by Acute Myeloid Leukemia (45, 31.5 %). Most patients received 2 or more treatment regimens before the transplant (103 patients, 71 %). A minority received myeloablative conditioning (33 patients, 23,1%) with a significant difference between transplants modalities, receiving myeloablative conditioning more frequently patients in related identical donors vs haploidentical (47.6 % vs 13.5 %, Chi square p <0.001).All but one patient were in complete response or in chronic phase (in the case of chronic myeloid leukemia) at the time of transplant. Minimal residual disease (MRD) assessment determined by flow cytometry was detectable in 34 patients (24.3 %) with no difference between haploidentical vs identical related allogenic transplant (22.4% vs 28.6 %, Chi square test p=0.44).
Relapse rate was significantly reduced in haploidentical transplant versus identical related donors (33.3 % vs 51.2 %, Chi square test p=0.003, RR: 0.48 CI 95 % 0.31-0.76).
With a median follow up of 274 days, the time free from relapse was significantly higher in transplant from haploidentical donors versus transplant from related identical donors [non reached, (1198 – non reached) vs 511 days (303-non reached), log rank test: 5.25, p = 0.022].
There was not a significant difference in overall survival between the two types of transplants (47,5 % vs 61,9%, Chi square test p=0.117, RR: 1.38 CI 95% 0.9-2.12).
The median survival time was similar between transplant types [754 days in haploidentical (565-199) vs 586 days in identical (369-non reached) log rank test: 0.704, p=0.401] because a possible higher non relapse mortality in haploidentical transplants (Chi square test p=0.037, RR:1.66, CI 95% 0.99-2.78) and possible better rescue therapies in relapsed patients after transplant.

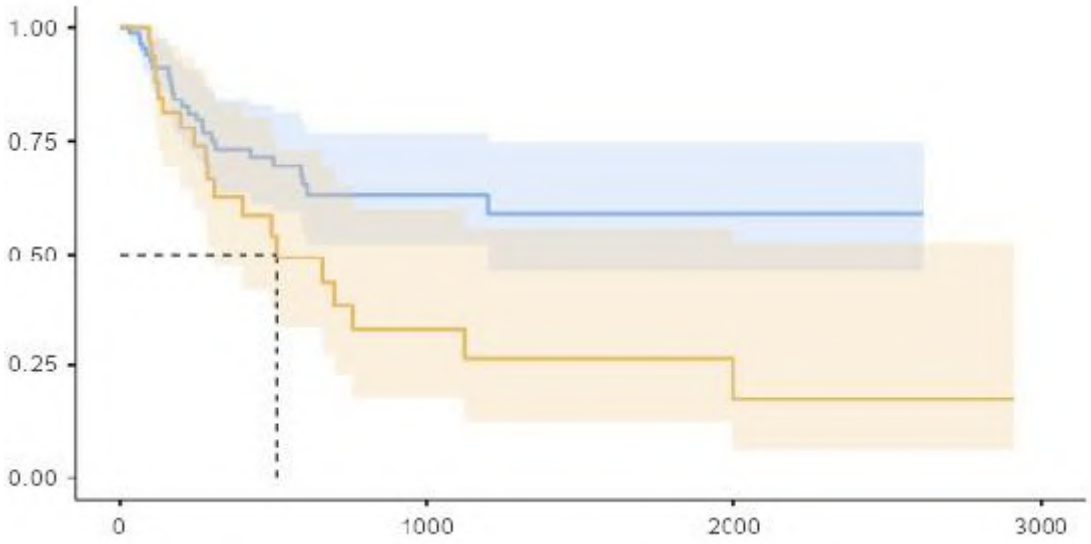

Figure1: relapse free survival, blue line: haploidentical , golden : identical related

Conclusions: Lower relapse rate was observed in transplants from haploidentical donors versus related identical donors without a difference in overall survival in this high risk leukemia patients despite a lower frequency of myeloablative conditioning use in haploidentical transplants suggesting enhanced graft versus leukemia effect in haploidentical transplants. Longer follow up and better supportive care could show that this finding translate in a better overall survival in the future.

Disclosure: We hace nothing to declare, the source of funding were own resources

P248

POST-TRANSPLANT OUTCOMES IN ADULT ALL: INSIGHTS FROM A SINGLE-CENTER EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a standard consolidation therapy for adult patients with high-risk acute lymphoblastic leukemia (ALL). The present study aimed to evaluate the post-transplant outcomes adult ALL including the cumulative incidence (CI) and severity of graft-versus host disease (GVHD), overall survival (OS), event-free survival (EFS), non-relapse mortality (NRM) and (CI) of relapse.

Methods: We conducted a retrospective study on adult patients with ALL who underwent allo-HSCT from HLA-identical sibling donors between January 2017 and December 2024. Conditioning regimens included Total Body Irradiation (TBI)-based protocols (associated with

etoposide or cyclophosphamide) or chemotherapy-only-regimens consisting of thiotepa–busulfan–fludarabine (TBF) or thiotepa–treosulfan–fludarabine (TTF). Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporine and short course of methotrexate with or without antithymocyte globulin (ATG). Stem cell sources were bone marrow (BM) or peripheral blood stem cells (PBSCs). Minimal residual disease (MRD) was assessed using multiparametric flow cytometry (6–8 colors) and/or RT-PCR in patients with Philadelphia chromosome–positive B-cell ALL (Ph-positive ALL).

Results: Fifty-three patients were included (20 women and 33 men) with a median age of 33 years (range, 18-55). Underlying disease included Ph-negative B-ALL, Ph-positive B-ALL and T-ALL in 24 (45%), 8 (15%) and 21 (40%) cases, respectively. The median time from diagnosis to allo-HSCT was 7 months (range, 4-135). Prior to transplant, 75% of patients were in first complete remission (CR1), 19 % in CR2. Three patients were transplanted with refractory disease. Minimal residual disease (MRD) status was available in 49 patients, of whom 53% were MRD-positive prior to allo-HSCT. Twenty-two patients (42%) received a TBI-based conditioning regimen, and BM was the source of graft in 60% of patients. The median time to engraftment was 14 days for neutrophil count (range, 10–23 days) and 20 days for platelet count (range, 15–38 days) with significant differences between BM and PBSCs ($p=0.011$ and $<10^{-3}$, respectively). CI of grade II-IV acute GVHD and chronic GVHD were 64% and 61%, respectively, with 22 patients presenting with the extensive form of chronic GVHD. The 2-year CI of relapse was 35%, with a median time of 7 months (range, 2–19 months). The 2-year CI of NRM was 14%, mainly attributable to infections. After a median follow-up of 25 months (range, 1-7 years), the 2-year OS and EFS were 64% and 52%, respectively, without significant differences between patients receiving a TBI-based conditioning and those receiving a CT-based regimen ($p=0.2$ and $p=0.16$), respectively. In subgroup positive MRD patients, TBI-based regimen was significantly associated with better EFS $p=0.048$ compared to CT-based regimen. This EFS benefit is explained by the significantly lower CI of Relapse observed in MRD+ patients receiving TBI ($p=0.036$).

Conclusions: Our experience showed favorable post-transplant outcomes in adult ALL patients with significantly lower relapse in the subset of patients with positive pretransplant MRD who received TBI-based conditioning. These findings support the need for broader access to TBI and targeted therapies to optimize outcomes in this high-risk population.

Disclosure: Nothing to declare.

P249

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR ADULT AND PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive precursor lymphoid neoplasm. Chemotherapy alone does not allow for long-term survival in high risk forms. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) offers a curative therapeutic alternative in these cases. We report the results of this procedure in a series of 56 pts.

Methods: From July 2007 to December 2024, 56 allo-HSCT were performed, including 41 geno-identical, 14 haplo-identical, 1 pheno-identical. At the time of transplant, 28 pts (50%) were in first complete remission (CR1), 26 pts (46, 4%) in second complete remission (CR2), and 2 pts in third CR. The median age of the pts is 20 years (5-56), with 21 pts (37,5%) under 18 years old. The sex-ratio (M/F) is 3. The average time from diagnosis to transplant was 19 months (3-72). Various conditioning regimens, without total body irradiation (TBI), were used, including Busulfan-Cytarabine-Melphalan in 13 pts (23,2%), Busulfan-Cyclophosphamide in 6 pts (10,7%), Busulfan-Cyclophosphamide-Thymoglobulin (5 mg/kg) in 4 pts (7%), and Busulfan-Cyclophosphamide-Etoposide in 19 pts (34%). For haploidentical HSCTs, conditioning regimens included Cytarabine-Busulfan-Cyclophosphamide-Thymoglobulin (10 mg/kg) in 6 pts (10,7%) and Busulfan-Thiotepa-Fludarabine in 8 pts (14,2%). GVHD prophylaxis consisted on association of ciclosporine-methotrexate (HLA-identical sibling), ciclosporine-methotrexate-MMF (Beijing Protocol), ciclosporine-MMF-PTCy (TBF). Peripheral blood stem cells (PBSC) as graft was used in 49 pts (87,5%), bone marrow (BM) graft in 1 pt, and a combination of BM and PBSC in 6 pts (Beijing Protocol). As of June 30, 2025, the minimum follow-up is 8 months, and maximum follow-up 215 months.

Results: Aplasia was observed in all pts with median duration of 16 days (8-45). The median day of neutrophils engraftment was 15 days (10-45). VOD occurred in 3 pts including 1 severe. Acute GVHD occurred in 20 pts (36, 3%) including 6 pts grade IV (30%). Chronic GVHD was seen in 13 pts (33,3%) with extensive form in 10 pts (25,6%). CMV reactivation is noted in 12 pts (21,4%). Relapse was observed in 15 pts (27,7%), after a median time of 3 months (2-18). After a median follow-up of 68 months (8-215), 24 pts are alive (42,8%) in CR and 32 pts (57,2%) are died including 18 (32%) of TRM (early infection: 1, acute GVHD: 7, chronic GVHD: 1, VOD: 1, late infection: 3, others: 5) and 14 pts of relapse. The overall survival (0S) and disease-free survival (DFS) at 18 years are 42,9% and 41,1% respectively. The OS and DFS for patients in the first CR and second CR are 64,3%, 23,1% (p : 0,008); and 60,7%, 23,1% (p :0,007), respectively.

Conclusions: TBI-free Allo-HSCT in high-risk T-ALL allows about half of pts to hope for long-term remission, as shown in our series, although with relatively high rates of TRM and relapse.

Disclosure: Nothing to declare

P250

DURABLE REMISSION AFTER ALLOGENEIC HSCT AND FLT3 INHIBITION IN PEDIATRIC REFRACTORY AML HARBORING A NOVEL FLT3 EXON 14 IN-FRAME INSERTION IDENTIFIED BY NEXT GENERATION SEQUENCING

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Background: Refractory pediatric acute myeloid leukemia (AML) remains a major therapeutic challenge. FLT3 (OMIM #136351) encodes a class III receptor tyrosine kinase on 13q12–q13, related to KIT, FMS, and PDGFR. In AML, activating FLT3 lesions are common—primarily internal tandem duplications (exons 14–15) and tyrosine kinase domain mutations (e.g., D835, I836, Y842, N676, F691). FLT3 variants are traditionally detected by PCR-based assays.

Methods: Targeted next-generation sequencing (NGS) was performed to identify actionable alterations in a child with AML refractory to multiple therapies.

Results: Targeted NGS identified a novel FLT3 exon 14 in-frame insertion, c.1780_1781insGGGTCCCTCCGCCTACCC (NC_000013.11:g.28034138_28034139insGGGTAGGCGGAGGGACCC; NM_004119.3(NP_004110.2): p.Phe594delinsTrpValProProProThrLeu), confirmed by Sanger sequencing, in a 13-year-old girl with refractory AML. She failed multiple chemotherapy regimens but achieved remission with chemotherapy plus sorafenib; relapse occurred after sorafenib discontinuation due to cardiomyopathy. With persistent disease after unsuccessful salvage, she underwent allogeneic HSCT with melphalan 140 mg/m² (day −11), fludarabine 30 mg/m² (days −6 to −3), and fractionated TBI 2 Gy twice daily on days −2 and −1 (total 8 Gy), followed by PBSC infusion. Sorafenib was restarted post-transplant at a reduced dose and continued for two years. She has been in complete remission for 56 months following her hematopoietic stem cell transplantation (HSCT) at the time of this report..

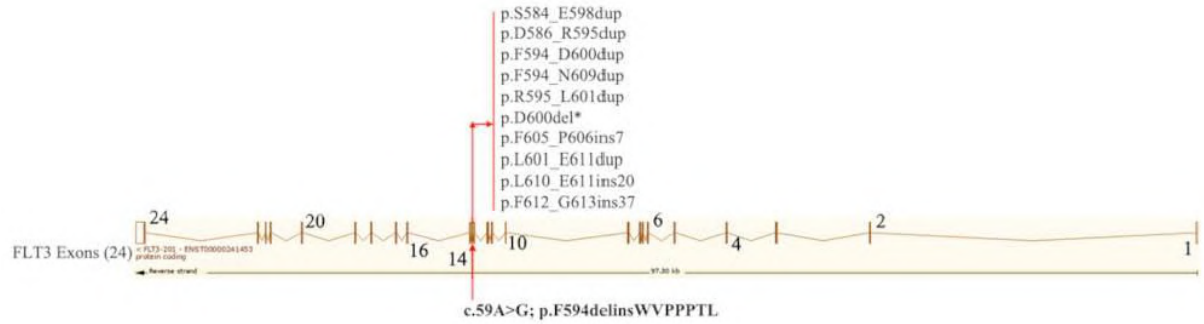

Figure 1: Exon map of FLT3 gene with the novel variant identified in exon 14 and known variants (ITD). Detailed exon map of FLT3 gene in reverse direction with the solid bars representing exons (right to left) and arrows showing the variants at specific exons. The number beside the gene name represents total number of exons in FLT3 gene.

Conclusions: In a child with refractory AML harboring a novel FLT3 exon 14 in-frame insertion, melphalan–fludarabine–TBI (8 Gy) conditioning with allogeneic HSCT, complemented by post-transplant FLT3 inhibition, achieved durable long-term remission, supporting the pathogenicity and therapeutic targetability of this novel mutation.

Clinical Trial Registry: None

Disclosure: No Conflict of interest.

P251

RISKS FACTORS FOR HEMORRHAGIC CYSTITIS IN LEUKEMIA PATIENTS FROM A COLOMBIAN BONE MARROW TRANSPLANTATION UNIT: A RETROSPECTIVE COHORT STUDY

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Background: Hemorrhagic cystitis (HC) is a common complication occurring after allogenic bone marrow transplantation and is associated with important morbidity and costs.

Methods: We retrospectively reviewed clinical records of leukemia patients who had undergone a bone marrow transplantation in our unit between January 1 st 2017 and July 30 th 2025.

Results: One hundred forty three (143) allogenic bone marrow transplants were performed, the most frequent transplant was from haploidentical donor (n=101, 70,6 %) versus allogenic transplant from a related identical sibling (n=42, 29,4%). The median age of patients was 36 years (11-66 years), and most patients were male (n:89, 62,2 %). The most frequent diagnosis was Acute Lymphoblastic Leukemia (n:82, 57,3 %) followed by Acute Myeloid Leukemia (n:45, 31,5 %). Most patients had received 2 or more regimens before proceeding to transplantation (n:103, 71 %). HC occurred in 28 transplants (19,6 %) and was grade 3 or 4 in 23 transplants (16,1 %).
Variables significant associated with HC in univariate analysis were age (Mann Whitney U test, p =0,016), type of transplant (haploidentical vs identical related donor**,** Chi square test p =0.016, RR: 3.75, CI 1.47-9.56), having received a combination of Busulfan at least 6.4 mg/kg and total body irradiation (TBI) dose of 200 or 400cGy as part of the conditioning regimen (Chi square test p < 0.001, relative risk (RR) : 4.8 , CI 1.93-11.9), having had mucositis (Chi square test p < 0.001, RR 4.46, CI 1.63-12.2) and having had Cytomegalovirus reactivation (Chi square test p=0.001, RR: 3.97, CI 1.56-10.1).
Having received a myeloablative (MAC) conditioning regimen was not significant associated with HC compared with a reduced intensity (RIC) or a non-myeloablative (NMA) regimen (Chi square test p=0.252, RR:0.58, CI 0.21-1.54).
HC was not associated with death (Chi square test p=0.675, RR: 1.09, CI 0.72-1.65).
In a multivariable logistic regression analysis having received conditioning with Busulfan and TBI, type of transplant, mucositis and CMV reactivation persisted as significant associated with HC while age was only marginally significant (Odd Ratio p=0,06, CI 1-1.07). This model had a sensibility of 94 % and an area under the curve of 0.847 for predicting HC.

Conclusions: HC is a common complication following allogenic transplant in leukemia patients; haploidentical transplant, mucositis, Busulfan plus TBI conditioning and CMV reactivation were variables significant related with HC occurrence.

Disclosure: we have no conflict of interest, the source of funding are own resources

P252

SAFETY AND EFFICACY OF LIPOSOMAL MITOXANTRONE-INTENSIFIED BUSULFAN-BASED CONDITIONING REGIMEN FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only effective curative method for hematological malignancies. However, some patients experience relapse after undergoing allo-HSCT, and reducing the post-transplant recurrence rate remains a major challenge of transplantation. Conditioning is the first step of allo-HSCT

and plays a significant role in preventing relapse after transplantation. The active ingredient of Liposomal Mitoxantrone (Lipo-MIT) is mitoxantrone, and the encapsulation with liposomes does not alter its inherent mechanism of action, which is expected to reduce toxicity and enhance antitumor effects after being encapsulated in liposomes, making it an ideal choice for modified conditioning regimen. However, its efficacy and safety in the conditioning of allo-HSCT remain uncertain. We conducted this study to evaluate the preliminary efficacy and safety of Lipo-MIT intensified busulfan (Bu)-based conditioning regimens (combined with cyclophosphamide or fludarabine) for allo-HSCT in patients with hematological malignancies.

Methods: A retrospective study was conducted at Xiangya Hospital of Central South University. Patients with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL) or myelodysplastic syndrome (MDS) aged ≥14 years old and underwent allo-HSCT after receiving Lipo-MIT intensified Bu-based conditioning were included. Lipo-MIT was administered at a dose of 30 mg/m²/day for one day.

Results: Data were collected from 28 eligible patients between March 2023 and October 2025, comprising 18 patients with AML, 8 patients with ALL (including 2 with T-ALL and 6 with B-ALL), and 2 patients with MDS. The median age was 41 years (range: 14-62). Prior to transplantation, 16 patients were in first complete remission (CR1) with negative minimal residual disease (MRD-), 5 were in CR1 MRD(+), 1 was in CR2 MRD(+), 2 had non-remission (NR), 3 had relapsed disease, and 1 was in partial remission (PR). Risk stratification: among AML patients, 11 were classified as high risk, 5 as intermediate risk, and 2 as standard risk. Among ALL patients, 7 were standard risk and 1 was high risk. MDS patients were all IPSS high risk.
Two patients died of serious infection before engraftment. Among the remaining patients, the median time to neutrophil engraftment was 13 days (range: 10-17 days), and of platelet engraftment was 13 days (range: 10-20 days). As of November 30, 2025, the median follow-up time was 13.82 months (range: 0.23-29.43 months).
The 12-month cumulative incidences of relapse, non-relapse mortality, disease-free survival, and overall survival were 7.4% (1.2-21.4%), 11.4% (2.7-27.0%), 76.4% (61.3-95.1%), and 88.6% (77.3-100.0%), respectively. By day 100 after allo-HSCT, 10 patients (35.7%) developed acute graft-versus-host disease (aGVHD), all of which were grade I-II. Until the follow-up cutoff date, chronic GVHD (cGVHD) developed in 5 patients (17.9%), including 2 mild cases and 3 moderate/severe cases. A total of 5 patients (17.9%) died after transplantation, with causes of death being relapse (1 case) and infection (4 cases).

Conclusions: It is concluded that Lipo-MIT-enhanced Bu-based conditioning regimens were feasible and effective for allo-HSCT in AML, ALL, or MDS patients. However, the sample size needs to be expanded for further observation and evaluation of long-term survival and recurrence rates.

Disclosure: The authors declare no competing financial interests.

P254

IMPLEMENTING EBMT RISK SCORE AS A PREDICTOR FOR OVERALL SURVIVAL IN PATIENTS WITH ACUTE LEUKEMIA AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT. SINGLE CENTER EXPERIENCE

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Background: Allogeneic hematopoietic stem cell transplant (HSCT) is a standard therapeutic procedure incorporated in the treatment algorithm of patients with acute leukemia. This procedure could be followed with numerous post-transplant complications and sometimes could be challenging to make a good estimation of the treatment benefit. EBMT risk score is a tool that is used in estimating the OS and TRM in patients where allogeneic HSCT is planned by using well defined variables.

Methods: We have analyzed 85 patients with acute leukemia treated with allo HSCT. We have used the well established form of EBMT risk score and its variables defined by Gratwohl et al. 2009 (Age, disease status, interval to HSCT, Donor, Gender of donor-recipient.) In our group of transplanted patients 69 (81%) were diagnosed with AML, while 16 (19%) with ALL. The average age of the patients was 39.5 years, in the AML group the median age was 42 years, while in the ALL group was 28 years. 76% of the patients had higher disease risk profile. 95% of the patients were transplanted in CR-1, while 5% in CR-2. We have calculated EBMT risk score to all of our patients. We grouped them in four groups (EBMT risk score 0/1, EBMT risk score 2, EBMT risk score 3, EBMT risk score >4).

Results: The 24 months overall survival (OS) post-transplant was 62.2 %, for patients with EBMT risk score of 0-2, while those with higher scores (3 and >4) had significantly worse OS of 45.4% (p value=0.05). We have also calculated the disease free survival (DFS) of these patients. The 36 months post-transplant DFS was 35.7% for those with EBMT risk score >4, 29.8% for those with score of 3, 53.3% for those with score 2 and 66.5% for the patients with EBMT risk score of 0-1. We have calculated that the DFS was statistically beter for patients with EBMT risk score of 0,1,2 compared with those with EBMT risk score of 3 and >4 (p=0.0257).

Conclusions: As a conclusion we have noticed that EBMT risk score could be an effective tool in anticipating the risk of allogeneic HSCT of patients with acute leukemia, translated in lower rates of OS and DFS for those patients that had higher EBMT risk score, especially 3 and >4.

Disclosure: No disclosures.

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SUBGROUP ANALYSIS OF THE GREATER CHINA REGION IN THE RANDOMIZED PHASE 3 AGILE STUDY OF IVOSIDENIB+AZACITIDINE VERSUS PLACEBO+AZACITIDINE IN PATIENTS WITH NEWLY DIAGNOSED MIDH AML

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Background: Ivosidenib (IVO) is an oral targeted inhibitor of mutant *IDH1 (mIDH)*. In the AGILE study (NCT03173248) on patients with newly diagnosed *mIDH1* AML, the median overall survival (OS) was 29.3 months for IVO+azacitidine (AZA) compared with 7.9 months for placebo (PBO)+AZA (HR, 0.42; 95% CI, 0.27, 0.65; *P*<0.0001), at a median follow-up of 28.6 months. We conducted an ad-hoc analysis of the AGILE phase 3 study to assess the efficacy and safety of IVO+AZA in newly diagnosed and unfit patients from the Greater China region.

Methods: In the double-blind AGILE study, patients were randomized 1:1 to receive either IVO 500 mg QD plus AZA 75 mg/m² SC or IV for 7 days in 28-day cycles or PBO+AZA. Data from the Greater China region for OS, event-free survival (EFS), blood count recovery, and safety are reported here. EFS was defined as the time from randomization until treatment failure (ie, the patient did not achieve complete response (CR), CR with incomplete hematologic recovery, or morphologic clearance of leukemic cells from the marrow after at least 24 weeks of treatment), relapse from remission, or death from any cause, whichever occurred first.

Results: From 23-Aug-2018 to 07-Jan-2021, 23 Greater China region patients were randomized: 12 to IVO+AZA (mean age 70.0 [6.71] years) and 11 to PBO+AZA (mean age 68.2 [8.89] years). Patients aged ≥75 years in the two arms were 25% and 18.2%, respectively, and male patients were 75% vs 45.5%, respectively. In the IVO+AZA arm, all patients had intermediate or high ELN risk, and one had extramedullary disease; in the PBO+AZA arm, 81.8% had intermediate or high risk. Median treatment duration was 164 days for IVO+AZA and 82 days for PBO+AZA. At a median follow-up of 7.2 months for EFS in the IVO+AZA arm, the median EFS was not reached in the IVO+AZA arm, and was 9.33

months (95% CI, 0.66-NE) in the PBO+AZA arm, the 12 month-EFS rate was 67.5% (IVO+AZA) vs 0 (PBO+AZA). At median follow-up of 22.4 months for OS in the IVO+AZA arm, median OS was 30.6 months (95% CI, 3.7-NE) for IVO+AZA vs 11.2 months (95% CI, 0.9-NE) for PBO+AZA. The CR rate was 50% (95% CI, 21.1%-78.9%) for IVO+AZA vs 27.3% (95% CI, 6.0%-61.0%) for PBO+AZA. Mean platelet count recovered from baseline (55.25 x 10^9/L) by cycle 4 (day 1) and stabilized within the normal range; mean neutrophil counts rapidly increased from baseline (0.652 x 10^9/L) on day 15(4.44 x 10^9/L) and remained above 1.5 x 10^9/L. For adverse events of special interest, no differentiation syndrome was observed in either group. In the IVO+AZA group, 1 case of ≥grade 3 QT interval prolongation occurred, while no ≥grade 3 cases were reported in the PBO+AZA group.

Conclusions: The data indicate that IVO+AZA provides significant therapeutic benefits for patients with newly diagnosed mIDH1 AML in the Greater China region with higher mOS, better hematologic responses, and faster blood count recovery, while maintaining a manageable safety profile vs PBO+AZA.

Clinical Trial Registry: NCT03173248

Disclosure: Nothing to declare

P257

TARGETING FLT3: A REAL-LIFE, SINGLE-CENTER ANALYSIS OF FLT3 INHIBITORS USE IN THE ALLOGENEIC TRANSPLANT SETTING

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Background: FLT3 mutations occur in about 30% of Acute Myeloid Leukemia (AML), conferring adverse prognosis and high relapse rates. Often coexisting with NPM1, RUNX1, and DNMT3A alterations, FLT3-mutated AML is highly heterogeneous. FLT3 inhibitors (FLT3is) improve outcomes across disease phases, including upfront, relapsed/refractory, and maintenance. Our study presents real-life experience with FLT3is in the allo-HSCT setting, assessing clinical efficacy, graft impact, and tolerability in a complex population.

Methods: We retrospectively analyzed 17 adult patients with FLT3-mutated AML who underwent allo-HSCT at our center between 2020-2025 and received FLT3is therapy before and/or after transplant. Based on primary indication and timing, patients were categorized into: 1. Post-transplant maintenance with Sorafenib once in complete remission (CR) (n=10); 2. Gilteritinib as second-line therapy bridging to transplant in refractory/relapsed (R/R) disease (n=3); 3. Post-transplant relapse treatment without prior FLT3is maintenance (n=2); 4. Complex pathways with sequential FLT3is exposure (n=2). Primary endpoints were efficacy, graft outcomes, and toxicity.

Results: Group 1: It demonstrated median OS of 22.5 months (range 10-99) and PFS of 20 months (3-75), with 2/10 patients relapsing during or after maintenance. Among relapsed patients, both were treated with Gilteritinib: one achieved transient response, the other successfully proceeded to second allo-HSCT. Overall, 8/10 are still alive (median follow-up 23 months, range 10-99).
Group 2: Gilteritinib successfully bridged all refractory/relapsed patients to transplant. All three patients maintained durable remissions when Gilteritinib was continued post-transplant, with median OS 44 months (11-53) and PFS 38 months (11-50). All patients are still alive and in CR.
Group 3: These 2 patients treated after post-transplant relapse showed poor outcomes with median OS 16.5 months (14-19) and median PFS 6.5 months (4-9). Neither patient survived.
Group 4: One patient received Azacitidine-Venetoclax-Sorafenib before transplant for R/R AML and continued with Sorafenib as maintenance after transplant. The second one received Azacitidine-Venetoclax-Sorafenib for a relapse one year after transplant. After 5 months, the treatment was shifted to Gilteritinib for a second relapse achieving a third remission. Both are still alive (median follow-up 32 months, range 22-42).
Graft outcomes and tolerability: FLT3is before transplant did not compromise engraftment across all groups, with median neutrophil recovery ranging from day +17 to +29 and platelet recovery from day +17 to +33. Acute GVHD incidence was low to moderate overall (range 20-50% across groups), while chronic GVHD varied from 0-100%. The most common grade 3-4 toxicities were manageable cytopenias requiring dose modifications. One case of myopericarditis occurred in group 4. Infectious complications, predominantly viral reactivations and bacterial infections, occurred in approximately 50% of patients and were manageable with standard therapy.

Characteristic	**Group 1: Sorafenib Maintenance (n=10)**	**Group 2: Gilteritinib Bridge (n=3)**	**Group 3: Post-Tx Relapse (n=2)**	**Group 4: Complex (n=2)**
Demographics				
Age, median (range), yrs	58 (22-66)	52 (31-71)	57 (50-58)	61 (54-60)
Sex, M/F	4/6	2/1	1/1	1/1
Disease characteristics				
NPM1 mutated, n (%)	6 (60%)	3 (100%)	1 (50%)	1 (50%)
Adverse-risk karyotype, n	3	1	1	1
Donor type				
- MUD 10/10	6	2	1	2
- MUD 9/10	2	0	0	0
- Sibling	2	1	0	0
- Haploidentical	0	0	1	0

Conditioning regimen				
Myeloablative	8	3	2	2
Reduced intensity	2	0	0	0
Outcomes				
OS, median (range), months	22.5 (10-99)	44 (11-53)	16.5 (14-19)	32 (22-42)
PFS, median (range), months	20 (3-75)	38 (11-50)	6.5 (4-9)	17 (17-17)
Relapse rate, n (%)	2 (20%)	0 (0%)	2 (100%)	2 (100%)
Alive at last follow-up, n (%)	8 (80%)	3 (100%)	0 (0%)	2 (100%)
GVHD				
Acute GVHD any grade, n	2	1	1	1
Acute GVHD grade ≥2, n	2	1	1	1
Chronic GVHD any grade, n	2	0	2	2
Toxicity				
Grade 3-4 AEs, n	2	2	0	2
Infectious events, n	5	1	0	2

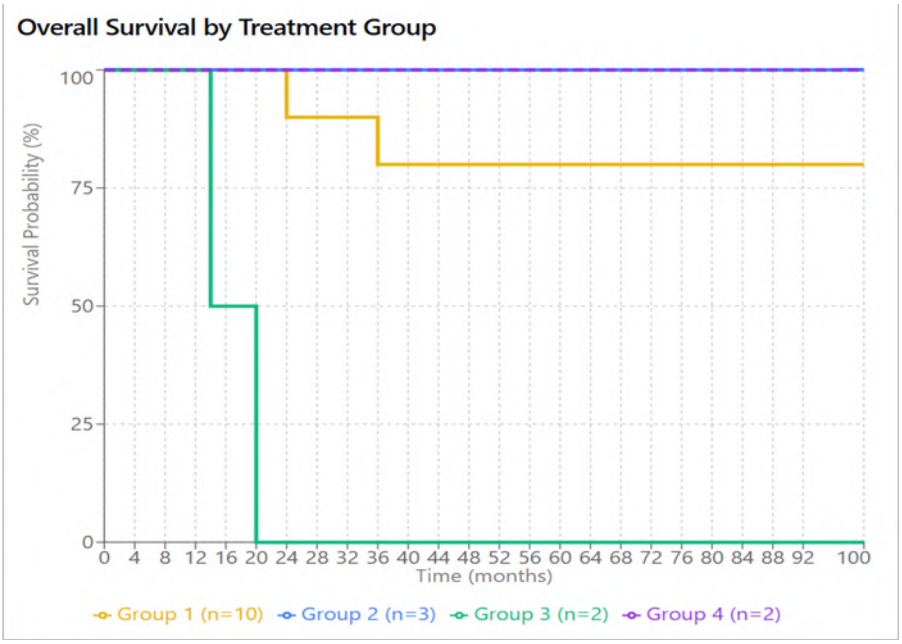

Figure 1. Kaplan-Meier survival curves: Overall Survival by treatment group: Group 1 (Sorafenib maintenance, n=10), Group 2 (Gilteritinib bridge, n=3), Group 3 (post-transplant relapse, n=2), and Group 4 (complex pathways, n=2).

Conclusions: This real-world experience demonstrates safe, effective integration of FLT3is into the allo-HSCT setting. Sorafenib maintenance achieved low relapse rates and high survival, while Gilteritinib successfully bridged refractory patients to transplant with

sustained remissions. Post-transplant relapse without prior FLT3is remains challenging, underscoring the value of early FLT3is use. Importantly, FLT3is did not impair engraftment or significantly increase GVHD. These findings support FLT3is as standard peri-transplant management, although further studies should refine patient selection and dosing.

Disclosure: Nothing to declare.

P258

CLINICAL CASE OF TREATMENT OF CONGENITAL ACUTE MYELOID LEUKEMIA

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Background: Congenital acute myeloid leukemia (AML) is a sporadic aggressive disease diagnosed within the first 28 days of life. Early diagnosis and treatment are crucial, emphasizing the responsibility of clinicians to act promptly, including intensive chemotherapy and, possibly, hematopoietic stem cell transplantation (HSCT). Survival rates remain low, mainly due to treatment-related mortality.

Methods: A patient with refractory congenital acute myeloid leukemia was treated at the Belarusian Research Center for Pediatric Oncology, Hematology, and Immunology. Diagnostic procedures were performed by the Center's clinical, molecular genetic, cytological, and other laboratories.

Results: The patient, a 20 days old boy born using IVF, was hospitalised with hyperleukocytosis and leukemic infiltrates on the skin. Bone marrow (BM) examination revealed hypercellularity, 68% blasts, M5 (FAB). An unbalanced rearrangement of the KMT2A gene was detected. Immunophenotyping: acute monocytic leukemia. Based on the diagnostic results, the final diagnosis was established: congenital acute myeloid leukemia.
Treatment began in the ICU: prophase (DNR, VP), ADE (DNR, VP, ARA-C) with a 1/3 dose reduction. Chemotherapy was stopped on day +6 due to infectious and toxic complications, with an initial response in the form of disappearance of leukemic infiltrates, a decrease in leukocytes, and the absence of blast cells in the peripheral blood. A month later, the myelogram showed 24% blasts, and leukemic infiltrates appeared on the skin. An AI block (ARA-C, IDA) was performed; on day +16 after the block – progression. FLAG+Mit was performed against the background of infectious complications, but it was unsuccessful; further progression was noted.
As a salvage therapy, a Clo+VP+Cy+Venetoclax block was performed with three infusions of allogeneic haploidentical donor NK cells (donor: father). A week after the latest NK cell infusion, the CBC showed WBC $1.4x10^9$/L, and the BM examination showed myelokaryocytes $2x10^9$/L. Over the next few days, the condition worsened - seizures, fever, cytopenia,

mechanical ventilation was started.
On day +40 from the start of Clo+VP+Cy+Venetoclax block, the child was diagnosed with secondary hemophagocytic lymphohistiocytosis with no response after month of therapy (dexamethasone, VP, CSA, intralumbar administration of cytostatics, ruxolitinib). Severe toxicity occurred, and the patient experienced several episodes of sepsis. The patient was diagnosed with left-sided lung mucormycosis. Due to persistent aplasia and failure of prior therapies, a decision was made to perform allogeneic related (haploidentical) HSCT as the definitive salvage option, emphasizing the criteria guiding this choice.
Allogeneic related HLA-mismatched peripheral blood HSCT with CD3αβCD19 depletion was performed (donor: father) after fludarabine, cyclophosphamide, ATG, and Rituximab conditioning. G-CSF stimulation on days +1 to +5. By day +9, WBC recovery was more than $1x10^9$/L, and granulocytes were more than $0.5x10^9$/L. On day +14 – 100% donor chimerism (peripheral blood).
Currently (+18 days after allo-HSCT), despite the restoration of granulocytopoiesis and combined antifungal therapy, the patient shows further progression of mucormycosis with lesions of the lungs, heart, skin, and liver.

Conclusions: Intensive polychemotherapy combined with immunotherapy can effectively induce remission in congenital refractory AML. Recognizing the importance of early intervention, allogeneic HSCT should be considered promptly when profound hematopoietic aplasia occurs.

Disclosure: Nothing to declare.

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REAL-WORLD EXPERIENCE WITH VENETOCLAX, AZACITIDINE, AND SORAFENIB IN RELAPSED/REFRACTORY FLT3-ITD AML: A SINGLE-CENTRE CASE SERIES

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Background: Azacitidine in combination with Venetoclax is increasingly used in acute myeloid leukaemia (AML), including cases with FLT3 mutations, where responses to therapy are often short lived due to rapid emergence of resistance mechanisms. FLT3-ITD and FLT3-TKD mutations are well recognized drivers of treatment failure, particularly under selective pressure from venetoclax-based therapy. Adding Sorafenib, a multikinase inhibitor with FLT3-inhibitory activity, to the Azacitidine and Venetoclax backbone is being explored as a strategy to enhance antileukemic activity and potentially improve outcomes in patients with FLT3-mutated relapsed or refractory AML.

Methods: We conducted a retrospective single-centre study at the Hospital of the Lithuanian University of Health Sciences Kaunas Clinics. Adult patients with relapsed or refractory FLT3-mutated AML treated with Azacitidine 75 mg/m², Venetoclax 400 mg once daily, and Sorafenib 400 mg BID between February and November 2025 were included. Key clinical, molecular, treatment, transplant, and survival data were extracted from medical records. Overall survival (OS) was defined from treatment initiation to death or last follow-up, and progression-free survival (PFS) from treatment initiation to relapse, progression, or death. Survival outcomes were analysed using the Kaplan-Meier method. Due to the low number of events, no comparative statistical testing was performed.

Results: A total of 4 patients with relapsed/refractory FLT3-ITD mutated AML were treated with the triplet combination of Venetoclax, Azacitidine, and Sorafenib. The cohort included patients with median age of 42 (range 21 – 75) with an ECOG performance status of (0 – 2), all of whom had received at least one prior line of therapy, and three had previously undergone allogeneic transplantation. The overall response rate (CR/CRi) was 100%, as all four patients achieved remission after the first treatment cycle. Among the three patients who had previously undergone allogeneic transplantation, all were successfully bridged to a second allo-HSCT following remission. One patient later experienced disease progression and subsequently died during the follow-up, while the remaining three remained alive and progression free at last contact. Median OS and PFS were not reached, with a median follow-up of 225 days (range 90 – 270 days). Estimated 6-month OS and PFS were both 100%, and the estimated 12-month OS and PFS were both 67%, demonstrating notable durability of disease control. Due to the very low number of events, statistical comparisons were not feasible. These findings highlight the activity of Venetoclax – Azacitidine combined with Sorafenib in heavily pretreated FLT3-ITD AML, including patients undergoing a second HSCT.

Conclusions: The combination of Venetoclax, Azacitidine, and Sorafenib demonstrated promising activity in heavily pretreated relapsed/refractory FLT3-ITD AML, with encouraging PFS and OS despite substantial prior therapy and high-risk disease biology. Although limited by small sample size and low event rates, these real-world findings provide a strong rationale for prospective evaluation of this triplet approach, including its integration into pre- and post-transplant therapeutic strategies. Larger multicentre studies are warranted to validate these early signals of efficacy.

Disclosure: Nothing to disclose.

Aplastic Anaemia

OS20-02

CSMD1 IS THE MOST COMMONLY MUTATED GENE IN APLASTIC ANEMIA PATIENTS TREATED WITH IMMUNO-SUPPRESSIVE THERAPY: EVIDENCE OF *IN VIVO* PRUNING SELECTION OF HEMATOPOIETIC CELLS

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Background: In our recent EBMT RACE phase-3, randomized, prospective trial (NCT02099747) investigating Immuno-Suppressive Treatment (IST) with/without Eltrombopag in Aplastic Anemia (AA), the CUB and Sushi Multiple Domains 1 (*CSMD1*) gene emerged as a commonly mutated gene. Here we investigate *CSMD1* mutations, looking for the frequency of mutations, their association with clinical variables and other somatic mutations, the dynamics of the mutated clones across the 2-year study period and a in silico structural analysis predicting functional consequences.

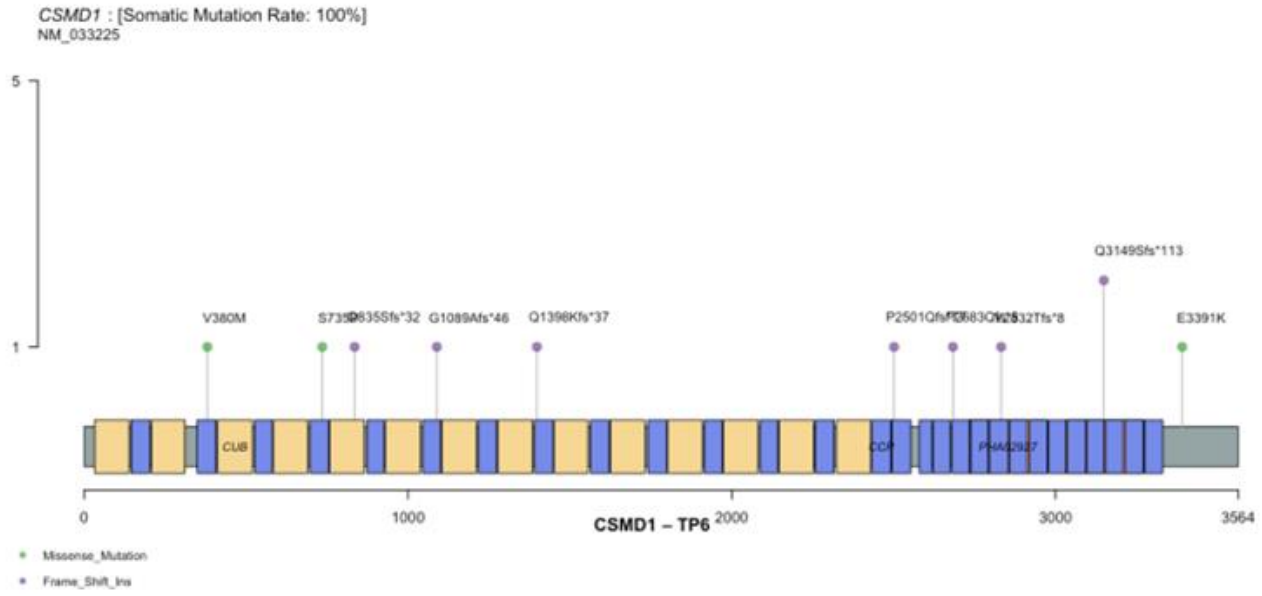
Methods: Somatic mutations analysis using the HaloHS 31 gene panel was performed at King's College London on 170, 150 and 103 patient bone marrow samples collected at baseline, 6 and 24 months after randomization, respectively. Appropriate variant caller protocols were utilized to identify candidate variants, using an arbitrary Variant Allele Frequency (VAF) threshold of 0.2% to define mutations.

Results: No *CSMD1* mutation was found at baseline (n=170). Then mutations in the *CSMD1* gene were found in 4/150 (2.7%) patients at TP6 and in 16/103 (15.5%) patients at TP24. Since many patients harbored more than one *CSMD1*-mutated clone, the mean number of *CSMD*1 mutations per patients was 0.07 and 0.47 at 6 and 24 months after IST, respectively. The presence of *CSMD1* mutations was not associated with age, disease severity at baseline, presence of somatic mutations in myeloid-cancer genes at baseline, treatment arm and hematological response. The VAF of *CSMD*1-mutated clones was usually very low, with 9/11 (81.8%) and 42/48 (87.5%) clones remaining below a 5% VAF at TP6 and TP24. Mutations in *CSMD1* were often associated with mutations in *ETV6, PHF6, PPM1D, PTPN11, RAD21* and *STAG2* genes.
The CSMD1 protein consists of 14 CUB domains alternated with 14 Sushi domains, followed by further 15 Sushi domains, and then a transmembrane domain and an intracytoplasmic tail at the C-terminus. Looking structurally at the specific mutations, no hotspot mutation was

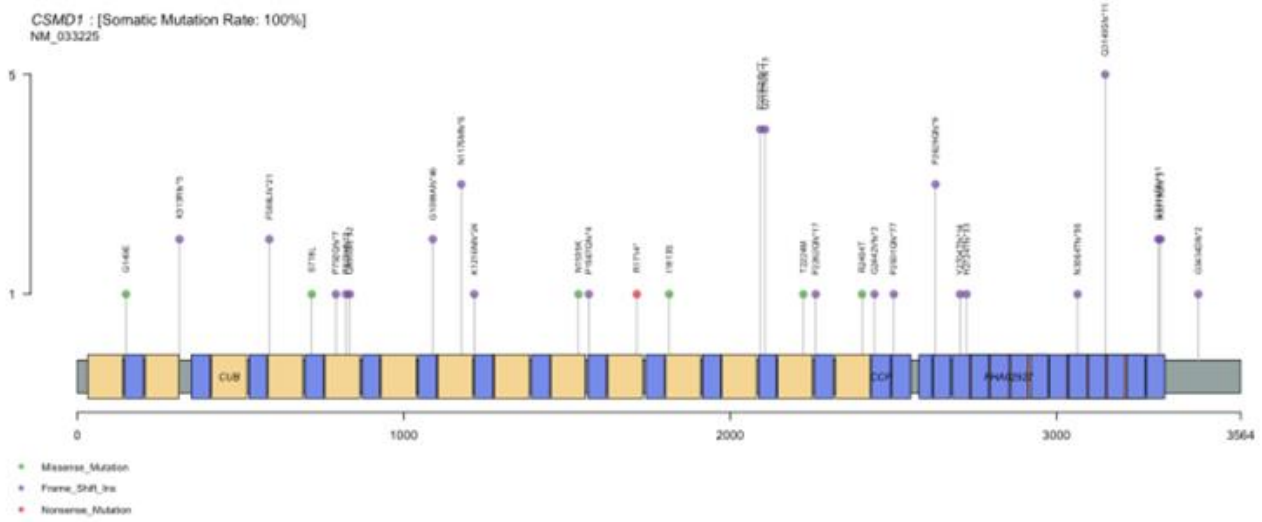
found; lollipop plots (**Figure 1**) illustrate that the majority of mutations are frameshift mutations located in the first half of the protein (thus not affecting the signal-transduction domain of its intracytoplasmic tail). Rather they result in truncated versions of the protein lacking its transmembrane domain, retaining their complement-regulatory activity associated with the multiple Sushi domains of its N-terminus. We hypothesize that the secretion of truncated CSMD1 proteins retaining complement regulator activity may result in an autocrine effect which may spare mutated hematopoietic cells from a complement-mediated damage triggered by immune-complexes associated with anti-thymocyte globulin treatment. Thus, major structural changes associated with *CSMD1* mutations would result in a gain-of-function phenotype accounting for negative clonal selection.

The Lollipop Plots for CSMD1

TP6



TP24



Conclusions: *CSMD1* is the most commonly mutated gene in AA patients after 2 years from IST, even more than *PIGA*), strongly suggesting a non-random mechanism of selections for the mutated HSC/HPC. Although *CSMD1* is also known as a tumor-suppressor gene, in the context of AA clones *CSMD1* mutations seems to rather represent an example of in vivo "*pruning selection*", with selected clones developing a transient survival advantage emerging at the time of treatment with anti-thymocyte globulin and subsequent hematological recovery.

Clinical Trial Registry: EBMT RACE trial (NCT02099747)

Disclosure: None

OS20-04

EXPANDING DONOR OPTIONS: RETROSPECTIVE REVIEW OF PRACTICE AND OUTCOMES FOR MISMATCHED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN PAEDIATRIC ACQUIRED SEVERE APLASTIC ANAEMIA (SAA)

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Background: In the absence of a fully matched donor, upfront mismatched donor transplantation as an initial strategy rather than immunosuppressive therapy in paediatric SAA needs to be evaluated.

Methods: Retrospective data were collected on HSCTs performed for paediatric patients (< 16 years) with idiopathic/acquired SAA from 1st January 2017 to 31st March 2025 across England and Ireland. Patients with inherited bone marrow failure syndromes were excluded.

Mismatched transplants were defined as single-allele mismatches by high-resolution typing of HLA-A, -B, -C, -DRB1, and -DQB1.

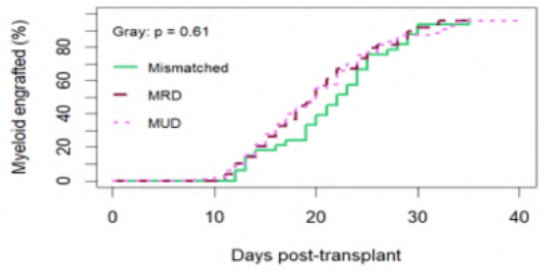
Results: 201 patients underwent HSCT for SAA, of whom 159 (79%) received HSCT from matched donors (56 related (MRD), 103 unrelated (MUD)), while 33 (16%) received HSCT from mismatched donors (4 related (MMRD), 29 unrelated (MMUD)). 9 (5%) were from haploidentical donors and excluded from this analysis. The two mismatched groups were combined due to the low number of MMRD HSCTs.
Median age at transplant was 9 years, with no significant differences between groups ($p = 0.8$). Median follow-up time was 36 months (IQR 17-57). No significant differences were observed in median engraftment time, cumulative incidence of engraftment at day 30 (Figure 1), or incidence of graft failure, acute graft-versus-host disease (aGVHD), or veno-occlusive disease (VOD) between MRD, MUD, and mismatched donor cohorts (Table 1). No difference in overall survival was observed in the three groups (Figure 1c, $p=0.2$). The mismatched cohort had a significantly longer time to HSCT from diagnosis (median 8 months, $p < 0.001$), a considerably higher pre-transplant serum ferritin level (median 2328, IQR 1370-3282, $p < 0.001$), and a higher proportion of major ABO incompatibility (36%, $p = 0.03$). There was a significantly higher incidence of viral reactivation/infection requiring treatment in the mismatched cohort. Eight treatment-related deaths were reported overall (MRD: 1, MUD: 4, mismatched: 3).
Within the mismatched cohort, donors were HLA-A mismatched in 55% (18/33), HLA-C mismatched in 24% (8/33), HLA-DQB1 mismatched in 9% (3/33), and HLA-B and HLA-DR mismatched in 6% (2/33). 66.7% (22/33) of patients had prior immunosuppressive therapy (IST), 18.1% (6/33) developed side effects from ciclosporin use before HSCT (mainly renal impairment), and 15.2% (5/33) were receiving chelation at the time of HSCT (MUD 0/103, MRD 1/56). 36.4% (12/33) of patients in the mismatched group developed invasive fungal or serious bacterial infections before HSCT. In line with the national recommendation, the conditioning regimen used in 94% (32/33) consisted of Fludarabine 150mg/m2, cyclophosphamide 120 mg/kg and Alemtuzumab 0.9/1.0 mg/kg, with 81.8% (27/33) of patients receiving a combination of a calcineurin inhibitor and MMF for GVHD prophylaxis. 78.8% (26/33) received a single fraction of total-body irradiation (TBI), with 65% (17/26) receiving 3 Gy and the remainder (9/26) receiving 2 Gy. The incidence of thrombotic microangiopathy (TA-TMA) in the mismatched cohort was 12% (4/33, 3 deaths).

Table 1: Outcomes of HSCT for SAA

	Total (n=192)	Matched Related Donor (MRD) (n=56)	Matched Unrelated Donor (MUD) (n=103)	Mismatched Donor (MMD) (n=33)	P value
Median age at HSCT in years (IQR)	9.2 (5.5-12)	9.7 (7.2-13.7)	9.2 (5.6-11.9)	8.7 (6.2-12.2)	0.2
Median time to transplant from	4.1 (3-6)	3.0 (3-5)	4.0 (3-5)	8.0 (5-11)	<0.001

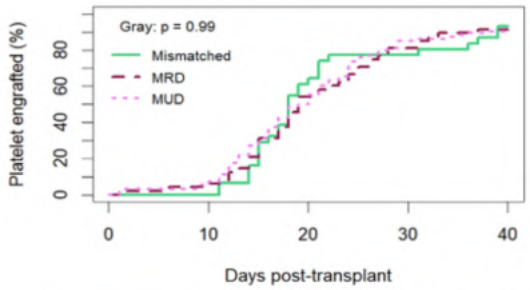
diagnosis in months (IQR)					
Median serum ferritin (mcg/L) (IQR)	953 (318-1786)	755 (300-1234)	768 (288-1441)	2328 (1370-3282)	<0.001
ABO Major/bidirectional	41 (21%)	7 (13%)	22 (21%)	12 (36%)	0.03
Median time to myeloid engraftment in days (IQR)	20 (15-24)	19 (14.5-24.0)	19 (15-24)	22 (19-25)	0.2
Median time to platelet engraftment	19 (15-26)	19 (15-26)	18 (14-24)	18 (15-21.5)	0.8
3-year overall survival (OS)	94 (91-98)	96 (91-100)	96 (92-100)	88 (77-100)	0.2
Cumulative incidence (CI) of myeloid engraftment at day 30(%) (Figure 1a)	91 (86-95)	93 (85-100)	88 (82-94)	94 (85-100)	0.6
CI of plat engraftment at day 30 (%) (Figure 1b)	84 (79-89)	83 (73-93)	86 (79-93)	77 (62-93)	0.99
Primary graft failure	6 (3%)	0 (0)	4 (4%)	1 (3%)	0.3
Secondary graft failure	6 (3%)	0 (0)	4 (4%)	1 (3%)	0.3
aGVHD (≥ grade 2 skin)	18 (9%)	4 (7%)	8 (8%)	6 (19%)	0.2
Veno-occlusive disease (VOD)	1 (0.5%)	1 (2%)	0 (0)	0 (0)	-
Viral reactivation/infection post-HSCT needing treatment	76 (40%)	15 (27%)	41 (40%)	20 (61%)	0.007
Treatment-related mortality	8 (4.1%)	1 (1.7%)	4 (3.8%)	3 (9%) (All deaths related to TA-TMA)	0.2

Figure 1a: Cumulative Incidence of Myeloid Engraftment



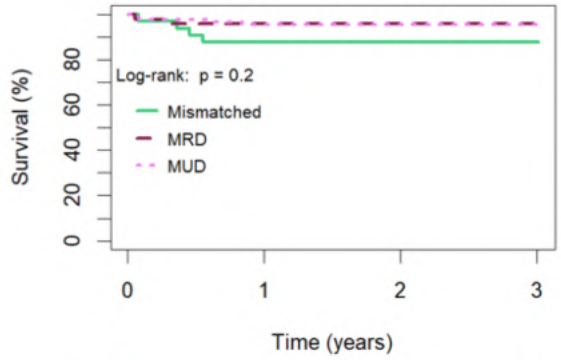
Mismatched	33	33	33	33	27	22	14	7	1	0	0
MRD	49	49	49	47	36	26	16	9	3	0	0
MUD	97	97	97	91	70	51	29	16	9	2	2

Figure 1b: Cumulative Incidence of Platelet Engraftment



Mismatched	31	31	31	29	22	12	7	7	5	5	1
MRD	48	47	46	44	33	22	17	10	6	4	3
MUD	96	93	93	85	66	48	33	19	9	7	5

Figure 1C: Overall survival



Mismatched	33	28	22	14
MRD	50	44	33	24
MUD	98	84	65	50

Conclusions: Mismatched HSCTs, primarily using MMUD, have outcomes comparable to those of fully matched donors. TA-TMA led to treatment-related mortality in this cohort. Prospective evaluation is needed to confirm optimal placement of mismatched donors within the therapeutic algorithm for paediatric SAA.

Disclosure: Nothing to declare.

B320

PREVIOUS ANTITHYMOCYTE-BASED IMMUNOSUPPRESSIVE THERAPY INCREASED THE RISK OF VIRUS REACTIVATION IN HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION FOR SEVERE APLASTIC ANEMIA

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Background: Allogeneic hematopoietic stem cell transplantation (HCT) and immunosuppressive therapy (IST) are two effective treatments for patients with severe aplastic anemia (SAA). For patients fail to respond to or relapse after IST, salvage haploidentical HCT is widely adopted. Several studies have demonstrated that salvage HCT leads to inferior outcomes compared to upfront HCT. This is partially attributed to impaired organ function, increased infections, and heavier transfusion burdens due to the delayed HCT. However, donors for haplo-HCT can be easily available in a really short time. To date, comparisons between upfront haplo-HCT and salvage haplo-HCT are limited.

Methods: Patients undergoing upfront (n = 437) or salvage haplo-HCT (n = 97, defined as haplo-HCT conducted after failure or relapse to ATG-based IST) between 2008 and 2022 at PKUPH were reviewed. To minimize the impact of selection bias and confounding factors, we performed a propensity score matching (PSM) analysis. Patient age, sex, and conditioning regimen were included in the propensity score model (1:1). Finally, 94 patients in each cohort (upfront cohort and salvage cohort) were included for analysis. No letermovir prophylaxis for cytomegavirus (CMV) reactivation was used during the study period.

Results: Overall, upfront or salvage haplo-HCT resulted in comparable survival. The 5-year overall survival (OS) were 89.71% and 85.33% in the upfront and salvage cohorts (P = 0.534), respectively. And the 5-year graft-versus-host disease/failure-free survival (GFFS) were 74.50% and 72.14% in the corresponding cohorts (P = 0.832), respectively. Multivariable analysis again confirmed that neither upfront nor salvage haplo-HCT was associated with worse survival outcomes. Moreover, the two cohorts had similar cumulative incidences of 28-day neutrophil engraftment, 100-day platelet engraftment, 100-day acute graft-versus-host disease (aGVHD), and 5-year chronic graft-versus-host disease (cGVHD). However, the cumulative incidence of 100-day virus reactivation was significantly higher in the salvage cohort, which is 82.31%, compared to the upfront cohort (70.04%). In particular, salvage haplo-HCT was associated with higher risks of Epstein-Barr virus (EBV) reactivation (19.36% vs. 11.20%, P = 0.042) and adenovirus (ADV) reactivation (11.44% vs 5.34%, P = 0.037). Multivariable analysis showed that salvage haplo-HCT was a risk factor for virus reactivation (hazard ritio [HR] = 1.471, P = 0.024). In subgroup analysis, we found that among patients who did not respond to IST, salvage haplo-HCT conducted 12 months after IST showed slightly inferior OS (78.50%, P = 0.072) and GFFS (66.83%, P = 0.109) compared to the upfront cohort, while salvage haplo-HCT conducted within 12 months resulted in comparable OS (89.86%, P = 0.842) and GFFS (75.33%, P = 0.956).

Conclusions: In conclusion, salvage haplo-HCT led to an increased risk of virus reactivation, especially EBV and ADV reactivation. However, comparable survival rates to those of upfront haplo-HCT were achieved. Preliminary subgroup analysis suggested that, for patients who failed to respond to IST, timely consideration of haplo-HCT could be beneficial.

Disclosure: Nothing to declare.

B321

IMPROVING THE OUTCOME OF STEM CELL TRANSPLANTATION IN PATIENTS WITH SEVERE APLASTIC ANEMIA

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Background: Stem cell transplantation (SCT) from an HLA–matched sibling donor (MSD) is considered the standard of care for younger patients with severe aplastic anemia (SAA). Due to the use of high resolution HLA matching, specifically designed conditioning regimens, together with improved supportive care and GvHD prophylaxis, SCT can be a therapeutic option also for patients lacking a suitable MSD . With changing donor types and transplant platforms, the question is whether the outcome has improved over time.

Methods: We retrospectively analyzed 194 patients with SAA undergoing SCT in two transplants Unit (IRCCS Policlinico San Martino IST, Genova and Fondazione Policlinico Universitario A.Gemelli, IRCCS, Rome.
Patients' characteristics are summarized in Table 1, according to three different time periods: 1976-1990 (n=69); 1991-2010 (n=81), 2011-2024 (n=44).
The median age (range) was respectively: 19 (5-48); 25 (9-60); 28 (13-70). The median interval from diagnosis to transplant was respectively: 85 days range 22-442) vs 149 (26-1482) vs 208 (28-1401).
There was a significant change in donor type (P<0.00001), with an increased use of alternative donor and increased use of fludarabine based conditioning regimen (P<0.00001).
GvHD prophylaxis also changed, from the initial use of methotrexate, then the association of methotrexate and cyclosporine and the more recent use of PTCY (P<0.00001).
Bone marrow was the predominantly stem cell source in all period, with a small number of patients receiving peripheral blood grafts in the more recent period. (P<0.00001).

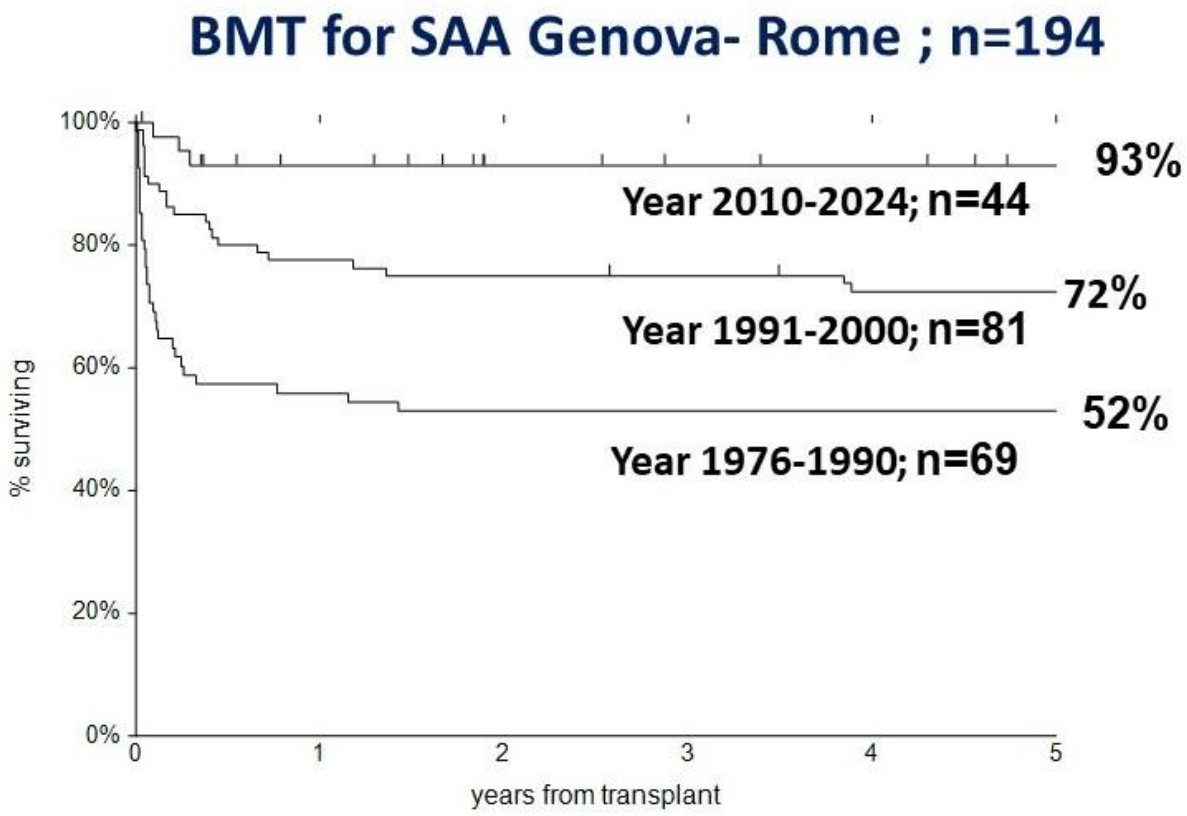
Table 1

PATIENTS (n=194)	1976-1990	1991-2010	2011-2024	
Number	69	81	44	
Gender (M/F)	45/24	48/33	25/19	P=0.5
Pt Age.median (range) years	19 (5-48)	25 (9-60)	28 (13-70)	P<0.001
Time diagnosis -SCT dd	85 (22-442)	149 (26-1482)	208 (28-1401)	P<0.001
Donor type Sibling	96 %	69%	39%	P<0.00001

Mismatched RD MUD Mismatched MUD CBU	3% 0 0 1%	9% 16% 5% 1%	14% 34% 11% 2%	
Conditioning regimen Cyclophosphamide Cyclophosphamide+TBI Fludarabine based	 73% 27% 0%	 54% 0% 46%	 20% 80%	P<0.00001
GvHD Prophylaxis Metotrexate Cyclosporine CSA+MTX PTCY	 21% 67% 12% 0	 0% 18% 82% 0	 0% 13% 68% 19%	P<0.00001
Stem cell source BM PBSC CBU	 100% 0% 0%	 98% 1% 1%	 75% 24% 1%	p<0,0001
GvHD II-IV GvHD III-IV cGvHD mod-severe	36 (52%) 18 (26%) 11 (16%)	14 (17%) 3 (4%) 10 (19%)	15 (34%) 2 (4%) 5 (12%)	p=0.004 P=0.0009 P=0.5

Results: Acute GvHD grade II-IV in the three time periods developed in 52%, 17% and 34% of patients (p=0.004); acute GvHD grade III-IV developed in 26%, 14% and 4% of patients (p=0.0009). Moderate-severe chronic GvHD developed in 16%, 19%, 12% (p=0.5). The 5 years actuarial survival was respectively: 52%, 72%, and 93% in the three time periods (P<0.0001) Figure 1.
Major causes of death were infections (14%, 12%, 2%) and GvHD (12%, 6%, 2%) (p<0.001).

Figure 1: 5 years actuarial survival according to time period



Conclusions: Improved outcome with time is clearly shown in this study, with a 5 year overall survival exceeding 90% beyond year 2010. This is seen despite older patients age (P<0.001), increased use of alternative donors (p<0.00001) and a longer interval between diagnosis and (P<0.001). Reduced GvHD and infectious complication appear to be the 2 crucial finding, possibly due to different conditioning regimens, better GvHD prophylaxis, and better supportive care.

Disclosure: No conflicts of interest to declare.

B323

ASSESSMENT OF DONOR ENGRAFTMENT KINETICS FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR TREATMENT OF SEVERE APLASTIC ANEMIA

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Background: Nonmyeloablative conditioning has decreased mortality after hematopoietic cell transplantation (HCT) for severe aplastic anemia (SAA) but management of mixed chimerism remains a challenge. Better understanding of its prevalence, kinetics, and clinical impact is needed.

Methods: We studied 140 pediatric patients who underwent HCT for SAA (Image 1).

Patient & HCT Characteristics	N=140
Age, median (range), years	11 (1-21)
Male/Female, n	74/66
Transplant Year	2005-2019
Stem Cell Source, n (%)	
Bone Marrow	128 (91.4)
Peripheral Blood	12 (8.6)
Donor Match, n (%)	
Matched Related (MRD)	68 (48.6)
Matched Unrelated (MURD)	43 (30.7)
Mismatched Related (MMRD)	11 (7.9)
Mismatched Unrelated (MMURD)	18 (12.9)
Conditioning Regimen, n (%)	
CY/ATG	69 (49.2)
FLU/CY/ATG	6 (4.3)
FLU/CY/TBI (2Gy)/ATG	23 (16.4)
FLU/Alem/CY	25 (17.9)
FLU/CY/TBI (4Gy), post-HCT CY	4 (2.9)
Other	13 (9.3)
Serotherapy, n (%)	
Yes	134 (95.7)
No	6 (4.3)
GVHD Prophylaxis, n (%)	
CSP	7 (5)
CSP+MTX	72 (51.4)
CSP+MMF	4 (2.9)
Tacrolimus	15 (10.7)
MTX+Tacrolimus	26 (18.6)
Other	16 (11.4)
Post-HCT Outcomes, n (%)	
Primary Graft Rejection (≤D+100)	3 (2.1)
Secondary Graft Rejection (>D+100)	2 (1.4)
Acute Grade II-IV GVHD	39 (27.9)
Extensive Chronic GVHD	12 (8.6)
Death	9 (6.4)

Abbreviations: ATG, Anti-Thymocyte Globulin; CSP, Cyclosporine; CY, Cyclophosphamide; D, Day; GVHD, Graft Versus Host Disease; HCT, Hematopoietic Cell Transplantation; FLU, Fludarabine; MMF, Mycophenolate; MTX, Methotrexate; n, Number; PTCY, Post-Transplant Cyclophosphamide; TBI, Total Body Irradiation

Rejection, GVHD, death, and when available, longitudinal lymphoid (CD3) and myeloid (CD33/CD15) chimerism, defined by full (>95%), high-level (50-95%), low-level mixed (5-49%), and rejection (<5%) were recorded. The association of chimerism with age, donor type, stem cell source, donor/recipient sex, TNC cell dose, and TBI-vs non-TBI-conditioning was assessed using generalized estimating equations, and the association with GVHD was assessed using Cox regression with chimerism level modeled as a time-varying covariate. Donor type and use of TBI were combined given the strong correlation between use of TBI and match status in the related population.

Results: Of the 140 patients, 4 experienced rejection (n=3) or death (n=1) prior to D+100. Among patients with lineage-specific chimerism data available, 92/96 (96%) and 81/87 (93%) had full donor myeloid engraftment at D+100- and 1-year post-HCT respectively. In contrast, 32/104 (31%) and 45/93 (48%) had full donor lymphoid engraftment at D+100 and 1-year post-HCT. Of patients with mixed (5-95%) donor lymphoid chimerism at D+100 (n=72) who had 1-year data available (n=54), 18 (33%) achieved full donor by 1-year (Table 1). One patient developed secondary graft rejection.

Table 1: Day +100 and Subsequent Chimerism Status at 1-year, 2-years, and 3-5 years post-HCT

	Day +100 Donor Chimerism*	Years post-HCT	Total (n)	Full Donor n, (%)	High-Level Mixed n, (%)	Low-Level Mixed n, (%)	Secondary Graft Rejection** n, (%)
Lymphoid (CD3)	Full Donor (n=32)	1	25	24 (96)	1 (4)	0	0
		2	15	15 (100)	0	0	0
		3-5	15	15 (100)	0	0	0
	High-Level Mixed (n=47)	1	39	17 (43.6)	22 (56.4)	0	0
		2	19	10 (52.6)	9 (47.4)	0	0
		3-5	17	12 (70.6)	5 (29.4)	0	0
	Low-Level Mixed (n=25)	1	15	1 (6.7)	13 (86.7)	0	1 (6.7)
		2	13	1 (7.7)	12 (92.3)	0	0
		3-5	9	3 (33.3)	6 (66.7)	0	0
Myeloid (CD33/CD15)	Full Donor (n=92)	1	73	70 (95.9)	2 (2.7)	0	1 (1.4)
		2	43	41 (95.3)	2 (4.7)	0	0
		3-5	38	38 (100)	0	0	0

	High-Level Mixed (n=4)	1	1	1 (100)	0	0	0
		2	1	1 (100)	0	0	0

*Of the 140 patients, 104 had lymphoid chimerism and 96 had myeloid chimerism data available at Day +100
**One patient with secondary graft rejection (CD3<5% and CD33<5%) did not have chimerism data available at Day +100 and is therefore excluded.
Abbreviations: HCT, Hematopoietic Cell Transplantation; n, Number
Definitions: Full Donor (>95%); High-Level Mixed (50-95%); Low-Level Mixed (5-49%); Rejection (<5%)

In univariate analysis, recipients of mismatched related donor (MMRD) grafts had 15.2% (95% CI, 7.4 to 23.0%) higher absolute mean lymphoid chimerism than MRD-graft recipients. Likewise, recipients of TBI-conditioning and mismatched unrelated donor (MMURD) or MURD-grafts had 25.4% (95% CI, 19.8 to 31.0%) and 0.4% (95% CI, -11.3 to 12.1%) higher absolute mean lymphoid chimerism respectively than the MRD group. Absolute mean lymphoid chimerism was 3.4% (95% CI, -10.9 to 17.7%) higher for the non-TBI MMURD group and 3.1% (95% CI, -6.6 to 12.8%) higher for the non-TBI MURD than the MRD group. Males transplanted from female donors had an absolute mean myeloid chimerism 5.1% (95% CI, -10.4 to 0.3%) lower than other patient/donor sex combinations. No other factors showed meaningful associations with myeloid or lymphoid chimerism.
The impact of chimerism on survival was not examined due to the limited number of deaths. As donor lymphoid chimerism increased 10%, the risk of acute and chronic GVHD increased 20% (95% CI, 0-45%) and 44% (95% CI, 11-88%), respectively. There was little evidence of an association between myeloid chimerism level and GVHD.

Conclusions: HCT after nonmyeloablative conditioning results in excellent myeloid engraftment in patients with SAA. Donor lymphoid chimerism is initially often mixed and increases thereafter. Our observation of just one secondary graft rejection suggests that early mixed lymphoid chimerism is not necessarily associated with subsequent graft rejection, particularly when full donor myeloid engraftment coexists. Future studies should examine donor engraftment kinetics in other non-malignant diseases where there may be greater barriers to engraftment.

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B324

QUALITY OF LIFE IN PATIENTS WITH APLASTIC ANEMIA IMPROVES DURING IMMUNOSUPPRESSIVE THERAPY AND CORRELATES WITH DEPTH OF RESPONSE: ANALYSIS OF THE SAAWP EBMT RACE STUDY

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Background: The combination of anti-thymocyte globulin (ATG) and cyclosporin (CsA) is an effective immunosuppressive treatment (IST) for aplastic anemia (AA). Recent research has focused on improving response rates and (event-free) survival through the addition of eltrombopag. However, both the disease and its treatment can affect quality of life (QoL), while data on QoL of AA patients remain scarce. In a recent study among AA patients treated with IST, patients with partial recovery of blood values (PR) experienced lower QoL than patients with complete recovery (CR). The EBMT RACE study, a multicenter randomized clinical trial comparing first-line ATG and CsA with or without eltrombopag, incorporated self-reported QoL assessments. No significant differences in QoL were found between treatment arms. This post-hoc analysis evaluated the effect of treatment response on QoL of AA patients treated within the RACE trial.

Methods: Patients were invited to complete the EORTC-QLQ-c30 questionnaire at baseline, 6, 12 and 24 months. The questionnaire consists of 30 items evaluating QoL. Subscales include overall Global Health status/QoL (GH), 5 functional scales and 9 symptom scales. We used the separate subscales (range: 0-100) to assess different aspects of QoL from baseline until a year after starting treatment. QoL scores of patients with PR and CR were compared using unpaired t-tests. Paired t-tests were used to analyze changes in QoL over time.

Results: 192 patients were included in the analysis, of whom 166 completed the questionnaire at baseline. At 6 and 12 months, 151 and 136 questionnaires were completed respectively. GH scores were lowest of all subscales at baseline (mean 52). After one year, GH scores had increased 18 points, with the biggest improvement (12 points) taking place in the first 6 months. Other subscales improved significantly as well, with pronounced changes in role functioning and social functioning (both increasing 22 points).

After 6 months, 45 patients in PR and 38 in CR completed the questionnaire, whereas after one year the number of completed questionnaires was 28 in the PR group and 53 in the CR group. Patients in CR scored 7 points higher on GH than patients in PR at both time points (p=0.053). Most outspoken between-group differences were seen in Fatigue, with differences of 9 (p=0.055) and 6 points (p=0.167) at 6 and 12 months respectively. Patients improving from PR at 6 months to CR at 12 months (n=17) had better QoL scores as well: a 7 point increase in GH (p=0.051) and a remarkable increase in social functioning of 12 points (p=0.045), whereas here fatigue improved only 2 points. Patients who remained in PR between 6 and 12 months (n=28) showed no clear change in QoL.

Conclusions: Overall, QoL of AA patients receiving ATG-based IST improved during the first year of treatment. There was a discernable trend that patients reaching PR as best response experienced lower QoL than patients in CR. Moreover, improving from PR to CR was associated with increasing GH and Social functioning scores. This study shows that QoL of AA-patients benefits from aiming for the best hematological response after IST.

Disclosure: Nothing to declare.

B325

QUALITATIVE ASSESSMENT OF PREDICTORS OF RESPONSE TO IMMUNOSUPPRESSIVE THERAPY IN APLASTIC ANAEMIA: A SYSTEMATIC LITERATURE REVIEW

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Background: Recommended aplastic anaemia (AA) treatments include haematopoietic stem cell transplantation or immunosuppressive therapy (IST) with horse antithymocyte globulin and cyclosporine (double therapy) ± eltrombopag (triple therapy). Predictive evidence of individual response to IST remains limited. This systematic literature review (SLR) was conducted to combine all findings to date and expand AA knowledge, with the primary objective of evaluating predictors of response to IST.

Methods: A PRISMA-compliant SLR was undertaken on PubMed and Embase published records (1980-2025). Studies reporting double or triple IST response rates and AA predictors (any disease severity/age) were included in this qualitative analysis. Dual screening with independent adjudication was performed, supported by a validated AI screening tool (Robot Screener, [Nested Knowledge; NK]) as a second reviewer. Data pertaining to the primary objective were extracted using AI and reviewed by humans. Information on predictors was categorised as clinical, immunologic, or genetic/molecular for the qualitative analysis.

Results: The search identified 2,335 candidate studies. Overall, 89 studies reported IST use for AA, of which 45 reported on predictors of response to IST in AA (**Figure 1**). Across the 45 studies (6,254 patients of all ages), key clinical predictors of improved response rate in AA included younger age and lower-severity AA (definitions varied by study), although children with non-severe AA (per Camitta criteria) had higher relapse rates.
Additional predictors were higher baseline absolute reticulocyte count (ARC), absolute lymphocyte count (ALC), and absolute neutrophil count (ANC), in effect, residual haematopoiesis. The presence of PNH clones was the most conflicting predictor. Some studies associate PNH positivity with improved overall survival (N=259, retrospective), others examined its association with complete response, showing mixed results—ranging from negative predictive value (N=98, paediatric RCT) to positive associations (N=125, prospective, all ages), with some studies finding no clinical outcome association (N=51, observational, adults). Furthermore, immunologic markers such as lower CD57+ CD8+ naïve T-cells, higher CD8+ memory stem T-cells, and higher natural killer cell proportions at baseline and post-treatment were associated with higher response rates.
Genetic and molecular findings were heterogeneous: interferon gamma (IFNG) and transforming growth factor beta 1 (TGFB1) polymorphism presence correlated with improved response. Longer telomere length showed improved response in one study (N=92, prospective, all ages), but no association with response in other studies (N=51, observational, adults and N=314, retrospective, paediatric). Sustained elevated thrombopoietin correlated with non-response. Delayed initiation of IST (>6 months from diagnosis) and older age (≥40 years) were associated with worse complete response.

Conclusions: Qualitative analysis of articles in this SLR showed age, haematopoietic reserve, and immune cell profiles as potential predictors of response to IST in patients with AA. Poorer response with delayed therapy underscores the importance of timely diagnosis and treatment. Despite study design variability and limited statistical power, these findings support the potential for personalised AA treatment, enabling clinicians to better assess the likelihood of haematologic recovery with IST. Further analyses are planned to elucidate details regarding the identified predictors, investigate conflicting findings and explore additional predictors.

Clinical Trial Registry: NA

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Stephanie MacLeod, Meryem Bektas, and Shahnaz Khan are currently employed by RTI Health Solutions.
Raj Gokani and Barbara Możejko-Pastewka are currently employed by Pfizer.
Kevin Kallmes is currently employed by Nested Knowledge and possesses stock in the following private companies: Nested Knowledge, Superior Medical Experts, Piraeus Medical.
Alicia Rovo is currently employed by Bern University Hospital, has provided consultancy for Novartis, Alexion Pharmaceuticals, Swedish Orphan Biovitrum GmbH, OrPha Swiss GmbH, GlaxoSmith Kline AG, Pfizer, Pierre Fabre Pharma AG, Vertex Pharmaceuticals GmbH, has

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AB T-CELL DEPLETION VERSUS PTCY IN UNRELATED DONOR HSCT FOR PEDIATRIC PATIENTS WITH APLASTIC ANEMIA

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Background: Hematopoietic stem cell transplantation (HSCT) from a fully matched unrelated donor (MUD) is an established treatment for patients with severe aplastic anemia (SAA) who do not respond to ATG and CsA therapy. To improve key outcomes, we used two platforms of GVHD prevention: αβ T-cell depletion (2012-2022) and post-transplant cyclophosphamide (PTCy) (2022-2025). This study presents a comparative retrospective analysis of these approaches.

Methods: The analyses included 61 patients with SAA, who received their first allogeneic HSCT from MUD using TCRαβ depletion (αβ-depletion group – G-αβ), n=47 and PTCy (PTCy group – G-PTCy), n=14 as the primary method for GVHD prevention from May 2022 to February 2025.
The main characteristics of the group are presented in Table 1.

Table 1. Clinical Characteristics of Patients

N=61	TCR αβ group, n=47	PtCy group, n=14	p

Date of HSCT	November 2012 - February 2022	March 2022 - July 2025	
Age (range)	12.4 (3-22.7), 21f/26m	7.4 (3.1-14.2), 4f/10m	0.003
gender	21 females and 26 males	4 females and 10 males	0.3
IST courses before HSCT	1 course - 3 2 courses - 44	1 course - 3 2 courses - 11	0.1
PNH+ vs -	5	0	
Refractory Relapse	36 10	11 3	0.9
Median time to HSCT	1.2 (0.5-11.8)	1.4 (0.8-3.5)	0.9
CMV serology D+/R+ D+/R- D-/R+ D-/R-	 29 6 10 2	 13 1 0 0	
Serotherapy ATG (rabbit) ATG (horse)	 20 27	 14 0	
Condition regimen TAI 4-6Gr cyclophosphamide 100mg/kg fludarabine 150mg/kg thiotepa 10mg/kg rituximab at 200mg/m^2	 47 47 47 12 35	 14 14 14 0 3	

GVHD prophylaxis	tacrolimus until day 180	CsA until day 365 MMF until day 60 PTCy on days +3, +4, 100mg/kg total dose	
Graft source	PBSC	BM	
CD34 (*10^6/kg)	7.15 (2.76-13.2)	6.7 (1.7-12.1)	
TCRαβ (*10^3/kg)	23 (1.1-184)	NA	
CD3 (*10^6/kg)	19.61 (7.27-66.5)	73.35 (17.6-748.2)	

Results: Primary engraftment was achieved in 45 patients in G-αβ and 13 in G-PTCy. Cumulative incidence (CI) of engraftment was 0.96 (95% CI 0.9–1) in G-αβ and 0.93 (95% CI 0.8-1) in G-PTCy with the medians for white blood cells (WBC) 14 (7-24) days in G-αβ and 21(15-26) days in G-PTCy, p=0.003; for platelets 12 (9-18) in G-αβ and 18 (11-24) days, p=0.001.
Secondary graft failure was reported in 8 cases at a median of 72 (18-194) days in G-αβ, CI 0.15 (95% 0.08-0.3) and in 1 patient in 66 days CI 0.07(95% CI 0.01-0.54), p=0.4. 3 patients in G-αβ and 1 patient in G-PTCy were successfully retransplanted.
Prolonged stable mixed chimerism in T-cell compartment was detected in G-αβ, but not in the G-PTCy.
Ten patients died in G-αβ and one in G-PTCy. In G-αβ five patients died of various complications with donor-type hematopoiesis, one patient died after graft failure while awaiting salvage HSCT, and in 4 cases lethal complications developed after the second HSCT. In G-PTCy one patient died from complications following primary graft failure after two consecutive HSCTs.
CI of aGVHD grade II-IV was 0.15 (95% 0.08-0.3) and 0.29 (95% 0.12-0.65) in G-αβ and G-PTCy, respectively, p=0.2. No cases of grade III-IV aGVHD were registered. CI of cGVHD was 0.11 (95% 0.05-0.25) and 0.33 (95% 0.15-0.74) in G-αβ and G-PTCy, respectively, p=0.06. EFS was 72% (95% 60-85) and 86% (95% 67-100) in G-αβ and in G-PTCy, respectively, p= 0.4. OS was 79% (95% 67-90) in G-αβ and 92% (95% 78-100) in G-PTCy, p=0.3 (fig.1). GVHD–Free, Relapse-Free Survival (GRFS) was 72% (95% 60-85) in G-αβ and 79% (95% 57-100) in G-PTCy, p=0.3 (fig.1). A median follow-up was 10.5 (3.7-13.2) years in G-αβ and 1.7 (0.8-3.6) in G-PTCy years.

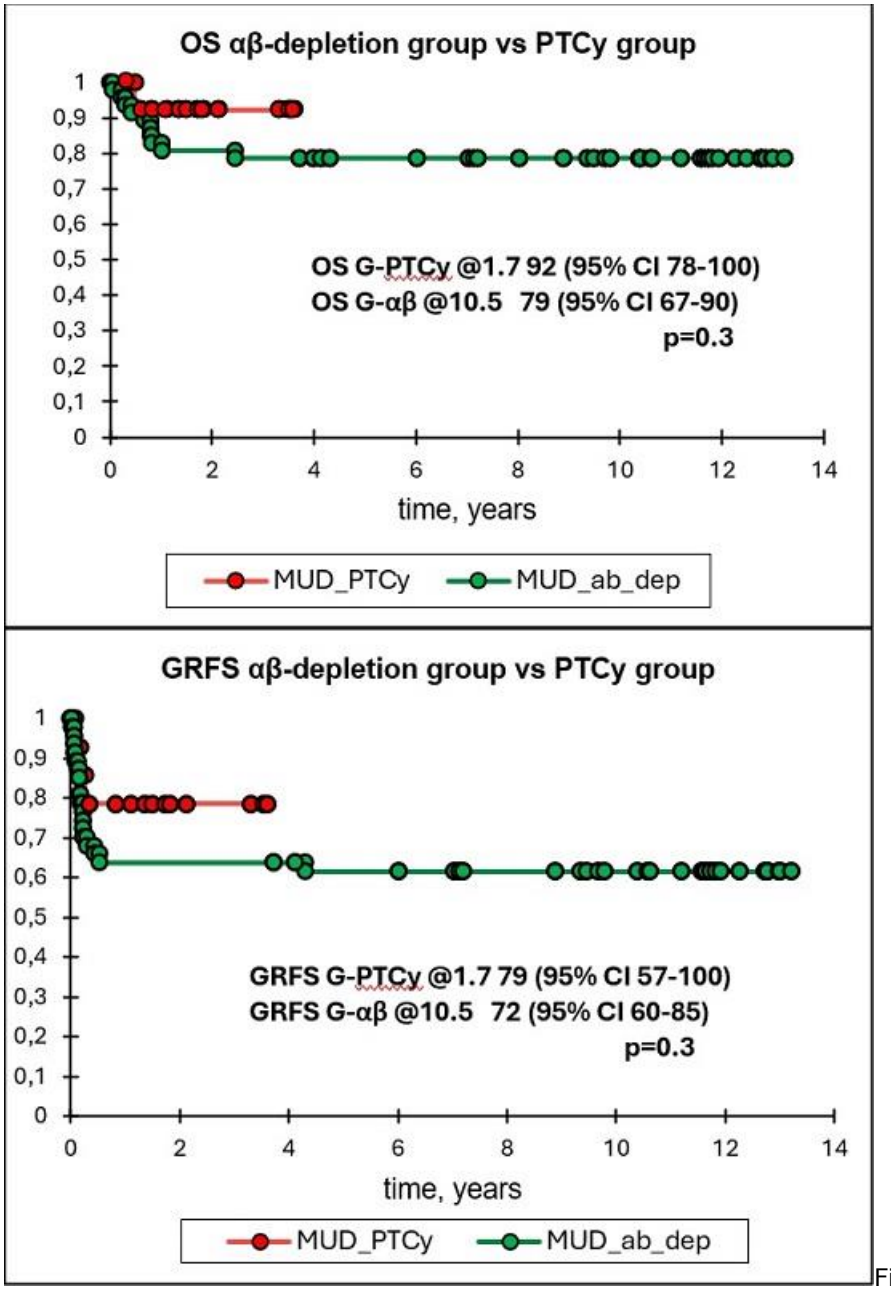

Fig.1 OS and GRFS for G-αβ and G-PTCy after MUD HSCT in pediatric patients with AA

Conclusions: PTCy and αβ T-cell depletion provided comparable engraftment and survival outcomes in unrelated donor HSCT for SAA. The PTCy group showed lower rejection rates but a higher incidence of chronic GVHD. Overall, PTCy appears to be an effective alternative GVHD prophylaxis, warranting further evaluation in larger cohorts.

Disclosure: Nothing to declare.

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EXCELLENT OUTCOMES AFTER HAPLOIDENTICAL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE IN CHILDREN WITH ACQUIRED SEVERE APLASTIC ANEMIA SUPPORT EARLY TRANSPLANTATION

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Background:

Severe aplastic anemia (SAA) in children and adolescents is a life-threatening condition with distinct therapeutic challenges. Immunosuppressive therapy (IST) is commonly used in patients lacking a matched sibling donor but is associated with lower response rates and higher risks of relapse and clonal evolution in pediatric patients. Matched unrelated donor transplantation represents an alternative but often requires prolonged donor searches, delaying definitive treatment and increasing transfusion burden and complication risk. Haploidentical HCT has emerged as a widely accessible alternative, allowing earlier access to curative therapy. We conducted a multicenter retrospective study evaluating the safety and efficacy of haploidentical HCT performed both upfront and after prior IST in pediatric patients with acquired SAA.

Methods:

This retrospective, longitudinal, non-randomized observational study included 60 pediatric patients with SAA transplanted at three HCT centers from 2012 to 2025. Clinical data were obtained from institutional databases and medical records, and statistical analyses were performed using EZR. All patients underwent haploidentical HCT with reduced-intensity conditioning. Most patients received low-dose cyclophosphamide (29–50 mg/kg), fludarabine (150 mg/m²), and total-body irradiation (200–400 cGy); three patients transplanted with peripheral blood received an alternative busulfan-based regimen. Antithymocyte globulin (ATG) was administered to 27 patients (45%), with total doses ranging from 3.3 to 6.4 mg/kg. Graft-versus-host disease (GVHD) prophylaxis consisted of post-transplant cyclophosphamide, mycophenolate mofetil, and cyclosporine.

Gender, n (%)	Female 28 (46.7%) Male 32 (53.3%)
Age at HCT, median (range)	9.9 years (2.9-17 years)
Previous immunosuppression for ≥3 months, n (%)	Yes 30 (50%) No 30 (50%)

Stem cell source, n (%)	Bone Marrow 56 (93.3%) Peripheral Blood 4 (6.7%)
Donor, n (%)	Father 38 (63.3%) Mother 9 (15%) Sibling 12 (20%) Other 1 (1.7%)
Donor age, median (range)	32.5 years (10-55 years)
Cytomegalovirus status for donor/recipient, n (%)	Negative/negative 0 (0%) Positive/negative 4 (6.7%) Positive/positive 56 (93.3%)
ABO compatibility, n (%)	Compatible 39 (65%) Minor incompatibility 10 (16.7%) Major incompatibility 11 (18.3%)
DSA status, n (%)	Positive 0 (0%) Negative 60 (100%)
Conditioning regimen, n (%)	Cyclophosphamide-based (93.3%) Busulfan-based 4 (6.7%)
ATG	Yes 27 (45%) No 33 (55%)
TBI dosis, n (%)	No 3 (5%) 200 cGy 14 (23.3%) 300 cGy 1 (1.7%) 400 cGy 42 (70%)
TNC (x108/kg), median (range)	5.6 (2.6-10.9)
CD34 (x106/kg), median (range)	4.5 (1.2-15)
Follow-up, median (range)	992.5 days (83-4619 days)

Results:

Primary graft failure occurred in 4 patients (6.7%) and secondary graft failure in 2 (3.3%), with a 1-year cumulative incidence of 10.0% (95% CI, 4.0–19.2). All patients with primary graft failure underwent rescue transplantation, and 4 of 6 patients with graft failure are alive.

No significant differences in graft failure were observed between TBI doses (200 vs. 400 cGy;p=0.59) or ATG use (p=1).

The 100-day cumulative incidence of grade II–IV acute GVHD was 15.0% (95% CI,7.3–25.2). The 2-year cumulative incidence of chronic GVHD of any grade was 6.8% (95% CI,2.1–15.1). Neither TBI dose nor ATG use was associated with differences in acute or chronic GVHD incidence.

The 100-day cumulative incidence of cytomegalovirus reactivation was 65.0% (95% CI,51.3–75.7), with a median onset at 40.5 days. Hemorrhagic cystitis occurred in 13.3% of patients (95%CI,6.2–23.3).

Five patients died, mainly due to infection (n=4) and graft failure–related complications, including one cytomegalovirus-related death. The 1-year event-free survival was 85.0%(95% CI,73.2–91.9).

The 1- and 2-year overall survival (OS) was 91.7%(95% CI,81.1–96.4). Notably, patients aged ≤12 years showed superior 2-year OS compared with those >12 years (97.9%vs.66.7%, p=0.00041).

Patients transplanted after 2020 showed higher 2-year OS than earlier transplants (95.0%vs. 85.0%), although this difference was not statistically significant (p=0.174). No other evaluated variables were significantly associated with overall survival.

Two-year overall survival did not differ between patients with and without prior IST (90.0%vs. 93.3%,p=0.61), nor did graft failure rates.

Conclusions: Haploidentical HCT is safe and effective in pediatric SAA, achieving excellent survival with low toxicity, particularly in children younger than 12 years, regardless of prior immunosuppressive therapy, serotherapy use, or TBI dose. These results strongly support

haploidentical transplantation as an early curative strategy.

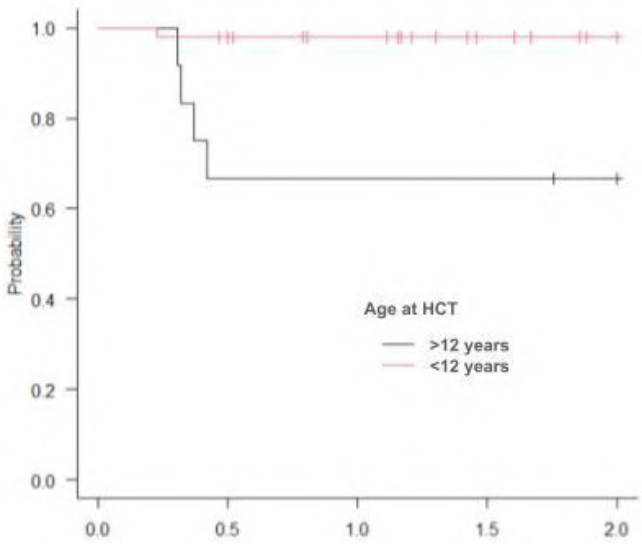

Figure 1. Overall survival according to age at transplantation. Patients aged ≤12 years showed significantly superior OS compared with those >12 years (97.9% vs. 66.7%, $p = 0.00041$).

Disclosure: Nothing to declare.

B328

AN EPIGENOME-WIDE ASSOCIATION (EWAS) STUDY IN FANCONI ANEMIA AND APLASTIC ANEMIA

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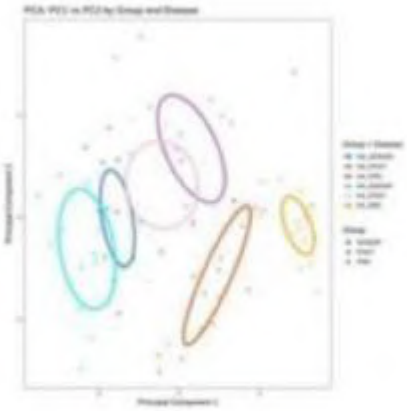
Background: The epigenetic landscape of Fanconi anemia (FA) and Aplastic Anemia (AA), and its evolution after Hematopoietic Cell Transplantation (HCT), remains poorly characterized.

Methods: We aimed to characterize disease-specific and shared DNA methylation (DNAm) patterns and to evaluate post-HCT epigenetic changes in donor-derived hematopoietic cells. We conducted an epigenome-wide association study (EWAS) using peripheral blood

mononuclear cells collected from 15 FA and 15 AA trios (PRE-HCT, POST-HCT and DONORS). Genome-wide DNAm was assessed with the Illumina Methylation Screening Array.

Results: Comparative EWAS identified distinct and shared epigenetic alterations (Table 1). Further, we tested the applicability of the FA episignature previously described [1], confirming its ability to distinguish FA patients from AA patients and donors. Notably, FA POST-HCT DNAm profiles appeared intermediate between PRE-HCT and DONOR, indicating a partial reversion of the signature toward the pre-transplant state (Figure 1).



FA PRE vs AA PRE	HLA-DPB1 promoter hypomethylation and gene body hypermethylation in AA vs FA
FA PRE vs FA DONOR	Significant hypermethylation in the gene bodies of *MILRET7BHG*, *XRCC3*, *PRDM16*, and *VARS1* in FA PRE vs DONOR
FA PRE vs FA POST	The promoter of *PPCDC* is hypermethylated and the gene body of *NFIX* is hypomethylated in FA PRE vs FA POST
FA POST vs DONOR	No significant differences in *MILRET7BHG* methylation comparing FA DONOR vs FA POST POST samples displayed intermediate methylation at *XRCC3*, *PRDM16*, and *VARS1** In *PPCDC* and *NFIX* loci, normalization of methylation pattern POST HCT, maintaining the DONOR pattern*

Conclusions: We identify a disease-specific HLA-DPB1 signature in AA and coordinated DNAm changes in FA involving XRCC3, PRDM16, VARS1, and MIRLET7BHG, which may contribute to disease pathophysiology. Critically, the post-HCT epigenetic shift in donor cells suggests a persistent influence of the patient's environment on engrafted hematopoietic system, with potential implications for long-term outcomes.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

B329

HIGH CD34⁺ CELL DOSE SIGNIFICANTLY REDUCES EBV REACTIVATION AND IMPROVES SURVIVAL IN APLASTIC ANEMIA PATIENTS UNDERGOING UCBT

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Background: Umbilical cord blood transplantation (UCBT) is effective for hematologic disorders, and recommended CD34⁺ cell doses have been established for malignant diseases. However, optimal CD34⁺ dosing for UCBT in aplastic anemia (AA) remains undefined. This study aimed to determine the appropriate CD34⁺ infusion dose for AA patients undergoing ATG-based UCBT.

Methods: We retrospectively analyzed 63 pediatric AA patients who received ATG-based UCBT at Hebei Yanda Lu Daopei Hospital and Beijing Lu Daopei Hospital from March 2013 to April 2024. The optimal infused CD34⁺ cell-dose threshold for predicting 180-day EBV viremia was determined using Fine-Gray competing-risk modeling with death as a competing event. Patients were then stratified into low-(≤0.16×10⁶/kg) and high-(> 0.16×10⁶/kg)CD34⁺ groups based on this cutoff. Clinical outcomes including 180-day EBV viremia, overall survival (OS), and GVHD-free/Failure-free survival (GFFS) were evaluated by univariable and multivariable analyses. Immune reconstitution was compared between groups by assessing serial lymphocyte-subset recovery.

Results: Patient Characteristics: Among 63 patients, 29 were male and 34 female, with a median age of 5 years (range, 1–16). Conditioning was predominantly BU/CY/FLU/ATG (98.4%). ATG formulations included Rabbit Anti-human T Lymphocyte Immunoglobulin (ATLG) (14.3%) and Rabbit Anti-human Thymocyte Immunoglobulin (rATG) (85.7%). Median cell doses were: MNC 0.61, CD3⁺ 0.06 and CD14⁺ 0.07 (×10⁸/kg),CD34⁺ 0.203(×10⁶/kg) . Neutrophil and platelet engraftment rates were 95.2% and 88.9%, with median times of 16 and 29 days, respectively.
Optimal CD34⁺ cell-dose threshold for predicting outcomes: The optimal CD34⁺ cell-dose threshold for predicting 180-day EBV viremia was identified as 0.16 × 10⁶/kg. CD34⁺high group had a significantly lower 180-day EBV viremia incidence compared with CD34⁺low group (7.89% [95% CI, 2.66–23.39] vs. 28.63% [95% CI, 15.29–53.61]; *P* = 0.024) (Figure 1A). The 5-year OS was higher in the CD34⁺high group (89.0%, 95% CI 78.9–99.2) vs. CD34⁺low group (75.6%, 95% CI 58.5–92.6), though the difference did not reach statistical significance (log-rank *P* = 0.126) (Figure 1B). A similar trend was observed for 5-year GFFS (Figure 1C).
Multivariable Fine-Gray competing-risk model results: Multivariable Fine-Gray competing risk model were constructed by entering the following covariates: ATG dose, HLA match, CD34⁺ ,

CD3⁺, CD4⁺ and CD8⁺ (Table 1). The infused CD34⁺ cell dose emerged as the strongest independent predictor of day-180 EBV viremia. CD34⁺high dose markedly reduced EBV risk (HR 0.05; 95% CI 0.00–0.82; P=0.035). A similar protective trend was observed for CMV viremia. ATG dose and infused CD3⁺, CD4⁺, and CD8⁺ cell counts did not demonstrate independent associations.
Immune reconstitution after UCBT: Immune reconstitution profiles were broadly comparable between groups (all P>0.05), with a modest advantage in CD4⁺T cells recovery among patients receiving high CD34⁺ cells (Figure 2).

Conclusions: Infused CD34⁺ dose >0.16×10⁶/kg emerged as the strongest independent predictor of reduced early EBV reactivation and showed favorable trends in long-term survival in pediatric AA undergoing UCBT. This data-driven cutoff remained robust in multivariable analyses and was accompanied by a modest advantage in late CD4⁺ immune recovery.

Disclosure: There's no Conflict of Interest to declare.

B330

A SYSTEMATIC REVIEW OF REAL-WORLD EVIDENCE ON THERAPIES FOR MODERATE APLASTIC ANAEMIA

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Background: Moderate aplastic anaemia (mAA) is clinically heterogeneous with substantial variation in its definitions, and no universally accepted guidelines or therapies. Treatment choices depend on blood counts, transfusion dependency or other significant symptoms and include supportive care, monotherapy (cyclosporine [CSA], tacrolimus, daclizumab, thrombopoietin receptor agonists [TPO-RA], androgens), double or triple therapy, (combining horse or rabbit anti-thymocyte globulin [hATG or rATG], CSA/tacrolimus, and eltrombopag [EPAG]/TPO-RA or androgens), and/or haematopoietic stem-cell transplantation (HSCT). Comprehensive documentation of the treatment landscape and impact is limited. To inform evidence-based decision-making, we conducted a systematic literature review (SLR) of therapeutic outcomes in mAA.

Methods: This artificial intelligence (AI)-assisted review followed a prespecified protocol. Study searches for any mAA therapy (adults and/or children) were conducted in Embase and PubMed/Medline (January 1980–November 2025). This SLR was assisted by validated human-in-the-loop AI review tools, with expert oversight over AI throughout. All searches, screening, extraction, and quality-control workflows were performed using AI and experts as independently adjudicated dual screeners and expert-curated extractions. Eligible study designs included randomised controlled trials (RCTs), observational, and non-randomised interventional studies; case reports were excluded. Key outcomes were overall survival (OS) and response rate (ORR).

Results: Of 2,539 unique records screened, 65 studies (5 RCT [n=374], 5 non-RCT single-arm [n=1,100], 14 prospective cohort [n=974], and 41 other observational [n=2,679]) reporting on patients with mAA were included. Studies spanned diverse eras (most reported in 2020-2025 [n=32]) and geographies (most reported in Asia [n=47]) with substantial heterogeneity in populations treated and outcomes reported. 'Non-severe' AA was reported in 43 and 'moderate' in 22 studies; Camitta criteria were mentioned in four studies, and Seattle criteria in one. Eleven studies closely matched the Camitta definition and 14 the Seattle criteria; 13 studies provided no definition.
OS was 83.9% for supportive care; for monotherapies it was: 84.3% for CSA; 98.0% for tacrolimus; 95.0% for daclizumab; 93.5% for EPAG; 72.7% for androgens. OS in double therapies was 94.3% for eATG+CSA; 86.0% for rATG+CSA; 93.3% for unspecified ATG+CSA; 94.4% for CSA+TPO-RA; 93.5% for CSA+androgens; and OS was 81.7% for HSCT. OS was not reported for triple therapy (**Table 1**).
ORR for monotherapies was: 48.5% for CSA; 38.6% for tacrolimus; 42.6% for daclizumab; 53.1% for EPAG; 42.6% for androgens. Among double therapies, ORR was 60.1% for eATG+CSA; 64.6% for rATG+CSA; 64.3% for unspecified ATG+CSA; 69.4% for CSA+TPO-RA; 41.7% for CSA+androgens. ORR for HSCT was 79.3%, and 100% in all 5 patients treated with triple therapy (ATG+CSA+EPAG; **Table 1**).
OS across the therapies was generally consistent but ORR seemed to vary widely. Outcome reporting by severity was highly variable.

Table 1. Overall Survival (OS) and Overall Response Rate (ORR) by Intervention Category for Moderate Aplastic Anaemia

Intervention Category	OS, n/N (%)	ORR, n/N (%)	Follow-up period (months)
Supportive Care	78/93 (83.9%)	--	3-278
CSA monotherapy	166/197 (84.3%)	242/499 (48.5%)	1-278
Tacrolimus monotherapy	99/101 (98.0%)	39/101 (38.6%)	14-36
Daclizumab monotherapy	57/60 (95.0%)	26/61 (42.6%)	1-278
EPAG monotherapy	43/46 (93.5%)	113/213 (53.1%)	1-278
Androgens monotherapy	40/55 (72.7%)	26/61 (42.6%)	1-174

eATG+CSA	216/229 (94.3%)	86/143 (60.1%)	1-221
rATG+CSA	86/100 (86.0%)	64/99 (64.6%)	1-166
Unspecified ATG+CSA	140/150 (93.3%)	171/266 (64.3%)	1-278
CSA/Tacrolimus+TPO-RA (including EPAG)	51/54 (94.4%)	109/157 (69.4%)	6-278
CSA+androgens	419/448 (93.5%)	10/24 (41.7%)	9-132
Triple therapy (ATG+CSA+EPAG)	--	5/5 (100.0%)	14-104
HSCT	49/60 (81.7%)	23/29 (79.3%)	1-166

Conclusions: Across heterogenous studies, OS and ORR have been documented for monotherapies, double, and triple therapies; HSCT was only reported in small, heterogeneous cohorts. Due to varied timepoints, missing data, and cohort selection, there was insufficient homogenous data for quantitative analysis. This SLR demonstrates a clear need for uniform definition of mAA and for comparative, prospective studies to enable the comparison of therapeutic effectiveness and to develop sufficient treatment algorithms.

Clinical Trial Registry: NA

Disclosure: **Disclosures of Conflicts of Interest:**
Britta Hoechsmann is a member of an advisory board for Pfizer and an advisory board for Novartis and got support for conducting a clinical trial by Novartis. ***Marc Bierings*** is a member of an advisory board for Pfizer. ***Frank R. Ernst, Raj Gokani and Barbara Możejko-Pastewka*** are currently employed by Pfizer and may own stock or stock options. ***Morag Griffin*** is a member of an advisory board for Pfizer, and Novartis; and has received lecture fees from Pfizer and Novartis. ***Kevin Kallmes*** is currently employed by Nested Knowledge, possesses stock in the following private companies: Nested Knowledge, Superior Medical Experts, Piraeus Medical. ***Stephanie MacLeod*** is currently employed by RTI Health Solutions. ***Sujith Samarasinghe*** is a member of an advisory board for Pfizer. ***Carlo Dufour*** is a member of an advisory board for Pfizer and a profit clinical trial advisory board for Novartis.
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B331

HAPLOIDENTICAL VS MATCHED UNRELATED DONOR TRANSPLANTATION IN SEVERE APLASTIC ANEMIA: A SINGLE-CENTER COHORT

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Background: In severe aplastic anemia (SAA), matched unrelated donors (MUD) are standard alternatives for allogeneic hematopoietic cell transplantation (HCT) when a matched sibling donor is unavailable. Recent data demonstrate excellent outcomes with haploidentical (Haplo) HCT using the BMT CTN 1502 protocol (DeZern et al., *Lancet Haematol*, 2022). Given the rapid identification and availability of Haplo donors, comparative evaluation of Haplo versus MUD HCT in SAA is warranted.

Methods: We conducted a retrospective study of consecutive patients with SAA who underwent HCT from either a haploidentical (Haplo) or matched unrelated donor (MUD) between March 2011 and March 2025. All Haplo recipients received a BMT CTN 1502–based protocol with post-transplant cyclophosphamide (PTCy). Among MUD recipients, 17 received fludarabine (Flu), cyclophosphamide (Cy), and total body irradiation (TBI) 2 cGy with anti-thymocyte globulin (ATG; 4.5 mg/kg), methotrexate (MTX), and cyclosporine (CsA), while six did not receive TBI. Of these, five received Flu/Cy/alemtuzumab and one received Flu/Cy/ATG with MTX/CsA. The primary endpoint was overall survival (OS); secondary endpoints included primary graft failure (PGF) and major infectious complications.

Results: Overall, 34 patients were included, with a median age of 27 years (IQR, 21–32); 17 were male. There were 23 MUD and 11 Haplo donors. Half of the cohort (n=17) had received prior immunosuppressive therapy before HCT. Graft source was bone marrow in 16 MUD and 9 Haplo recipients, and peripheral blood in the remainder. There were no significant differences between groups in $CD34^+$ cell dose or donor–recipient CMV/ABO compatibility. Neutrophil recovery occurred at a median of 21 days in the MUD group and 22 days in the Haplo group (p=0.60). Platelet engraftment occurred at 19 days for MUD and 26 days for Haplo recipients (p=0.47). PGF occurred in four MUD patients, all of whom underwent second HCT.
The cumulative incidence of bloodstream infection at day +60 was 54.4% (95% CI, 21–79) in the Haplo cohort and 26.1% (95% CI, 10–45) in the MUD cohort (p=0.30). At day +100, clinically significant EBV reactivation (>30,000 copies/mL) occurred in 20% (95% CI, 3–49) of Haplo recipients and 56.5% (95% CI, 34–74) of MUD recipients (p=0.09). CMV reactivation was comparable (0% Haplo vs. 4.3% MUD; p=0.56).
At day +100, grade II–IV and III–IV acute GVHD occurred in 29.5% (95% CI, 6–59) and 10.1% (95% CI, 1–38) of Haplo recipients, respectively, and in 22% (95% CI, 8–41) and 0% of MUD recipients (p=0.82 and p=0.13). At 24 months, moderate-to-severe chronic GVHD was 0% in Haplo versus 4.8% (95% CI, 1–20) in MUD recipients (p=0.57).
With a median follow-up of 30.3 months (95% CI, 24–56), the 24-month overall survival was

90.9% (95% CI, 74.3–97). Survival was comparable between the Haplo and MUD groups, 90.9% (95% CI, 51–99) and 91.1% (95% CI, 69–98), respectively (p=0.90).

Conclusions: Haploidentical HCT using a PTCy platform is an effective and feasible alternative to MUD HCT in SAA, with comparable engraftment, GVHD, and survival outcomes.

Disclosure: Nothing to declare.

B332

THIOTEPA-BASED BUSULFAN-SPARING CONDITIONING OPTIMIZES ENGRAFTMENT AND MITIGATES CHRONIC GVHD IN PEDIATRIC HAPLOIDENTICAL HSCT FOR SAA: A MATCHED CASE-CONTROL STUDY

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Background: For pediatric patients with severe aplastic anemia (SAA) undergoing haploidentical hematopoietic stem cell transplantation (HSCT), balancing the need for robust engraftment against the risks of conditioning-related toxicity remains a critical therapeutic challenge. We hypothesized that a Thiotepa (TT)-intensified, Busulfan-sparing regimen could optimize the therapeutic index by leveraging Thiotepa's unique dual properties—profound immuno-ablation and myelo-ablation—while specifically minimizing Busulfan-associated organ damage.

Methods: In this retrospective study, 30 pediatric SAA patients (TT-group) were matched 1:2 with 60 historical controls based on age and disease status. All patients received a standard conditioning backbone of Fludarabine, Cyclophosphamide, and Rabbit ATG. The TT-group utilized a modified protocol where Thiotepa (10 mg/kg) was substituted for one day of Busulfan, resulting in significantly de-escalated total Busulfan exposure (median 3.50 vs. 6.40 mg/kg, $P < 0.001$). Standard consensus criteria were used for GVHD and toxicity grading. Primary endpoints included engraftment kinetics, GVHD incidence, safety profiles, and survival.

Results: 1. Graft Characteristics & Engraftment: Graft cellularity was well-balanced between groups, with comparable mean CD34+ cell doses (6.88 ± 1.78 vs. 6.70 ± 1.63 × 10^6/kg, $P = 0.638$) and MNC doses (7.23 ± 2.11 vs. 7.80 ± 2.17 × 10^8/kg, $P = 0.249$). The TT-group achieved a 100% engraftment rate (30/30). Recovery kinetics were significantly accelerated, with faster neutrophil (median 11 vs. 12 days, $P = 0.033$) and platelet reconstitution (median 10.5 vs. 12.0 days, $P = 0.025$) compared to controls. 2. GVHD Reduction: With a median follow-up of 313 days for the entire cohort, the TT-group demonstrated a striking reduction in chronic GVHD incidence (10.00% vs. 30.00%, $P = 0.034$), suggesting that the intensified Thiotepa regimen fosters a potent tolerogenic environment. Acute GVHD rates (Grade 2-4) remained comparable ($P = 0.916$). 3. Safety & Toxicity: Gastrointestinal toxicity was more frequent in the TT-group (40.00% vs. 20.00%, $P = 0.043$) but was fully reversible.

Notably, a numerical increase in TA-TMA/VOD incidence was observed in the TT-group (13.33% vs. 1.67%; P = 0.074). While this represents a clinically notable signal warranting vigilance, crucially, all cases resolved with supportive care, and no associated mortality occurred. Incidence of Grade 3-4 liver injury was comparable (P = 0.607). 4. Survival & Viral Reactivation: Overall Survival (OS) was 100% in the TT-group, with zero transplant-related mortality (TRM). Additionally, a strong trend toward reduced CMV reactivation was noted in the TT-group (30.00% vs. 51.67%, P = 0.051), indicating preserved immune reconstitution.

Conclusions: Thiotepa intensification facilitates a Busulfan-sparing strategy that ensures rapid, stable engraftment and significantly reduces chronic GVHD in pediatric SAA. Despite a signal for manageable endothelial toxicity, this regimen establishes a compelling new paradigm with a superior efficacy-safety profile, effectively trading short-term, reversible toxicity for enhanced long-term immunological recovery and survival. These findings strongly support the design of prospective, randomized trials to validate this regimen as a standard of care.

Disclosure: Nothing to declare.

B333

SECOND ALLOGENEIC STEM CELL TRANSPLANTATION FOR SEVERE APLASTIC ANEMIA: REAL-WORLD OUTCOMES FROM A SINGLE CENTRE IN PAKISTAN

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Background: Primary and secondary graft failure following second allogeneic Hematopoietic Stem Cell Transplantation (HSCT) for Aplastic Anemia (AA) remain critical complications associated with high morbidity and mortality. Large Western cohort studies report favorable survival with salvage HSCT. However, data from low- and middle-income countries (LMICs) is scarce. This study reports real-world outcomes of second HSCT for AA from one of Pakistan's largest transplant centers.

Methods: We conducted a retrospective analysis of 37 patients with AA who underwent a second matched related donor or haploidentical HSCT with unmanipulated/unselected peripheral/bone marrow stem cells at the Armed Forces Bone Marrow Transplant Centre (AFBMTC) from 2002 to 2025 out of a total cohort of 495 patients undergoing HSCT for AA. Our primary outcomes were engraftment kinetics and overall survival (OS). Secondary endpoints included disease-free survival (DFS), graft-versus-host disease–free relapse-free survival (GRFS), and transplant complications. We performed Kaplan–Meier with log-rank test, Mann–Whitney U, chi-square/Fisher's exact, and multivariate analysis using Cox regression where required.

Results: The median age of the study cohort at second HSCT was 16 years (IQR 9.5-25.5), and the male-to-female ratio was 1.3:1. The median interval between the first and second HSCT was 145 days (IQR: 25-406). Among all patients receiving a second transplant, 78.4% received grafts from related donors and 21.6% from haploidentical donors. Indications for second transplant were primary graft failure (48.5%), secondary graft failure (45.5%), and poor graft function (6.1%). The most common graft source was PBSCs (45.9%). Conditioning regimens included fludarabine, cyclophosphamide, and ATG (39.4%), followed by no conditioning (33.3%), non-ATG regimens (15.2%), ATG alone (3%), and other regimens (9.1%). Median time to neutrophil engraftment and platelet engraftment was 13 days (IQR: 10-22) and 27 days (IQR: 21-40), respectively. Neutrophil engraftment was significantly associated with conditioning (p=0.001), occurring in 100% with ATG-based regimens, 55.6% without conditioning, and 0% with non-ATG regimens. Transplant-related mortality was 32.4%, caused by graft failure (48%), infectious complications (8.1%), and organ failure (8.1%). The incidence of grade II-IV aGVHD was 11%, and chronic GVHD was 10.8%. Survival outcomes were OS: 50%, DFS: 43.2%, and GRFS: 32.4%. On univariate analysis, OS and DFS were significantly associated with HSCT type (OS $p < 0.001$), neutrophil engraftment (OS/DFS $p < 0.001$), and CMV reactivation (OS $p < 0.001$). On multivariate Cox regression these associations were no longer significant, reflective of the limited statistical

power in our small study population.

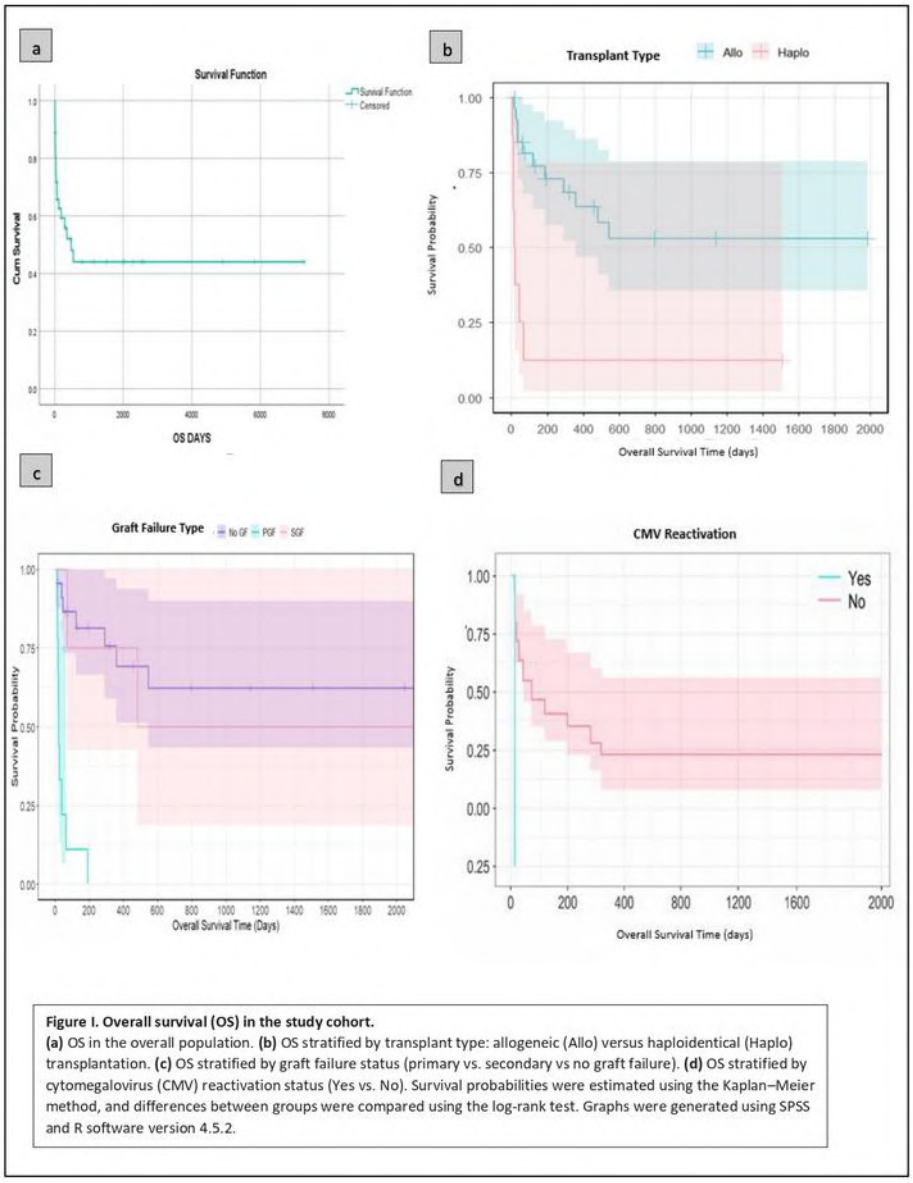

Figure I. Overall survival (OS) in the study cohort.
(a) OS in the overall population. **(b)** OS stratified by transplant type: allogeneic (Allo) versus haploidentical (Haplo) transplantation. **(c)** OS stratified by graft failure status (primary vs. secondary vs no graft failure). **(d)** OS stratified by cytomegalovirus (CMV) reactivation status (Yes vs. No). Survival probabilities were estimated using the Kaplan–Meier method, and differences between groups were compared using the log-rank test. Graphs were generated using SPSS and R software version 4.5.2.

Conclusions: In comparison to outcomes reported by large Western registry-based studies, survival in our region remains inferior. This is mainly attributable to the use of unmanipulated stem cells due to the excess cost associated with CD34 selection/αβ T-cell depletion, which is otherwise standard of care in graft failure. Other causes include delayed engraftment and infectious complications. Results from our study underscore the need for optimal conditioning strategies, better infection control measures, and early referral pathways in LMIC settings.

There is a need for multicenter collaborations across South Asia to provide more high-quality evidence to refine salvage transplant approaches for AA globally.

Disclosure: Nothing to declare

P260

PEDIATRIC ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN FANCONİ ANEMIA: A CASE SERIES OF SINGLE CENTER EXPERIENCE

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Background:

Fanconi anemia (FA) is a a rare multi-organ hereditary disease characterized by defective DNA repair mechanism that manifests as congenital malformations, progressive bone marrow failure, and a predisposition to malignancy. Hematological abnormalities occur in patients with FA at a median age of 7 years (range, birth to 31 years). Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) remains the only potential curative treatment for bone marrow failure in patients with FA. We aimed to present our transplant experiences in pediatric patients with FA at Acibadem Adana Hospital, Pediatric Bone Marrow Transplantation Unit.

Methods:

A total of 650 allogeneic hematopoietic stem cell transplantations were performed at Acıbadem Adana Hospital Pediatric Bone Marrow Transplantation Unit in Turkey from 2013 to 2025. 17 of 650 pediatric patients were FA. In this retrospective analysis of medical records and treatment modalities were evaluated.

Results:

In this retrospective analyses, 17 patients were evaluated, age ranging from 3 to 17 years with an average of 8.9 years. Ten patients were males, seven were female. Five patients had HSCT from an unrelated donor. We included all patients conditioning with ATG, fludarabine and cyclophosphamide. Two patients experienced secondary graft failure and this patients underwent a second transplant. Nine CMV reactivation developed in our patients. Acute GVHD ≥ Grade III was observed in only one patient. Chronic GVHD was seen in three patients. Two patients died. One of them died on day 38 due to central posterior reversible encephalopathy syndrome. Another patient, who underwent second transplant due to primary graft failure, died on the 27th post-transplant day due to sepsis and veno-occlusive disease. No serious toxicity was observes in other patients. 15 patients are alive and still following up GVHD free.

Conclusions:

HSCT is the only potentially curative treatment option for the hematologic complications that occur in patients with FA. In this retrospective study, we showed the results of our reduced toxicity myeloablative conditioning regimen is excellent overall survival, negligible GVHD, and low toxicity among in pediatric patients with FA even in those with high-risk pre-HSCT clinical features or those with no HLA-identical family donor who transplanted match unrelated donor.

Disclosure: No disclosure.

P261

EXPERIENCE IN HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ACQUIRED APLASTIC ANEMIA BETWEEN 2010-2015 IN A SINGLE CENTER

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Background: With evolving advances in conditioning regimens, immunosuppression and supportive care, Allogeneic Hematopoietic stem cell transplantation (HSCT) remains a curative option in acquired severe and very severe aplastic anemia (SAA/VSAA) and should be carefully considered after evaluating response to immunosuppression, age, comorbidities and donor availability.

Methods: The objective of this study was to assess the outcomes of Allogeneic HSCT in patients with AA during the last 15 years in a single center.All AA adult patients who underwent an HSCT at a single center between 2010-2025 were retrospectively identified.

Results: In total, 13 patients with SAA/VSAA underwent an Allogeneic HCT between 2010-2025 at a single institution, the median follow-up was 126 months. 7 out of 13 (54%) were females, 6 (46%) were males and the median age at HCT was 44 years (60-18). The median duration from diagnosis to alo-HSCT was 223 days (41-1573), with only one patient undergoing alo-HSCT upfront and the remaining patients after insufficient response to immunosuppresive therapy (IST). Most patients had received prior IST (12 (92%)), the majority with Cyclosporine (CsA) plus rabbit ATG (rATG) (11 (85%)). In all patients, the graft source was bone marrow, and the median total nucleated cells (TNC) and CD34+ stem cell doses were above the recommended threshold of 3×10^8/kg and 3×10^6/kg respectively. Most of the donors were matched (10 (77%), half of them unrelated). Two patients had mismatched unrelated donors and one patient a haploidentical unrelated donor.
All the patients received anti-thymocyte globulin (ATG) based conditioning regimens, 10 (77%) of them, received fludarabine based regimens, with modifications according to individualized assessment of their comorbidities. Two patients received post-transplant high-dose cyclophosphamide (PTCy) for GVHD prophylaxis as they were receiving mismatched unrelated or haploidentical unrelated donors respectively. For acute graft versus host disease

(GVHD) prophylaxis most of the patients received CsA plus methotrexate (MTX) (11 (85%)) except for 2 patients who received Mycophenolate Mofetil (MMF) plus CsA due to mismatched and haploidentical transplantation.
During follow-up 3 patients (23%) died due to transplant-related complications, all had received matched transplants and all experienced primary graft failure. One of these patients is the oldest in the cohort (60 years old), and another was the only patient that developed mild acute GVHD. No patients developed grade III-IV aGVHD. The rate of cytomegalovirus (CMV) reactivation was 46% and the rate of Epstein-Barr virus (EBV) reactivation was 15% (2 patients, both developing post-transplantation lymphoproliferative disorder (PTLD)).

Table 1. Characteristics of the patients.

Characteristics	All patients no. = 13
Gender:	
Male	6 (46%)
Female	7 (54%)
Median age (years)	44
Disease severity:	
Severe Aplastic anemia (SAA)	12 (92%)
Very severe Aplastic anemia (VSAA)	1 (8%)
Immunosuppresive therapy:	
Cyclosporine (CsA) + rabbit ATG (rATG)	11 (85%)
Horse anti thymocyte globulin (hATG)	2 (15%)
No immunosuppresive therapy	1 (8%)
Median duration from diagnosis to alo-HSCT	223 (days)
<1 year from diagnosis to alo-HSCT	9 (69%)
≥1 year from diagnosis to alo-HSCT	4 (31%)
Median Follow-up	126 months
Graft source:	
Bone marrow	13 (100%)
Stem cell dose:	
Median TNC (total nucleated cells) dose	3.7 × 108/kg
Median CD34 dose	4 × 106/kg
Donor:	
Matched related donor (MRD)	5 (39%)
Matched unrelated donor (MUD)	5 (39%)
Mismatched unrelated donor	2 (15%)
Haploidentical (Haplo) unrelated donor	1 (8%)
Donor/recipient sex match:	
Donor (male)/ receptor (male)	5 (39%)
Donor (female)/receptor (male)	1 (8%)
Donor (female)/receptor (female)	4 (31%)
Donor (male)/receptor (female)	3 (23%)

Characteristics	All patients no. = 13
ABO compatibility:	
compatible	6 46%)
minor incompatibility	4 (31%)
major incompatibility	3 (23%)
Conditioning regimen:	
- Cy-rATG	3 (23%)
- Flu based	10 (77%)
Cy-Flu-rATG	8 (62%)
Cy-Flu-rATG-TBI	1 (8%)
Flu-rATG	1 (8%)
GVHD prophylaxis	
CsA-MTX	11 (85%)
CsA-MMF	2 (15%)
Engraftment:	
Median time to ANC engraftment	24 (days)
Median time to platelets engraftment	25 (days)
Primary graft failure rate	3 (23%)
GVHD:	
Grade III-IV aGVHD	0
Grade 1-II aGVHD	1 (8%)
Rate of CMV reactivation	6 (46%)
Rate of EBV reactivation	2 (15%)
PTLD	2 (15%)
Chimerism analysis at last follow-up:	
Mixed chimerism	4 (31%)
Full chimerism	9 (69%)
Deaths	3 (23%)

Conclusions: Although the small sample size limits the strength of the findings, it seems that in our cohort the outcome of MUD transplants for acquired AA is similar compared with MRD transplants. Transplants from non conventional donors (mismatched and haploidentical) also showed comparable outcomes in our series, reflecting the improvement in conditioning,

GVHD prophylaxis and supportive care. In our population the patients who experienced primary graft failure had the worst outcomes.

Disclosure: Nothing to declare.

P262

CASE REPORT: THE USE OF PEGCETACOPLAN PERI-HAEMATOPOIETIC STEM CELL TRANSPLANT FOR PAROXYSMAL NOCTURNAL HAEMOGLOBINURIA / APLASTIC ANAEMIA

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Background: Parxyosmal nocturnal haemoglobinuria (PNH) is a rare, acquired condition that results in chronic complement-mediated haemolysis. Pegcetacoplan is a pegylated peptide that targets the proximal complement C3 and is a novel management strategy for PNH refractory to terminal complement inhibitors (eculizumab and ravalizumab). The only potential cure for PNH is allogeneic haematopoietic stem cell transplant (allo-HSCT), however allograft is infrequently performed solely for PNH and usually is undertaken for coexistent aplastic anaemia.

Methods: We describe the case of a 23-year-old female diagnosed with classical PNH with a somatic PIGA variant in March 2022. Initially managed at a tertiary hospital in Sydney, Australia with ravalizumab. She remained transfusion-dependent and severely pancytopenic. Repeat bone marrow biopsy in July 2022 was consistent with development of severe aplastic anaemia. Bone marrow failure panel did not detect any underlying pathogenic variants. She did not have an adult fully matched sibling donor so underwent immunosuppression with horse anti-thymocyte globulin (hATG), cyclosporin and eltrombopag. Six months following immunosuppresion and eltrombopag, the patient remained severely pancytopenic with no haematological response (ANC 0.5x10*9/L Hb 82g/L Plt 26x10*9/L). At this point, due to ongoing haemolysis she was changed to pegcetocoplan 1080mg twice weekly and referred for allo-HSCT. On extended testing of her younger siblings an 11-year- old male sibling was found to be HLA match.

Results: Given the presence of a large Type 2 and 3 PNH clone, and ongoing haemolysis, a decision was made that she remained on pegcetacoplan throughout conditioning. This was done to reduce the risk of thrombosis and veno-occlusive disease (VOD). The conditioning regimen consisted of rATG, fludarabine, cyclophosphamide and one fraction of 2.00 Gy total body irradiation as per the protocol by DeZern et al (Blood 2023). Graft-versus-host disease (GVHD) prophylaxis consisted of post-transplant cyclophosphamide, tacrolimus and mycophenolate. We elected to use peripheral blood stem cells to ensure rapid engraftment as the donor was age 11 and of low weight relative to the recipient, and given the recipient had been severely neutropenic for 5 months. On day +9 she developed septic shock (*Klebsiella*

pneumoniae and *Streptococcus mitis*) requiring intensive care admission. Due to development of severe sepsis pegcetacoplan was ceased on D+9. Neutrophil and red cell engraftment occurred at D+26, with platelet engraftment occurring at D+41. The patient had no evidence of acute GVHD and two years post allograft has no cGVHD and is off immune suppression with no detectable PNH clone, normal blood count and full donor chimerism. *Figure 1* demonstrates clearance of the PNH clone and neutrophil engraftment.

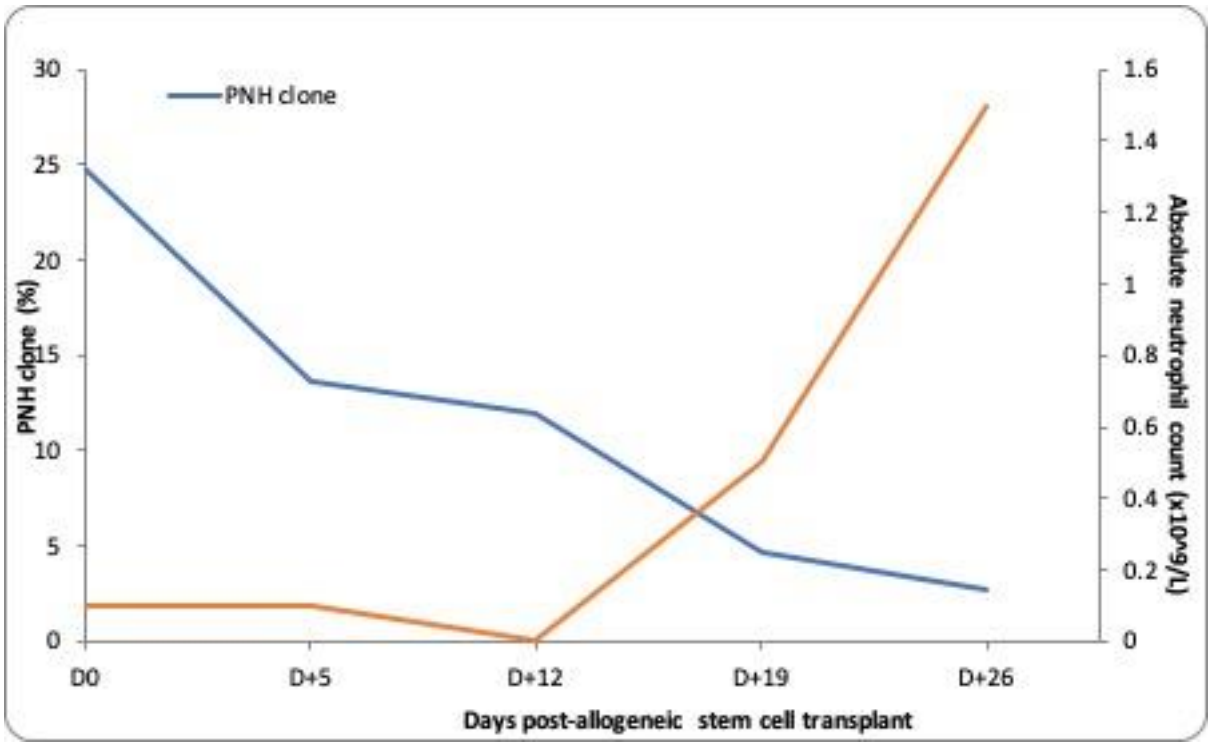

Figure 1: Rate of clearance of PNH clone and engraftment post-transplant

Conclusions: Use of eculizumab during the peri-transplant period has been described. We are not aware of any previously described cases of pegcetacoplan as a bridging therapy to allograft for patients with PNH and AA. The case demonstrates that this novel complement inhibitor can be used during the transplant conditioning and continued after stem cell infusion with successful engraftment and clearance of the PNH clone.

Disclosure: Nothing to declare.

P263

AUTOLOGOUS UMBILICAL CORD BLOOD TRANSPLANTATION WITHOUT CHEMOTHERAPY-BASED CONDITIONING IN A CHILD WITH SEVERE APLASTIC ANEMIA: A CASE REPORT

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Background: Severe aplastic anemia (SAA) is a rare, life-threatening hematopoietic disorder characterized by profound bone marrow failure and severe pancytopenia, requiring prompt diagnosis and treatment, typically including immunoablative therapy or allogeneic hematopoietic stem cell transplantation. Here, we report a 2.5-year-old boy with SAA treated with an immunoablative regimen without chemotherapy, followed by autologous umbilical cord blood transplantation (auto-UCBT).

Methods: The boy was diagnosed with SAA at 2.5 years of age. At diagnosis, testing was negative for Fanconi anemia and germline inherited bone marrow failure syndromes. In the absence of a matched sibling donor, immunosuppressive therapy was chosen.

Results: Immunoablation was initiated with four doses of equine antithymocyte globulin (Atgam, 40 mg/kg), after which a substantial number of residual T lymphocytes was observed (818/μL). To intensify the immunoablation, the patient subsequently received a 3-day course of antithymocyte globulin (Grafalon, 5 mg/kg), followed by a 2-day course of antithymocyte globulin (Thymoglobulin, 3.75 mg/kg), administered with methylprednisolone and cyclosporine A. Subsequently, the child underwent auto-UCBT containing 0.13×10^6 CD34+ cells/kg and continued treatment with cyclosporine A and prednisone. Leukocyte recovery above 1000/μL was achieved on post-transplant day +26, and neutrophil recovery above 500/μL on day +28. Transfusions of packed red blood cells and platelet concentrates were required until day +28 and +38 respectively. The post-transplant period proceeded without severe complications. Immunosuppression with cyclosporine A has been continued for 11 months after auto-UCBT, as the patient has not yet met the criteria for complete remission.

Conclusions: Early neutrophil recovery may indicate better underlying stem cell reserve, due to auto-UCBT infusion, though this interpretation remains speculative. Auto-UCBT after immunosuppression-based protocol appears to be a promising curative option for pediatric SAA patients with stored autologous cord blood and without available matched sibling. A key prerequisite for autoUCBT in SAA is excluding inherited bone marrow failure syndromes via clinical assessment, and germline genetic testing.

Disclosure: Nothing to declare

Bone Marrow Failure

OS20-07

ALEMTUZUMAB-CONDITIONED HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION CONFERS EXCELLENT SURVIVAL WITH LIMITED GVHD IN FANCONI ANEMIA

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Background: Fanconi anemia (FA) is the most common inherited bone marrow failure, and Hematopoietic cell transplantation (HCT) can cure hematological complications associated with the disease. When a matched donor is unavailable, a haploidentical donor may be a suitable option. Given the DNA frailty intrinsic to the disease, FA patients should receive a reduced-intensity conditioning (RIC) regimen while ensuring engraftment and low rates of Graft-Versus-Host Disease (GVHD). We present outcomes for patients with FA who underwent haploidentical transplantation with alemtuzumab-based conditioning and GVHD prophylaxis with a modified post-transplant cyclophosphamide (PTCY).

Methods: A retrospective, longitudinal, non-randomized, observational study including 44 patients with a median age of 8.9 years (range 3.5-44.8), transplanted in six HCT centers, between 2019 and 2025. Patients were classified as having bone marrow failure (FA-BMF) or aberration of indeterminate potential associated with FA (FA-AIP), such as 1q duplication. Patients with advanced disease (AML or MDS) were not included. All subjects received bone marrow from haploidentical donors and conditioning with Fludarabine 150mg/m², Total Body Irradiation (TBI) 200cGy, and Alemtuzumab 0,6-0,7mg/kg. GVHD prophylaxis consisted of PTCY 50-60 mg/kg (total dose), Cyclosporin, and Mycofenolate Mofetil. The database was revised, and statistical analyses were performed using EZR. Patients' characteristics are summarized in Table 1.

Gender, n (%)	Female 21 (47.7%)

	Male 23 (52.3%)
Age at HCT, median (range)	8.9 years (3.5-44.8)
FANC mutation, n (%)	FANCA 23 (52%) FANCG 5 (11.3%) Other 2 (4.5%) Unidentified 14 (31.5%)
Disease status at HCT, n (%)	FA-BMF 39 (88.6%) FA-AIP 5 (12.8%)
Donor, n (%)	Father 24 (54.5%) Mother 3 (6.8%) Other 17 (38.6%)
Donor age, median (range)	30.5 years (6-46)
Cytomegalovirus status for donor/recipient, n (%)	Negative/negative 3 (6.8%) Positive/negative 3 (6.8%) Positive/positive 38 (86.4%)
DSA status, n (%)	Positive 2 (4.5%) Negative 42 (94.5%)
TNC (x108/kg), median (range)	5.21 (2.6-10.5)
CD34 (x106/kg), median (range)	5.3 (1.6-13.1)
Follow-up, median (range)	25.5 months (6-67.1)

Results: With a median follow-up of 25.5 months, the 1- and 2-year overall survival (OS) was 93.2% (95%CI:80.3-97.7%). Four patients died, three from transplant-related complications (bleeding, viral, and fungal infection), while one 44-year-old patient died from oral cancer four years post-transplant.

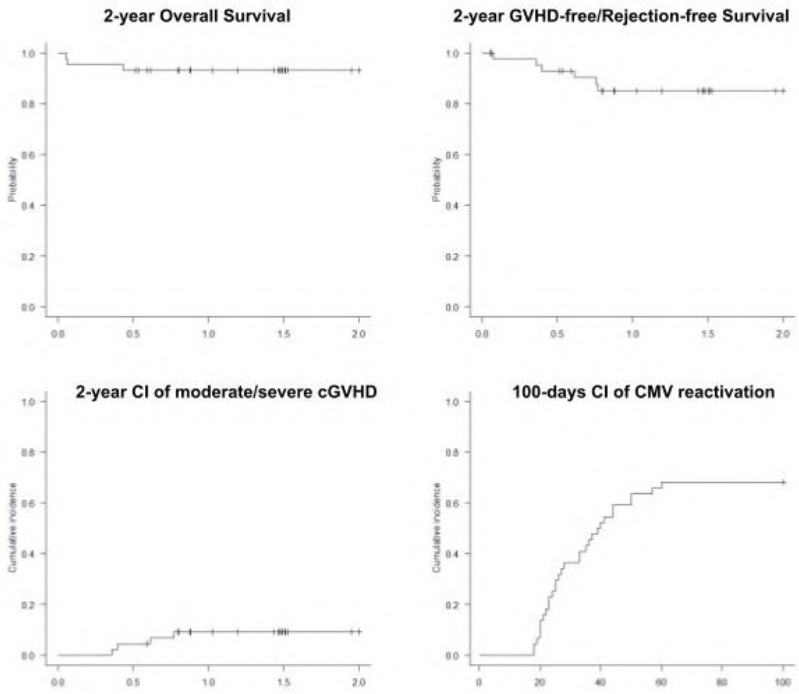
Only one patient experienced primary graft failure (GF) and was successfully rescued. There were no secondary graft failures. The 1-year cumulative incidence of GF was 2.3% (95%CI:0.2-10%). All engrafted patients sustained complete donor chimerism at the last follow-up.

Early cytomegalovirus (CMV) reactivation was frequent, with a 100-day CMV reactivation CI of 68.2% (95%CI:51.8-80%). Patients didn't receive letermovir prophylaxis but were successfully treated with preemptive therapy, with no evidence of CMV disease. The incidence of hemorrhagic cystitis was 20.6% (95%CI:10.1-33.7%).

The 100-day cumulative incidence of grade II-IV acute GvHD (aGVHD) was 4.5% (95%CI:0.08-13.8%), and the 2-year CI of any-grade and moderate/severe chronic GvHD (cGVHD) were 22.9% and 9.2% respectively (95%CI:11.7-36.3% and 2.9-20.1%).

Long-term outcomes and quality of life are significantly affected by GF and GVHD; therefore, patients were also evaluated for extensive (grade III-IV aGVHD, moderate/severe cGVHD) GVHD associated with rejection as a composite endpoint. The 2-year GVHD-free/Rejection-free survival was 85.1% (95% CI:69.9-93%). Given the low incidence of events in this cohort, no risk factor for worse outcomes (such as donor/patient age or sex mismatch) was identified in the statistical analysis.

Conclusions: The modified haploidentical approach incorporating alemtuzumab and PTCY achieves excellent survival outcomes in FA by decreasing rejection and TRM. The RIC approach minimizes toxicity, but careful consideration of TBI exposure and GVHD-associated malignancy risk remains a concern. The addition of alemtuzumab reduced the incidence and severity of GVHD compared to previously reported data. Haploidentical donors are promptly available and should be considered before disease progression to MSD/AML.



Disclosure: Nothing to declare.

OS20-08

DISEASE STATUS AND HIGH TOXICITY INFLUENCE OUTCOMES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ADOLESCENTS AND ADULTS WITH FANCONI ANEMIA: A SPANISH MULTICENTER EXPERIENCE

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Background: Allogeneic hematopoietic cell transplantation (HCT) remains the only curative option for bone marrow failure (BMF) or clonal evolution in Fanconi anemia (FA). However, most available evidence is derived from pediatric cohorts, and outcomes in adolescents and adults remain poorly defined. To address this gap, we conducted a study to characterize the clinical profile and transplantation outcomes of FA patients aged ≥12 years.

Methods: This national retrospective multicenter study through the Spanish Group for Hematopoietic Transplantation and Cell Therapy (GETH-TC) included all FA patients who underwent first HCT at ≥12 years of age between 2000–2024 across 17 centers. Primary endpoints were overall survival (OS) and event-free survival (EFS). Secondary endpoints included engraftment, graft failure (GF), acute and chronic graft-versus-host disease (aGVHD, cGVHD), relapse, non-relapse mortality (NRM), and secondary malignancies.

Results: Forty-five patients were included. Median age at diagnosis was 12 years (range, 2-38). Median time from diagnosis to HCT was 7 years (range, 3m-34y). The median age at HCT was 20 years (range, 12–44). Disease status at transplant was BMF 49%, MDS 45% and AML 13%. The donor was a MSD in 35.6%, MUD in 33.3% and alternative donor in 31%. Most patients received a fludarabine-based reduced-intensity conditioning regimen and 42,2% TBI. The cumulative incidence (CI) of neutrophil recovery by day 30 was 88.6% (95% CI, 78.8–98.5%), with a median engraftment time of 13 days (range, 8–41). GF occurred in 6 patients (4 primary and 2 secondary), with a CI at day 100 of 8.8% (95% CI, 2.2–17.7%). The CI of grade II–IV aGVHD at day 100 was 36.4% (95% CI, 21.9–50.4%), and grade III–IV was 24.4% (95% CI, 13.3–37.8%). The 2-year CI of moderate/severe cGVHD was 12.2%

(95% CI, 2–22.4%). Infections and organ toxicities were frequent (table1). Relapses and NRM occurred early, plateauing after month 6. The 2-year CI of relapse reached 31% (95% CI, 16.7–45.2) and NRM of 16.7% (95% CI, 5.2–28.1).
With a median follow-up of 88.1 months (IQR, 27–166), 2-year OS and EFS were 57% (95% CI, 42–72) and 51% (95% CI, 36–65), respectively. Survival differed significantly by disease status (p=0.013): patients with BMF had a 2-year OS of 68% (95% CI, 50-85%), compared with 16% (95% CI, 0-34%) in MDS/AML cohort. Secondary malignancies occurred in 5 patients, with a median of 63 months (range, 8–177) post-HCT, predominantly squamous cell carcinoma (n=4). At last follow-up, 22 patients were alive. Among the 23 deaths, main causes were organ toxicity and infection (n=11), relapse (n=7), GVHD (n=3) and secondary malignancies (n=2).

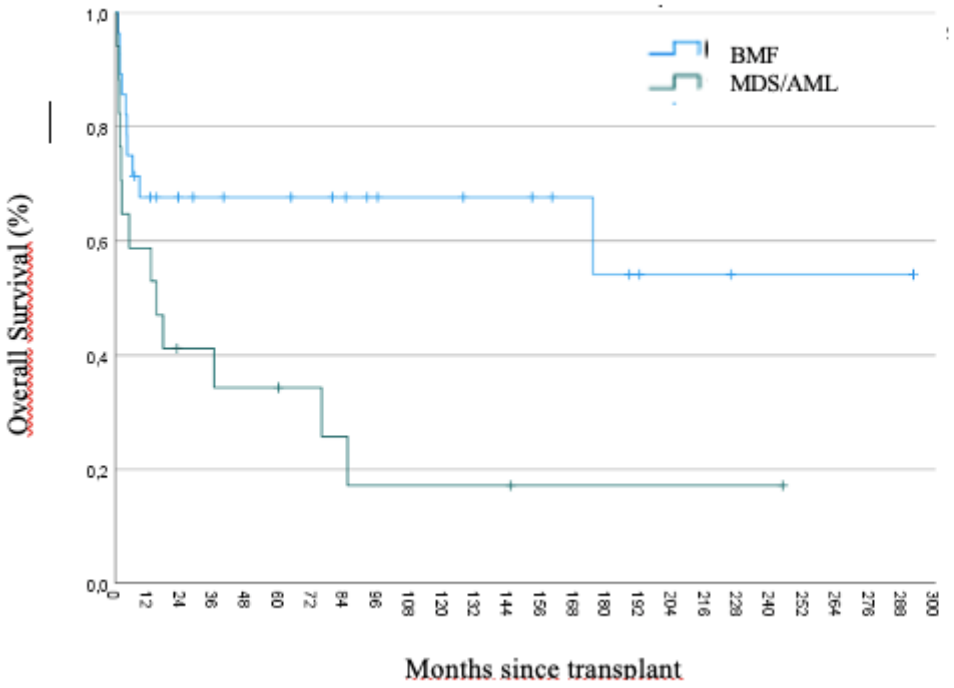
Table 1. Patient, donor, and transplant characteristics and complications in patients with Fanconi anemia		
	Total patients (n=45)	%
Patient characteristics Gender		
• Male	20	44.4%
• Female	25	55.6%
Median age (range) at diagnosis of FA, yrs.	12 (2-38)	
Median time from diagnosis to HSCT (range), yrs.	7 years (3 m-34 y)	
The median age at HSCT, yrs.	20 (12–44)	
	20	44.4%
	25	55.6%
• Adolescents (12–17 years)	22	49%
• Adults (≥18 years)	17	38%
	6	13%
Disease status at transplant		
• BMF	90 (80-100)	
• MSD		
• AML		
	18	40%
	15	33%
Median clinical performance status score (Lansky- Karnofsky), %	7	15.5%
	5	11%
Congenital malformations		

Table 1. Patient, donor, and transplant characteristics and complications in patients with Fanconi anemia		
• None • <3 • ≥3 • Unknown Treatment pre-HSCT • ≥20 blood product transfusions • Androgens • Eltrombopag • Cytoreduction in SMD/AML	18 14 2 4	40% 35% 5% 18.2%
Donor characteristics Donor Type • MSD • MUD • MMFD • MMUD • Haploidentical donor	 16 15 3 9 2	 35.6% 33.3% 6.6% 20% 4.4%
Transplant characteristics CMV serological status D/R • +/+ • +/- • -/- • -/+ Blood group D/R • Matched • Mistmatched • Unknown Conditioning regimen • FLU-CY • FLU/Cy/BU • Others	 21 14 7 3 30 13 2 38 3 4 26 19 4	 46% 31% 15.5% 6.6% 69.8% 28.8% 4.4% 84.4% 6.6% 8.8% 57.8% 42,2% 21%

Table 1. Patient, donor, and transplant characteristics and complications in patients with Fanconi anemia		
Total Body irradiation (TBI)	10	52.6%
	5	26%
• No		
• Yes		
• TBI dose	38	88.4%
○ 2Gy	7	15.6%
○ 3Gy		
○ 4Gy		
Serotherapy	27	60%
	9	20%
• Yes	9	20%
• No		
GvHD prophylaxis	23	51.1%
	20	44.4%
• CsA plus a second immunosuppressive drug	2	4.4%
• CsA alone		
• Others	3.7 (range, 0.5-5.2)	
Source of hematopoietic progenitors	5.5 (range, 1.8-13)	
• BM		
• PB		
• CBU		
Cell dose infused		
• Median TNCx10^8/Kg (BM)		
• Median CD34+x10^6/kg (PB)		
HSCT adverse events		
Infections	27	60%
• Viral reactivation	3	6.6%
• Viral disease	15	34.1%
• Bacterial infection	12	26.7%
• Fungal infection		
Organ toxicities	39	86%
	17	37.8%
• Mucocutaneous	13	28.8%

Table 1. Patient, donor, and transplant characteristics and complications in patients with Fanconi anemia		
• Bladder • Renal dysfunction • Pulmonary • Hepatic (veno-occlusive disease)	4 4	8.8% 8.8%

Figure 1. Overall survival in patients with Fanconi anemia according to disease status at transplantation



Conclusions: HCT in adolescents and adults with FA results in high engraftment rates but is associated with substantial toxicity, reflecting the vulnerability of older FA patients to treatment-related damage. Survival was strongly conditioned by disease status at transplant, with markedly inferior outcomes in those with MDS/AML. These findings underscore the need for early referral, optimized conditioning strategies, and tailored supportive care to mitigate toxicity and improve outcomes, particularly in the setting of clonal evolution.

Clinical Trial Registry: No.

Disclosure: No.

B335

T CELL-DEPLETED HAPLOIDENTICAL AND MATCHED UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION REPRESENT SAFE AND EFFICIENT THERAPEUTIC APPROACHES FOR PEDIATRIC PATIENTS WITH BONE MARROW FAILURE SYNDROMES

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Background: Hematopoietic stem cell transplantation (HSCT) is a valuable treatment option for patients with bone marrow failure syndromes (BMF). Limited availability of matched donors and disease-associated increased acute and long-term toxicity pose significant challenges. Thus, T cell-depleted haploidentical donor models (T-haplo-HSCT), may offer a promising alternative.

Methods: Nine patients with BMF, including three Fanconi anemia (FA), two dyskeratosis congenita (DC), two Schwachman-Diamond syndrome (SD), and two Diamond-Blackfan anemia (DBA), underwent HSCT. Four (2DC, 2SD) received matched-unrelated grafts (MUD; median age: 2 years; range 1-19): two bone marrow (BM), one cord blood (CB), one peripheral blood stem cells (PBSC). Five patients (3FA, 2DBA) received a CD3+/CD19+ or α/CD19+ T-cell-depleted graft (median age: 11 years; range 9-20). The indication for HSCT in all was transfusion-dependent pancytopenia caused by BMF. Five patients received a conditioning regimen based on fludarabine and cyclophosphamide (FC) and three fludarabine, thiotepa, treosulfan (FTT), along with ATG-Grafalon® or thymoglobulin. One SD patient received a MUD-PBSC, conditioned with fludarabine, thiotepa and melphalan (FTM). Immunosuppression (IST) consisted of tacrolimus (or cyclosporine) and mycophenolate mofetil (MMF) in all nine patients.

Results: The graft consisted of 7.6 x 10^8 TNC/kg (range: 6-9.2 x 10^8) and 10 x 10^6 T-cell depleted CD34+ cells/kg (range: 2,51-18,37 x 10^6). Leukocyte engraftment was achieved after a median of 20 days (range: 10-20) in MUD and only 11 days (range: 9-14) in T-haplo-HSCT. The median follow-up was longer for MUD (37.5 months; range: 8-62) compared to T-haplo-HSCT (6 months; range: 5-24). Overall survival was 5/5 in T-haplo-HSCT patients and 2/4 for MUD-HSCT. One deceased patient received MUD-PBSC and developed GvHD grade IV of skin and gut, along with infectious complications within 6 months post HSCT, the other one died of progressive liver disease 5.5 years post HSCT. One patient received two consecutive MUD-BM grafts due to primary graft failure. Transfusion independence was achieved in all MUD patients (median: 63 days; range: 18-134 days after transplant) and T-haplo-HSCT patients (median: 11 days; range: 10-18 days after transplant). Median Chimerism was 97% (85-100) in MUD-HSCT and 100% (87-100) in T-haplo-HSCT.
The FC and FTT conditioning regimens were tolerated with manageable transplant-related toxicity, except for extensive squamous dermatitis and mucositis in one FA patient with MDS

who received full myeloablative conditioning (Flu/Cy/Treo). One case of veno-occlusive disease (VOD) in a T-haplo-HSCT patient with FA resolved completely after treatment with defibrotide. Two cases of severe grade III-IV acute GvHD affecting the skin and gut, and one case of chronic graft-versus-host disease of the lung (cGvHD), were observed in the MUD group. Among T-haplo-HSCT recipients, mild grade I aGvHD of the skin was seen in one patient, and another patient experienced ocular cGvHD. With preemptive antibiotic treatment during neutropenia and antiviral prophylaxis, there were no life-threatening infectious complications, except for one case of septicemia in a MUD patient.

Conclusions: This single-center, retrospective series supports feasibility and safety of T-haplo-HSCT in rare BMF syndromes and indicates favorable outcomes in T-haplo-HSCT with fast engraftment, low GVHD, and a reduced risk of severe toxicity compared to MUD-HSCT in children.

Clinical Trial Registry: N/A

Disclosure: Conflict of interest:
AT: travel grants from Medac, Vertex and Jazz
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P264

GROWTH IMPAIRMENT AND PROGRESSIVE SHORT STATURE IN PEARSON SYNDROME

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Background: Pearson syndrome (PS) is a rare unique primary mitochondrial disorder (PMD) caused by single large-scale mitochondrial DNA deletions (SLSMDs), characterized by bone marrow failure, predisposition to myeloid malignancy, lactic acidosis, and progressive multi-organ complications. Spontaneous recovery of anemia is observed in two-third of patients. Recently, PS patients have opportunity to participate in clinical trials such as a cell therapy called mitochondrial augmentation therapy (MAT, ClinicalTrials.gov, NCT06017869). The marked clinical heterogeneity and lack of reliable biomarkers pose major challenges in

evaluating treatment efficacy and defining clinically meaningful endpoints. In the MAT trial some clinical improvement such as weight gain and stabilized height standard deviation score (SDS) was reported (Jacoby, et al 2022). Although short stature and abnormal growth are common clinical features in PMD, there is still limited data on growth in children with PS.

Methods: We retrospectively evaluated anthropometric data (height, weight, and body mass index (BMI) SDS from 25 patients with PS (14 males /11 females) during disease course. A diagnosis of PS was suspected from typical bone marrow features including vacuolized marrow precursors and ring-sideroblasts and subsequently confirmed by detection of SLSMDs in blood cells.

Results: Patients presented with anemia, occurring at a median age of 5 months (range 0 to 31 months). Variable organ failures developed during the course including, pancreas insufficiency in 14 patients (56%), renal disease in 8 (56%), endocrine dysfunctions in 7 (28%) and cardiac dysfunction or arrhythmia in 5 (20%). Fourteen patients required tube feeding and/or parenteral nutrition due to feeding difficulties and/or failure to thrive. The median age at last follow-up was 49 months (range: 7–183 months); 11 patients were alive and 14 had died (acute metabolic acidosis: n=9, arrhythmia: n=2, respiratory infection: n=2, and acute liver and renal failure: n=1).
The most recent median height, weight, and BMI SDS were −2.12 (range: −7.32 to 1.08), −1.70 (range: −12.25 to 0.11), and −1.44 (range: −4.74 to 2.19), respectively; 50%, 40%, and 35% of patients, respectively, had values below −2 SDS. Longitudinal data from 18 patients showed that height and weight SDS declined progressively with age in most patients (median -0.2, -1.9 and -3.4 SDS, $p<0.01$ and median -0.9, -1.7 and -3.7 SDS, $p<0.01$ in the age group of <36 months, 36-<72 months and >=72 months, respectively), whereas BMI SDS fluctuated without a clear age-related trend. Initiation of nutritional support improved weight and BMI SDS in some patients, while height SDS continued to decline without catch-up growth. Patients with at least one of the organ failures in the first 36 months of life exhibited an earlier decline in height SDS achieving -2 SDS than those without organ failure ($p=0.03$).

Conclusions: Patients with PS are generally short and underweight, and their short stature worsens over time. The presence of organ failure further exacerbates growth impairment. The results suggest that height SDS, in particular, could be a reliable marker of disease progression and treatment response in PS and serve as a meaningful clinical endpoint in future clinical trials.

Disclosure: Nothing to declare

P265

OUTCOMES OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION AS THE ONLY TREATMENT AVAILABLE FOR PATIENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA IN VENEZUELA

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Background: Nowadays, the therapy with Eculizumab has proven to be effective in controlling the symptoms and preventing complications associated with Paroxysmal Nocturnal Hemoglobinuria (PNH). However, because of its high cost, this therapy is not available in Venezuela; therefore, allogeneic Stem Cell Transplantation (HCT) is the only therapeutic option for these patients in Venezuela.

Methods: A retrospective study was conducted, and all the patients who underwent an allogeneic HCT for PNH in the Bone Marrow Transplant Center Abraham Sumoza from 2019 to 2025 were included.

Results: Patients' characteristics:
A total of 3 patients were included; all were male patients with a median age of 30.3years
The three cases presented classic PNH, the main indication for allogeneic HCT was hemolysis with constant need for red blood cell transfusion, the median time between diagnoses of PNH and AHCT was 26 months, and the therapies received before the AHCT were steroids, androgens, folic acid, and iron supplementation.
HCT and donor characteristics
There was only 1 patient who had an Identical Matched Related Donor (MRD), and two with HLA- haploidentical donor. The conditioning regimens used were: RIC with a combination of Busulfan, Fludarabine, and Cyclophosphamide for the HLA-haploidentical HCT cases, and MAC that consisted of a combination of Busulfan and Cyclophosphamide. In two of the cases, the source of the graft came from granulocyte colony-stimulating factor-mobilized Peripheral Blood CD34 cells, with a median dose of 2.35 × 10^6 cells/kg. As Graft vs Host Disease (GVHD) prophylaxis, high-dose Cyclophosphamide on days 3 and 4 followed by CsA and Micofenolato Mofetilo starting on day 5 was used for the HLA-haploidentical HCT, and the combination of CsA plus 4 doses of Metrotexate was used for the patient who received MAC conditioning.
Engratment:
Evidence of neutrophile and platelet recovery was seen on days 16 and 11, respectively, for the patient who received the MAC conditioning; this patient did not attend the follow-up consultation. Only one case of primary graft failure was registered and eventually passed away due to infection. At the time this study was conducted one of the patients was still in the recovery phase of the HCT.

Retrospective studies have shown the rate of graft failure is low in these patients; therefore, we presumed that the only case in this study was associated with a low dose of CD34 cells and perhaps the fact that they were harvested from bone marrow.

Conclusions: Allogenic HCT is recognized worldwide as the only curative treatment for patients with PNH, offering an Overall Survival (OS) of 70 to 80% at 5 years of follow-up after HCT. However, there is no guide on how or when to proceed to HCT as front-line therapy.
In our institution, it is feasible to carry out an allogeneic HCT as front-line therapy for PNH patients, using a RIC regimen and an identical MRD or HLA-haploidentical donor. Long-term follow-up is necessary to evaluate OS, incidence of GVHD, and other complications post HCT.

Disclosure: Nothing to declare.

Autoimmune Diseases

GS2-10

LONG TERM EVALUATION OF EFFICACY AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION FOR SYSTEMIC SCLEROSIS – NISSC-1 LONG TERM EXTENSION

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Background: Systemic sclerosis (SSc) is a rare and heterogenous autoimmune disease with the highest mortality rate amongst all rheumatic diseases and still very limited treatment options. In the ADWP EBMT non interventional NISSC-1 study [Henes J et al. Hematologica 2021] that included 80 adults treated with a first aHSCT with a 24 months median follow-up, 81.8% progression free survival (PFS) and 90% overall survival (OS) were observed at 2 years, but the NISSC-1 long term follow-up data were not yet available.

Methods: Long-term extension follow-up of all the NISSC-1 patients was obtained from the participating centres. Primary endpoint was progression free survival (PFS), defined as survival from baseline without evidence of SSc progression. Main secondary endpoints were overall survival (OS), non-relapse mortality (NRM), and incidence of progression.

Results: Among the NISSC-1 80 patients who had undergone aHSCT, with a median follow-up of 9.2 (IQR : 8.9-9.6) years, at respectively five and ten years, the PFS was 72% (60.6-80.6) and 58.5% (44.7-69.9) and the OS was 86% (76.2-92) and 71% (56.1-81.6). The non-relapse mortality was 7.6% (3.1-14.8) and 13.5% (5.7-24.8) and the incidence of progression 20.4% (17.4-42.3) and 26.3% (16.9-36.7) at five and ten years.
Late complications showed six malignancies diagnosed in five patients (two breast cancer, one lung cancer, one pancreatic cancer and two myelodysplasias), which occurred after a median of 80 months (range 30-121). Three patients experienced a major adverse cardiac event (MACE) and 12 had a late serious infection (after 29 months; 11-115). In nine patients one or two secondary AID appeared (51 months; 3-99).

Conclusions: This multicenter EBMT NISSC-1 long-term extenion study with 80 SSc patients and a median follow-up of 9.2 years after first aHSCT is the longest experience reported so far in the literature. We demonstrate a long-lasting effect of aHSCT in SSc with an overall survival >70% in this extremely high risk selected patients. Incidence of progression from 20.4% to 26.3%, suggesting that patients remain at risk of relapse/progression after 5 years. The extended timeframe of nearly ten years enables robust assessment of late complications.

Disclosure: Nothing to declare

OS20-01

CO-INFUSION OF ANTI-CD19 AND ANTI-BCMA CAR-T CELLS FOR RELAPSED OR REFRACTORY NMOSD: A PHASE 1 CLINICAL TRIAL AND MECHANISTIC INSIGHTS

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Background: Neuromyelitis optica spectrum disorder (NMOSD) is a severe autoimmune disease of the central nervous system, characterized by pathogenic antibodies against aquaporin-4 (AQP4). B-cell depletion with monoclonal antibodies controls neuromyelitis optica spectrum disorder (NMOSD) but requires continuous dosing and fails to eradicate long-lived autoreactive clones. We identified the cellular source of AQP4 antibodies and evaluated dual-target chimeric antigen receptor (CAR)-T cells directed at CD19 and BCMA in refractory disease.

Methods: Using single-cell RNA/B-cell-receptor (BCR) sequencing and in-vitro antibody re-expression we traced AQP4-IgG production to both $BCMA^+$ plasma cells and $BCMA^-CD19^+$ memory B cells. We then conducted an open-label, single-center, phase 1 dose-escalation study (NCT05828212). Adults with relapsed or refractory, AQP4-IgG-seropositive NMOSD received lymphodepletion followed by a single infusion of autologous anti-CD19 and anti-BCMA CAR-T cells ($1{\cdot}0 \times 10^6$ or $2{\cdot}0 \times 10^6$ cells kg^{-1} for each product). Primary endpoint was safety; secondary endpoints included relapse rate, AQP4-IgG titers, disability scores. Exploratory endpoints include immune reconstitution, peripheral blood levels of anti-CD19 and anti-BCMA CAR-T cells, serum immunoglobulins, and complement components.

Results: Nine patients (median age 45 y, range 23–65; 8 women) were treated between Apr 4, 2023, and Mar 28, 2024. Grade 1 cytokine-release syndrome occurred in eight (89%); no immune-effector-cell–associated neurotoxicity was observed. Grade ≥3 cytopenia was transient and reversible. All patients entered clinical remission; seven (77·8%) remained relapse-free and off all NMOSD therapy after a median follow-up of 505 days (291–687). Serum AQP4-IgG became undetectable in every participant within three months. One patient relapsed at eight months with de-novo pathogenic B-cell clones; single-cell analysis revealed loss of $CD16^+$ non-classical monocytes, reduced regulatory $CD4^+$ T cells, expansion/exhaustion of $CD8^+$ effector T cells, and enrichment of interferon-γ and lymphotoxin signaling.

Conclusions: Simultaneous CD19 and BCMA CAR-T-cell therapy was safe, induced deep molecular remission, and permitted drug-free disease control in most patients with highly refractory NMOSD. Relapse arose from newly generated autoreactive clones within a pro-inflammatory immune milieu, indicating that long-term success may depend on adjunctive strategies aiming at immune-regulation. Controlled trials are warranted.

Clinical Trial Registry: https://clinicaltrials.gov/study/NCT05828212

Disclosure: Nothing to declare.

OS20-03

CAR-T ACTIVITY FOR AUTOIMMUNE DISEASES ACROSS EBMT CENTERS IN 2025: A SURVEY ON BEHALF OF EBMT ADWP AND CTIWP

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Background: CAR T-cell therapy represents an emerging, promising approach in the field of autoimmune diseases (ADs), providing a deep B cell depletion and striking clinical responses through their ability to infiltrate tissues. This strategy is rapidly expanding globally, offering a treatment option to patients with refractory systemic lupus erythematosus (SLE), systemic sclerosis (SSc), and other difficult-to-treat ADs. As interest rapidly increases, the real-world landscape regarding where and how centers are beginning to implement this transformative therapy remains largely unknown.

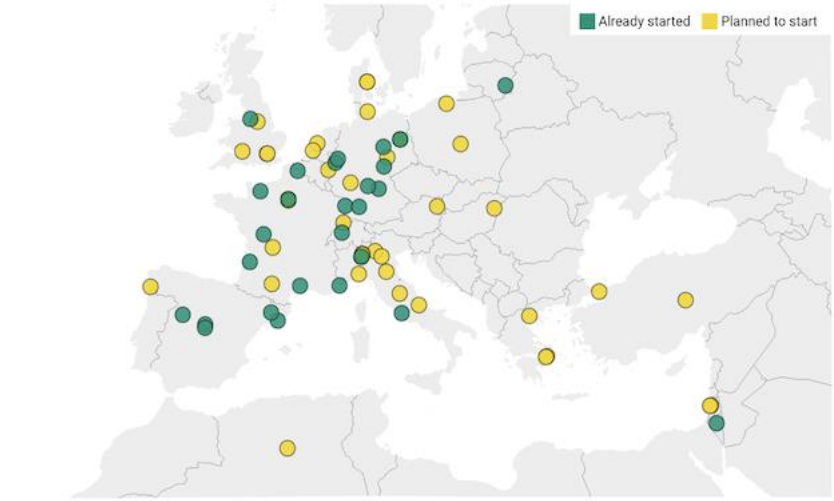
Methods: To address this knowledge gap, we conducted a cross-sectional survey across EBMT centers on behalf of the Autoimmune Disease Working Party (ADWP) and the Cellular

Therapy Immunobiology Working Party (CTIWP). The aim was to characterize current activity, indications, challenges, and future directions in the emerging field of CAR T-cell therapy for ADs.

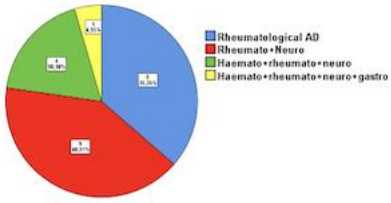
Results: The survey was distributed to 557 EBMT centers, with 103 (18%) centers responding directly to the complete survey and additional 66 centers who provided information regarding their experience with CAR T cells for ADs, resulting in 169 (30%) total responses. Overall, 29 centers had already initiated (2019-2025) CAR T-cell therapy for AD indications, while 41 others reported their plans to start within 2025, spanning most surveyed countries (Figure 1A). Among centers already treating ADs with CAR T cells, rheumatological and neurological diseases were the most frequent indications, and most treatments were administered within clinical trials (Figure 1B-C). SLE was the leading planned indication, particularly lupus nephritis, followed by SSc, idiopathic inflammatory myopathies, and multiple sclerosis. Most responding centers performing or planning to perform CAR T-cell therapy also had established HCT programs for ADs (60%) and reported multidisciplinary management models (72%) with AD specialist and CAR T specialist on-site. Autologous CAR T-cell products were most commonly available, though some centers had or will have access to both autologous and allogeneic products (20%). CD19 was the predominant target antigen (86%), followed by BCMA, CD19/CD20, or CD19/CD22 (Figure 1D). The most frequently used co-stimulatory domains were 4-1BB and CD28 (60% and 23%, respectively, Figure 1E). Lymphodepletion regimens largely mirrored those used in hematologic settings, with the majority of centers (93%) combining fludarabine and cyclophosphamide; only a small proportion of centers reported incorporating busulfan or bendamustine into their lymphodepleting regimens (5% and 2%, respectively). A total of 147 patients with ADs were reported as having received treatment, including five who had concurrent hematologic malignancies (3%). One center alone accounted for 63 treated patients (43%). Follow-up practices varied considerably across centers: 45% reported using joint disease-specific multidisciplinary visits; another 50% conducted in parallel separate hematology and disease-specialist visits; and in 5% of centers, follow-up procedures had not yet been defined.

Figure 1

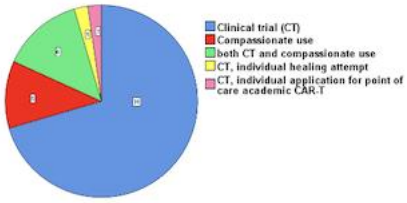
A. Geographical distribution of centers performing CAR T-cell therapy for ADs



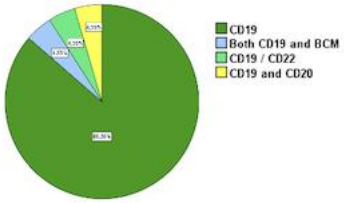
B. Indications for CAR T-cells in ADs across centers



C. Type of CAR T programme across centers



D. CAR T-cell antigen specificity



E. Co-stimulatory domain used

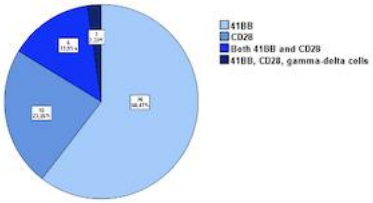


Figure Legend

A. Outlined the locations of all participating centers. Sites already active in delivering CAR T-cell therapy are highlighted in green, while centers scheduled to begin soon are shown in yellow. B. Overview of CAR T-cell therapy indications for autoimmune diseases across participating centers that already started performing CAR T-cell therapies. C. Overview of CAR T programme types across participating centers. D. CAR T-cell antigen specificity: targeted antigens across centers. E. Co-stimulatory domains employed in CAR design across centers. *Abbreviations: AD – Autoimmune Diseases; Haem – Haematological; Rheum – Rheumatological; Neuro: Neurological; Gastro – Gastrointestinal: CT – Clincial Trial*

Conclusions: This multinational EBMT survey provides the first broad overview of the rapidly evolving adoption of CAR T-cell therapy for ADs. The field is expanding quickly, with increasing numbers of centers initiating programs, targeting both rheumatological and neurological diseases. Standardization of indications, right patient selection, multidisciplinary

follow-up strategies, and reporting data in large multinational registries will be essential to guide this strategy toward wider clinical implementation.

Clinical Trial Registry: NA

Disclosure: G.O.; R.G. *equal contribution*
T.A.; A.R. *equal contribution*

OS20-05

THE "WINDOW OF OPPORTUNITY" IN CAR-T FOR LUPUS NEPHRITIS: AUTOLOGOUS BISPECIFIC CD19/BCMA RESCUE IN PATIENTS REFRACTORY TO UNIVERSAL-CD19 CAR-T — A TALE OF TWO BIOPSIES

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Background: Universal CD19 CAR-T therapy faces high relapse rates in Systemic Lupus Erythematosus (SLE) due to host rejection and the escape of CD19-negative/BCMA+ long-lived plasma cells (LLPCs). While autologous bispecific CD19/BCMA CAR-T offers a definitive immunological salvage by depleting the entire B-cell lineage, the potential for renal recovery in advanced disease remains undefined. We hypothesized that while bispecific CAR-T can reliably reset the immune system, the clinical outcome is dictated by the pre-existing Renal Chronicity Index (CI).

Methods: We analyzed two patients with refractory Class V Lupus Nephritis (LN) who failed prior single-target CD19 CAR-T therapy and were salvaged with autologous bispecific CD19/BCMA CAR-T. We correlated immunological depth of response (B-cell aplasia, serology) with histological markers of kidney damage (biopsy Chronicity Index) and clinical outcomes (proteinuria).

Results: 1. Immunological Uniformity (The "Salvage" Success):
Both patients achieved robust CAR-T expansion and deep immunological remission post-rescue, overcoming the limitations of prior therapies.
•Seroconversion: Anti-dsDNA and ANA turned negative in both patients within 45 days.
•Biomarker of Eradication: Sustained B-cell aplasia (0/μL) and low IgG levels confirmed the complete destruction of the pathogenic LLPC reservoir.
2Divergent Renal Outcomes (The "Point of No Return"):
Despite identical immune clearance, clinical trajectories diverged sharply based on histological chronicity.
•Patient 1 (Functional Cure): Had a history of active inflammation but preserved renal architecture. Following a "lag phase," her massive proteinuria normalized (<0.15 g/24h) by Month 9, allowing for Drug-Free Remission.
•Patient 2 (33y, Class V LN, 11y history):
◦Clinical Status: Despite successful salvage (no CRS/ICANS vs. Grade 2 CRS in prior trial)

and serological improvement, she presented with massive nephrotic syndrome (Proteinuria 13.14 g/24h, Albumin 23.4 g/L) at 1-month post-rescue.
◦The "Smoking Gun": Renal biopsy revealed a Chronicity Index (CI) of 5 (Glomerulosclerosis 1, Fibrous Crescents 2, Interstitial Fibrosis 1).
◦Mechanism: While CAR-T successfully extinguished the autoimmune "fire," the "burnt structure" (fibrosis and sclerosis) prevented proteinuria resolution. The massive proteinuria reflects irreversible podocyte injury and basement membrane damage, rather than active immune complex deposition.

Table 1: Immunological Rescue vs. Histological Reality

Parameter	Patient 1 (Functional Cure)	Patient 2 (Irreversible Damage)	Clinical Implication
Prior History	Refractory LN (11y)	Refractory Class V LN (11y)	Long disease duration
Prior CAR-T	Failed Universal-CD19 CART	Failed Universal CD19 CART	Need for "Salvage"
Rescue Therapy	Autologous 19-BCMA	Autologous 19-BCMA	Successful Engraftment
Immunology	Seroconversion (Neg)	Seroconversion (Neg)	Universal Immune Efficacy
Renal Biopsy	Active Inflammation	Chronicity Index (CI) = 5	The Determining Factor
Proteinuria	Normalized (<0.15 g)	Persistent Massive (13.1 g)	Structural Damage
Outcome	Drug-Free Remission	Symptomatic Management	Limit of Regeneration

Conclusions: Autologous 19-BCMA CAR-T is a highly effective salvage strategy for immunological relapse, reliably inducing deep serological remission where universal CD19 therapy fails. However, our data unmask a critical limitation: Immunological cure does not guarantee organ restitution if the "Window of Opportunity" is missed. A Chronicity Index (CI) ≥ 5 may predict persistent proteinuria despite successful B-cell eradication. This underscores the urgent need to deploy dual-targeting CAR-T earlier in the disease course, before irreversible organ damage precludes functional recovery.

Disclosure: Nothing to declare

OS20-06

GENOMIC INSTABILITY AND HIGH MUTATION BURDEN IN FIBROBLASTS OF SYSTEMIC SCLEROSIS PATIENTS ARE IMPROVED IN CLINICAL RESPONDERS TO AUTOLOGOUS HSCT

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Background: Diffuse cutaneous systemic sclerosis (dcSSc) is a lethal rheumatic disease that is characterized by progressive skin and visceral fibrosis. Autologous hematopoietic stem cell transplant (AHSCT) is known to improve the quality of life and survival of dcSSc patients. However, the mechanism of action is poorly understood. We and others have recently shown that, similar to cancer cells, genomic instability is an important feature of dcSSc fibroblasts. In this cross-sectional study, we compared the genomic instability and mutational landscape in skin/fibroblasts from dcSSc patients not treated with AHSCT (dcSSc patients) vs treated with AHSCT (post-AHSCT patients).

Methods: We recruited 25 dcSSc patients and 9 post-AHSCT patients (median 12 months posttransplant). We performed whole exome sequencing (WES) on microdissected dermis from each patient and determined the mutational frequencies by comparing DNA sequences from the microdissected dermis with autologous DNA from buccal samples using two pipelines (MuTect2 and Strelka). We also generated dermal fibroblasts (DFs) from the patients and from age&sex-matched healthy controls, and measured the number of double strand breaks (DSB, using pH2AX immunostain).

Results: We identified frequent recurrent mutations in dcSSc patients, including in genes commonly mutated in cancer. The most frequently mutated gene was MUC16, also called CA125. (Fig. 1A). MUC16 mutations were associated with SSc severity (Fig.1A, patients with severe dcSSc are marked red). AHSCT resulted in decreased MUC16 mutations (in particular) as well as recurrent mutations (in general) – the number of mutations per genome was 678 in the dcSSc patients vs 74 in the postAHSCT patients ($p<0.01$), with particularly low number of mutations in AHSCT responders (dark green in Fig. 1B, non-responders are marked in yellow). Importantly, the number of DSBs was higher in dcSSc patients compared to post-AHSCT patients (mean 15 vs 5 pH2AX foci per nucleus, $p<0.05$) as well as compared to healthy controls (mean 5 pH2AX foci per nucleus, $p<0.05$). Preliminarily, patient fibroblasts also appeared resistant to apoptosis, further supporting their cancer-like characteristics.

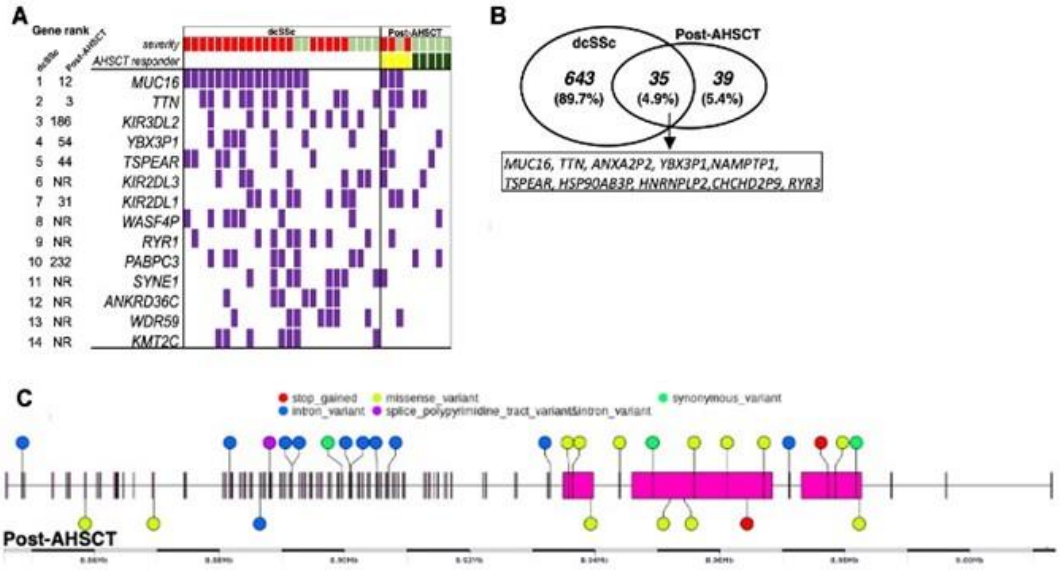

Fig. 1. A. MUC16 is the most frequently mutated gene in the dermis of dcSSc patients. B. AHSCT reduces recurrent mutations. C. Map showing types/locations of the recurrent mutations present in MUC16.

Conclusions: Genomic instability-associated high mutation burden in fibroblasts from dcSSc patients is virtually abrogated in AHSCT responders. We speculate that the AHSCT conditioning chemo/radiotherapy kills the cancer-like fibroblasts and that these cells are replaced by healthy fibroblasts, which might originate from hematopoietic stem cells.

Disclosure: Nothing to declare (no conflict of interest).
Funding: Canadian Institute for Health Research, National Scleroderma Foundation. MO is supported by Arthritis-Society-STAR/IMHA award (Award 00049).
Disclosure of encore abstract: Similar abstract will be presented at the 9th Systemic Sclerosis World Congress on March 5-7, 2026 in Athens, Greece.

B338

DANICOPAN ADD-ON THERAPY DEMONSTRATES POSITIVE EFFICACY AND SAFETY IN ADVANCED AGE ADULTS WITH PNH AND CLINICALLY SIGNIFICANT EXTRAVASCULAR HEMOLYSIS: PHASE 3 ALPHA TRIAL SUB-ANALYSIS

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Background: Danicopan (oral factor D inhibitor) add-on therapy showed significant clinical improvements in adult patients with ravulizumab- or eculizumab-treated paroxysmal nocturnal hemoglobinuria (PNH) and clinically significant extravascular hemolysis ([csEVH] hemoglobin [Hb] <9.5 g/dL; absolute reticulocyte count [ARC] ≥120×10^9/L), in phase 3 ALPHA trial (NCT04469465). There is limited evidence whether this translates to advanced age patients (≥65 years [y]). This study characterized efficacy and safety of danicopan add-on therapy in advanced age patients with PNH and csEVH from ALPHA trial.

Methods: This sub-analysis focused on primary treatment period, during which adult patients (≥18y) with PNH and csEVH with ≥6 months of ravulizumab or eculizumab treatment were randomized 2:1 to add-on danicopan or placebo for 12 weeks. Outcomes were evaluated by age at study enrollment (≥65y and <65y): change from baseline in Hb concentration, ARC, and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score up to 12 weeks; proportion of patients who were transfusion-independent at 12 weeks; and proportion of patients with adverse events (AEs) during 12-week period.

Results: Eighty-six patients were enrolled into ALPHA; 57 randomized to add-on danicopan (≥65y, n=16; <65y, n=41), and 29 randomized to add-on placebo (≥65y, n=6; <65y, n=23). Mean (SD) baseline clinical characteristics were similar between age groups in danicopan (≥65y vs <65y: Hb, 7.6 [0.9] vs 7.7 [1.0] g/dL; ARC, 216.0 [40.4]×10^9/L vs 260.0 [109.8]×10^9/L; FACIT-F, 36.0 [8.5] vs 33.2 [12.2]) and placebo arms (≥65y vs <65y: Hb, 8.3 [0.8] vs 7.8 [0.1] g/dL; ARC, 201.1 [69.1]×10^9/L vs 228.6 [125.7]×10^9/L; FACIT-F, 38.3 [9.2] vs 29.9 [10.9]). In danicopan arm, both age groups showed increase in mean (SD) Hb from baseline to week 1 (≥65y vs <65y: 2.7 [1.0] vs 1.9 [1.0] g/dL); maintained in patients aged ≥65y and improved in those aged <65y through week 12 (≥65y, 2.8 [1.7] g/dL, 50.0% with ≥2.0 g/dL increase; <65y: 3.1 [1.4] g/dL, 56.1% with ≥2.0 g/dL increase). Both age groups demonstrated meaningful reduction in ARC (≥65y, −51.2 [74.4]×10^9/L; <65y, −105.3 [97.7]×10^9/L) and increases in FACIT-F score (≥65y, +4.9 [6.4]; <65y, +9.4 [7.9]). Conversely, placebo arm showed no improvements in Hb, ARC or FACIT-F from baseline to week 12 (≥65y vs <65y: Hb, 0.5 [0.6] vs 0.8 [0.9] g/dL; ARC, 9.0 [39.0]×10^9/L vs 0.1 [54.2]×10^9/L; FACIT-F, −4.0 [6.1] vs 4.6 [9.4]). In danicopan arm, proportion of transfusion-independent patients at week 12 was similar between age groups

(≥65y vs <65y: 75.0% vs 80.5%) and higher than placebo arm (30.4% vs 16.7%). Proportion of patients experiencing AEs in danicopan arm was similar between age groups (≥65y vs <65y: 68.8% vs 78.0%) and lower in placebo arm (≥65y vs <65y: 50.0% vs 65.2%).

Conclusions: This sub-analysis demonstrates that danicopan add-on to ravulizumab or eculizumab has positive efficacy and safety profile in advanced age patients with PNH and csEVH. During 12 weeks of danicopan therapy, patients reported meaningful improvements in Hb and ARC, maintained transfusion avoidance, and reported low rate of AEs.

Disclosure: **Austin Kulasekararaj** holds stock options in Pfizer; reports honoraria from Agios, Alexion (AstraZeneca Rare Disease), Amgen, Celgene/Bristol Myers Squibb, Novartis, Pfizer, Roche, Samsung, Sobi; reports being a consultant (includes expert testimony) for AbbVie, Alexion (AstraZeneca Rare Disease), Celgene/Bristol Myers Squibb, Janssen, Novartis, Novo Nordisk, Pfizer, Roche, Samsung, Sobi. **Morag Griffin** reports being a consultant (includes expert testimony) for Sobi, BioCryst, Amgen, Omeros, Regeneron, Pfizer, Alexion (AstraZeneca Rare Disease), Novartis. **Robert Brodsky** reports research funding from Alexion (AstraZeneca Rare Disease). **Jun-ichi Nishimura** reports honoraria and research funding from Alexion (AstraZeneca Rare Disease); reports being a consultant (includes expert testimony) for Sobi, Asahikasei, Alexion (AstraZeneca Rare Disease), Novartis, Roche, Chugai. **Christopher Patriquin** reports being a consultant (includes expert testimony) for Novartis, Sobi, Roche, Alexion (AstraZeneca Rare Disease), Takeda, BioCryst, Sanofi. **Hubert Schrezenmeier** is an inventor (together with others) of patent application(s) that describe the use of complement inhibitors for therapeutic applications, holds patents and receives royalties; reports honoraria from Alexion (AstraZeneca Rare Disease), Novartis; reports being a consultant (includes expert testimony) for Alexion (AstraZeneca Rare Disease), Novartis, Omeros, Sobi. **Wilma Barcellini** reports being a consultant (includes expert testimony) for Sobi, Recordati, Alexion (AstraZeneca Rare Disease), Novartis, Sanofi, Roche; reports research funding from Alexion (AstraZeneca Rare Disease). **Anna Gaya** reports honoraria from Alexion (AstraZeneca Rare Disease), Novartis, Roche, Sobi; reports being a consultant (includes expert testimony) for Alexion (AstraZeneca Rare Disease), Novartis, Roche. **Flore Sicre-de-Fontbrune** reports honoraria from Novartis, Sobi, Samsung, Alexion (AstraZeneca Rare Disease); reports research funding from Novartis, Sobi, Alexion (AstraZeneca Rare Disease). **Jong Wook Lee** reports honorarium from Alexion (AstraZeneca Rare Disease); reports being a consultant (includes expert testimony) for Kyowa Kirin, Novartis, Alexion (AstraZeneca Rare Disease). **Yogesh Patel**, **Ying Tang**, **Gleb Filippov**, and **Mohammed Mahdi** are employees of Alexion, AstraZeneca Rare Disease.

B339

HETEROGENEOUS NON-HEMATOLOGIC AUTOIMMUNE COMPLICATIONS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC LEUKEMIA: INCIDENCE, SPECTRUM, AND OUTCOMES IN A SINGLE-CENTER COHORT

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Background: Autoimmune diseases (ADs) are rare, non-GvHD immune-mediated complications, often underdiagnosed after Allo-HSCT. The precise mechanisms remain poorly understood due to the complex interactions between impaired immune-system reconstitution and various transplant-related factors. The clinical manifestations vary widely, depending on the underlying disease, ranging from hematologic to non-hematologic, organ-specific, or systemic involvement. Diagnosis and treatment of ADs are challenging, and the response to immunosuppressive therapies is often either incomplete or transient, with no standardized guidelines addressing the optimal approach to managing this potentially life-threatening complication. We aimed to evaluate the incidence, risk factors, and treatment of non-hematologic ADs after HSCT in pediatric patients with leukemia. To our knowledge, this study provides the first report of non-hematologic ADs in pediatric leukemia patients following Allo-HSCT.

Methods: We retrospectively analyzed 140 pediatric leukemia patients (95 ALL, 43 AML, 2 CML) who underwent Allo-HSCT from Jan 2017 to Mar 2023 at the Children's Medical Center, the country's central HSCT department.

Results: The incidence of non-hematologic ADs after Allo-HSCT was 5.7% (8/140), with a median time to the onset of autoimmunity of 13.73 months [7.54-29.31]. The median age at transplant was 9.04 years [0.83-17.9] for the non-AD group and 9.62 years [7-15] for the AD group (p=0.515). Observed ADs included Nephrotic Syndrome (n=3), Autoimmune Hepatitis accompanied by nephrotic syndrome (n=1), Vitiligo (n=2), Scleroderma (n=1), and Transverse myelitis (n=1).
All patients underwent a non-TBI myeloablative conditioning regimen (Busulfan, Cyclophosphamide, +/- rabbit-ATG). The majority of patients received HSCT from a fully matched donor, with PB as the primary graft source (127 non-AD, 8 AD). No statistically significant differences were observed between the two groups regarding donor or recipient gender, donor relationship, graft source, HLA matching, cytomegalovirus reactivation, aGvHD, or graft rejection. The relapse rate was 29.5% in the non-autoimmune group and 12.5% in the autoimmune group (p=0.439). cGVHD was significantly higher in the Autoimmune Group (75% vs. 36.4%, p=0.05).
Three patients with nephrotic syndrome were treated with systemic steroids and Mycophenolate in 2 cases, and cyclosporin in 1. The patient with autoimmune hepatitis and nephrotic syndrome received steroids, tacrolimus, and azathioprine. Two patients with vitiligo, initially resistant, were finally treated with prednisolone and Ruxolitinib. The patient with Transverse myelitis was treated with corticosteroid pulse, IVIG, and plasmapheresis.

The patient with Scleroderma was treated with systemic steroids and sirolimus. All achieved complete response.
The 3-year OS and DFS rates were 61% and 58.7% in the non-autoimmune group, compared with 83% and 82.3% in the autoimmune group (p=0.096 and 0.81, respectively).

Conclusions: Post-HSCT non-hematologic ADs in pediatric leukemia patients are diverse and differ from those in non-malignant diseases. The rate of AD incidence is consistent with prior research findings. cGvHD was associated with the development of ADs in this study, potentially due to a shared mechanism with autoimmunity, attributable to dysregulated immune reconstitution and impaired self-tolerance post-HSCT. Additionally, the relapse rate may reflect an increased graft-versus-leukemia effect in autoimmune patients. Early recognition and standardized management strategies are essential, as timely, tailored immunomodulatory therapy leads to high response rates and may improve long-term outcomes.

Disclosure: Nothing to declare.

B340

FROM VISION TO REALITY: EVALUATING SAFETY OF THE FIRST IN HOUSE IMPLEMENTED CD19 CAR-T IN UNITED ARAB EMIRATES FOR SLE PATIENTS

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Background: SLE poses a substantial burden in the UAE and Middle East, with an age-standardized incidence of ~8.6/100,000 per year, a prevalence of ~103/100,000, and a mean diagnostic age of 28 years in Emirati patients. Biologic B-cell–targeted therapies such as rituximab and BAFF (BlyS) inhibitor therapy such as belimumab have advanced disease control by reducing autoantibody production and modulating immune activation. For refractory cases, autologous stem cell transplantation provides an immune reset, achieving remission in approximately two-thirds of patients but with notable treatment-related mortality. CD19 CAR-T cell therapy offers a deeper and more durable immune reprogramming by eliminating a broad spectrum of B-cell populations, with early data showing sustained disease control. This poster presents the first implementation and safety outcomes of locally manufactured CD19 CAR-T therapy in the UAE.

Methods: Patients meeting stringent disease-specific criteria—including the 2019 ACR/EULAR SLE classification, active organ involvement (≥1 BILAG A or ≥2 BILAG B), persistent seropositivity, and failure of at least two to three immunosuppressive agents—are first evaluated by rheumatologists. Multidisciplinary meetings with rheumatology and

hematology ensure coordinated assessment and eligibility. Three candidates were identified and underwent comprehensive screening to confirm fitness for the CAR-T process, including tolerance of leukapheresis, lymphodepletion chemotherapy, and appropriate immunosuppressive washout. Autologous leukapheresis was performed using the Spectra Optia platform to collect approximately 2 × 10^9 $CD3^+$ T cells, subsequently transduced in a GMP-compliant facility using the CliniMACS Prodigy system and a CD19-targeted lentiviral vector. After rigorous quality control—including sterility, immunophenotyping, and vector copy number—patients received lymphodepletion with fludarabine (25 mg/m^2 for three days) and cyclophosphamide (1,000 mg/m^2 for one day). A single infusion of 1.0 × 10^6 CD19 CAR-T cells/kg was administered, with expansion monitored by flow cytometry and clinical response evaluated through serologic markers and organ assessments. Adverse events were graded per 2018 ASTCT consensus criteria.

Results:

Characteristics	Patient 1	Patient 2	Patient 3
Age	61	39	42
Sex	F	M	F
Disease Duration	21 years	25 years	7 years
Indication	SLE with refractory ITP and AIHA (BILAG A)	SLE with antiphospholipid syndrome & acquired haemophilia (BILAG A)	Refractory lupus nephritis (IV/V A) (SELENA-SLEDAI 17)
ICU Admission	1 day	0	0
WBC Recovery	Day +11	Day +9	Day +7
CAR-T Expansion	Day +10 (69.0%)	Day +10 (47.18%)	Day +10 (41.20%)
CRS	Grade 1 (Tocilizumab)	Grade 1 (Tocilizumab)	Grade 0
ICANS	0	0	0
Admission (days)	30	22	14
Post CAR-T Follow-up	12 months	7 months	4 months
Post-discharge Infections	CMV reactivation (valganciclovir)	URTI	CMV reactivation (valganciclovir)
Hypogammaglobulinemia	No	No	No
B cell Recovery	D+124	D+54	Pending
Clinical condition	Drug-free remission; active, exercising, No episode of ITP or AIHA (BILAG D)	Drug-free lupus remission; improved life quality & fatigue; LMWH prophylaxis (BILAG D)	Off all IS; Prednisolone 3 mg daily; C3/C4 NL; remission (SLEENA-SLEDAI 2)

The three patients with systemic lupus erythematosus (SLE) treated with CD19 CAR-T therapy had a mean age of 47 years (range 39–61) and included two females and one male. Median disease duration was 21 years (range 7–23), with significant baseline comorbidities including refractory immune thrombocytopenia, autoimmune hemolytic anemia, recurrent thrombosis, life threatening bleeding episodes complicated with acquired hemophilia A and class IV/V active lupus nephritis. Hematologic recovery was rapid, with a mean WBC

recovery by Day +9 (range Day +7 to Day +11), and CAR-T expansion averaged 52% (range 41–69%). Treatment demonstrated a favorable safety profile: two patients developed grade <3 cytokine release syndrome resolving after a single tocilizumab dose, and no grade ≥4 CRS or ICANS occurred. One patient developed Local Immune Effector Cell–Associated Toxicity Syndrome (LICATS), which resolved within a month on steroids. Two patients experienced CMV reactivation, managed successfully with oral valganciclovir. All patients are alive and off immunosuppressive therapy at a median six-month follow-up, with one maintaining remission for one year.

Conclusions: UAE's locally produced CD19 CAR-T therapy for SLE shows feasibility, safety, and powerful efficacy, inspiring a bold new era of accessible cellular treatments transforming autoimmune care worldwide for patients.

Clinical Trial Registry: NA

Disclosure: no conflict

B341

REDUCTION OF INTERLEUKIN-6 AND INTERLEUKIN-8-MEDIATED INFLAMMATION AND PROLIFERATION IN SKIN FIBROBLASTS IN SYSTEMIC SCLEROSIS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION MEASURED BY GENE EXPRESSION ANALYSES

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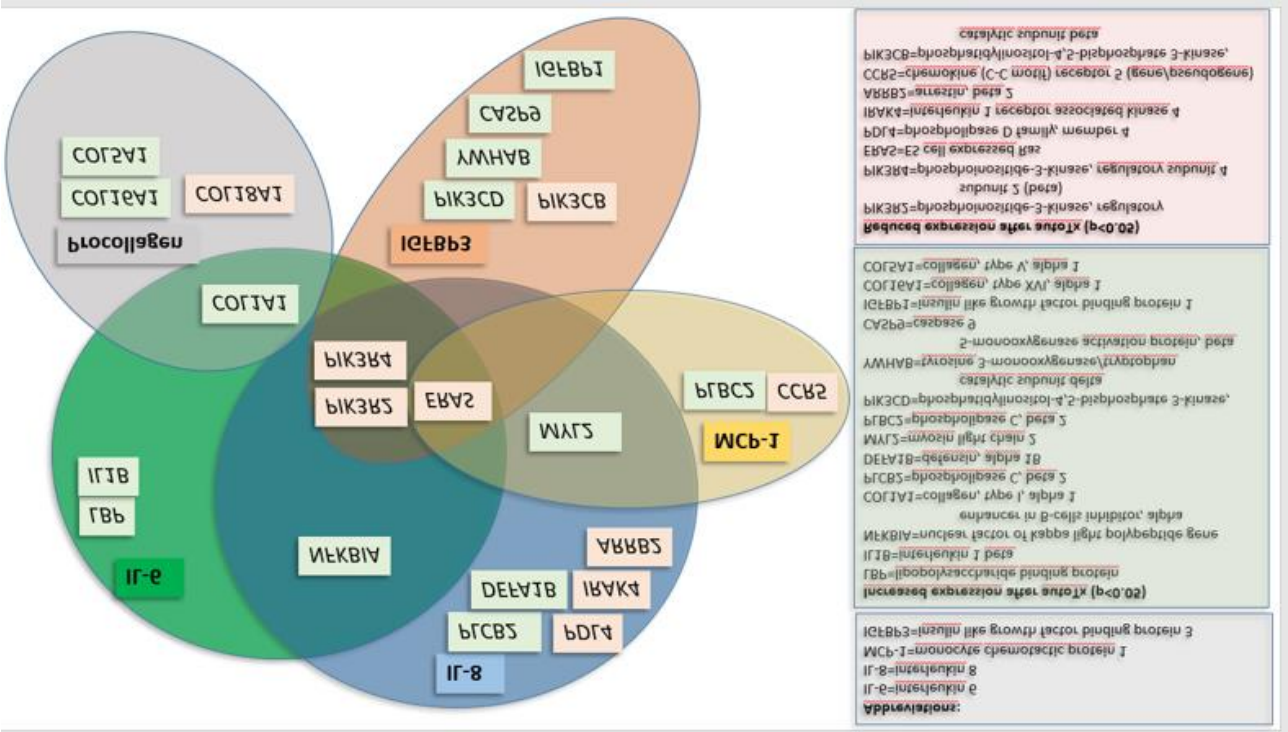
Background: Systemic sclerosis (SSc) is an autoimmune connective tissue disease defined by fibrosis of the skin and internal organs. Early severe courses of SSc should be treated with intensified therapy such as hematopoietic stem cell transplantation (autoTx). The effect of the therapy is evident, particulary, in a reduction in skin fibrosis and its complications. However, it is not yet sufficiently clear which pathogenetic mechanisms can be influenced by autoTx.

Methods: Here we investigated cultures of skin fibroblasts derived from 4 SSc patients by skin biopsy (4 months) prior to and after successful autoTx. SSc patients (n=4, aged 43 to 59 years, male/female: 2/2) underwent a skin biopsy of the lateral abdominal wall or forearm. After 4 passages of the cell culture according to standard procedure (native or TGF-beta stimulated), the cell supernatant was tested for concentrations of the following

chemokines: interleukin-6, interleukin-8, MPC-1 (monocyte chemotactic protein–1), procollagen, IGFBP3 (insulin-like growth factor binding protein 3); in addition, the genes (n=341) belonging to the gene family of the above-mentioned chemokines were examined and evaluated with microarray (mRNA concentrations) before and after autoTx. The differences in expression before and after autoTx were evaluated using t-test (and Fisher's correction). The ethics committee of the Saarland Medical Association has approved the experimental study (EK120/23).

Results: IL-6, IL-8, MCP-1, and IGFPB3 secreted by skin fibroblasts showed a reduced cell supernatant concentration in SSc patients after autoTx whereas the procollagen secretion increased: IL-6 (native) 0.13 vs. 0.07 ng/ml, p=0.06; IL-8 (TGF-beta stimulated) 1688 vs. 728 ng/ml, p=0.01; MCP-1 (native) 0.38 vs. 0.36, p=0.79; IGFBP3 (native) 18.7 vs. 5.5, p=0.02; procollagen (native) 800 vs. 1232 pg/ml, p=0.03. Following gene expression analysis of the cell supernatant, Figure 1 shows the change in expression of the respective gene when it increases (green) or decreases (red) significantly ($p<0.05$) in comparison to pre-autoTx. For several chemokines at the same time, the significant upregulation of the NFKBIA gene (nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha) appears to be important for the inhibition of inflammation, and the MYL2 gene (myosin light chain 2) preferentially for the activation of repair mechanisms; On the other hand, PIK3R2 (phosphoinositide-3-kinase, regulatory subunit 2beta), PIK3R4 (phosphoinositide-3-kinase, regulatory subunit 4), and ERAS (ES cell expressed Ras) are significantly downregulated by autoTx as inflammation/proliferation-mediating genes.



Conclusions: Consecutive skin biopsies in SSc patients after therapy with autoTx show activation of certain genes at the molecular level with predominantly anti-inflammatory

and/or anti-fibrotic regenerative effects. The extent to which the data suggest staging with skin biopsy for therapy management in SSc remains unclear due to the small number of cases.

Clinical Trial Registry: n.a.

Disclosure: Nothing to declare

B342

SAFETY OF RAVULIZUMAB USE IN PREGNANCY: INSIGHTS FROM A GLOBAL PHARMACOVIGILANCE ANALYSIS

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Background: Ravulizumab, a second-generation C5 complement inhibitor and an analog of eculizumab, is approved for the treatment of hematologic and complement-mediated disorders including paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) in adults and pediatric patients, as well as rare autoimmune diseases (generalized myasthenia gravis [gMG] and neuromyelitis optica spectrum disorder [NMOSD]) in adults. PNH and aHUS are disorders associated with high maternal and fetal morbidity in pregnancy. There are multiple reports on the use of eculizumab (approved for the same four indications) in pregnant patients where no safety signals have been observed. However, the safety profile of ravulizumab with respect to use during pregnancy and lactation, including its potential effects on fetal development and breastfed infants remain incomplete. This analysis aims to provide insights into pregnancy-related safety following ravulizumab exposure using data from global post-marketing surveillance.

Methods: Here, we analyze all pregnancy cases reported globally in the post-marketing setting of ravulizumab, with ≥1 documented dose of exposure. Data from both spontaneous and solicited cases recorded in the Alexion pharmacovigilance database from the initial market approval up to June 26, 2025 were included in the analysis. Descriptive statistics were used to summarize patient demographics, treatment patterns, and pregnancy outcomes.

Results: Among the 256 identified pregnancy cases with ≥1 dose of ravulizumab exposure, hematologic conditions represented a substantial proportion of underlying maternal diagnoses (PNH [n=117], aHUS [n=56]). Of the non-hematologic conditions, underlying maternal diagnosis included gMG (n=29) and NMOSD (n=12). Among 79 cases with data on pregnancy outcomes, the distribution of ravulizumab exposure included full-pregnancy exposure in 26.6%, ravulizumab to eculizumab switch during pregnancy in 26.6% and incomplete exposure details reported in 43.1%. Pregnancy outcomes included live births (n=51), spontaneous abortions (n=22), fetal deaths (n=3), and elective terminations (n=3). Moreover, in a subset of 38 pregnancies (PNH [n=19]) more detailed information was available on ravulizumab exposure. Maternal co-morbidities reported, predominantly in PNH,

were aplastic anemia (n=4), Budd-Chiari syndrome (n=2), hypertension including gestational (n=3), and gestational diabetes (n=1). In this subset, 29 were live births (PNH [n=15]), of which, 16 had ravulizumab exposure throughout all trimesters, 3 had exposure beyond 12 weeks but discontinued prior to delivery, and 8 had exposure limited to the first trimester (≤12 weeks).

Conclusions: This analysis provides real-world insights on the use of ravulizumab in pregnancy and suggests no unexpected safety signals, similar to analyses on the use of eculizumab during pregnancy. These findings may inform clinical decision-making. As additional data are needed, a global observational study (NCT06312644) evaluating the safety of ravulizumab during pregnancy is currently ongoing.

Disclosure: Heather Sherrard was an employee of Alexion, AstraZeneca Rare Disease at the time of the analysis.
Cynthia Carrillo Infante, Arshad Mujeebuddin and Cory Williams are employees of Alexion, AstraZeneca Rare Disease.

B343

MMR SEROLOGIC STATUS IN MULTIPLE SCLEROSIS AFTER AUTOLOGOUS STEM CELL TRANSPLANTATION

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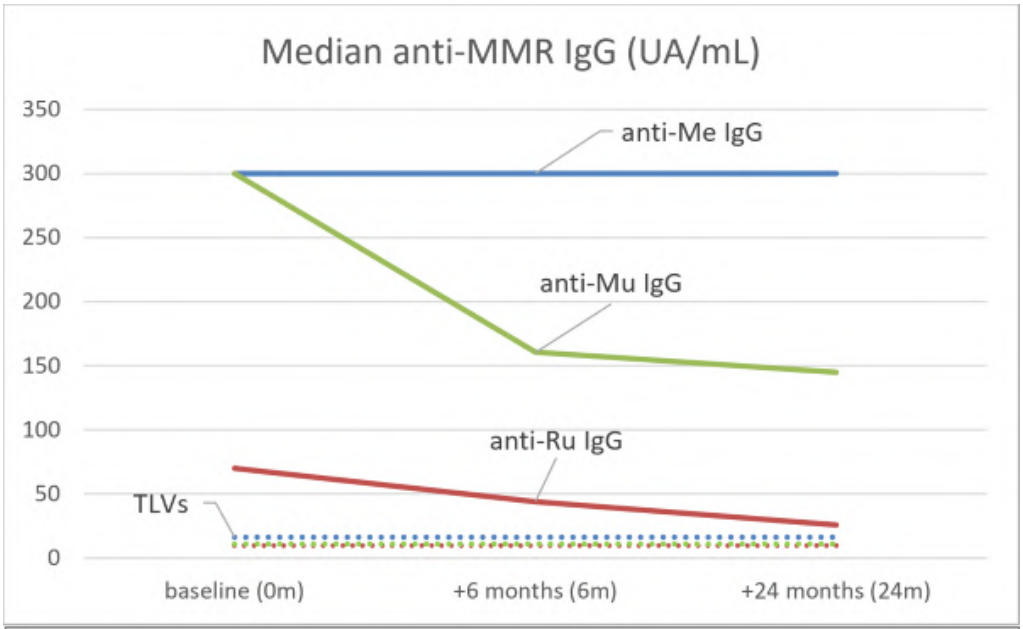
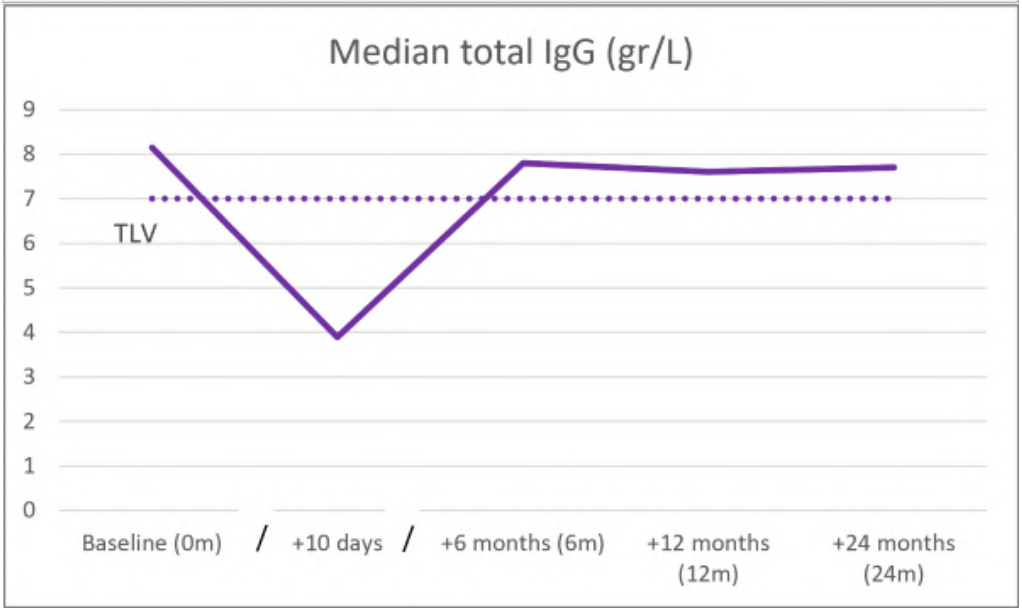
Background: Multiple sclerosis (MS) patients undergoing autologous stem cell transplantation (ASCT) after carmustine, cytarabine, etoposide, melphalan (BEAM) or cyclophosphamide (Cy) chemotherapy plus rabbit anti-thymocyte globulin (rATG) are considered as naïve to vaccines and offered revaccination; live vaccines as measles/mumps/rubella (MMR) are not recommended before 24 months from ASCT with concern about vaccine-induced infectious disease.

Methods: We retrospectively analysed MMR specific IgG at baseline (0m), 6 months (6m); 24 months (24m) in MS patients transplanted in Florence over a 10-year period (29/04/2015 - 07/04/2025). Due to a laboratory-technique change, qualitative data (positive, intermediate, negative) were available for the whole study population while quantitative IgG titles were available only for a subgroup. Median IgG titles at 0m, 6m, 24m were compared with median total IgG trend in the same patients at the same time points and in two additional at 10 days and 12 months (12m) after ASCT.

Results: Among 65 patients transplanted in the index period, 39 had at least one post-ASCT assessment at 6m or 24m (M/F ratio: 8/31; median age: 40; median prior lines of therapy: 3, range 1-7; BEAM-rATG/CY-rATG conditioning: 36/3; rATG dose 7.5 mg/5 mgKg: 37/2).

None of patients experienced clinical MMR infection or received immunization after ASCT.Data were available at all the timepoints (0m; 6m; 24m) for 16/39 patients (41%); 14/39 (35.9%) were evaluable at baseline and at a single post-ASCT timepoint (eight at 6m; six at 24m), whereas 9/39 (23.1%) had the 24m assessment only. All the patients except for two (28/30) maintained baseline MMR serologic status post-ASCT. The two patients who lost either MMR (ID23) or rubella immunity (ID35) had both low titles at baseline; prior to ASCT, they had received interferon and 3 lines of therapy (interferon, fingolimod, ocrelizumab), respectively. The 9 patients evaluable at 24m only were all MMR IgG positive, hence putatively maintaining a pre-ASCT positivity.
In the whole cohort 37/39 (94.9%) patients maintained MMR baseline immune status at 6m and 29/31 (93.5%) at 24m.
Regarding MMR IgG title,14/39 (35.9%) patients were evaluable between 0-6 and 24 months: median values over time in comparison with median total IgG and relative threshold limit values (TLVs) are shown in figure 1. Measles specific IgG were the most stable, while mumps and rubella declined over time. Total IgG decreased earlier with a nadir at +10 days and full recovery before 6m after ASCT.





Conclusions: In our real-life population of ASCT-treated MS, the vast majority of patients retained MMR immunity with a slight decline of vaccine titres over time confirming that MMR revaccination could be safely postponed after 24 months from ASCT and probably offered only in selected patients at high risk (i.e. low titles at baseline, work exposure). The different time trend between total and specific IgG titres, rapidly returning to normal and stable values and declining over time, respectively, may represent an indirect demonstration of a reassortment of IgG idiotypes following plasma cells and B cells repertoire modification in the context of the well-known immune-reset after ASCT in MS.

Disclosure: Nothing to declare.

B344

INFECTIOUS COMPLICATIONS IN DUTCH MS-PATIENTS WITHIN THE FIRST YEAR AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A FOREIGN COUNTRY

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Background: Autologous hematopoietic stem cell transplantation (aHSCT) is only imbursed to a limited extent as a treatment for Multiple Sclerosis (MS). This results in Dutch patients looking for aHSCT treatment abroad. The aim of the study is to investigate infectious complications and mortality in self-referred MS patients who have traveled abroad to undergo HSCT.

Methods: Through retrospective cohort examination of 53 patient files of Dutch MS-patients who have been treated on their own initiative with aHSCT in a foreign country, the number of infections and mortality within a year after the treatment, have been analysed using descriptive statistics. The results are compared to data that have been found through literature research concerning MS-patients who have undergone aHSCT in their own country.

Results: 53 patients were included (71.7% women, the average age at the time of treatment is 41.6 (range: 24-62). Of these 50.9% had relapsing remitting MS (RRMS), 26.4% had secondary progressive MS (SPMS) and 22.6% had primary progressive MS (PPMS). The treatment they received was in the following countries: 37 patients in Mexico, 12 in Russia (Moscow), 1 in Norway, 1 in Sweden, and 2 in Belgium. The number of infections the patients had was compared with that of 507 American MS-patients who underwent aHSCT in the United States (62.3% women), average age 36.6 (range: 17-60), 81.7% had RRMS, 18.3% had SPMS, none had PPMS. The Dutch patients had, on average, 1 infection during the year after aHSCT. The American reference group had, on average, 0.51 infections in the year after aHSCT. In the population as a whole, people on average have 2-4 infections per year. The mortality (0 deceased patients) among the Dutch patients was compared to patients who underwent aHSCT in their own country (United States (507 patients, 1 deceased (0.19%)).

Conclusions: This study shows that among patients with MS who travel abroad on their own initiative to undergo aHSCT, there is no increased mortality after returning home compared with MS patients treated within their own country. The number of infections is, while higher than the group treated in their own country, still low and not statistically significant. Compared with the literature, patients who self-referred include a higher proportion with

progressive MS, a condition known to make patients more prone to infections due to a usually higher level of disability and higher age compared to patients with RRMS.

Disclosure: Nothing to declare

B345

NUMBER OF CD34 CELLS EMPLOYED IN AUTOLOGOUS HEMATOPOIETIC STEM-CELL TRANSPLANTATION FOR PERSONS WITH MULTIPLE SCLEROSIS IS NOT RELATED TO THE NEUROLOGICAL OUTCOME OF THE PROCEDURE

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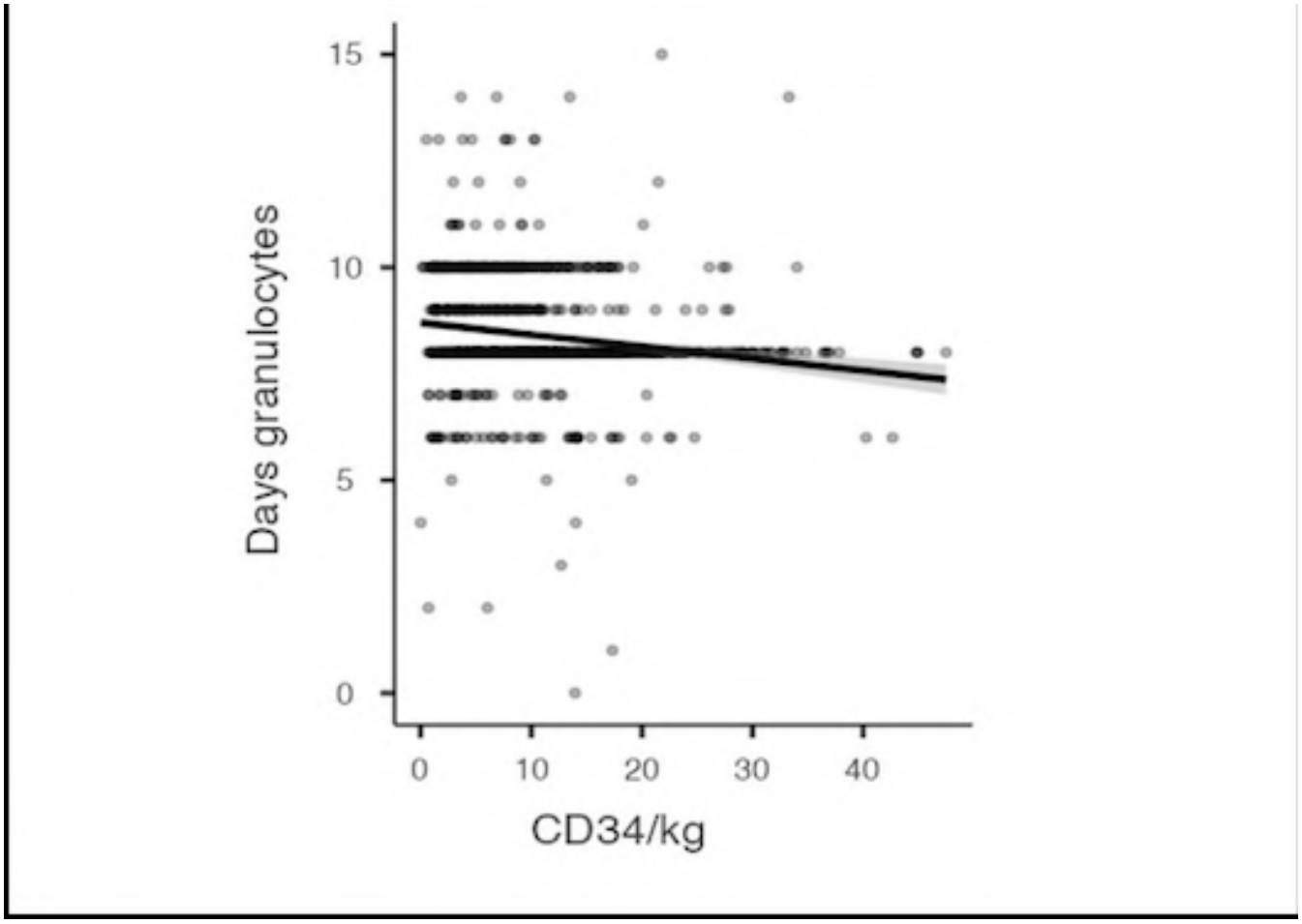
Background: CD34 is expressed on hematopoietic stem and progenitor cells (HSPCs) and is widely used to assess graft adequacy in transplantation. Autologous HSCT (aHSCT) has become an effective treatment for multiple sclerosis (MS), but the relationship between infused $CD34^+$ cell dose and neurological outcomes remains unclear.

Methods: We retrospectively analyzed 1 417 MS patients (64.6% women; median age 46 years) who underwent aHSCT at HSCT Mexico between June 2015 and March 2025. Mobilization used cyclophosphamide (50 mg/kg) and filgrastim (10 µg/kg/day); products were infused fresh without cryopreservation. Conditioning followed the "Mexican Method" (high-dose cyclophosphamide + rituximab). Neurological response was defined as stabilization or improvement in EDSS after transplant. Median $CD34^+$ dose was 8.27×10^6 cells/kg (IQR 4.4–12.9).

Results: Median recovery for granulocytes > 0.5×10^9/L and platelets > 20×10^9/L was 8 and 10 days. Correlations between $CD34^+$ dose and hematologic recovery were weak ($r = -0.169$ and -0.012). Among 564 patients with follow-up, 460 (81%) achieved neurological stabilization or improvement, with similar rates across MS subtypes (RRMS 81.3%, PPMS 82.5%, SPMS 83%). The correlation between $CD34^+$ dose and neurological response was negligible ($r = 0.016$).



Conclusions: Thus, aHSCT induces neurological benefit in MS independent of CD34⁺ dose, supporting the efficacy of the outpatient "Mexican Method".

Disclosure: Nothing to declare.

B346

BEYOND STEM CELLS; DUAL NK-CELL POPULATION IN STEM CELL GRAFT MAY CONTRIBUTE TO IMMUNE RESET POST AUTOLOGOUS STEM CELL TRANSPLANTATION FOR MULTIPLE SCLEROSIS

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Background: Autologous stem cell transplantation (ASCT) is emerging as an important therapeutic modality for patients with relapsing-remitting multiple sclerosis (MS) after previous lines of highly effective disease-modifying treatments. We previously described immune recovery post ASCT in MS and reported early NK-cell reconstitution post ASCT. Now we further investigate the immune cell composition of the stem cell graft for 12 patients.

Methods: 16 patients undergoing ASCT for MS were monitored with serial lymphocyte subset analyses (CD4, CD8, NK and B cells) monthly for three months and at 6 and 12 months. Autologous stem cells were mobilized with Cyclophosphamide 1.5 mg/m^2 and G-CSF and patients underwent ASCT after conditioning with Cyclophosphamide and ATG. In 12 patients, the non-stem cell component of the graft was analyzed by flow cytometry for lymphocyte subsets using defrosted cryovials.

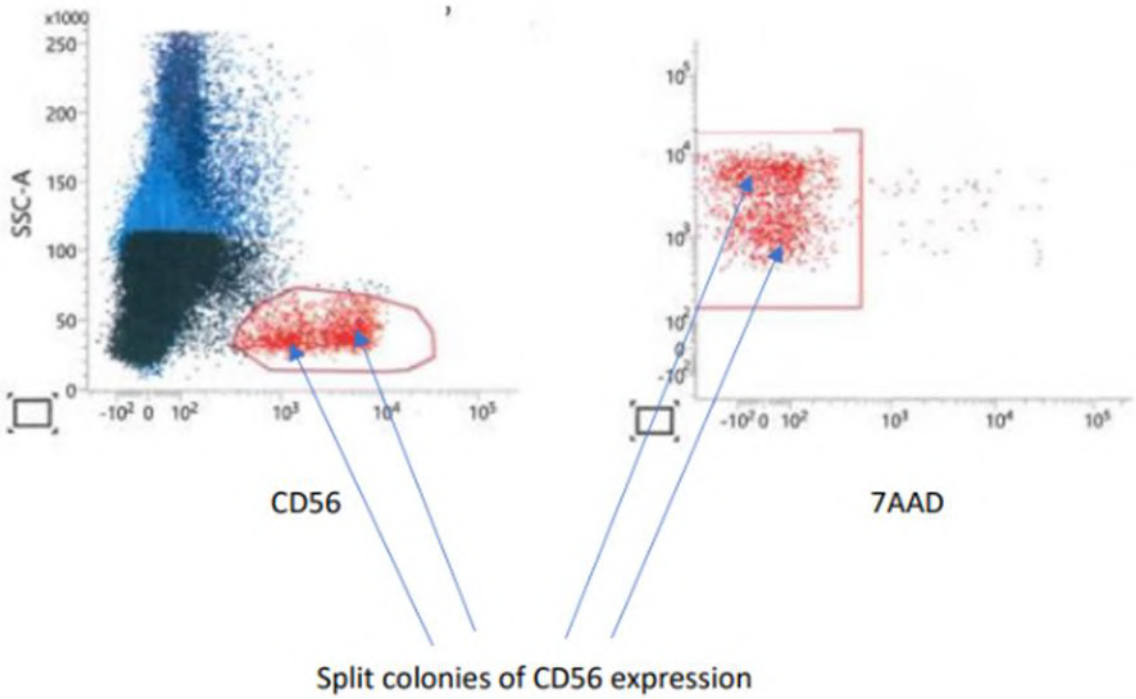
Results: Patient and disease characteristics for the 12 patients analyzed are summarized in table 1. There was a high degree of variability in immune cell composition in stem cell product for all the patients studied. Nonetheless, early NK-cell reconstitution was a consistent feature in this patient cohort. In the early post-transplant period (day +30), the highest absolute number of NK cells was seen with a decline to low normal numbers in subsequent time points. 8 of the 12 patients studied showed a dual population of NK cells in the stem cell product, with variable CD56 expression, possibly representing CD56 dim and CD56 bright populations, although more work is required to characterize these populations further.

Table 1: Patient and Disease Characteristics for 12 Patients who Underwent ASCT for MS Between 2019 and 2023

Number of Patients	12
Sex No. (%)	
Male	5 (42%)
Female	7 (58%)
Age (years)	
Median	29.5
Range	24- 49
Duration of MS (years)	
Median	6
Range	1-23
Expanded Disability Status Scale (EDSS) Score	
Median	3.75

Lines of Therapy	
Median	2
Last Immunosuppresive Therapy prior to ASCT No. (%)	
Alemtuzumab	4 (33%)
Natalizumab	5 (42%)
Ocrelizumab	3 (25%)
Duration between Last Disease-Modifying Therapy and ASCT (months)	
Median	12

Figure 1: Flow Cytometric Analysis Demonstrating Dual NK-Cell Colonies



Conclusions: There is no clear correlation between immune-cell composition of the graft and dynamics of reconstitution post ASCT for MS. We focused our interest on the consistent early NK reconstitution encountered in this patient cohort. The presence of two distinct NK-

cell populations in the majority of stem cell grafts needs to be studied further. CD56 bright NK cells have been reported to effect immune modulation and autoreactive T cell control.

Disclosure: Nothing to declare.

B347

AUTOLOGOUS STEM CELL TRANSPLANTATION FOR ANTI-SYNTHETASE SYNDROME: LONG-TERM OUTCOMES FROM TWO REFRACTORY CASES

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Background: Anti-synthetase syndrome (ASSD) is a rare, heterogenous autoimmune disorder characterized by the presence of anti-aminoacyl-tRNA synthetase antibodies, such as anti-Jo-1. Although pathogenesis remains unclear, immune dysregulation with loss of self-tolerance is the hypothesised key pathogenic mechanism. The treatment paradigm for ASSD is not well-defined, particularly in steroid-refractory cases. Various therapies have been trialed, including intravenous immunoglobulin (IVIg), immunosuppressants like cyclophosphamide and rituximab, and more recently chimeric antigen receptor T-cell (CAR-T) therapy.

Methods: This case series presents two cases successfully treated with autologous stem cell transplant (ASCT) using nonmyeloablative conditioning, consisting of cyclophosphamide and thymoglobulin. Disease activity was assessed using biomarkers such as creatine kinase (CK) and measures of respiratory function, including Forced Expiratory Volume in 1 second (FEV_1), Forced Vital Capacity (FVC), and Diffusing Capacity of the Lungs for Carbon Monoxide (DLCO).

Results: **Case 1:** A 65-year-old man presented in 2019 with anti-Jo1–positive ASSD, manifesting as arthritis, interstitial lung disease (ILD) and myositis with myocardial involvement. Initial therapy of pulse methylprednisolone, cyclophosphamide, and IVIg induced a partial response. Over the following 18 months, he experienced multiple relapses despite sequential immunosuppressive strategies including mycophenolate mofetil, rituximab, ciclosporin, tacrolimus, and repeated corticosteroid pulses. Due to persistent progression and limited treatment options, the patient underwent an ASCT in July 2021. Post-transplant, he achieved sustained clinical and biochemical remission with follow up now extending beyond 4 years. He remains stable on a reducing dose of prednisone, weaned to 5mg for the last 2 years from the initial 50mg dose, and maintenance IVIg.
This first case illustrates an optimal outcome following ASCT, with sustained remission allowing a significant reduction of DMARD therapy and corticosteroid use with durable disease control despite multiorgan involvement initially. Disease response to various treatments is summarised in Figure 1.

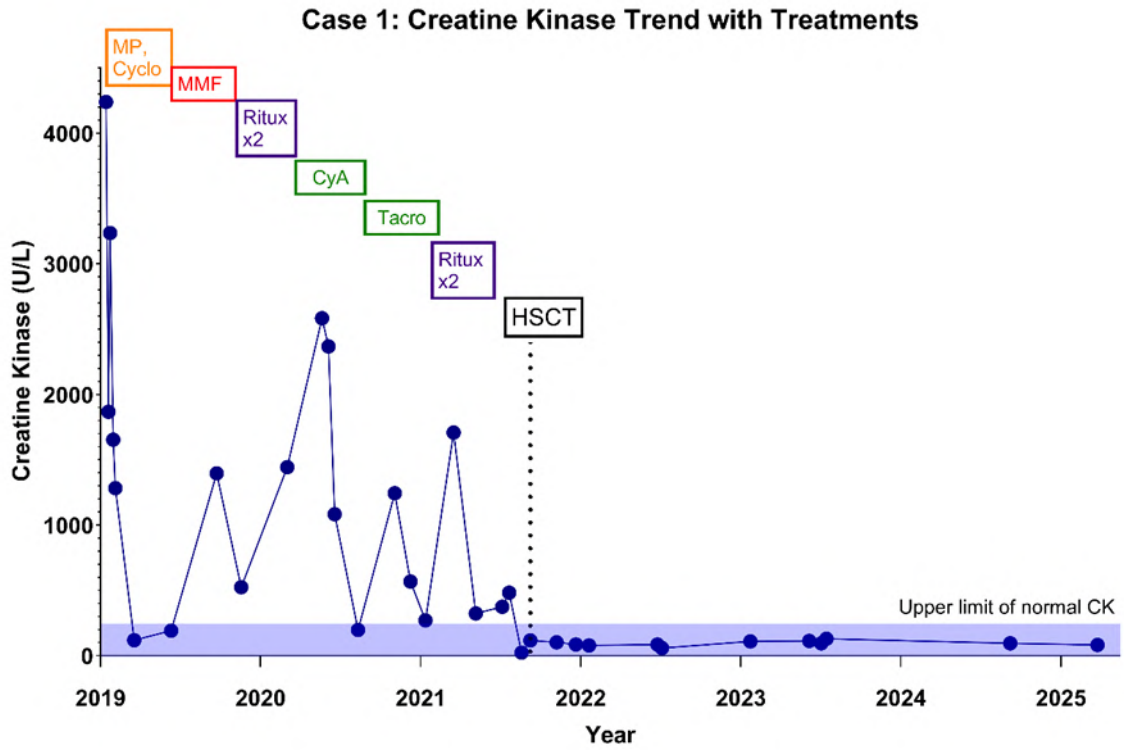

Figure 1: Creatine Kinase trend with treatments

Case 2: A 46-year-old woman with Jo-1–positive ASSD initially responded to glucocorticoids, cyclophosphamide, and hydroxychloroquine but experienced multiple relapses requiring escalation to IVIg, tofacitinib, and rituximab. Progressive disease led to an ASCT in March 2024, followed by nine months of stability. Two later flares were controlled with lower-dose prednisone, maintenance IVIg, and six-monthly rituximab. CAR-T therapy remains on hold due to improvement. Pre-relapse flow cytometry showed B-cell reconstitution and an inverted CD4:CD8 ratio driven by elevated CD8+ T cells.
This second case, while less favourable, demonstrates that ASCT can control the most aggressive ASSD phenotypes, enabling disease stability with lower-toxicity maintenance therapy. It also provides insight into ASSD pathophysiology, suggesting lymphocyte subset monitoring may help predict relapse and informing how ASCT and emerging options like CAR-T might be sequenced.

Conclusions: Our cases support ASCT as a viable option for selected ASSD patients amid growing interest in advanced cellular therapies such as CAR-T. While CAR-T shows promise, its long-term outcomes and accessibility remain uncertain. In contrast, ASCT offers multi-year follow-up data and comparatively lower cost, at approximately $60,000 AUD (internal costings).

Disclosure: Nothing to declare.

B348

OUTCOMES OF AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH MULTIPLE SCLEROSIS: EXPERIENCE FROM SOUTH AFRICA

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Background: Multiple sclerosis (MS) is a chronic, immune-mediated demyelinating disease that remains a major cause of neurological disability in young adults. While disease-modifying therapies (DMTs) can delay progression, many patients with highly active relapsing–remitting MS (RRMS) continue to experience breakthrough disease. Autologous haematopoietic stem cell transplantation (ASCT) offers durable immune reconstitution and remission but remains underutilised in upper-middle-income settings such as South Africa.

Methods: We conducted a retrospective review of all MS patients who underwent ASCT between 1 January 2009 to 31 December 2024 at two JACIE-accredited tertiary centres (Wits Donald Gordon Medical Centre, Johannesburg; and Netcare Pretoria East Hospital, Pretoria). Data were extracted from institutional transplant records and analysed using descriptive statistics and Kaplan–Meier survival estimates.

Results: Thirty-two patients were included (median age 42 years; 53% female; 94% RRMS). Median disease duration was 7.4 years, and 97% had received prior DMTs. Conditioning included cyclophosphamide (97%), anti-thymocyte globulin (69%), and fludarabine (34%). Treatment-related adverse events occurred in 63%, most commonly neutropenic fever (50%) and mucositis (16%), with no transplant-related mortality. Median neutrophil and platelet engraftment occurred at 10 and 14 days, respectively. Disease-free survival was 100% at one year and 91% (95% CI, 68–98%) at five years. Approximately 90% of evaluable patients demonstrated neurological improvement or stabilisation at one year.

Conclusions: ASCT is safe, feasible, and highly effective for aggressive, treatment-refractory RRMS in South Africa. Its earlier use in selected patients may offer durable remission and substantial cost savings compared with long-term DMTs. Expansion of accredited national ASCT programmes and registry-based outcome monitoring is warranted.

Disclosure: No conflicts of interest and no funding was required for this project.

B349

ANTI-CD38 MONOCLONAL ANTIBODY FOR TREATING IMMUNE THROMBOCYTOPENIA:A CASE REPORT

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Background: Immune thrombocytopenia (ITP) is an autoimmune disorder characterized by platelet destruction mediated by anti-platelet antibodies. Some patients who do not respond to conventional treatments are classified as refractory ITP, which occurs in approximately 0.4-3.8% of adults. The residual CD138/38-positive lymphocyte population is a key factor contributing to treatment failure. Daratumumab, an anti-CD38 monoclonal antibody, targets and eliminates CD38-positive cells (including plasma cells). In a multicenter Phase II study, 21 previously treatment-resistant ITP patients receiving daratumumab monotherapy achieved remission rates of 38%-48%, demonstrating the potential therapeutic value of Anti-CD38 monoclonal antibodies in refractory ITP.

Methods: This report describes a middle-aged female patient who developed thrombocytopenia during pregnancy. After undergoing repeated diagnostic tests including bone marrow aspiration, biopsy, loss-of-cell immunophenotyping, chromosomal analysis, fusion gene testing, and autoimmune disease evaluation, the patient met the diagnostic criteria for idiopathic thrombocytopenic purpura (ITP). Despite treatment with first-line therapies such as glucocorticoids, intravenous immunoglobulin (IVIG), platelet-receptor agonists, and decitabine, the platelet count remained persistently below 10×10^9/L, leading to a diagnosis of refractory ITP. The patient received daratumumab targeted therapy (16 mg/kg, once weekly for 1-8 weeks), with continuous monitoring of Platelet count, NK cell ratio and adverse reactions.

Results: After treatment with daratumumab, the patient's platelet count rapidly returned to normal within 8 weeks, with all values remaining ≥100×10^9/L. No adverse events such as infusion reactions or infections occurred during treatment, demonstrating good tolerability. The therapeutic mechanism may involve inhibiting antibody-dependent cell-mediated platelet destruction (ADCC) and reducing platelet phagocytosis by spleen macrophages.

Conclusions: Daratumumab demonstrated significant efficacy and favorable safety in this refractory ITP patient, providing clinical evidence for Anti-CD38 monoclonal antibody therapy in such cases. Further large-scale studies are required to clarify its long-term safety profile and optimal dosing regimen.

Disclosure: The authors declare no conflict of interest.Correspondence: Min Dong :mindonghn@hainmc.edu.cn

Haemoglobinopathies

OS21-02

ASS-T CELL DEPLETED HAPLOIDENTICAL HSCT FOR PEDIATRIC AND ADULT PATIENTS WITH SICKLE CELL DISEASE: INTERIM ANALYSIS OF THE T-HAPLO-HSCT FOR SCD TRIAL (NCT04201210)

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Background: Sickle cell disease (SCD) is one of the most common and severe monogenic disorders worldwide. Matched sibling donor (MSD) stem cell transplantation (HSCT) is the standard curative treatment. Haploidentical stem cell transplantation offers a potential alternative for patients with no available MSD. aß T cell-depleted haploidentical HSCT (aß-Haplo-HSCT) provides nearly universal donor availability, along with a well-controlled graft composition, consisting of a high stem cell dose and low aß T cell count. This results in rapid engraftment and minimal acute (aGVHD) or chronic graft-versus-host disease (cGVHD). Therefore, aß-Haplo-HSCT could become a viable alternative for patients with an elective transplant indication where the highest level of safety and efficacy is required.

Methods: We report the outcomes of 84 SCD patients (45 males/39 females; 13 HbSß°; median age was 14 years [range 4-40]; median follow-up 49 months [range 2-146]) who received 88 transplants between 2013 and 2025. All patients underwent a standardized, myeloablative conditioning regimen, which included ATG (Grafalon; 45mg/kg for haplo-HSCT respectively 30mg/kg for MSD HSCT), treosulfan, fludarabine, and thiotepa (FTT), followed by post-transplant immunosuppression with tacrolimus and mycophenolate mofetil for 240 and 180 days, respectively for haplo-HSCT and MSD HSCT.

Results: Thirty-five patients received an MSD transplant, and 49 underwent an aß-Haplo-SCT. The overall survival (OS) for the entire cohort was 93%. Disease-free survival (DFS) was 98%, with 6% experiencing graft failure (GF), which was rescued with a second transplant. The incidence of Grade 1/2 aGVHD was 24%, mild-to-moderate cGVHD occurred in 8% and 1 case of severe cGVHD. All cases resolved by 24 months post-transplant. Following a single-center pilot series with 43 patients (15 MSD and 28 aß-Haplo SCT), 57

patients enrolled in a prospective international multicenter trial (T-Haplo-HSCT for SCD; NCT04201210), stratified by donor availability. Forty-one evaluable patients are included in the analysis (20 MSD and 21 aß-Haplo SCT). In 35 MSD transplants, median age was 13.75 years, with a median follow-up of 49.4 months. The overall survival (OS) and disease-free survival (DFS) were both 97%, with a median chimerism of 96.8%. The incidence of grade 1/2 aGVHD and mild/moderate cGVHD was 20% and 5.7%, respectively. In 49 aß-Haplo-SCT, median age was 14 years, with a median follow-up of 46 months. The OS and DFS were 90% and 92%, respectively, with a median total chimerism of 96.8%. The incidence of grade 1/2 aGVHD and mild/moderate cGVHD was 20% and 5.7%. The patients treated in the multicenter Haplo-HSCT for SCD trial had an OS of 100% and a DFS of 91%, with a DFS of 100% after re-transplant. Transient grade 1/2 aGVHD was observed in only 5%, with no cGVHD. The time to neutrophil (16.5 versus 26.5 days) and platelet (16 versus 24 days) engraftment in the haplo-SCT arm was, as expected, significantly shorter compared to MSD HSCT.

Conclusions: aß-depleted haploidentical HSCT is currently being evaluated in a prospective stratified international trial (NCT04201210). The interim results of the ongoing trial show promising outcomes, comparable to MSD HSCT.

Clinical Trial Registry: **NCT04201210,**
https://clinicaltrials.gov/study/NCT04201210

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OS21-04

A DECADE OLD EXPERIENCE OF OPTIMISING CONDITIONING TO IMPROVE HEMATOPOIETIC STEM CELL TRANSPLANTS OUTCOMES IN SICKLE CELL DISEASE

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Background: Best outcomes of Hematopoietic stem cell transplantation (HSCT) for Sickle cell disease(SCD) are reported for children <12 years of age with matched sibling donor(MSD). Haplo-family donor(HFD) transplant is emerging as a promising alternative. Our experience in HFD HSCT for SCD with APOLLO protocol has been reported. With this study we aim to evaluate a decade long post HSCT overall survival(OS), acute graft vs host disease(GVHD) free & graft failure(GF) free survival for SCD patients. And factors affecting HSCT outcomes.

Methods: A retrospective observational study including all patients who underwent HSCT for SCD at Centre for Bone marrow transplant & cellular therapy at Indraprastha apollo

hospitals, New Delhi, India from June 2014 to November 2025. Required data retrieved from the hospital records and collected in a case record form. Modification of APOLLO protocol since June2024, which includes reduction of dose of thiotepa to 5mg/kg/day and addition of 4Gy Total Body Irradiation(TBI) was done for children >10 years of age.

Results: Total 197 patients were studied. Majority,86.8%(171/197) belong to African ethnicity having multiple comorbities with veno-occlusive crisis(VOC) being most common in 81.2%(160/197) patients. HFD HSCT was done for 53%(105/197) and 46.7%(92/197) underwent matched HSCT [88/92 with MSD/Matched related donor(MRD) and 4/92 with Matched unrelated donor(MUD)]. GCSF + Plerixafor mobilized Peripheral blood stem cell (PBSC) was the major source of stem cells. Pretransplant immunosuppression (PTIS) was given in all except 1 patient, 72%(142/197) received APOLLO protocol based PTIS. Conditioning regimen was myeloablative(Busulfan based) in 13.3%(26/197) and reduced toxicity/Apollo protocol(Fludarabine based) in 86.8%(171/197) patients along with Anti-thymocyte globulin(ATG) and 2Gy/4Gy TBI. Sirolimus, mycofenolate mofetil and Post-transplant cyclophosphamide (PTCY) based GVHD prophylaxis was used predominantly i.e 76.1%(150/197)(Table1).The median duration of follow up in Matched HSCT was 38.7 months(1 to 141months) and HFD HSCT was 32.3 months (1 to 136 months). Matched donor recipients have a significant better OS & acute GVHD free survival as compared to HFD{ 93.1% vs 81.7%(P value: 0.013) & 92.4% vs 75.2%(P value: <0.001)(Figure1A,C) with comparable GF free survival[96.7% vs 95.2%(P value: 0.509)].
Age at HSCT was a significant factor affecting OS irrespective of HSCT type with age <10 years showing best outcomes [91.4% in <10 years vs 78.2% in > 10 years (P value: 0.026)].
Upon evaluation against the type of HSCT, children <10 years of age had comparable OS in both matched and HFD cohort.[95% in matched vs 89.7% in HFD(P value:0.27)](Figure1B). Out of 64, 78.1%(50/64) patients of >10years age were treated on APOLLO protocol and new modified APOLLO protocol was given to 19/50 patients. Those treated on Modified APOLLO protocol had a better trend in OS[89.4% (17/19) vs 70.96%(22/31) P value:0.230](Figure1D) with better tolerability than those on APOLLO protocol, although not statistically significant.

TABLE 1: Showing Comparison of matched vs halo-family donor HSCT for sickle cell disease.

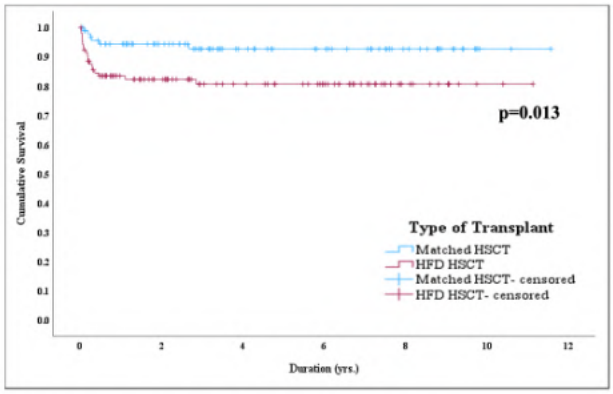
Variables	**Total** n=197	**Type of HSCT** No of patients(%)		**P value**
		Matched HSCT n= 92 (46.7%)	HFD Haplo HSCT n= 105 (53.3%)	

AGE <10 years >10 years	133(67.5%) 64 (32.5%)	63 (68.5%) 29 (31.5%)	70 (66.7%) 35 (33.3%)	0.786
GENDER Male Female	111(56.3%) 86 (43.7%)	52 (56.5%) 40 (43.5%)	59 (56.2%) 46 (43.8%)	0.963
COMORBIDITIES VOC Blood Transfusion >2-3 ACS Stroke AVN SLD	160(81.2%) 82 (41.6%) 34 (17.3%) 18 (9.1%) 7 (3.6%) 1 (0.5%)	70 (76.1%) 32 (34.8%) 15 (16.3%) 8 (8.7%) 2 (2.2%) 0 (0%)	90 (85.7%) 50 (47.6%) 19 (18.1%) 10 (9.5%) 5 (4.8%) 1 (1%)	0.084 0.068 0.740 0.840 0.452 1.000
ETHNICITY African Indian Others	171(86.8%) 22 (11.2%) 4(2%)	82(89%) 8(8.7%) 2 (2.3%)	89(84.7) 14(13.3) 2(2%)	0.586
GRAFT SOURCE Bone Marrow Peripheral blood stem cells Cord Blood	17 (8.6%) 179(90.9%) 1 (0.5%)	17 (18.5%) 74 (80.4%) 1 (1.1%)	0 (0%) 105 (100%) 0 (0%)	0.000* 0.000* 0.467
CONDITIONING REGIMEN Bu-Cy-ATG-2GyTBI (Myeloablative) Thio-Flu-Cy-ATG± 2Gy/4Gy TBI (APOLLO Protocol) Thio(5mg/kg)-Flu-Cy-ATG-4Gy TBI (Modified APOLLO) Thio-Treo-Flu-ATG	25(12.7%) 138(70%) 22(11.2%) 10(5%) 2(1%)	18(19.6%) 56(60.86%) 8(8.7%) 10(10.8%) 0(0%)	7(6.7%) 82(78%) 14(13.3%) 0(0%) 2(2%)	0.007* 0.008* 0.302 <0.001* 0.500

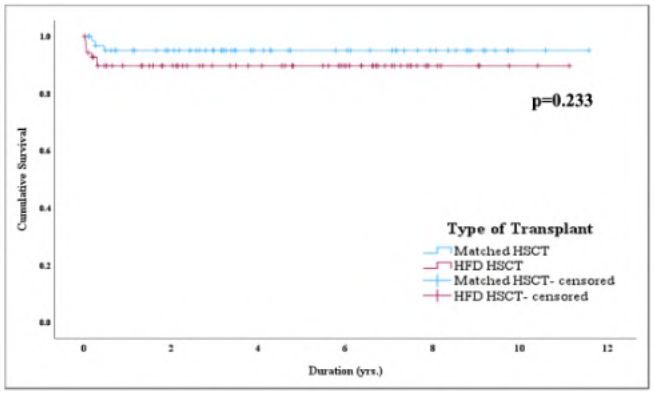
± 2Gy TBI (Reduced Toxicity) Others				
PTIS Hydra-Aza-Hyper transfusion Flu-Dex based PTIS Flu-Cy-Dex based APOLLO PTIS No PTIS	44(22%) 10(5%) 142(72%) 1(1%)	35(38%) 0(0%) 56(61%) 1(1%)	9(8.5%) 10(9.5%) 86(82%) 0(0%)	0.000* <0.001* 0.001* 0.467
GVHD PROPHYLAXIS CNI + MTX Siro + MMF Siro + MMF + PTCY Others	35 (17.8%) 1 (0.5%) 150(76.1%) 11 (5.6%)	35 (38%) 1 (1.1%) 54 (58.7%) 2 (2.2%)	0 (0%) 0 (0%) 96 (91.4%) 9 (8.6%)	0.000* 0.467 0.574 0.064
ACUTE GVHD Yes No	164(83.2%) 33 (16.8%)	85 (92.4%) 7 (7.6%)	79 (75.2%) 26 (24.8%)	0.001*
MUCOSITIS OVERALL GRADE Grade 0 Grade 1 Grade 2-3	111(56.3%) 39 (19.8%) 47 (23.8%)	59 (64.1%) 17 (18.5%) 16 (17.3%)	52 (49.5%) 22 (21%) 31 (29.5%)	0.191 0.664 0.046*
POST-TRANSPLANT CMV REACTIVATION Yes No	90(45.7%) 107(54.3%)	33(35.9%) 59(64.1%)	57(54.3%) 48(45.7%)	0.010*
BK VIRUS REACTIVATION Yes No	21(10.7%) 176(89.3%)	8(8.7%) 84(91.3%)	13(12.4%) 92(87.6%)	0.430

VENO-OCCLUSIVE DISEASE Yes No	4(2%) 193(98%)	1(1.1%) 91(98.8%)	3 (2.9%) 102 (97.1%)	0.624
PRES Yes No	5(2.5%) 192(97.5%)	0(0%) 92(100%)	5 (4.8%) 100 (95.2%)	0.062
GRAFT FAILURE No PGF SGF	189(95.9%) 5(2.5%) 3(1.5%)	89(96.7%) 1(1.1%) 2(2.2%)	100 (95.2%) 4 (3.8%) 1(1%)	0.594 0.374 0.600

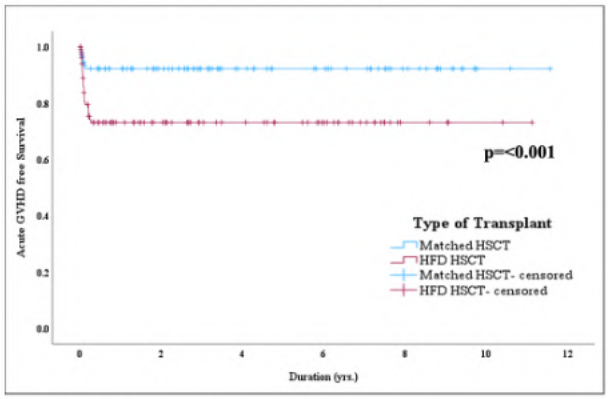
VOC-Veno-occlusive crisis, ACS-Acute chest syndrome, AVN-Avascular necrosis, SLD-Sickle lung disease, Bu-Busulfan, Cy-Cyclophosphamide, ATG-Anti-thymocyte globulin, TBI-Total body irradiation, Flu-Fludarabine, Treo-Treosulfan, Hydra-Hydroxyurea, Aza-Azathioprin, Dex-Dexamethasone, CNI-Calcineurin inhibitor(Cyclosporine/tacrolimus), MTX-Methotrexate, MMF-Mycofenolatemofetil, PTCY-Post transplant cyclophosphamide, Siro-Sirolimus, CMV-Cytomegalovirus, GVHD-Graft versus host disease, PRES- Posterior reversible encephalopathy syndrome.
*Significant pvalue<0.05



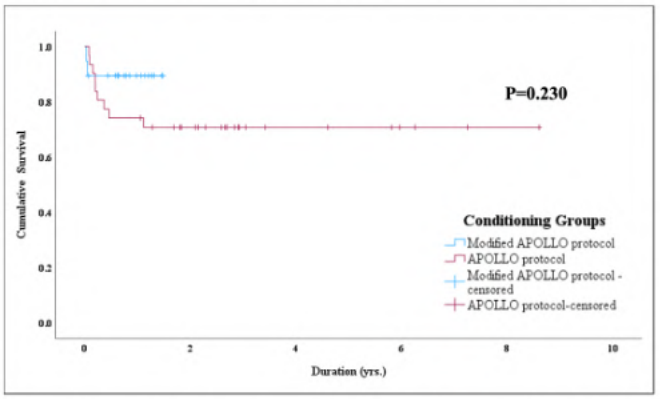
A) Overall survival for Matched vs HFD HSCT patients



B) Overall survival for Matched vs HFD HSCT patients in children < 10 years of



C) Acute GVHD free survival for Matched vs HFD HSCT patients



D) Overall survival in children>10 years on Modified APOLLO vs APOLLO protocol

Figure 1: Showing the survival outcomes for: A) Overall survival (OS) in matched vs HFD HSCT, **B)** OS matched vs HFD HSCT in children <10 years of age, **C)** Acute GVHD free survival in matched vs HFD HSCT, **D)** OS for children >10years treated on Modified APOLLO vs APOLLO protocol
HFD: Haplo-family donor, HSCT: Hematopoietic stem cell transplant, GVHD: Graft vs host disease.

Conclusions: We conclude that SCD children when transplanted below 10 years of age have the best chances of survival even in the setting of HFD HSCT. Children >10 years of age perform poorly, but we report better survival chances and lesser toxicities by using modified APOLLO protocol for this cohort, needing further study to validate.

Disclosure: No conflict of interest.

OS21-06

LOWER GVHD RATES IN MISMATCHED DONORS WITH PTCY AS COMPARED TO MATCHED UNRELATED DONORS WITHOUT PTCY AFTER PEDIATRIC FULL BONE MARROW HSCT FOR HEMOGLOBINOPATHIES

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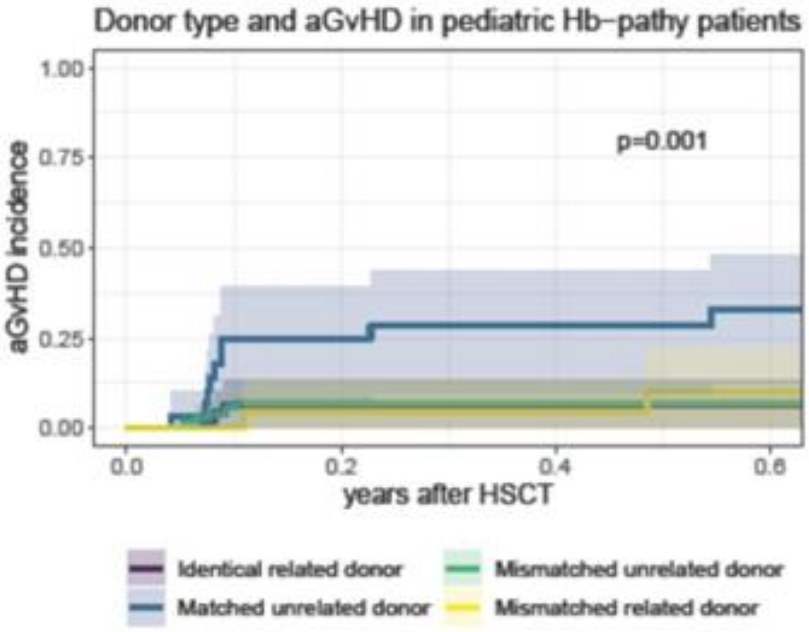
Background: Allogeneic hematopoietic stem-cell transplantation (HSCT) is currently the only available curative therapy for children with hemoglobinopathies. The lack of HLA-matched donors for most patients drove successful HLA-mismatched unrelated and haploidentical HSCT by αβ-depletion or post-transplant cyclophosphamide (PTCy). While PTCy proved effective in preventing graft versus host disease (GvHD) in mismatched HSCT, its additive role in GvHD prevention in HLA-matched unrelated donor bone marrow HSCT needs to be determined and weighted against its potential side effects in pediatric hemoglobinopathy patients.

Methods: We report 171 HSCTs in 154 pediatric hemoglobinopathy patients transplanted in our hospital between 2012 and 2024. Eighty sickle cell disease patients and seventy-four transfusion dependent thalassemia patients were evaluated. Patients received grafts from identical related donors (IRD, n=46), matched unrelated donors (MUD, n=28), mismatched (8/10 or 9/10) unrelated donors (MMUD, n=71) and mismatched (haplo-identical) related donors (MMRD, n=26). Almost all patients (89%) received full BM, 6% PBSC and 5% cord blood. Conditioning was myeloablative, treosulfan-based in 89% and busulfan-based in 11%. Patients received serotherapy with anti-thymocyte globulin (92%) or alemtuzumab (8%). In addition, GvHD prophylaxis for matched patients (IRD and MUD) consisted of ciclosporin A and methotrexate 10mg/m2 on days 1, 3 and 6, whereas mismatched patients (MMUD and MMRD) predominantly received PTCy 50mg/kg on days 3 and 4 followed by ciclosporin A and mycophenolate mofetil. We compared the incidence of overall survival, acute- and chronic GvHD, mixed chimerism, retransplant and viral reactivations between these different donor groups. Log-rank and cox-proportional-hazard models were used for uni- and multivariate comparisons.

Results: Overall survival was 96.5% and did not differ between the donor groups. Strikingly, the incidence of acute and chronic GvHD was the highest in MUD transplants: 9/28 MUD recipients (32%) developed >grade II aGvHD, compared to respectively 6.5%, 7.0% and 7.7% of IRD, MMUD and MMRD recipients ($p<0.001$, Figure 1). In addition, moderate/severe cGvHD occurred in 36% of MUD recipients compared to 2,2%, 4.2 and 3.8% of IRD, MMUD and MMRD recipients, respectively ($p<0.001$). In addition, aGvHD rate was increased in hemoglobinopathy patients with leukocytosis in the three months before conditioning: 7/23 patients (30%) with leukocytes >12*10^9/l developed aGvHD compared to 12/148 patients (8.1%) without leukocytosis. The occurrence of mixed chimerism, graft failure, as well as reactivation of cytomegalovirus, Epstein-Barr virus and adenovirus did not differ between the donor groups. In multivariate analysis, both donor type (MUD: HR 4.7, $p=0.016$) and pre-

HSCT leukocyte count (HR 1.16 per 10^9 leukocytes/l increase, p=0.019) were associated with the development of aGvHD (Table 1).



Multivariate evaluation of risk factors for aGvHD in pediatric hemoglobinopathy patients				
Risk factor	**Event Rate**	**HR[1]**	**95% CI[1]**	**p-value**
Diagnosis				>0.9
Transfusion Dependent Thalassemia	7 / 88 (8.0%)	—	—	
Sickle cell disease	12 / 83 (14%)	1.03	0.36, 2.96	
Donor type				0.016
Identical related donor	3 / 46 (6.5%)	—	—	
Matched unrelated donor	9 / 28 (32%)	4.67	1.18, 18.4	
Mismatched unrelated donor	5 / 71 (7.0%)	1.02	0.23, 4.49	
Mismatched related donor	2 / 26 (7.7%)	1.21	0.19, 7.72	
Leukocytes pre-HSCT (per 10^9/l)		1.16	1.03, 1.32	0.019
[1] HR = Hazard Ratio, CI = Confidence Interval				

Conclusions: In the pediatric hemoglobinopathy patient cohort presented here, PTCy effectively reduced GvHD rates in HLA-mismatched HSCT to the level of HLA-identical HSCT. The significantly higher rate of GvHD in children receiving full bone marrow grafts from MUD donors demonstrates the need for additional GvHD prophylaxis in this group. In addition, pre-HSCT leukocytosis -and possible related systemic inflammation and endovascular activation-provide an interesting base for future studies to further limit HSCT toxicity and substantiate the use of HSCT to cure hemoglobinopathies.

Disclosure: Nothing to declare

B350

THE NEED FOR A SUBSEQUENT HCT IS A LATE & CONTINUOUS RISK AND WITH SIGNIFICANT IMPACT IN OVERALL SURVIVAL IN HAEMOGLOBINOPATHIES: AN ANALYSIS OF HWP

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Background: Allogeneic hematopoietic cell transplantation (HCT) is the best established curative option for sickle cell disease (SCD) & transfusion dependent thalassemia (TDT). Primary and particularly secondary graft failure are important risks impacting on event free survival.

Methods: Data on pediatric and adult patients with TDT and SCD receiving a HCT from January 2000 to December 2022 were extracted from the EBMT Hemoglobinopathy registry database. Only first transplants were included.

Results: 2,045 consecutive patients underwent transplanted in centers distributed accross 33 countries in Europe, Asia and Africa: 1,532 were for TDT and 513 for SCD. Median age at transplant was 9 years (IQR 5, 15; range 1-49) with 62% HCT up to the age of 10 years. The median year of HCT was 2012 (IQR 2006, 2017). A total of 1,425 patients received a matched related donor HCT (70%), 435 patients a matched unrelated donor HCT (21%) and 174 patients a haploidentical HCT (8.6%). Bone marrow as a stem cell sourse was used in

74% of HCT and 75% received a cell dose >3 x 10^8 TNC/kg. Half of HCT were donor-recipient gender mismatched: 512 female to male (26%) and 476 male to female (24%). 60% HCT (n=504) were ABO compatible whereas minor ABO incompatibility was present in 15% HCT (n=129), major ABO incompatibiolity in 19% HCT (n=163) and biderictional ABO incompatibility in 4.8% HCT (n=40). CMV donor to patient was as follows: neg/neg 207 HCT (12%), neg/pos 242 HCT (14%), pos/neg 185 HCT (11%), pos/pos 1,076 HCT (63%). 89% HCT received myeloablative conditioning.
134 patients (6.5%) received a second HCT: 111 with TDT (83%, 7.2% of first HCT) and 23 with SCD (17%, 4.4% of first HCT). The time to subsequent HCT was ≤3 months in 20% cases. A second HCT was undertaken for reasons other than graft failure in 9.4% of the cases, including clonal evolution. The age and year at HCT was no different from first HCT. There were no differences in conditioning regimens and use of TBI, and only small reduction in use of serotherapy between first and second HCT.
The estimated incidence of subsequent HCT continues to increase over time with no apparent plateau. With median follow up of 5 years (IC95%, 4.6-5.1) the incidence at 1 year was 2.8% (2.1-3.6), at 2 years 3.9 (3.1-4.9), at 3 years 4.7 (3.7-5.7) and at 5.7 years (4.6-6.9). With median follow up of 4.8 years (IC95%, 3.3-6.7) from a second HCT, the overall survival at 1 years was 70.3% (62.7-76.6), at 2 years 66.7% (58.9-73.4), at 3 years 66.7% (58.9-73.4) and at 5 years 62.6% (54.1-69.9).

Conclusions: Real-world data confirms a small but significant risk of the need for a subsequent HCT in haemoglobinopathies. This, unlike in malignancies, usually is a late event (after day +100) and the incidence does not achieve a plateau over time. The OS following a subsequent HCT is inferior to first HCT and continues to decline over time with no plateau unlike the outcomes of first HCT, highlighting the need for improvement to avoid graft failure.

Disclosure: N/A

B351

EARLY DETECTION OF CLONAL HEMATOPOIESIS IN SICKLE CELL DISEASE: RESULTS FROM AN ACTIVELY MONITORED COHORT

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Background: Clonal hematopoiesis (CH) is increasingly recognized as a frequent, age-related phenomenon associated with adverse outcomes, including hematologic malignancies and cardiovascular disease.
Whether CH occurs more frequently in patients with sickle cell disease (SCD)—who are exposed to chronic inflammation, increased hematopoietic turnover, and repeated therapeutic interventions—remains unclear, as recent studies have reported conflicting results. Clarifying the prevalence and spectrum of CH in SCD patients has become critical since several cases of CH have been reported in the setting of allogenic stem cell transplantation and gene therapy (GT) for SCD, raising concerns about treatment-related

risk. In particular, TP53 mutations detected before transplantation have been linked to hematological malignancies in patients with graft rejection, and several cases of acute leukemia occurred following GT. Together, these observations underscore the need for a better understanding of CH in this population.

Methods: We screened peripheral blood samples from our actively followed cohort of 147 patients with sickle cell disease (SCD) at Necker Hospital. A targeted high-throughput approach was performed using an in-house panel covering 38 CH-associated genes, sequenced on our MiSeq (Illumina) plateform (validated LOD = 0.1%). Variants with an allelic frequency (VAF) above 0.9% and below 40% were considered clonal. Mutations previously identified with Agilent's NGS capture system were confirmed using a Quiagen amplicon-based NGS assay. Both sequencing strategies ensured high sensitivity and confidence for detecting CHIP-related variants down to ~0.9% VAF.

Results: Median age at blood sampling was 27 ± 10.4 years and SCD subtypes included SS or S/β^0 thalassemia (n = 125) and SC (n = 22).
After quality filtering, MiSeq sequencing yielded 20 suspect variants in 17 patients (11.5%), with a median variant allele frequency (VAF) of 1.2% [0.9-21%] (min-max). The most frequently affected genes were *ASXL1* (30%), *PPM1D* (25%), *RUNX1* (25%) and *DNMT3A* (20%). Amplicon-based confirmation reduced this list to 7 true CH mutations in 5 patients (3.4%) of a median age of 34,3 years (18-57 years). This group included 3 SS patients (all receiving hydroxyurea at the time of sampling) and 2 SC patients. Validated variants displayed VAFs ranged from 0.95% to 26%. We identified 4 single nucleotide variants and 3 deletions, classified as coding in *TP53*, *DNMT3A* and *RUNX1*, stop in *PPM1D* and frameshift mutation in *ASXL1*, *DNMT3A* and *PPM1D*. A patient who recently experienced bone marrow transplant failure was found to harbor two clonal hematopoiesis variants in *TP53* and *PPM1D*. Following immunomodulatory therapy and prior to a second bone marrow transplantation, the *TP53* variant was no longer detectable.

Conclusions: Initial sequencing identified numerous low-VAF variants, but amplicon confirmation reduced the true CH prevalence from 11.5% to 3.4%. These findings highlight the necessity of rigorous validation of low-frequency variants and suggest that background CH remains uncommon in this young SCD population. CH was detected in both SS and SC patients, highlighting that CH is not restricted to the most severe SCD genotypes. Given the dynamic behavior observed in a post-transplant setting, longitudinal monitoring of CH may be particularly relevant in patients undergoing transplantation or gene therapy.

Disclosure: none

B352

TREOSULFAN-BASED CONDITIONING IS ASSOCIATED WITH BETTER OUTCOMES IN ADOLESCENTS AND YOUNG ADULTS UNDERGOING MATCHED RELATED DONOR TRANSPLANTATION FOR THALASSEMIA MAJOR

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Background: Outcomes of allogeneic transplantation for Thalassemia Major (TM) in adolescents and young adults (AYA) remain suboptimal in resource-limited settings due to late referral, iron overload, and high-risk disease biology. Evidence comparing Treosulfan-based regimens with conventional Busulfan-based conditioning in this age group is limited.

Methods: We performed a retrospective analysis of AYA patients (≥12 years) with TM who underwent matched sibling or family donor transplantation at our centre between 1994–2022. Conditioning consisted of either Busulfan–Cyclophosphamide (Bu/Cy ± ATG) or Treosulfan–Fludarabine–Thiotepa (FTT). Standard institutional protocols were followed for GVHD prophylaxis, supportive care, and engraftment monitoring. Overall survival (OS) and thalassemia-free survival (TFS) were estimated using Kaplan–Meier analysis. Multivariable Cox regression was used to assess prognostic factors.

Results:

	Total [N=124] n (%)/ Median(range)	Busulfan based [N = 46] n (%)/ Median(range)	Treo based [N = 73] n (%)/ Median(range)	P-value
Median age [years]	15 (13-25)	15 (13-25)	15 (13-25)	0.459
Age > 18 years	13 [10.5%]	3[6.5%]	9[12.3%]	0.370
Median Ferritin (ng/ml)	3490[361 – 16761]	3850 (1036-11185)	3315(361-16761)	0.570
Previous splenectomy	29[23.4%]	15 [32.6%]	13 [17.8%]	0.078
Lucarelli Class I II III Vellore Low risk Vellore high risk	 3 [2.5%] 11 [8.8%] 110 [88.7%] 29 [23.4%] 81 [65.3%]	 3[6.5%] 4[8.7%] 39[84.8%] 10[21.7%] 29[63%]	 0[0%] 5[6.8%] 68[93.2%] 18[24.7%] 50[68.5%]	 0.078 1.000

Stem Cell Source Bone Marrow PBSC	 47 [37.9%] 77 [62.1%]	 43[93.5%] 3[6.5%]	 4[5.5%] 69[94.5%]	 0.000
Donor MSD MRD	 112 [90.3%] 12 [9.7%]	 44[95.7%] 2[4.3%]	 64[87.7%] 9[12.3%]	 0.199
Median time to Neutrophil count > 0.5 x 10^9/L (days)	16 [8 – 43]	14.5[8-25]	16[11-43]	0.096
Median time to Platelet count > 20 x 10^9/L (days)	21 [10 – 66]	26[10-66]	19.50(10-42]	0.001
Graft Failure [n=103] Primary Secondary	12 [9.7%] 4 [3.2%] 8 [6.4%]	3[9.1%] 1[3.03%] 2[6.06%]	7[10%] 2[2.85%] 5[7.14%]	 1.000
Sinusoidal obstruction syndrome	48 [38.7%]	25[54.3%]	23[31.5%]	0.021
Hemorrhagic Cystitis	11 [8.9%]	9[19.6%]	2[2.7%]	0.003
Infections	55[44.3%]	18[39.1%]	35[47.9%]	0.449
Acute GVHD Evaluable Grade 1-4 Grade 3-4 Steroid Refractory Chronic GVHD Evaluable All Limited Extensive	 n = 111 38(34.2%) 24(19.4%) 13[11.7%] (n=89) 28(31.4%) 15(16.8%) 13(14.6%)	 n=40 14[35%] 9[22.5%] 3[7.5%] n=28 4 [14.2%] 2[7.1%] 2[7.1%]	 n=69 24[34.8%] 15[21.75%] 10[14.5%] n=60 24[40%] 13[21.6%] 11[18.3%]	 1.000 0.026
Treatment related mortality (Day 100)	33[26.6%]	18[39.1%]	11[15%]	0.002
5-year Overall Survival	63.6 + 4.5%	54.8 $\pm$ 7.6%	72.2 $\pm$ 5.4%	0.017
5-year Thalassemia Free Survival	60.1 + 4.5%	51.1 $\pm$ 7.5%	70.1 $\pm$ 5.5%	0.018

A total of 124 AYA patients underwent MRD transplant. Median age was 15 years (13–25); 88.7% were Lucarelli Class III, and 65.3% belonged to the Vellore high-risk subgroup. The

median ferritin level was 3490 ng/mL (range: 361 – 16761). Conditioning comprised Bu/Cy in 46 (37.1%) and FTT in 73 (58.9%) patients. Peripheral blood stem cells were used in 94.5% of FTT recipients versus 6.5% in the Bu/Cy group.
Engraftment occurred in 111 patients (89.5%); median neutrophil and platelet engraftment times were 16(range: 8 - 43) and 21(range: 10 - 66) days, respectively. Primary graft failure occurred in 3.2% and secondary graft failure in 6.4%. Treatment-related mortality by Day 100 was 26.6% and significantly lower with FTT (15%) compared to Bu/Cy (39.1%, p=0.002).
Sinusoidal obstruction syndrome (SOS) occurred in 38.7%, with significantly lower incidence in the FTT group (31.5% vs 54.3%, p=0.021). Haemorrhagic cystitis was also less frequent with FTT (2.7% vs 19.6%, p=0.003). Grade II–IV acute GVHD occurred in 34.2% of evaluable patients, with similar rates in the FTT and Bu/Cy groups (34.8% vs 35%; p=1.000). Chronic GVHD was higher with Bu/Cy (40% vs 14.2%; p=0.026).
The median duration of follow-up after excluding early deaths was 59 months (range: 1 - 289 months). For the entire cohort, 5-year OS and TFS were 63.6$\pm$ 4.5% and 60.1$\pm$ 4.5% respectively. FTT was associated with superior OS 72.2% vs 54.8% (p=0.017) and TFS 68.7% vs 51.1% (p=0.018). Platelet engraftment was faster, complete chimerism at Day 30 was higher (92.8% vs 78.6%, p=0.023), and regimen-related toxicity was reduced in the FTT cohort.
In Lucarelli Class III patients overall, FTT showed significantly improved survival, with a 5-year OS of 71.9% vs 52.5% for Bu/Cy (p=0.014) and a 5-year TFS of 69.3% vs 52.5% (p=0.029). In the Vellore High-Risk subset, the benefit was even more pronounced, with 5-year OS of 75.2% vs 40.2%

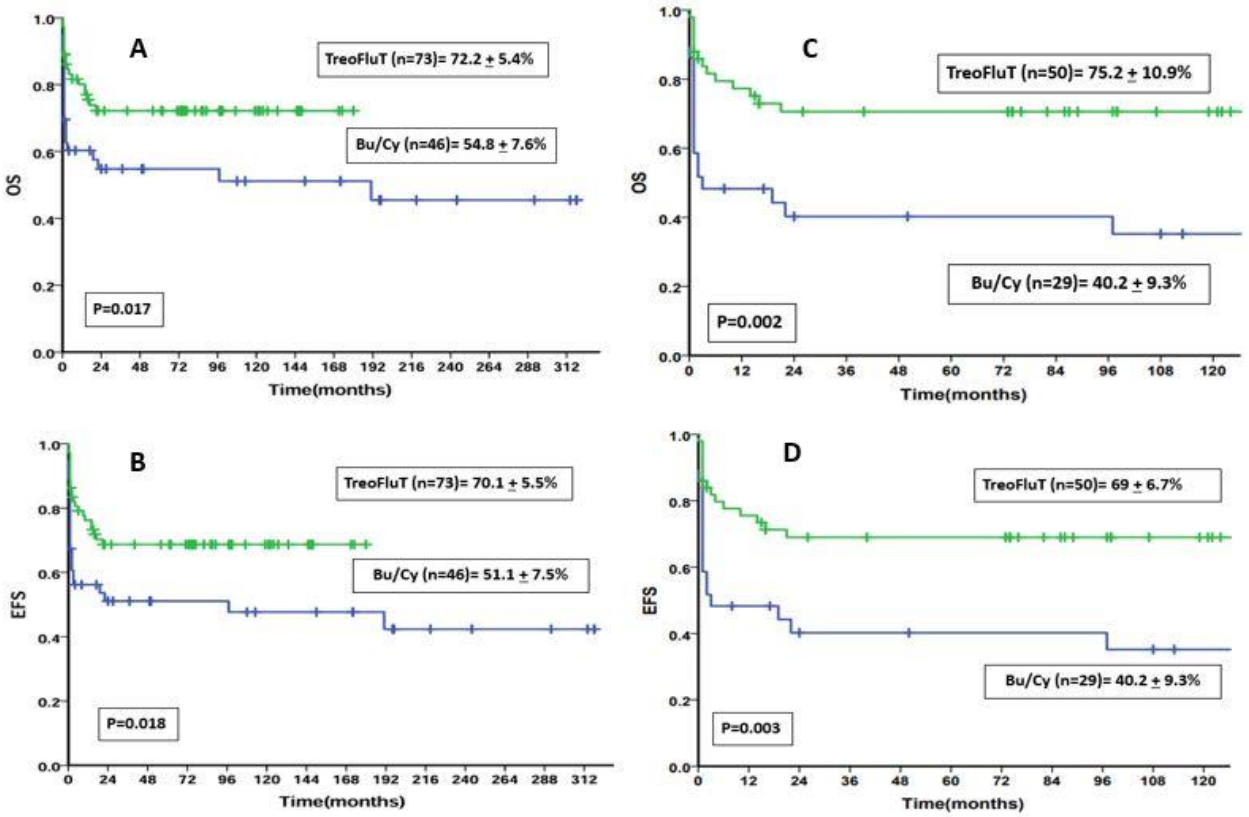

Figure A - 5-year overall survival of Treosulfan and Busulfan based regimens, Figure B- 5-year Thalassemia free survival of Treosulfan and Busulfan based regimens , Figure C 5 year Overall free survival of Treosulfan and Busulfan based regimens for Class III Vellore High Risk patients, Figure D- 5-year Thalassemia free survival of Treosulfan and Busulfan based regimens for Class III Vellore High Risk patients

Conclusions: Treosulfan-based conditioning significantly reduces early toxicity and improves long-term OS and TFS in AYA patients with TM undergoing MRD transplantation, including those in high-risk subgroups. These findings support Treosulfan-based conditioning as the preferred regimen for AYA patients in resource-constrained settings.

Disclosure: Nothing to declare

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POST-TRANSPLANT CYCLOPHOSPHAMIDE VERSUS ATG AS GVHD PROPHYLAXIS IN MATCHED SIBLING DONOR PBSC TRANSPLANTATION FOR B-THALASSEMIA MAJOR – A SINGLE CENTER EXPERIENCE

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Background: Hematopoietic stem cell transplantation (HCT) remains a cost-effective curative treatment for transfusion-dependent thalassemia major(TDT).Myeloablative conditioning (BU/CY) and CSA/MTX as GvHD prophylaxis has been the standard of care for decades in Matched Sibling Donor(MSD) HCT. Adding ATG both to mitigate the high rejection rate and minimize GvHD when using peripheral blood(PBSC) for MSD has shown satisfactory results in Thalassemia-Free Survival(TFS).However, in Egypt, the high-cost and irregular availability of ATG has been a major shortcoming.Post-transplant Cyclophosphamide(PT-CY) has emerged as a cost-effective,readily available option in the haplo-setting with favorable graft rejection and GvHD outcomes.

Methods: **Aim:** To evaluate whether PT-Cy can be used(in cost-constrained countries)as an alternative to ATG for GvHD prophylaxis in MSD-PBSC-HCT for TDT, focusing on Engraftment, Thalassemia-Free Survival and GvHD
Study design: In a comparative study, a prospective group of 41 consecutive patients transplanted between August 2023-January 2025(Group A) with TDT who underwent MSD-PBSC-HCT, conditioned with BU/CY and GvHD prophylaxis using PT-CY 40mg/kg/day(Day+3,D+4) plus CSA were compared to a retrospective historical control of 55 consecutive patients transplanted between 2021-2023(Group B),conditioned with BU/CY+rabbit ATG 7mg/kg/day(Day-3-Day-1)and GvHD prophylaxis using CSA/MTX.

Results:

Baseline characteristics were rather balanced,apart from Pesaro class 3 patients being more prevelent in group A.
The median follow-up was 20 months(1-31) vs 44 months(1-61) in Groups A&B respectively(Table.1).
Primary Endpoints: In Group A vs B respectively,
1-yTFS was non-significantly different between the two groups(78%vs83.6%,p=0.59).
Chimerism analysis was available for 28 and 26 patients,respectively. Full donor chimerism(FDC) was significantly lower in Group A(53.5%vs 88.5%, p=0.007). Mixed chimerism(MC) and Primary graft failure(GF) were observed in(28%vs7.7%,p=0.14)and(21.4% vs 3.8%,p=0.1),respectively.Notably, at a median of 6-months post-immunosuppression withdrawal(ISW), four patients(9.8%) with stable mixed chimerism in group A experienced late graft rejection versus non in group B. Hence,TFS showed a clinically relevant drop in group A post-ISW (68%vs83.6%,p=0.09).
Acute and chronic GvHD were significantly lower in groupA, (2.4%vs 38.2%,p=0.001) and (2.4%vs32.7%,p=0.001) for aGvHD II-IV and Moderate-severe cGvHD respectively.Two patients in group B died from aGvHD(3.6%).
CMV reactivation was significantly lower in group A(2.4%vs20%,p=0.01).
Secondary Endpoints:
OS and TRM were similar in both groups(85.5% and 14.5% p=0.99),respectively.
Neutrophil and platelet engraftment were delayed in Group A(mean 20.78vs17.36

days,p=0.001) and(20.31vs18.3 days,p=0.317), respectively.
Bacterial infections were higher in Group A(51.2%vs23.6%,p=0.005) with comparable Infection-related-mortality(4.8%vs7.2%,p=0.97).
Hemorrhagic cystitis was non-significantly higher in Group A(14.6%vs7.3%,p=0.317).
VOD was comparable (14.6%vs12.7%,p=0.787).
Thalassemia-Free,GvHD-Free Survival was 60%vs49.1%,p=0.3

Characteristics	**BU CY/ PT-CY+CSA (Group A) (n=41)**	**BU CY / ATG MTX+CSA (Group B) (n=55)**	**P-value**
Median Age	5 (0.58 -15)	6 (2-18)	0.161
Male, n (%)	23 (56%)	33 (60%)	0.701
Primary Disease BTM Class 1 BTM Class 2 BTM Class 3 BTM/SCD Congenital Dyserythropoietic anemia Sideroblastic anemia	 1 (2.4%) 17 (47.2%) 18 (50%) 1 (2.4%) 2 (4.8%) 2 (4.8%)	 11 (20.4%) 29 (53.7%) 14 (25.9%) 1 (1.8%) 0 0	0.01 0.082
Ferritin >1500 n (%)	22 (53.7%)	26 (47.3%)	0.536
Splenectomy	1 (2.4%)	6 (10.9%)	0.233
Donor (Trait/Normal)	17/23 (42.5%)	21/33 (38.9%)	0.724
Mean CD34 count (x10^6/kg)	6.83 (4-9.6)	7.24 (3.5-10)	0.097
Median follow-up (months)	20 (1-31)	44 (1-61)	0.001
Results	**BU CY/ PT-CY+CSA (Group A) (n=41)**	**BU CY / ATG MTX+CSA (Group B) (n=55)**	**P-value**

OS	85.5%	85.5%	0.99
TFS (1-year)	78%	83.6%	0.59
TFS (6months post-ISW)	68%	83.6%	0.09
Full Donor Chimerism	15/28 (53.3%)	23/26 (88.5%)	0.007
Primary Graft failure	6/28 (21.4%)	1/26 (3.8%)	0.1
aGvHD (Grade II-IV)	2.4%	38.2%	0.001
cGvHD (Moderate-Severe)	2.4%	32.7%	0.001
CMV reactivation	2.4%	20%	0.01

Conclusions: Replacing ATG by PT-CY has significantly reduced aGvHD/cGvHD risks together with reducing CMV reactivation while maintaining comparable OS. However, the higher rates of MC and late graft rejection were observed. The clinically relevant trend toward lower TFS and graft instability in the PT-Cy group warrants caution and further optimization of immunosuppression strategies.
Study limitations: Non-randomized.
Retrospective nature of the control arm(with possible non-identical practice)
The small sample size and shorter follow-up in PT-CY arm.
Recommendations: A larger prospective RCT is recommended to confirm these findings. Augmentation or a slow-tapering of Immunosuppression is probably mandatory in stable MC to suppress residual host immunity with vigilant chimerism monitoring(preferably lineage-specific chimerism to guide ISW).

Disclosure: Nothing to declare

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ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR PEDIATRIC HEMOGLOBINOPATHIES: LONG-TERM OUTCOMES IN A LARGE SINGLE-CENTER COHORT

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Background: Allogeneic hematopoietic stem cell transplantation (HCT) has long represented the only curative therapy for transfusion-dependent thalassemia (TDT) and sickle cell disease (SCD), supported by extensive long-term follow-up. Gene-editing–based therapies have recently broadened the therapeutic landscape for hemoglobinopathies; however, their positioning within current treatment algorithms remains to be defined. In this context, contemporary HCT results from experienced centers remain crucial for patient-specific treatment selection. We report the long-term outcomes of pediatric patients with hemoglobinopathies transplanted at I.R.C.C.S. Policlinico San Matteo, Pavia, Italy.

Methods: We retrospectively analyzed 134 consecutive patients with TDT or SCD who underwent allogeneic HCT between 2009 and 2025. Myeloablative conditioning was based on busulfan or treosulfan. Stem cell sources included bone marrow, peripheral blood stem cells, or combined bone marrow plus cord blood grafts. Donors were matched family (MFD), matched unrelated (MUD), or partially matched family donors (PMFD). Overall survival (OS), event-free survival (EFS), graft-versus-host disease-free/relapse-free survival (GRFS), and thalassemia-free survival (TFS) were estimated using the Kaplan-Meier method. Cumulative incidences of transplant-related mortality (TRM), graft failure (GF), and acute and chronic GVHD were estimated using competing-risk methods. Events included death and graft failure.

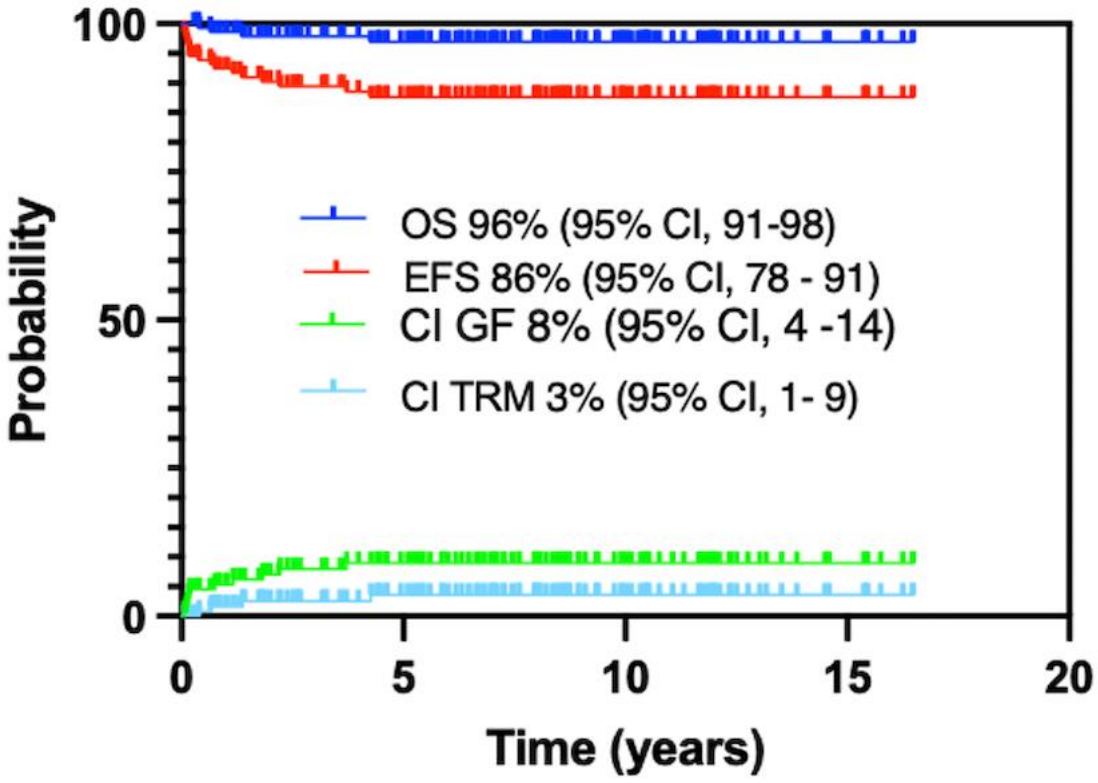
Results: A total of 134 patients underwent first allogeneic HCT, including 71 with TDT and 63 with SCD (Table 1). At 5 years, OS was 97% (95%CI: 91-99), EFS 86% (95%CI: 79-91), GRFS 85% (95%CI: 78-90), and TFS 90% (95%CI: 83–94). Donor type significantly affected outcomes: 5-year OS was 100% after MFD HCT, 97% after MUD HCT (95%CI: 90–99), and 79% after PMFD HCT (95%CI: 38–94; p=0.004), with similar trends for EFS (p=0.01).
The cumulative incidence of grade II–IV acute GVHD was 12.7% (95%CI: 8–19). Chronic GVHD was rare (4%, 95%CI: 1.5–9), with moderate to severe forms below 3%. The incidence of acute GVHD (any grade) differed by donor type (p=0.020), being lowest after MFD HCT. Five-year TRM was 3% (95%CI: 1.4–9.5) and was higher in patients aged ≥11 years (p=0.021) and after PMFD HCT (p=0.002). The cumulative incidence of GF was 8.4% (95%CI: 4–14).
At 1-month post-HCT, median donor chimerism was 99% (IQR 93–100). At last follow-up donor chimerism remained stable in 76% of patients, whereas progressive mixed chimerism (defined as ≥10% decline between consecutive timepoints) occurred in 13%. Excluding GF,

6% of patients had donor chimerism <50% at last follow-up, yet remaining transfusion-independent and free from disease-related symptoms. In competing-risk analysis, donor chimerism ≤90% at 1 month was a strong predictor of graft failure (sHR 50, 95%CI:12.5-200; p<0.001).

Table 1.

		Total pop.(N=134)	Thal. (N=71)	SCD (N=63)	p value
Patient characteristics	Female (n, %)	63 (47.0%)	30 (42.3%)	33 (52.4%)	0.241
	Age at HCT, years (median, IQR)	7.1 (3.3-10.7)	5.39 (2.57–8.90)	7.83 (5.13–12.58)	0.03
	Median follow-up (Y, IQR)	7.26 (3.25-10.36)	7.45 (3.99-10.53)	7.25 (2.64-10,13)	0.63
Donor type	MFD (n, %)	46 (34.3%)	18 (25.4%)	28 (44.4%)	0.002
	MUD (n, %)	78 (58.2%)	51 (71.8%)	27 (42.9%)	
	PMFD (n, %)	10 (7.5%)	2 (2.8%)	8 (12.7%)	
Conditioning	Bus+Thio+Flu+ATG (n, %)	55 (41.0%)	27 (38.0%)	28 (44.4%)	0.505
	Thio+Treosul+Flu+ATG (n, %)	78 (58.2%)	43 (60.6%)	35 (55.6%)	
Stem cell source	BM (n, %)	97 (72.4%)	48 (67.6%)	49 (77.8%)	0.327
	BM + Cord (n, %)	14 (10.4%)	7 (9.9%)	7 (11.1%)	
	Cord (n, %)	1 (0.7%)	1 (1.4%)	0 (0.0%)	
	PBSC (n, %)	22 (16.4%)	15 (21.1%)	7 (11.1%)	
GVHD prophylaxis	CsA+MTX+ATG (n, %)	122 (91.0%)	68 (95.8%)	54 (85.7%)	0.110
	PTCy (n, %)	11 (8.2%)	3 (4.2%)	8 (12.7%)	
	TCD (n, %)	1 (0.7%)	0 (0.0%)	1 (1.6%)	
Engraftment	PMN eng., days (median, IQR)	19 (17-23)	20.5 (18–24)	18.0 (15.25–22)	0.18
Graft composition	TNC $\times 10^8$/kg (median, IQR)	5.0 (3.2-8.1)	5.76 (3.79–8.78)	4.78 (3.17–7.27)	0.44
	CD34+ $\times 10^6$/kg (median, IQR)	6.6 (4.2-9.11)	6.76 (5.25–9.41)	5.62 (3.81–8.31)	0.32
	CD3+ $\times 10^6$/kg (median, IQR)	61.2 (40-118)	65.66 (41.96–148.03)	55.47 (33.35–83.72)	0.23

Figure 1. Survival and graft failure.



Conclusions: Allogeneic HCT for pediatric hemoglobinopathies was associated with excellent long-term survival, low TRM, and low incidence of severe GVHD. Donor type significantly influenced outcomes, with MFD transplantation providing the most favorable results, while age ≥11 years was associated with higher TRM. Early donor chimerism ≤90% at 1 month strongly predicted graft failure; however, patients without GF maintained clinical cure despite mixed chimerism. Even in the era of gene therapy, HCT remains a safe and effective option for selected patients.

Disclosure: No disclosure.

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RELIABLE ENGRAFTMENT AND COMPARABLE OUTCOMES ACROSS DONOR SOURCES WITH BUSULFAN65–FLUDARABINE–THIOTEPA CONDITIONING IN PAEDIATRIC SICKLE CELL DISEASE

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Background: HSCT is an established and increasingly accessible curative option for children with severe sickle cell disease (SCD) and transplant activity is expanding rapidly. Outcomes with MSD are excellent, whereas data on alternative donors remain limited and often associated with graft failure or GVHD. These are therefore generally reserved for patients with a severe, progressive disease phenotype. Experience from other inborn errors has shown that pre-emptive HSCT, performed before significant comorbidities develop, offers the best chances of survival in conditions with an otherwise poor long-term natural history.

Methods: We report on 35 symptomatic SCD patients aged 1-17 years (median 6) transplanted between 2014 and 2025 on an institutional protocol (including an established psychosocial support framework) with a uniform conditioning: busulfan tAUC 65ng*h/ml, fludarabine 150mg/m² and thiotepa 10mg/kg (plus cyclophosphamide 29mg/kg in MMFD). Donors were haploidentical MMFD (n=11), (M)MUD (10/10: n=3; 9/10: n=4), or MSD/MFD (n=17). All patients received serotherapy depending on donor source and HLA match: alemtuzumab 0.4mg/kg for MMFD, 0.8mg/kg for (M)MUD and ATG Grafalon® 45mg/kg for MSD/MFD. GVHD prophylaxis was post-transplant cyclophosphamide (PTCY), tacrolimus, MMF for MMFD and CSA-MMF for all other donors. One MMFD patient received a TCRa/b depleted PBSC graft because of pre-existing chronic kidney failure. All other but two MUD grafts were unmanipulated bone marrow. The three patient cohorts did not significantly differ with regards to age, disease severity, CMV status, cell source and number, and busulfan AUC (table).

Results: After a median follow-up of 3.3 years (range 0.4-9.1), 34/35 patients are alive (97%) without clinical signs of SCD or active GVHD. One patient in the MMFD group died from severe COVID-19 triggered bronchiolitis obliterans. Neutrophil and platelet engraftment were observed on median days +19 (significantly slower in the MSD/MFD group [p=0.005]), and +20 (not impacted by donor type [p=0.182]), respectively. There were no graft failures, and donor chimerism was >90% in all MMFD and 86% and 88% of (M)MUD and MSD/MFD recipients, respectively (p=0.462). All patients with mixed chimerism had either undetectable HbS levels or in the range of their heterozygote donor. Rates of acute GVHD in the MMFD, (M)MUD and MSD/MFD groups were °III-IV: 9%, 0% and 0% (p=0.325), and °II-IV: 27%, 29% and 0% (p=0.063), respectively. NIH moderate/severe chronic GVHD occurred in 9%, 14%, and 0% (p=0.330), respectively. Infectious complications and immune reconstitution were comparable across donor groups with no significant differences (not shown). There was one mild-moderate VOD case each in the MMFD and the MSD/MFD groups. In summary, overall survival, SCD-free survival and mod./sev. chronic GVHD, SCD-free survival rates were 97%, 97%, 94% for all patients with 91%, 91%, 91% with MMFD, 100%, 100%, 86% with (M)MUD, and 100%, 100%, 100% with MSD/MFD, respectively (p=0.325-0.330; table).

patient characteristics									
	all patients		MMFD		(M)MUD		MSD/MFD		p= *
n=	35		11		7		17		
HbSS genotype	30	86%	11	100%	5	71%	14	82%	0.206
VOC	29	83%	8	73%	7	100%	14	82%	0.325
ACS	17	49%	7	64%	3	43%	7	41%	0.481
stroke	4	11%	2	18%	1	14%	1	6%	0.594
age (years; median, range)	6	(1-17)	6	(1-8)	5	(3-17)	8	(2-15)	0.289
HSCT characteristics									
	all patients		MMFD		(M)MUD		MSD/MFD		p= *
donor age (median, range)	21	(1-52)	34	(29-38)	29	(18-49)	10	(1-52)	<0.001
HLA match 10/10 9/10 7/10 6/10 5/10	20 4 4 2 5		 4 2 5		3 4		17		n/a
CMV (R/D) -/- other	3 32	9% 91%	0 11	0% 100%	0 7	0% 100%	3 14	18% 82%	0.176
BM as stem cell source	32	91%	10	91%	5	71%	17	100%	0.075
TNC (*10^8/kg; median, range)	4.4	(1.1-77)	5.1	(1.6-77)	7.1	(2.5-27)	2.8	(1.1-4.8)	0.184
busulfan AUC (median, range, ng*h/ml)	64	(53-73)	63	(53-70)	65	(58-73)	66	(60-72)	0.312
outcome									
	all patients		MMFD		(M)MUD		MSD/MFD		p= *
overall survival	34/35	97%	10/11	91%	7/7	100%	17/17	100%	0.325
SCD-free survival	34/35	97%	10/11	91%	7/7	100%	17/17	100%	0.325
mod./sev. chronic GVHD, SCD-free survival	33/35	94%	10/11	91%	6/7	86%	17/17	100%	0.330
aGVHD °III-IV	1	3%	1	9%	0	0%	0	0%	0.325
aGVHD °II-IV	5	14%	3	27%	2	29%	0	0%	0.063
cGVHD mod./sev.	2	6%	1	9%	1	14%	0	0%	0.330
graft failure	0	0%	0	0%	0	0%	0	0%	n/a
neutrophils >0.5G/l (median, range)	19	(13-30)	18	(13-22)	19	(13-20)	21	(14-30)	**0.005**
platelets >50G/l (median day)	20	(10-41)	22	(13-34)	17	(10-25)	22	(11-41)	0.182
chimerism >90-100% 50-90% <50%	32 3 0	91% 9% 0%	11 0 0	100% 0% 0%	6 1 0	86% 14% 0%	15 2 0	88% 12% 0%	0.462

ACS: acute chest syndrome; AUC: area under curve; VOC: vaso-occlusive crisis.
(*chi-square for categorical and ANOVA for grouped variables)

Conclusions: These results, obtained in a relatively young and otherwise healthy pediatric cohort treated with a Bu65–Flu–TT conditioning regimen, demonstrate reliable engraftment and similarly favorable outcomes across MSD/MFD, (M)MUD, and MMFD donors. These findings may pave the way for broader consideration of very early HSCT from alternative donors in children with SCD.

Disclosure: Nothing to declare

B358

THE IMPACT OF TREOSULPHAN-BASED CONDITIONING AND INTEGRATED FOLLOW UP IMPROVES EVENT FREE SURVIVAL IN CHILDREN UNDERGOING HSCT FOR SICKLE CELL DISEASE

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) remains as one of the curative therapies for sickle cell disease (SCD). Busulphan-based myeloablative conditioning is effective, is associated with significant immediate and late toxicity in this cohort with pre-existing organ damage due to vasculopathy. We report our experience using uniform Treosulphan-based conditioning in children patients undergoing HSCT for SCD and the outcomes of integrated follow up between SQUH, Muscat and ASH, Chennai.

Methods: We performed a retrospective study conducted at the Apollo Speciality Hospital, Chennai collected data from patient records. We included children with SCD who underwent HSCT at our centre from October 2010 to October 2025 over a fifteen-year period and children from Muscat had an integrated follow up protocol. The conditioning combined Treosulphan with Fludarabine and Thiotepa with or without serotherapy. Children who had a haplo-identical transplant received 2 Gy TBI along with plasma exchange and rituximab based on donor specific antibodies.
We analysed the impact of the Treosulphan based conditioning regimen on the engraftment, graft failure, sinusoidal obstruction syndrome, viral reactivation, PRES, graft versus host disease, and and Overall Survival. The study has been approved by our Institutional Ethics Committee and we performed the statistical analysis using SPSS software.

Results: A total of 74 children with sickle cell disease underwent HSCT, of whom 14 (18.9%) were of Indian ethnicity and 60 (81.1%) were of other ethnicities. The cohort included 47 males (63.5%) and 27 females (36.5%). Forty-six children (62.2%) were aged ≤13 years, while 28 (37.8%) were older than 13 years, with a median age of 10.5 years. The underlying diagnosis was SCD in 64 children (86.4%), S beta thalassemia in 7 (9.5%), and SD disease in 3 (4.1%).The indication for HSCT included recurrent vaso-occlusive crises in 59 (79.7%), acute chest syndrome in 14 (18.9%), stroke in 12 (16.2%), avascular necrosis of the femur or osteomyelitis in 8 (10.8%), and hepatopathy in one child (1.4%). We used peripheral blood stem cells in 50 (67.5%), bone marrow in 23 (31.1%), and cord blood in 1 (1.2%) as stem cell source. Donors were matched family donors in 60 (81%), haploidentical donors in 13 (17.6%), and a matched unrelated donor in one child (1.4%).
We documented acute graft-versus-host disease in 7 children (9.5%), involving the gastrointestinal tract and chronic graft-versus-host disease in 5 children (6.8%), predominantly affecting the skin and musculoskeletal system. We did not document any primary or secondary graft failure but mixed chimerism was observed in 3 children (4.1%)

who remain clinically stable with sickle-free survival on follow-up of up to five years. At last follow-up, 68 children (91.9%) are alive with similar event free survival. The cause of death was graft-versus-host disease in 3 children and overwhelming sepsis in 3 children.

Conclusions: Treosulphan-based conditioning is a safe and effective conditioning regimen for children with sickle cell disease from different ethnic backgrounds. Seamless follow up between two HSCT units has improved event free survival to 91.9%. The combination of reduced gonadotoxicity and hepatotoxicity results in intact survival.

Disclosure: NIL

B360

LONG TERM FOLLOW-UP OF THALASSEMIA PATIENTS SHOWS REASONABLE OUTCOMES AFTER TRANSPLANTATION- A SINGLE CENTER EXPERIENCE FROM INDIA

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Background: Allogeneic transplantation (ASCT) is the only available curative therapy for a patient with Thalassemia as far as most of the countries are concerned. In India thalassemia continues to be a significant public health problem. Graft failure (GF), Veno-occlusive disease (VOD) or Sinusoidal obstruction syndrome (SOS) and Graft versus Host Disease (GVHD) are some of the unwarranted effects due to ASCT which can lead to Transplant related mortality (TRM). Most of the studies previously have shown a TRM ranging from 5-24% in these children.
We show that TRM can be improved in patients with thalassemia with satisfactory long-term outcomes with pretransplant optimization and improvements in supportive care.

Methods: Patients with a diagnosis of transfusion dependent thalassemia who underwent ASCT (Matched related transplant/Unrelated transplant) using Flu-Bu-Cy-ATG or Flu-Treo-Cy-ATG protocol between 2017 and 2025 were included in the study. No liver biopsies were performed prior to transplantation. Hydroxyurea was used in most of the patients prior to transplantation to decrease the liver size. Baseline demographic information, clinical and laboratory data, and details of transplantation, including donor characteristics, graft characteristics, and clinical outcomes, including graft rejection, TRM, GVHD, and death, were retrieved from the hospital records.

Results: One hundred forty-five patients with transfusion dependent thalassemia underwent transplant during this period with a median age of 8 years (IQR:5-9 years) with 66% being male. Median pre-transplant ferritin was 1720 ng/ml (IQR:1260-2220), median liver size was 2 cm (IQR:2.0-3.5), median hydroxyurea exposure was 9 years (IQR:4.7-14.4 years), median number of blood transfusions before transplant was 94 (IQR: 58-142). Patients were

classified as Lucarelli class 1 in 47(35.5%), class 2 (n=59,44.4%) and class 3 (n=27,20%) out of 133 patients. Eighty-four percent (123) underwent matched sibling donor transplant, and the rest underwent matched unrelated donor transplant. Five patients received treosulfan instead of busulfan as part of conditioning. 64% patients were ABO group matched. Median CD34 dose was 3.7 x 10^6/kg (IQR:2.4-5.0). The median TNC infused was 8 x 10^8 cells/kg available in 73/145 patients. The median time to neutrophil engraftment was 18 (IQR:16-21) days and platelet engraftment was 17 (14-21) days. More than 95% donor chimerism at day +100 was seen in 84.3% patients and in 73.8% patients at the time of stopping immunosuppression. Most common transplant related complications seen were veno-occlusive disease (VOD) in 21.4% (86% mild), infections in 47.6% (bacterial predominant), graft versus host disease (GVHD) in 20.0% (16.6% acute, 8.3% chronic), hypertension in 22.8%, graft rejection in 6.2%. The overall survival of the cohort was 97.9% with a median follow up of 3 years. The thalassemia free and gvhd free survival of the cohort was 82.1%.

Conclusions: Our real-world data shows excellent post-transplant outcomes in Indian children with thalassemia similar to the ones reported in western literature.

Clinical Trial Registry: None.

Disclosure: None.

B361

TREOSULFAN BASED MYELOABLATIVE CONDITIONING IN ADOLESCENT AND ADULT PATIENTS WITH HEMOGLOBINOPATHY

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Background: Hematopoietic stem cell transplantation (HSCT) is currently the standard curative treatment for transfusion-dependent thalassemia (TDT) and sickle cell disease (SCD), as outcomes remain poor despite optimal supportive care. Busulfan is the traditional alkylator for myeloablative conditioning. Due to a narrow therapeutic window and lack of standardized drug monitoring, busulfan is associated with a high risk of severe toxicity, such as sinusoidal obstruction syndrome (SOS). Treosulfan, an increasingly preferred alternative, has a wider therapeutic window, offering notable advantages. It is not metabolized in the liver, does not cross the blood-brain barrier, and has low endo-/epithelial toxicity, which reduces the need for extensive drug monitoring. However, treosulfan has been linked to graft failure and mixed chimerism (MC). This retrospective analysis summarizes the outcomes for adolescent and young adult (AYA) patients with SCD and TDT- groups at high risk for rejection and MC - who were transplanted with a treosulfan-based conditioning regimen.

Methods: 35 AYA patients (28 SCD/SCD-β-Thal, 7 TDT) (median age: 23 years; range: 16-39) received either a matched sibling donor (MSD) or an aß T cell-depleted haploidentical HSCT (T-haplo-HSCT; n=17, MSD; n=18), indicated by severe transfusion-related iron overload or SCD-related complications. All patients received a conditioning regimen consisting of treosulfan (3 x 14 g/m²), thiotepa (2 x 5 mg/kg BW), fludarabine (4 x 40 mg/m²), and ATG-Grafalon®, with the only difference being in the timing of ATG (upfront 3 x 15 mg/kg BW in T-haplo-HSCT, 3 x 10 mg/kg BW in MSD-HSCT on days -3 to -1). Immunosuppression involved a combination of calcineurin inhibitors and mycophenolate mofetil.

Results: Overall survival (OS) and disease-free survival (DFS) were 94%, respectively. One patient in each group died at 11 and 14 months, respectively, due to acute gastrointestinal bleeding and SCD-related chronic complications. Neutrophil engraftment was achieved at a median of 21 days (range 8-38) and platelet engraftment was achieved at a median of 20 days (range 13-48) post-transplant. Two patients experienced graft failure (GF) in the context of HHV-6 reactivation combined with macrophage activation syndrome and recent EBV infection. All GF cases underwent successful re-transplantation and are now disease-free. Mixed chimerism was observed in 11 patients (median 91%; range 86–94%), with median CD14+ split-chimerism at 99.5%. All TDT patients became transfusion-independent, and all SCD patients were free of vaso-occlusive crises after transplant. Ten patients developed mild aGVHD (grades I–II), all resolving completely with intensified immunosuppressive therapy. No severe acute GVHD (grades III–IV) was observed. There was no moderate or severe cGVHD, and mild cGVHD was not systematically documented. No additional severe infectious complications occurred. Three patients developed mild hepatic SOS, all responding well to defibrotide and fully recovering. No significant differences in all outcome parameters were observed between MSD and T-haplo-HSCT.

Conclusions: Treosulfan-based conditioning proved to be safe, myeloablative, and highly immunosuppressive. It emerges as an excellent alternative to busulfan in this high-risk population, with no cases of conditioning-related graft failure, no significant mixed chimerism, and neither severe GVHD nor SOS.

Disclosure: Nothing to declare.

B362

ESTABLISHING PRE-TRANSPLANT AUTOMATED RED CELL EXCHANGE FOR SICKLE CELL DISEASE: SAFETY AND FEASIBILITY RESULTS FROM A START-UP HSCT PROGRAM IN TANZANIA

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Background: Automated red blood cell exchange (a-RCE) is a key preparatory intervention before allogeneic hematopoietic stem cell transplantation (allo-HSCT) in patients with sickle cell disease (SCD), as it enables rapid reduction of sickle haemoglobin and minimizes sickling-related toxicity, improving organ protection, engraftment, and transplant outcomes.

Methods: Allo-HSCT represents the only curative therapy for SCD. As part of the first structured start-up transplantation program in Tanzania, we evaluated the feasibility, safety, and operational integration of a-RCE as a pre-transplant intervention intended to reduce sickling-related complications. Tanzanian staff didn't have previous experience in HSCT and procedures such as automatic RCE. From January 2023 to September 2025, 23 patients with severe sickle cell disease underwent allogeneic HSCT. The median patients age was 8 years (IQR 4-12). Overall, median pre-transplant level of HbS and haemoglobin were 78% (IQR 48-97) and 7,5 g/dL (IQR 5,8-10,8), respectively. All donors were HLA-matched siblings and 16 of them had sickle cell trait donor; two donor–recipient pairs exhibited major and minor ABO incompatibility. All patients had a tunneled central venous catheter placed prior to transplant. After dedicated training, Tanzanian clinical and technical staff performed automated red cell exchange using the Spectra Optia Apheresis System prior to conditioning, with fully compatible, irradiated, leukocyte-filtered packed red blood cells, to achieve a pre-transplant HbS level <30%.

Results: Overall, 20 patients underwent a-RCE prior to allo-HSCT , while one patient, presenting with 43% HbS, received two top-up transfusions 15 days before the transplant, having undergone automated RCE three months earlier for recurrent severe vaso-occlusive crises. An additional two patients treated in the first two months of the program received manual exchange transfusions. The median time between automated RCE and transplant was 17 days (IQR 12-24). 45% of patients (9/20) had a prior history of transfusion, with no documented alloimmunization. 70% of patients (14/20) with Hb level < 8 g/dl received top-up transfusions before the procedure. 80% (15/20) of patients required two RCE sessions, while 20% (4/20) underwent a single session and one patient required three. A mean of 3 (range 2–5) RBC units were exchanged per procedure. Median HbS level decreased from 78% (IQR 58-97) pre-RCE to 22% (IQR 12-33) post-RCE. Procedures were well tolerated, with stable post-procedure hemoglobin values. One patient developed transient haemolytic reaction during the second RCE session, despite pre RCE negative cross matches and IAT, leading to procedure interruption with full recovery. All patients reached stable donor engraftment without SCD-related complications.

Conclusions: In low-resource settings, safety and feasibility of a-RCE are strongly influenced by infrastructure, expertise, sustainability and reliable blood supply. Our experience demonstrates that, following targeted capacity building, a-RCE can be effectively incorporated into pre-transplant workflows, achieving the expected reduction in sickle hemoglobin with manageable, adverse effects and reducing allo-HSCT toxicities. a-RCE is now used in the same Centre also for SCD indications outside allo-HSCT. These findings highlight the importance of structured training in expanding access to advanced therapies for patients with SCD in LMIC, while a reliable and economically sustainable supply chain remains essential to ensure their availability.

Disclosure: None.

B363

HIGH PLATELET TRANSFUSION BURDEN FLAGS ENDOTHELIAL RISK BUT NOT GVHD, AFTER PEDIATRIC SICKLE CELL HSCT

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Background: Severe thrombocytopenia in the early post-HSCT period carries a risk of life-threatening bleeding, prompting platelet transfusions to maintain counts above 50000/μL in patients with sickle cell disease (SCD). Achieving this threshold often requires substantial platelet support during days 0–30. However, emerging evidence suggests that higher transfusion intensity may not be uniformly beneficial and may contribute to downstream harm. Platelets exert immuno-inflammatory effects that can amplify endothelial injury, and evaluating whether early platelet transfusion burden predicts acute GVHD (aGVHD) or endothelial syndromes could address a knowledge gap and help refine supportive care without implying causation.
Objectives: Primary: Assess whether high early platelet transfusion burden is associated with grade II–IV aGVHD by day +100.
Secondary: Explore associations with endothelial complications, hepatic veno-occlusive disease (VOD), posterior reversible encephalopathy syndrome (PRES), diffuse alveolar hemorrhage (DAH) and characterize severity signals including engraftment kinetics and RBC transfusion needs.

Methods: We retrospectively reviewed 80 pediatric and young adult SCD recipients of myeloablative HLA-identical sibling HSCT (2005–2024). The exposure was cumulative apheresis platelet units transfused during days 0–30 (median 12; IQR 7.8–15.3). "High burden" was defined a priori as the upper quartile (Q3; ≥15.25 units); a median split (≥12 vs <12) served as sensitivity testing. Platelet burden was also evaluated as a continuous variable for descriptive correlations. Outcomes followed standard institutional/EBMT criteria. Fisher's exact test evaluated categorical associations; Spearman correlation and OLS regression summarized trajectories. Given sample size, findings are exploratory.

Results: Primary outcome: Grade II–IV aGVHD occurred in 5.0% of high-burden vs 10.5% of low-burden patients (1/20 vs 6/57; OR 0.45; p = 0.67). Median-split sensitivity analyses were consistent, providing no evidence that higher early platelet burden increases aGVHD risk.
Endothelial complications: VOD occurred only in the high-burden group (3/20 vs 0/57; p≈0.016). Although notable, this small number and the multifactorial nature of VOD (conditioning exposure, iron status, graft source) limit inference. PRES and DAH were rare, and pooled analyses excluding VOD showed no association with platelet burden.
Severity signals (transfusion and engraftment): Platelet burden correlated strongly with RBC

transfusion needs (ρ = 0.66; $p<10^{-10}$). OLS regression estimated +0.19 RBC units per +1 platelet unit (95% CI 0.14–0.24; $R^2 \approx 0.42$). Higher platelet burden was associated with later platelet and ANC recovery ($\rho \approx 0.30$; $p \approx 0.02$ and $p \approx 0.008$, respectively). These relationships likely reflect clinical complexity rather than direct effects of transfusion.

Conclusions: In pediatric SCD HSCT, higher early platelet transfusion burden was not associated with increased grade II–IV aGVHD. A small enrichment of VOD in the high-burden group is hypothesis-generating and warrants validation incorporating factors including busulfan exposure, iron overload, graft source, and infection history. Independently, strong correlations with RBC support and delayed engraftment indicate that early platelet burden may function as a practical marker of early clinical severity, useful for risk stratification and targeted surveillance. Future work should evaluate a risk-adapted, platelet-trajectory anchored model in which day 0–30 platelet burden helps guide CNS-focused surveillance, hepatic monitoring in high-risk windows, and standardized thresholds to minimize unnecessary exposure.

Disclosure: Alexander Ngwube : Vertex Therapeutics (paid consultant one-time, ended November 2025) and Beam Therapeutics (paid consultant one-time, ended December 2025)

B364

63 HLA-IDENTICAL RELATED HAEMOTOPOIETIC STEM CELL TRANSPLANTS IN SICKLE CELL DISEASE

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Background: Despite the progress in management, sickle cell disease (SCD) still carries high morbimortality. Waiting for gene therapy, allogeneic haematopoietic stem cell transplantation (HSCT) is the only curative treatment.

Methods: A single-center descriptive study was conducted in patients with SCD who underwent HSCT from an HLA-identical sibling donor between May 2010 and May 2025.
Stem cell source: bone marrow.
Transfusion therapy began 3 months before HSCT. Since 2015, hydroxyurea was initiated/intensified 1 month before to keep reticulocytes <100,000/mm³. During transplant, platelets were maintained >50,000/µL, hemoglobin >11 g/dL, and hypertension and hypomagnesemia were prevented to reduce neurological complications. Ovarian tissue is cryopreserved since 2015.
Conditioning regimen:

- Until January 2015: Busulfan, cyclophosphamide, alemtuzumab. Graft versus host disease (GVHD) prophylaxis: cyclosporine A (CsA) and methotrexate.
- After January 2015: Thiotepa, Treosulfan, Fludarabine, anti-thymocyte globulin (myeloablative conditioning but reduced toxicity).GVHD prophylaxis: CsA, mycophenolate mofetil (MMF) (Jan 2015–Feb 2019); tacrolimus, MMF (Feb 2019–May 2024) or tacrolimus, MMF and *post*-transplant cyclophosphamide (PTCy) (January 2025–May 2025).

Epidemiological, clinical, and analytical parameters were collected. Data are presented as percentages and medians (p25–p75).

Results: 63 HSCT were performed in 62 patients, 29 females (46%), median age of 6.45 years (3.07–9.82), 11 patients with the first conditioning, 52 with the second (GVHD prophylaxis: CsA/MMF 10/52, tacrolimus/MMFF 39/52 and tacrolimus/MMF/PTCy 3/52). Donor median age: 6.54 years (4.31–9.54). 48.4% sickle cell trait, 20.6% with major group incompatibility.All patients grafted but 3 patients had autologous reconstitution (AR): one developed recurrent symptoms and underwent a successful second HSCT (same donor); one lost follow up (month +14) with mixed chimerism (MC) and come back in AR with a refractory HLH due to EVB causing decease (month +41); the third is alive but without follow-up (month +4). Complete chimerism (CQ) was achieved in 41/63 (65.1%), mixed in 19/63 (30.1%). Overall survival (OS) and event-free survival (EFS) (death and graft failure) were 96% and 95% respectively, median follow-up of 5 years (2.5–6.7). First conditioning: OS 91% and EFS 90%. Second conditioning: OS 97% and EFS 96%.
Time to neutrophil and platelets engraftment: 19 days (17–22) and 23 (20–28) respectively. Complications of HSCT included: hypertension 52/63 (82.5%), CMV reactivation 43/63 (68.3%), acute renal failure 10/63 (15.9 %) and neurological complications 12/63 (19.4%) all recovered: subarachnoid haemorrhage (n=6), seizures (n=9), posterior reversible encephalopathy syndrome (n=5) or drug-related toxicity (n=4). Acute GVHD in 23/63 (36.5%): 52.2% stage I (n=12), 30.4% stage II (N=7), stage III (n=1) with good response to treatment and two patients developed grade IV causing one death on day +51 (first conditioning), the other with good response. One patient developed skin chronic GVHD score 1 with favorable evolution. One patient developed Hodgkin lymphoma 4.7 years after HSCT (QC, 7 months of immunosuppressive therapy) and, due to progression, he underwent a second HSCT with a favorable outcome.

Conclusions: The results of our study, the largest HSCT series in Spain, is similar to the international cohort and confirms the role of HSCT for children with SCD . Long-term follow-up remains essential to identify late complications.

Disclosure: Nothing to declare.

B365

CORRELATION OF HB S LEVEL WITH CHIMERISM POST BONE MARROW TRANSPLANT IN PATIENT WITH SICKLE CELL DISEASE

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Background: Hematopoietic stem cell transplant is the only curative treatment for sickle cell disorder which is recommended in selective patients in terms of prevent furthers serious complications of the disease and improved the quality of life (Payal Desai, 2022).Chimerism analysis is an crucial molecular test that used for assessment of engraftment after bone marrow transplant in patient with sickle cell disease. In addition to that, HbS level measurement has also been used along with chimerism by many transplant centers. In fact, there is no study that has been done to evaluate the correlation between Hb S level and chimerism in sickle cell disease post-transplant. Therefore, our research will evaluate whether the Hb S level is sufficient to predict the chimerism level and monitor the successful of engraftment or failure in SCD patient post HSCT following at SQUH.

Methods: In this single center retrospective study, we included patients with SCD who underwent HSCT at the transplant unit of Sultan Qaboos University Hospital (SQUH) and those who were transplanted abroad and returned for their post-transplant care to SQUH between January 2006 and December 2023. We included pediatric and adult patients. Clinical, laboratory and epidemiological data of relevance were collected for this cohort from the electronic health records. Patients were excluded if no chimerism or Hb S level results were available. Results were presented as appropriate using medians, means and proportions. The correlation was assessed using univariable and multivariable logistic regression. Scatter plot and linear regression analyses were performed to assess the correlation between hemoglobin S (Hb S) level and donor chimerism at multiple post-transplant intervals (3 months, 6 months, 1 year, and 2 years). All analyses and graphs were performed using R program software.

Results: A total of 117 patients were included in the study, comprising 71 males (60.7%) and 46 females (39.3%), with a mean age of 28.8 years. Most transplants were performed abroad, primarily in India (n = 64), while 53 transplants were carried out at SQUH. The majority of donors were sickle cell trait carriers (n=68,58.1%). Engraftment failure occurred in six patients (5.1%).No statistically significant correlation was observed at 3 months ($p = 0.374$) or 6 months ($p = 0.768$). This lack of correlation may have been influenced by donor sickle cell trait status, as majority of donors were carriers. At one-year post-transplant, a trend toward significance was observed ($p = 0.0573$), and a strong, statistically significant positive correlation emerged at two years ($p < 0.001$).

Conclusions: Hb S monitoring is a valuable indicator for long-term post-transplant follow-up, showing significant correlation with donor chimerism at 1 and 2 years. This relationship is influenced by donor sickle-trait status, underscoring the need for further analyses stratified by donor genotype.

Disclosure: I declare that there are no conflicts of interest in this study.

B366

DIFFERENT APPROACHES TO HSCT IN TRANSFUSION-DEPENDENT B-THALASSEMIA

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Background: β-thalassemia is a huge problem for the Central Asian region, causing the death of dozens of patients every year. Allogeneic hematopoietic stem cell transplantation (HSCT) is the only available curative treatment option in the region. The aim of this study is to explore different approaches to HSCT in transfusion-dependent β-thalassemia (TDT).

Methods: We analyzed the results of 50 HSCTs on patients with TDT treated according to different protocols. Patients' ages at the time of HSCT ranged from 2 to 14 years (average 5 years). Retrospective statistical analysis of HSCT results was performed.

Results: All patients received normal transfusion rates and chelation therapy in preparation for HSCT. Myocardial iron overload was detected in 3 cases and hepatic iron overload - in 29 cases before HSCT. 39 children had splenomegaly before HSCT. In 35 cases, long-term pre-transplant immunosuppressive therapy was administered, including fludarabine, dexamethasone, and monoclonal antibodies against CD20 and CD38. 15 patients were transplanted without long-term immunosuppression. 16 patients received transplant from a matched related donor (MRD), 20 patients - from an 10/10-matched unrelated donor (MUD), 10 – from an 9/10 MUD, 4 – from a haploidentical donor (haplo). All patients received a myeloablative conditioning regimen. The source of stem cells was peripheral blood for 42 patients and bone marrow – for 8 ones. 40 children received 100 mg/kg post-transplant cyclophosphamide for graft-versus-host disease (GVHD) prophylaxis. Additionally, 48 children received calcineurin inhibitors, 20 - mycophenolate mofetil, 12 -ruxolitinib. In 47 cases the engraftment was achieved with a median engraftment time of 21 days. Primary non-engraftment was observed in 1 patient, who demonstrated restoration of native hematopoiesis. 5 patients died: 3 due to severe GVHD, 2 – due to infection. Acute GVHD grade 3 was in 5 cases, chronic GVHD was detected in 10 patients. Mixed chimerism was seen in 20 cases, causing complete graft rejection in 5. Therapy with donor lymphocyte infusion was effective in 15 children. Transfusion dependence persisted for median duration of 6 months in 5 cases. In the group of patients received long-term pre-HSCT immunosuppression was significantly lower rate of severe GVHD ($p=0.03$), but significantly higher rate of severe infections ($p=0.04$). The rate of severe GVHD was higher in MUD group in comparison to haplo group ($p=0.04$). There was no difference in severe GVHD between 9/10 MUD and 10/10 MUD ($p=0.2$).

Conclusions: Multivariate statistical analysis shows age, primary organ iron overload, immune hemolysis as the major negative prognostic factors for the results of HSCT for TDT. Long-term immunosuppression can prevent severe GVHD but increases the risk of severe infections. Haplo HSCT is feasible and can be an alternative approach for HSCT strategy.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

B367

THIRTY YEARS LATER: UNEXPECTED, UNHERALDED, AND UNEXPLAINED RE-EMERGENCE OF THALASSEMIA FOLLOWING LONG-TERM ALLOGENEIC ENGRAFTMENT

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Background: Limited data are available on the long-term (30 years) survival of allogeneic hematopoietic engraftment, regardless of the underlying disease. Patients with TDT who underwent transplantation in the 1980s represent a unique natural model to assess the long-term potential of transplanted hematopoietic stem cells to sustain hematopoiesis over several decades.

Methods: We report five patients transplanted in the 1980s and early 1990s who experienced an unexpected, unheralded, and unexplained graft loss and thalassemia recurrence more than 30 years after transplantation.

Results: Case 1: A 16-month-old male underwent transplantation in 1982 after conditioning with dimethyl busulfan and cyclophosphamide from an HLA-identical sister without thalassemia trait. The early post-transplant course was successful. No data were available for decades until 2014, when the patient (age 32) presented with severe anemia (Hb 6.5 g/dL) and 5% donor chimerism by STR. He resumed regular transfusions and was later lost to follow-up.
Case 2: A 3.7-year-old male underwent HCT in 1985 from an HLA-identical brother with thalassemia trait. Engraftment was initially monitored by blood group typing. From 2012 onward, hemoglobin levels progressively declined, reaching 6.5 g/dL by July 2016 (day +11,402), when STR analysis showed 19% donor chimerism. Transfusions were restarted. Donor chimerism further declined to 16% by 2019. He remains on regular transfusions and chelation.
Case 3: A 3.6-year-old female received an HLA-identical sibling transplant in 1994. Full donor chimerism was confirmed in 2010. Subsequently, Hb declined to 9 g/dL, and donor chimerism fell to 25% by 2016. By July 2024 (day +11,046), Hb was 7.5 g/dL with 17% donor cells, prompting resumption of transfusions.

Case 4: A 2.5-year-old female was transplanted in 1994 from an HLA-identical sister, with complete early chimerism. During her second pregnancy in April 2021 (day +9,720), Hb declined and transfusions resumed. Chimerism decreased to 26% in 2022 and 20% in 2023. She underwent a second transplant in October 2023 and is currently well.
Case 5: A 26-year-old male with sickle cell disease/thalassemia underwent transplantation in 1990 from an HLA-identical sister with thalassemia trait. After five years of full donor engraftment, he remained stable until late 2024, when Hb levels fell. In January 2025 (day +12,600), electrophoresis revealed 20% HbS and 7% HbF; FISH showed 61% Y/X metaphases, and blood typing indicated mixed A+/O+ red cells. He is under watchful monitoring.

Conclusions: All patients underwent transplantation in the 1980s or early 1990s, mostly receiving classic oral busulfan–cyclophosphamide myeloablative conditioning and HLA-identical sibling grafts. None received antithymocyte globulin or developed chronic GvHD, and all maintained excellent long-term quality of life. No clear immunologic trigger preceded graft loss.
Where follow-up was available, recurrence manifested as progressive anemia and declining donor chimerism, culminating in re-expansion of autologous hematopoiesis without accompanying leukopenia or thrombocytopenia.
These cases suggest that long-term exhaustion of allogeneic engraftment may occur decades after transplantation and highlight the remarkable durability, and possible "immortality", of autologous thalassemic stem cells, which may remain quiescent yet viable for decades after myeloablation. Systematic evaluation of long-term survivors in this unique cohort is warranted.

Disclosure: Nothing to declare

B368

HLA-MATCHED RELATED DONOR TRANSPLANTATION IN CHILDREN WITH TRANSFUSION-DEPENDENT THALASSAEMIA: A SINGLE-CENTRE EXPERIENCE IN A RESOURCE-LIMITED SETTING – LADY RIDGEWAY HOSPITAL FOR CHILDREN, SRI LANKA

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Background: Transfusion-dependent thalassaemia (TDT) is a significant health burden in low- and middle-income countries (LMIC) such as Sri Lanka. In LMIC, Haematopoietic stem cell transplant (HSCT) remains the only curative option as it's a low-cost treatment modality compared to gene therapy.

Methods: We present the outcomes of 18 children with confirmed TDT who underwent matched family donor transplants at LRH between December 2021 and Dec 2025. Patients were classified into the Pesaro groups, none of the patients was in class1. 15

children were in class 2, and 3 were in class 3. Class 1 and 2 children received oral Busulfan/Cyclophosphamide either with rabbit or horse Antithymocyte globulin. Class 3 received Thioptepa/Treosulfan/Fludarabin.
All received graft vs host disease prophylaxis with Intravenous Cyclosporin and short course of Methotrexate.

Results: All patients were under the age of 14 years at the time of transplants. and 11%(*n=2*) were under 7 years, while 88% (*n=16*) were over 7 years. The median age of the patients at the transplant was 10 years and 5 month (range 4 years 6 months to 12 years 7 months).
Karnofsky-Lansky score before transplantation was > 90 in all patients. The male-to-female ratio was 1.25:1, and all were 10/10 HLA-matched donor transplants. 55% (*n = 10*) of the patients received stem cells from their brothers, 38% (*n = 7*) from their sisters, and 5 % (*n=1*) from their father. 38% (*n=7*) had sex-matched donors, while 73% (*n=13*) had blood group-matched donors. Of the four group-mismatched donors, three were major mismatches.
72%(*n = 13*) received bone marow graft and 27% received peripharal blood stemcells. The mean CD34 stem cell dose was 7.3 x 10^6 /Kg. All patients engrafted, and the median time to engraftment was 17 days (range,15 -26 days). Platelet engraftment occurred at a median time of 20 days (range, 15 – 27 days). The median duration of follow-up was 539 days (range 51 - 1452 days).
Median donor chimerism was 99% (range 72.07 – 100%) at the last follow-up. Twelve patients achieved sustained full donor chimerism, and four had stable mixed chimerism. Despite being a LMIC, 5% transplant-related mortality (TRM), 95% overall survival (OS) rates, with a 95% thalassaemia-free survival rate and GvHD free thalassaemia free survival (GFGS) being 88.9 % at the time of writing. All 18 children are alive, transfusion-independent, and maintaining excellent quality of life.

Conclusions: This report represents a single-centre experience of HLA-matched sibling donor HSCT in children with TDT in a government-funded transplant centre in Sri Lanka. Our findings confirm that HLA-matched related donor HSCT is a safe, and cost-efficient curative option for children with TDT, even in low-resource settings. Careful patient selection, appropriate conditioning regimens,and experienced multidisciplinary care, enabled excellent outcomes.
Scaling up access to HSCT for thalassaemia in Sri Lanka and similar settings will require increased infrastructure, training, and early identification of suitable patients before irreversible organ damage occurs. Given its curative potential and cost advantage over lifelong transfusion and chelation, HSCT should be prioritised in national thalassaemia management strategies.

Disclosure: No disclosure.

B369

HAPLOIDENTICAL STEM CELL TRANSPLANTATION AS A CURATIVE STRATEGY FOR SEVERE SICKLE CELL DISEASE: A SINGLE-CENTER REPORT

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Background: Haploidentical hematopoietic stem cell transplantation (haplo-HSCT) has emerged as a curative option for patients with severe sickle cell disease (SCD) who lack an HLA-matched sibling donor. Improvements in conditioning regimens and graft manipulation have broadened transplant accessibility. We report our single-center experience using post-transplant cyclophosphamide (PTCy) platform.

Methods: Descriptive review on patients with high-risk SCD who underwent haplo-HSCT from related donors between December 2022 and December 2025. Conditioning: thiotepa, fludarabine, rabbit antithymocyte globulin (ATG) and 2 Gy TBI, except for the first patient, who received treosulfan. Graft versus host disease (GVHD) prophylaxis: mycophenolate mofetil with tacrolimus or sirolimus and PTCy, abatacept was added in the last two patients. All patients received hydroxyurea before transplantation and peri-transplant transfusion support. The first patient additionally received azathioprine for two months andrequired rituximab and plasmapheresis due to alloimmunization. Bone marrow was the graft source in all but one. Outcomes analyzed included engraftment, chimerism, GVHD, and toxicities. Data is presented as percentages and medians (p25; p75).

Results: Six haplo-HSCT were performed in five patients, median age at transplantation: 16.9 years (15.7; 17.3), 3 males. Donor median age 39.2 years (14.4; 43.5), no major group incompatibility, 1/6 with CMV mismatch. All patients achieved engraftment, with median neutrophil and platelet recovery of 20 (17.5; 23.3) and 41 days (36; 71), respectively.
The first patient experienced early graft rejection on day +40 following HHV-6 reactivation and secondary hemophagocytic lymphohistiocytosis and successfully underwent a second haplo-HSCT (different related donor; thymoglobulin, thiotepa, and fludarabine conditioning and peripheral blood stem cells source). The remaining patients maintained full donor chimerism. Delayed platelet recovery required thrombopoietin receptor agonists in 3/6. Overall survival (OS) was 100%, and event-free survival (considering death or graft failure) was 83%, with a median follow-up of 2.5 years (1.7–2.8).
Acute GVHD occurred in 66.7% of patients (grade I, n=2; grade III, n=2) with good response to treatment. Three patients developed overlap syndrome with intestinal involvement (no biopsy confirmation in 66.7% cases), treated with photopheresis and ruxolitinib: one is off treatment, one is tapering immunosuppression, and one remains on immunosuppressive therapy. One patient (20%) developed chronic GVHD (liver and ocular

involvement), after photopheresis, he remains without immunosuppressive treatment, only receiving topical treatment. CMV reactivation occurred in 2/6, hypertension (4/6), reversible acute kidney injury (3/6), mucositis (2/6) and neurologic toxicity (2/6): two cases of PRESS, one suffering from subarachnoid hemorrhage, seizures and encephalopathy with rising ammonia levels that required chelation therapy and hyperfiltration with neurological sequelae.

Conclusions: Haplo-HSCT using PTCy was feasible in this small cohort of adolescents with severe SCD, resulting in 100% OS and high rates of sustained donor engraftment. Early transplant-related toxicities were frequent, underscoring the need for careful supportive care. Given that hemoglobinopathies are non-malignant diseases, the risk of chronic GVHD remains a major concern due to its potential long-term impact on quality of life. Despite the limited sample size, these results support haplo-HSCT as a curative alternative for patients lacking an HLA-identical donor and emphasize the need for further optimization of transplant strategies.

Disclosure: Nothing to declare.

P266

HEMATOPOIETIC CELL TRANSPLANTATION IN PEDIATRIC UNSTABLE HEMOGLOBINOPATHIES: TWO RARE CASES WITH SUSTAINED DONOR CHIMERISM AND LONG-TERM FOLLOW-UP

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Background: Unstable hemoglobinopathies are rare inherited disorders. In severe cases, symptoms may appear early in life. This can include marked hemolytic anemia, fetal hydrops, and a need for transfusions. Currently, hematopoietic cell transplantation (HCT) is considered the only curative treatment available. Reports on HCT, particularly for severe variants, are limited. Existing literature often presents fragmented information and lacks comprehensive details regarding donor chimerism and long-term outcomes. This knowledge gap is especially pronounced in the pediatric population.

Methods:

We describe two pediatric patients with severe unstable hemoglobinopathies. The participants underwent HCT at a tertiary care center in Brazil. We evaluated several factors, including age at transplantation, donor type, and conditioning regimen. Additionally, we assessed hematologic engraftment, donor chimerism, and long-term clinical outcomes.

Results:

Case 1 involved a male patient diagnosed with the hyperunstable hemoglobin variant Zurich–Albisrieden. He presented with fetal hydrops and required transfusions from birth. At age 3 years, he underwent HCT from a matched sibling donor, utilizing a myeloablative conditioning regimen. Neutrophil and platelet engraftment were observed on day +28 and +35, respectively. Mild infections and suspected endothelial toxicity were managed conservatively. Donor chimerism reached > 95% within the first year post-transplant and has been maintained to the present. The patient remains transfusion-independent, with iron overload managed by therapeutic phlebotomy.

Case 2 involved a female patient with severe unstable hemoglobinopathy resulting from the co-inheritance of Hb Bristol-Alesha [β67(E11)Val→Met] and the α212 Patchwork allele. At age 1 year, she underwent haploidentical HCT from her mother after a non-myeloablative conditioning regimen of fludarabine, cyclophosphamide, and low-dose total-body irradiation. However, she experienced secondary graft failure prior to day +100. At 4 years old, she underwent a second haploidentical HCT from her father, with a myeloablative conditioning consisting of fludarabine, busulfan, and antithymocyte globulin. Neutrophil and platelet engraftment were observed on days +12 and +20, respectively, with early and sustained donor chimerism. The patient developed grade II acute cutaneous graft-versus-host disease, which responded effectively to corticosteroid treatment. After more than 8 years of follow-up, she remains transfusion-independent, with preserved cardiopulmonary function.

Table1. Characteristics and outcomes of patients

Variable	Case 1	Case 2
Sex	M	F
Hb variant	Zurich–Albisrieden	Bristol-Alesha + α212
Onset	Fetal hydrops	Congenital HA
HSCT age (y)	3	1 / 4
Donor	MSD	Haplo
Conditioning	MAC	NMAC → MAC
Engraftment	ANC +28	PLT +12; ANC +20
GVHD	No	Acute II
Chimerism	Full	Full
Transfusion-free	Yes	Yes
Follow-up	>8y	>7 y

Abbreviations: HA, hemolytic anemia; HSCT, hematopoietic stem cell transplantation; MSD, matched sibling donor; Haplo, haploidentical donor; MAC, myeloablative conditioning; ANC, absolute neutrophil count; PLT, platelets; GVHD, graft-versus-host disease; Flu, fludarabine; Cy, cyclophosphamide; TBI, total body irradiation; Bu, busulfan; ATG, anti-thymocyte globulin.. Source: Authors' own data.

Conclusions:

Currently, the literature reports few cases of transplantation in patients with unstable hemoglobinopathies. This study describes two pediatric patients exhibiting a severe phenotype. HCT resulted in durable donor chimerism and long-term transfusion independence for both patients. These findings suggest that HCT may serve as a curative treatment for severe unstable hemoglobinopathies. Moreover, myeloablative conditioning has demonstrated greater efficacy, even in the context of haploidentical transplantation.

Disclosure: Nothing to declare.

P268

EVALUATING THE SAFETY, EFFICACY, AND OUTCOMES OF A TARGETED INVASIVE PRENATAL SCREENING PROGRAM FOR HEMOGLOBINOPATHIES IN RURAL AND SEMI-URBAN INDIA

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Background: Hemoglobinopathies, such as thalassemia and sickle cell disease, are prevalent genetic disorders in India, disproportionately affecting rural and underserved populations. While there have been advances in prenatal diagnostics in metropolitan areas, access to these services still remains limited in rural regions. This study aims to evaluate the implementation and outcomes of an invasive prenatal diagnostic (IPND) program for prevention of hemoglobinopathies by Sankalp India Foundation across five states in India.

Methods: The program screened gestational women within 20 weeks of gestational age across 82 districts in five states in India, from June -2023 to September -2024. The program followed a targeted screening approach consisting of, a three-step model: HPLC testing, molecular confirmation, and invasive prenatal diagnosis for affected fetus (amniocentesis at >16 weeks and chorionic villus sampling at <14 weeks of gestation) supported by comprehensive counselling at each stage along with robust counselling at every step. Fetal samples were collected at local centers and sent to centralized laboratories for the analysis of causative mutations. Couples with a fetus diagnosed with severe hemoglobinopathy received counselling and were allowed to make informed decisions regarding medical termination of pregnancy (MTP), in accordance with the country's legal and ethical guidelines.

Results:

From June 2023 to September 2024, 81,139 women were screened across 24 centers in five states, identifying 6,323 (7.8%) carriers: 2,181 (34.5%) beta thalassemia, 3,618 (57.2%) sickle cell disease, and 524 (8.3%) other hemoglobinopathies (Hb-D Punjab, Hb-E, Hb-Lepore, etc.). Among 5,983 (94.6%) partners screened, 11 (0.2%) couples had benign variants, while 802 (13.4%) couples were at significant risk of having a fetus with a severe hemoglobinopathy.

A total of 536 (66.8%) couples registered for invasive prenatal diagnosis, and 495 (92.4%) completed the procedure. Among these, 495 singleton and five twin pregnancies were analyzed, with 381 (77%) undergoing amniocentesis at a median gestational age of 18.3 weeks (IQR 16.9–20.3) and 119 (24%) undergoing CVS at 13.1 weeks (IQR 12.3–13.8). Antibiotic prophylaxis was given in 393 (80%) cases. Two spontaneous abortions (0.6%) occurred post-amniocentesis without prophylaxis; Anti-D was administered in only two (0.4%) cases.

Of 500 fetal samples analyzed, 476 (95.2%) met quality standards, with 27 (5.4%) requiring culture or repeat testing due to maternal contamination or insufficient fetal cells; three couples required repeat procedures, with one refusal. Eight (1.6%) couples returned for testing in subsequent pregnancies.

Fetal analysis revealed 251 (50.2%) heterozygous carriers, 112 (22.4%) negative, and 137 (27.4%) affected. Couples received genetic and psychological counseling for medical termination of pregnancy (MTP), resulting in 88 (64.2%) terminations, while 49 chose to continue the pregnancy. Median turnaround time for counseling and MTP was 1.7 weeks (IQR 1.4–2.6).

Conclusions: This initiative demonstrates the feasibility of delivering IPND services in low-resource settings through a decentralized sample-collection model integrated with analysis at centralized laboratories. By integrating genetic counselling, effective sample management, and timely facilitation of informed -MTP facilitation, the program provides a scalable framework for reducing the burden of hemoglobinopathies in India.

Disclosure: The authors declare no competing financial interests.

Inborn error of immunity, hematopoiesis and metabolism

OS21-05

PROSPECTIVE MULTICENTRE ANALYSIS OF FLUDARABINE EXPOSURE IN CHILDREN RECEIVING FLUDARABINE-TREOSULFAN-THIOTEPA FOR NON-SCID INBORN ERRORS OF IMMUNITY: PRELIMINARY FINDINGS FROM HAPLO+4KIDS

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Background: Fludarabine (FLU) has largely replaced cyclophosphamide in paediatric reduced toxicity conditioning regimens as it provides potent lymphodepletion to prevent immune mediated graft rejection while offering a more favourable toxicity profile. FLU-Treosulfan±Thiotepa is now a recommended conditioning regimen for children with inborn errors of immunity (IEI). Despite widespread use, FLU paediatric dosing practices have been variable, including different dosing strategies using body surface area (BSA) and body weight, resulting in considerable heterogeneity in drug exposure. While reported target exposure ranges for paediatric HSCT vary, cumulative exposure (cAUC) > 25mg.h/L is associated with significantly higher transplant related mortality (TRM) attributed to infection and organ toxicity, while cAUC < 15mg.h/L is associated with graft failure. The Haplo+4Kids trial are conducting the first prospective study to systematically measure drug exposure for FLU-treosulfan-thiotepa within a unified conditioning platform. The preliminary results for FLU will be presented.

Methods: All patients enrolled in the Haplo+4Kids trial received standard conditioning with Thiotepa (5mg/kg BD on day -7), Treosulfan (10-14g/m^2/day on days -6, -5 and -4) and Fludarabine (40mg/m^2/day on days -6, -5, -4 and -3). Serotherapy was alemtuzumab for matched unrelated donor and ATG-Grafalon for TCRab-depleted mismatched family/unrelated donor. FLU was infused over 1 hour, with PK samples collected at 0, 1, 3 and 22 hours post end of infusion. A fully validated liquid chromatography-tandem mass spectrometry assay was used to measure fludarabine concentration. Pharmacokinetic (PK) analysis was conducted using a 3-compartment population PK model using InsightRX. FLU exposure using measured PK data was compared with model-based dosing (MBD) predictions without measured PK data to assess the appropriateness of MBD.

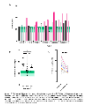
Results: FLU PK analysis has been conducted for 32 non-SCID IEI patients. Median age at HSCT was 2.7 years (0.16 - 16.3 years). All patients except one (25% dose reduction for renal impairment) received standard FLU dosing. The median cAUC was 28.1mg.h/L (16.4-49.3mg.h/L), with 20/32 patients (62%) achieving cAUC >25 mg.h/L, a level which has previously been associated with increased toxicity and transplant related mortality (Figure 1A) (Table 1). All 11 infants (<1 year) achieved exposures >25mg.h/L, with a median of 36mg.h/L (28.1-49.3mg.h/L). Infants also achieved significantly higher cAUCs than older children ($p<0.0001$) (Figure 1B) and demonstrated significantly lower body surface area normalised clearance values ($p<0.0001$).
Model predicted exposures differed significantly from the measured-predicted exposures generated after incorporating concentration-time data into the model (Figure 1C). Measured exposures (median 28.1, 16.4-49.3) were consistently higher and more variable than model predicted exposure alone (median 21.6, 17.1-30.8; $p<0.0.001$). Had model-based dosing alone been utilised, potentially suboptimal achieved exposures would have been missed for 14/32 patients (44%).

Table 1

	Patient Age (Years)		
	< 1 (n= 11)	1-13 (n= 16)	³ 13 (n= 5)

Weight (kg), Median (range)	6.5 (4.2 - 10.7)	14.9 (7.5 - 35)	55.2 (23.8 -72.2)
BSA (m^2), Median (range)	0.36 (0.28 -0.53)	0.65 (0.4 - 1.2)	1.6 (0.9 - 1.9)
Creatinine (pre 1st flu infusion) (mmol/L), Median (range)	21 (12 – 37)	23.5 (17-85)	44 (31 – 76)
cAUC (mg.h/L), Median (range)	36 (28.1 – 49.3)	24.2 (16.4 – 35.6)	30.1 (24.5 - 35.2)
Patients with cAUC 20-25 mg.h/L n (%)	0 (0)	9 (56)	2 (40)
Patients with cAUC <20 mg.h/L n (%)	0 (0)	2 (12.5)	0 (0)
Patients with cAUC >25 mg.h/L n (%)	11 (100)	5 (31)	3 (60)
MBD dosing cAUC (mg.h/L), Median (range)	27.4 (22.2 - 30.8)	18.6 (17.1 - 26.6)	24.2 (20.9 - 25.5)
Percentage difference between measured PK and MBD cAUC, Median (range)	32.2 (6.2 - 101.3)	29.8 (-14.1-87.4)	30.3 (-3.9 - 63.0)

Figure 1



Conclusions: Preliminary data indicate considerable interpatient variability in fludarabine exposure in paediatric HSCT patients. Body surface area-based dosing may lead to overexposure, particularly for infant patients. MBD without measured PK data was inaccurate in estimating individual fludarabine exposure in our study cohort, underscoring the importance of real-time therapeutic drug monitoring to enable personalised dosing to achieve a targeted drug exposure to optimise engraftment whilst minimising the risk of toxicity.

Clinical Trial Registry: Haplo+4Kids – ISRCTN11859866 - https://www.isrctn.com/ISRCTN11859866

Disclosure: Nothing to declare.

OS21-07

PATIENT-CENTERED, MULTIDISCIPLINARY DELPHI PROCESS TO DEVELOP EUROPEAN CONSENSUS FOR LATE EFFECTS POST-HSCT FOR PATIENTS WITH INBORN ERRORS OF IMMUNITY ON BEHALF OF IEWP AND ESID

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Background: While data on long-term outcomes after haematopoietic stem cell transplantation (HSCT) are growing, existing guidance remains dominated by cohorts with haematological malignancies and often focuses on early follow-up. For patients with inborn errors of immunity (IEI), late effects are uniquely influenced by the underlying immune defect, treatment toxicity, and immune reconstitution, necessitating tailored survivorship care. This project developed the first European, multidisciplinary consensus guidance specifically for late effects post-HSCT in the IEI population. Our objective was to develop and validate the first European, patient-centered, multidisciplinary consensus guidance for the surveillance and management of late effects following HSCT in patients with IEI.

Methods:

Figure 1: External expert group; collaborators:

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A rigorous, stepwise consensus process was followed: (1) Systematic Literature Review: A comprehensive search of PubMed/Medline and additional databases from April–November 2023 (with updates in March 2024, March 2025, and September 2025) identified 24,768 publications. Inclusion criteria encompassed all study types (including case reports and expert views) involving adult and/or paediatric recipients of HSCT for IEI, with long-term follow-up data (>2 years post-HSCT). Exclusion criteria were *in vitro* or animal studies, non-English language publications, studies with no or few IEI-HSCT patients, and studies reporting only short-term outcomes (<2 years). Following screening and duplicate removal, two independent reviewers applied these criteria for selection and critically appraised the level of evidence, with disagreements resolved by a third reviewer. This resulted in 278 publications for inclusion. (2) Drafting & Grading: Initial recommendations were drafted and graded using the GRADE framework. (3) Internal Consensus: A two-round Delphi process was conducted with a core multidisciplinary panel of 18 internal experts, including 5 junior specialists, 2 nurse specialists, 2 psychologists, 1 patient representative, and 8 senior bone marrow transplant (BMT) and immunology experts. (4) External Validation: A third Delphi round was performed with an independent European validation group of 15 senior BMT and immunology experts (collaborators; figure 1). (5) Integration & Implementation: This included an internal review of external feedback and collaboration with the International Patient Organisation for Primary Immunodeficiencies (IPOPI) to develop a patient leaflet. Consensus was defined *a priori* at ≥80% and further categorized: 100% (unanimous), 90–99% (very strong), and 80–89% (consensus).

Results: The systematic review informed the initial 77 recommendations. The internal Delphi successfully generated consensus on all 77 recommendations across core domains. External validation refined the guidance, with consensus reached on 70/77 recommendations (90.9%). Of these, unanimous consensus was achieved for 29 (37%), very strong consensus for 25 (32%), and consensus for 16 (21%) recommendations. The final guidance is now undergoing internal review, constituting the first part of the implementation step.

Conclusions: This work demonstrates a robust model for guideline development, resulting in the first comprehensive European consensus for post-HSCT survivorship care in IEI. The integration of a parallel patient-resource development process ensures the final guidance will serve as a clinically valid and practical tool to standardize and improve long-term follow-up care for this unique patient population across Europe.

Disclosure: Nothing to declare

Paed4-01

HEMATOPOIETIC STEM CELL TRANSPLANTATION IN 752 CHILDREN WITH OSTEOPETROSIS: A STUDY OF THE INBORN ERRORS WORKING PARTY OF THE EBMT

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Background: Osteopetrosis (OP) is a group of rare inherited conditions characterized by dysfunctional osteoclasts, leading to hypocalcemia, cytopenia, bone fractures and vision loss. Hematopoietic stem cell transplantation (HSCT) is the only curative approach for most children with OP but is complicated by high incidence of graft failure (GF), veno-occlusive disease (VOD) and transplant-related mortality (TRM). To define prognostic risk factors in this setting, the IEWP of the EBMT performed a large registry study on HSCT in OP.

Methods: We analyzed the outcomes of children with OP receiving HSCT in EBMT centers between 1990 and 2022. Endpoints were overall survival (OS) and event-free survival (EFS) according to year of HSCT, donor type, stem cell source and conditioning regimen.

Results: We studied 752 children affected by OP, with a median age at transplant of 0.7 years (range: 0-15). Genetic results were available for 435 patients: *TCIRG1* 66.4%, *CLCN7* 12.9%, *SNX10* 6.6%, *RANK* 5.9%, and others 8.2%. The median follow-up was 7 years (range 0-33.8 years). Conditioning regimen was Busulfan/Fludarabine (n=316; 43.9%), Busulfan/Cyclophosphamide (n=237; 32.9%), Treosulfan/Fludarabine/Thiotepa (n=131; 18.2%), or other (n=36; 5%). Donors were matched sibling donor (MSD; n=208, 29.2%), matched related (MRD; n=78, 11%), matched unrelated (MUD, 10/10 or 6/6; n=174; 24.4%), mismatched related (MMRD; n= 168; 23.6%), mismatched unrelated (MMUD, n= 84; 11.8%). Stem cell source was bone marrow (BM, n=476; 63.8%), peripheral blood (PB, n=201; 26.9%) or umbilical cord blood (UCB, n=63; 8.4%).
The 3-year Kaplan-Meier estimate of OS was 69% (95% CI, 66-73). Survival improved over time: 3-year OS was 50% (42-59%), 66% (60-73%) and 78% (73-82%) for patients transplanted between 1990-2000, 2001-2011 and 2012-2022, respectively (p<0.001).
Risk factor analysis was performed for patients transplanted between 2007-2022 (n= 497, 66%), reflecting adoption of modern transplant procedures. In this group, the 3-year OS, EFS and CI of graft failure (GF) was 75% (71-79%), 62% (57-66%) and 21% (17-26%), respectively.
In multi-variate analysis (MVA), OS was lower in patients with poor performance status (HR, 1.73; p=0.047), splenomegaly (HR, 2.26; p=0.007). Centre size was associated with OS, with better outcomes in large centers (p<0.001), motivating the inclusion of center in the MVA model.
In MVA, EFS was lower in patients with poor performance score (HR, 2.11; p<0.001), splenomegaly (HR, 2.92; p<0.001), use of HLA mismatched donors (HR, 1.85; p=0.001) and PB as stem cell source (HR, 1.67; p=0.001).
The 30-day CI of VOD was 22% (16-24%). In MVA exposure to Busulfan/Fludarabine (HR, 5.35; p<0.001) was an independent risk factor. Arterial pulmonary hypertension and hypercalcemia were described in 12.1% and 18.5% evaluable patients, respectively.
OP-related clinical phenotype HSCT showed improved cytopenia (p<0.001), growth (p<0.001), and intracranial hypertension (p<0.001). Second HSCT was performed in 104 patients, with a 3-year OS and EFS of 56% (46-66%) and 40% (30-50%), respectively.

Conclusions: This is the largest study to date describing HSCT outcomes in children affected by OP. Survival has significantly improved over the last decade, especially when an HLA matched donor is unavailable. Due to the complexity of OP patients, it is recommended that HSCT is performed in large centers.

Disclosure: no conflicts of interest

Paed4-08

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH ATAXIA-TELANGIECTASIA - A MULTICENTER STUDY BY EBMT/IEWP

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Background: Ataxia-telangiectasia (A-T) is a rare DNA-repair disorder characterized by progressive neurodegeneration, immunodeficiency, and a high risk of malignancy. The role of allogeneic hematopoietic stem cell transplantation (alloHSCT) in A-T remains controversial due to concerns regarding toxicity and transplant-related mortality. We report a multicenter experience evaluating feasibility, outcomes, and indications for alloHSCT in patients with A-T.

Methods: We retrospectively analyzed 16 A-T patients undergoing alloHSCT in 8 centers. Indications included malignancy (n=5; EBV+ B-NHL n=1, ALL n=1, T-ALL n=3) and pre-emptive transplantation for immunodeficiency (n=11; CID/SCID phenotypes, severe infections, granuloma, HIGM phenotype, or abnormal newborn screening). Conditioning regimens included reduced-intensity or non-myeloablative fludarabine-based protocols using cyclophosphamide, busulfan or treosulfan, and serotherapy (ATG or alemtuzumab). Overall survival (OS), transplant-related toxicity, graft-versus-host disease (GVHD), and donor chimerism were assessed.

Results: Median age at alloHSCT was significantly lower in the pre-emptive group compared with the malignancy group (2.5 vs 8 years; $P = 0.013$). Median follow-up was 6 years (range 5–9) for pre-emptive HSCT and 11 years (range 2–16) for malignancy-associated HSCT.

Overall survival did not differ significantly between groups (log-rank $P = 0.31$). In the pre-emptive cohort, alloHSCT resulted in sustained correction of immunodeficiency with resolution or improvement of severe infections and granulomatous disease. Peripheral blood donor chimerism at last follow-up was significantly higher in the malignancy cohort, nevertheless both groups achieved high T cell chimerism levels.

Conclusions: Allogeneic HSCT in A-T is feasible when using carefully selected reduced-intensity conditioning regimens. Pre-emptive alloHSCT appears effective in correcting immunodeficiency and may reduce the risk of malignancy. Outcomes in malignancy-associated HSCT were comparable when performed in complete remission. These data support further prospective evaluation of pre-emptive alloHSCT as a disease-modifying strategy in selected A-T patients.

Disclosure: No conflict of interest

B370

HEMATOPOIETIC CELL TRANSPLANTATION FOR PRIMARY IMMUNODEFICIENCIES IN CHILDREN: THE UKRAINIAN EXPERIENCE (2018–2025)

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Background: Hematopoietic cell transplantation (HCT) remains the only curative treatment for many primary immunodeficiencies (PIDs). In Ukraine, although 11 medical centers are involved in transplantation activities, the National Specialized Children's Hospital "Ohmatdyt" (NSCH) is the only institution providing sustained paediatric HCT across haematologic, oncologic, metabolic disorders, and PIDs.
Since 2022, Ukraine has implemented a national expanded newborn screening program, increasing the number of screened conditions from 4 to 21, including severe combined immunodeficiency (SCID). This study summarizes the clinical experience and outcomes of paediatric HCT for PIDs performed at our center between March 2018 and July 2025, with emphasis on early diagnosis and transplant timing.

Methods:

We conducted a retrospective analysis of 25 children with PIDs who underwent allogeneic HCT between 2018 and 2025. Conditioning regimens were based on a modified EBMT/ESID Protocol D with individualized adjustments according to clinical status, infectious burden, donor availability, and transplant-related risk. GVHD prophylaxis was donor-adapted: matched sibling donors (MSD) received cyclosporine A (CsA) and methotrexate (MTX); matched unrelated donors (MUD) received CsA, MTX, and antithymocyte globulin (ATG); haploidentical donors received post-transplant cyclophosphamide (PTCy), CsA, and mycophenolate mofetil (MMF).

Results:

Baseline patient and transplant characteristics are summarized in Table 1. Ten patients (40%) had SCID and 15 (60%) had non-SCID PIDs. The median time from diagnosis to HCT was 3.3 months in SCID and 12.9 months in non-SCID PIDs. Importantly, five SCID cases were identified through the national newborn screening program, enabling pre-symptomatic diagnosis and early referral for transplantation.

Tab 1. Patient and Transplant Characteristics (March 2018 – July 2025)

Characteristic	Value
Patients, n	25
Male, n (%)	21 (84)
Age < 1 year, n (%)	6 (24)
Mean age, years	4
Diagnosis category, n (%) and details, n	**SCID 10 (40);** IL2RG - 3; AK2 - 1; ADA-II deficiency - 1; RAG1 - 1; IL7RA - 1; Artemis - 1; Omenn - 1; CARD11 - 1
	PID 15 (60) WAS - 3; XLP - 2; CGD - 1; STAT1 GOF 1; DOCK8 - 1; GATA2 defficiency - 1; Hyper-IgM (CD40LG) 1; NBS - 1; CID - 1; ADA II 1; CVID - 1; IPEX 1
Median time to HCT, months	SCID 3,3; non-SCID 12,9
Median follow-up, years	2,5
Donor type, n (%)	MSD 8 (32); Haplo 1 (4); MUD 12 (48); MMUD 4 (16)
Graft source, n (%)	PBSC 16 (64); BM 7 (28)
GVHD prophylaxis, n (%)	CsA+MTX 10 (40); CsA+MMF 13 (52); none 2 (8)
Chimerism, n (%)	Complete 16 (64); Mixed 8 (32)
aGVHD, n (%)	15 (60)

Tab 1. Patient and Transplant Characteristics (March 2018 – July 2025)

Characteristic	Value
cGVHD, n (%)	6 (24)
aGVHD grade, n (%)	I–II 9 (60); III–IV 6 (40)

HCT – hematopoietic stem cell transplantation; **SCID** – severe combined immunodeficiency; **PID** – primary immunodeficiency; **MSD** – matched sibling donor; **Haplo** – haploidentical donor; **MUD** – matched unrelated donor; **MMUD** – mismatched unrelated donor; **PBSC** – peripheral blood stem cells; **BM** – bone marrow; **GVHD** – graft-versus-host disease; **aGVHD** – acute GVHD; **cGVHD** – chronic GVHD; **CsA** – cyclosporine A; **MTX** – methotrexate; **MMF** – mycophenolate mofetil.

WAS – Wiskott–Aldrich syndrome, **XLP** – X-linked lymphoproliferative disease, **CGD** – chronic granulomatous disease, **STAT1 GOF** – STAT1 gain-of-function disease, **NBS** – Nijmegen breakage syndrome, **CID** – combined immunodeficiency, **ADA-II** – adenosine deaminase 2 deficiency, **CVID** – common variable immunodeficiency, **IPEX** – immune dysregulation, polyendocrinopathy, enteropathy, X-linked syndrome

Twenty-two patients received treosulfan-based conditioning; one received melphalan, and two neonatally screened infants underwent HCT without conditioning. Median neutrophil engraftment occurred on day +18. Complete donor chimerism was achieved in 18 patients, while 6 exhibited mixed chimerism.
Acute GVHD occurred in 15 patients (grade I–II: n=9; grade III–IV: n=6), and chronic GVHD was observed in 6 patients, with ongoing immunosuppression required in 2 at last follow-up. Two deaths were recorded: one transplant-related death due to severe grade IV acute GVHD and one early death on day +13 due to acute cardiovascular failure associated with engraftment syndrome. Day +100 transplant-related mortality was 4% (1/25).

With a median follow-up of 2.5 years, **overall survival was 92%**, as shown in **Figure 1**.

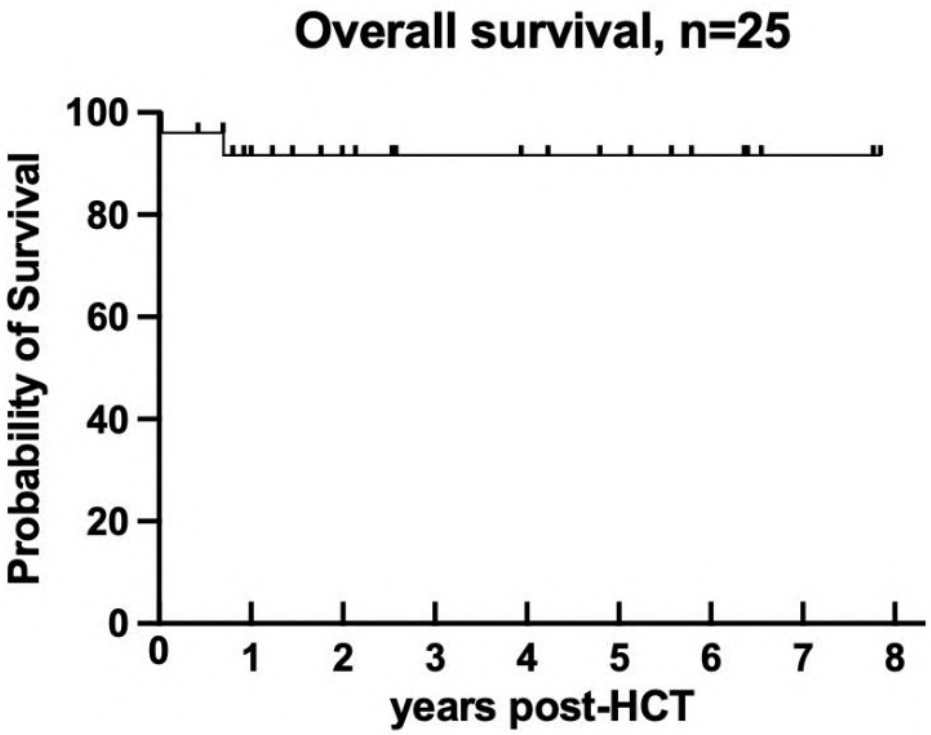

Figure 1. Kaplan–Meier estimate of overall survival after allogeneic HSCT in children with primary immunodeficiencies (n = 25). Tick marks indicate censored observations.

Conclusions: Allogeneic HCT is a feasible and effective curative strategy for children with PIDs in Ukraine, achieving high overall survival and low early transplant-related mortality. The implementation of a national expanded newborn screening program enabled earlier identification of SCID and timely transplantation, contributing to improved outcomes. Notably, 14 of the 25 HCT procedures were performed after the onset of full-scale war, demonstrating sustained and increasing transplant activity despite ongoing conflict. Centralization of paediatric PID transplantation within a single high-volume expert center

allows to optimize resoursces and maintain care quality during wartime conditions. These data reflect the growing capacity and resilience of the Ukrainian paediatric HCT program and highlight the importance of continued expansion of newborn screening and structured referral pathways for children with PIDs.

Disclosure: Nothing to declare

B371

OUTCOMES OF ALLOGENEIC HSCT IN NIJMEGEN BREAKAGE SYNDROME WITH TREOSULFAN-BASED CONDITIONING REGIMEN - A MULTICENTER STUDY

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Background: Nijmegen breakage syndrome (NBS) is a DNA repair disorder characterised by combined immunodeficiency and susceptibility to lymphoid malignancies. Currently HSCT is considered in NBS to prevent malignancy. Minimal-intensity regimens are used in NBS due to risks of toxicity. We recently demonstrated experience of treosulfan 30g/m^2 versus low doses of busulfan. The aim of the current study was to compare efficacy of treosulfan dose 30g/m^2 versus 21g/m^2.

Methods: From 2017 to 2025, 40 NBS patients received allogeneic HSCT with treosulfan-containing conditioning in 5 Russian centers. The median age at NBS diagnosis was 5 years (0.05-15.7), at HSCT 7.4 years (0.5-16.2). Fifteen patients had leukemia/ lymphoma before HSCT (median time of remission to HSCT 10 months (1.4-74)). To 2020, treosulfan 30g/m^2 was used in 16 (Treo30 group) and after 2020 treosulfan 21g/m^2 in 24 patients (Treo21 group). All received fludarabine 150mg/m^2, 24 cyclophosphamide (22–40mg/kg, 1–30mg/kg, 1–20mg/kg). In 37 patients, rabbit ATG (thymoglobulin, Genzyme) 3-7,5mg/kg, in 1 patient horse ATG (ATGAM) 100mg/kg, and in 2 patients no serotherapy was used.
In 25 patients matched unrelated (19–10/10, 6–9/10 HLA-matched), in 9 mismatched related, in 6 matched sibling donor was used. In 19 TCRab/CD19 depletion, in 14 post-transplant cyclophosphamide (25-80 mg/kg), and in 7 patients (4 MSD, 3 MUD) no T-cell depletion was used. 29 patients received various regimens of immunosuppression (16 calcineurin inhibitor-based, 13-other) and 11 patients no immunosuppression (10 after TCRab/CD19 depletion, 1 after Pt-Cy in MSD).

Results: The median follow-up time in survivors was 8,0 years (4,7-8,8) and 2,7 (0,8-5,3) in Treo30 and Treo21 groups, respectively, p<0,001. Overall survival was 0,81 (95%CI 0,62-1,0) after Treo30 and 0,76 (95%CI 0,56-0,95) after Treo21, p=0,7.
All patients reached primary engraftment. The median time of neutrophil engraftment was 13,5 days (10-21) in Treo30 and 19 days (11-28) in Treo21 groups, p=0,009, which was due to higher proportion of TCRab/CD19 depletion in Treo30. The median time of engraftment after TCRab/CD19 depletion was 13 days (10-21) versus 19 days (13-28) after non-depleted grafts, p=0,0003. No patients developed graft rejection.
Severe organ toxicity was seen in 14 patients, 6 received Treo30 and 8 Treo21. Incidence of acute GVHD was 0,5 (95%CI 0,31-0,82) in Treo30 and 0,63 (95%CI 0,46-0,85) in Treo21 (p=0,88), of chronic GVHD 0,31 (95% CI 0,15-0,65) in Treo30 and 0,25 (95% CI 0,13-0,5) in Treo21 groups (p=0,79). The incidence of significant viral infections was 0,38 (95%CI 0,2-0,71) after Treo30 and 0,38 (95%CI 0,22-0,63) after Treo21 (p=0,94).
Two patients (both after Treo30) developed rhabdomyosarcoma (in 7 and 37 months post-HSCT, 1 of them died). Four patients (all after Treo21) developed leukemia relapse (2 received CAR-T therapy and alive, 2 died).
At last follow-up, 8 patients had mixed chimerism, 5 after Treo21 and 3 Treo30, p=0,22. Six of them had hypogammaglobulinemia requiring regular immunoglobulin replacement.

Conclusions: Both doses of treosulfan 21g/m^2 and 30g/m^2 were well tolerated by NBS patients. However, lower dose of 21g/m^2 was associated with higher risk of mixed chimerism and leukemia relapse versus increased incidence of secondary malignancy after higher dose of 30g/m^2.

Disclosure: The authors declare no conflict of interest.

B372

FACTORS ASSOCIATED WITH MIXED CHIMERISM IN CHILDREN WITH NON-MALIGNANT DISEASES TRANSPLANTED WITH A TREOSULFAN-BASED REGIMEN

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Background: Treosulfan is an alkylating agent used for conditioning for hematopoietic stem cell transplant (HSCT). Children with non-malignant diseases have been shown to have increasing incidence of mixed chimerism when undergoing HSCT at a younger age with melphalan-based (Fitch, et al, 2024) and with busulfan-based conditioning (Dvorak, et al, 2025). This has not yet been evaluated in the context of Treosulfan-based conditioning. Our group has previously published that, conditioning with treosulfan and fludarabine is insufficient for achieving long term donor chimerism in patients with diseases of neutrophil function (Jacoby, et al, 2023).

Methods: We retrospectively reviewed charts of patients undergoing first HSCT for non-malignant disease from 2008 – 2024. In order to isolate the effects of age and conditioning on our ability to myeloablate these patients, we excluded patients with immunologic graft failure and patients with recent chemotherapy for malignancy. Parameters evaluated included diagnosis, age at transplant, cell dose, thiotepa administration, serotherapy administration, and the main outcome was chimerism status at 12 months from HSCT.
All patients received treosulfan and fludarabine, some patients received additional serotherapy (either ATG or alemtuzumab) and/or thiotepa (10 mg/kg on day -2 before HSCT).
Comparison of categorical variables was analyzed using the Fisher exact test, multiple categorical variables together were compared using multiple logistic regression. Mixed chimerism was defined as <95% donor chimerism in whole blood. Immunologic graft rejection was defined as either primary or secondary graft failure with subsequent pancytopenia.

Results: We reviewed 111 consecutive transplants that met inclusion criteria. Patient characteristics are shown in Table 1. Patients undergoing HSCT at an age younger than 6 years had a significantly higher mixed chimerism than patients older than 6 years (52.8% vs 20.8%, p = 0.0057). Similarly, patients not receiving thiotepa had higher incidence of mixed chimerism than patients who received thiotepa (66.1% vs 20.4%, p <0.0001). On multivariate logistic regression lack of thiotepa administration was strongly correlated with mixed chimerism while age <6 and serotherapy administration were not.
Subgroup analysis confirms that thiotepa addition for treosulfan-based conditioning is necessary for durable engraftment in disorders of neutrophil function - of 13 patients transplanted without thiotepa the average 12 month donor chimerism was 25.5% (range 0-64%), whereas the three patients transplanted with thiotepa had 12 month donor chimerism of 90, 100, and 100%.

	Total	Mixed Chimerism (n = 51)	Full Donor Chimerism (n = 60)
Age < 6 years	87	46	41
Age > 6 years	24	5	19
IEI	82	43	39
Red Cell/Platelet	16	5	11
Metabolic	13	6	7
Serotherapy +	89	42	47
Serotherapy -	22	9	13
Thiotepa +	49	10	39

Thiotepa -	62	41	21

Conclusions: Treosulfan and fludarabine conditioning does not ensure durable engraftment in patients with non-malignant diseases especially in disorders of neutrophil dysfunction. Increased mixed chimerism is associated with age <6 years old, suggesting the previous observations of Fitch and Dvorak may be more universal. Still, the addition of thiotepa to conditioning was the most consistent predictor of full donor chimerism.

Disclosure: I have received consultation honoraria/speaker fees from Sanofi, related to belumosudil

B373

MULTICENTER EXPERIENCE OF HSCT IN RAS-ASSOCIATED AUTOIMMUNE LEUKOPROLIFERATIVE DISEASE (RALD) – IEWP EBMT STUDY

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Background: RALD – is a rare phenocopy of inborn error of immunity, caused by somatic gain-of-function mutations in KRAS/NRAS genes. The main clinical features are autoimmunity (mainly immune cytopenia) and lymphoproliferation. Case descriptions of RALD are limited and only few cases of HSCT have been reported to date. The aim of the current study was to estimate efficacy of HSCT in RALD.

Methods: Through IEWP EBMT, 7 RALD patients who received HSCT were identified: 4 in Russia and 3 in the UK. The median age at diagnosis was 1.7 years (range 0.8-9.4). In four patients, KRAS c.37G>T and in three, NRAS c.38G>A mutations were identified. All patients had immune cytopenia (hemolytic anemia (AIHA) (n=7), thrombocytopenia (n=5)) and lymphoproliferative syndrome, 3 severe/recurrent infections, 2 neutropenia, 2 systemic lupus erythematosus, 1 ulcerative colitis and osteomyelitis with myeloid cell infiltration, and 1 erythroid myelodysplasia. All had peripheral blood monocytosis (median 4x10*9/L) and hypergammaglobulinemia (median IgG 20g/L). All patients received 2 or more lines of immunosuppression, 4 required regular antibiotics, 2 regular IVIG with no complete remission achieved in any.

Results: The median age at HSCT was 4.8 years (range 2.3-10.2). Six patients received treosulfan/thiotepa-based myeloablative conditioning (MAC) and one busulfan-based MAC. Serotherapy included rabbit ATG in 4, alemtuzumab in 2 and none in 1. Four patients additionally received rituximab. The donor source included haploidentical parents in 4, matched sibling in 1, matched unrelated donor in 1, and 6/8 unrelated cord blood in 1. For graft-versus-host disease (GVHD) prophylaxis, in haploidentitcal grafts TCRab/CD19 depletion was used in 3 and posttranspant cyclophosphamide with ruxolitinib in 1. In the remaining, ciclosporin alone and in combination with prednisolone/mycophenolate mofetil was used.
Neutrophil engraftment occurred in 5 patients (median 16 days, range 11-24 days). One patient developed primary graft rejection and three early secondary rejection. All patients with graft failure received second HSCT (in 2.5, 3, 5.3 and 9 months), 2 from the same donors and 2 with donor change. In second HSCT, conditioning regimens were switched to melphalan/cyclophosphamide and irradiation in two and to busulfan in 1 (after treosulfan) and to treosulfan in one (after busulfan). No patients had severe acute or chronic GVHD. Four patients after the first HSCT and four patients after the second HSCT developed viral reactivation requiring therapy.
All patients are alive with median follow-up after the last HSCT of 5.5 years (range 1-7.4). At last follow-up, 3 patients had 100% donor and 3 82-94% donor chimerism, (mixed T cell with full donor myeloid chimerism in 2). One patient with mixed chimerism has lupus nephritis, and one AIHA. No other patients have disease symptoms, one has hypogammaglobulinemia (after post-HSCT rituximab).

Conclusions: HSCT is a feasible option to control symptoms of RALD. Our case series demonstrate a very high risk of graft failure, however, salvage HSCT is a viable option in these patients. Mixed chimerism may lead to uncomplete disease control. Larger series are needed to elaborate optimal timing and HSCT regimens in this condition.

Disclosure: The authors declare no conflict of interest.

B374

OUTCOMES OF LATE-ONSET KRABBE DISEASE TREATED WITH HAEMATOPOIETIC STEM CELL TRANSPLANTATION: SINGLE-CENTRE EXPERIENCE

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Background: Krabbe disease is a rare lysosomal storage disorder caused by deficiency of the galactocerebrosidase (GALC) enzyme, resulting in psychosine accumulation, progressive demyelination, and neuronal loss. The late-onset form presents with variable combinations of spasticity, ataxia, and cognitive decline. Haematopoietic stem cell transplantation (HSCT) may modify disease progression by providing donor-derived microglial enzyme activity that helps clear psychosine and preserve myelin integrity. However, HSCT carries significant

morbidity and mortality, and published outcomes in late-onset Krabbe disease are limited and heterogeneous. We report survival, neurodevelopmental, radiological, and HSCT outcomes of children with late-onset Krabbe disease, including the first patient to receive transplant for the attenuated form in the UK.

Methods: We performed a retrospective review of all patients with juvenile-onset Krabbe disease who received HSCT at Birmingham Children's Hospital between 2015 and 2025. Clinical, biochemical and genetic data were collected. Transplant details included donor type, stem-cell source and dose, conditioning regimen and engraftment kinetics. Neurological function was assessed using serial clinical examinations. Brain MRI scans were reviewed pre- and post-transplant, and white matter changes were scored using a semi-quantitative system of disease burden. Electrophysiological studies were analysed longitudinally where available. Survival, transplant-related toxicity, and neurological trajectory were evaluated up to the last follow-up.

Results: Six patients underwent HSCT for late-onset Krabbe disease during the study period. Four were symptomatic and two presymptomatic at the time of transplantation. The median age at HSCT was seven years (range 2–12). Conditioning regimens included Fludarabine/Busulfan and Busulfan/Cyclophosphamide with serotherapy. Donor sources were mismatched cord (3/6) and MUD (3/6). Notably, two patients had graft failure and required rescue with a second graft using a haploidentical donor. At a median follow-up of 87.5 months post-transplant, five patients were alive, and one died from CMV pneumonitis at day +147. Transplant-related complications included viral reactivation in three patients and acute skin graft-versus-host disease (GvHD) in two patients. None of the surviving patients developed chronic GvHD. Four surviving patients had full donor chimerism at most recent assessment. One patient developed mixed chimerism, stabilising at 94% six years post-HSCT. All surviving patients demonstrated neurological stabilisation, with improvement or preservation of motor and cognitive function compared to their pre-transplant course. Post-HSCT galactocerebrosidase levels normalised within 3 months of transplant, while MRI showed stabilisation of white matter abnormalities in all survivors. Electrophysiological studies showed stable conduction velocities over time.

Conclusions: Our review of a single – centre cohort of patients with late-onset Krabbe disease demonstrated that HSCT appears to modify the natural history of the disease, resulting in prolonged survival and stabilisation of neurodegenerative progression when performed in appropriately selected patients. Transplant was generally well tolerated without a significant morbidity however graft failure remains a significant problem in this group of patients, with two out of six patients in our cohort requiring a second graft. Larger, collaborative studies are required to refine prognostic markers, optimise donor and conditioning strategies, and establish standardised pre-HSCT evaluation and follow-up protocols to maximise the benefits of HSCT in this leukodystrophy.

Disclosure: Nothing to declare

B375

HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) IN NEUROPATHIC MUCOPOLYSACCHARIDOSIS TYPE-II (MPS-II) PRESERVES NEURODEVELOPMENT AND SHOULD BE ROUTINE PRACTICE

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Background: MPS-II (Hunter Syndrome) is a rare X-linked lysosomal storage disease resulting in multi-system accumulation of heparan and dermatan sulfate with genetic deficiency of iduronate-2-sulfatase enzyme. In its more common "neuropathic or severe" form, it causes progressive neurodegeneration, severe functional limitations, and early death. It is often thought that enzyme replacement therapy (ERT) is the treatment of choice, and that allogeneic HSCT isn't indicated and is less effective than it is in MPSIH (Hurler Syndrome).
ERT has many limitations in controlling disease progression including attenuating antibodies, and that it doesn't penetrate the BBB and affect CNS correction. However, Graft-derived leukocytes cross the BBB and deliver enzyme to the brain as microglia, with no immune response against the deficient enzyme protein, since it is not foreign to the graft source. Despite some evidence supporting early HSCT, there is still very little systemically reviewed data available to support a paradigm shift in guidance towards early diagnosis and treatment with HSCT rather than ERT.

Methods: We report dramatic outcome differences between 2 siblings, one treated with ERT, and another with HSCT, emphasising the importance of early intervention, and cellular therapy in optimising patient outcomes.
The older sibling (Sibling-A) was diagnosed at 4 years of age (post-symptom onset) and received weekly ERT.
The younger sibling (Sibling-B) was diagnosed at birth via newborn biochemical and genetic testing showing same diagnosis. He underwent a 10/10 HLA MUD HSCT (BM source) at the age of 3 months. He was conditioned with Busulfan and Fludarabine following the standard European Guidelines. Alemtuzumab Serotherapy and GVHD prophylaxis with Ciclosporin-A were used. A second transplant at the age of 1 year was required after secondary engraftment failure (myeloid chimerism falling below 17% after 6 months). The same donor donated PBSC and conditioning was with Fludarabine, Thiotepa and Treosulfan. Alemtuzumab serotherapy, Cyclosporin-A and mycophenolate mofetil used as GVHD prophylaxis.
Defibrotide was used for VOD prophylaxis in second transplant due to experiencing mild VOD during first transplant.
Multisystem evaluation including neurodevelopmental assessments were recorded over 6–7 follow-up-years.

Results: Despite sharing the same biochemical and molecular diagnosis, the siblings experienced significantly divergent developmental and multisystem outcomes.

Sibling-A showed some early somatic improvements but has expectedly experienced severe irreversible neurocognitive decline. He initially plateaued then progressively lost most of the acquired developmental and language skills.
Sibling-B achieved stable 100% donor chimerism after the second HSCT with mild transplant related acute complications including mild skin GVHD resolving with short-course of systemic steroids, and with no chronic complications. Circulating mixed leukocytes measured normal levels of iduronate-2-sulphatase activity. He has been showing highly preserved neuro-cognitive development within normal limits for age.

Comparison of Developmental Milestones and Functional Status of both Siblings

Milestone / Skill	Sibling A – Older Sibling (Late ERT)	Sibling B – Younger Sibling (Early HSCT)
Sitting unsupported	Initially no delay but later requiring supportive chair most of the time.	Achieved at 10 months (mild delay due to transplant period). Currently sits independently without issues (normal balance).
Crawling	Achieved on time.	Achieved at 12 months.
Walking independently	Initially no delay, but toe-walker. Later becoming very stiff, walking like "an old man" for short distances and requiring constant support.	Delayed – achieved at 2 years old (24 months) after recovery from transplants. Currently walks and runs normally for age with no gait abnormality or fatigue.
First words	Delayed – only began saying a few single words around 3–4 years old.	Slightly delayed – spoke first words around 18–24 months.
Combining words	Never achieved meaningful phrases; at best had <5 single words, which were later lost (no phrase speech).	Achieved by 3 years old, speaking in 3-4-word sentences.
Later speech and communication abilities	No functional speech at 10 years old; non-verbal aside from occasional sounds. Uses some signs or gestures but largely unable to communicate needs.	Age-appropriate speech at 7 years; fluent in communicating wants and needs. Mild word-finding difficulty at times but essentially normal language for age.
Hearing	Newborn hearing screen failed; diagnosed bilateral moderate SNHL in early childhood. Uses hearing aids since toddlerhood but hearing progressively deteriorated to	Newborn hearing screen failed with mild conductive loss in infancy. Developed mild bilateral SNHL by age 5 (≈30 dB). Uses bilateral hearing aids

Comparison of Developmental Milestones and Functional Status of both Siblings		
	severe mixed loss by age 8–10 (requires loud prompts even with aids).	consistently with good benefit; hearing is stable and mild with aids.
Vision	Mild corneal clouding and mild hyperopia. Refusing corrective glasses due to cognitive delay.	Clear corneas and normal vision with very mild hyperopia effectively corrected with glasses.
Cardiac	No cardiomyopathy, mild mitral valve thickening by age 8 (trace prolapse) but normal function.	Normal cardiac exams and echocardiograms to date; no valvular disease or cardiac dysfunction.
Airway/Sleep	Chronic rhinorrhea and loud snoring from infancy. Developed obstructive sleep apnoea by age 9 (AHI 14) requiring invasive interventions.	No chronic upper airway obstruction. No sleep apnoea on studies post-HSCT; normal sleep quality without intervention.
Continence (Toilet training)	Never achieved; remains fully incontinent (doubly) and in diapers at age of 10 years. No awareness of toileting needs.	Daytime toilet trained by ~4 years old; reliably dry and clean during day. Achieved night-time dryness by ~5–6 years old.
Fine motor skills	Markedly impaired; cannot perform purposeful drawing or writing. Has clawed hands with joint contractures and carpal tunnel syndrome, requiring surgical release. Cannot use utensils well – eats with assistance.	Age-appropriate fine motor skills; able to draw shapes, use utensils, and manipulate objects. No hand deformities or carpal tunnel signs.
Gross motor skills / Mobility	Frequently uses wheelchair due to fatigue and poor safety awareness. At risk of falls due to inattentiveness and joint stiffness.	Runs, jumps, and climbs like an ordinary child. Enjoys physical play (e.g. trampoline). No mobility aids needed. Good endurance for age-appropriate activities.
Behaviour	Severe hyperactivity, impulsivity, and aggressive behaviours. Episodes of hitting, kicking, and head-banging daily. Requires behavioural medication (risperidone) and constant supervision. Unable to follow	Generally good behaviour for age. Mildly impulsive or "silly" at times but no abnormal aggression. Follows instructions appropriate for age, though can be shy in new environments. No special supervision needed beyond normal parenting.

Comparison of Developmental Milestones and Functional Status of both Siblings		
	instructions or understand discipline due to cognitive level.	
Educational placement	Enrolled in a special needs school with one-on-one support. Curriculum focused on life skills and sensory activities. Not engaged in academic learning due to cognitive impairment.	Enrolled in mainstream primary school at the appropriate age. Requires no classroom aid, performing at or only slightly below grade level in academic skills. Interacts well with classmates.
Current age and status	10 years old – **Severely affected.** Profound cognitive impairment (functioning at <3-year-old level). Fully dependent on caregivers for all aspects of care. Quality of life is poor due to behavioral issues and loss of skills, despite ongoing ERT.	7 years old – **Minimally affected.** Mild developmental delays but essentially functional in an age-appropriate range. Independent in ADLs for age, with good quality of life and participation in normal activities.

Conclusions: In neuropathic MPS-II, definitive therapy with HSCT in early infancy preserves neurodevelopment and significantly reduces the multi-system disease burden compared with initiating ERT in later childhood. This sibling case-comparison supports the rationale for the need of newborn screening and prompt referral for HSCT. We have separately developed a gene therapy programme to further improve outcomes of cellular therapy in MPS-II and are reporting those outcomes at this meeting.

Clinical Trial Registry: Not applicable

Disclosure: Nothing To Declare

B376

IMPAIRED P53-MEDIATED DNA DAMAGE RESPONSE IN A HUMAN *ETV6::RUNX1* IPSC MODEL SHOWS GENOMIC INSTABILITY IN PRE-LEUKEMIC CELLS

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Background: The *ETV6::RUNX1* (*E::R*) fusion gene is a prevalent pre-leukemic state in childhood B-cell precursor acute lymphoblastic leukemia that requires secondary somatic mutations for leukemic transformation. We utilized a human iPSC model to investigate whether *E::R* intrinsically impairs DNA damage repair (DDR) pathways, thereby creating a permissive environment for the accumulation of these secondary genomic hits.

Methods: We utilized a previously described human iPSC model (Jepsen *et al*., HemaSphere 2025) comparing wind-type (WT) iPSCs against CRISPR/Cas9-generated *E::R* knock-in clones. To simulate genotoxic stress, cells were treated with the topoisomerase II inhibitor etoposide (1-40 nM) or vehicle control, and DDR activation was assessed via immunoblotting for phosphorylated p53 (Ser15) and PARP cleavage (n=3). To validate the findings in a hematopoietic context, iPSCs were differentiated into hematopoietic stem and progenitor cells (HSPCs; Terheyden-Keighley *et al*., Stem Cells Transl Med 2024) and characterized via multiparameter flow cytometry. Additionally, we employed a newly established serum-free differentiation protocol to direct HSPCs towards the B lineage to further study these pathways in B-cell progenitors (Bhave *et al*., Sci Rep 2025).

Results: Western blot analysis confirmed robust expression of the E::R fusion protein in knock-in clones. Upon induction of DNA damage with etoposide, WT iPSCs exhibited a strong, dose-dependent activation of the p53 pathway, evidenced by high levels of p-p53 (Ser15) and significant PARP cleavage. In sharp contrast, *E::R* iPSC clones displayed attenuated phosphorylation of p53 at Ser15 and reduced PARP cleavage across all tested concentrations. Notably, preliminary data suggests that this suppression occurs independently of the canonical MDM2 upregulation pathway often cited in murine models. Furthermore, we successfully differentiated these lines into hematopoietic progenitors with a CD34+CD38-CD90+CD45RA+/- phenotype (HSC/MPP/MLP), demonstrating that this model accurately recapitulates the early hematopoietic hierarchy required to study these defects in the lineage of origin. We have further validated a protocol to differentiate these HSPCs into the B-lineage, providing a physiologically relevant system to confirm these defects in committed B-progenitors.

Conclusions: Our findings demonstrate that pre-leukemic *ETV6::RUNX1* expression leads to significant impairment of the p53-mediated response to DNA damage in a human model system. This "dampened" DDR may allow pre-leukemic cells to evade apoptosis following genotoxic stress, facilitating the survival of clones carrying secondary mutations. By extending our model to include HSPCs and B-lineage progenitors, we are now positioned to characterize the precise impact of this repair defect on genomic stability during the vulnerable stages of B-cell development.

Disclosure: Nothing to declare

B377

GLOBALISING HAEMATOPOIETIC STEM CELL TRANSPLANTATION FOR CEREBRAL X-LINKED ADRENOLEUKODYSTROPHY: A UK–INDIA MULTICENTRE EXPERIENCE

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Background: X-Linked Adrenoleukodystrophy (X-ALD) is a rare genetic disorder (1:20,000–50,000) caused by ABCD1 gene mutations which encodes a peroxisomal membrane protein responsible for transporting very long chain fatty acids (VLCFAs). Impaired metabolism leads to VLCFA accumulation in the CNS/PNS and adrenal cortex, resulting in a spectrum of presentations including Cerebral ALD (CALD), axonopathy, and adrenal insufficiency. Haematopoietic stem cell transplant (HSCT) can halt disease progression in early CALD, when the patients have no significant neurology deficits (Neurology Function Score (NFS) ≤1) and limited demyelinating lesions in the brain (Loes score ≤9).

Methods: We retrospectively reviewed survival, neurological, and radiological outcomes following HSCT for CALD at UK and Indian centres, comparing results to a contemporary non-HSCT cohort. This included all patients transplanted at Birmingham Children's Hospital between 2005 and 2025 and the first patient transplanted at Sir Ganga Ram Hospital. Clinical, biochemical, and genetic data were collected. Donor type, graft source, conditioning regimen, and engraftment kinetics were collected. Neurological function was assessed using serial MRI and neurocognitive testing. Survival, transplant morbidity, and neurological trajectory were analysed to last follow-up.
A non-HSCT comparator cohort (n=6) was analysed for outcome comparison.

Results: Five patients underwent six HSCTs (median age 11 years, range 5-13). Lesions included fronto-pontine (n=2), posterior (n=2), and midbrain/pons/medulla (n=1). Donors included HLA-mismatched unrelated (n=2), matched unrelated (n=2), HLA-identical sibling (n=1) and haploidentical parent (n=1). Graft sources were PBSC (n=3), marrow (n=2), and cord (n=1). All patients received myeloablative conditioning with Fludarabine and Busulfan or Fludarabine/Treosulfan/Thiotepa plus ATG/Alemtuzumab. Neutrophil and platelet engraftment was achieved in all (median day +20 and +16). One patient required a second HSCT for secondary graft failure. No significant toxicity was observed in the first five patients. Patient transplanted from the haploidentical donor experienced viral reactivation and acute skin and gut GVHD. One patient had mild chronic skin GVHD. All patients achieved full donor chimerism at 3-year median follow-up.
Loes scores at HSCT were 2, 2, 2.5, 7.5 and 6. Imaging post HSCT remained stable at median follow up of 2,5 years. Neurological function scores stayed at 0 at 3 years and IQ scores remained stable.
The six non-HSCT CALD patient presented with neurology symptoms (NFS 1-6) and abnormal radiology (median Loes 14). Three died 2, 11 and 26 years after presentation. Two have severe cognitive and motor impairment 3 years post presentation, while one remains ambulant (NFS 4) 1 year post presentation.

Conclusions: Allogeneic HSCT provided robust outcomes for CALD patients, demonstrating excellent engraftment, acceptable toxicity, and 100% survival. Neurological and radiological stability was maintained in all transplant recipients, contrasting sharply with the rapid decline and 50% mortality observed in the non-HSCT comparator cohort. Our multi-center experience reinforces HSCT as an effective, disease-modifying therapy. Crucially, the successful haploidentical transplant, performed as the first in a resource-limited centre, broadens the feasibility of HSCT for CALD globally, proving successful outcomes with alternative donor sources. These findings reinforce HSCT as an effective disease-modifying therapy for CALD when performed early in the disease course.

Disclosure: Nothing to declare

B378

FIRST REPORTED ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ALLO-HSCT) FOR RAD50 DEFICIENCY: INITIAL CLINICAL EXPERIENCE IN TWO PEDIATRIC PATIENTS

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Background: Biallelic loss-of-function variants in RAD50 is an extremely rare DNA double-strand break repair disorder characterized by genomic instability, impaired ATM signaling and defects in lymphocyte development. Published reports of RAD50 deficiency are scarce and describe a heterogeneous phenotype including microcephaly, growth delay, variable immune dysfunction and sometimes progressive bone marrow failure. Unlike other DNA repair disorders such as Nijmegen breakage syndrome or LIG4 deficiency, no allo-HSCT cases have been reported in RAD50-deficient patients, and transplant-related biological risks, particularly sensitivity to alkylating agents, remain undefined. This lack of clinical experience leaves a critical gap in understanding HSCT feasibility, conditioning tolerability, immune reconstitution and genomic stability under transplant-related stress.

Methods: We report two pediatric patients with compound heterozygous mutation in RAD50 gene confirmed by whole-genome sequencing who underwent allo-HSCT.
Case #1. An 8-year-old girl presented with progressive trilineage cytopenia and bone marrow hypoplasia, DEB testing and telomere length were normal. Within one year, bone marrow dysplasia with a del(5q) clone and blasts up to 6–7% evolved, consistent with MDS on the background of inborn error of immunity.
Unrelated-donor allo-HSCT (conditioning regimen: fludarabine 150 mg/m², busulfan 4 mg/kg, ATG 5 mg/kg and rituximab 375 mg/m², with PTCy-based GVHD prophylaxis) was complicated by HHV-6 infection, severe infusion-associated rash, and subsequent graft rejection by day +60. Six months later a second haploidentical HSCT from the mother (conditioning regimen: fludarabine 150 mg/m², treosulfan 21 g/m², rituximab 375 mg/m² and alemtuzumab 0.4 mg/kg with PTCy-based GVHD prophylaxis) resulted in timely engraftment and was complicated by megakaryocytic lineage hypofunction, viral reactivation, COVID-19 infection, and mild skin GVHD.
Case #2. A 10-year-old girl with syndromic features (microcephaly, reticular skin hyperpigmentation, oral leukoplakia and onychodystrophy) developed severe pancytopenia with markedly hypocellular marrow and pathologically shortened telomeres, consistent with telomere biology disorder. The course was marked by transfusion dependence, recurrent infections and refractory thrombocytopenia despite romiplostim and eltrombopag therapy.

At the age of 13, haploidentical HSCT from the mother (conditioning regimen: fludarabine 150 mg/m², treosulfan 30 g/m², ATG 5 mg/kg, cyclophosphamide 40 mg/kg and rituximab 375 mg/m² with a CD3-depleted graft) was performed and resulted in primary graft failure by day +20. Three months later a second haploidentical HSCT from the father (conditioning regimen: TLI 4 Gy, fludarabine 150 mg/m², thiotepa 8 mg/kg, ATG 5 mg/kg and rituximab 375 mg/m² with PTCy-based GVHD prophylaxis) resulted in timely engraftment and was complicated by severe generalized HSV infection, engraftment syndrome, acute kidney injury and toxic encephalopathy.

Results: At last follow-up (+16 and +10 months after HSCT, respectively), both patients demonstrated complete donor chimerism with stable graft function.

Conclusions: These cases represent the first reported allo-HSCT procedures in patients with RAD50 deficiency, demonstrating that transplantation is feasible. However, an attempt to reduce the conditioning intensity, by analogy with other DNA repair disorders, resulted in severe graft dysfunction. We believe our experience should be taken into account when selecting a treatment strategy for this ultra-rare DNA repair disorder.

Disclosure: Nothing to declare.

B379

SUCCESSFUL HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A CHILD WITH WOLMAN DISEASE REFRACTORY TO HIGH-DOSE ENZYME REPLACEMENT THERAPY: COMPLETE DONOR CHIMERISM AND SUSTAINED METABOLIC RECOVERY

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Background: Wolman disease is a severe lysosomal storage disorder caused by biallelic mutations in the LIPA gene, resulting in markedly reduced lysosomal acid lipase (LAL) activity. Affected infants develop malabsorption, hepatosplenomegaly, dyslipidemia, and growth failure, and the condition is typically fatal without treatment. Enzyme replacement therapy (ERT) improves early survival; however, many patients continue to exhibit clinical progression despite receiving high-dose, long-term therapy. Hematopoietic stem cell transplantation (HSCT), by providing donor-derived enzyme production, offers a potential curative option, although real-world experience remains limited. We report the transplant course and 18-month outcome of a 29-month-old child whose symptoms persisted despite prolonged high-dose ERT.

Methods: The patient was a 29-month-old male with genetically confirmed homozygous *LIPA* mutation and severe LAL deficiency (<0.03 nmol/punch/h). Despite high-dose ERT initiated at 6 months of age, he continued to exhibit hepatosplenomegaly, malabsorption,

hypertriglyceridemia, and significant growth delay. Pre-HSCT evaluation also showed mild elevation in liver enzymes and poor nutritional status.
HSCT was performed using bone marrow from his fully matched (6/6) mother. Conditioning Regimen (with editable doses): Treosulfan 42 g/m² (Days −6 to −4), Fludarabine 150 mg/m² (Days −6 to −2), Thiotepa 10 mg/kg (Day −2), Anti-thymocyte globulin (ATG) 20 mg/kg total dose (Days −6 to −5). GVHD Prophylaxis: Tacrolimus (target trough 6-15 ng/mL), Methotrexate (Days +1, +3).
Supportive care included nutritional optimization and standard antimicrobial prophylaxis. No transplant-related toxicity, organ dysfunction, or infectious complications were observed.

Results: **Table 1. Clinical and Metabolic Parameters Before and After HSCT**

Parameter	Before HSCT	After HSCT (12 months)
LAL enzyme (nmol/punch/h)	<0.03	4.73
Weight (kg)	10	16.2
Height (cm)	78	91
Triglycerides (mg/dL)	223	84
Cholesterol (mg/dL)	203	161

Table comparing key metabolic and growth parameters before and 18 months after HSCT, showing normalization of LAL enzyme activity, improved triglyceride and cholesterol levels, and significant gains in weight and height.

Both neutrophil and platelet engraftment occurred on Day +14. Donor chimerism reached 85% on post-transplant Day +30 and increased to 100% by post-transplant Day +60, remaining fully donor-derived at post-transplant Months +3, +6, and +12. LAL enzyme activity normalized by post-transplant Month +3 (4.73 nmol/punch/h) and remained stable at post-transplant Months +6 and +12.
Metabolic parameters improved consistently: triglycerides decreased from 223 mg/dL to 84 mg/dL, cholesterol from 203 mg/dL to 161 mg/dL, and liver enzymes normalized. Clinically, the patient showed clear resolution of malabsorption, with improved appetite and energy level, and demonstrated substantial catch-up growth by the end of the first post-transplant year (weight increased from 10 to 16.2 kg; height from 78 to 91 cm) *(Table 1)*.
Hepatosplenomegaly regressed markedly on follow-up, and no acute or chronic GVHD was observed throughout the 18 months.

Conclusions: This case shows that HSCT can provide rapid engraftment, durable full donor chimerism, and sustained metabolic correction in a child with Wolman disease unresponsive to high-dose ERT. Despite pre-transplant clinical morbidities, the absence of toxicity or GVHD and remarkable clinical improvement highlight HSCT as a viable treatment option with a case-specific conditioning regimen. These findings support the evaluation of HSCT in patients who do not benefit adequately from ERT and add longer-term outcome data to the limited global experience in Wolman's disease.

Disclosure: Nothing to declare.

B380

HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR INBORN ERRORS OF IMMUNITY: IMPACT OF CONDITIONING REGIMENS

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Background: Inborn errors of immunity (IEIs) are genetically inherited diseases characterized by susceptibility to severe and opportunistic infections, malignancy, and immune dysregulation. Early diagnosis during childhood and timely referral for hematopoietic stem cell transplantation (HSCT) are critical for improving survival and long-term immune reconstitution. HSCT represents the only curative treatment for many severe forms of IEI; however, graft failure and loss of donor chimerism remain major challenges.
The aim of this study was to evaluate the demographic and clinical characteristics, transplant-related features, chimerism outcomes, graft failure, and survival of pediatric patients with IEI undergoing HSCT, with particular focus on the impact of conditioning regimens.

Methods: We retrospectively reviewed pediatric patients diagnosed with IEI who underwent HSCT between February 2019 and August 2024 at our Pediatric Bone Marrow Transplantation Center. Data were extracted from medical records. Transplant indications, donor and graft characteristics, conditioning regimens, chimerism status, graft-versus-host disease (GVHD), and outcomes were analyzed. Conditioning protocols were applied according to the 2021 EBMT/ESID Guidelines for HSCT in Primary Immunodeficiencies.

Results: A total of 36 patients (25 males, 69.4%) underwent 40 HSCT procedures; four patients required a second transplant. Median age at diagnosis was 40 months (range: 14–121 months), and median age at transplantation was 12 months (range: 2–94 months). Underlying diagnoses included combined immunodeficiency in 16 patients (44%; SCID n=15, DOCK8 deficiency n=1), immune dysregulation syndromes in 11 patients (30%; primary HLH n=9, IL-10 receptor deficiency n=1, RASGRP1 deficiency n=1), phagocytic system defects in 7 patients (19%; congenital neutropenia n=3, LAD n=2, chronic granulomatous disease n=2), and syndromic bone marrow failure in 2 patients (5%; Wiskott–Aldrich syndrome n=1, cartilage–hair hypoplasia n=1).
Chimerism analysis revealed full donor chimerism at engraftment in 22 patients. At 6 months post-transplant, 13 patients maintained full chimerism, while 9 patients who reached one-year follow-up remained fully chimeric. Among four patients with chimerism levels <10%, one experienced primary graft failure, and three required a second HSCT following recurrence of disease-related symptoms. At one-year follow-up, 10 patients exhibited chimerism <10%. Loss of chimerism was significantly less frequent in patients receiving busulfan-containing conditioning regimens.
GVHD occurred in 10 patients (25%); no grade IV GVHD was observed. GVHD incidence was

significantly higher in patients receiving busulfan-based conditioning. Overall survival was 88.8%, with 32 patients alive at last follow-up.

Conclusions: HSCT provides excellent survival outcomes in pediatric patients with IEI when performed early and according to guideline-based protocols. Conditioning regimens play a pivotal role in stable donor chimerism and long-term graft sustainability. Our findings highlight treosulfan- and busulfan-based conditioning as key determinants of chimerism outcomes, emphasizing the importance of individualized transplant strategies to optimize long-term success in IEI patients.

Disclosure: None.

B381

ALLOGENEIC STEM CELL TRANSPLANTATION AS A CURATIVE STRATEGY FOR PYRUVATE KINASE DEFICIENCY: A SINGLE-CENTER EXPERIENCE

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Background: Pyruvate kinase deficiency (PKD) is an autosomal recessive enzymatic defect that causes congenital chronic hemolytic anemia with complications such as iron overload, bilirubin gallstones, extramedullary hematopoiesis, pulmonary hypertension, thrombosis, and others. The heterogeneous clinical manifestations lead to significant morbidity and reduced quality of life. The long-term effect of disease-modifying therapy in PKD requires further evaluation. Allogeneic hematopoietic cell transplantation (allo-HCT) is the only potentially curative treatment for patients with PKD.

Methods: We present 4 patients with PKD who underwent allo-HCT at RM Gorbacheva Research Institute over two years (Table 1). The diagnosis was confirmed by mutations in the *PKLR* gene in all children. Patients had a high degree of dependence on blood transfusions from an early age. Three patients had secondary cardiomyopathy, NYHA class 0, 1 patient underwent cholecystectomy for calculous cholecystitis. The median ferritin level before transplantation was 1032 µg/L (range 245-2440). The median age was 4.8 years (range 1.5-14.6), and the median time from diagnosis to HCT was 52 months (13.6-177.8). All patients received a myeloablative conditioning regimen based on treosulfan, fludarabine, and thiotepa. The sources of hematopoietic cells were bone marrow from matched sibling donor (MSD) – 1, matched unrelated donor (MUD) – 3 with median CD34+ cell dose of 4.2 x 10^6/kg (range 2.4-6). Prophylaxis of graft-versus-host disease (GVHD) included post-transplant cyclophosphamide (PTCy, 50 mg/kg on days 3 and 4) with ruxolitinib at a dose of 0,3 mg/kg; abatacept was added at a dose of 10 mg/kg (4 doses on days −1, 5, 14, and 28) in 1 patient.

Table 1. Patients characteristics

	Case 1	Case 2	Case 3	Case 4
Patient sex	female	male	female	male
PKLR genotype	*PKLR*: c.1529G>A; c.1079G>A	*PKLR*: c.1529G>A, c.994G>A	*PKLR*: c.1+C4529G>A c.1318G>T	PKLR: c.948C>A c.848T>A
Splenomegaly	12,8*5,4	17,1*7,7	8,2*4,0	7,1*3,4 -N
Liver elastography	6,43 kPascal (F2 - F3)	4,8 kPascal (F0-F1)	7,49 kPascal (F2 - F3)	5,64 kPascal (F0-F1)
Number of transfusions	63	>100	18	19
Ejection fraction (EF), %	68%	58%	65%	65,9%
Age at allo-HCT, years	7	14	1,7	3
Ferritin before allo-HCT	245	614	2440	1450
Donor sex	male	female	male	female
Type donor	MUD	MUD	MUD	MSD
Conditioning regimen	Treo42Flu150Tio8	Treo42Flu150Tio8	Treo30Flu150Tio8	Treo42Flu150Tio8
GVHD prophylaxis	PTCyRuxoAba	PTCyRuxo	PTCyRuxo	PTCyRuxo
Hematopoietic cell transplant source	BM	BM	BM	BM
Complications	Oral mucositis grade1; bloodstream infection	Oral mucositis grade1; infections skin, anal fissure;	Febrile neutropenia Macrophage	Febrile neutropenia

		hepatotoxicity grade 2	Activation Syndrome	
GVHD	No	No	No	No
Outcome	alive	alive	alive	alive
Follow-up time (months)	1	8	13	22

Results: With follow-up time of 10 months (range 0.8-22.5) all patients are alive. Primary engraftment was achieved in all patients with median time of 20 days (14-23) for neutrophils. Despite this, one patient experienced secondary graft rejection on day +141, and still requiring blood transfusions and continued chelation therapy. One patient has 100% chimerism, two patients have stable mixed chimerism that does not require any further therapy.

Conclusions: Allo-HSCT is a therapeutic alternative to long-term transfusion therapy and allows for definitive correction of PKD in certain severe cases.

Disclosure: Nothing to declare.

B383

SUCCESSFUL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A CHILD WITH IMMUNODEFICIENCY ASSOCIATED WITH ITGB4 MUTATION: EXPANDING THE PHENOTYPE

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Background: ITGB4 mutations are classically linked to junctional epidermolysis bullosa with pyloric atresia (JEB-PA), reflecting the integrin's essential role in epithelial adhesion. Increasing evidence suggests broader immunological functions of integrins in leukocyte adhesion, migration, and epithelial–immune signaling. Immunodeficiency associated with *ITGB4* variants is exceedingly rare, and HSCT experience is limited. We report what appears to be the first successful allogeneic HSCT performed for ITGB4-associated combined immunodeficiency in a child with syndromic features of JEB-PA.

Methods: An 18-month-old male presented with recurrent severe infections, chronic diarrhea, growth failure, and extensive blistering since birth. Immunological evaluation showed reduced CD3+, CD4+, and CD19+ lymphocytes, low serum IgA, and markedly elevated IgE. Whole exome sequencing identified a homozygous *ITGB4* missense variant (p.Pro305Leu), confirming JEB-PA with combined immunodeficiency. Despite IVIG and antimicrobial prophylaxis, infections persisted, warranting HSCT.
A fully HLA-matched (10/10) paternal donor was selected. Reduced-intensity conditioning

consisted of fludarabine (30 mg/m²/day × 5) and treosulfan (12 g/m²/day × 3). Peripheral blood stem cells (CD34+ dose 8.0 × 10⁶/kg) were infused. GVHD prophylaxis included cyclosporine and mycophenolate mofetil. Chimerism, immune reconstitution, and clinical recovery were monitored serially.

Results: Neutrophil engraftment occurred on day +14 and platelet engraftment on day +20. Donor chimerism was 82 percent at day +28, 70 percent at day +100, and 72 percent at day +180. No acute or chronic GVHD developed. At 6 months, T- and B-cell subsets normalized, allowing discontinuation of IVIG. Clinically, infections resolved, chronic diarrhea improved, and significant amelioration of blistering and wound healing was observed. By 12 months, the child showed catch-up growth to the 25th percentile. No transplant-related epithelial or gastrointestinal toxicity occurred.

Conclusions: This case broadens the recognized phenotype of *ITGB4*-related disorders, supporting a pathogenic role of β4 integrin in immune homeostasis. Allogeneic HSCT resulted in stable engraftment, full immune reconstitution, and substantial clinical improvement, indicating its curative potential for ITGB4-associated immunodeficiency even in the presence of JEB-PA. Early genomic diagnosis is essential for identifying these rare immuno-epithelial syndromes and enabling timely HSCT before irreversible complications occur.

Clinical Trial Registry: Not applicable

Disclosure: None

B384

SINGLE CENTER EXPERIENCE OF ALLOGENEIC HSCT WITH POSTTRANPLANT CYCLOPHOSPHAMIDE IN INBORN ERRORS OF IMMUNITY

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Background: Inborn errors of immunity (IEI, or primary immunodeficiency) is a big group of genetic disorders of immune system. Better diagnostics, improving survival and decreasing morbidity post-HSCT over the past decade have led to significant expansion of indications for HSCT in IEI. Posttransplant cyclophospamide (Pt-Cy) has been becoming a standard of GVHD prophylaxis for HLA-mismatched transplantations. The aim of the study was to analyze HSCT results after Pt-Cy in IEI.

Methods: From 2015 t0 2025, 59 patients with IEI received allogeneic HSCT with Pt-Cy in our center. The median age at diagnosis was 2.2 years (at birth-28.7), at HSCT 2.6 (0.2-29.4). 18 patients had severe combined immunodeficiency (SCID), and 41 other IEI (19 of them developed malignancy before HSCT). Treosulfan-based conditioning was used in 48

patients (31 with thiotepa/melphalan), busulfan-based regimen in 10 (all older than 13), 1 received thiotepa/melphalan regimen. In 36 ATG and in 10 rituximab was used. In 5 patients matched sibling (MSD), in 22 matched unrelated (MUD)(12-10/10, 10-9/10 HLA-matched), in 32 mismatched related (MMRD) donor was used. In MMRD group 17 patients were SCID, 12 of them had active infections at HSCT. Graft source in 49 patients was bone marrow and in 10 patients peripheral blood stem cells. The median of CD34 cells in graft was 5.2 (range 1.8-15.6). In addition to Pt-Cy, GVHD prophylaxis included: in 26 calcineurin or mTOR inhibitor-based, in 30 ruxolitinib-based regimens, and in 3 (MSD) no prophylaxis was used.

Results: The median follow-up in survivors was 2.3 years (range 0.3-10.1). The overall survival (OS) was 0.79 (95%CI 0.69-0.9). OS was 0.96 (95%CI 0.87-1.0) in MUD and 0.65 (95%CI 0.48-0.82) in MMRD, and all 5 patients survived after MSD, p=0.035. Neutrophil engraftment occurred in 53 patients (median 22, range 13-33 days), 3 patients had severe infections early after HSCT before engraftment, and 3 had non-engraftment and received second HSCT (all died after second HSCT).
The incidence of acute GVHD was 0.26 (95%CI 0.17-0.4).Of 16 patients, acute GVHD was of grade 3 in 5 of grade 4 in 1 (was associated with CMV disease). The incidence if chronic GVHD was 0.13 (95%CI 0.07-0.27). No significant differences in acute and chronic GVHD rate were seen between the donor groups, p=0.94 and 0.86, respectively. The incidence of viral infection requiring therapy was 0.35 (95%CI 0.24-0.49), without differences between the donor groups, p=0.12. One SCID patient developed EBV-posttransplant lymphoproliferative disease transformed to lymphoma and died. The causes of death in all patients were infections.

Conclusions: Pt-Cy is a feasible option for GVHD prophylaxis in allogeneic HSCT for IEI. Decreased survival in MMRD group is related to high amount of patients undergoing HSCT with active infections (mainly SCID) or no complete control of inflammatory complications (like hemophagocytic lymphohistiocytosis), as no increased risks of development of acute and chronic GVHD, and viral infections is seen in this group.

Disclosure: The authors declare no conflict of interest.

B385

CLINICAL PICTURE AND IMMUNE RECONSTITUTION POST-HAEMATOPOIETIC CELL TRANSPLANTATION IN PAEDIARIC PATIENTS WITH CHRONIC GRANULOMATOUS DISEASE – LATIN AMERICAN SINGLE EXPERIENCE

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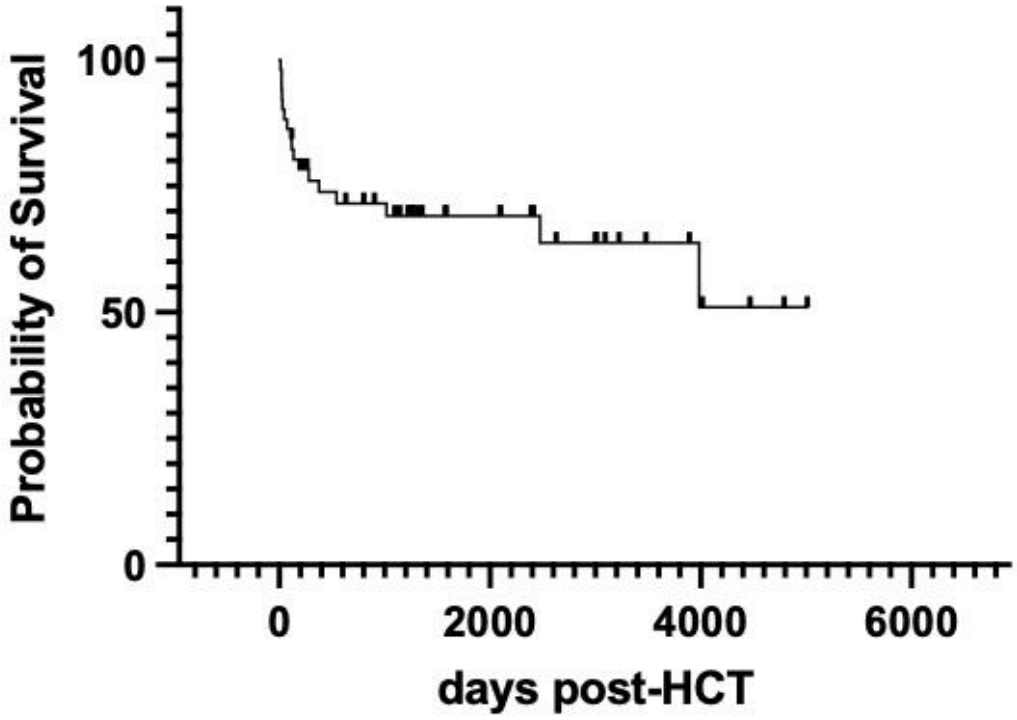
Background: Haematopoietic cell transplantation (HCT) is a curative treatment option for Chronic Granulomatous Disease (CGD). Post-HCT clinical features and immune reconstitution of patients from Latin America remain poorly described.
On behalf of the LASID Working Group of HCT**,** we aim to report the outcomes of CGD patients who received HCT at 8 different centers from Latin America: Argentina (3), Chile (2), Colombia (1), Mexico (1), Uruguay (1).

Methods: Retrospective data collection from 58 clinical records from post-HCT CGD patients (p).
2p were excluded due to insufficient information.

Results: Of 56p included, 54p (96.4%) were male and 51p (91.1%) X-linked CGD. Median age at diagnosis 27.9 months [0-164].Median follow-up 3.6 years [0-13], median age at transplant 43 months [1-197]. 8p (14.3%) required a second conditioned HCT and 1p (1.8%) a third procedure. The main reason was primary graft failure (5p, 55.6%).
Pre-HCT patients had: 47 (84%) at least one severe infection, 38 (67.9%) lung disease, 27 (48.2%) growth failure, and 14 (25%) CGD colitis. Of the 51p (91.1%) who received BCG vaccine, 23p (45.1%) developed associated complications (13p BCGitis, 10p BCGosis).
Regarding HCT, patients received bone marrow stem cells (n=19), peripheral blood (n=25) or cord (n=12) from matched (n=20) or mismatched (n=11) unrelated donors, matched sibling donor (n=10), haploidentical (n=9) or mismatched family donors (n=6).
47p (83.9%) received myeloablative conditioning, with busulfan-fludarabine being the most commonly used regimen (39p, 83%). Only 9p (16.1%) received a reduced toxicity conditioning regimen. 43p (76.8%) received serotherapy with Anti-Thymocyte Globulin. Cyclosporine and MMF as GvHD prophylaxis in most patients (20p, 35.7%).
In the post-HCT evolution, 17p (30.4%) developed acute, and 9 (16.1%) chronic GvHD. 14p (25%) had CMV, 6 (10.7%) EBV, 2 (3.6%) HHV6, and 1 (1.8%) ADV viremia. 1 (1.8%) developed EBV-PTLD.
At last follow-up, 34 patients were certified to be alive, resulting in a 14-year OS of 51%. Of the 17p that passed away, an infectious complication was the reason in 12. During the follow-up: 21/47 (44.7%) had significant infections, 21/38p (55.3%) stabilized lung disease, 11/27 (40.1%) improved growth and 13/14 (92.9%) resolved colitis.
Among the 37 patients who underwent both donor chimerism and DHR testing, a statistically significant correlation was observed between DHR results and chimerism ($r = 0.5630$; $p < 0.003$).



Conclusions: This study provides valuable insights into outcomes after HCT in patients with CGD at different centers of Latin America.
In our cohort, most patients had multiple severe pre-HCT complications. Despite high mortality, HCT led to myeloid reconstitution with improvement in infection rate, growth, lung disease and colitis.
These results support HCT as a curative option for CGD and highlight the need for earlier referral and better transplant strategies in Latin America.

Disclosure: Nothing to declare.

B386

SUCCESSFUL CORD BLOOD TRANSPLANTATION IN AN INFANT WITH LEUKOCYTE ADHESION DEFICIENCY TYPE III: A CASE REPORT AND 1 YEAR FOLLOW-UP

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Background: Leukocyte Adhesion Deficiency type III (LAD-III) is the rarest form of leukocyte adhesion defects and is caused by biallelic mutations in *FERMT3*, leading to impaired integrin activation in leukocytes and platelets. Patients present with severe immunodeficiency and a Glanzmann-like bleeding phenotype due to dysfunctional GPIIb/IIIa. Diagnosis typically occurs in infancy following evaluation for recurrent infections, mucocutaneous bleeding, and abnormal platelet function. Hematopoietic stem cell transplantation (HSCT) is considered the only curative treatment. We describe the clinical course and post-transplant outcome of a female infant with genetically confirmed LAD-III who underwent allogeneic cord blood transplantation.

Methods: The patient presented at four days of life with petechiae, gross hematuria, hematomas, leukocytosis, anemia, and mild thrombocytopenia. Platelet aggregation testing revealed absent aggregation to all agonists. Whole-genome sequencing identified a homozygous *FERMT3* p.(Arg573*) nonsense mutation, confirming LAD-III. Comprehensive hematologic, immunologic, and genetic evaluations excluded alternative causes. Due to the absence of an HLA-identical related or unrelated donor, an HLA-compatible cord blood unit (CBU) was selected from international registries. The patient underwent a stem cell transplant from an unrelated CBU at 4 months old, following Treosulfan, Fludarabine, Thiotepa, and Alemtuzumab conditioning. Standard antimicrobial prophylaxis, immunoglobulin supplementation, and post-transplant monitoring were performed according to institutional protocols.

Results: Neutrophil engraftment occurred on day +19 and platelet engraftment on day +41. Only complication registered during the HSC infusion was a blood pressure spike due to hemodinamic imbalance which quickly resolved with medical treatment. The patient did not develop any infectious complications. Cystoscopy performed during hospitalization showed complete resolution of previously documented hemangioma-like submucosal bladder lesions, with residual hemosiderin deposits and no active bleeding. Patient showed no evidence of acute GvHD. Immunosuppression with cyclosporine was discontinued in September 2025. Donor chimerism progressively improved: 85% in T cells and 100% in B cells and PMN 4 months post transplant, rising to 98.3% T-cell donor chimerism by 6 months post HSCT. Immune reconstitution was robust, with adequate lymphocyte subpopulations: RTEs were 2920 cell/uL 6 months post transplant; CD3+ 7180 cell/uL and CD4+ 5032 cell/uL 1 year post transplant. Patient showed normal mitogen responses, and serum IgG levels within acceptable range. TRECs/KRECs were >100,000/mL 6 months post transplant. The patient started routine vaccinations 6 months post HSCT. At the 1-year follow up evaluation the patient is clinically well, with appropriate growth, normal psychomotor development, no evidence of GvHD and no ongoing treatment.

Conclusions: This case highlights the effectiveness of cord blood transplantation as a curative option for LAD-III in the absence of matched donors. The patient achieved timely engraftment, full donor chimerism, resolution of bleeding manifestations, and robust immune recovery with an excellent clinical outcome. We believe CBUs represent a viable and potentially lifesaving strategy for patients with ultra-rare immunodeficiencies such as LAD-III.

Disclosure: N/A

P269

HEMATOPOIETIC STEM CELL TRANSPLANTATION WITHOUT CONDITIONING IN IL2RG-MUTATED SCID AND SEVERE ACTIVE CMV INFECTION: RAPID IMMUNE RECONSTITUTION AND INFECTION CONTROL

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Background: In severe combined immunodeficiency (SCID), early hematopoietic stem cell transplantation (SCT) is curative, but active infections prior to SCT such as cytomegalovirus (CMV) are associated with increased morbidity and mortality. Considerations of optimal transplant approach in these infants with active infection include omitting conditioning regimen, even with increasing the risk for necessity of a second procedure due to incomplete B-cell recovery and the need for ongoing immunoglobulin replacement.

Methods: Retrospective review of clinical charts was used to report on a 4-month-old male with genetically confirmed interleukin-2 receptor gamma (IL2RG)-mutated SCID (T−B+NK−) presenting with severe CMV infection, including severe encephalitis with multiple brain calcifications and CMV retinitis. Pre-transplant management included intense combined antiviral therapy with foscarnet and ganciclovir. At 6 months of age, the patient received an unmanipulated bone marrow graft from a matched sibling donor, without conditioning or serotherapy; immunosuppression was limited to cyclosporine A. Immune reconstitution and clinical outcomes were monitored longitudinally.

Results: Despite intensive antiviral therapy pre-transplant, the SCT was performed while CMV was actively replicating - CMV DNA in CSF was still high positive (350 000 copies of CMV /ml. We noted fast immune reconstitution, with first naive CD4+ T cells in peripheral blood as early as day +8 (30/uL). The patient encountered engraftment syndrome on day +11, treated with short course of steroids. Despite steroids, CMV PCR became negative in blood since D+24. Additional virus specific T cell therapies were not needed. At D+21 the donor chimerism was already dominant (62%), patient was discharged at D+31 and remained free of GvHD, severe infections and demonstrated stable donor chimerism through 24 months of follow-up post-transplant. The immune reconstitution continued well (at 6months post SCT, naïve CD4 were 480/ul, with complete donor chimerism also in CD19 and IgG substitution independence at 10 months).

Conclusions: The case supports the preference for unconditioned SCT in T−B+NK− IL2RG SCID with severe active CMV or other severe infection, especially with available matched sibling donor – an option included in recent ESID/IEWP EBMT recommendations (1). SCT without conditioning can achieve rapid T-cell reconstitution and infection control and spare

the patient from dangerous organ toxicity, in the presented case also with adequate B cell reconstitution without the need for a second procedure.

References:

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Disclosure: Nothing to declare.

P271

SUCCESSFUL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR DIAPH1 MUTATION: A CASE REPORT

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Background: Loss of function mutations in Diaphanous related formin 1 (*DIAPH1)* are associated with seizures, cortical blindness, and microcephaly syndrome (SCBMS). It is rare entity which has an autosomal recessive inheritance. The affected children mostly have microcephaly, early-onset epilepsy, severe visual impairment and hearing loss. Also, it causes combined immune deficiency which is associated with major T, natural killer (NK), and innate lymphoid cells (ILCs) defects. Consequently, recurrent pulmonary infections and bronchiectasis are frequently observed in association with this. For today, there is no specific treatment for DIAPH1 deficiency and hematopoietic stem cell transplantation (HSCT) may be an option.

Methods: We report a 5 years-old female patient with DIAPH1 mutation who received HSCT at the Bone Marrow Transplantation Unit at Medicalpark Pendik Hospital, Istanbul.

Results: The patient had been presented with microcephaly, cortical blindness, and seizures starting in first month postnatally. She had been operated because of ventricular septal defect. Also, she had recurrent pulmonary infections requiring hospitalization many times and mouth sores. Pediatric immunology tests revealed low CD4 and CD8 T lymphocyte counts, leading to a diagnosis of T-B+NK+ combined immunodeficiency. Whole exome sequencing test identified homozygous pathogenic variant p.(Arg351Ter) in DIAPH1 gene. The patient, whose signs of infection persisted despite antibacterial prophylaxis and regular intravenous immunoglobulin (IVIG) replacement, was referred for HSCT.
The conditioning regimen consisted of; fludarabine 180 mg/m^2 on days -7 to -2, treosulfan 36 gr/m^2 on days -6 to -4, rabbit anti-thymocyte globulin (rATG) 15 mg/kg on days -2 to -1. Because, EBV-DNA level was 1993 copies/ml in the pre-transplantation tests, rituximab at a dose of 375 mg/m^2 was administered before starting the conditioning regimen. HSCT was performed from a fully matched unrelated male donor. Peripheral blood stem cells with a dose of 4.4x10^6 CD34/kg were infused. For graft versus host disease (GVHD) prophylaxis, she received methotrexate on days +1, +3, +6 along with tacrolimus starting on day -2. Neutrophilic engraftment was achieved on day +14, while platelets were engrafted on day +15 post-HSCT. The post-transplant period was uneventful apart from having seizures. GVHD

did not develop. Chimerism test performed one month after transplantation was %100 donor cells. At 6 months follow up, no complications occurred. Peripheral blood cell counts and immunoglobulin levels are normal, and there is no need for IVIG.

Conclusions: This rare combined immunodeficiency can be fatal due to pulmonary infections. HSCT can be a curative treatment for immune deficiency component of this syndrome. However, prospective studies involving a larger patient population are needed on this subject.

Disclosure: The Authors declare no conflict of interest.

P272

CLINICAL CONSIDERATIONS FOR HEMATOPOIETIC CELL TRANSPLANTATION IN PATIENT WITH CONCOMITANT CHRONIC GRANULOMATOUS DISEASE AND MCLEOD SYNDROME

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Background: The CYBB gene, responsible for X-linked chronic granulomatous disease (X-CGD), is located adjacent to the XK gene, which is responsible for McLeod syndrome (MLS). A contiguous deletion of both genes results in a phenotype exhibiting both X-CGD and MLS. MLS is a genetic disorder that causes neuroacanthocytosis. It is characterized by the loss of XK protein along with Kx antigen on red blood cell (RBC) surfaces and late-onset neurocognitive symptoms.
The absence of XK protein leads to a high risk of sensitization from allogenic RBC transfusions, producing anti-Kx or anti-Km antibodies. This makes subsequent transfusions difficult because of the risk of acute hemolytic transfusion reactions. Therefore, performing hematopoietic cell transplantation (HCT) -the only radical cure for X-CGD, which often requires several transfusions- is challenging.
Here, we report a case of X-CGD with MLS who underwent HCT and experienced a stable mid-term clinical course.

Methods: A retrospective chart review was completed for a case of X-CGD associated with MLS who underwent HCT.

Results: A Japanese boy was diagnosed with X-CGD and MLS in his infancy base on a family history. Genetic testing confirmed a deletion of both CYBB and XK genes. The patient suffered from recurrent infections and refractory inflammatory bowel disease due to X-CGD. He required an RBC transfusion from a random donor at age 6, but fortunately, pre-HCT testing confirmed he was not sensitized to the Kx antigen.
At age 7, he underwent HCT from a matched unrelated donor. He received a reduced intensity conditioning regimen composed of targeted busulfan, fludarabine, anti-thymocyte

globulin, and total body irradiation (3 Gy). To specifically prevent Kx sensitization, rituximab was added to this regimen, and RBCs were depleted from the donor bone marrow graft prior to infusion.
The post-HCT course was successful. The patient received 7 units of RBCs from random donors without any hemolytic events. Neutrophil engraftment occurred on day +19 with full donor chimerism. Every immunosuppressants, were successfully tapered and discontinued one year after HCT. Three years have passed since HCT, and the patient is living well without SCT-related complications such as chronic GVHD, severe infections and neurological complications associated with MLS.

Conclusions: We successfully performed HCT in a patient with X-CGD and MLS. Our strategy was based on using rituximab and RBC depletion from the graft, and conditioning including low-dose total body irradiation may also have contributed to preventing sensitization.
Past reports have shown that inadequate measures can lead to severe hemolysis. Thus, HCT for X-CGD with MLS requires additional interventions to prevent hemolysis and a meticulous transfusion plan. Although, a fully established, standard method does not yet exist, our approach may be considered a promising optimal method.
Fortunately, no neurological complications associated with MLS have developed after three years of follow-up.
In conclusion, while this HCT method can safely cure X-CGD, improving prognosis and quality of life by eliminating recurrent infections, the long-term impact of HCT on the late-onset neurocognitive symptoms of MLS remains unclear. Further studies involving more cases and vigilant long-term follow-up are essential.

Disclosure: Nothing to declare

P273

EXPERIENCE IN PREPARING FOR ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN A PATIENT WITH WISKOTT-ALDRICH SYNDROME

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Background: Grafts from unrelated donors in patients with Wiskott-Aldrich syndrome (WAS) carry a high risk of severe complications, particularly graft-versus-host disease (GVHD). Allogeneic hematopoietic stem cell transplantation (HSCT) in WAS patients is also associated with a significant risk of graft dysfunction, such as failure, rejection, or persistent mixed chimerism in the myeloid compartment. These outcomes have been consistently reported in large clinical studies.

Methods: A patient with a genetically confirmed diagnosis of WAS received treatment at the Belarusian Research Center for Pediatric Oncology, Hematology, and Immunology, where he later underwent allogeneic HSCT from an HLA-compatible unrelated donor.

Results: The patient was born from the third pregnancy and second delivery. He has a five-year-old half-brother with a genetically confirmed diagnosis of WAS, who underwent umbilical cord blood HSCT at the Center at eight months of age.
On the second day after birth, the patient was transferred to the intensive care unit due to thrombocytopenia ($15*10^9$/L). Given his complex medical history, he was first seen at the Center for Pediatric Oncology, Hematology, and Immunology at 20 days old. Genetic testing identified a WAS gene mutation (c.631C>T, p.Arg211Ter (rs1602178165)). Standard immunological tests showed reduced T-lymphocytes ($0.225*10^9$/L) and B-lymphocytes ($0.517*10^9$/L).
At admission, the patient had loose stools, blood in every bowel movement, rotavirus enterocolitis, poor weight gain, aphthous stomatitis, and congenital pneumonia. After treating the rotavirus infection, he began preparation for hematopoietic stem cell transplantation (HSCT). He was admitted to the transplantation unit with enterocolitis and pneumonitis, likely of immunological origin.
Both the Center's experience and global data indicate a high incidence of intestinal graft-versus-host disease (GVHD) in WAS patients after transplantation. Due to persistent gastroenteritis and malabsorption, with no evidence of infection and negative viral tests (including CMV and EBV), the patient began conditioning with infliximab 10 mg/kg on days -10 and -2, ATG (Genzyme), treosulfan, fludarabine, thiotepa, and rituximab.
The patient underwent allogeneic bone marrow HSCT from an unrelated HLA-compatible donor. GVHD prophylaxis included cyclosporine and methylprednisolone. Two mesenchymal stem cell transplants were also administered to prevent GVHD.
In the early post-transplant period, the patient developed grade I GVHD (skin 2) on day +14. Engraftment was confirmed on day 11, with cytopenia lasting 18 days. On day +13, 100% PCR chimerism was achieved. Enterocolitis and pneumonitis resolved after the initial infliximab administration but recurred following enterovirus infection on day +8 after HSCT. The patient's condition stabilized after the infection was cleared.
As of day +85 post-transplant, the patient shows no signs of graft-versus-host disease (GVHD) and maintains 100% donor chimerism.

Conclusions: Based on our Center's experience and global data, patients with Wiskott-Aldrich syndrome require thorough preparation for HSCT to minimize post-transplant complications, with the intestine being the most vulnerable organ. Due to early signs of enterocolitis, persistent malabsorption, hemorrhagic colitis, and previous intestinal infections, the medical team determined that additional pre-transplant preparation was necessary. Two infliximab administrations were performed, resulting in stabilization of the patient's enterocolitis and pneumonitis.

Disclosure: No conflict of interests.

P274

HEMOPHAGOCYTING LYMPHOHISTIOCYTOSIS – ISOLATED CNS MANIFESTATION

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Background: Hemophagocyting lymphohistiocytosis (HLH) is an aggressive life-threatening syndrome of excessive immune activation. The familial form typically presents in early childhood as a sepsis-like condition. However, HLH can have diverse clinical presentations, which are even more diagnostically challenging, especially in atypical or isolated manifestations. Isolated central nervous system HLH (CNS-HLH) is a rare and difficult to diagnose due to nonspecific symptomatology and absence of systemic manifestations.

Methods: Case report:

Results: A 4-year-old patient with genetically confirmed familial HLH (UNC13D) underwent allogeneic hematopoietic stem cell transplantation (HSCT) from matched unrelated donor at the age of 8 months. In the post-transplant period, a gradual decrease in donor T cell chimerism was observed. We have been using a „watch and wait" strategy for a long period of time with stable mixed CD3+ T Ly chimerism of 30 % donor which is generally compatible with long term HLH control and our patient was without signs of disease reactivation. Before relapse, 3.5 years after 1st HSCT, chimerism was 28% of donor in CD3+ T ly. Neurological symptomatology slowly developed in the absence of systemic manifestations of HLH: ataxia, tremor, later convulsions up to refractory status epilepticus requiring intensive care. Based on the examination of the cerebrospinal fluid (proteinuria, pleocytosis) and MRI findings (diffuse/multifocal white matter lesions) isolated CNS HLH was diagnosed. At relapse, the detected donor chimerism 16 % in CD3 T cells – the drop happened unrecognized within 3 months. Intensive immunosuppressive treatment with alemtuzumab was indicated and subsequently 2nd allogeneic HSCT. After complicated HSCT, the patient is without signs of active CNS HLH, but with severe neurological impairment with progression.

Conclusions: Isolated CNS HLH is a rare form of HLH and CNS damage by the HLH process is largely irreversible. By clinical and MRI findings it mimics other, more common neurological diseases of childhood and thus represents a significant diagnostic challenge. It should be considered in a patient with neurological symptoms, especially with concurrent pleocytosis, proteinuria and abnormalities on brain MRI associated with HLH. Our patient shows that relying on disease control at lower level of mixed chimerism to spare the patient a second HSCT maybe a risky approach and challenge to monitoring even longterm after 1st HSCT.

Disclosure: Nothing to declare

Hodgkin Lymphoma and T cell Lymphoma

OS02-06

EARLY ALLOGENEIC TRANSPLANTATION AS PART OF FIRST-LINE THERAPY IN HIGH-RISK T-CELL LYMPHOMA: RESULTS OF A PROSPECTIVE PHASE 2 STUDY

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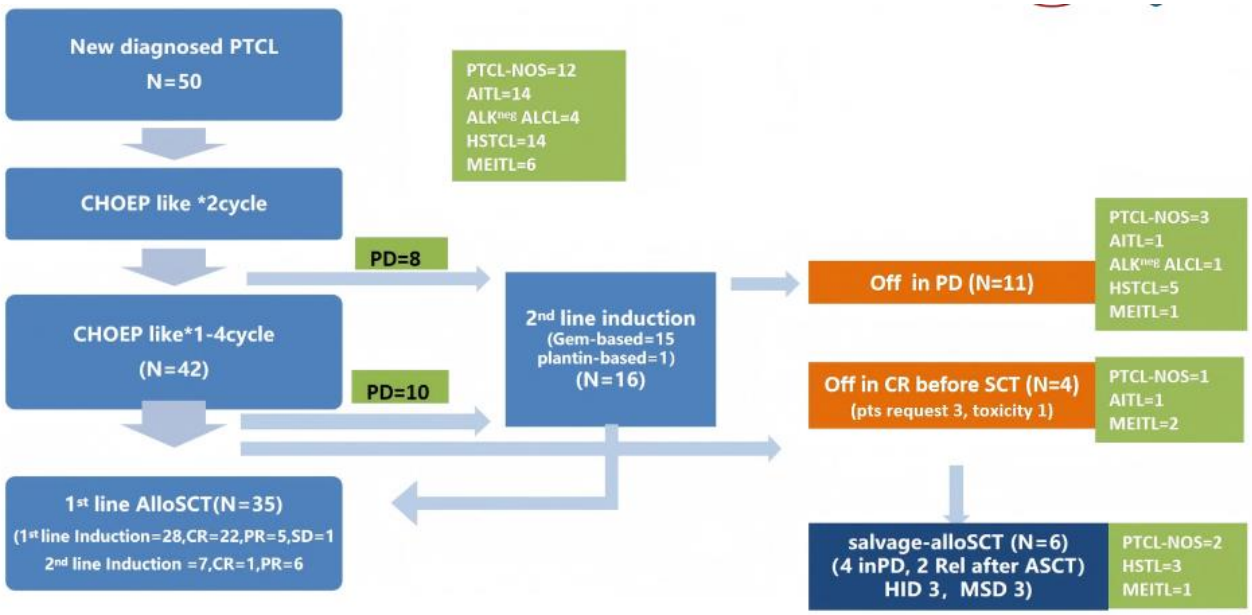
Background: Allogeneic stem cell transplantation (alloSCT) cures about 50% of patients (pts) with T-cell lymphoma (PTCL). However, more than one-third of pts progress or relapse early failing to reach alloSCT (Schmitz et al. BLOOD 2021). We shortened conventional therapy and followed by alloSCT to prevent early progression (PD).

Methods: This was a prospective phase 2 study conducted in high-risk PTCL pts (no ALK+ ALCL, no stage 1 with aaIPI 0). Pts with PET-neg CR or PR after 3 cycles of CHOEP(or variant) underwent alloSCT, in pts with early PD salvage therapy followed by alloSCT was planned. Pts received myeloablative conditioning with BuCy, MeCCNU, and Ara-C or TBI (8 Gy). GVHD prophylaxis consisted of cyclosporine A, MMF, and short-term MTX, plus ATG (10mg/kg) for unrelated or haplo-transplants. The study was planned according to Simon’s optimal two-stage study design with a total of 47 pts to be included (Clinicaltrials.gov, NCT03672084).

Results:



Fifty newly diagnosed patients were enrolled: 12 pts with PTCL-NOS, 4 ALK-neg. ALCL, 14 AITL, 6 MEITL, and 14 pts (28%) with hepatosplenic T-cell lymphoma (HSTL) (see flowchart). Thirty-five pts responded (28 to first-, 7 to second-line therapy) and proceeded to alloSCT(On-study). 15 pts went off-study due to PD (n=11), patient request for autoSCT (n=3), and heart toxicity (n=1); 6 of these pts finally underwent alloSCT. Until Nov 30, 2025, with a median follow-up of survivors of 1259 days two-year overall survival (OS) and progression-free survival (PFS) was 74.7% and 56.7%, respectively. Incidence of PD or relapse(RI) was 40%, NRM was 2%.

On-study pts: 26/32 pts had durable CR post alloSCT, six pts relapsed (3 HSTCL, and 1 MEITL,ALK-neg ALCL, PTCL NOS each). Four responded to salvage therapy including donor stem cell infusion. Two-year-PFS and -OS were 77.6% and 90.7%. The D100 and 1y transplant-related mortality (TRM) were 0% and 3%, respectively. The cumulative incidences of acute and chronic GVHD were 45.7% and 62.8%.

Off-study pts: Eight of 9(no alloSCT) died of lymphoma, 1 keep CR with chidamide maitaining. Six pts (4 PD, 2 failing autoSCT) received salvage alloSCT and 4 are alive (3 CR, 1 with lymphoma). Their 2y-PFS and -OS were 20% and 33.9%.

Twenty pts (40%) diagnosed with HSTCL or MEITL had a significantly worse survival compared to other subtypes, with the 2y PFS of 31.3% vs 65.2% (p=.088), and 2y OS 59.8% vs 82.1% (p=.048), this probally due to the higher RI (55% vs 27%, p=0.018). None of these pts survived without alloSCT.

Table1 Patient Characteristics

	On-Study Group(n=35)	**Off-Study Group(n=15)**	**Total(N=50)**

Gender (Male /Female)	22/13	11/4	33/17
Age median (range) (years)	45(4-63)	46(24-64)	45.5(4-64)
Histology PTCL-NOS AITL ALK-ALCL HSTL MEITL	 8 12 3 9 3	 4 2 1 5 3	 12 14 4 14 6
B symptoms at diagnosis	26(74.3%)	13(86.7%)	39(78%)
BM involvement at diagnosis	17(48.6%)	7(46.7%)	24(48%)
2y OS from Diagnosis	90.7%±5.1%	33.9%±13.2%	74.7%±6.7%
2Y PFS from Diagnosis	77.6%±7.5%	20.0%±10.3%	56.7%±7.6%
Status at last contact Alive in CR Alive with lymphoma Dead	 30 2 3	4 (3 post salvage alloSCT) 1(post salvage alloSCT) 10	 34 3 13
No. of AlloSCT	35(100%)	6(40%)	41 (82%)
No. of lines of therapy before AlloSCT 1 2 >2	 28(80.0%) 7 (20.0%) 0	 1 4 2	
Disease status @ AlloSCT CR/PR/SD	23/11/1	1/0/5	
Conditioning regimen Bu/Cy ±ATG BU/FLU/Cy ±ATG TBI/Cy/ based±ATG	 16 11 8	 2 1 3	
Graft BM+PBSC PBSC	 8 27	 0 6	

MNC, median (range) x108/kg	8.7 (5.4-29.2)	8.98 (7.4-12.1)	8.7 (5.4-29.2)
CD34+ median (range) x106/kg	2.83 (0.47-7.2)	2.32 (1.9-6.4)	2.7 (0.47-7.2)
Engraftment of WBC (day)	12 (10-25)	14.5 (11-27)	12 (10-27)
Engraftment of PLT (day)	14(10-159)	17(10-100)	14(10-159)

Conclusions: *Early* alloSCT as 1st line consolidation was feasible in two-thirds of pts with low TRM resulting in excellent survival. All but one pts without alloSCT died of lymphoma. Notably, 40% of study pts suffered from HSTCL or MEITL. For these pts, underrepresented in other studies, alloSCT is the only curative option although outcomes were worse than in major T-cell entities (2-yr OS 60% vs 82%).

Clinical Trial Registry: Registered at clinicaltrials.gov, NCT03672084

Disclosure: NO

OS02-07

AVOIDING SALVAGE CHEMOTHERAPY IN EARLY PD-1 INHIBITOR RESPONDERS: OUTCOMES OF LOW-DOSE NIVOLUMAB-BASED SECOND-LINE THERAPY (NICE-40) FOR HODGKIN LYMPHOMA

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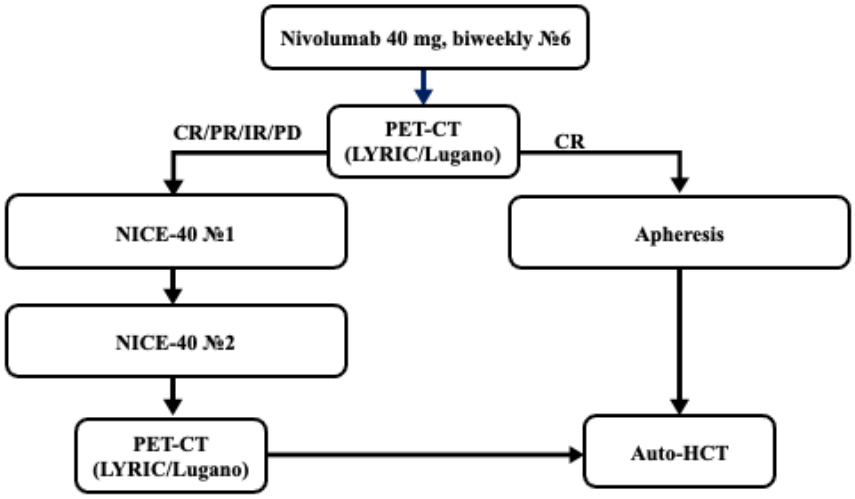
Background: PD-1 inhibitors enable high response rates in relapsed/refractory classical Hodgkin lymphoma (r/r cHL), prompting investigation of PET-adapted strategy. In this approach, responders to PD-1 monotherapy may potentially avoid salvage chemotherapy before auto-HCT, reducing overall toxicity. For non-responders, adding PD-1 inhibitors to chemotherapy improves efficacy, allowing a significant proportion of patients to achieve an optimal pre-transplant status. However, widespread use of PD-1 inhibitors raises financial toxicity concerns. Pharmacologically supported low-dose regimens represent a viable strategy to reduce costs and expand patient access.

Methods: This prospective, multicenter clinical trial enrolled adults with r/r cHL (NCT04981899) after first-line therapy failure. Patients (pts) received 6 nivo-40 cycles

(biweekly), followed by response-adapted therapy (LYRIC/Lugano): pts achieving early CR (CR) after 6 cycles proceeded directly to auto-HCT, while those with less than CR received combined chemoimmunotherapy (nivo-40 plus ICE, NICE-40) followed by auto-HCT. The primary endpoint was objective response rate (ORR); secondary endpoints included 3-year overall survival (OS) and progression-free survival (PFS).



Results: In total, 33 pts (median age 38 [20–66]) were enrolled across three sites (Dec 2020–Nov 2025). Primary refractory/early relapse occurred in 58% (n=19)/24% (n=8); B-symptoms in 27% (n=9), extranodal disease in 39% (n=13) at the time of enrollment. Post nivo-40 monotherapy: CR - 46% (n=15), partial response (PR) - 21% (n=7), indeterminate response (IR) - 30% (n=10), and progression - 3% (n=1) pts. Among non-CR, 1 continued nivo-40 due to patient/physician decision, 17 proceeded to NICE-40: ORR 76% (13/17) with CR 41% (n=7), PR 35% (n=6), IR 24% (n=4). Auto-HCT was performed in 88% (n=29): 45% (13/29) post nivo-40, 52% (15/29) post NICE-40, 1 post third-line.Post-HCT maintenance was given to 55% (n=16): brentuximab vedotin (n=9, 31%) and nivo-40 (n=7, 24%). With a median follow-up of 37 months (range 4–57), the 3-year OS was 92% (95% CI 72–98%), PFS - 79% (95% CI 59–90%). A trend toward superior PFS was observed in pts achieving CR after nivo monotherapy (93% [95% CI 61–99%] vs. 67% [95% CI 37–85%], p=0.11). Pre-HCT PET status (CR vs. non-CR) did not affect PFS (81% [51–94%] vs. 74% [39–91%], p=0.8). In the safety analysis performed for study treatment, the rate of adverse events (AEs) of any grade occurred in 42% (n=14), including 42% (n=14) of grade 1-2 AEs and 12% (n=4) of grade 3-4 AEs (related to hematological toxicity).

Conclusions: NICE-40 is an effective second-line regimen prior to auto-HCT in r/r cHL. Using a PET-adapted strategy, we identified that 45% of patients can successfully avoid

salvage chemotherapy and proceed directly to auto-HCT after nivo-40 monotherapy, achieving favorable outcomes while reducing toxicity and financial burden.

Clinical Trial Registry: NCT04981899

Disclosure: Nothing to declare

B387

PD-1 INHIBITOR PROLGOLIMAB ACHIEVES HIGH RESPONSE RATE BUT AUTO-HCT REMAINS ESSENTIAL FOR SUSTAINED PROLONGED REMISSION IN SECOND-LINE TREATMENT OF RELAPSED/REFRACTORY HODGKIN LYMPHOMA (PROLGO-HL)

Liudmila Fedorova[1], *Polina Kotselyabina*[1], *Kirill Lepik*[1], *Anastasia Semenova*[2], *Valeria Shpirko*[2], *Stanislav Volchenkov*[3], *Natalia Konoplya*[4], *Andrey Chekalov*[1], *Vladislav Markelov*[1], *Ilya Zyuzgin*[3], *Gayane Tumyan*[2], *Natalia Mikhailova*[1], *Alexander Kulagin*[1]
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Background: The introduction of PD-1 inhibitors into the second-line treatment for classic Hodgkin lymphoma (cHL) has raised question about the role of autologous hematopoietic cell transplantation (auto-HCT). It remains unclear whether patients achieving deep responses to PD-1 blockade can safely omit transplantation. Given the early and late complications associated with auto-HCT, clarifying this question in immunotherapy era is clinically important. This study aims to determine if auto-HCT may be omitted in patients who achieved an early complete response (CR) with PD-1 inhibitor prologolimab (Prolgo) monotherapy in second-line treatment of cHL.

Methods: This prospective, multicenter, single-arm, phase 2 clinical trial includes adult patients with histologically confirmed relapsed/refractory (r/r) cHL after first-line therapy (NCT05757466). All patients were naïve to PD-1 inhibitors. According to study protocol (Fig.1) patients with CR after 6 cycles of Prolgo (1 mg/kg every 2 weeks) continue monotherapy for up to 24 cycles. If CR is not achieved pts are switched to combination therapy (Prolgo 1 mg/kg D1,15; Bendamustine 90 mg/m2 D1,2, 28-day cycle, for up to 3 cycles). Response assessments are performed every 3 months by PET-CT using LYRIC criteria. The primary endpoint was overall response rate (ORR). Secondary endpoints included overall (OS), progression-free survival (PFS), duration of response (DOR), and adverse events (AE). The intention-to-treat (ITT) population was used for the safety analysis, and the per-protocol (PP) population - for the efficacy analysis. Four patients were excluded from the PP analysis for the following reasons: significant protocol deviation (n=2), early withdrawal of consent (n=1), and grade 3 AE (n=1).

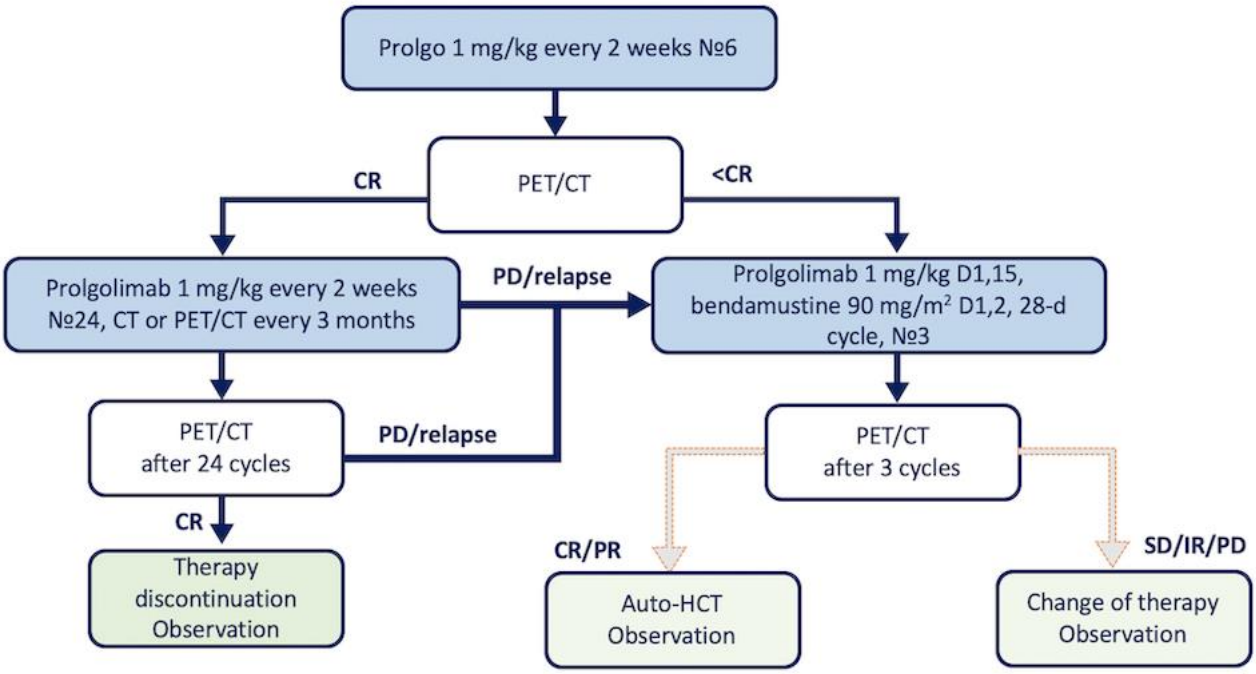

Figure 1 Study protocol

Results: 32 pts with r/r cHL were enrolled in the study from 04.2023 to 11.2025. Median follow-up was 19 months (range,2-31).
In the PP analysis all patients (n=28) completed 6 cycles of Prolgo: 9 pts (32%) achieved CR, 8 (29%) – partial response (PR), 1 (4%) – stabilization, 9 (32%) – indeterminate response, 1 (4%) – disease progression. Among patients who achieved CR after 6 cycles (n=9), 7 pts (78%) had already completed 24 cycles of therapy. Relapse was occurred in 4 pts (44%). Median DOR was 23.3 months (95%CI 20.3-NA). 17/19 pts without CR were switched to the Prolgo-bendamustine arm. Fourteen pts completed combination therapy, among which CR was achieved in 11 (79%) pts and PR in 1 (7%). Auto-HCT was performed at 8 pts (57%).
At the end of therapy per protocol, 19/21 (90%) pts achieved an objective response. Median PFS was 24.1 (95%CI 22.5-NA) and 1-year PFS was 87% (95%CI 74-100%). One patient in CR died of an infectious AE on D+88 after auto-HCT.
In the safety ITT analysis (n=32), the rate of grade 1-2 AE was 63%, grade 3 - 16%. Therapy was discontinued due to AE in 2 pts.

Conclusions: This real-world study demonstrates high response rate within the Prolgo-HL protocol in patients with r/r cHL. However, significant relapse rate in early CR maintenance arm bring into question the benefit of omitting auto-HCT in unselected group of patients with r/r cHL. Further stratification of low risk patients needed to identify population for whom forgoing auto-HCT is feasible.

Clinical Trial Registry: NCT05757466

Disclosure: The investigational drug (prolgolimab) was provided by BIOCAD. The sponsor had no role in the study design, data collection, analysis, interpretation, or decision to submit the manuscript for publication.

B388

FIVE-YEAR FOLLOW-UP OF NIVOLUMAB-BASED COMBINATIONS AND TRANSPLANT STRATEGY AFTER PD-1 INHIBITOR FAILURE IN RELAPSED/REFRACTORY CLASSIC HODGKIN LYMPHOMA

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Background: The optimal management of relapsed/refractory classic Hodgkin lymphoma (r/r cHL) after checkpoint inhibitors (CPI) failure remains an unmet need. While combination regimens with CPI show promise, their long-term outcomes are not systematically described. The role of allo-HCT and alternative strategies for ineligible patients are undefined. Thus, the aim of this study was to assess long-term outcomes of nivolumab (nivo) combined with chemo- or targeted therapy after mono-CPI failure, and to evaluate the prognosis of patients consolidated with allo-HCT versus those continuing conservative therapy.

Methods: The retrospective study included 123 patients with r/r cHL after mono-CPI failure. All patients were treated with combination of nivo (3 mg/kg or 40 mg every 2 weeks) and chemo- or targeted therapy: bendamustine 90 mg/m² D1,2 of a 28-day cycle (n=55), vinblastine 10 mg every 2 weeks (n=42), brentuximab vedotin (BV) 1.8 mg/kg every 3 weeks (n=20), or gemcitabine 800-1000 mg every 2 weeks (n=6). The response was evaluated every 3 months by PET-CT using LYRIC criteria. The survival outcomes and adverse events (AE) were analyzed.

Results: Baseline characteristics are listed in Table 1. Median follow-up was 65 months (2–103). The ORR was 54% (n=67): complete response (CR) 29%, partial response (PR) 25%, stabilization 14%, progression 14% and indeterminate response 18%. 5-year OS was 82.6% (95% CI: 75.5–90.3). Median PFS was 11.5 months (95% CI: 9.4–13.7 mo) with 5-year PFS of 13.1% (95% CI: 6.6–26.3). Median TTNT was 7.1 months (95% CI: 5.9–8.7), 5-year TTNT was 5.5% (95% CI: 2.6–11.7). AE occurred in 81 patients (66%), including grade 3-4 in 17 (14%).
Additional therapy was required in 116 patients (94%), which included: another combination regimen with CPI (51%), chemotherapy (15%), mono-CPI (25%), auto-HCT (3%) or allo-HCT consolidation (7%). Median number of therapy lines following the first combination regimen was 4 (range, 0-10).
29 patients (24%) underwent allo-HCT at any timepoint after combination. Disease status at allo-HCT was CR in 8 (28%), PR in 7 (24%), SD in 1 (3%), IR in 3 (10%), PD in 10 (34%) patients. No significant difference in OS was found between patients receiving only

conservative therapy (n=94) and those undergoing allo-HCT consolidation: 5-year OS: 84.9% vs. 74.8%, p=0.58.
We also analyzed whether performing allo-HCT as consolidation after first combination therapy affected subsequent survival outcomes. Comparing OS and TTNT between the group of patients with allo-HCT consolidation (n=8) and those who continued with other treatment options (n=115), we found no difference in OS (5-year OS 87.5% vs 85.9% respectively, p=0.51); however, a statistically significant difference in TTNT was demonstrated (5-year TTNT 87.5% vs 15%, p<0.001).

Table 1. Patient's characteristics

Patient's characteristics	n=123
Age, years (range)	33 (17-69)
Female/Male, n (%)	59/64 (48/52)
Primary refractory/early relapse, n (%)	77/17 (63/14)
Prior brentuximab vedotin, n (%)	61 (50)
Prior autologous hematopoietic cell transplantation, n (%)	45 (37)
Prior allogeneic hematopoietic cell transplantation, n (%)	3 (2)
Prior exposure to the combination agent, n (%)	54 (44)
Prior lines of therapy, median (range)	5 (2-11)
Median time from last nivolumab infusion, months (range)	1 (0-25)

Conclusions: The use of combination regimens with CPI represents an effective and safe strategy. This approach is beneficial for patients who have failed multiple therapy lines including CPI, including its use as a bridge to allo-HCT, as well as for patients who are not candidates for transplantation.

Disclosure: None.

B389

AUTOLOGOUS TRANSPLANT IN T-CELL LYMPHOMAS

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Background: For certain T-cell lymphomas, consolidation with autologous transplant in first-line treatment represents an important alternative to improve survival. The optimal conditioning regimen in these lymphomas is not well established.

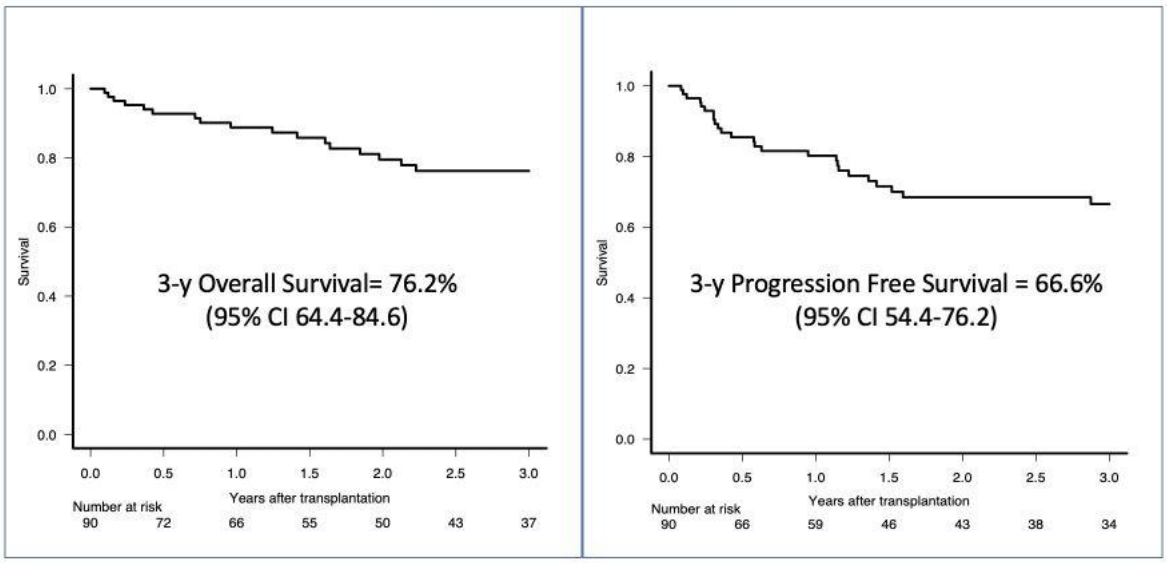
Methods: This is a retrospective study of patients with newly diagnosed T-cell lymphoma who received an autologous transplant as consolidation between 2015 and 2025. The following entities were included: Peripheral T-cell Lymphoma (PTCL-NOS), Anaplastic Large Cell Lymphoma ALK-negative (ALCL ALK-), Anaplastic Large Cell Lymphoma ALK-positive (ALCL ALK+), and Angioimmunoblastic T-cell Lymphoma (AITL). Centers were invited to participate through the Argentine Group for Bone Marrow Transplant and Cellular Therapy (GATMO-TC). Overall survival (OS) and progression-free survival (PFS) were evaluated.

Results: A total of 90 patients were included (median age 49.1 years; range 18.0–70.9; 54 males, 60.0%). Lymphoma subtypes were: PTCL-NOS n = 43 (47.8%), ALCL ALK- n = 27 (30.0%), AITL n = 15 (16.7%), and ALCL ALK+ n = 5 (5.6%). At diagnosis, 26 cases were stage I–II (28.9%) and 64 (71.1%) stage III–IV; 20 (22.5%) had bone marrow involvement; and 40 cases (49.9%) had extranodal involvement. Other pre-transplant characteristics are shown in the table. Median infused CD34+ cells were 4.49 (range 1.6–17.4). Conditioning regimens were BEAM n = 35 (38.9%), CBV n = 26 (28.9%), bendamustine-based n = 24 (26.7%) and others n = 5 (5.5%). All patients achieved myeloid reconstitution. Transplant-related mortality at one year was 2.4% (95% CI 0.5–7.7). Three-year overall survival was 76.2% (95%CI 64.4-84.6) and three-year progression-free survival was 66.6% (95% CI 54.4-76.2) (Figure). Considering the three main conditioning regimens (BEAM, CBV and bendamustine-based), no differences in OS or PFS were observed. Four patients had a prior diagnosis of HIV; in this subgroup, PFS and OS were both 100%.
Variables associated with better 3-year PFS were: Ann Arbor stage I–II vs III–IV at diagnosis (86.1% vs 59.3%; p = 0.015); ECOG 0 vs 1 vs 2 (74.0%, 66.6%, 14.6%; p < 0.001); and best pre-transplant response CR vs PR (72.4% vs 33.3%; p = 0.003). On multivariate analysis, ECOG performance status remained statistically significant.
Variables associated with better 3-year OS were: ECOG 0 vs 1 vs 2 (82.0% vs 82.5% vs 21.4%; p < 0.001); best pre-transplant response CR vs PR (82.1% vs 33.3%; p < 0.001); lymphoma subtype ALCL ALK- vs PTCL-NOS vs ALCL ALK+ vs AITL (92.1% vs 75.6% vs

66.7% vs 50.3%; p = 0.034); and number of prior lines 1 vs 2 vs 3 (78.6% vs 72.3% vs 33.3%; p = 0.021). All four variables remained significant in the multivariate model.

Table. Baseline pre-transplant characteristics of patients with T-cell lymphoma (n=90)

Variable	Results
Age at transplant, median (range)	49.1 (18.0–70.9)
Gender, female/ male, n (%)	36 (40.0)/ 54 (60.0)
ECOG performance status, n (%) 0 1 2	 64 (72.7) 15 (17.0) 9 (10.2)
Lines of therapy, n (%) 1 2 3	 77 (85.6) 10 (11.1) 3 (3.3)
Previous Brentuximab, n (%)	15 (16.7)
Better response, n (%) Complete response Partial response Unknown	 80 (88.9) 9 (10.0) 1 (1.1)



Conclusions:

Consolidation with autologous transplant in patients with T-cell lymphoma offers survival rates above 70%. Carmustine based regimens like BEAM or, CBV, and bendamustine-based regimens were all equally effective. Achieving complete response prior to transplant and requiring fewer lines of therapy to achieve it are the most important variables for clinical decision-making.

Disclosure: Nothing to declare.

B391

THE ROLE OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ADVANCED PRIMARY CUTANEOUS T-CELL LYMPHOMA - A MULTICENTER RETROSPECTIVE ANALYSIS

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Background: Primary cutaneous T-cell lymphomas (CTCL) comprise a rare and heterogeneous group within non-Hodgkin lymphomas which have their primary mostly indolent manifestation in the skin. In advanced stages, these lymphomas can advance to an aggressive course and are associated with a poor overall prognosis and a high recurrence rate. For this reason, the treatment of these patients is particularly challenging. In this context, allogeneic hematopoietic stem cell transplantation (allo-HSCT) can lead to long-lasting remissions by inducing a graft-versus-lymphoma effect and thus represents a potentially curative treatment option. Due to the rarity of the disease spectrum, there is still very limited data on the role of allo-HSCT in primary CTCL.

Methods: We investigated long-term efficacy and safety of allo-HSCT in patients with advanced primary CTCL by means of a multicentric retrospective study analyzing patient data from six German transplant centers to determine overall survival (OS), relapse-free survival (RFS) and the incidence of relapse (RI) following allo-HSCT. In addition, the remission status of the disease prior to allo-HSCT, the intensity of the conditioning regimen, the occurrence of graft-versus-host disease (GvHD) and the clinical impact of different post-transplant strategies were considered.

Results: A total of 28 patients with advanced primary CTCL were included, the majority suffering from Mycosis Fungoides (MF) (*n=12*, 42%). Half of the patients with MF and Sézary Syndrome (SS) had stage IV disease. In addition, patients had received extensive prior treatment, with a median of four previous lines of therapy. On average, 65.5 months passed between the initial diagnosis and transplantation. 23 patients (82%) were in partial (*n=19*, 68%) or complete remission (*n=4*, 14%) at the time of transplantation. 18 patients (64%) underwent myeloablative conditioning and in-vivo T-cell depletion was performed in 16 patients (57%; antithymocyte globulin: *n=6*; post-transplant cyclophosphamide: *n=9*; alemtuzumab: *n=1*). With a median follow-up of 58 months, 17 patients (60%) had died, with infections (*n=8*, 47%) followed by disease relapse (*n=7*, 41%) being the most common causes of death. The median OS after allo-HSCT was 15 months with an estimated one-year OS of 55%. The RI was 64% *(n=18)* after transplantation with a median RFS of 14 weeks and an estimated one-year RFS of 36%. Acute GvHD was seen in 15 patients (53%), with most cases being mild (*n=10* for grade I and II, 66%) and mainly affecting the skin (*n=13*, 86%). Chronic GvHD subsequently developed in 13 patients (46%). In patients suffering from relapse a partial or even complete short- to medium-term therapeutic response was achieved in 7 patients (38%) with the use of various post-transplant strategies (donor lymphocyte infusions (*n=5*), antibody therapy (*n=2*), radiotherapy (*n=2*)).

Conclusions: Although allo-HSCT can prolong RFS compared to conventional therapies, the durability of response is limited. Standardized transplant and post-transplant strategies to maintain disease remission are currently lacking and may be essential to fully exploit the curative potential of allo-HSCT in advanced CTCL.

Disclosure: Daniel Wolff received research funds from Novartis and honoraria from Novartis, Sanofi, Incyte, Therakos, Neovii, Behring.

B392

A COMPARATIVE ANALYSIS OF TRANSFORMED HODGKIN'S LYMPHOMAS FROM MARGINAL ZONE LYMPHOMA: A POPULATION-BASED COHORT STUDY

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Background: Histological transformation of marginal zone lymphoma (MZL) to Hodgkin's lymphoma (HL) is a rare but clinically significant event, with its risk factors and outcomes remaining poorly characterized. Our study represents the largest comparative analysis to date, aiming to elucidate the distinct clinical features and outcomes associated with this transformation.

Methods: Our study retrospectively analyzed 23,609 MZL patients diagnosed between 2000 and 2021 from the SEER17 registry database. Competing risk and Cox regression analyses were employed to evaluate transformation rates and outcomes, respectively. Additionally, we investigated the prognostic impact of time-to-transformation on outcomes in t-HL patients and conducted a comparative analysis of clinical characteristics and survival profiles between *de novo* HL and t-HL (transformed HL) cases.

Results: Our cohort comprised 23 609 MZL patients, of whom 38 (0.16%) developed t-HL. The median follow-up duration was 112 months (95% CI 110-113) for the overall cohort, 112 months (95% CI 110-113) for non-transformed MZL (nt-MZL) patients, and 148 months (95% CI 107-198) for t-HL patients. Compared to patients with nt-MZL, those with t-HL exhibited younger age at the time of MZL diagnosis and advanced Ann Arbor Stage. By competing risk analysis and Gray's test, the overall cumulative transformation rates (CTRs) at 5, 10 and 20 years were estimated to be 0.09% (95% CI 0.05%–0.13%), and 0.16% (95% CI 0.10%–0.22%) and 0.27% (95% CI 0.17%–0.37%), respectively. The transformation occurred within 10 years in most patients (76%, 29/38) at a median time of 57.5 months. Multivariate analysis further indicated that splenic MZL subtype ($P < 0.001$) and younger age (HR 0.966, 95% CI 0.948-0.984, $P < 0.001$) were associated with an increased risk of developing t-HL, whereas receipt of radiotherapy for MZL was linked to a reduced risk (HR 0.109, 95% CI 0.016-0.752, $P = 0.025$). Late transformation (transformation after 38 months of MZL diagnosis [T38]) was identified as an independent predictor of adverse outcomes in t-HL patients. Lastly, comparative survival analysis revealed a significantly worse prognosis for t-HL patients compared to those with *de novo* HL.

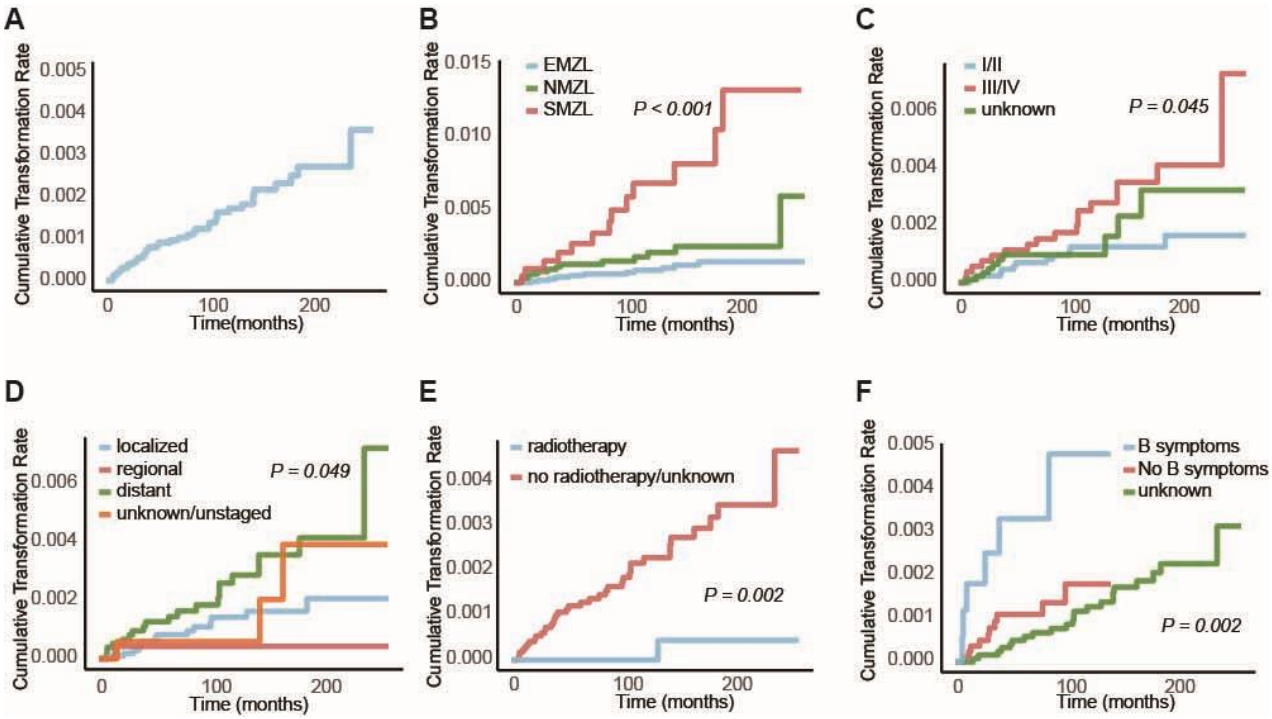

Figure 1. The cumulative incidence of histological transformation in MZL were statistically different among subgroups. (A) Estimated cumulative transformation rates by Fine–Gray's competing risks model. Comparisons of estimated cumulative transformation rate by competing risks model in the SEER database based on MZL subtype (B), Ann Arbor stage (C), disease stage (D), receipt of radiotherapy (E) and B symptoms (F). SEER indicates the Surveillance, Epidemiology, and End Results.

Conclusions: Our study provides comprehensive insights into the characteristics and survival of t-HL patients. We identified MZL subtype and younger age as risk factors for t-HL development, while radiotherapy for MZL was associated with a reduced risk. Importantly, late transformation emerged as an independent predictor of adverse outcomes. Furthermore, we demonstrated significantly worse survival in t-HL compared to *de novo* Hodgkin Lymphoma. These findings highlight critical prognostic factors and underscore the need for tailored management strategies in t-HL.

Disclosure: Nothing to declare

B393

ROLE OF TARGETED IMMUNE THERAPIES IN RELAPSED/REFRACTORY LYMPHOMA (HODGKINS): A MULTICENTER EXPERIENCE FROM VARIOUS TRANSPLANT CENTERS IN PAKISTAN. A LOWER MIDDLE INCOME COUNTRY PERSPECTIVE

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Background: Relapsed/refractory lymphoma (RR-HL) remains a therapeutic challenge, with limited durable responses to conventional salvage chemotherapy. Immunotherapy, particularly CD30-targeted antibody drug conjugates, has emerged as a promising option. This study aimed to evaluate the role, safety and efficacy of targeted immunotherapy in RR-HL patients treated at various bone marrow transplant centers in Pakistan, with focus on clinical responses, transplant outcomes, and treatment-related adverse events.

Methods: We conducted a retrospective review of 63 patients with RR-HL treated cases. All patients had received first-line ABVD followed by salvage ICE/GDP before immunotherapy (brentuximab vedotin ± bendamustine or alternative agents). Safety endpoints included adverse events graded by CTCAE, while efficacy endpoints were response rates, progression to autologous stem cell transplant (ASCT), and post-ASCT PET outcomes as over all survival and progression free survival.

Results: The median age was 38.6 years (range 23–65) and was 64% men. These patients received 3 to 5 cycles of Brentuximab vedotinb+bendamustine. The majority of patients had stage IV disease (72%). Pre-treatment labs were commonly abnormal: ESR >20 was found in 80%, anemia in 60%), and LDH in 72%. All patients relapsed after first-line ABVD, 1/3 achieved CR to salvage ICE, 0/1 to GDP. Immunotherapy Toxicities were diarrhea (28%), nausea/vomiting (20%), rash/mucositis (16%), cytopenias (24%), respiratory (32%), and infections (24%). One death of treatment related was recorded. ASCT was completed in 60 patients (95%); 100-day PET confirmed CMR in 56%, PR in 12%, and progression in 16%. Over all survival and progression free survival results will be shared at time of poster/oral presentation.

Conclusions: Immunotherapy/ targeted therapy showed clinically relevant activity in heavily-pretreated RR-HL patients, allowing many patients to proceed to ASCT with a high remission rate. Toxicities were frequent, but overall manageable and with one death. Our results reiterate the feasibility of immunotherapy in RR-HL as a bridge to transplant in keeping with international experience, although more extensive prospective studies are required in South Asian cohorts.

Disclosure: Nothing to declare.

P275

SAFETY AND EFFICACY OF LENALIDOMIDE IN PATIENTS WITH RELAPSED OR REFRACTORY ADULT T-CELL LEUKEMIA/LYMPHOMA AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A MULTICENTER PROSPECTIVE OBSERVATIONAL STUDY

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Background: Relapse of adult T-cell leukemia/lymphoma (ATL) after allogeneic hematopoietic stem cell transplantation (allo-HCT) remains associated with extremely poor outcomes, and effective salvage therapies are limited. Lenalidomide, approved in Japan for relapsed or refractory (r/r) ATL, has immunologic activity but may exacerbate graft-versus-host disease (GVHD) after transplantation. This multicenter prospective observational study evaluated the efficacy, safety, tolerability, and immunologic effects of lenalidomide in patients with r/r ATL following allo-HCT.

Methods: The primary endpoint was 1-year overall survival (OS) from relapse. Secondary endpoints included clinical response, 1-year OS from lenalidomide initiation, safety, tolerability, and GVHD incidence. Immune profiling was performed at baseline and at weeks 2, 4, and 12.

Results: Twenty-seven patients from 10 institutions received lenalidomide post-allo-HCT at physician-determined doses and schedules. The median age at registration was 62 years (interquartile range [IQR], 58–65), and 14 patients (51.9%) were female. The median time from relapse to lenalidomide initiation was 30 days (IQR, 10–52), and the median time from transplantation to initiation was 171 days (IQR, 77–418). The 1-year OS from relapse was 48.1% (95% CI, 28.7–65.2), with a median OS of 0.92 years (95% CI, 0.43–1.60). From the start of lenalidomide, the 1-year OS was 33.3% (95% CI, 16.8–50.9), and the median OS was 0.47 years (95% CI, 0.19–1.08).
Regarding clinical response, the best overall response included complete response in 3 patients (11.1%), partial response in 4 (14.8%), stable disease in 10 (37.0%), and progressive disease in 10 (37.0%). The median starting dose was 5 mg (IQR, 5–10), and the median maximum dose was 10 mg (IQR, 5–15). The median duration of lenalidomide therapy was 33 days, and only 22.2% of patients remained on treatment at week 12, indicating limited tolerability. Discontinuation was primarily due to disease progression or adverse events. Grade ≥3 adverse events were common, including neutropenia (33.3%), thrombocytopenia (29.6%), and febrile neutropenia (18.5%). Worsening of acute GVHD occurred in 5 patients and exacerbation of chronic GVHD in 3. Transplant-related mortality 12

months after relapse was 11.1% (95% CI, 2.7–26.3).
Immune profiling demonstrated increases in activated CD8+ T cells, effector regulatory T cells, and NK cells in clinical responders between weeks 2 and 4, indicating pharmacodynamic immunomodulatory activity of lenalidomide.

Conclusions: Lenalidomide showed immunologic activity and clinical benefit in a subset of patients with r/r ATL after allo-HCT; however, its broader use was limited by substantial toxicity, GVHD exacerbation, and short treatment duration. These findings underscore the importance of individualized patient selection and warrant further clinical trials to optimize the post-transplant use of lenalidomide for r/r ATL.

Clinical Trial Registry: UMIN 000029635

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HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR T-CELL LYMPHOMAS IN A MIDDLE-INCOME COUNTRY: FEASIBILITY, DELAYS, AND REAL-WORLD OUTCOMES FROM A NATIONAL REFERRAL CENTER IN MEXICO

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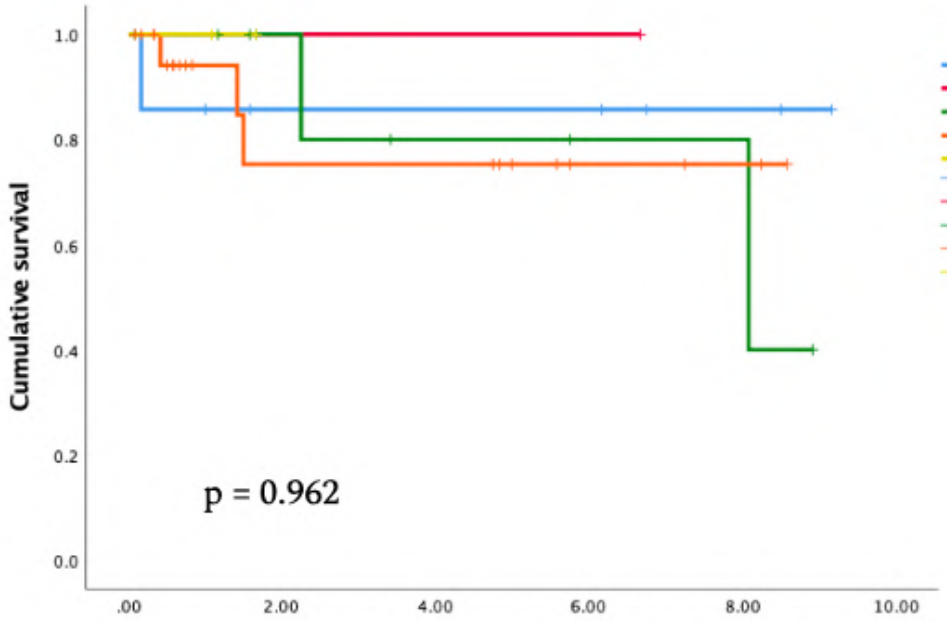
Background: Despite its established role in T-cell lymphomas, the feasibility and real-world use of hematopoietic stem cell transplantation (HSCT) in middle-income settings remain poorly defined, particularly regarding delayed access.

Methods: We conducted a retrospective cohort study including 40 adult patients with confirmed T-cell lymphomas who underwent HSCT at a national referral cancer center. Demographic characteristics, disease subtype, timing and type of HSCT, early post-transplant outcomes, and survival were analyzed. Primary outcomes included overall survival (OS), progression-free survival (PFS), and post-HSCT PFS. Secondary variables included time from diagnosis to HSCT, transplant indication (CR1 vs relapsed/refractory [R/R]), and feasibility indicators such as day +100 response, infectious complications, and transplant-related mortality (TRM).

Results: The cohort primarily included young adults (median age 36 years), with extranodal NK/T-cell lymphoma being the most frequent subtype (52.5%). Marked delays in access to HSCT were observed, with a median interval of 22 months from diagnosis to transplantation.

As a result, 57.5% of patients underwent HSCT in the R/R setting, whereas only 42.5% were transplanted in CR1. Most patients received autologous HSCT (87.5%), while 12.5% underwent allogeneic HSCT.
Early post-transplant outcomes demonstrated high feasibility despite resource limitations: day +100 complete response was achieved in 90% of patients, and no transplant-related mortality occurred. Infectious complications were observed in 57.5% of all patients and in all allogeneic recipients.
Median OS and PFS for the entire cohort were 60 and 48 months, respectively. Survival outcomes differed by lymphoma subtype: PTCL-NOS/AITL showed the most favorable results, with median OS and PFS of 60 months; ALCL had a median OS of 60 months and median PFS of 48 months; whereas extranodal NK/T-cell lymphoma exhibited poorer outcomes, with a median OS of 44 months and median PFS of 43 months. Post-HSCT PFS varied significantly by subtype, with the poorest outcomes observed in ENKTL (10 months), compared with ALCL (27 months) and PTCL-NOS/AITL (60 months). Patients transplanted in the relapsed/refractory (R/R) setting exhibited approximately twice the risk of post-transplant progression compared with those transplanted in CR1, although differences in OS and PFS did not reach statistical significance.



	Years								
No. at risk	1	2	3	4	5	6	7	8	9
PTCL-NOS	6	4	4	4	4	4	2	2	1
AITL	1	1	1	1	1	1			
ALCL	8	5	4	3	3	2	2	2	
ENKTL	10	8	8	8	6	3	3	2	
T-LBL	2								

Metric	Value
Median time from diagnosis to HSCT	22 months
HSCT performed in CR1	42.5%

HSCT performed in relapsed/refractory setting	57.5%
Autologous HSCT	87.5%
Allogeneic HSCT	12.5%
Most frequent subtype	ENKTL (52.5%)
Day +100 complete response	90%
Transplant-related mortality	0%

Conclusions: HSCT was feasible, safe, and effective in this middle-income setting, achieving high early response rates and no TRM. However, substantial delays in access to transplantation resulted in a majority of patients undergoing HSCT in the R/R setting, which was associated with increased post-transplant progression. The predominance of aggressive ENKTL and delayed referral likely contributed to shortened post-HSCT PFS. These findings highlight the need to improve timely access to HSCT and address system-level barriers that disproportionately affect patients with high-risk T-cell lymphomas in resource-limited environments.

Disclosure:

Nothing to declare.

P277

PEMBROLIZUMAB PLUS GEMCITABINE, VINORELBINE, AND DOXORUBICIN FOLLOWED BY AUTOLOGOUS STEM CELL TRANSPLANTATION IN 24 RELAPSED/REFRACTORY CLASSICAL HODGKIN LYMPHOMA PATIENTS

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Background: Relapsed/refractory (R/R) classical Hodgkin lymphoma (cHL) remains challenging, particularly in patients failing multiple therapy lines. PD1-inhibitor based salvage regimens before autologous stem cell transplantation (ASCT) are associated with significantly higher PFS. Previously reported results with pembrolizumab, gemcitabine, vinorelbine, and doxorubicin (P-GVD) followed by ASCT (Moskowitz, et al. JCO 2021) achieved better outcomes.

Methods: We retrospectively analyzed 24 consecutive patients (pts) with R/R cHL treated with P-GVD followed by ASCT between Dec 2023 and Aug 2025. Median age was 36 years (22–57); sex ratio M/F: 0.4. Patients received the regimen after ≥2 prior lines (range 2–5); 4 relapsed and 20 were refractory. The status of the pts at transplantation was: coplete remission (CR) in 13 patients (11 metabolic CR, mCR), and partial remission (PR) in 11 pts (with metabolic assessment in 2). Conditioning regimen was BeEAM (Bendamustine: 300 mg/m², Aracytine: 800 mg/m², Etoposide: 800 mg/m² and Melphalan: 140 mg/m²). Peripheral HSC was collected by cytapheresis after mobilization with G-CSF alone. The median CD34+ cells dose was 2.66×10⁶/kg (1.05–9.19). Brentuximab-vedotin maintenance was given in 9 pts (39%). The median follow-up at 31/10/2025 is 18 months (4-24).

Results: Median duration of aplasia was 8 days (6–14); neutrophil recovery occurred at day +11 (9–15). One patient died at 3 months from a metabolic complication. At 3-month post-ASCT evaluation, 16 pts were in CR (15 mCR) and 7 in PR. Two progressed at a median time of 3 months (1-6); one achieved CR after geno-identical allo-HSCT (full donor chimerism), and one remains under assessment. At a median follow-up of 18 months (4–24), 23 pts (95.8%) were alive: 16 in CR, 6 in PR, and 1 under evaluation. The overall survival (OS) at 2 years is 95,8% and the event-free survival (EFS) is 87,5%.

Conclusions: Currently, patients with R/R cHL receive salvage therapy with immune checkpoint inhibitors. Pembrolizumab-GVD prior to ASCT provides deep pre-transplant responses and excellent post-ASCT outcomes. This strategy increases transplant eligibility and supports a tailored approach incorporating post-ASCT consolidation.

Disclosure: Nothing to declare

P278

IMMUNE RECONSTITUTION AND LONG-TERM OUTCOMES AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN RELAPSED AND REFRACTORY T-CELL LYMPHOMAS

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Background: Refractory and relapsed T-cell lymphomas represent a rare and biologically heterogeneous group of non-Hodgkin lymphomas associated with poor prognosis and limited therapeutic options. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains

a potentially curative approach in this setting. However, post-transplant outcomes are frequently compromised by high rates of severe infections and systemic inflammatory response, with the underlying mechanisms remaining incompletely understood. In particular, the dynamics of immune reconstitution (IR) after allo-HSCT and their impact to post-transplant complications and survival remain poorly defined. We therefore analyzed IR and its association with post-transplant outcomes in patients with T-cell lymphoma undergoing allo-HSCT.

Methods: We performed a retrospective analysis of patients with relapsed or refractory T-cell non-Hodgkin lymphoma (AITL, n=9; ALCL, n=5; PTCL-NOS, n=5; MF, n=2; NKTL, n=1; EATL, n=1; MEITL, n=1; SPTCL, n=1) who underwent allo-HSCT at our institution. Clinical and transplant-related data were collected. Immune reconstitution markers were assessed prior to transplantation and serially up to one-year post-transplant. Associations between immune recovery, transplant-related complications, and clinical outcomes were analyzed.

Results: In total, 25 patients were analyzed. The median age was 50 years, and 15 patients were male. Donors were matched related (n=4), matched unrelated (n=8), or haploidentical (n=13). 75% of patients presented with active disease at the time of conditioning. After a median follow-up of >6 years, 1-, 3-, and 5-year overall survival rates were 60%, 50%, and 50%, and progression-free survival rates were 48%, 48%, and 41%, respectively. Severe non-hematological toxicities (grade III–IV) were observed in 50% of patients. The 1-year cumulative incidence of non-relapse mortality was 36%, most commonly due to septic shock (n=4). Grade III–IV acute GvHD occurred in 16% of patients. Comprehensive IR data are already collected longitudinally, and analyses evaluating their impact on treatment outcomes, including comparisons with B-cell non-Hodgkin lymphoma cohorts undergoing allo-HSCT, are ongoing.

Conclusions: Our study shows that allo-HSCT can provide durable responses in patients with T-cell lymphoma, although severe infections remain a major challenge. Through a detailed and comprehensive analysis of IR and its impact on clinical outcomes, our findings offer the opportunity to gain insights into the interplay between immune recovery, infection, and relapse, which may help guide strategies to improve post-transplant outcomes.

Disclosure: Nothing to declare.

P279

NURSING MANAGEMENT OF A CHEMOTHERAPY PATIENT WITH ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA AND AN INFECTED LOWER-LIMB WOUND: A CASE STUDY

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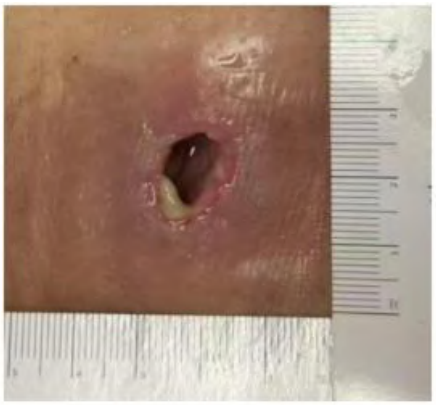
Background: To share the nursing experience of a patient with angioimmunoblastic T-cell lymphoma (AITL) who developed a lower-limb infected wound during chemotherapy.

Methods: A 71-year-old male was admitted on 14 July 2025 with a diagnosis of AITL and nephrotic syndrome. Physical examination on admission revealed multiple palpable enlarged lymph nodes throughout the body; marked abdominal distension; moderate pitting edema of the lower limbs; and an ulcerated wound located below the left inguinal region, measuring approximately 2 cm × 1.5 cm with a depth of about 1.5 cm. The wound showed yellow purulent discharge. Wound secretion culture indicated *Acinetobacter baumannii* complex infection. Pain assessment showed an NRS score of 0; NRS-2002 score was 6; and ADL indicated mild dependence. Serum albumin was 19.3 g/L. The chemotherapy regimen consisted of CHP + VP16 (cyclophosphamide, vincristine, dexamethasone, and etoposide). Wound care focused on infection control and local management, following the principles of "debridement – infection control – moist wound healing." Nursing interventions were adjusted according to the wound-healing stage, with strict aseptic technique throughout.
Infection Phase (Day 1–Day 5): Debridement and dressing changes combined with anti-infective therapy: normal saline irrigation, povidone-iodine disinfection, removal of necrotic tissue, repeated saline irrigation; application of a mixture of mupirocin, growth-factor gel, and zinc sulfadiazine in a thick layer; silver-containing dressings, covered with gauze and secured with an elastic bandage.
Exudation Phase (Day 6–Day 14): Continued anti-infection treatment with exudate management: saline irrigation → povidone-iodine disinfection → saline irrigation; thick application of a mixture of growth-factor gel, detoxifying-promoting-tissue-regeneration ointment, and zinc sulfadiazine; povidone-iodine gauze packing for drainage; gauze coverage and elastic bandage fixation.
Repair Phase (Day 15–Day 23): Promotion of wound healing: saline irrigation, povidone-iodine disinfection, saline wiping; thick application of the growth-factor gel + detoxifying-regeneration ointment + zinc sulfadiazine mixture; gauze coverage and elastic bandage fixation.
In addition, close monitoring of blood counts and biochemical indicators, vital-sign surveillance, accurate recording of fluid intake and output, medication administration per medical orders, as well as dietary guidance, activity recommendations, and psychological support were provided.

Results: After 23 days of systematic and targeted nursing interventions, the patient's clinical indicators and symptoms improved markedly, meeting all expected nursing goals. The wound achieved complete healing.

Wound Infection Phase


Wound Exudation Phase

Wound Repair Phase

Conclusions: Patients with AITL are prone to skin infections and wound ulceration due to impaired immunity. In this case, nephrotic-syndrome–associated hypoalbuminemia and generalized edema further increased infection risk and hindered wound healing, making nursing care more challenging. Comprehensive management and precise, stage-based wound care—including aseptic dressing changes, debridement, and the targeted use of advanced wound dressings and topical agents—can effectively promote wound healing in such high-risk patients.

Disclosure: Nothing to Disclosure

P280

AUTOLOGOUS STEM CELL TRANSPLANTATION IN 175 PATIENTS WITH RELAPSED OR REFRACTORY CLASSICAL HODGKIN LYMPHOMA; LONG-TERM FOLLOW UP IN A SINGLE-CENTRE SERIES

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Background: Classical Hodgkin lymphoma (cHL) has high rates of cure, but in 15% to 20% of general patients (pts) and between 35% and 40% of those in advanced stages, the disease will progress or will relapse after initial treatment. For pts refractory to first-line chemotherapy or who relapse after initial treatment, outcomes are considerably worse. Salvage high-dose chemotherapy (HDT) followed by autologous stem cell transplant (ASCT) is the standard of care.

Methods: A retrospective study was performed with data collected from pts charts. The analysis involved 175 cHL pts who were consecutively submitted to HDT followed by ASCT in a single institution from April 1998 to December 2024 (27 years). The median age is 28 years (13-64) and a sex-ratio of 0,88 (82M /93F). It is cHL refractory and early relapse (120 pts), and late relapse (55 pts). Immunotherapy was administered as salvage treatment to 20 pts before transplantation. Disease status at transplantation is: 103 pts in partial response (PR), 55 pts in complete response (CR) including 10 pts in unconfirmed CR (CRμ) and 17 pts in failure. Peripheral HSC was collected by cytapheresis after mobilization with G-CSF alone. The median rate CD34 + cells is 3 x 106/kg (1,03-16,8). Several HDT conditioning regimens were used: BEAM: 78 pts, BeEAM with Bendamustine: 87 pts, Busulphan-Cyclophosphamide: 07 pts and TEAM with Tiothepa : 03 pts). The median follow-up at 01/12/2025 is 110 months (11-315).

Results: The median time to graft (PNC > 0.5x109/l) was 12 days (08-24). Eight early deaths were observed including 6 infections, 1 pulmonary embolism and 1 heart failure (TRM: 4,5%). Of the 167 pts that can be evaluated in post-transplantation, 128 pts (76%) achieved a CR, 33 pts (20%) achieved a PR and 6 pts achieved stable disease (3,5%). A relapse was observed in 52 pts (31%) after a median duration of 06 months (2-52). At 01 of December 2025, 115 pts (65,7%) are alive (108 in CR, 07 in PR), 60 pts (34,3%) died (43 pts from progression disease and other reason for 17 pts). The overall survival (OS) at 27 years is 58% and the event-free survival (EFS) is 54%. The survival of pts who have received immunotherapy is 90% at 2 years versus 77% without immunotherapy (P=0,38).

Conclusions: Our retrospective analysis shows good outcomes in patients who had R/R disease. Patients can be cured with second-line salvage chemotherapy and with HDT followed by ASCT. The introduction of the novel agents, including antibody-drug conjugates and PD-1 blocking antibodies has transformed the management of cHL in multiple settings.

Disclosure: Nothing to declare

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ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANT AS SALVAGE THERAPY FOR MATURE T CELL LYMPHOMA: CLINICAL EXPERIENCE AND OUTCOMES

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Background: Mature T cell lymphomas (MTCLs) are a heterogeneous group of aggressive neoplasms that present a significant haematological challenge in Asia, where they account for up to 20–25% of all non-Hodgkin lymphomas. Subtypes such as Peripheral T-Cell Lymphoma, Not Otherwise Specified (PTCL-NOS) and Anaplastic Large Cell Lymphoma (ALCL) are frequently associated with chemo-refractoriness and dismal survival outcomes following

standard therapies. Furthermore, rare entities like Gamma-Delta (γδ) T Cell Lymphoma are notoriously resistant to multi-agent chemotherapy, often carrying a median survival of less than 18 months. While allogeneic haematopoietic stem cell transplantation (AlloHCT) remains the sole intervention with curative potential for relapsed or refractory (R/R) disease, there is a paucity of granular data regarding its feasibility in Southeast Asia. This study aims to contribute real-world evidence on the practical feasibility and toxicity profile of AlloHCT in a Philippine tertiary centre.

Methods: We conducted a retrospective observational analysis of three consecutive adult patients with R/R mature T cell lymphoma who underwent AlloHCT at our institution. The study assessed key outcomes including engraftment kinetics, the incidence of graft-versus-host disease (GvHD), and disease-free survival. The cohort included high-risk histology: PTCL-NOS, γδ-TCL, and ALCL.

Results: All three patients had exhausted multiple lines of prior therapy. Case 1 underwent haploidentical HCT with FLU-CY-TBI conditioning salvage chemotherapy. He achieved neutrophil engraftment on day 13, developed cutaneous acute graft-versus-host disease (aGVHD) on day 28, and maintains a sustained remission of 5 years. Case 2 presented with highly refractory disease having failed three prior lines, notably experiencing immediate relapse following a prior autologous stem cell transplantation. Following salvage with pralatrexate, she proceeded to haploidentical HCT with FLU-CY-TBI conditioning, achieving engraftment on day 13 and a durable remission of 4 years. Finally, Case 3, pre-treated with four prior lines (including CHOP, radiotherapy, and brentuximab vedotin), underwent a matched sibling donor transplant utilising FLU-BU conditioning post-chemotherapy salvage. He engrafted on day 12 with cutaneous aGVHD onset at day 38 and remains disease-free at 3 years. All patients achieved successful engraftment with manageable toxicity profiles, demonstrating the efficacy of this approach in chemo-refractory settings.

Conclusions: This case series confirms the feasibility and curative efficacy of AlloHCT as a salvage strategy for Filipino patients with high-risk MTCL. The study demonstrates that the graft-versus-lymphoma effect can induce sustained survival even in patients with chemo-refractory disease or prior autologous transplant failure. Furthermore, the successful implementation of haploidentical platforms highlights that donor availability need not be a barrier to life-saving therapy in this region.

Disclosure: No

P284

A CASE REPORT OF MULTI-DRUG COMBINATION THERAPY FOR RELAPSED/REFRACTORY ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA

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Background: Peripheral T-cell lymphomas (PTCLs) are a heterogeneous group of non-Hodgkin lymphomas characterized by aggressive clinical behavior and poor prognosis.

Angioimmunoblastic T-cell lymphoma (AITL) accounting for approximately 20%-30% of PTCL case. The standard first-line treatment for AITL typically involves the CHOP regimen(cyclophosphamide,doxorubicin, vincristine,and prednisone) or CHOP-like protocols. However, many patients exhibit primary refractoriness or experience relapse after initial response, resulting in a 5-year overall survival rate of only 30% to 40%. For patients with relapsed/refractory (R/R) AITL, there is currently no established standard therapeutic approach.

Methods: We conducted a single-case retrospective analysis of a 54-year-old male patient with R/R AITL who had progressed following prior treatment with first-line CHOPE (CHOP plus etoposide) and second-line GDP (gemcitabine, doxorubicin liposome and corticosteroid) regimens. After one cycle of chidamide, mitoxantrone, azacitidine and corticosteroid therapy at our linstitution, the original lesions showed significant shrinkage with partial resolution; however, a new lesion emerged, indicating disease progression. The pathological specimens were re-evaluated, and immunohistochemical analysis demonstrated a lack of CD7 expression in the tumor cells, thereby ruling out the feasibility of CAR-T cell therapy. The treatment regimen was subsequently modified to a multi-agent combination: chidamide (20 mg twice weekly), decitabine (10 mg d1-5), mitoxantrone liposome (20 mg d2), bevacizumab (600mg day 1), bortezomib (2mg d1, 4, 8) and dexamethasone (20mg d1-4), repeated every 21days. During treatment, serial assessments of complete blood counts, liver and renal function, and imaging studies were performed to evaluate therapeutic response.

Results: Following completion of two cycles of the revised combination regimen, positron emission tomography–computed tomography (PET-CT) demonstrated complete remission (CR) with resolution of previously enlarged lymph nodes. Due to financial constraints, the patient declined allogeneic hematopoietic stem cell transplantation. The same chemotherapeutic regimen was continued and sustained through five cycles, with follow-up PET-CT confirming persistent CR. The patient has completed seven cycles of therapy with favorable tolerability. The main adverse event was grade III thrombocytopenia which resolved with supportive management; no severe infections or significant organ dysfunction were observed. After eight cycles of combination therapy, maintenance treatment with chidamide monotherapy or chidamide in combination with bortezomib is planned.

Conclusions: Chidamide, a histone deacetylase inhibitor, enhances tumor cell sensitivity to chemotherapeutic agents through epigenetic modulation. Decitabine exerts antitumor effects via inhibition of DNA methylation. Bevacizumab targets vascular endothelial growth factor (VEGF) , ameliorating tumor microenvironment-associated vascular abnormalities and immunosuppression. Bortezomib induces apoptosis in tumor cells by inhibiting the proteasome pathway. The six drug combination regimen leverages multidimensional synergy among epigenetic regulation, cytotoxicity, anti-angiogenesis and immune modulation, potentially overcoming resistance to conventional chemotherapy. The predominant adverse event was hematological toxicity, which was manageable with supportive care. No intolerable non-hematological toxicities were observed, indicating controllable treatment tolerability. For patients with R/R AITL who are ineligible for transplantation or CAR-T therapy—particularly when target antigens such as CD7 are negative and cellular therapies are not feasible—this combination represents a promising therapeutic option with high efficacy and low toxicity. Larger-scale clinical studies are warranted to confirm its efficacy and to determine the optimal maintenance strategy.

Disclosure: Nothing to declare

B cell Non-Hodgkin Lymphoma

OS02-04

OUTCOMES AFTER ANTI-CD19 CAR T-CELL THERAPY IN PRIMARY MEDIASTINAL B-CELL LYMPHOMA: A LARGE REAL-WORLD REGISTRY ANALYSIS FROM THE EBMT LYMPHOMA WORKING PARTY

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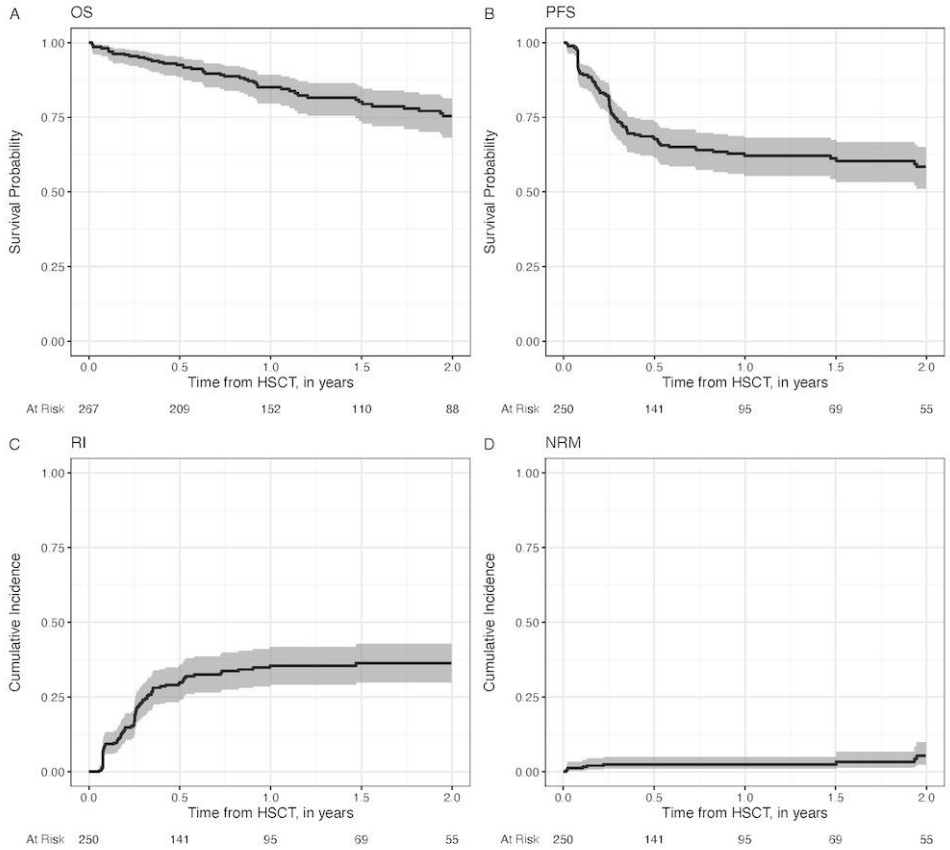
Background: Anti-CD19 CAR T-cell therapy is increasingly used in relapsed/refractory (R/R) primary mediastinal B-cell lymphoma (PMBCL), but dedicated large-scale analyses are scarce. In particular, the clinical factors associated with treatment outcomes in this population remain to be better defined.

Methods: We performed a retrospective registry-based analysis within the EBMT, including adults with PMBCL treated with commercial anti-CD19 CAR T-cell products between 2018–2025. Patients with secondary mediastinal involvement from other large B-cell lymphoma subtypes or with prior allogeneic transplantation were excluded. The primary endpoint was progression-free survival (PFS) from infusion. Secondary endpoints included overall survival (OS), relapse incidence (RI), and non-relapse mortality (NRM). OS and PFS were estimated using the Kaplan–Meier method; RI and NRM were assessed using competing-risk models.

Group comparisons were performed with log-rank tests. Subgroups of interest included CAR-T construct (axicabtagene ciloleucel [axi-cel], lisocabtagene maraleucel [liso-cel], tisagenlecleucel [tisa-cel]) and age (<30, 30–45, >45 years).

Results: A total of 284 patients met the inclusion criteria. Three commercial CAR T-cell products were infused: axi-cel (n=248), liso-cel (n=23), and tisa-cel (n=13). Median age was 35 years (range, 18–77), and 55% were female. The HCT comorbidity index was 0 in most patients (69%), 1–2 in 12%, and ≥3 in 20%. Ten percent had previously received autologous transplantation. At lymphodepletion, 6% were in CR, 27% in PR, and 67% had progressive disease.
With a median follow-up of 1.5 years, 2-year outcomes were OS 75.5%, PFS 58.4%, RI 36.3%, and NRM 5.3% (Figure 1). Two-year PFS was numerically higher with liso-cel (64.6%) than with axi-cel (56.9%) or tisa-cel (58.3%). However, baseline characteristics differed across products: liso-cel recipients were more frequently infused in CR/PR (67% vs. 29% with axi-cel and 38% with tisa-cel), which likely contributed to their lower early RI. No significant difference was observed in OS or NRM between constructs. Age had no significant impact on OS, PFS, RI, or NRM across the three predefined age groups.
The most influential prognostic variable was disease status at lymphodepletion. Patients with progressive disease at lymphodepletion had inferior PFS (HR 2.28, 95% CI 1.60–4.99, p<0.001) and higher RI (HR 2.77, 95% CI 1.53–5.01, p<0.001), while no significant effect was observed on OS or NRM. Other baseline characteristics—including time from diagnosis to CAR-T, sex, prior autologous transplantation, and year of infusion—showed no significant association with outcomes.



Conclusions: This is the largest real-world study to date evaluating CAR T-cell therapy in PMBCL. Survival outcomes were favorable across all age groups and across the three CAR-T constructs. Our findings support the broad use of anti-CD19 CAR T-cell therapy in R/R PMBCL and underscore the importance of disease control prior to infusion.

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OS02-08

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AFTER FAILING CAR-T THERAPY FOR PATIENTS WITH RELAPSED/REFRACTORY LARGE B CELL LYMPHOMA: SPANISH MULTICENTER GETH-TC/GELTAMO STUDY

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Background: Chimeric antigen receptor T-cell therapy (CAR-T) therapy has changed the treatment paradigm for patients with relapsed/refractory (R/R) large B cell lymphoma (LBCL) who relapse after ≥2 lines. Recently, it has been positioned in earlier lines and has currently been considered the second-line treatment choice in patients with primary refractory or early relapsed disease. For patients who relapse after CAR-T therapy, whether in ≥3rd or 2nd line, allogeneic hematopoietic stem cell transplantation (allo-HSCT) could be considered a potentially curative treatment in eligible patients. Unfortunately, data regarding efficacy, toxicity and potential role of new treatment strategies to be used to achieve chemosensitivity prior to allo-HSCT in this subpopulation of patients are scarce. Therefore, the aim of this study is to analyse the long term outcomes of patients with LBCL that fail CAR-T cell therapy and receive an allo-HSCT.

Methods: We performed a retrospective multicenter study including patients from centers of GETH-TC/GELTAMO with R/R LBCL after CAR-T therapy who underwent allo-HSCT. The primary endpoints were progression-free survival (PFS), overall survival (OS), NRM and the efficacy of different salvage treatments prior to allo-HSCT. Disease status was defined as complete remission (CR), partial response (PR) and refractory disease (stable disease or progression) assessed by PET/CT.

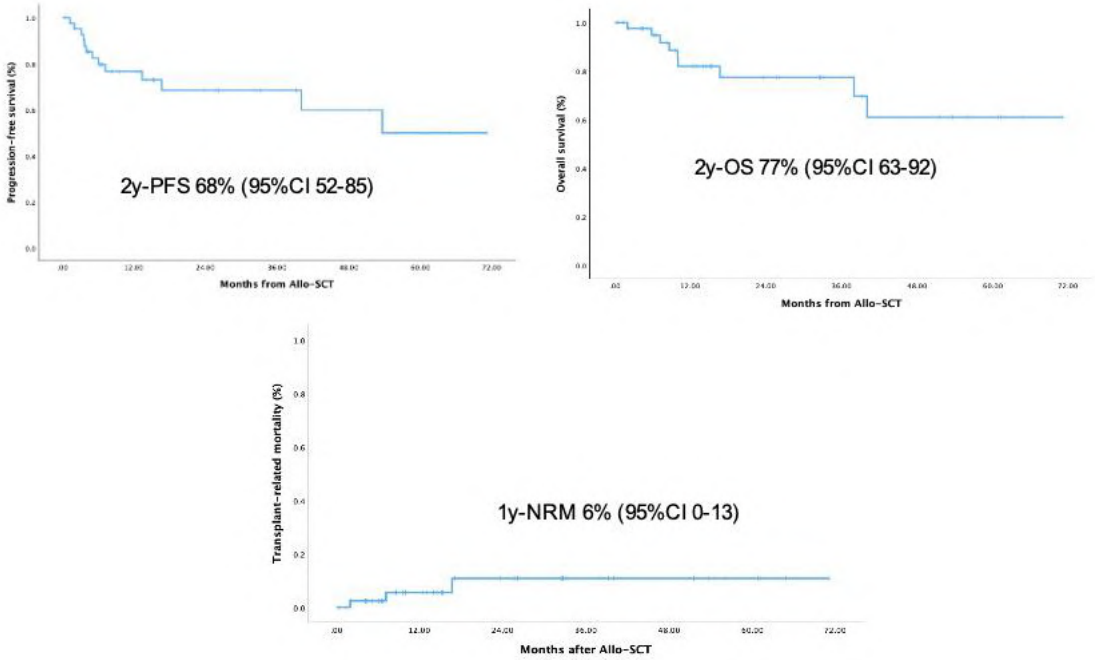
Results: Fourty-three patients [70% male, median age at allo-HSCT 50 years (20-70)] were included. 75% of the patients received axi-cel; 19/44 (44%) had achieved CR after CAR-T as best response. Median time from CAR-T infusion to relapse was 5 months (range 0-43). The median number of lines between CAR-T and allo-HSCT was 1 (range 1-4) and the median

time 13 months (range 4-53). Most of the patients received targeted therapies as a bridging to allo-HSCT such as bispecific antibodies (23%), polatuzumab (28%) and anti-PD1/PDL1 based regimens (21%). Baseline characteristics are summarized in Table 1. The CR rate with allo-HSCT at day +100 was 74%. After a median follow-up of 17 months (range 6-29), 34/44 (79%) of the patients are alive and 31/34 (91%) of them are free of disease. PFS at 2 years was 68% (95%CI 52-85) and 2y-OS 77% (95%CI 63-92). NRM at day 100 and 1 year was 2% (95%CI 0-7) and 6% (95%CI 0-13), respectively, Figure 1. The main causes of death were disease progression in 67% and infections in 33%. CI of grade III-IV acute GVHD was 16% and moderate/extensive chronic GVHD 14%. None of the variables showed an impact on survival and NRM, most probably due to the small sample size.

Table 1: Baseline characteristics	**N=43**
Sex (Male /Female)	30 (70%) / 13 (30%)
Lymphoma subtype	
DLBCL	24 (56%)
HGBCL	5 (12%)
PML	10 (23%)
tFL	4 (9%)
IPI at diagnosis	
0-2	22 (55%)
>2	18 (45%)
Missing	3 (7%)
ASCT	
Yes	9 (21%)
No	34 (79%)
Prior CAR-T therapy	
CAR-T line	
2L	7 (16%)
3L	29 (67%)
>3L	7 (16%)
CAR-T type	
Axi-cel	32 (75%)
Tisa-cel	6 (14%)
Clinical Trial	5 (12%)
Disease status pre-CAR-T	
Complete response	3 (7%)
Partial response	7 (17%)
Stable disease	6 (14%)
Progression	26 (62%)
Missing	1 (2%)

Best response to CAR-T	
Complete response	19 (44%)
Partial response	12 (28%)
Stable disease	4 (9%)
Progression	8 (19%)
Allo-HSCT	
Number of lines between CAR-T and allo-HSCT (median, R)	1 (1-4)
Salvage therapy pre-allo-HSCT	
Rituximab-Polatuzumab-Bendamustine	10 (28%)
Biespecific antibodies	10 (23%)
Anti-PD1/PDL1 ± Brentuximab	9 (21%)
CIT	6 (14%)
Tafasitamab-Lenalidomide	3 (7%)
Others	3 (7%)
HCT-CI	
0-2	20 (47%)
>2	22 (51%)
Missing	1 (2%)
Disease status pre-allo-HSCT	
Complete response	24 (56%)
Partial response	16 (37%)
Stable disease	1 (2%)
Progression	2 (5%)
Donor type	
Identical sibling	16 (38%)
Haploidentical	18 (43%)
Identical unrelated donor	8 (19%)
Mismatched unrelated donor	0 (0%)
Source	
PB	43 (100%)
BM	0 (0%)
Conditioning type	
MAC	4 (9%)
RIC	39 (91%)
TTBUFLU	17 (39%)
BUFLU	4 (9%)
BUMEL	5 (12%)
TREOFLU	8 (19%)
Other	9 (21%)

GVHD prophylaxis	
PTCy + Tacrolimus ± MMF	23 (53%)
PTCy + Sirolimus ± MMF	11 (26%)
ATG based	3 (7%)
Tacrolimus + Sirolimus	3 (7%)
Other	3 (7%)



Conclusions: Our data confirmed that allo-HSCT is a feasible and a potentially curative option for eligible patients with R/R LBCL failing after CAR-T therapy, with a high PFS and low NRM. Most of the patients received targeted therapies as a bridging to allo-HSCT such as bispecific antibodies, polatuzumab and anti-PD1/PDL1 based regimens. Further prospective studies are needed to confirm these results.

Disclosure: Nothing to declare.

OS13-04

CELLULAR THERAPIES IN PRIMARY CENTRAL NERVOUS SYSTEM LYMPHOMA: REAL-WORLD EBMT OUTCOMES WITH CAR-T CELLS AND ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT

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Background: Sufficient treatment of relapsed or refractory (r/r) primary central nervous system lymphoma (PCNSL), particularly after the failure of autologous hematopoietic cell transplantation, remains an unmet medical need. Although emerging evidence suggests that CAR T-cell therapy may offer a promising therapeutic approach with high response rates, published data indicate that responses are often not durable, with most patients ultimately relapsing. Although evidence supporting allogeneic hematopoietic cell transplantation (allo-HCT) for PCNSL is limited, data from the EBMT suggest a potential for durable disease control in selected patients.

Methods: Adult patients with PCNSL reported to the EBMT-registry who received either CD19-directed CAR-T cell therapy or allo-HCT transplantation between 01/2018 and 09/2023 were included.

Results: Of 70 patients, 23 underwent allo-HCT and 47 received CAR T-cell therapy (axi-cel in 66%, tisa-cel in 25.5%, and liso-cel in 8.5% of cases). Overall, 64% of patients were male, and 55% had a performance status < 90%, without significant differences between the two groups. Patients receiving CAR T-cell therapy were older (median 59 vs. 54 years, p = 0.04) and more frequently had refractory disease prior to cellular treatment (56% vs. 23%, p = 0.02). Most patients (57%) had previously undergone autologous HCT. Median time from diagnosis to treatment was 27 and 17 months for the allo-HSC and CAR-T cohorts, respectively (P=0.3). Myeloablative conditioning regimens were used in 55% of allo-HCT patients. Thiotepa was part of the conditioning regimen in 49% of cases, and total body irradiation in 26%.
With a median follow-up of 22.8 months (22.8 after CAR T-cell therapy and 19.2 after allo-HCT), the 18-month overall survival (OS) for the whole cohort was 39.4% (95% CI: 26.2–52.4), and 44.7% (27.2–60.8) for patients treated with CAR-T cell therapy versus 30.0% (12.4–49.8) for patients treated with allo-HCT. The 18-month progression-free survival (PFS) was 27.5% (15.6–40.8) for all patients, 27.1% (12.9–43.5) for CAR T-cell-treated patients and 28.9% (10.7–50.2) for allo-HCT–treated patients. Relapse incidence (RI) after 1.5 years was higher after CAR T-cell therapy, at 66.5% (46.3–80.5), compared with 37.4% (16.0–

58.9) after allo-HCT, while non-relapse mortality (NRM) was 6.5% (1.0–19.7) after CAR T-cell therapy and 33.7% (12.8–56.2) after allo-HCT.
A Cox model using propensity score overlap weighting, including age, disease status before the evaluated treatment, time from diagnosis, and year of procedure, did not demonstrate significant differences between the two groups in survival outcomes.

Conclusions: In this large real-world cohort of r/r PCNSL, both CAR T-cell therapy and allo-HCT achieved a clinically meaningful 18-month PFS of over 25%, with approximately one-third of patients alive at 18 months. Although allo-HCT was associated with lower numerical relapse rates, the high NRM offset this benefit, resulting in similar PFS compared with CAR T-cell therapy. These data underline that both CAR T-cell therapy and allo-HCT are viable treatment options for patients with an otherwise dismal prognosis. However, careful patient selection for allo-HCT is essential, and further studies are needed to develop less toxic conditioning regimens.

Disclosure: Igor Kos received travel support from Johnson and Johnson and Honoraria from AstraZeneca; Ron Ram received Honoraria from Novartis, Gilead, BMS.

OS18-05

THE IMPACT OF TIME IN PATIENTS WITH LARGE B CELL LYMPHOMA CANDIDATES FOR AXI-CEL THERAPY: SPANISH MULTICENTER GETH-TC/GELTAMO STUDY

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Background: Chimeric antigen receptor T-cell therapy (CAR-T) has changed the treatment of relapsed/refractory (R/R) large B cell lymphoma (LBCL). However, its availability is not immediate, as it requires several steps from identifying the candidate to receiving the product. Because of this waiting time, not all candidates for CAR-T therapy ultimately receive treatment, with disease progression being the main reason for non-administration. In recent years, infusion capacity has increased with the incorporation of additional CAR-T centers, reducing the need for interregional referral. Together with the learning curve, this likely has

shortened waiting times and allowed more patients to be treated, although these data are not yet available. Therefore, our objective was to analyze the waiting time from relapse to CAR-T infusion among eligible patients in Spain.

Methods: We performed a retrospective multicenter study based on GETH-TC database of CAR-T. We included patients from GETH-TC/GELTAMO centers with R/R LBCL who were eligible for axi-cel therapy [in 2nd and ≥3rd lines (L)]. Primary endpoints were to assess the time from approval to infusion in the overall cohort, in 3L+ divided in two time periods: before and after June 2022 (point at which more centers were allowed to infuse CAR-T cell products), and in the 2L cohort, as well as the proportion of candidates who ultimately received the product.

Results: 469 patients fulfilled the inclusion criteria. Baseline characteristics are summarized in **Table 1**. Apheresis was performed in 459 patients (98%) and 424 (92%) received the infusion. Among available data, cause of not reaching the apheresis was disease progression in all patients; and causes of not receiving axi-cel were disease progression (n=9), manufacturing failure (n=1), patient decision (n=1) and complete remission after bridging (n=4). Infusion delay was confirmed in 33% of infused patients; causes were infections (n=21), bed capacity (n=20), progression (n=8), second apheresis or reception delay (n=3) and bridge therapy-related issues (n=22). Median time from national approval to apheresis was 11 days (range 4-13), from apheresis to product reception 26 days (range 24-28) and from vein-to-vein 40 days (range 34-44). In the 3L+ cohort there was a significant reduction in the apheresis-reception time (27 vs 25 days, p<0.001) and in the apheresis-infusion time (43 vs 39 days, p=0.009) when comparing the first and second period. Times in the 2L subgroup were similar to those of the most recent period in the 3L+ cohort. No differences in waiting times were observed between patients referred from non-infusion centers and those treated at CAR-T cell infusion centers.

Table 1: Patients with R/R LBCL potential candidates for axi-cel

	N=469
Median age, years (range)	62 (19-83)
Sex (male/female)	264 (56%) / 205 (44%)
Lymphoma subtype DLBCL NOS tFL Double hit HGBCL NOS PML Other Missing	 311 (66%) 56 (12%) 32 (7%) 18 (4%) 28 (6%) 15 (3%) 9 (2%)

Primary refractory	
Yes	99 (21%)
No	175 (37%)
Missing	195 (42%)
Center	
Infusion	170 (36%)
Referral	292 (62%)
Missing	7 (2%)
Holding therapy	
No	297 (63%)
Yes	40 (9%)
Missing	132 (28%)
Apheresis	
Yes	459 (98%)
No	10 (2%)
Bridging therapy	
Yes	279 (61%)
No	86 (19%)
Missing	94 (20%)
Infusion	
Yes	424 (92%)
No	35 (8%)
CAR-T line	
3L+	328 (70%)
2L	141 (30%)
Infused patients (N=424)	
Disease status pre-CAR-T	
Complete response	25 (6%)
Partial response	66 (15.5%)
Stable disease	41 (9.5%)
Progression	195 (46%)
Missing	97 (23%)
CAR-T line	
3L+	290 (68%)
2L	134 (32%)
Infusion delay	
Yes	141 (33%)

No	147 (35%)
Missing	136 (32%)

Conclusions: In our cohort of patients 90% of initial candidates made it to CAR-T cell infusion. Disease progression remains the main reason for not reaching the apheresis and infusion. Although waiting times have improved slightly, there remains room for improvement, particularly through the identification of factors associated with delays. Further efforts in this direction may help to reduce the loss of potential candidates. Finally, we did not observe delays in patients coming from referral centers compared to those from CAR T centers.

Disclosure: Nothing to declare.

B394

PHASE 2 ELARA TRIAL FINAL ANALYSIS: CLINICAL OUTCOMES OF TISAGENLECLEUCEL IN PATIENTS WITH RELAPSED/REFRACTORY FOLLICULAR LYMPHOMA (R/R FL)

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Background: Tisagenlecleucel, an autologous anti-CD19 chimeric antigen receptor (CAR)-T cell therapy has been approved in the US and Europe for adults with r/r FL after ≥2 lines of prior therapy based on the phase 2 ELARA trial (EUCT number: 2023-508127-13-00) in 2022. Final analysis from the ELARA trial after a median follow-up (mFU) of >5 years is reported here.

Methods: Eligible patients with r/r FL (grade 1-3A) previously treated with ≥2 lines of systemic therapy (including an anti-CD20 monoclonal antibody and alkylating agent) received a single tisagenlecleucel infusion (0.6-6 × 10^8 CAR+ viable T cells). Bridging therapy was permitted. Here we report the long-term efficacy and safety analysis, including duration of response, progression-free survival, and overall survival in all patients and patients with high-risk disease characteristics. Cellular kinetics were determined by the measurement of transgene levels by quantitative polymerase chain reaction.

Results: As of May 28, 2025 (mFU: 61.0 months [range: 3.1–67.0 months]), all patients (N=97) were evaluated for safety and 94 patients for efficacy. At baseline, patients with high-risk disease characteristics included 60% with high Follicular Lymphoma International Prognostic Index score (FLIPI ≥3), 62% with progression of disease within 2 years of frontline systemic therapy, 64% with bulky disease (>7 cm or 3 lesions >3 cm), 68% with double refractory to prior CD20 antibody and alkylating agent, and 21% with high tumor burden (total metabolic tumor volume >510 mL). The overall response rate (86.2%) and complete response (68.1%) remained consistent with previous data in overall patients and high-risk disease characteristics subgroups (Dreyling M, *Blood* 2024). Efficacy outcomes at final follow-up are reported in **Table 1**. CAR transgene persistence (T_{last}; time to last quantifiable transgene level) was observed up to 60.9 months; the median T_{last} was 8.6 months (range: 0.6–60.9 months). Tisagenlecleucel demonstrates a favourable safety profile at final analysis with reports of blood and lymphatic system disorders in 11 patients

(13.1%), infection and infestations in 34 patients (40.5%), >1 year after infusion. Adverse events reported >4 years after tisagenlecleucel infusion will be presented at congress. Second primary malignancies (defined as any new cancer occurring post-infusion regardless of tisagenlecleucel relationship) were reported in 7 (7.2%) patients, including 2 events each of basal cell carcinoma, myelodysplastic syndrome, squamous cell carcinoma of skin (n=2), and 1 event each of acute myeloid leukemia, bladder transitional cell carcinoma, Bowen's disease, malignant melanoma, and metastatic squamous cell carcinoma (n=1). In total, 22 patients died during the study; causes of death include disease progression (n=8), AEs (n=13, predominantly infections), and euthanasia.

Table 1: Efficacy outcomes of tisagenlecleucel in patients with r/r FL

Efficacy	**N=94**
Median DOR, month	NR
4-year DOR, % (95% CI)	
In all responders	61% (48.8–71.1)
In patients achieving CR	71.2% (57.7–81.1)
Median PFS, month	53.2
5-year PFS, % (95% CI)	
In all patients	46% (35.0–56.3)
In patients achieving CR	59.8% (46.2–71.1)
5-year PFS in high-risk disease characteristics subgroups, %	
High FLIPI	35.5
POD24	41.1
Bulky disease	45.1
Double refractory	50.5
High tumor burden	NE
Median OS, month	NR
5-year OS, % (95% CI)	
In all patients	74.1% (63.0–82.3)
5-year OS in high-risk disease characteristics subgroups, %	
High FLIPI	64.4
POD24	74.6
Bulky disease	71.1
Double refractory	79.8
High tumor burden	65.5

CI, confidence interval; CR, complete response; DOR, duration of response; FLIPI, Follicular Lymphoma International Prognostic Index, NE, not estimable; NR, not reached; OS, overall

Table 1: Efficacy outcomes of tisagenlecleucel in patients with r/r FL
survival; PFS, progression-free survival; POD24, progression of disease within 2 years of frontline systemic therapy.

Conclusions: After a median follow-up of >5 years, tisagenlecleucel continues to demonstrate durable responses and prolonged survival in patients with r/r FL including patients with high-risk disease characteristics. No new safety signals were reported. More than 75% of patients were alive, and approximately half remained progression-free at this final analysis, indicating the curative potential of tisagenlecleucel in r/r FL after ≥2 lines of prior therapy.

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Clinical Trial Registry: 2023-508127-13-00 (https://euclinicaltrials.eu/?lang=en)

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B395

REAL-WORLD STUDY OF SECOND-LINE LISOCABTAGENE MARALEUCEL AND AXICABTAGENE CILOLEUCEL EFFECTIVENESS, SAFETY, AND HEALTH CARE RESOURCE UTILIZATION IN PATIENTS WITH RELAPSED OR REFRACTORY LARGE B-CELL LYMPHOMA

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Background: Lisocabtagene maraleucel (liso-cel) and axicabtagene ciloleucel (axi-cel) are chimeric antigen receptor (CAR) T cell therapies approved for second-line (2L) treatment of relapsed or refractory (R/R) large B-cell lymphoma (LBCL). While pivotal trials of each agent established superior efficacy versus standard of care, the absence of direct comparisons underscores the importance of real-world comparative data to support informed treatment selection, toxicity management, and site-of-care planning. This study investigated the real-world effectiveness, safety, and health care resource utilization (HCRU) of liso-cel and axi-cel in the 2L treatment setting.

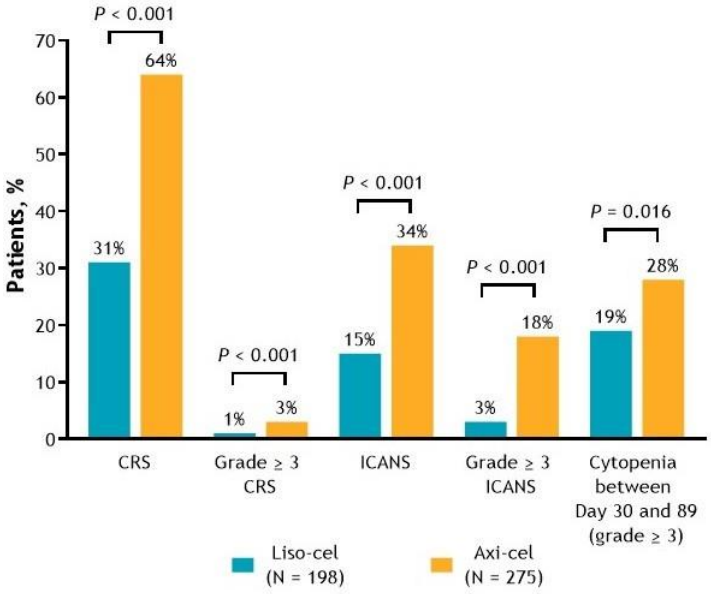
Methods: Patients with LBCL who received 2L liso-cel or axi-cel (April 2022–April 2025) were selected from the United States Flatiron Health Research Database, an oncology-specific platform combining electronic health records and other real-world data. Both overall survival (OS) and progression-free survival (PFS) were evaluated using the Kaplan-Meier method. Descriptive statistics were used to describe safety endpoints (cytokine release syndrome [CRS], immune effector cell–associated neurotoxicity syndrome [ICANS], cytopenia) and HCRU (tocilizumab/steroid use, hospitalization).

Results: The study included 473 patients with LBCL who received 2L CAR T cell therapy, of whom 198 received liso-cel versus 275 who received axi-cel (median [interquartile range (IQR)] age, 72 years [63–77] vs 63 years [54–70]; elevated lactate dehydrogenase, 39% vs 33%; high-grade B-cell lymphoma, 41% vs 40%; receipt of bridging therapy, 78% vs 71%; bulky disease, 68% vs 74%; relapsed within 1 year of first-line treatment, 72% vs 86%; and median [IQR] follow-up time, 8 months [4–14] vs 12 months [5–22]).
Early survival outcomes among patients in liso-cel versus axi-cel groups were similar at 6 months with no statistically significant differences observed (OS, 89% [95% confidence interval, 84%–94%] vs 89% [85%–93%]; PFS, 69% [63%–77%] vs 71% [66%–77%]). CRS and ICANS of any grade were less frequent with liso-cel than axi-cel (CRS, 31% vs 64%; ICANS, 15% vs 34%), as were grade ≥ 3 CRS/ICANS (CRS, 1% vs 3%; ICANS, 3% vs 18%; **Figure**). Grade ≥ 3 cytopenia between Day 30 and Day 89 after CAR T cell therapy infusion was less common with liso-cel than axi-cel (19% vs 28%). Patients in the liso-cel group were less likely to receive treatment for CRS/ICANS versus the axi-cel group (**Table**). Infusion in an outpatient setting was more common with liso-cel than axi-cel (21% vs 6%) and was associated with a lower rate of hospitalization after infusion (47% vs 62%; **Table**). For patients infused at an inpatient setting, liso-cel was associated with shorter length of

stay (8 days vs 12 days) and lower rates of rehospitalization (33% vs 40%) compared with axi-cel.

Conclusions: In this retrospective real-world analysis, liso-cel demonstrated similar effectiveness and a more favorable safety and HCRU profile versus axi-cel as a 2L therapy for R/R LBCL. Despite limited follow-up, these real-world findings suggest liso-cel could deliver safety advantages without compromising efficacy in a broad population of patients with 2L LBCL.

Figure. RW adverse events after infusion



P values are as per Fisher's exact text.
Axi-cel, axicabtagene ciloleucel; CRS, cytokine release syndrome; ICANS, immune effector cell–associated neurotoxicity syndrome; liso-cel, lisocabtagene maraleucel.

Table. Management of real-world adverse events and CAR T cell infusion hospitalization and postinfusion hospitalizations

Adverse event management, n (%)	Liso-cel (N = 198)	Axi-cel (N = 275)	*P* value[a]
Evidence of CRS in 2L Received therapy for	61 (31) 38 (19) 36 (18)	177 (64) 145 (53) 136 (49)	< 0.001 0.002 > 0.9

Table. Management of real-world adverse events and CAR T cell infusion hospitalization and postinfusion hospitalizations

CRS Received tocilizumab for CRS			
Evidence of ICANS in 2L Received therapy for ICANS Received dexamethasone for ICANS Received siltuximab, anakinra, and/or other methylprednisolone administration for ICANS	30 (15) 15 (8) 12(6) 4 (2)	94 (34) 67 (24) 42 (15) 27 (10)	< 0.001 0.032 0.2 0.3
HCRU-related metric	**Liso-cel (N = 146)**	**Axi-cel (N = 205)**	
Infused in inpatient setting, n (%) Median duration of infusion hospitalization, days Rehospitalized, n (% of IP infusions) ICU admission at rehospitalization, n (% of IP infusions) Median duration of first rehospitalization, days	116 (79) 8 38 (33) 3 (3) 3	192 (94) 12 77 (40) 7 (4) 4	
Infused in outpatient setting, n (%) Hospitalized after	30 (21) 14 (47)	13 (6) 8 (62)	

Table. Management of real-world adverse events and CAR T cell infusion hospitalization and postinfusion hospitalizations

infusion, n (% of OP infusions)			

Top: Therapies cannot be attributed to CRS versus ICANS; attribution is inferred. [a]Fisher's exact text.
Bottom: Among 351 patients with ≥ 3 months of electronic health record activity after infusion and known infusion setting.
Axi-cel, axicabtagene ciloleucel; CAR, chimeric antigen receptor; CRS, cytokine release syndrome; HCRU, health care resource utilization; ICANS, immune effector cell–associated neurotoxicity syndrome; ICU, intensive care unit; IP, inpatient; liso-cel, lisocabtagene maraleucel; OP, outpatient.

Clinical Trial Registry: Not applicable.

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ALLOGENEIC TRANSPLANTATION AFTER FAILURE OF CAR-T CELLS AND EXPOSURE TO BISPECIFIC ANTIBODIES: FEASIBILITY, SAFETY AND SURVIVAL OUTCOMES

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Background: Clinical outcome after Chimeric Antigen Receptor (CAR)T-cell failure in large B-cell lymphoma (LBCL) is dismal. Allogeneic stem cell transplantation (alloSCT) represents a potential curative salvage for relapsed/refractory LBCL, although concerns remain about feasibility and safety in patients exposed to CAR-T and bispecific antibodies (BsAb).

Methods: We retrospectively analysed outcomes of 19 LBCL patients who underwent alloSCT consolidation after failure of CAR-T cells and exposure to BsAb in 3 academic centres, with the aim to describe safety, feasibility and survival outcomes in a heavily pre-treated population.

Results: Median age at alloSCT was 52 years (range 23-68). Prior CAR-T product were axicabtagene ciloleucel (n=8) or tisagenlecleucel (n=11); BsAb was glofitamab (n=18) or epcoritamab (n=1). Patients had received a median of 4 (range 3-9) prior lines of therapy, including autologous SCT in 5 (26%). Median number of BsAb cycles was 8 (range 2-12). Disease status at alloSCT was complete response (n=17) obtained with either BsAb (n=13) or subsequent treatments (n=4), or partial response (n=2) obtained with subsequent treatments. All patients received reduced intensity conditioning, while Graft-versus-Host-Disease (GvHD) prophylaxis was PTCy-based in 10 (52%). Other baseline characteristics are summarized in **Table 1**. Cumulative incidence of 30-days neutrophil engraftment was 100% (median time 17 days, range 10-25), while 30-days cumulative incidence of platelet engraftment was 94% (median time 20 days, range 10-45). The 100-days cumulative incidence of grade II-IV acute GvHD was 26% (95% confidence interval [CI] 9-51); 1-year cumulative incidence of chronic GvHD was 22% (95%CI 6-46). Full donor chimerism was documented at +30 and +90 in all evaluable patients. Median absolute lymphocyte counts at 3, 6 and 12 months after alloSCT were 515, 710 and 1365 cells/μL, respectively. The median number of infectious events per patient was 2 (range 0-5). One fatal fungal infection was observed; all other viral (n=6 patients) and bacterial (n=15 patients) infections resolved with appropriate antimicrobial therapy. Viral reactivations occurred in 9 (47%) patients before and in 5 (26%) patients after day +180, with resolution of all 4 cases of end-organ disease (colitis). Uncommon toxicities included one steroid-responsive hemolytic anemia, one anti-GM2-ganglioside IgM-positive acute demyelinating polyneuropathy diagnosed 10 months after alloSCT, successfully managed with intravenous immunoglobulins with complete recovery, and one case of iatrogenic encephalopathy on a likely microangiopathic basis,

possibly related to cyclosporine. With a median follow-up of 23 months (IQR 12-46), 1-year overall and progression-free survival were 94% (95%CI 68-99) and 89% (95%CI 62-98), respectively. Only one LBCL relapse 5 months after alloSCT and one case of transplant-related mortality occurred. One-year GvHD- and relapse-free survival (GRFS) was 71% (95%CI 43-87).

Table 1.

	Patients n=19
Age at alloSCT, median (range)	52 (23-68)
Median time from last treatment, days (range)	48 (20-98)
Median time from last BsAb, days (range)	71 (22-369)
ECOG 0, n (%)	15 (79%)
HCT-CI score, median (r)	2 (0-4)
0-2, n pts	12 (63%)
≥ 3, n pts	7 (37%)
Donor type, n (%)	
Matched related donor	3 (16%)
Matched unrelated donor	9 (47%)
Haploidentical donor	7 (37%)
Conditioning regimen type, n (%)	
FluCyTBI2Gy	6 (32%)
ThioFluCy	9 (47%)
ThioBuFlu	4 (21%)
GvHD prophylaxis, n (%)	
PTCy-based	10 (52%)
ATG-based	6 (32%)
CSA+MTX +/- MMF	3 (16%)

Conclusions: AlloSCT consolidation after CAR-T cells and BsAb exposure is feasible in selected, fit and responding patients, providing durable disease control with acceptable toxicity. Despite heavy pre-treatment, no unexpected safety signals emerged, with relatively low GvHD rates across donor type, and limited transplant-related mortality. In conclusion,

alloSCT consolidation should be offered to all eligible patients failing both T-cell redirecting strategies, and carefully evaluated also in patients achieving complete remission with BsAb after CAR-T cells failure.

Disclosure: Nothing to declare

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ALLOGENEIC TRANSPLANTATION OUTCOMES IN PATIENTS WITH HIGH-GRADE LYMPHOMA AFTER RELAPSE FOLLOWING CAR-T THERAPY: A MULTICENTER RETROSPECTIVE COMPARATIVE STUDY

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Background: Relapsed or refractory (R/R) high-grade lymphomas remain a major clinical challenge. Although chimeric antigen receptor T-cell (CAR-T) therapy has improved response rates, relapses still occur and often require allogeneic hematopoietic stem cell transplantation (allo-HCT). The impact of prior CAR-T exposure on allo-HCT outcomes remains unclear.

Methods: **Objectives:** To compare progression-free survival (PFS) and overall survival (OS) between patients with high-grade lymphoma undergoing upfront allo-HCT and those treated with CAR-T therapy followed by allo-HCT.
Methods: We conducted a multicenter retrospective comparative study across five centers in Andalusia, Spain. Patients with diffuse large B-cell lymphoma (DLBCL) or primary mediastinal B-cell lymphoma (PMBCL) undergoing allo-HCT between 2015 and 2025 were included. Sixty-two patients were analyzed: CART-NO (upfront allo-HCT, n=46) and CART-YES (CAR-T followed by allo-HCT, n=16).
Demographic, clinical, disease-related, transplant-related, and post-transplant response variables were collected. OS and PFS were estimated using Kaplan–Meier methods.

Results:

Table 1. Baseline and transplant characteristics and outcomes according to prior CAR-T exposure

Variable	CAR-T No (n=46)	CAR-T Si (n=16)	p value
Baseline characteristics			
Age, years	45.3 (12.6)	48.8 (11.0)	0,26
Male sex	29 (63.0%)	12 (75.0%)	0,542
ECOG 0	28 (62.2%)	5 (41.7%)	0,408
ECOG 1	10 (22.2%)	5 (41.7%)	
ECOG ≥2	7 (15.5%)	2 (16.7%)	
Diagnosis: DLBCL	36 (78.3%)	12 (75.0%)	0,743
Diagnosis: PMBCL	10 (21.7%)	4 (25.0%)	
Stage IV at diagnosis	31 (67.4%)	12 (75.0%)	0,71
≥4 prior lines of therapy	12 (26.1%)	6 (37.5%)	0,523
Prior autologous SCT	32 (69.6%)	5 (31.2%)	**0,014**
Overall response before allo-HCT (CR/PR)	41 (89.1%)	7 (43.8%)	**0,001**
Transplant characteristics			
Age at transplant, years	46.0 (12.6)	50.0 (11.1)	0,25
HLA-identical donor	34 (73.9%)	8 (50.0%)	0,12
Outcomes			
Overall survival, months	51.5 (48.8)	25.0 (23.7)	0,215
Post-allo-HCT response: CR	27 (84.4%)	9 (64.3%)	0,202
Post-allo-HCT response: PR	1 (3.1%)	0 (0%)	
Post-allo-HCT response: PD	4 (12.5%)	5 (35.7%)	
Vital status: alive	24 (52.2%)	8 (50.0%)	1
Vital status: dead	22 (47.8%)	8 (50.0%)	

Footnote: Data are presented as mean (standard deviation) or number (percentage). Comparisons between groups were performed using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables. Statistically significant p values (<0.05) are shown in bold.

Figure 1: Alluvial plots showing disease status before and after allogeneic hematopoietic stem cell transplantation (allo-HCT).

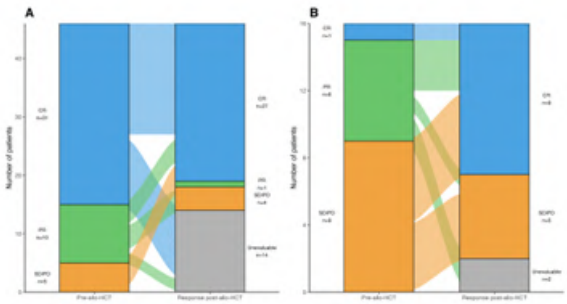


Figure 2: Kaplan-Meier curve, Overrall survival

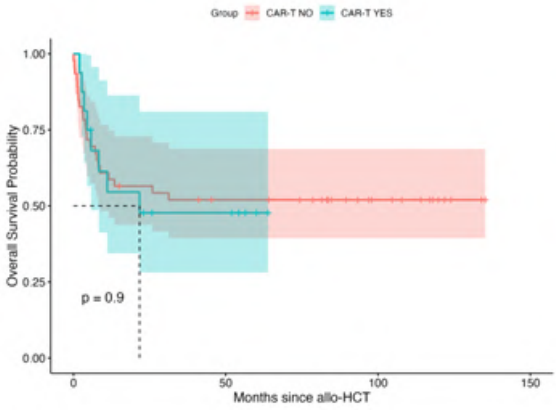
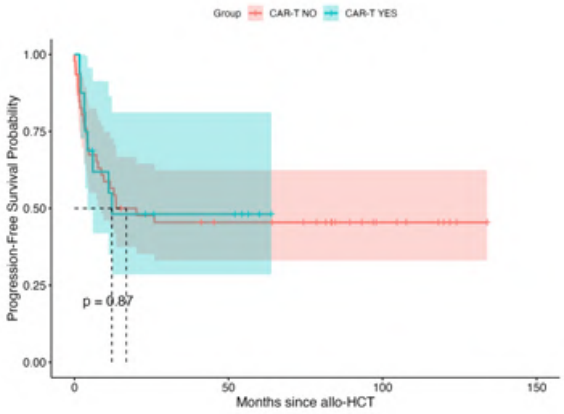


Figure 3: Kaplan-Meier curve, Progression-free survival



Baseline demographic and clinical characteristics were comparable between groups. Mean age was similar (CART-YES 45.3 vs CART-NO 48.8 years; p=0.26), with no significant differences in sex, ECOG performance status, diagnosis, disease stage, or number of prior treatment lines (Table 1).CART-YES patients less frequently had prior autologous transplantation (31.2% vs 69.6%; p=0.014) and showed a significantly lower overall response rate (CR/PR) before allo-HCT (43.8% vs 89.1%; p=0.001), reflecting a more refractory disease profile. Transplant-related characteristics, including age at transplant and HLA-matched donor availability, were similar between cohorts (Table 1).
Regarding response to allo-HCT, most CART-NO patients were in complete response (CR) before transplant (31/46), with fewer in partial response (PR, 10/46) or stable/progressive

disease (SD/PD, 5/46). Post-transplant, CR was largely maintained (27 patients), although 14 patients were unevaluable due to early death, and only a minority showed PR (n=1) or SD/PD (n=4). In contrast, CART-YES patients presented with more refractory disease before allo-HCT, with fewer patients in CR (1/16) and a higher proportion in PR (6/16) or SD/PD (9/16). After allo-HCT, a marked improvement in disease status was observed, with 9 patients achieving CR, while 5 remained with active disease and 2 were unevaluable (Figure 1).
With a median follow-up of 36.5 months, overall mortality was 47.8% in CART-NO and 50% in CART-YES (median follow-up 16.4 months), without significant differences. Kaplan–Meier analyses showed similar OS and PFS, with early post-transplant events and parallel curves. Median OS was not reached in CART-NO and was approximately 21 months in CART-YES (log-rank p=0.82). PFS was also comparable between groups (log-rank p=0.87) (Figures 2–3).

Conclusions: Our data suggest that prior CAR-T therapy does not negatively impact survival after allogeneic transplantation. Although CART-YES patients showed slightly higher overall mortality and marginally lower OS, and a trend toward improved PFS, these differences were not statistically significant. Notably, despite lower response rates before allo-HCT, CART-YES patients showed a higher degree of response consolidation after transplantation. The main limitation of this study is the small sample size, which may limit statistical power and generalizability. Larger studies are needed to confirm these findings and clarify the impact of prior CAR-T therapy on allo-HCT outcomes.

Disclosure: Nothing to declare

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AUTOLOGOUS STEM CELL TRANSPLANTATION WITH REDUCED-DOSE THIOTEPA CONDITIONING IN PRIMARY CNS LYMPHOMA: SAFETY AND OUTCOMES IN A REAL-WORLD COHORT

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Background: High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) is a standard consolidation strategy for fit patients with primary central nervous system lymphoma (PCNSL) achieving response after first-line induction with MATRix regimen. Standard conditioning commonly includes thiotepa combined with BCNU; however, therapy-related toxicity remains a concern, particularly in older patients or those with multiple comorbidities. We explored whether a reduced-dose thiotepa conditioning regimen could maintain efficacy while improving tolerability.

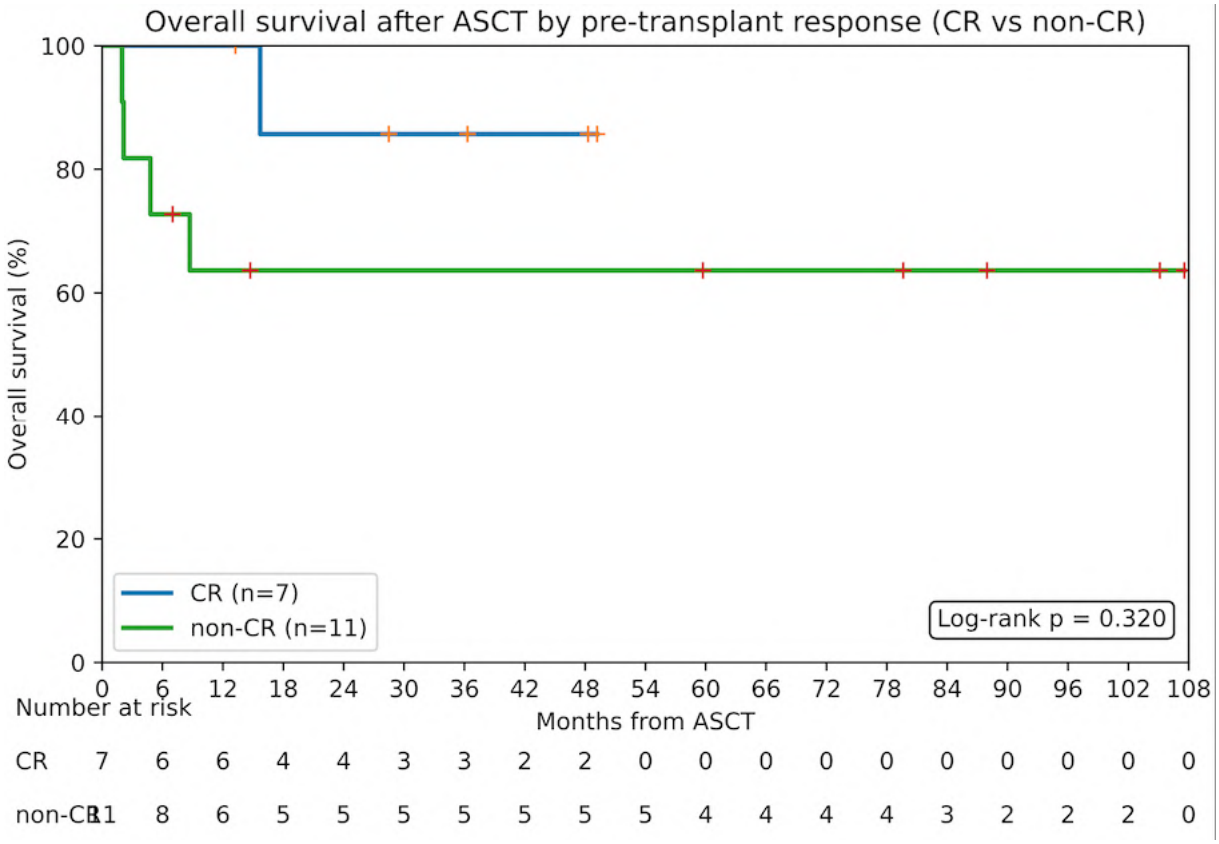
Methods: We retrospectively analyzed all consecutive adult patients with newly diagnosed PCNSL treated at ASST Niguarda in Milan between January 2014 and November 2025 who were eligible for ASCT. All patients received four cycles of MATRix induction chemotherapy.

Patients achieving at least a partial response proceeded to ASCT using a modified conditioning regimen consisting of thiotepa 5 mg/kg/day for two consecutive days (total dose 10 mg/kg) combined with standard-dose BCNU (400 mg/mq). Patients who did not proceed to ASCT were excluded from the analysis. Primary endpoints were overall survival (OS), progression-free survival (PFS), and non-relapse mortality (NRM), calculated from the date of ASCT. Toxicity and transplant-related complications were assessed descriptively.

Results: Eighteen patients underwent ASCT and were included in the analysis. Median follow-up was 59.7 months and median age at transplantation was 58 years (range 36-72). Complete characteristics of the population are listed in Table 1.

Variable	**Patients (n=18)**
Male, n (%)	5 (28%)
Median Age at Transplantation, years (range)	58 (36-72)
ECOG ≥ 2, n (%)	11 (61%)
IELSG ≥ 2, n (%)	8 (44%)
Complete Response Before ASCT, n (%)	7 (39%)
Infused CD34+ cells, mediana (range)	8.8 ×10⁶/kg (2.6-27.22)

Estimated OS at 1 and 2 years was 77.8% and 72.2%, respectively, while PFS at 1 and 2 years was 72.2% and 66.7%. Patients achieving complete remission prior to ASCT showed more favorable outcomes, with a 2-year OS of 85.7% and a 2-year PFS of 71.4%, compared with 63.6% and 63.6%, respectively. Exploratory subgroup analyses suggested that age, IELSG score, and disease status at transplant influenced outcomes.
The most common toxicity was febrile neutropenia which occurred in 62% of patients. Other non-hematologic toxicities were infrequent, with no grade ≥3 organ toxicity or mucositis observed. No cases of non-relapse mortality were observed at day +100 or at 1 year.



Conclusions: In this real-world cohort of PCNSL patients undergoing ASCT in first remission, a conditioning regimen incorporating reduced-dose thiotepa demonstrated a favorable safety profile with preserved disease control. Despite the absence of a comparative control group, survival outcomes appear comparable to those reported in the literature, while severe transplant-related toxicities were limited. This approach may represent a viable strategy to reduce treatment-related toxicity, particularly in patients achieving complete remission or in older and more comorbid populations. Prospective, controlled studies are warranted to confirm these findings and to better define the role of thiotepa dose reduction in ASCT conditioning for PCNSL.

Disclosure: Nothing to declare.

B400

POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS (PTLD): RESULTS OF THE MULTICENTER OBSERVATIONAL RETROSPECTIVE COHORT STUDY OF THE ITALIAN LYMPHOMA FOUNDATION (FIL_PTLD)

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Background: Post-transplant lymphoproliferative disorders (PTLDs) are rare lymphomas that arise as complications of solid organ transplantation (SOT) and hematopoietic stem cell transplantation (HSCT). The Fondazione Italiana Linfomi (FIL) conducted the multicenter, observational, retrospective FIL_PTLD cohort study to assess PTLD management across Italian haematology centers. Primary objectives include the characterization of clinical features and survival outcomes, as well as the identification of prognostic factors affecting disease progression and mortality.

Methods: Adult patients diagnosed with PTLD between January 2011 and December 2021 were retrospectively included. The sample consisted of 241 patients that have been enrolled across 21 Italian centers. Overall Survival (OS) and Progression-Free Survival (PFS) were estimated using Kaplan-Meier method, and compared across groups with Cox model. In particular, the sample was stratified based on type of transplant (SOT vs HSCT) and

correlation with EBV infection; a statistical subanalysis was performed on the subcohort of patients diagnosed with diffuse large B-cell lymphoma (DLBCL).

Results: Most cases followed SOT (92.5%), including thoracic organ (24.1%) and abdominal organ (68.5%) transplants; only 7.5% occurred after HSCT. The median time from transplantation to PTLD diagnosis was 7.8 years (range 2.2-14.8), with shorter latency ($p<0.001$) observed in EBV-positive cases (3.6 years). Early-onset PTLD (within 2 years post-transplant) occurred in 25.4% of patients. EBV-encoded RNA (EBER) status was available for 201 patients: 91 (45,3%) were EBV-positive, with early-onset in 38 (41.8%). The predominant histological subtype was monomorphic PTLD (88.8%), with DLBCL in 66.4% and Burkitt lymphoma in 7.5%. Extranodal localization was observed in 73.9% of cases, central nervous system involvement in 5%. About half of patients had elevated serum LDH (50.2%) and advanced Ann Arbor stage (57.3%). Immunosuppression reduction (RIS) was reported in 162 cases (67.2%). Treatment consisted of RIS alone (7.9%), rituximab monotherapy (41.3%) or associated to chemotherapy (32.5%), or other (18.3%). Overall response rate (ORR) was 71.4%, with 56.3% achieving complete response; 19.3% developed progressive disease. With a median follow-up of 77 months, 5-year and 10-year OS rates were 55% (95% CI, 48–61) and 46% (95% CI, 38–53), respectively; 5-year and 10-year PFS rates were 47% (95% CI, 40–53) and 40% (95% CI, 32–47), respectively. Multivariable analysis with Cox model identified age (HR per 1-y 1.03; $p=.001$), advanced stage (HR 2.4; $p=.001$), and ECOG performance status ≥2 (HR 2.84; $p<.001$) as independent predictors of inferior OS. The same prognostic factors were identified as having a significant impact on PFS. However, EBER positivity (HR 1.26; $p=.335$), elevated LDH (HR 1.29; $p=.247$), extranodal localization (HR 1.49; $p=.163$) and short latency from transplant ≤ 24 months (HR 1.41; $p=.182$) were not significantly associated with survival.

Conclusions: The FIL_PTLD study is the first Italian retrospective observational study evaluating outcome and management of PTLD. The study confirms that PTLD in adults predominantly arises after SOT and frequently presents in the late-onset form. Treatment approaches were heterogeneous across centers. Advanced age, poor performance status, and advanced stage at diagnosis were associated with worse overall and progression-free survival.

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PREDOMINANCE OF CD4+ T-CELLS IS ASSOCIATED WITH IMPROVED OUTCOMES IN PATIENTS WITH DIFFUSE LARGE B-CELL LYMPHOMA TREATED WITH AXICABTAGENE CILOLEUCEL

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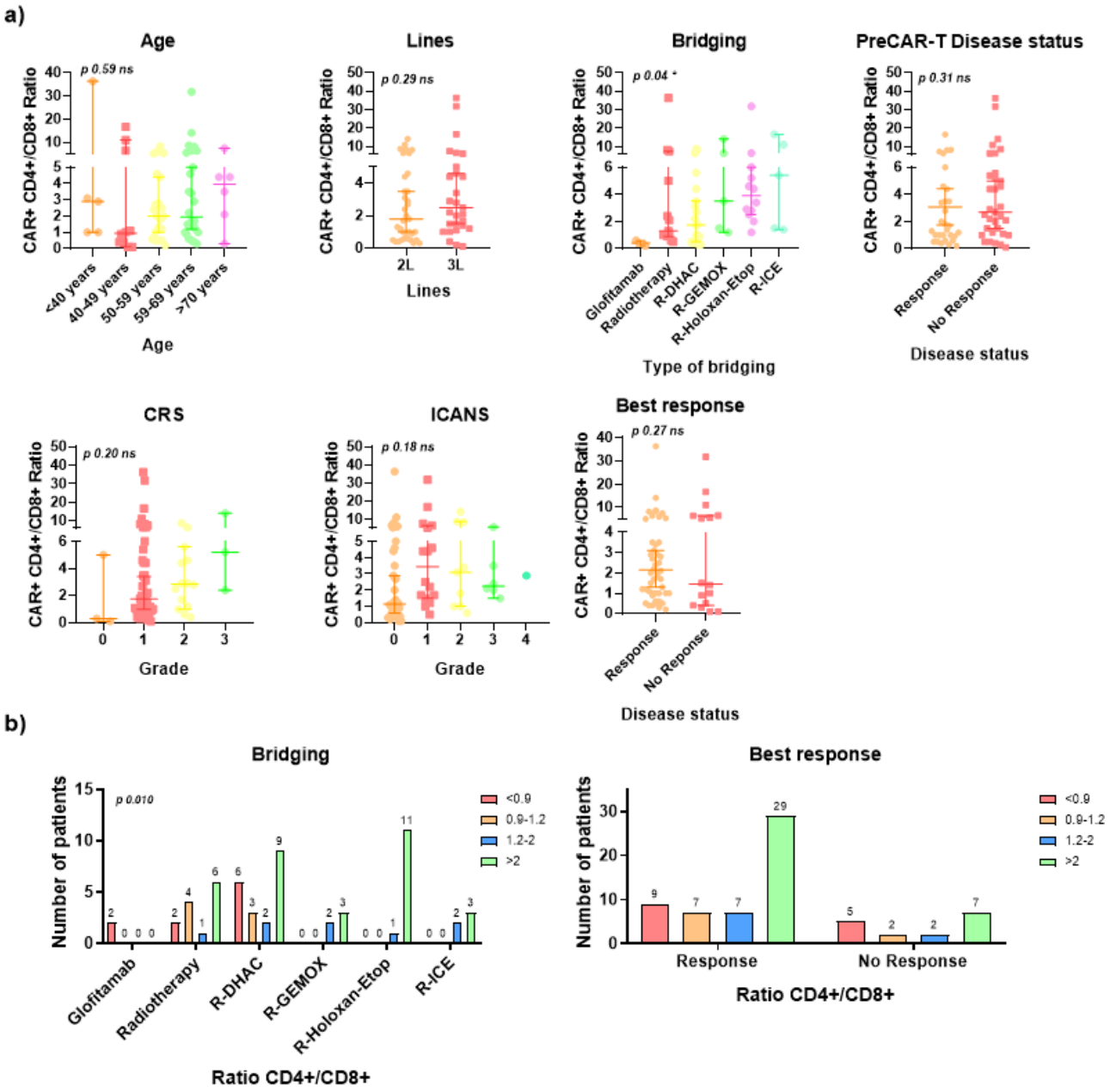
Background: Emerging evidence suggests that both CAR-T kinetics and subsets may influence treatment response and toxicity. Understanding these parameters could help to optimize patient outcomes in diffuse large B-cell lymphoma (DLBCL) treated with CAR-T therapies. This study evaluates the association between baseline CD4+/CD8+ ratios and both toxicity and response outcomes.

Methods: Retrospective observational study conducted between January 2021 and May 2025 at Bordeaux University hospital. CAR-T cell monitoring and CD4+/CD8+ ratio analysis were performed by multiparametric flow cytometry by indirect staining. Only patients with DLBCL treated with axi-cel were included. Lymphocyte CAR+ ratio CD4+/CD8+ from the infusion bag (day 0) were analyzed according to age, treatment line, bridging therapy, CRS and ICANS development and best response. Only patients with disponible data or detectable CAR-T were included 68/74 (91.8%).

Results: A total of 68 patients were included (female:male 19:49) with a median age of 58 years (range 28–73). CAR-T was administered in 2nd and 3rd line in 36 (52.9%) and 30 (44.1%) patients. Pre-CAR-T disease status (n=63) showed 31 responders (R, 49.2%) and 32 non-responders (NR, 50.8%). Among patients who received bridging therapy (n=64), the most frequently used regimen was R-DHAC (19, 29.7%), followed by radiotherapy (13, 20.3%), R-Holoxan-etoposide (12, 18.8%), R-GEMOX (5, 7.8%), R-ICE (6, 9.4%) and glofitamab (2, 3.1%). For CRS (n=68), grade 0 in 3 (4.4%), grade 1 in 48 (70.6%), grade 2 in 9 (13.2%), grade 3 in 7 (10.3%), and grade 4 in 1 (1.5%). For ICANS (n=68), grade 0 in 36 (52.9%), grade 1 in 16 (23.5%), grade 2 in 9 (13.2%), grade 3 in 6 (8.8%), and grade 4 in 1 (1.5%). Regarding treatment response (n=68), R 51 (75%), while NR 17 (25%).
The median CD4+/CD8+ ratio of 2.1 (IQR 1.0–4.9; range 0.1–36.3). The CD4+/CD8+ CAR+ ratio showed no differences across age groups (*p 0.59*, *ns*). 2nd line patients exhibited ratios closer to 1 compared with 3rd line (1.8 vs 2.5) (*p 0.29, ns*). Across bridging regimens, higher ratios were observed in patients who received immunochemotherapy. Ratios were: glofitamab 0.4, radiotherapy 1.3, R-DHAC 1.75, R-GEMOX 3.5, R-Holoxan-Etoposide 3.9, and R-ICE 5.4 (*p 0.04,* *). Pre-CAR-T disease status showed ratios of 1.6 for R and 2.7 for NR (*p 0.31, ns*). Regarding outcomes, ratios increased with CRS severity (1.0 for grade 0, 2.0 for grade 1, 2.92 for grade 2) (*p 0.20, ns*). Patients with ICANS had higher ratios (2.7 vs 1.15), with medians of 3.45, 3.1, 2.25 and 2.9 for grades 1–4 (*p 0.18, ns*). For best response, ratios were 2.2 for R and 1.5 for NR (*p 0.27, ns*). Overall, 29/51 responders (56.9%) had ratios >2, while 6/17 NR patients (35.3%) had ratios <0.9.



Conclusions: Higher CD4+/CD8+ ratios with predominance of CD4+ T-lymphocytes were associated with better response outcomes and increased severity of CRS and incidence of ICANS. Older age and specific bridging regimens influenced lymphocyte CD4+ and CD8+ distributions. These findings support the potential prognostic relevance of CD4+/CD8+ ratios and lymphocytes subsets in patients undergoing CAR-T therapy.

Disclosure: No disclosures.

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EFFICACY AND SAFETY OF ENSARTINIB-BASED REGIMENS IN ALK-POSITIVE LYMPHOMA: A REAL-WORLD RETROSPECTIVE STUDY

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Background: Anaplastic lymphoma kinase-positive (ALK+) lymphomas are aggressive malignancies driven by ALK rearrangements. Although conventional chemotherapy is effective for most patients (patients), approximately 30% experience a relapsed or refractory (R/R) disease, with a poor prognosis. Ensartinib has demonstrated efficacy in ALK+ non-small cell lung cancer, but its role in ALK+ lymphoma is unclear. This real-world study aimed to evaluate the efficacy and safety of ensartinib-based regimens in ALK+ lymphoma.

Methods: Between December 1, 2021, and February 20, 2025, patients with R/R ALK+ lymphoma who received ensartinib were included in this multicenter retrospective study. The outcomes included overall response rate (ORR), disease control rate (DCR), progression-free survival (PFS), overall survival (OS), and safety.

Results: A total of 9 patients (6 females; 5 adults; median age 31 years [range: 5-63]) were included, of whom 8 had anaplastic large cell lymphoma and 1 had diffuse large B-cell lymphoma. All patients had an ECOG performance status of 0, with B symptoms and elevated LDH (>ULN). Prior treatments included chemotherapy alone (55.6%), chemotherapy plus transplantation (33.3%), or chemotherapy with radiotherapy (11.1%). Among all patients, 22.2% received ensartinib alone, 22.2% received ensartinib plus R-CHOP regimen, and 55.6% received ensartinib plus other chemotherapy regimens. As of the data cutoff date (March 20, 2025), the median duration of ensartinib-based regimens treatment was 28.1 (range: 0.5-76.5) months. The ORR and DCR were both 100% for all patients (7 [77.8%] complete response; 2 [22.2%] partial response). After a median follow-up of 9.3 (range: 0.9-37.5) months, the PFS and OS were immature. No progression/death occurred as of March 20, 2025. Adverse events (AEs) of any grade occurred in 4 of 9 patients (44.4%), including rash (22.2%), elevated liver enzymes (11.1%), and edema (11.1%). No patients experienced grade ≥3 AEs or severe AEs. No dose adjustments or deaths due to AEs occurred.

Conclusions: Ensartinib-based regimens demonstrated promising preliminary efficacy and manageable toxicity in patients with R/R ALK+ lymphoma, warranting further prospective validation.

Disclosure: Nothing to declare

B403

LONG-TERM FOLLOW-UP OF CD19 CAR-T FOR R/R B-NHL: KI-67 AS A PROGNOSTIC FACTOR FOR SUSTAINED REMISSION

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Background: Patients with relapsed/refractory B-cell non-Hodgkin lymphoma (R/R B-NHL) typically experience dismal outcomes. Although CD19 chimeric antigen receptor-T (CAR-T) cell therapy has shown considerable efficacy, the factors influencing its long-term efficacy remain unclear.

Methods: We retrospectively analyzed 79 R/R B-NHL patients treated with CD19 CAR-T cell therapy at our center to evaluate efficacy, long-term survival, and prognostic factors.

Results: Among all evaluable patients, the overall response rate was 89.7%, with a 3-year duration of response (DOR) of 44.9% (95% CI, 34.2%-59.0%), a 3-year progression-free survival (PFS) of 40.2% (95% CI, 30.3%-53.4%), and a 3-year overall survival (OS) of 48.3% (95% CI, 38.0%-61.3%). Long-term adverse events (AEs) included hypogammaglobulinemia, which occurred in 73 of 74 evaluable patients (92.4%), viral reactivation (5.1%), and secondary malignancy (5.1%). Notably, high tumor Ki-67 (> 60%) was associated with lower peak CAR-T cell expansion ($P < 0.01$), reduced area under the curve of expansion from day 0 to 28 ($P < 0.0001$), and inferior complete response rate, DOR, and PFS (all $P < 0.05$). However, CAR-T cell persistence was not significantly associated with long-term remission or survival (all $P > 0.05$).

Conclusions: CD19 CAR-T cell therapy yielded sustained remissions in patients with R/R B-NHL, with manageable long-term AEs. High tumor Ki-67 expression serves as a poor prognostic factor and is linked to limited CAR-T cell expansion, whereas CAR-T cell persistence does not influence long-term prognosis.

Disclosure: Nothing to declare

P285

CLINICAL OUTCOMES AND PREDICTORS OF INTENSIVE CARE ADMISSION IN LYMPHOMA PATIENTS TREATED WITH BISPECIFICS

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Background: CD3/CD20 bispecific antibodies, classified as bispecific T-cell engagers (BiTEs), have seen a rapid expansion in their use for lymphoma treatment. As their toxicity profiles and management strategies become better understood, identifying patients at higher risk of severe adverse events is increasingly important. Identifying risk factors for toxicity is essential to optimize patient management. This aim of this study is to analyze risk factors and clinical evolution of patients treated with bispecific antibodies requiring admission to the ICU.

Methods: Retrospective unicentric analysis on clinical predictors and adverse events in patients receiving bispecific therapy who require ICU admission form June 2019 to June 2025.

Results:

	No. of UCI Patients (n=5, 8.1%)	No. of Non-UCI Patients (n=57, 91.9%)
ECOG pre-treatment, median (range) Frailty Score pre-treatment, median (range)	1 (1-2) 3 (1-3)	0 (1-3) 2 (1-4)
Pre bispecific status • First line • Progressive disease • Partial response	5 (100)	18 (31.6) 36 (63.2) 3 (5.2)
Patients with life-threatening event	5 (100)	2 (3.5)
Inpatients monitoring for treatment administration	5 (100)	41 (71.9)
Toxicity cause • CRS • CRS and ICANS • ICANS • Documented Sepsis • Flare	2 (40) 1 (20) 1 (20) 1 (20)	27 (46.6) 2 (3.4) 1 (1.7) 3 (5.2) 4 (6.9)
CD3/CD20 bispecific antibodies cycle at time of toxicity • 1st dose step up	1 (20) 1 (20) 3 (60)	7 (26.9) 6 (23.1) 4 (15.4) 9 (34.6)

• 2nd dose step up • 3rd dose step up • Full dose step up		
Characteristics at ICU admission • Fever • Hypotension • SOFA score, median (range)	4 (80) 5 (100) 3 (2-6)	
Interventions • Dexamethasone dose mg, median (range) • Tocilizumab, median (range) • Antibiotic therapy • Vasoactive drugs • Mechanical ventilation • Renal replacement therapy	70 (10-230) 2 (1-3) 5 (100) 5 (100) 0 (0) 0 (0)	20 (10-800) 1 (1-3) 30 (51.7)
Deaths • Progression • Toxicity	3 (60) 3 (100) 0 (0)	10 (17.5) 9 (90) 1 (10)

The study included 62 patients, 32 women (51.6%) and 30 men (48.4%), who received odronextamab (n=14, 22.6%), glofitamab (n=13, 20.9%), epcoritamab (n=16, 25.8%), or mosunetuzumab (n=19, 30.7%). Diagnoses comprised follicular lymphoma (n=34, 54.9%), DLBCL (n=25, 38.7%), mantle cell lymphoma (n=2, 3.2%), and marginal zone lymphoma (n=2, 3.2%). The median age at treatment initiation was 62 years (range 26–85).
CRS occurred in 33 patients (53.2%), predominantly grade 1–2 (85.7%), with 5 cases (14.3%) of grade 3. ICANS was observed in 4 patients (6.3%): two with grade 1 and two with grade 3, the latter deemed non-ICU candidates due to pre-existing comorbidities. Patients admitted to the ICU had significantly worse baseline ECOG performance status (χ^2=6.5, p=0.03), with no differences in Frailty Score. Forty-six patients (74.2%) were hospitalized preventively, no difference in ICU admission was observed between patients managed as outpatients (χ^2=1.8, p=0.1). 46 patients (74.2%) had preventive hospitalization, we foun7 patients (11.2%) developed severe complications requiring ICU-level supportive care: 2 patients (3.2%) with grade 3 CRS receiving full-dose treatment, 1 (1.6%) with a severe flare, 1 (1.6%) with sepsis, and 2 (3.2%) with neurotoxicity who were not considered ICU candidates. Median ICU stay was 3 days. ICU-admitted patients received

significantly more doses of tocilizumab (χ^2=6.7, p=0.03), but not steroids (χ^2=8.1, p=0.4). No deaths occurred during ICU admission; however, 3 patients died after being discharge due to disease progression. No significant difference in progression was observed among patients admitted to the ICU (χ^2=2.6, p=0.1). Table 1.

Conclusions: No significant differences in treatment-related toxicity were seen between ICU and ward patients. Mortality was mostly due to disease progression, with one therapy-related death in a non-ICU candidate. Outpatient administration appears feasible, as complications were infrequent and mild. Early recognition of severe complications is crucial to optimize outcomes.

Disclosure: Nothing to declare.

P286

MANAGEMENT OF RELAPSED/REFRACTORY (R/R) B-NON HODGKIN LYMPHOMA (B-NHL) WITH ANTI-CD20/ANTI-CD3 BISPECIFIC ANTIBODIES (BSABS). A SINGLE CENTER EXPERIENCE

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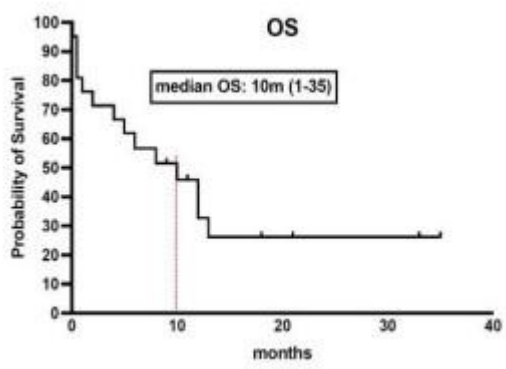
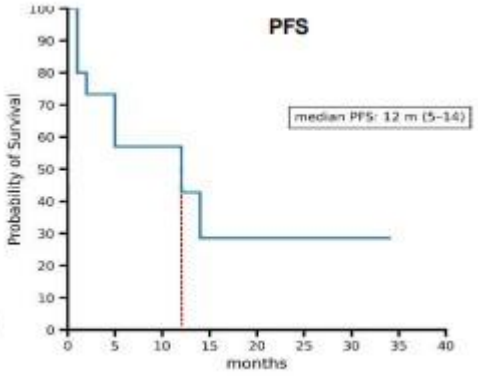
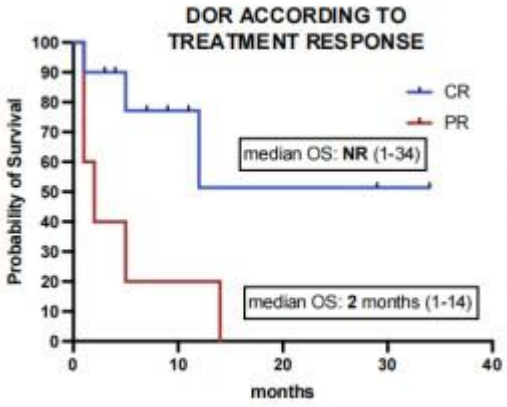
Background: Patients with R/R B-NHL are associated with unfavorable outcomes. Consequently, BsAbs appear to be a game changer in the treatment of B-NHL. Glofitamab, epcoritamab, and mosunetuzumab are all anti-CD20/anti-CD3 BsAbs, showing comparable efficacy and class distinct safety profiles. In view of their favorable profiles, we sought to describe our experience in treating patients with R/R DLBCL, FL or MCL in our department.

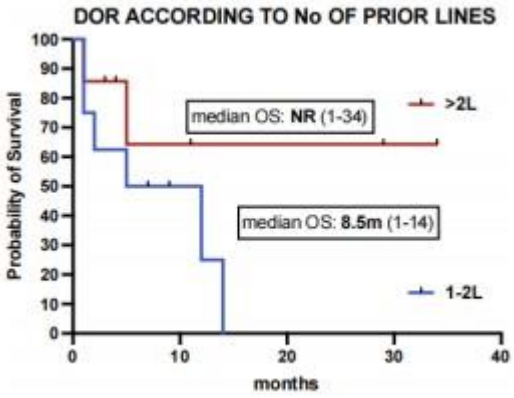
Methods: This is a real world, retrospective, observational, single Center study, based on data from 21 consecutive patients with DLBCL, FL and MCL, treated with BsAbs between 2021 - 2025. Efficacy was estimated based on ORR, OS, PFS and DOR after treatment. Safety was evaluated by retrieving data on adverse events, especially those considered to be treatment class specific, particularly CRS, ICANS, hematological toxicity, necessity for IVIG replenishment and incidence of opportunistic infections.

Results:









From a total of 21 patients (13 females, 8 males), 9 had DLBCL, 2 Grey Zone lymphoma, 2 PMBCL, 5 FL, 1 MCL and 2 Richter transformation. The median age upon 1st administration of a BsAbs was 59 years. Thirteen patients received Glofitamab, five epcoritamab and three mosunetuzumab. All had received at least 1 prior line of treatment. BsAbs preceded CAR-Ts in eight and allogeneic transplantation in one (bridging therapy). CRS (grade I n=5, grade II n=4, grade III n=4) occurred in 13 patients: 12 (1st cycle), 1 (3rd cycle). Any grade of CRS was associated with markedly elevated ferritin levels (>1000μg/mL). One patient developed ICANS grade II. Hematological toxicity was reported in all subjects and was well managed with G-CSF. Only 3 received IVIG replenishment. Best response assessment after BsAbs was feasible in 18/21 patients. ORR was 83.3% (15/18). Ten patients achieved CR, 5 PR and 3 had PD. Median time to best response was 1.76 months (0.8-4.2). With a median FU of 21 months (0.1-35) the median OS was 10 months (0.1-35). Median PFS for responders was 12 months (95% CI, 5–14). For complete responders, the median OS was not reached, whereas in partial responders it was only 2 months. Notably, patients with fewer prior lines of treatment had lower median OS, than more heavily pretreated ones. The former all had primary refractory disease and thus a more aggressive course. This imposed the earlier integration of BsAbs in the treatment sequence and it might explain the poorer survival of these patients. Most of the patients died due to disease progression or sepsis, three patients manifested CMV disease (encephalitis n=1, colitis n=2) and 1 HLH.

Conclusions: Anti-CD20/anti-CD3 BsAbs have already entered routine clinical practice for the treatment of R/R B-NHL. The majority of our patients benefited from BsAbs. Infections, nonetheless, remain a substantial challenge and a major cause of mortality. In accordance with the literature, CRS was manageable. Further real world evidence is required to estimate the suitable timing of articulation with CAR T-cell therapy and the optimal treatment sequencing.

Disclosure: Nothing to declare.

P287

MARIBAVIR TREATMENT IN AGGRESSIVE EBV-ASSOCIATED POSTTRANSPLANT LYMPHOPROLIFERATIVE DISORDER (EBV+ PTLD)

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Background: Epstein-Barr Virus-associated post-transplant lymphoproliferative disorders (EBV+ PTLD) have variable prognoses based on histology, stage, and ability to reduce immunosuppression. Standard treatment includes reducing immunosuppression (RIS) and R-CHOP chemoimmunotherapy. Novel therapies like EBV-specific cytotoxic T lymphocytes or chimeric antigen receptor T cell therapy are often not feasible. Maribavir (MBV) has demonstrated the ability to inhibit EBV BGLF4 viral protein kinase activity, thereby reducing viral genome copies and infectivity.

Methods: A 53-year-old woman with morbid obesity was diagnosed with HTLV-1-associated adult T cell leukemia/lymphoma (ATLL), stage IV, with lymphadenopathy, skin, and bone marrow involvement in August 2023. She received the VCAP-AMP-VECP regimen plus intrathecal chemotherapy for 4 cycles with Ropeginterferon alfa-2b for skin involvement. Following complications, including sepsis and right frontal lobe stroke, she underwent reduced-intensity conditioning (FB2 regimen) with 8/8 matched unrelated donor allogeneic peripheral blood stem cell transplantation on 2024/4/18. GVHD prophylaxis with cyclosporine and mycophenolate was tapered within three months due to *Pneumocystis jirovecii* pneumonitis. Disease relapsed in June 2025 with multiple extramedullary nodal lesions. Treatment included carmustine, brentuximab vedotin, venetoclax, azacitidine, and two donor lymphocyte infusions (5M/kg CD3+ T cells each). She developed severe liver and GI GVHD (bilirubin 15.4 mg/dL), requiring steroids, tacrolimus, mycophenolate, abatacept, ATG (1mg/kg), and ruxolitinib (40mg daily). Post-discharge, she was readmitted with *E. coli* urosepsis, carbapenem-resistant *Acinetobacter baumannii* pneumonia, and *Candida dubliniensis* infection, requiring ICU care with mechanical ventilation and hemodialysis.

Results: In September 2025, progressive neck lymphadenopathy developed with intermittent fever and rising EBV viral load. PET scan showed distinct lymphadenopathy patterns. Excisional biopsy confirmed EBV+ PTLD (EBER positive). Treatment consisted of immunosuppression reduction, maribavir 800mg daily for three weeks, single-dose

Ropeginterferon 250mcg, and one donor lymphocyte infusion (2M/kg CD3+ T cells). EBV viral load decreased from 23,300 IU/mL to 2,000 IU/mL with concurrent lymphoma regression. The patient continues low-dose tacrolimus and ruxolitinib for ongoing GI GVHD and maintains disease-free status.

Conclusions: Approximately half of EBV+ PTLD cases show relapse or resistance to initial RIS or Rituximab-based treatments. While no clinical trials have proven maribavir efficacy in EBV+ PTLD, this case demonstrates promising results in a complex post-transplant setting with multiple complications, highlighting the need for further research in this unmet medical need.

Disclosure: Nothing to disclosure

P288

AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PRIMARY CNS LYMPHOMA: A SINGLE-CENTER EXPERIENCE OVER 10 YEARS

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Background: Primary central nervous system lymphoma (PCNSL) is a rare and aggressive subtype of non-Hodgkin lymphoma (NHL). Despite advances in high-dose methotrexate–based induction therapies, the optimal consolidation strategy remains controversial. Autologous hematopoietic stem cell transplantation (auto-HSCT) has been used as a consolidation option in selected patients.

Methods: We retrospectively analyzed patients with PCNSL who underwent auto-HSCT in our center over the last 10 years. During this period, a total of 148 NHL patients received auto-HSCT, of whom 6 patients were diagnosed with PCNSL. Clinical data including demographic characteristics, pathological features, induction regimens, use of radiotherapy, conditioning protocols, and transplant-related outcomes were collected.

Results: A total of six patients with primary CNS lymphoma underwent autologous HSCT during the study period. All patients had diffuse large B-cell lymphoma histology. The mean age at diagnosis was 60 years (range 45–78), and four patients were female. Tumors demonstrated aggressive biological features, with Ki-67 proliferation indices ranging from 70% to 99%, and included both ABC and GCB cell-of-origin subtypes.
All patients received high-dose methotrexate–based induction therapy, followed by consolidative radiotherapy prior to transplantation. Conditioning consisted of BEAM in all cases, and autologous HSCT was successfully performed in every patient. No early (≤100-day) transplant-related mortality was observed.
With a median follow-up of 9.4 months (range 3,2–79.5), two patients remained alive at last follow-up, while four patients died, primarily due to disease progression. Three deaths occurred within the first year following transplantation, reflecting the aggressive clinical

course of the disease. One patient developed secondary acute myeloid leukemia after relapse.
Overall, despite intensive multimodal therapy including radiotherapy and autologous HSCT, long-term survival remained limited in this real-world cohort.

Conclusions: In this single-center experience, autologous HSCT was feasible in selected patients with PCNSL treated with a multimodal approach including radiotherapy. However, long-term survival remained limited, highlighting the aggressive nature of PCNSL and the need for improved consolidation strategies.

Clinical Trial Registry: Not applicable.

Disclosure: The authors declare no conflict of interest.

Chronic Lymphocytic Leukemia

B405

OUTCOME OF SINGLE- AND DOUBLE-REFRACTORY HIGH-RISK CHRONIC LYMPHOCYTIC LEUKEMIA (CLL): THE IMPACT OF CELLULAR THERAPY

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Background: Guidelines suggest that patients with CLL refractory to both BTKi and BCL2i (double-refractory; DR) and those who have failed BTKi in the presence of *TP53* abnormalities and/or complex karyotype (high-risk single-refractory; SRHR) should be considered for alloHCT. The aim of this retrospective single-center study was to assess the prognosis of patients with SRHR and DR CLL, respectively, and the outcome of cellular therapy (CT; alloHCT and/or CART) in these high-risk categories.

Methods: SRHR was defined as CLL refractory to either BTKi or venetoclax (including relapse within 24 months after venetoclax cessation) in the presence of TP53 abnormalities and/or complex karyotype. DR was defined as refractory to both BTKi and venetoclax. Patients fulfilling these criteria were identified from electronic institutional databases. AlloHCT was performed according to institutional standards (PMI 30630979) from matched related or unrelated donors, and CART with the 3G-CD19 CART Heidagenlecleucel within a clinical trial (PMI 39192036). Primary endpoint for SRHR was event-free survival (EFS;

defining events progression to DR, transformation, and death) and for DR transformation-free survival (TFS; defining events transformation and death).

Results: Between 2016 and 2025, 37 patients were identified fulfilling SRHR criteria and 29 patients DR criteria. Since 18 patients evolved from SRHR to DR during their disease course, they appeared in both cohorts. Median age was 61 (41-83) years. In the SRHR cohort, 70% were BTKi-refractory and 30% venetoclax-refractory, and the HR-defining abnormality was TP53 in 89%. In the DR cohort, all patients were both BTKI- and venetoclax-refractory by definition, and 71% harbored TP53 abnormalities. Median EFS of the SRHR cohort was 23 months and median TFS of the DR cohort was 13 months; median OS of the SRHR and DR cohorts was 51 and 21 months, respectively (p=0.039). In the SRHR group 12 patients underwent CT after study entry (alloHCT 10; CART 2), while 16 additional patients received CT only after having reached DR status (alloHCT 9; CART 7). CT significantly improved EFS for SRHR (HR 0.15; 95%CI 0.06-0.34) and TFS for DR (HR 0.19; 95%CI 0.06-0.62), respectively, compared to patients not undergoing CT. Although PFS after alloHCT tended to be better than after CART (HR 0.46; 95%CI 0.16-1.29; p 0.076), OS was similar with both strategies. In individual patients, alloHCT failure could be salvaged with CART and vice versa. NRM was 16% after alloHCT and 0% after CART. Postponing CT until reaching DR status resulted in a numerically inferior OS from CT (4y-OS DR vs SRHR 29% vs 61%; HR 2.87; 95%CI 0.93-8.9; p 0.095).

Conclusions: These results demonstrate for the first time that the outlook of patients with SRHR CLL is dismal but still better than in patients with DR disease. In both settings, alloHCT and CART are feasible and may overcome clinical and biological disease refractoriness, with better results when used in SRHR status rather than DR status. However, the optimum timing and sequencing of CART and alloHCT, respectively, and the impact of CT on the natural course of SRHR/DR CLL remain to be determined.

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THE ROLE OF GENETIC SUSCEPTIBILITY GENES IN THE NECESSITY OF ALLOGENEIC TRANSPLANTATION FOR RICHTER SYNDROME

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Background: Richter syndrome (RS) has historically been considered curable only through allogeneic hematopoietic stem cell transplantation (allo-HSCT). However, recent advances in chimeric antigen receptor (CAR) T-cell therapy are challenging this paradigm. This study investigates the potential utility of genetic susceptibility testing in guiding clinical decisions regarding the need for allo-HSCT in RS patients who achieve complete remission (CR) following CAR-T therapy.

Methods: A retrospective analysis was performed on the clinical data of a 63-year-old male patient with RS. The patient was initially diagnosed with chronic lymphocytic leukemia (CLL), which later transformed into plasmablastic lymphoma (PBL); clonal relatedness to the original CLL was confirmed by immunoglobulin gene rearrangement and genetic profiling. Following BCMA-targeted CAR-T cell therapy, the patient achieved CR. High-throughput DNA sequencing was conducted on peripheral blood samples to screen for pathogenic variants across more than 900 genes associated with hematologic and immune disorders. Clinical outcomes and therapeutic strategies were evaluated in conjunction with the patient's genetic and disease course.

Results: Genetic analysis identified four pathogenic or likely pathogenic variants: TNFRSF13C c.62C>G (p.P21R) (variant allele frequency 54.29%), associated with impaired BAFF receptor function and increased susceptibility to non-Hodgkin lymphoma (NHL) and immunodeficiency; ALPK2 c.5557C>G (p.Q1853E) (46.7%), linked to loss of tumor suppressor activity and elevated risk of angioimmunoblastic T-cell lymphoma and colorectal cancer; STK11 c.1062C>G (p.F354L) (48.67%), associated with reduced AMPK signaling, Peutz-Jeghers syndrome, and predisposition to multiple malignancies; and BTLA c.590A>C (p.N197T) (100%), resulting in aberrant T-cell inhibitory signaling and increased risk of B-cell lymphomas. Additionally, 12 variants predicted to be potentially deleterious by in silico analysis were detected. The overall genetic profile indicated a high inherited risk for hematologic neoplasms, leading to a recommendation for allo-HSCT. However, the patient declined transplantation and instead received consolidation therapy with a Bruton tyrosine kinase (BTK) inhibitor. Fourteen months after CAR-T therapy, the patient experienced relapse, with pathological confirmation of classical Hodgkin lymphoma (cHL). Immunoglobulin gene rearrangement analysis revealed no clonal relationship to the prior CLL/PBL, suggesting a de novo second primary malignancy. The patient achieved CR again following treatment with ABVD and D-AVD chemotherapy regimens and was subsequently scheduled for allo-HSCT.

Conclusions: This case demonstrates that multiple germline pathogenic variants affecting critical pathways—such as B-cell survival (TNFRSF13C), apoptosis and metabolic regulation (STK11), and immune checkpoint signaling (BTLA)—contribute to an underlying high tumor susceptibility. Although CAR-T therapy induced durable remission initially, the persistent genetic predisposition may have facilitated the development of a secondary malignancy.

Evidence suggests that STK11 mutations impair DNA damage repair mechanisms, accelerating malignant transformation, while TNFRSF13C deficiency may compromise CAR-T cell persistence due to altered microenvironmental support. These findings underscore the importance of considering allo-HSCT as a consolidative strategy in genetically high-risk RS patients, even after achieving CR with CAR-T therapy, to mitigate long-term risks of relapse and secondary cancers.

Disclosure: Nothing to declare

Multiple Myeloma

OS15-01

LONG-TERM PROGRESSION-FREE SURVIVAL BENEFIT WITH CILTACABTAGENE AUTOLEUCEL IN STANDARD-RISK RELAPSED/REFRACTORY MULTIPLE MYELOMA

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Background: The CARTITUDE-4 study (NCT04181827), which enrolled patients with lenalidomide-refractory multiple myeloma (MM) after 1–3 prior lines of therapy (pLOT), demonstrated a significant benefit of ciltacabtagene autoleucel (cilta-cel) over established triplet regimens. However, the benefit of cilta-cel for patients with standard-risk cytogenetics remains less defined. Here, we report outcomes in patients with standard-risk cytogenetics from the intent-to-treat and as-treated populations in CARTITUDE-4.

Methods: In CARTITUDE-4, patients randomised to the cilta-cel arm underwent apheresis and bridging treatment with either pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd), followed by lymphodepletion therapy with cyclophosphamide and fludarabine, and then a single cilta-cel infusion. Progression-free survival (PFS) was assessed using a validated computerised algorithm. The intent-to-treat population included 208 patients; 32 patients progressed or died on bridging therapy, resulting in an as-treated population of 176 patients. Patients with high-risk cytogenetics, defined as del(17p), t(14;16), t(4;14), gain/amp(1q) (n=105), or with unknown cytogenetics (n=12), were excluded from the as-treated analysis. The 12-month minimal residual disease (MRD)-negative complete response (CR) was defined per the International Myeloma Working Group criteria as the proportion of participants with CR or better prior to and at 12 months (+/- 3 months), achieving MRD-negative status at 12 months (+3 months) after cilta-cel infusion, as determined by next-generation sequencing (10^{-5}), prior to progressive disease or subsequent anti-myeloma therapy. For the as-treated population, PFS rates were measured from the time of cilta-cel infusion.

Results: In CARTITUDE-4, in the intent-to-treat population, at a median follow-up of 33.6 months, patients with standard-risk cytogenetics had a 30-month PFS rate (95% CI) of 71.0% (58.8–80.2) in the cilta-cel arm (N=69) vs 43.2% (31.3–54.5) in the standard-of-care (SOC) arm (N=70). Patients with standard-risk cytogenetics in the as-treated population (n=59) had a 30-month PFS rate of 80.5% (95% CI, 67.2–88.8). In CARTITUDE-1 (NCT03548207), which evaluated cilta-cel in patients with heavily pretreated relapsed/refractory MM (RRMM; ≥3 pLOT), the 30-month PFS rate among patients with standard-risk cytogenetics (negative for del(17p), t(14;16), or t(4;14); n=68) was 59.9% (95% CI, 47.2–70.5). In the CARTITUDE-4 as-treated population with standard-risk cytogenetics, 8 PFS events occurred within 1 year and 4 PFS events beyond 1 year of cilta-cel infusion. Twenty-six patients achieved MRD-negative CR at 12 months after cilta-cel; 100.0% of these patients were progression free at 30 months. Fourteen patients were not evaluable for MRD due to: calibration failure (n=12), no sample availability for testing (n=1) or indeterminate results post baseline (n=1).

Conclusions: PFS rate at 2.5 years for patients with standard-risk RRMM was higher in CARTITUDE-4 compared with CARTITUDE-1, supporting the use of cilta-cel as early as second line in the treatment course. In CARTITUDE-4 (as-treated population), 80.0% of patients with standard-risk cytogenetics were progression free and off treatment at 2.5 years. In patients with standard-risk cytogenetics who achieved MRD-negative CR at 1 year, this rate increased to 100.0%. The low rate of progression events in cilta-cel-treated patients with standard-risk cytogenetics shows the profound benefit of a single cilta-cel infusion in this population. © *American Society of Hematology (2025). Reused with permission*.

Clinical Trial Registry: https://clinicaltrials.gov/study/NCT04181827

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OS15-02

EFFECTIVENESS OF BRIDGING THERAPY CORRESPONDS TO IMPROVED OUTCOMES AFTER CILTACABTAGENE AUTOLEUCEL: PHASE 3 CARTITUDE-4 STUDY OF PATIENTS WITH RELAPSED, LENALIDOMIDE-REFRACTORY MULTIPLE MYELOMA

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Background: Effective tumour burden reduction using bridging therapy has been associated with better progression-free survival (PFS) and safety outcomes in patients treated with ciltacabtagene autoleucel (cilta-cel). A single infusion of cilta-cel in CARTITUDE-4 (median follow-up, 33.6 months) significantly improved PFS (hazard ratio [HR] weighted, 0.29 [95% CI, 0.22–0.39]) and overall survival (OS; HR, 0.55 [0.39–0.79]; *P*=0.0009) versus standard of care in patients with relapsed and lenalidomide-refractory multiple myeloma after 1–3 prior lines of therapy. Here, we investigate the correlation between bridging therapy response pre-cilta-cel infusion with the efficacy and safety outcomes post-infusion.

Methods: The CARTITUDE-4 study design has previously been described. Patients in the cilta-cel arm underwent apheresis, received ≥1 cycle of bridging therapy (investigator's choice) with either pomalidomide, bortezomib and dexamethasone (PVd) or daratumumab, pomalidomide and dexamethasone (DPd), lymphodepletion (cyclophosphamide and fludarabine), and then a single cilta-cel infusion 5–7 days post-initiation of lymphodepletion.

Results: Among 196 patients who received cilta-cel in CARTITUDE-4 (176 as study treatment, 20 as subsequent therapy), 172 (87.8%) received DPd and 24 (12.2%) received PVd during bridging period (median number of bridging cycles, 2 [range, 1–6]). Following bridging therapy and pre-lymphodepletion, 42 patients had very good partial response or better (≥VGPR), 70 had partial response (PR), 61 had minimal response (MR)/stable disease (SD), 20 had progressive disease (PD) and 3 were not evaluable. Thirty-month PFS rates (95% CI) from cilta-cel infusion were 75.9% (59.8–86.2), 72.9% (60.4–82.1), 56.5% (42.8–68.1) and 30.0% (12.3–50.1), respectively. Thirty-month OS rates (95% CI) were 85.1% (69.9–93.0), 91.4% (81.9–96.1), 74.8% (61.6–84.0) and 40.0% (19.3–60.0), respectively.

No movement or neurocognitive treatment-emergent adverse events (MNTs) were reported in patients with ≥VGPR or PR. There was 1 MNT case in patients with PD and 1 in a patient with a best response of SD (unconfirmed PD at cilta-cel infusion). Cranial nerve palsy was reported in 11.9%, 7.1%, 8.2% and 5.0% of patients with ≥VGPR, PR, MR/SD and PD, respectively. Fatal infections occurred in 2.4%, 4.3%, 13.1% and 15.0%, respectively. Rates of prolonged (grade 3/4 cytopenia that did not recover to grade 2 by day 60 post-cilta-cel) thrombocytopenia were lowest among patients who achieved ≥VGPR (9.5%), followed by patients with PR (11.4%) or MR/SD (11.5%) after bridging, and markedly higher in those with PD (50%). Prolonged neutropenia was lowest in patients achieving ≥VGPR before cilta-cel (2.4%) vs 9.8–15.7% in patients with PR or lower. Non-relapse mortality was 7.1%, 8.6%, 18.0% and 30.0% in patients with ≥VGPR, PR, MR/SD, and PD, respectively.

Conclusions: In patients from CARTITUDE-4, better response to bridging therapy correlated with longer PFS and OS. No MNTs were observed in patients who achieved ≥PR following bridging therapy. Patients with poorer responses to bridging therapy were more likely to develop fatal infections, prolonged thrombocytopenia and neutropenia, and had higher rates of non-relapse mortality following cilta-cel infusion. These data emphasize the importance of optimizing bridging therapy for disease control prior to receiving cilta-cel. © *American Society of Hematology (2025). Reused with permission*.

Clinical Trial Registry: https://www.clinicaltrials.gov/study/NCT04181827

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DARATUMUMAB/BORTEZOMIB/LENALIDOMIDE/DEXAMETHASONE WITH DARATUMUMAB/LENALIDOMIDE MAINTENANCE IN TRANSPLANT-ELIGIBLE PATIENTS WITH NEWLY DIAGNOSED MULTIPLE MYELOMA: ANALYSIS OF SUSTAINED MINIMAL RESIDUAL DISEASE NEGATIVITY IN THE PHASE 3 PERSEUS TRIAL

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Background: Minimal residual disease (MRD) negativity and sustained MRD negativity are associated with longer survival and are strong prognostic clinical endpoints. PERSEUS (NCT03710603) evaluated subcutaneous Dara + VRd induction/consolidation + DR maintenance vs VRd induction/consolidation + R maintenance in TE NDMM. DVRd significantly improved progression-free survival (PFS), complete response or better rate (≥CR), and MRD negativity rate. Nearly two-thirds of patients on DR maintenance could stop treatment after achieving sustained remission, leading to DVRd being recommended by NCCN as a preferred TE NDMM regimen. Here, we report the impact of sustained MRD negativity status on PFS in PERSEUS.

Methods: TE patients with NDMM age 18–70 years were randomized 1:1 to DVRd (DVRd induction/consolidation + DR maintenance) or VRd (VRd induction/consolidation + R maintenance). The primary endpoint was PFS; MRD negativity rate (MRD negativity 10^{-5} and ≥CR) was a key secondary endpoint. Sustained MRD negativity, assessed in the intent-to-treat population, was defined as confirmed MRD negativity ≥12 months apart and without MRD positivity in between. Functionally high risk (FHR) was defined as disease progression ≤18 months from treatment initiation, excluding pre-progression deaths.

Results: A total of 709 patients were assigned to DVRd (n=355) or VRd (n=354). At 47.5-month median follow-up, ≥12-month sustained MRD negativity rates were higher overall with DVRd (64.8%; n=230) vs VRd (29.7%; n=105); this pattern persisted across clinically relevant subgroups, including age ≥65 years and high-risk cytogenetics. Similarly, ≥24-month sustained MRD negativity rates were higher with DVRd (55.8%; n=198) vs VRd (22.6%; n=80). Patients with ≥12-month sustained MRD negativity vs those without had improved 48-month PFS rates regardless of treatment arm (**Table**). Compared with VRd, DVRd reduced FHR rates (3.1% vs 6.8%), and rates of FHR or pre-progression deaths were lower with DVRd vs VRd (5.4% vs 11.0%) in the first 18 months.

Conclusions: In TE NDMM, nearly two-thirds of patients treated with DVRd induction/consolidation and DR maintenance achieved ≥12-month sustained MRD negativity, associated with >95% 48-month PFS rate. Moreover, ≥24-month sustained MRD negativity rates with DVRd were 2.5 times as high as VRd, and FHR incidence was halved with DVRd vs VRd. Collectively, these data further support the PERSEUS regimen as standard of care for TE NDMM. *© 2025 American Society of Clinical Oncology, Inc. Reused with permission. This abstract was accepted and previously presented at the 2025 ASCO Annual Meeting. All rights reserved.*

Table: Median and 48-month PFS among patients who did and did not achieve sustained MRD neg

	Achieved sustained (≥12 month) MRD negativity (10^{-5})			Without achieving sustained (≥12 month) MRD negativity (10^{-5})		
	DVRd (n=230)	**VRd (n=105)**		**DVRd (n=125)**	**VRd (n=249)**	
Median PFS, months (95% CI)	NE (NE–NE)	NE (NE–NE)	HR=0.83 (95% CI 0.3–2.3) *P*=0.7149	NE (47.9–NE)	NE (45.3–NE)	HR=0.80 (95% CI 0.6–1.2) *P*=0.2489
48-month PFS rate, % (95% CI)	95.3 (91.4–97.5)	94.2 (87.6–97.4)		60.3 (48.0–70.5)	54.9 (47.7–61.4)	

Hazard ratio, HR; NE, not estimable.
Median PFS and 95% CI are from Kaplan-Meier estimates.
P-value is from unstratified log-rank test

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Robin L Carson - **Employment** - J&J. **Stocks** - J&J.
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OS15-04

REAL-WORLD COMPARISON OF STANDARD-OF-CARE IDECABTAGENE VICLEUCEL AND CILTACABTAGENE AUTOLEUCEL IN RELAPSED/REFRACTORY MULTIPLE-MYELOMA: A STUDY ON BEHALF OF THE CTIWP AND THE CMWP OF THE EBMT

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Background: Idecabtagene vicleucel (ide-cel) and ciltacabtagene autoleucel (cilta-cel), two B-cell maturation antigen (BCMA)–directed chimeric antigen receptor (CAR) T-cell therapies, have demonstrated remarkable efficacy in relapsed/refractory multiple myeloma (RRMM). We hereby compare safety, efficacy, and survival among patients with RRMM treated with standard-of-care ide-cel or cilta-cel.

Methods: The CTIWP and the CMWP performed a retrospective study based on the European Society of Blood and Marrow Transplantation registry, including all patients receiving ide-cel or cilta-cel between 2020 and 2024 for RRMM with available one year follow-up outcome data.

Results: Overall, 785 patients met the inclusion criteria, with 599 (76.3%) patients receiving ide-cel and 186 (23.7%) patients receiving cilta-cel. The median age was 65 years in both groups (range: 18.4-89.2), 60.9% of the patients were male, and 93.5% had an Eastern Cooperative Oncology Group performance status of 0-1. Most patients received CAR T-cell therapy after at least three lines of treatment. There was no difference regarding exposure to prior BCMA-directed therapy between both groups (6.1% in the ide-cel group versus 5.3% in the cilta-cel group). More patients were penta-refractory in the ide-cel group, 21%, versus 9.8% in the cilta-cel group.
Median follow-up was 12.1 (range, 6.5 to 23.7) months. The 30-day incidence of all grade cytokine release syndrome (CRS) was higher in the ide-cel group, being 77% versus 63% in the cilta-cel group ($p<0.001$), the corresponding grade >=3 CRS was 6% versus 2% ($p=0.048$). There was no difference in the day 30 incidence of all grade ICANS, 10% in the ide-cel group, versus 12% in the cilta-cel group ($p=0.4$), while the day 30 incidence grade >=3 ICANS was 2% in both groups. More patients achieved a response (complete response [CR]+very good partial response [VGPR] +partial response) in the cilta-cel group, 95.4%, versus 88.2% in the ide-cel group. At one-year, overall survival (OS) and progression-free survival (PFS) were significantly higher in the cilta-cel group, being 84% and 78%, respectively versus 78% and 53% respectively, in the ide-cel group ($p=0.024$ and $p<0.001$ respectively). At 12 months, the cumulative incidence of CAR T-cell related mortality (4% in the ide-cel group versus 7% in the cilta-cel group; $p=0.4$) was similar in both groups. In multivariable analysis (Cox model), MM status at time of CAR T-cell therapy (not being in CR/VGPR) and prior exposure to BCMA-directed therapies were associated with a lower OS. Use of ide-cel was also associated with a lower PFS (HR, 0.38 (0.25-0.56), $p<0.001$).

Conclusions: This large real-world comparison of anti-BCMA CAR T-cell therapy for RRMM demonstrates that use of cilta-cel translates to superior efficacy and PFS. Regarding safety, there was no difference in non-relapse mortality between treatment groups. The higher rate of CRS, (including grade>=3), in the ide-cel group, could be related to the fact that patients in the cilta-cel cohort were treated more recently with improvements in CRS prevention and treatment over time.

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OS15-05

OUTCOMES OF PATIENTS WITH T(4;14) MULTIPLE MYELOMA AFTER AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION: A REPORT BY THE EBMT CHRONIC MALIGNANCIES WORKING PARTY

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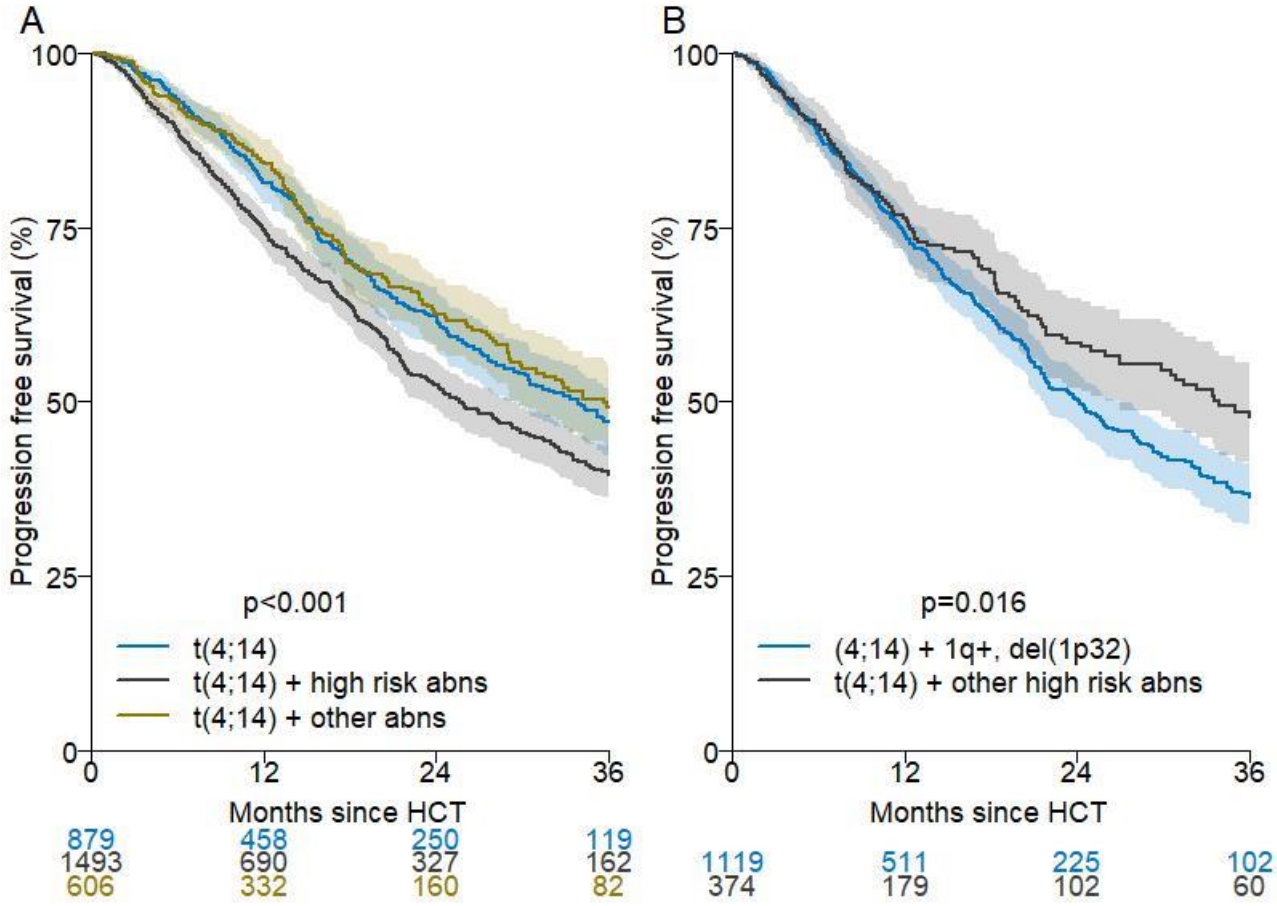
Background: Upfront autologous hematopoietic cell transplantation (auto-HCT) remains the standard of care for younger fitter patients with newly diagnosed multiple myeloma (MM). Both single and tandem auto-HCT strategies are used, depending on the disease risk profile. Fluorescence in Situ Hybridisation (FISH) cytogenetic abnormalities are important prognostic markers of progression-free (PFS) and overall survival (OS) in MM. We here report on the outcomes of patients with t(4;14) multiple myeloma following auto-HCT.

Methods: MM patients aged ≥18 years old with t(4;14) who underwent their first auto-HCT between 2016 and 2022 were selected from the EBMT registry. OS and PFS were analyzed using Kaplan-Meier methods. The cumulative incidence of relapse (RI) and non-relapse

mortality (NRM) were analyzed together in a competing risks framework. Patients were stratified into three groups by the presence of co-existing cytogenetic abnormalities as follows: (1) t(4; 14) as the only detected abnormality, (2) International Myeloma Society (IMS)-defined high risk myeloma based on either t(4;14) with co-existing chromosome 1 abnormalities (1q+ or del(1p32)),or, alternatively, del(17p), t(14;16), or t(14;20), and (3) t(4;14) with any other abnormalities. Additional analysis was performed for the cohort with t(4;14) with 1q+ or del(1p32).

Results:



Overall, 3,103 patients were included. The median age at the first auto-HCT was 60 years (IQR, 54, 65). 1,706 (55%) were male. 573 (23%), 999 (40%), and 898 (36%) patients had ISS stage I, II or III myeloma, respectively. 914 (30%) patients had t(4;14) only, 1,564 (50%) had additional high-risk abnormalities of whom 1,169 (75%) had 1q+ or del(1p32), and 625 (20%) had other abnormalities. The median time from diagnosis to auto-HCT was seven months (IQR, 5, 9). 2,301 (74%) patients achieved a VGPR or better at auto-HCT and 2,312 (75%) patients received Melphalan 200mg/m2 conditioning.
The 3-year PFS and OS for the whole group were 44% (95%CI, 41-46%) and 72% (95%CI, 70-75%), respectively. The 3-year PFS estimates stratified by the three cytogenetic

subgroups were (1) 47% (42-52%), (2) 40% (36-43%) and (3) 49% (43-55%) (p<0.001) (Figure 1A). The respective OS outcomes were 79% (75-83%), 66% (62-69%), and 77% (73-82%) (p<0.001), respectively. RI at 3 years was 53% (50-56%) for the whole group and 50% (46-55%), 56% (53-60%), and 48% (42-54%) for the three subgroups (p<0.001). NRM did not differ between groups (p=0.5) and reached 3% (2-4%) at three years for the entire cohort.
Patients with t(4;14) and either 1q+ or del(1p32) had inferior PFS compared with patients with other high-risk abnormalities [3-year PFS 36% (32-41%) vs. 48% (41-55%), p=0.016] (Figure 1B) due to a higher RI [3-year RI, 59% (55-64%) vs. 48% (41-56%), p=0.018]. There was no difference in OS between the two groups [3-year OS 65% (61-69%) vs. 69% (63-75%), p=0.4] or in NRM.

Conclusions: Patients with t(4;14) and additional co-existing high-risk cytogenetic abnormalities, especially either 1q+ or del(1p32), continue to have significantly poorer outcomes after auto-HCT [vs OS of 81% at 4 years in the IFM-2009 trial Transplant Arm cohort (RVd+ASCT)].

Disclosure: The Authors declare no conflicts of interest.

OS15-07

MODELING LONG-TERM PROGRESSION-FREE SURVIVAL IN TRANSPLANT-ELIGIBLE AND TRANSPLANT-INELIGIBLE NEWLY DIAGNOSED MULTIPLE MYELOMA TREATED WITH DARATUMUMAB, BORTEZOMIB, LENALIDOMIDE, AND DEXAMETHASONE

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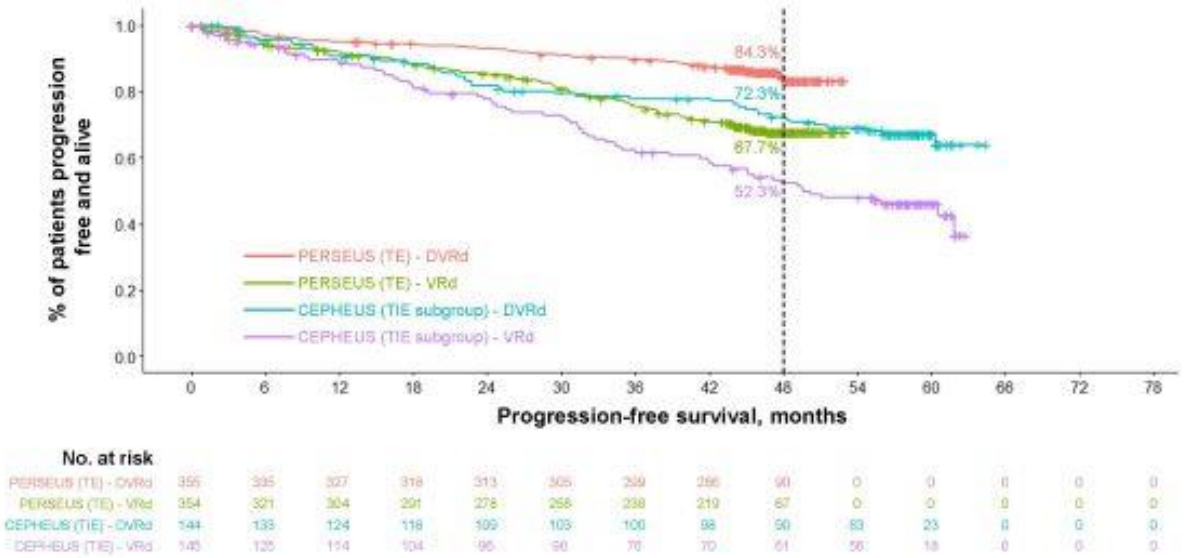
Background: Quadruplet therapy consisting of daratumumab, bortezomib, lenalidomide, and dexamethasone (DVRd) plus DR maintenance therapy showed superior efficacy to VRd with R maintenance in patients with transplant-eligible (TE) newly diagnosed multiple myeloma (NDMM) in the PERSEUS trial, and the CEPHEUS trial showed superiority of DVRd over VRd in transplant-ineligible (TIE) or transplant-deferred patients with NDMM; this analysis aims to extrapolate progression free-survival (PFS) data from the PERSEUS trial intent-to-treat (ITT) population and the TIE subgroup of CEPHEUS to estimate long-term outcomes of DVRd in the frontline setting.

Methods: Following UK National Institute for Health and Clinical Excellence (NICE) guidance on survival data extrapolation, 7 parametric distributions were fitted to model PFS data: exponential, Weibull, gamma, Gompertz, log-logistic, log-normal, and generalized gamma. Individual parametric curves were fit for the DVRd and VRd groups. Long-term extrapolations were capped by UK general population data for 2020–2022 on disease-specific and all-cause mortality, utilizing the median age of the population and the proportion of male patients in the cohort at the initiation of treatment (per NICE guidance). PFS projections begin at the median age of the population.

Results: In PERSEUS, 709 TE patients were randomized (DVRd, n=355; VRd, n=354), with median age 60 years and 59% male. In CEPHEUS, 289 TIE patients were randomized (DVRd, n=144; VRd, n=145), with median age 72 years and 51% male. Observed Kaplan-Meier estimates of PFS at 48 months in TE patients in PERSEUS were 84.3% vs 67.7% in the DVRd and VRd groups, respectively; for TIE patients in CEPHEUS, they were 72.3% vs 52.3% (**Figure**). Based on PFS modeling in the PERSEUS TE population, the range of estimated median PFS across all distributions was 158–255 months (13.2–21.2 years) for the DVRd group and 76–119 months (6.3–9.9 years) for the VRd group. The exponential distribution (best fit) gave PFS estimates of 205 vs 87 months (17.1 vs 7.3 years) for DVRd and VRd, respectively. For the CEPHEUS TIE population, the range of estimated median PFS across distributions was 96–118 months (8.0–9.8 years) for the DVRd group and 52–54 months (4.3–4.5 years) for the VRd group, with the exponential distribution (best fit) giving estimates of 100 vs 53 months (8.3 vs 4.4 years) for DVRd and VRd, respectively.

Conclusions: Across all 7 distributions, PFS projections were significantly longer with DVRd than VRd in both TE and TIE patients with NDMM. As expected, projected PFS with DVRd was longer for TE patients (205 months from baseline age of 60 years) than TIE patients (100 months from age 72 years). These extrapolations provide supportive projections beyond the observed PFS data, helping to inform treatment decisions and reinforcing the benefit of DVRd with a daratumumab-containing maintenance regimen in all patients with NDMM.

Figure: Observed PFS in TE and TIE patients treated with DVRd or VRd in the PERSEUS and CEPHEUS studies



Clinical Trial Registry: Clinicaltrials.gov: NCT03710603 (PERSEUS), NCT03652064 (CEPHEUS); EudraCT number: 2018-002992-16 (PERSEUS)

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Thierry Facon - Nothing to declare.
Vania Hungria - **Consulting**- Regeneron/GSK/BMS/Sanofi/Kite/J&J. **Honoraria-** Pfizer/AbbVie/Amgen/GSK/BMS/Sanofi/Takeda/J&J.
Nizar J Bahlis - **Consulting**- Sanofi/BMS/Takeda/GSK/Kyte/Karyopharm Therapeutics/Amgen/J&J/Celgene/Genentech/Roche/Novartis/Abbvie/Pfizer. **Honoraria**- Sanofi/BMS/Takeda/GSK/Kyte/Karyopharm Therapeutics/Amgen/J&J/Celgene/Genentech/Roche/Novartis/Abbvie/Pfizer.
Philippe Moreau - **Honoraria** - Abbvie/Amgen/Celgene/GSK/J&J/Pfizer/Sanofi. **Consulting**- Abbvie/Amgen/Celgene/GSK/J&J/Pfizer/Sanofi.
Mario Boccadoro - **Honoraria** - AbbVie/Amgen/BMS/Celgene/J&J/Novartis/Sanofi. Consulting- GSK/J&J. **Funding** - Amgen/BMS/Celgene/J&J/Mundipharma/Novartis/Sanofi.

Fredrik Borgsten - **Employment** - J&J. **Stocks** - J&J.
Annette Lam - **Employment** - J&J. **Stocks** - J&J.
Marjorie Nobrega - **Employment** - J&J.
Viktor Kovacs - Nothing to declare.
Jianping Wang - **Employment** - J&J. **Stocks** - J&J.
Melissa Rowe - **Employment** - J&J. **Stocks** - J&J. **Funding** - J&J.
Anna Sitthi-Amorn - **Employment** - J&J. **Stocks** - J&J.
Robin L Carson - **Employment** - J&J. **Stocks** - J&J.
Meletios A Dimopoulos - **Honoraria** - Amgen/AstraZeneca/Beigene/BMS/GSK/J&J/Menarini/Regeneron/Sanofi/Swixx BioPharma/Takeda. **Consulting**- Amgen/AstraZeneca/Beigene/BMS/GSK/J&J/Menarini/Regeneron/Sanofi/Swixx BioPharma/Takeda. **Other** - Amgen/BMS/Celgene/J&J/Takeda.
Paula Rodríguez-Otero - **Honoraria** - Abbvie/Celgene/GSK/H3 Biomedicine/J&J/Pfizer/Regeneron/Roche/Genentech/Sanofi. **Consulting**- Abbvie/BMS/GSK/J&J/Pfizer/Roche/Sanofi. **Speakers' Bureau** - BMS/GSK/J&J/Sanofi. **Other** - Pfizer.
Saad Z Usmani - **Consulting**- Abbvie/AstraZeneca/BMS/Celgene/Genentech/GSK/J&J/Oricell Therapeutics/Regeneron. **Funding** - BMS/Gilead Sciences/GSK/Gracell TherapeuticsJ&J/K36 Therapeutics.

OS15-08

THE EBMT MULTIPLE MYELOMA EARLY RELAPSE (ER) SCORE IDENTIFIES FUNCTIONALLY HIGH RISK PATIENTS ACROSS CYTOGENETIC SUBGROUPS IN THE CURRENT ERA OF INDUCTIONS. AN EBMT-CMWP REPORT

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Background: Early relapse (ER) within 12 months of Autologous Hematopoietic Cell Transplantation (AHCT) is deemed functionally high risk disease. We developed the EBMT early relapse (ER) score based on the International Staging System (ISS), Performance Status and Disease Status (pre-AHCT) (Beksac et al, BMT 2023). This score was based on data from patients aged 40-70 years transplanted with Melphalan 200mg/m2 between 2014 and 2017 and was later validated by the WAUSTIM collaborative group (ASH 2024).
To validate the score in a more recent patient cohort following treatment with more effective induction regimens taking into account the cytogenetic risk classification.

Methods: We selected MM patients from the EBMT Registry who received their first AHCT between 2020 and 2022. We assessed the predictive performance of the EBMT ER score both in terms of discrimination and calibration. Furthermore, we explored possible refinements of the original model and the interplay with cytogenetic risk.

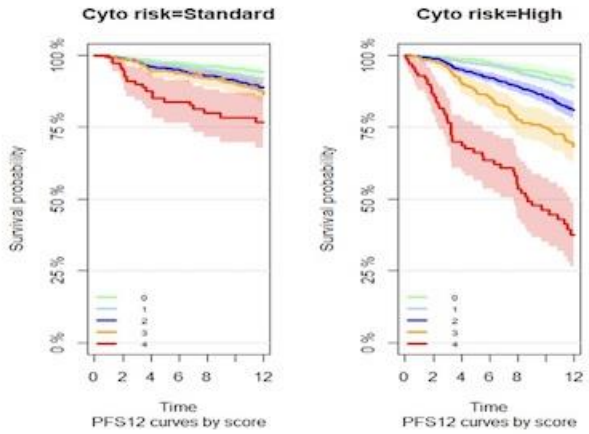
Results: In total 8,833 patients were eligible for the analysis. Median age at AHCT was 61 (range 23-83) years. IgG /IgA/light chain: 53.0%/18.8%/25.4%. Disease status at AHCT was CR/VGPR/PR: 20.8%/51.2%/25.1%. ISS at diagnosis was I/II/III: 34.5%/ 37.5%/ 28.1%; Karnofsky score prior to AHCT-1: ≤70/80/90/100: 6.9%/ 25.9%/ 35.6%/ 31.6%. Cytogenetic risk was standard/high (t(4;14),t(14;16),17pdel): 63.1%/36.9%. Patients received Mel 200/ Mel140: 69.0%/ 10.2%. Regardless of Melphalan dose, 12-month PFS (PFS-12) was 87.9% (95% CI 87.0-88.7) with an ER incidence of 10.4%. which is similar to that observed in the original EBMT study (Mel200 training: 14.7%, Mel200 validation: 11.6%, Mel140: 16.9%).
The EBMT ER score distribution was: 0/1/2/3/4: 22.9% /35.3%/ 31.0%/ 8.4%/ 2.4%. PFS-12 (95% CI) according to scores were as follows: score 0: 94% (92-95); score 1: 91% (90-92); score 2: 86% (84-87); score 3: 78% (75-82); score 4: 58% (50-66) resulting in Hazard Ratios (HRs) compared with the score 0 group: score 1: 1.45; score 2: 2.38; score 3: 3.69; score 4: 9.52 (all p values<0.005). The EBMT ER score behaved similarly in both the original and current populations with a clear separation of curves between groups. Neither age nor Melphalan dose had an impact on PFS-12. There were more ISS III and fewer ISS I cases in the high cytogenetic risk group. In addition, more high cytogenetic risk patients had undergone tandem AHCT (27.6 vs.10.6%). EBMT ER scores 3 or 4 were more frequent among high cytogenetic risk patients (13.0% vs. 9.5%). Cytogenetic high risk vs standard risk PFS-12: 82.7% (95% CI: 81.1-84.4) vs. 90.9% (95%CI: 89.9-91.8); p-value<0.0001). HR for cytogenetics high risk was 1.72 (95% CI: 1.48-1.99 (p<0.0001). In a Cox model, high risk cytogenetics was introduced for each ER score; high cytogenetics risk interacted significantly with scores 3 or 4; there was no significant interaction with score groups 1 or 2.

Conclusions:

Table-1: Distribution and impact of EBMT ER Score on PFS-12 across all patients, standard-risk or high risk patients

		All pts		cyto risk=Standard		cyto risk=High	
EBMT ER score	N (%)	PFS12	95%CI	PFS12	95%CI	PFS12	95%CI
0	2,023 (22.9%)	94%	(92-95)	94%	(93-96)	92%	(89-95)
1	3,118 (35.3%)	91%	(90-92)	92%	(90-93)	89%	(86-91)
2	2,734 (31.0%)	86%	(84-87)	89%	(87-91)	81%	(78-84)
3	744 (8.4%)	78%	(75-82)	86%	(82-91)	68%	(62-75)
4	214 (2.4%)	58%	(50-66)	77%	(68-86)	38%	(26-49)

Figure-1: PFS-12 curves according to EBMT ER score among standard and high cytogenetic risk patients



We have here validated the score regardless of conditioning dose or age. We observed an association between ISS and cytogenetic risk. Cytogenetic risk added to the ER score provided additional predictive value. In conclusion, the EBMT ER score is a widely applicable predictive tool capable of indentifying functionally high risk patients.

Disclosure: Authors have no conflict of interest to declare.

B406

INTENSIFIED CONSOLIDATION WITH TANDEM AUTOLOGOUS VERSUS AUTOLOGOUS/REDUCED-INTENSITY CONDITIONING ALLOGENEIC STEM CELL TRANSPLANTATION FROM RELATED OR UNRELATED DONORS IN FIRST-LINE THERAPY IN 149 HIGH-RISK MYELOMA PATIENTS

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Background: Autologous/reduced-intensity conditioning allogeneic stem cell transplantation (SCT) has curative potential in multiple myeloma (MM), by combining the dual effect of the direct cytotoxicity of autologous SCT (ASCT) and the graft-versus-myeloma effect of reduced-intensity conditioning allogeneic SCT (RICallo-SCT).

Methods: This analysis included all consecutive patients with newly diagnosed high-risk (HR) MM who received a 2nd ASCT or a RICallo-SCT as intensified consolidation. The indication for performing a 2nd autologous or RICallo-SCT was the presence of <VGPR after 1st ASCT or a HR genetic profile with del(17p), t(4;14) and t(14;16). Additional del13q14 and R-ISS III were temporarily defined as HR. If an HLA identical donor was available, RICallo-SCT was preferred. The 2nd ASCT or RICallo-SCT was performed 3-6 months after the 1st ASCT. The RICallo regimen included fludarabine 30mg/m2 for 3 days plus total-body irradiation 2 Gy (analogous to Seattle Protocol). Prophylaxis of graft-versus-host disease (GvHD) consisted of cyclosporine and mycophenolate mofetil.

Results: 149 HR MM patients underwent a 2nd ASCT (n=84) or RICallo-SCT (n=65) between January 1, 2000 and December 31, 2022. 33 patients received graft from matched related donors (MRD) and 32 patients from matched unrelated donors (MUD).
Tandem-ASCT: with a median follow-up of 93 months of surviving MM patients, median progression-free survival (PFS) and overall survival (OS) were 36 and 78 months, respectively. The ≥VGPR rate rose from 61 (n=51) to 83% (n=70). The relapse mortality rate after one year was 4% and after ten years 46%. Non-relapse-mortality (NRM) was 0% at day 100, 1% (n=1) at one year and 11% (n=9) at ten years.
RICallo-SCT: median PFS and OS were 33 and 80 months, respectively. The ≥VGPR rate increased from 62 (n=40) after 1st ASCT to 86% (n=56) after RICallo-SCT. The relapse mortality rate after one year was 8% (n=5) and after ten years 39% (n=25). NRM was 12% (n=8) at day 100, 15% (n=10) at one year and 25% (n=16) at ten years. Acute GvHD and treatment-related complications were the only reason of the 10 NRM in the first year.
MRD- vs. MUD-RICallo: There was no difference in median PFS between MUD and MRD groups (26 vs 33 months; p=0.4). However, patients in the MUD cohort had an inferior median OS compared to the MRD cohort (46 vs 107 months; p<0.05). The reason for the different OS was the significantly higher occurrence of acute GvHD-triggered deaths in the MUD (n=9; 28%) than in the MRD group (n=1; 3%) (p<0.01).
MRD-RICallo vs Tandem-ASCT: Compared to the Tandem-ASCT group, a trend for better OS was observed in the MRD RICallo group in the long-term follow-up from 36 months onwards. One reason for this is the slightly higher relapse mortality in the Tandem-SCT patients (n=38; 46%) compared to the MRD transplanted patients (n=11; 33%) in the first 10 years.

Conclusions: For selected patients with HRMM, MRD-RICallo-SCT according to the Seattle protocol is a treatment option. However, our results indicate that MUD carries a higher risk

due to a significantly increased treatment-related mortality rate and therefore cannot be recommended.

Clinical Trial Registry: Ethics Committee of the Medical Faculty, Leipzig University (IRB 00,001,750; registration number 118/18-e)

Disclosure: Nothing to declare.

B407

UPDATED EXPLORATORY MULTIVARIABLE ANALYSES DEMONSTRATE DIFFERENTIAL IMPACT OF DUFFY GENOTYPE ON PROGRESSION-FREE SURVIVAL WITH LENALIDOMIDE-BORTEZOMIB-DEXAMETHASONE (RVD) ALONE OR RVD+ASCT IN NEWLY DIAGNOSED MULTIPLE MYELOMA (NDMM)

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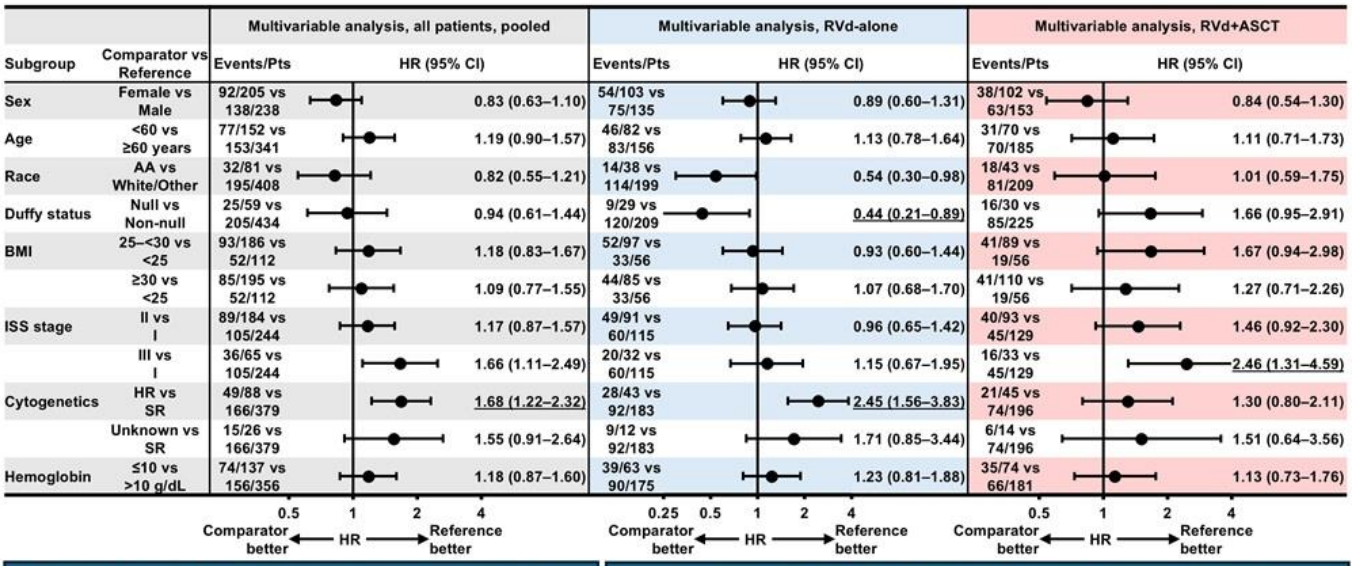
Background: The erythrocyte Duffy null phenotype, which is associated with lower absolute neutrophil count, plays a key role in cytokine homeostasis, and has known effects on the inflammasome, is present in ~66% of African American (AA) and <1% of White patients and may impact MM pathobiology. We previously reported analyses of progression-free survival (PFS) by Duffy genotype in an initial cohort in the DETERMINATION phase 3 trial (Merz, EBMT 2025) exploring Duffy null status as a pathobiological explanation for differential relative PFS with RVd-alone vs RVd+ASCT in White (n=540/722, 74.8%; median 44.3 vs 67.2 months; hazard ratio [HR] 1.67, 95%CI 1.29–2.15) and AA patients (n=132/722, 18.3%; median not reached [NR] vs 61.4 months; HR 1.07, 95%CI 0.61–1.89), in the context of enhanced access to care in DETERMINATION and race being a social construct. We report updated findings in an expanded cohort of ~500 patients.

Methods: Patients were classified as C/C (Duffy null) or non-C/C (Duffy non-null) based on genomics analysis of baseline peripheral blood samples for SNP rs2814778. PFS was evaluated, overall and by treatment, with Cox proportional hazards regression in univariate and multivariable models, with heterogeneity of treatment effect assessed by a test for interaction.

Results: Of 592 enrolled patients with data on Duffy status, 12% (n=71) had the Duffy null genotype (AA: 63.3%, n=62/98; White/other race: 1.1%, n=5/465). Of these, 493 were randomized (68.3% of intent-to-treat population) to RVd-alone (n=238) and RVd+ASCT (n=255); the cohort was broadly representative of the intent-to-treat population. Of the 493 patients, 53/81 (65.4%) AA and 5/408 (0.4%) White/other race patients were Duffy null (Table 1). In Duffy null vs non-null patients, pooled PFS (arms combined) was similar (median 56.7 vs 62.5 months; HR 0.94, 95%CI 0.62–1.42). In Duffy non-null patients, PFS with RVd-alone vs RVd+ASCT (120/209 vs 85/225 events/patients; median 46.7 vs 67.5 months; HR 1.76, 95%CI 1.33–2.34) favored RVd+ASCT. Findings were consistent in an analysis of the limited number of AA Duffy non-null patients (6/13 vs 3/15 events/patients; median PFS 64.4 months vs NR; HR 5.29, 95%CI 1.20–23.4). In Duffy null patients, PFS with RVd-alone vs RVd+ASCT (9/29 vs 16/30 events/patients; median NR vs 44.0 months; HR 0.64, 95%CI 0.27–1.50; Duffy status interaction p-value 0.005) was not significantly different, but the HR favored RVd-alone. A similar trend was observed in AA Duffy null patients (8/25 vs 15/28 events/patients; median PFS NR vs 45.3 months; HR 0.66, 95%CI 0.27–1.60). On multivariable analysis (Figure), Duffy null vs non-null was a significant prognostic factor for longer PFS with RVd-alone with a lower HR (0.44) than for AA vs White/other race (HR 0.54).

Baseline patient and disease characteristics by Duffy status were assessed for imbalances

	RVd-alone, n=238		RVd+ASCT, n=255		All, N=493	
Characteristic	**Duffy null, n=29 (12.2%)**	**Duffy non-null, n=209 (87.8%)**	**Duffy null, n=30 (11.8%)**	**Duffy non-null, n=225 (88.2%)**	**Duffy null, n=59 (12.0%)**	**Duffy non-null, n=434 (88.0%)**
Median age, y	56.0	57.0	57.5	54.0	57.0	56.0
Age ≥60 y, %	24.1	35.9	36.7	26.2	30.5	30.9
Male, %	24.1	61.2	63.3	59.6	44.1	60.4
AA / White, other, %	86.2 / 13.8	6.3 / 93.8 (n=208)	96.6 / 3.4 (n=29)	6.7 / 93.3 (n=223)	91.4 / 8.6 (n=58)	6.5 / 93.5 (n=431)
ECOG PS >0, %	55.2	57.9	50.0	49.3	52.5	53.5
BMI ≥30 kg/m^2, %	44.8	34.4	60.0	40.9	52.5	37.8
ISS I / II / III, %	58.6/37.9/3.4	46.9/38.3/14.8	46.7/36.7/16.7	51.2/36.4/12.4	52.5/37.3/10.2	49.1/37.3/13.6
LDH >ULN, %	20.7	20.1	33.3	18.8 (n=224)	27.1	19.4 (n=433)
HR cytogenetics, %	28.0 (n=28)	18.2 (n=198)	13.3	19.4 (n=211)	19.0 (n=58)	18.8 (n=409)
R-ISS I / II / III, %	32.1/67.9/0 (n=28)	31.8/60.6/7.6 (n=198)	26.7/60.0/13.3	33.3/62.9/3.8 (n=210)	29.3/63.8/6.9 (n=58)	32.6/61.8/5.6 (n=408)
Hemoglobin ≤10 g/dL, %	37.9	24.9	53.3	25.8	45.8	25.3
Median ANC x10^9L (IQR)	3.1 (2.1–4.4)	3.4 (2.8–4.7)	2.6 (2.2–4.2)	3.3 (2.4–4.4)	2.8 (2.1–4.3)	3.4 (2.6–4.6)



*Race and Duffy status were included along with the same additional variables in separate multivariable analyses. Data shown for other variables (sex, age, BMI, ISS stage, cytogenetics, hemoglobin) are from the multivariable analysis incorporating Duffy status; findings were consistent in the multivariable analysis incorporating race.

Conclusions: Duffy status was associated with a differential treatment effect more pronounced than previously observed by race in these exploratory analyses of DETERMINATION. In Duffy non-null patients, PFS favored RVd+ASCT, but in Duffy null patients, PFS HRs favored RVd-alone, with similar trends in analyses restricted to AA patients. In multivariable analyses, Duffy status was prognostic for PFS with RVd-alone and a stronger prognostic factor than race.

Clinical Trial Registry: NCT01208662, www.ClinicalTrials.gov

Disclosure: **Lauren Merz:**Consultancy: 23andMe,Johnson & Johnson. **Rebecca Zon:**Consultancy,Stock options: Triveni Bio. **Susanna Jacobus:**None. **Mehmet Samur:**Consultancy: NCGM genome,K36 Therapeutics,AbbVie. **Jeffrey Zonder:**Consultancy: Regeneron,BMS,Prothena,Janssen; Research Funding: BMS,RLL LLC,Janssen; Current Employment (spouse): BMS. **Abdullah Khan:**Research Funding: Sanofi,BMS; Honoraria: Sanofi,Amgen. **Hani Hassoun:**None. **Larry Anderson:**Consultancy: Pfizer,BMS,BeiGene,Sanofi,Amgen,Karyopharm,Celgene,Prothena,Cellectar,Johnson & Johnson,GSK,AbbVie; Research Funding: BMS,BeiGene,AbbVie; Honoraria: BMS,BeiGene,Sanofi,Amgen,Karyopharm,Celgene,Prothena,Cellectar,Johnson & Johnson,GSK,AbbVie. **Yvonne Efebera:**Honoraria: Pfizer,GSK,Kite,Janssen,Sanofi,BMS,Orca,Oncopeptides; Research Funding: Pharmacyclics (via Alliance),GSK (via Alliance). **Tondre Buck:**None. **Racquel Innis-Shelton:**None. **Monique Hartley-Brown:**Consultancy: IMF,GSK,Amgen,Alliance,Pfizer,MMRF,BMS/Celgene,Sanofi; Research Funding: Karyopharm,GSK,Amgen,Johnson & Johnson,Pfizer,MMRF,BMS/Celgene,Sanofi; Honoraria:

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B408

SOLUBLE BCMA AS AN EMERGING BIOMARKER IN BCMA T-CELL-REDIRECTING THERAPIES

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Background: Soluble BCMA (sBCMA) is a promising biomarker for monitoring tumour burden and treatment response in multiple myeloma (MM) patients treated with BCMA T-cell-redirecting therapies; however, its clinical utility remains insufficiently established in routine practice, while potentially enabling early and dynamic assessment of clinical benefit.

Methods: We conducted a prospective observational study including 36 MM patients treated with BCMA-directed CAR-T cells (n=20) or bispecific antibodies (n=16) between March 2022 and October 2024. Clinical and laboratory variables, treatment characteristics, tumour burden markers, sBCMA levels measured by ELISA, and response according to the International Myeloma Working Group 2016 criteria were collected at baseline, pre-infusion/initiation, day +28, day +56, day +100, month 6, month 12, and progression. The statistical analysis was performed to address the study objectives: to explore its correlation with classical tumour burden markers, to assess the clinical value of sBCMA as a dynamic biomarker and to characterize early kinetic differences between responders and those who subsequently progressed.

Results: Baseline characteristics are shown in **Table 1**. Regarding correlation with tumour markers, baseline sBCMA demonstrated a moderate association with bone marrow plasma cell infiltration ($\rho = 0.41$; $p = 0.011$) and with serum monoclonal protein ($\rho = 0.34$; $p = 0.040$), while no significant correlations were found with other tumour burden or inflammatory markers. sBCMA levels decreased markedly by month 1 across the cohort, followed by stabilisation in patients who maintained clinical response. In contrast, persistently elevated or rising values over sequential timepoints were consistently observed in those who later experienced progression. When analysed by treatment modality, both CAR-T and bispecific-treated patients showed comparable overall dynamic patterns, with an early and deeper decline more frequently observed following CAR-T therapy. These trajectories support the role of sBCMA as a dynamic marker in the monitoring of patients receiving BCMA-directed therapies. Finally, when assessed according to clinical response, patients achieving at least partial response showed a mean decrease in sBCMA at month 1 from baseline of 42.5 ng/mL, whereas non-responders exhibited a mean increase of 29.7 ng/mL, indicating a clear separation between responder and non-responder profiles at early treatment timepoints (**Figure 1**).

	Total (N=36)	CAR-T (n=20)	Biespecific (n=16)	p-valor
Age, median years (range)	62 (39 - 82)	57 (39-75)	67 (51-82)	0.005
Sex, male (%)	22 (61.1%)	10 (50%)	12 (75%)	0.126
Involved isotype, IgG (%)	21 (58.3%)	11 (55%)	10 (62.5%)	0.650
Involved light chain, kappa (%)	19 (52.8%)	11 (55%)	8 (50%)	0.765
R-ISS **- I** **- II** **- III**	6 (16.7%) 20 (55.6%) 10 (27.8%)	3 (15%) 12 (60%) 5 (25%)	2 (12.5%) 10 (62.5%) 4 (25%)	0.871
Pure extramedullary disease (%)	3 (8.3%)	2 (10%)	1 (6.25%)	1
Prior therapies **- Number of prior lines (range)** **- Triple-class exposed (%)** **- Triple-class refractory (%)**	3 (0-7) 33 (91.7%) 30 (83.3%)	3 (0-6) 17 (85%) 16 (80%)	3 (2-7) 16 (100%) 14 (87.5%)	0.974 0.238 0.672
Baseline disease burden **- Bone marrow plasma cell infiltration, median % (range)** **- Serum monoclonal component, median g/dL (range)** **- Free light chain kappa, median mg/L (range)** **- Immunoglobulin G, median mg/dL (range)**	9.5 (0-86) 1.2 (0-3.9) 14 (0.4-4845.1) 1265 (118-4990)	8.5 (0-86) 1.3 (0-2.7) 13.9 (0.7-1194.5) 1470 (140-3300)	15.5 (0-58) 1 (0-3.9) 61.1 (0.4-4845.1) 901 (118-4990)	0.689 0.554 0.714 0.774

Soluble BCMA, median (range)	61.6 (12.8-176)	66.7 (12.8-118.4)	52.8 (15.1-176)	0.787

Table 1. Baseline clinical characteristics, disease burden parameters and soluble BCMA levels in patients treated with BCMA-directed CAR-T cells and bispecific antibodies.

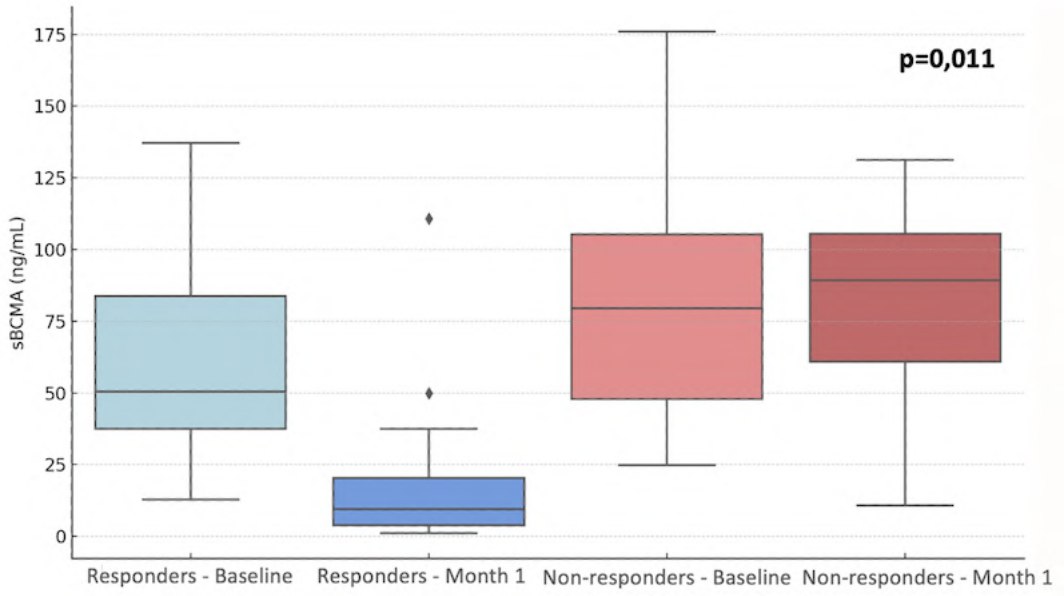

Figure 1. Distribution of sBCMA levels at baseline and month 1 in responders and non-responders treated with BCMA-directed therapies.

Conclusions: sBCMA is a serum biomarker that correlates with established tumour burden indicators. The results of this study demonstrate its value as a dynamic biomarker with early and distinct response patterns, suggesting that it may serve as an early response-predictive biomarker. Although further studies are required to validate these findings, they support its potential incorporation into monitoring strategies for MM patients treated with BCMA-redirecting approaches.

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B409

THE EXPERIENCE OF AUTOSCT IN PATIENTS WITH MULTIPLE MYELOMA ON DIALYSIS

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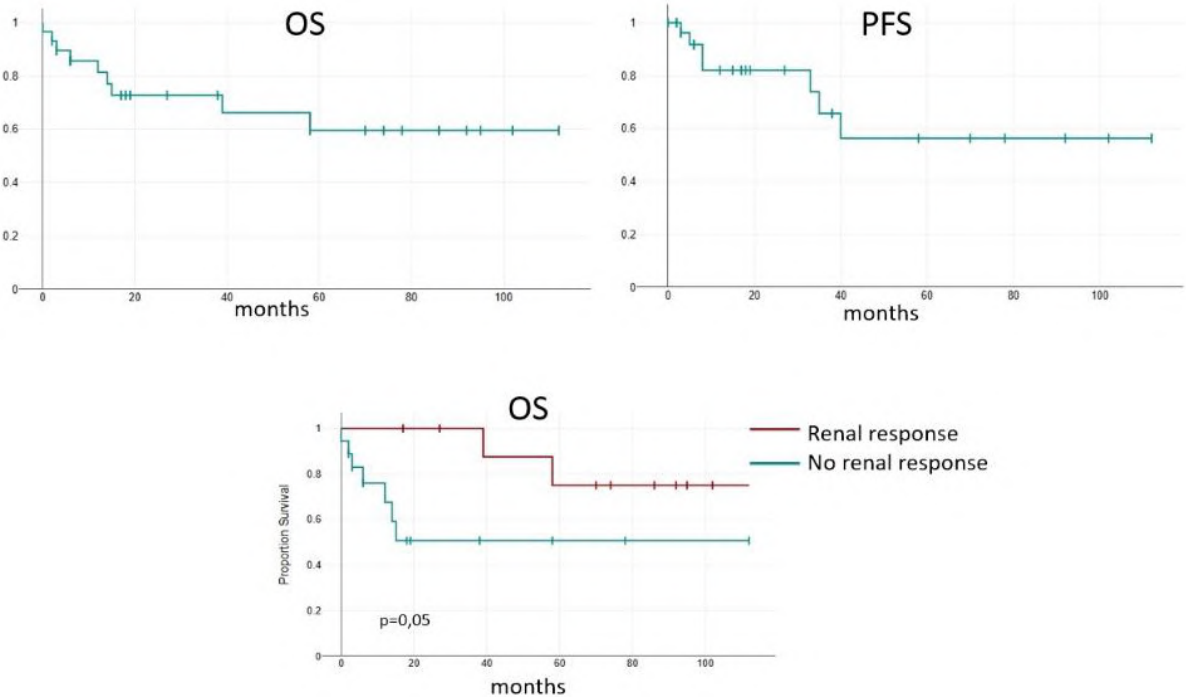
Background: Renal failure is a common complication of multiple myeloma. Only 20% of patients achieve independence from dialysis during induction therapy. Auto-HSCT remains a key step in the treatment of multiple myeloma, but patients on dialysis are often excluded from high-dose therapy protocols due to treatment-related toxicity.

Methods:

From 2015 to 2025, 29 patients in age 39-66 years (median 58) on hemodialysis underwent autoSCT at the Moscow Clinical Science and Research Center 52. 6 pts underwent tandem transplantation. 8 patients (27%) had high cytogenetic risk mutations.All patients were on program hemodialysis at the time of autoSCT, with a median GFR of 11.2 ml/min/1.73m2. Anuria was observed in 4 patients (14%), oliguria in 5 (17%), and normal diuresis in 20 patients (69%). In induction patients received bortezomib (100%), lenalidomide-containing courses - 17 patients (59%), anti-CD38-monoclonal antibodies - 8 pts (27%). Before auto-HSCT 11 patients (38%) achieved CR, 11 patients (38%) - VGPR, 7 (29%) - PR. High doses of cyclophosphamide or etoposide with G-CSF were used to mobilize PBSC. Pretransplant conditioning was carried out with melphalan at a dose of 140 mg/m2 (10 patients (34%), 19 patients (66%) added bendamustine 150 - 200 mg/m2 to melphalan. Median number of transfused PBSC: 4.5*10^6 CD34+ cells/kg.

Results: The median of leukocyte engraftment was 12 days (7 - 35 days). Infectious complications are represented by mucositis grade 3-4 (13 patients (45%), pneumonia (4 patients (14%)), sepsis (12 patients (41%)), clostridial colitis (3 patients (10%). Reactivation of HSV-1,2, HHV-6 and CMV infection was noted in 8 patients (27%). Non-infectious complications included gastrointestinal bleeding (1 patient), toxic cardiomyopathy (1 patient), atrial fibrillation (1 patient) and delirium (2 patients). Invasive aspergillosis was diagnosed in 1 patient. Transplant-associated mortality was 7% (2 patients). On day +100 after autologous T-cell therapy, all patients showed a deepening of the response: 19 (66%) patients achieved CR, 3 (10%) achieved VGPR, and 2 (7%) maintained PR. 11 patients (38%) achieved renal response and independence from dialysis, and 2 patients managed to reduce the frequency of dialysis to 2 times per week.
Renal response was achieved in patients with normal diuresis, but not in patients with oligo- and anuria (p=0.019). 2 patients subsequently underwent allogeneic kidney transplantation. In patients who achieved a renal response, there was no progression of renal failure even after the development of MM relapse.
The median follow-up was 18 months (1-112 months). The median OS and PFS were not reached.



3-year OS in patients who achieved renal response is significantly higher than in patients who remained on dialysis (100% vs.50%, p=0.05).

Adding bendamustine to the conditioning did not improve the OS and PFS in dialysis patients.

Conclusions: Dialysis-dependent renal failure in MM patients is not a contraindication to autologous SCT. AutoSCT promotes a deeper hematological response, and achieving a renal response and independence from hemodialysis in patients. Adding bendamustine to conditioning does not have an advantage over melphalan monotherapy in patients with dialysis-dependent renal failure.

Disclosure: No disclosure.

B410

BORTEZOMIB MAINTENANCE AFTER ALLOGENEIC TRANSPLANT IN NEWLY DIAGNOSED MYELOMA PATIENTS: LESS CHRONIC GVHD BUT NO IMPACT ON SURVIVAL

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Background: Despite modern therapies, allogeneic (allo) hematopoietic cell transplantation (HCT) remains the only potentially curative approach for MM, unfortunately associated with a high rate (>50%) of relapse. Maintenance therapy could potentially prolong survival and decrease relapse, but its role following allo HCT remains unclear.

Methods: We retrospectively compared the outcomes of newly diagnosed MM patients who underwent upfront tandem autologous (auto) transplant followed 3-4 months later by a nonmyeloablative allo HCT with or without maintenance with bortezomib (BTZ) 1.3 mg/m^2 SC every 2 weeks x 26 doses initiated on D+120 (R. LeBlanc et al. BMT 2022). Patients without partial response to induction therapy, to auto HCT or with progressive disease before allo HCT were excluded. Primary endpoints included comparison of overall survival (OS) and progression-free survival (PFS). Secondary endpoints included relapse, non-relapse mortality (NRM), incidences of acute and chronic GVHD, probability to receive systemic immunosuppressants (IS) post HCT and risk factors for relapse.

Results: Among 176 newly diagnosed MM patients who received upfront auto/allo HCT between May 2001 and December 2024 from an 8/8 sibling or unrelated donor, 116 received no maintenance while 60 patients had at least one dose of BTZ. Both cohorts were comparable for age, sex distribution and staging. More patients in the BTZ group had high-risk cytogenetics (defined as t(4;14) with ISS II or III, del(17p13), t(14;16), t(14;20) and chromosome 1 abnormalities regardless of ISS in ≥10% plasma cells at diagnosis). Most common induction regimen was VAD (59.5%) in the no BTZ and CyBorD (77%) in the maintenance group. Sibling donors were more common in the no-BTZ group (91% vs 35%). More patients in the BTZ group achieved ≥VGPR prior (92% vs 69%; $p< 0.0001$) and after allo HCT (98% vs 90%; $p< 0.0001$). Median follow-up was 16.0 years (95%CI: 15.0-17.1) in the no-BTZ group and 7.4 years (95%CI: 6.1-7.9) in the BTZ group. OS and PFS at 5 years were comparable at 79.9% in no-BTZ group vs 82.2% with BTZ and 54.2% vs 48.6%, respectively (Fig.1 A, B), with no impact of ISS or cytogenetics. Patients achieving complete response status post allo HCT had significant higher PFS compared to those with VGPR in both groups. NRM at 5 years was similar in both groups (8% vs 5.8%, $p=0.72$). We observed no difference in incidence of grade II-IV acute GVHD (17.2% vs 16.7%, $p=0.97$), but moderate/severe chronic GVHD was significantly lower following BTZ (46.7% vs 80.2%; $p< 0.0001$), with delayed onset (6.5 months vs 4.9 months; $p< 0.0001$), leading to reduced IS intake at 3 years (25% vs 54.5%; $p< 0.01$, Fig. 1C). Chronic GVHD had no significant impact on either OS or PFS in patients receiving BTZ maintenance.

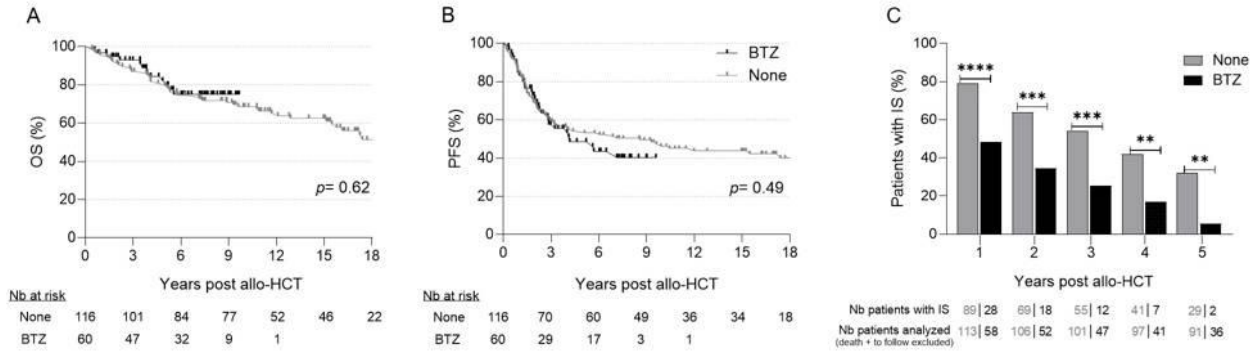

Figure 1. (A) Kaplan-Meier estimates of overall survival (OS) and (B) progression-free survival (PFS) in patients receiving BTZ maintenance or not. (C) Probability of taking oral systemic immunosuppressants after allogeneic transplant in patients with and without BTZ maintenance (Chi square or Fisher test: **p<0.01; ***p<0.001; ****p<0.0001).

Conclusions: BTZ maintenance in newly diagnosed MM patients receiving upfront tandem auto/allo HCT was associated with lower chronic GVHD incidence, reduced IS intake, but no impact on survival despite more patients with high-risk cytogenetics in this group. More effective novel maintenance strategies in the post-allo transplant setting are required to decrease relapse.

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SC: consultancy for the clinical program of ExCellThera, royalties from the sales of UM171
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Other authors declare non-conflict of interest

B411

AUTOLOGOUS STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA: A 10-YEAR SINGLE-CENTER EXPERIENCE

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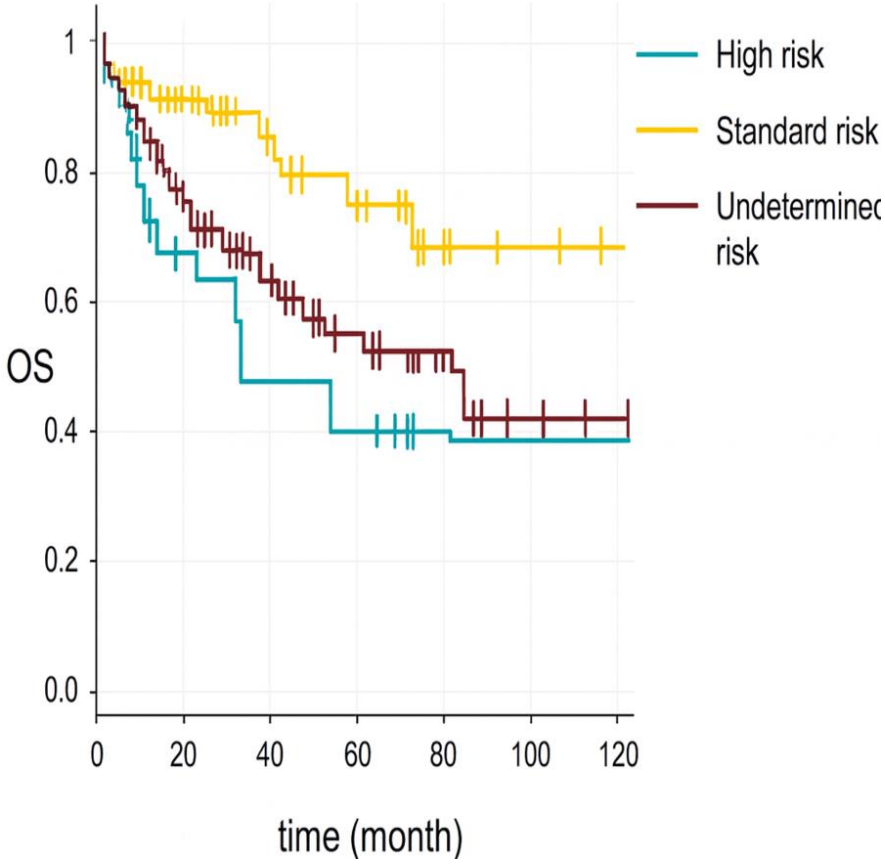
Background: Multiple myeloma (MM) is one of the most common hematologic malignancies. Autologous hematopoietic stem cell transplantation (ASCT) is the gold-standard consolidation therapy for eligible MM patients. This retrospective single-center study evaluates short- and long-term outcomes in MM patients undergoing ASCT between 2015 and 2025.

Methods: Retrospective analysis of N=314 MM patients (442 ASCTs; 138 tandem) treated from 2015 to 2025 at our center. Patient characteristics: median age 59 years (range 22–72); 49% male; 19% with high-risk cytogenetics; 35% with soft-tissue (extramedullary) disease; median 2 prior therapy lines (range 1–5). Conditioning regimen was Melfalan (N=212), Melfalan+Bendamustin (N=230). Transplant details: median CD34+ cell dose 4.3×10^6/kg; median neutrophil engraftment 13 days; platelet engraftment 13 days. Median follow-up was 16 months (range 1–118).

Results: Overall outcomes: median OS not reached; median PFS 57 months. Three-year OS ~73%; PFS ~62%. Risk stratification: Standard-risk patients had better survival than high-risk patients. Three-year OS was 92.3% (standard) vs 54% (high); three-year PFS was 80% vs 48%. Soft-tissue involvement: Patients without extramedullary disease had better outcomes. Three-year OS 82% (no soft tissue) vs 70%; PFS 65% vs 45%. Pre-transplant response: Patients with ≥VGPR before ASCT had better PFS (3-year PFS 64%) than those with <VGPR (37.7%). Tandem ASCT: Improved outcomes were observed in patients with soft-tissue disease and in those not in complete remission before ASCT. In patients with soft tissue desease OS tandem vs mono ASCT was 70% vs 45% ($p<0.05$), PFS 60% vs 25% ($p<0.05$). Conditioning regimens: In high-risk or soft-tissue subgroups, melphalan + bendamustine showed a trend toward better survival than melphalan. For high cytogenetic group OS Melfalan vs Melfalan+Bendamustine was 40% vs 70% ($p>0.05$), PFS 18% vs 50% ($p>0.05$). For soft tissue subgroup group OS Melfalan vs Melfalan+Bendamustine was 45% vs 50% ($p>0.05$), PFS 19% vs 61% ($p>0.05$). Transplant mortality: early ASCT-related t mortality was 3.2%, in this group infection as a reason 84%. Progression desease 16%.



Conclusions: ASCT remains a critical therapeutic modality for multiple myeloma, yielding high short- and long-term survival rates in a contemporary cohort. Long-term follow-up data highlight the importance of risk stratification and can inform optimized transplant strategies. The addition of bendamustine to melphalan conditioning may improve outcomes in high-risk or extramedullary MM, though differences were not statistically significant. Further larger studies are needed and are planned to validate these findings and refine treatment protocols at our center.

Disclosure: Nothing to declare.

B412

PROGNOSTIC DIFFERENCES AMONG PATIENTS WITH MULTIPLE MYELOMA UNDERGOING UPFRONT AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN JAPAN, TAIWAN, AND MALAYSIA: IMPACT OF PRE-TRANSPLANT PI/IMID-BASED THERAPIES

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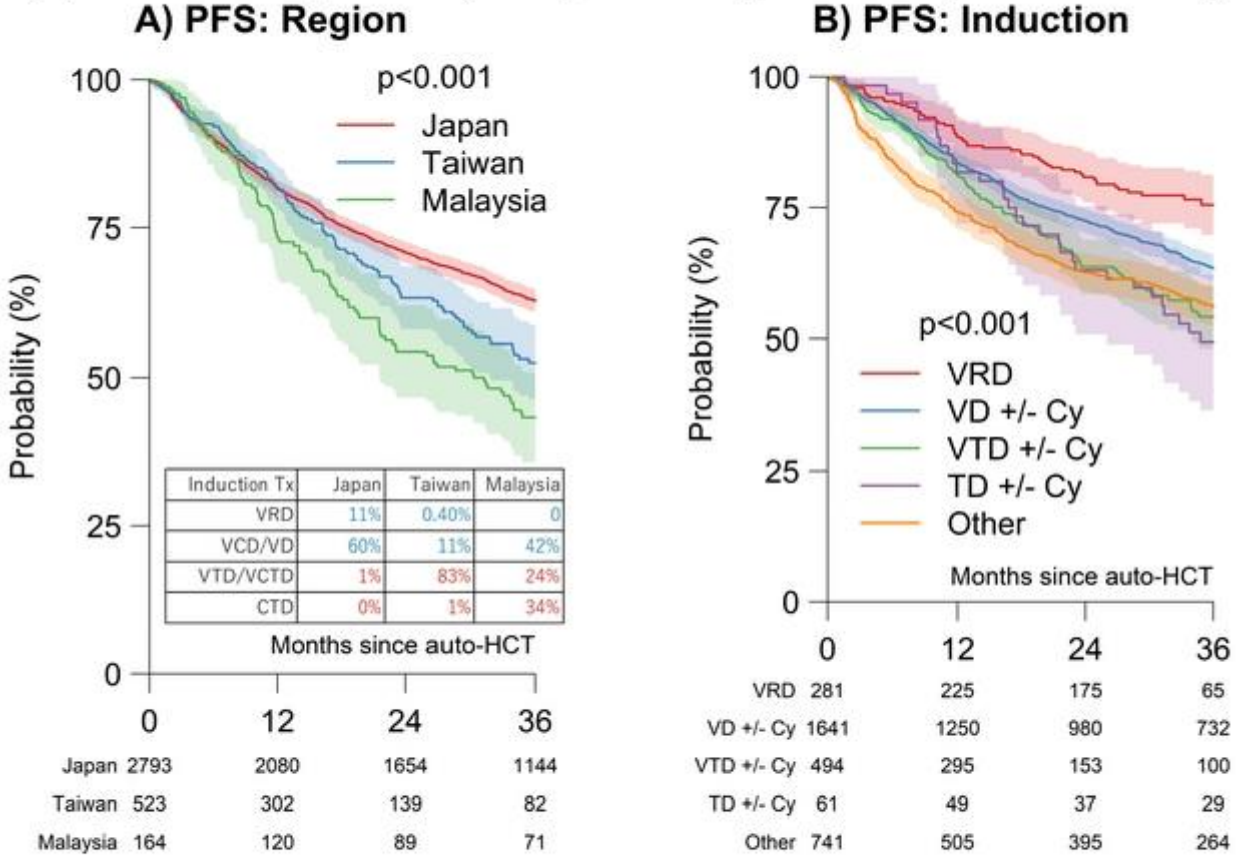
Background: Autologous hematopoietic cell transplantation (AHCT) is considered standard of care in eligible, newly diagnosed multiple myeloma (NDMM) patients after induction therapy. In our previous publication on more than 60000 patients worldwide (Garderet et al., AJH 2024) marked outcome differences were noted between regions and countries for progression-free survival (PFS) (Figure 1A) and overall survival (OS). Because of missing information on pre-transplant therapy, we collected and analyzed the impact of pre-transplant induction therapy from three Asia-Pacific countries with marked outcome differences.

Methods: NDMM patients undergoing upfront AHCT from 2013–2017 were collected through the Worldwide Network for Blood and Marrow Transplantation and the Asia-Pacific Blood and Marrow Transplantation Group. Endpoints included OS (primary) as well as PFS, relapse incidence, and non-relapse mortality (secondary). Kaplan–Meier and log-rank tests were used for survival comparisons. Cox multivariate analyses (MVA) and 6-month landmark models were applied, adjusting for baseline differences.

Results:

Figure 1. PFS according to (A) Japan, Taiwan and Malaysia and (B) induction regimens (VRD, VD+/-Cy, VTD+/-Cy and TD+/-Cy)



A total of 3,820 patients were evaluated (Japan n=3,127; Taiwan n=524; Malaysia n=169) with a median follow-up of 46 months. Induction therapies differed substantially between the Asian countries. In Japan VCD was used in 35%, VD in 24.8% and VRD in 11% of the patients. In Taiwan VTD was administered to 72.1% and in Malaysia VCD in 42.0%, CTD in 29.6% and VTD in 23.7%. The proportion of patients who received maintenance varied across countries and resulted in 100% in Taiwan (1.2% lenalidomide and 30.5% thalidomide), in 32.7% in Malaysia (4.2% and 21.4%, respectively) to 7.1% in Japan (5.2% and 0%, respectively). Induction regimens were significantly associated with PFS and OS (p<0.001) after AHCT (Figure 1B). VRD showed the highest 36-month PFS (76%, 95% CI 70-81%) versus VCD/VD (63%, 95% CI 61-66%), VTD/VCTD (54%, 95% CI 48-60%) and

CTD/TD (49%, 95% CI 37-62%). OS at 36 months was likewise superior with VRD (89%, 95% CI 85-93%) compared with VCD/VD (85%, 95% CI 83-87%), VTD/VCTD (75%, 95% CI 70-80%) and CTD/TD (72%, 95% CI 60-83%). In 6-month landmark analysis, lenalidomide maintenance showed better PFS (70% vs 64%) and OS (90% vs 84%) compared with no maintenance. In MVA, VRD was associated with significantly improved PFS compared with VTD/VCTD (HR 0.68, 95% CI 0.49, 0.93, P = 0.02) and improved OS compared with VTD/VTCD (HR 0.56, 95%CI 0.34, 0.91, P = 0.02). Differences in PFS and OS between VRD and VCD/VD were not statistically significant. Probably due to the small number of patients who received lenalidomide maintenance (n = 87), it showed only a trend toward improved OS (HR 0.49; 95% CI, 0.20–1.20; P = 0.12) in the adjusted MVA.

Conclusions: VRD induction was associated with superior PFS and OS compared with VTD/VTCD, contributing to observed international outcome differences. Maintenance using lenalidomide or thalidomide was not significant. Access to lenalidomide—both for induction and maintenance—varied markedly across countries and likely influenced prognosis. National approval and reimbursement policies enabling consistent access to PI/IMiD-based therapies are essential for optimizing outcomes in MM patients undergoing ASCT.

Clinical Trial Registry: Not aplicable

Disclosure: Consultancy: Takanori Teshima reports consultancy from Kyowa Kirin, Nippon Shinyaku, Takeda, Roche Diagnostics, and Meiji Seika Pharma.
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Honoraria: Hiroyuki Takamatsu has received honoraria from J&J, Sanofi, and Bristol-Myers Squibb; Shohei Mizuno has received honoraria from J&J, Sanofi, and Bristol-Myers Squibb; Takanori Teshima has received honoraria from AbbVie, Astellas, AstraZeneca, Asahi Kasei Pharma, Kyowa Kirin, Novartis, Chugai, Gilead, Pfizer, Janssen, Otsuka, Bristol-Myers Squibb, Takeda, Daiichi Sankyo, Nippon Shinyaku, MSD, Meiji Seika Pharma, Nippon Kayaku, SymBio, Genmab, Sanofi, Amgen, Kissei, Pharma Essentia Japan, Ono, and Roche Diagnostics; Damiano Rondelli has received honoraria from Vertex.
All other authors declare no conflicts of interest.

B413

COMPARISON OF DARA-VTD AND TRIPLE THERAPY AS INDUCTION REGIMENS PRIOR TO AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION IN NEWLY DIAGNOSED MULTIPLE MYELOMA

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Background: Daratumumab combined with bortezomib, thalidomide, and dexamethasone (Dara-VTD) has emerged as an effective first-line induction regimen for patients with newly diagnosed plasma cell myeloma (PCM). However, real-world data comparing its efficacy and safety with standard bortezomib-based triplet therapies prior to autologous hematopoietic cell transplantation (AHCT) remain limited. This single-center retrospective study compares outcomes of patients undergoing AHCT after induction with either four cycles of Dara-VTD or four to six cycles of bortezomib-based triplet therapy without daratumumab.

Methods:

We analyzed 224 consecutive patients with newly diagnosed PCM who underwent AHCT. Of these, 112 patients received Dara-VTD between 2023 and 2025, and 112 received bortezomib-based triplet therapy (TT) between 2019 and 2024, predominantly VTD (n=80). The median age was 62 years (IQR: 56–66). The groups were comparable with respect to age, sex, cytogenetic risk, and type of monoclonal protein. Patients in the Dara-VTD group had a significantly higher baseline disease burden, reflected by higher International Prognostic Scoring System (IPSS) scores (median 3 vs. 2; p=0.0372) and Revised International Staging System (R-ISS) stages (median 3 vs. 2; p=0.0011).

Results:

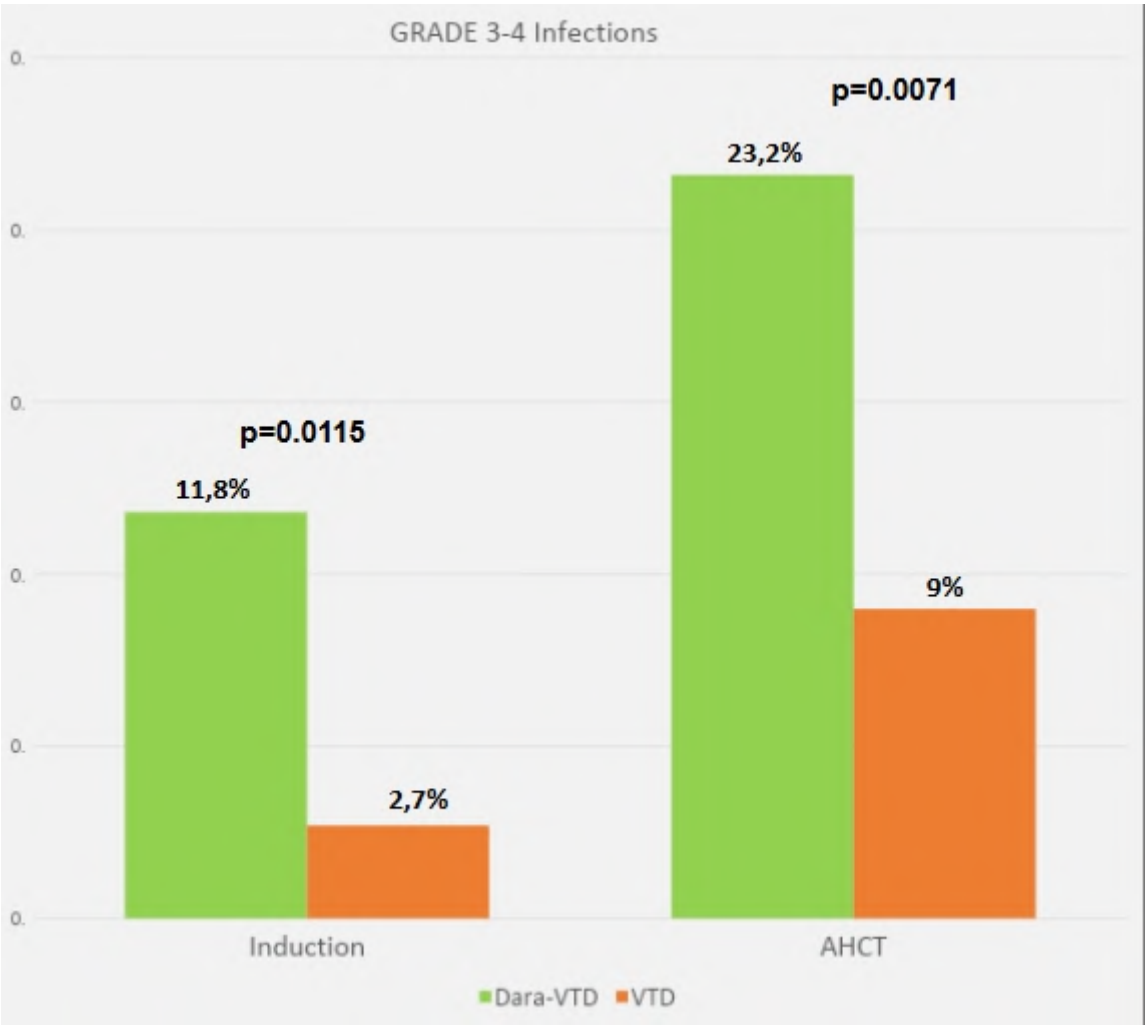
A significantly higher proportion of patients treated with four cycles of Dara-VTD achieved at least a very good partial response (VGPR) prior to AHCT compared with the TT group (89% vs. 73%; p=0.0002). Minimal residual disease (MRD) negativity assessed by multicolor flow cytometry with a sensitivity of 10^{-6} was also more frequent in the Dara-VTD group (46% vs. 18%; p=0.0001). Grade 3–4 infections during induction therapy occurred more often in patients receiving Dara-VTD (16.96% vs. 2.7%; p=0.0095).

During AHCT, patients in the Dara-VTD group achieved higher $CD34^+$ cell yields and received a higher median number of infused $CD34^+$ cells (4.42 vs. 3.66 $\times 10^6$/kg; p=0.0063). Despite this, hematopoietic recovery was delayed. Median neutrophil engraftment occurred on day +12 in the Dara-VTD group compared with day +11 in the TT group (p<0.0001), and platelet recovery was delayed to day +14 versus day +12, respectively (p<0.0001). Grade 3–4 infections during the transplantation period were significantly more frequent in the Dara-VTD group (23.2% vs. 9%; p=0.0071). No early transplant-related mortality was observed in either group. Most infectious complications were of bacterial etiology.

Conclusions:

Induction with four cycles of Dara-VTD results in significantly deeper responses, including higher MRD-negative rates, prior to AHCT in newly diagnosed PCM. However, these benefits are accompanied by an increased incidence of severe infectious complications during both induction and transpla
ntation, as well as delayed hematopoietic recovery. The relationship between delayed neutrophil recovery, daratumumab exposure, and infection risk warrants further investigation. In addition, the impact of daratumumab on overall hematopoietic reconstitution during AHCT requires further evaluation. While Dara-VTD improves depth of response, its adverse hematologic and infectious effects during transplantation highlight the need for refined risk stratification and optimized supportive care strategies. Future studies should focus on identifying predictors of toxicity to improve the safety of this highly effective

regimen.



Disclosure: Nothing to declare.

P290

IS THERE STILL A CURATIVE ROLE FOR ALLOGENEIC TRANSPLANTATION IN MULTIPLE MYELOMA? LONG-TERM OUTCOMES IN YOUNG PATIENTS UNDERGOING HLA-IDENTICAL ALLOGENEIC HAEMATOPIETIC STEM CELL TRANSPLANT

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Background: The role of allogeneic haematopoietic stem cell transplantation (allo-HSCT) in multiple myeloma (MM) remains controversial in the era of novel agents, mainly due to concerns regarding non-relapse mortality (NRM) and relapse. However, durable remissions and long-term survival suggest a potential curative role in selected patients, particularly when transplanted young and in early treatment phase. Herein we report the long-term overall survival (OS), relapse-free survival (RFS), graft-versus-host disease–free relapse-free survival (GRFS), and cumulative incidence of relapse and NRM in a cohort of young MM patients exposed to bortezomib- and/or thalidomide-based therapies.

Methods: We retrospectively analysed 46 MM patients aged <65 years (median age 53.7, range 33–63) undergoing allo-HSCT with curative intent at our institution. All patients had received prior treatment with proteasome inhibitors and/or immunomodulatory drugs. Conditioning was myeloablative in 36.9% and reduced-intensity in 63.1%. Donors were HLA-identical siblings (matched related donor - MRD) in 43.5% and unrelated donors (MUD) in 56.5%. Nearly half of the patients (47.8%) underwent allo-HSCT within the first two lines of therapy. OS, RFS and GRFS were estimated by Kaplan–Meier analysis, while cumulative incidence of relapse and NRM were assessed using competing-risk models. Long-term follow-up was available for surviving patients.

Results: With extended follow-up exceeding 10 years, median OS was 33.8 months for the entire cohort, with evidence of a long-term survival plateau. Median RFS was 36.5 months, while median GRFS was 12.5 months. Five- and ten-year overall survival were approximately 40% and 25%, respectively, while non-relapse mortality stabilised at around 25% within the first 24 months after transplantation. Acute GVHD occurred in approximately 60% of patients, most commonly grade II–III, and chronic GVHD developed in 25% of cases, frequently with multi-organ involvement (moderate 90%, severe 10%). Despite the absence of post-transplant cyclophosphamide, GVHD was clinically manageable and did not preclude long-term survival, supporting a clinically relevant graft-versus-myeloma effect in selected young patients. Cumulative incidence analysis showed progressive disease-related mortality over time, while NRM remained relatively stable after the first 24 moths. Importantly, patients receiving allo-HSCT from sibling donors had a significantly superior OS compared with those transplanted from unrelated donors (median OS 77.7 vs 16.5 months, p=0.04 – figure 1A). Younger patients (<55 years) and those transplanted early (figure 1B) demonstrated the most favourable long-term outcomes, with a subset achieving durable remission suggestive of cure.

	Number of patients (%)
Median age	53.7 (33.1-63)

Sex	
Male	29 (63)
Female	17 (37)
GVHD prophilaxys	
CNI+MTX	42 (91.3)
PTCy	0 (0)
Others*	4 (8.7)
Donor	
Sibling	20 (43.5)
MUD	15 (32.6)
MMUD	11 (23.9)
Haplo	0 (0)
Cord blood	0 (0)
Graft source	
BM	5 (10.9)
PBSC	41 (89.1)
Conditioning intensity	
MAC	17 (36.9)
RIC	29 (63.1)
Lines of therapy pre-HSCT	
<3	22 (47.8)
3-6	24 (52.2)

Fig. 1A

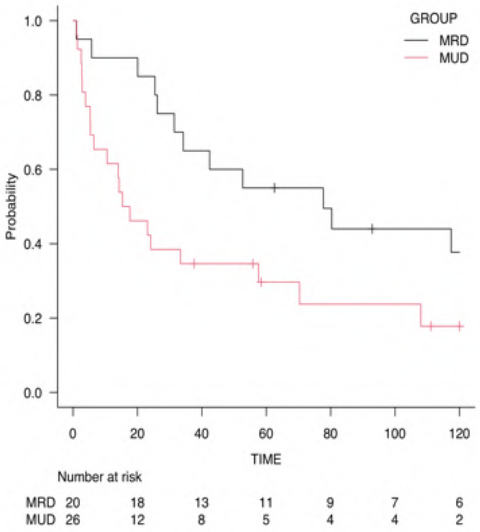
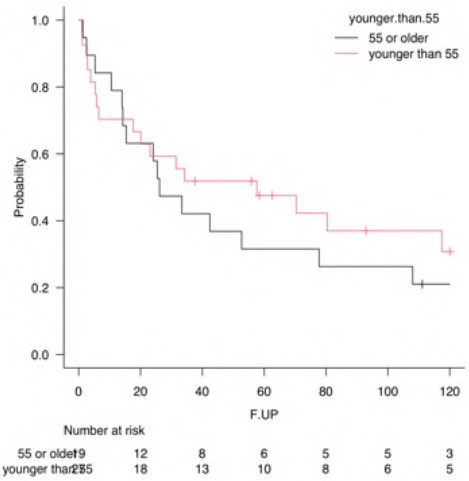


Fig. 1B



Conclusions: Despite advances in non-transplant therapies, allo-HSCT retains a potential curative role in carefully selected young MM patients. Early transplantation and the availability of an HLA-identical sibling donor appear to be critical determinants of long-term survival and disease control. These findings support reconsidering allo-HSCT as a curative strategy rather than a purely palliative option in the modern treatment landscape of MM.

Disclosure: Not applicable.

P291

ZERO PERCENT TREATMENT-RELATED MORTALITY, HIGH EFFICACY AND LONG-TERM SAFETY OF AUTOLOGOUS HEMATOPOIETIC CELL TRANSPLANTATION FOR MULTIPLE MYELOMA IN THE ERA OF QUADRUPLETS

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Background: Quadruplets have been introduced as the mainstay of induction treatment in multiple myeloma (MM) patients eligible for autologous hematopoietic cell transplantation (AHCT). We studied the long-term safety and efficacy of AHCT in a large real-world cohort of MM patients receiving quadruplets compared to historic controls induced with triplets.

Methods: We enrolled consecutive patients, of our JACIE-accredited center, that received AHCT over the last decade (2013-2023) for MM. Patients were divided into 2 groups: 79 patients were induced with daratumumab-based quadruplets (Group A) versus 187 patients with bortezomib-based triplets (Group B). All patients received high-dose melphalan (200 mg/m^2) as conditioning regimen, with dose reduction (140 mg/m^2) in 6 patients with chronic kidney disease. Median patient age at transplant date was 59 (41-71) years for group A and 57 (35-70) for group B. Disease status at transplantation was complete response (CR), very good partial response (VGPR), partial response (PR) and progressive disease (PD) in 34/28/11/5 in group A vs 55/64/63/5 in group B. Variables included in the analysis were also CD34+ stem cell yield, time to neutrophil and platelet engraftment and post-transplant outcome regarding overall survival.

Results: We studied 266 consecutive patients with multiple myeloma. No second AHCT or allogeneic transplantation was performed in the study period. There were no transplant-related deaths. Within this period, 5-year OS was 83% in Group A patients vs 60% in Group B patients (p=0.003). There was no statistically significant difference in the disease status at transplantation between the two groups. CD34+ stem cell yield was not different in the two groups, 3.91 (1.70-9.48) in group A vs 3.89 (1.38-9.63) x 10^6/kg in group B (p=ns). There was no impact in median time to neutrophil engraftment, 10.6 (in group A (9-13) vs 11.5 (7-26) days in group B (7, (p=ns). However, patients in group A had significantly shorter median time to platelet engraftment, 12.8 (8-26) vs 14.2 (7-68) days (p=0.045).

Conclusions: Our data confirm that AHCT is safe and effective for MM in the era of quadruplets. Daratumumab-based quadruplets offer an optimal graft yield and seem to exert an enhanced impact on platelet engraftment, probably due to their alkylator-sparing advantage. The significant benefit in overall survival highlights the importance of incorporating novel agents into the first-line setting, even in transplant-eligible patients, so as to improve total outcomes in this still incurable disease.

Disclosure: Nothing to declare for all authors.

P293

INTEGRATED PRE- AND POST-TRANSPLANT RISK SCORE FOR PROGRESSION AFTER A SINGLE AUTOLOGOUS STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA

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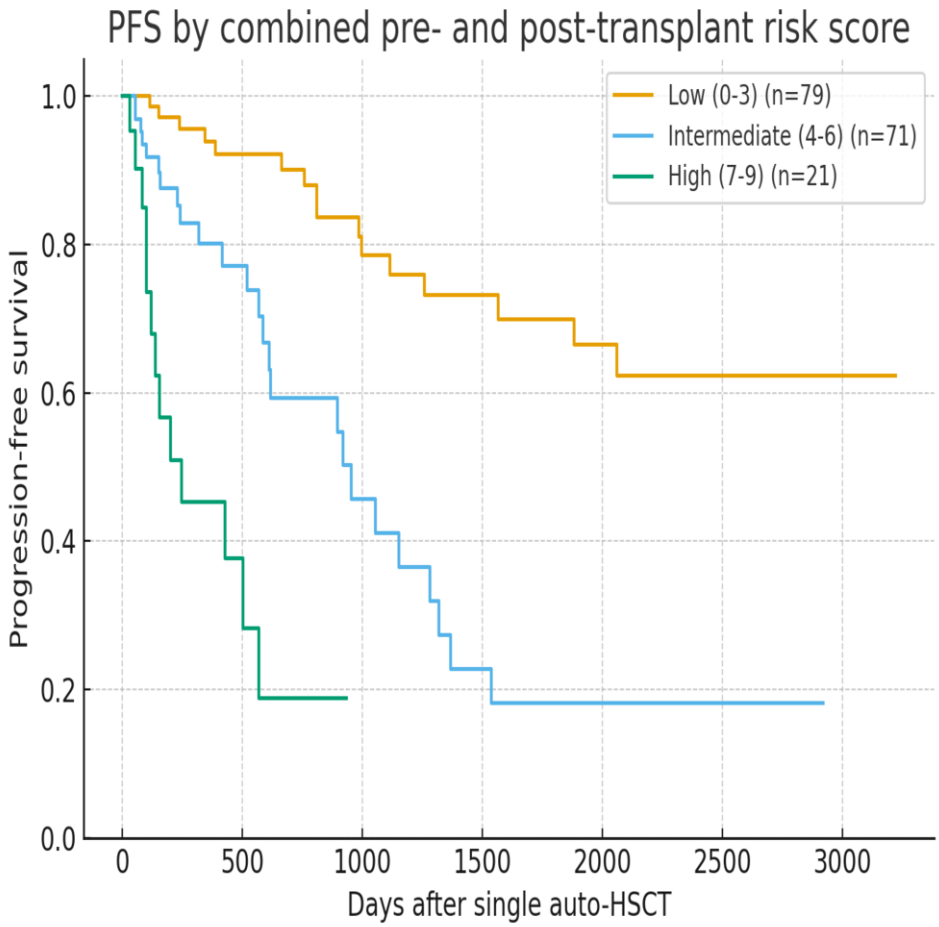
Background: Autologous stem cell transplantation (ASCT) remains a key component of therapy in multiple myeloma (MM), but long-term outcomes are heterogeneous, even in the era of novel agents and maintenance. There is a need for tools that integrate pre- and post-transplant factors to estimate progression risk, guide the use of a second ASCT and tailor maintenance or treatment intensification. We aimed to identify predictors of progression after single ASCT and to develop a clinical risk score combining pre- and post-transplant variables.

Methods: We retrospectively analysed 171 MM patients who underwent single ASCT at our center. Median age at ASCT was 59 years, and 45.2% were male. According to mSMART cytogenetics, 18.8% had high-risk, 31.5% standard-risk and 44.7% unknown status. A soft tissue/extra-medullary component was present in 27.9% of patients. Conditioning regimens included melphalan monotherapy in 45.7% and bendamustine-containing regimens in 54.3%. Pre-ASCT responses were PR 17.8%, VGPR 44.7%, CR 29.4%, sCR 2.5% and stable disease 1.0%. Median follow-up was 443.5 days (≈1.2 years). PFS was defined as time from ASCT to progression/relapse or death; OS as time to death from any cause. Kaplan–Meier estimates were used for survival, and Cox proportional hazards models for uni- and multivariable analyses, including clinical, cytogenetic, treatment and response variables. A combined pre/post-transplant risk score was then built.

Results: Median OS was not reached; 3-year OS was 74.5%. Median PFS was 1115 days (≈3.1 years), and 3-year PFS was 51.0%. In multivariable analyses, independent adverse factors for PFS were the presence of a soft-tissue component (HR≈2.2, p=0.026) and worse response at day +100 (per-category deterioration on the AX scale, HR≈1.38, p≈0.0001). Standard-risk mSMART cytogenetics were protective (HR≈0.45 vs non-standard/unknown, p=0.027), and achieving CR/sCR before ASCT markedly reduced the risk of progression (HR≈0.18 vs ≤PR/SD, p≈0.00006). Lenalidomide maintenance showed a trend toward lower risk (HR≈0.62, p≈0.11). Age, sex, Durie–Salmon stage, ISS, number of prior lines, haemodialysis, type of induction and conditioning (including bendamustine-containing vs non-bendamustine regimens; HR≈0.81, 95% CI 0.46–1.43, p=0.47) were not significantly associated with PFS (all p>0.05).
Based on Cox coefficients, we constructed a 0–9 point risk score integrating pre-transplant soft-tissue involvement, mSMART risk, depth of response before ASCT, day +100 response and lenalidomide maintenance. Three risk groups were defined: low (0–3), intermediate (4–6) and high (7–9 points). Low-, intermediate- and high-risk groups comprised 79, 71 and 21 patients, respectively. Median PFS was not reached in the low-risk group (3-year PFS 76.5%), 618 days (≈1.7 years) in the intermediate-risk group (3-year PFS 34.4%) and 201 days (≈0.6 years) in the high-risk group (3-year PFS 8.9%). The score showed good prognostic performance for PFS with a concordance index of 0.76.



Conclusions: We developed and implemented a combined pre- and post-transplant risk score for MM patients undergoing single ASCT. This score is being integrated into routine practice in our center to guide treatment strategies, including maintenance, consideration of a second ASCT and intensity of follow-up.

Disclosure: Nothing to declare.

P294

CLINICAL OBSERVATION ON THE NKG2D AND CS1 TARGETED CAR-T TREATMENT OF RELAPSED/REFRACTORY MULTIPLE MYELOMA PATIENT WITH BCMA AND GPRC5D DELETION

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Background: Although combination regimens based on bortezomib, lenalidomide, and daratumumab have significantly improved survival in patients with relapsed or refractory multiple myeloma (MM), clinical management remains challenging. In recent years, targeted therapies against BCMA and GPRC5D—including CAR-T cell therapies, CD3×BCMA or CD3×GPRC5D bispecific antibodies, and CD3×BCMA×GPRC5D trispecific antibodies—have markedly enhanced clinical outcomes. However, loss of BCMA and GPRC5D antigen expression in patients experiencing disease recurrence or progression after CAR-T therapy or trispecific antibody treatment substantially limits subsequent therapeutic options, underscoring the need for novel therapeutic strategies.

Methods: A 61-year-old female patient with an 11-year history of MM experienced repeated disease progression despite multiple prior treatments, most recently including a CD3×BCMA×GPRC5D trispecific antibody. Baseline evaluation revealed 25% bone marrow (BM) plasma cells and multiple lytic bone lesions. Serum immunofixation electrophoresis confirmed IgAλ type myeloma, with IgA at 27.42 g/L and λ free light chain at 9.72 g/L. Urine immunofixation demonstrated λ light chain restriction, with urinary λ free light chain at 98 mg/dL. Flow cytometry analysis showed absence of BCMA and GPRC5D surface expression on plasma cells, while CS1 and NKG2D were highly expressed, making these targets suitable for autologous CAR-T cell therapy. Peripheral blood mononuclear cells were collected from the patient to generate two separate autologous CAR-T cell products targeting CS1 and NKG2D. The lymphodepletion regimen consisted of fludarabine 30 mg/m² and cyclophosphamide 300 mg/m² administered from day −5 to −3. On November 18, 2024, CS1 CAR-T cells (0.86 × 10^6 cells/kg) were infused, followed by NKG2D CAR-T cells (1.0 × 10^6 cells/kg) on November 26, 2024.

Results: Following CAR-T cell infusion, the patient developed grade 1 cytokine release syndrome (CRS), manifesting as fever and fatigue, with no evidence of immune effector cell-associated neurotoxicity syndrome (ICANS); symptoms resolved with symptomatic management. By day 28 post-infusion, the patient achieved complete remission, as evidenced by the absence of abnormal plasma cells in bone marrow, undetectable serum M protein on electrophoresis, and normalization of serum free light chain ratios. Eleven months after remission, a palpable mass was identified adjacent to the right orbit. Laboratory evaluation revealed recurrent monoclonal λ light chain elevation in both serum and urine. Bone marrow examination showed 1% plasma cells. Biopsy of the orbital mass confirmed extramedullary plasmacytoma. Flow cytometric analysis at relapse demonstrated re-expression of BCMA (81.51% positive) and GPRC5D (40.97% positive) on neoplastic plasma cells.

Conclusions: This case illustrates that sequential CS1- and NKG2D-targeted CAR-T cell therapy induced a durable remission lasting 11 months in a patient with relapsed/refractory MM and prior loss of BCMA and GPRC5D antigen expression, demonstrating therapeutic potential in this high-risk population. The re-emergence of BCMA and GPRC5D expression at relapse restored eligibility for BCMA- and GPRC5D-directed therapies. These findings highlight the importance of dynamic monitoring of antigen expression profiles to guide personalized treatment decisions. Future studies may explore combination strategies—such as immune checkpoint inhibitors or immunomodulatory agents—following CS1- or NKG2D-directed CAR-T therapy to further improve response durability and efficacy.

Disclosure: Nothing to declare

P295

AUTOLOGOUS STEM CELL TRANSPLANTS NEGATE OUTCOME DIFFERENCES BETWEEN DUAL AND TRIPLE THERAPIES IN MULTIPLE MYELOMA: REAL-WORLD DATA FROM A MIDDLE-INCOME COUNTRY

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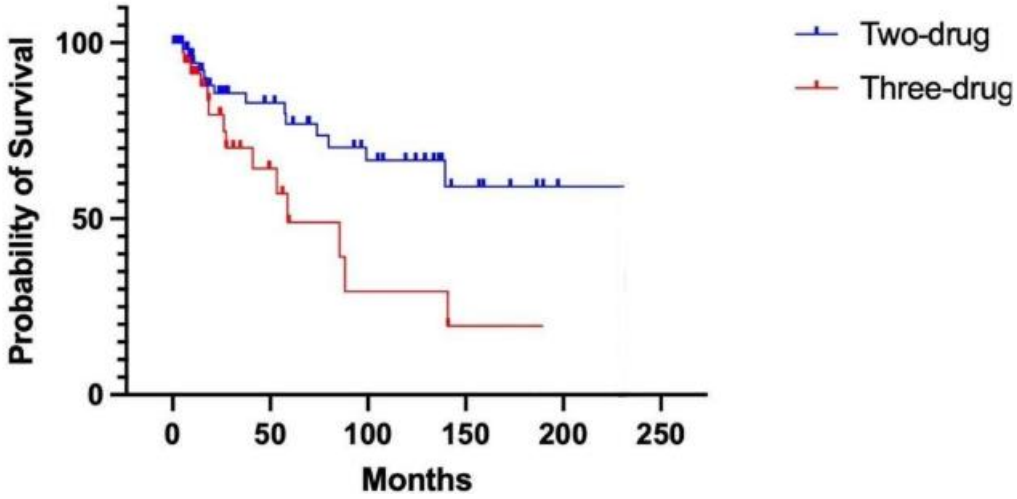
Background: To evaluate the impact of autologous stem cell transplantation (ASCT) and induction regimen (doublet vs. triplet) on overall survival (OS) and progression-free survival (PFS) in multiple myeloma (MM) patients treated in a resource-constrained setting.

Methods: This retrospective cohort included 105 MM patients diagnosed between 1991 and 2025. After excluding 17 due to incomplete data, 88 remained: 56 received doublet therapy (corticosteroid + immunomodulator) and 32 received triplet therapy (addition of a proteasome inhibitor). Survival was assessed using Kaplan–Meier and Cox regression analyses adjusted for ISS stage, age, and ASCT status. A predefined subgroup analysis evaluated outcomes within ISS stage III patients.

Results: Median OS appeared longer in the doublet group (230 vs. 59 months; p = 0.0061), largely reflecting a higher prevalence of ISS stage III disease in the triplet cohort (50% vs. 25%). After adjustment, induction regimen was not independently associated with OS (HR 0.9
1, 95% CI 0.36–2.12). ASCT was the strongest predictor of survival (HR 0.34, 95% CI 0.13–0.86), with ASCT recipients demonstrating significantly longer OS (189 vs. 73.7 months; p = 0.0015). PFS did not differ between regimens (56.6 vs. 56.2 months; p = 0.5941). Among ISS stage III patients (n = 30), OS did not differ by induction therapy (p = 0.6765).



Conclusions: In resource-limited settings, ASCT is the primary driver of long-term survival in MM. When ASCT is feasible, doublet induction yields adjusted survival outcomes comparable to triplet therapy, supporting its use as a pragmatic and cost-effective option.

Disclosure: Nothing to declare

P296

SAFETY, ENGRAFTMENT KINETICS, AND TRANSPLANT-RELATED COMPLICATIONS OF AUTOLOGOUS STEM CELL TRANSPLANTATION IN MULTIPLE MYELOMA: INSIGHTS FROM A RESOURCE-CONSTRAINED REAL-WORLD COHORT

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Background: Autologous stem cell transplantation (ASCT) remains a critical component of therapy for transplant-eligible patients with multiple myeloma (MM), offering deeper responses and improved disease control. While randomized trials have established its efficacy, real-world data—particularly from resource-constrained settings and patients with baseline renal dysfunction—remain limited. We report comprehensive transplant outcomes, toxicities, and early disease control from a single-center real-world cohort.

Methods: We retrospectively analyzed 64 consecutive MM patients who underwent ASCT over a 5 year period in a newly established transplant centre. Majority of transplants were under state sponsored health insurance scheme reflecting a predominantly publicly funded, real world transplant population. Demographic characteristics, transplant parameters,

engraftment kinetics, transplant-related complications, hospitalization duration, transplant-related mortality (TRM), and post-transplant outcomes were assessed.

Results: Sixty-four patients underwent ASCT, including 62.5% males (40) and 37.5% females (24), with a median age of 55 years. Renal failure at presentation was observed in 43.8% (28). Patients received a median of 4 induction cycles prior to transplant and the most common induction regimen was VRd in 52%(33/64) cases. Conditioning consisted of melphalan 200 mg/m² in 62.5% (40) and melphalan 140 mg/m² in 37.5% (24), primarily due to renal dysfunction or advanced age. The median infused $CD34^+$ stem cell dose was 6 × 10^6/kg.
Hematopoietic recovery was rapid, with a median neutrophil engraftment at Day 10(range, 9-25) and median platelet engraftment at Day 14(range 12-26). Delayed engraftment beyond Day 20 occurred in 7.8% (5/64).
Transplant-related toxicities were frequent but largely manageable. Mucositis occurred in 100% (64), with grade 1–2 in 53.1% (34), grade 3 in 31.3% (20), and grade 4 in 15.6% (10). Febrile neutropenia developed in 90.6% (58). Microbiologically documented infections were identified in 31.3% (20), including gram-negative bacterial infections in 12.5% (8/64)—most commonly Escherichia coli—gram-positive infections in 6.3% (4/64), and fungal infection in 1.6% (1/64). 60% 0f patients needed total parenteral nutrition support for a median of 5 days(range 3-6). Septic shock requiring inotropic support occurred in 4.7% (3). One patient (1.6%) died due to transplant-related complications, resulting in a TRM of 1.6%. The median duration of hospitalization was 20 days (range: 18–40). Despite a high burden of early transplant-related toxicities, complications were predominantly reversible with intensive supportive care. Importantly, no graft failure was observed, and hematopoietic recovery was durable in all evaluable patients.
At a median follow-up of 24 months, disease relapse was documented in 14% (9/64), all of whom received second-line therapy with a progression free survival of 86%.

Conclusions: This real-world experience demonstrates that ASCT in multiple myeloma is feasible and effective, with prompt engraftment, acceptable toxicity, and low TRM, even in a substantial proportion of patients with renal dysfunction and also in resource limited setting. Despite high rates of mucositis and febrile neutropenia, infectious complications were manageable, and early disease control was encouraging. These findings reinforce the continued role of ASCT as safe, effective and generalizable therapeutic strategy for myeloma across diverse real world and resource limited settings.

Clinical Trial Registry: Not Applicable.

Disclosure: Nothing to declare.

P297

PROGNOSTIC FACTORS FOR SURVIVAL IN PATIENTS WITH MULTIPLE MYELOMA UNDERGOING AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION IN COLOMBIA

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Background: Autologous hematopoietic stem cell transplantation (ASCT) remains a cornerstone of treatment for eligible patients with multiple myeloma (MM). However, survival outcomes after ASCT are heterogeneous and depend on patient and treatment-related factors, particularly in real-world settings from low and middle-income countries.

Methods: We conducted a retrospective observational study including adult patients with MM who underwent ASCT at a referral center in Northeastern Colombia between 2009 and 2024. The objective was to identify factors associated with progression-free survival (PFS) and overall survival (OS) at 100-days, 1-year and 5-years post-transplant. Baseline demographic, clinical, biochemical, and transplant-related variables were collected. Survival was estimated using the Kaplan–Meier method, and multivariable Cox proportional hazards regression models were used to identify factors independently associated with PFS and OS.

Results: A total of 150 patients were included. The median age at transplantation was 58 years (range, 53–63), and 48% were male. Most patients underwent ASCT after first-line therapy (63%). All patients received melphalan-based conditioning. Post-transplant strategies included consolidation (61% received) and maintenance therapy which was implemented routinely after 2015 (62% and 89% received from 2009-2014 and 2015-2024 respectively). The 5-year OS was 64.5%, and median OS was not reached during follow-up. Two patients died within the first 100 days after ASCT. No significant differences in OS or PFS were observed according to sex, age (>65 years) or ISS stage. In multivariable analysis, maintenance therapy was independently associated with improved OS at 1-year and 5-years (HR 0.14; 95%CI 0.02 - 0.77; p= 0.024 and HR 0.39; 95%CI 0.20 - 0.76; p= 0.002 respectively). A higher body mass index was associated with an increased risk of disease progression or relapse (HR 1.06; 95%CI 1.01 - 1.11; p= 0.012). Elevated dehydrogenase lactate at diagnosis was consistently associated with inferior outcomes, including a significantly shorter 1-year PFS (HR 4.39; 95%CI 1.04–18.42; p= 0.043) and reduced 5-year OS (HR 3.64; 95%CI 1.66–8.01; p= 0.043). First-line chemotherapy VRD prior ASCT improved 5-year OS (HR 0.13; 95%CI 0.02 - 0.62; p= 0.01) and administering melphalan for two days as a conditioning regimen and a higher pre-transplant hematopoietic stem cell transplant comorbidity index (HR 4.74; 95%CI 1.05-21.21; p = 0.042) were associated with decreased overall 5-year survival (HR 1.89; 95%CI 1.03-3.49; p = 0.039). Post-transplant consolidation-therapy was associated with a significant reduction in mortality (HR 0.38;

95%CI 0.20 - 0.72; p= 0.003), as was maintenance-therapy (HR 0.39; 95%CI 0.20 - 0.76; p= 0.006).

Characteristic	Desease-Free Survival		Overall Survival	
	1 year HR (95%CI) p-value	5 year HR (95%CI) p-value	1 year HR (95%CI) p-value	5 year HR (95%CI) p-value
Overall	86.9%	41.18%	94.12%	64.57%
Gender Female	0.79 (0.24 - 2.61) 0.71	1.2 (0.70 - 2.37) 0.83	0.73 (0.19 - 2.72) 0.64	0.88 (0.48 - 1.62) 0.7
Age>65y	0.41 (0.05 - 3.25) 0.4	0.72 (0.32 - 1.62) .43	1.34 (0.27 - 6.68) 0.7	0.82 (0.36 - 187) 0.6
IMC	1.01 (0.95 - 1.08) 1.08	1.06 (1.01 - 1.11) 0.012	0.99 (0.92 - 1.05) 0.7	0.99 (0.96 - 1.02) 0.65
LDH elevated	4.39 (1.04 - 8.42) 0.04	1.85 (0.86 - 3.99) 0.11	2.9 (0.41 - 21.1) 0.27	3.64 (1.66 - 8.01) 0.001
ISS 1	0.71 (0.04 - 11.45) 0.81	0.94 (0.32 - 2.7) 0.91	1.39 (0.12 - 15.34) 0.78	0.80 (0.25 - 2.49) 0.70
ISS 2	4.05 (0.49 - 32.93) 0.19	0.94 (0.32 - 2.7) 0.91	1.39 (0.12 - 15.34) 0.78	2.56 (1.00 - 6.54) 0.04
ISS 3	1.08 (0.09 - 11.94) 0.94	1.79 (0.68 - 4.69) 0.23	1.76 (0.18 - 16.97) 0.62	1.94 (0.73 - 5.14) 0.17
Ciotgenetic High Risk	6.30 (0.57 - 69.53) 0.13	2.55 (0.63 - 10. 35) 0.18	1.76 (0.18 - 16.97) 0.62	2.39 (0.64 - 8.91) 0.19
Extramedullary disease	1.08 (0.31 - 3.71) 0.895	0.88 (0.46 - 1.65) 0.67	0.55 (0.11 - 2.65) 0.45	2.39 (0.64 - 8.91) 0.19

HCTI 0	REF	REF	REF	REF
HCTI 1-2	0.65 (0.13 - 3.26) 0.61	-	0.94 (0.17 - 5.17) 0.9	0.99 (0.46 - 2.12) 0.98
HCTI >=3	0.98 (0.24 - 3.92) 0.97	-	1.32 (0.24 - 7.21) 074	1.73 (0.80 - 3.73) 0.15
Hematologic response prior to ASCT RC	RC 0.38 (0.12 - 1.14) 0.08	0.38 (0.12 - 1.14) 0.08	0.26 (0.2 - 2.59) 0.16	0.67 (0.27 - 1.62) 0.37
Hematologic response prior to ASCT sRC	3.00 (0.76 - 11.87) 0.11	3.00 (0.76 - 11.8) 0.08	0.49 (0.08 - 27.82) 0.43	0.58 (0.22 - 1.53) 0.27
Melphalan 2d	1.73 (0.53 - 5.70) 0.3	1.99 (1.09 - 3.63) 0.02	1.09 (0.27 - 4.36) 0.9	1.89 (1.03 - 3.49) 0.039
Consolidation therapy	0.78 (0.23 - 2.56) 0.68	0.67 (0.37 - 1.23) 0.2	0.69 (0.14 - 2.37) 0.4	0.38 (0.20 - 0.72) 0.003
Maintenance therapy	0.53 (0.15 - 1.82) 0.31	0.54 (0.29 - 1.01) 0.57	0.14 (0.22 - 0.77) 0.02	0.39 (0.20 - 0.76) 0.006

Conclusions: In this real-world cohort of patients with MM undergoing ASCT, survival outcomes were influenced by specific clinical and therapeutic factors. Split-dose melphalan conditioning and a higher comorbidity burden were associated with inferior OS, whereas post-transplant consolidation and maintenance therapies conferred significant survival benefits. These findings support individualized transplant strategies and highlight the importance of local real-world evidence to optimize post-transplant outcomes.

Disclosure: The authors declare no conflicts of interest.

P301

DRUG INDUCED THROMBOTIC MICROANGIOPATHY (TMA) IN A CASE OF MULTIPLE MYELOMA

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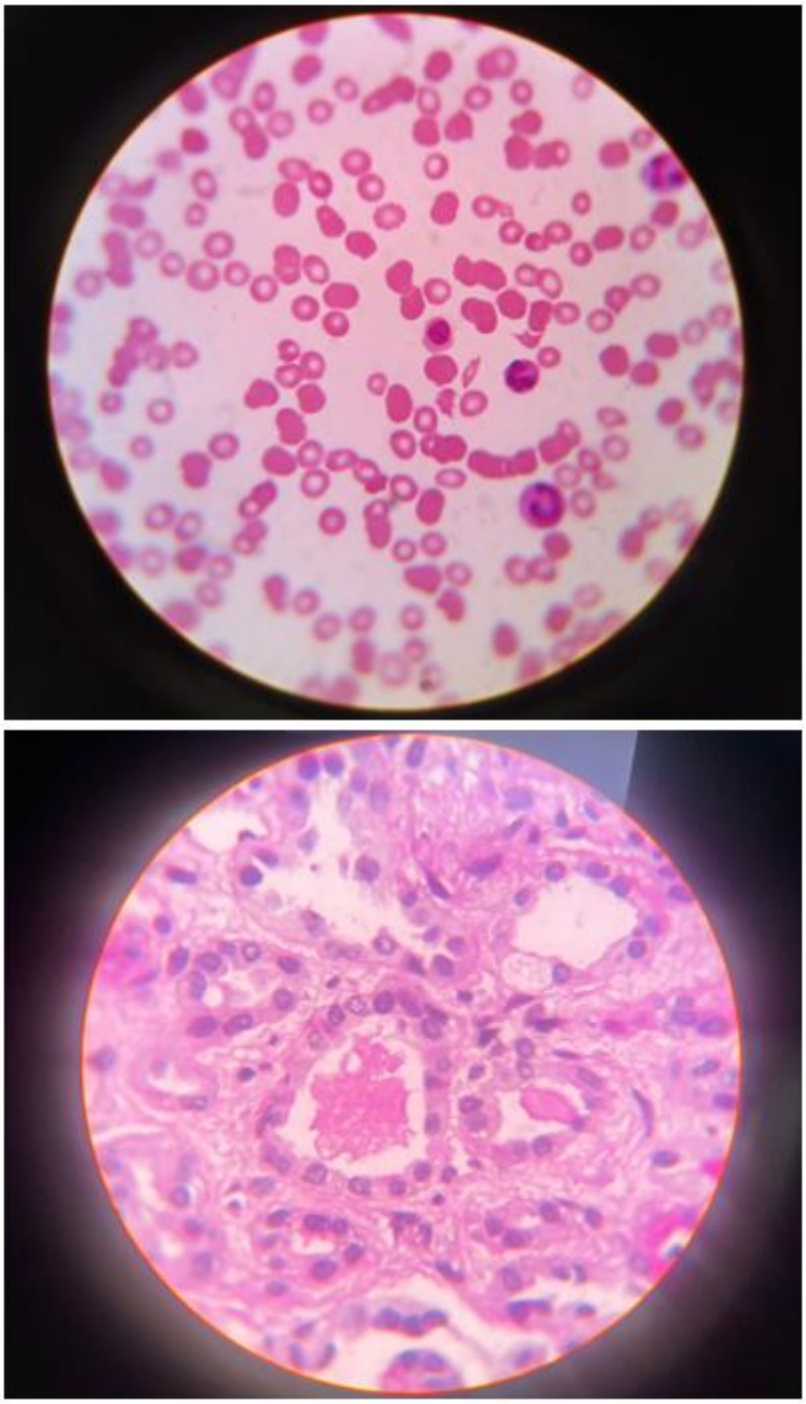
Background: Carfilzomib is a second-generation proteasome inhibitor commonly used in the treatment of relapsed / refractory multiple myeloma. Carfilzomib is used for second-line treatment , following disease progression or resistance to initial treatment regimens. Carfilzomib has been implicated in drug-induced thrombotic microangiopathy (TMA), a rare but severe adverse event, characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute kidney injury resulting from endothelial injury and microvascular thrombosis leading to end-organ damage.

Methods: A 51-year-old female was diagnosed with IgG kappa multiple myeloma, ISS stage I, in October 2024. At the time of diagnosis, no high-risk cytogenetic abnormalities were identified. Bone marrow aspirate showed 59% plasma cells. Serum protein electrophoresis revealed an M-band of 0.90 g/dL, and the kappa free light chain was 101.64 mg/L First-line chemotherapy with 4 cycles of VRd regimen (bortezomib, lenalidomide, dexamethasone) and 2 cycles of VCD (bortezomib, cyclophosphamide, dexamethasone) was initiated. Bone marrow done as part of pre BMT work up in which aspirate had 19 % plasma cells and biopsy showed sheets of plasma cells. In view of persistent disease she was started on therapy with carfilzomib, cyclophosphamide, and dexamethasone (KCD regimen). First cycle of KCD was tolerated well.
She received the Day 1 dose of carfilzomib of the second cycle as scheduled. Four days later, she presented to the emergency department with complaints of fatigue, vomiting, and reduced urine output. Laboratory investigations revealed acute kidney injury, with serum creatinine elevated to 6.2 mg/dL. Hemoglobin dropped to 8.2 g/dL, and platelet count was 27,000/µL. There was elevated serum lactate dehydrogenase to 2101 IU/L, decreased serum haptoglobin, and the presence of schistocytes (6%) on peripheral blood smear (Fig 1), suggestive of microangiopathic hemolytic anemia (MAHA). Complement studies showed an initially normal C3 level, which subsequently decreased, while C4 remained within normal limits. Other causes of TMA like TTP, aHUS, DIC and malignancy were ruled out.



Results: • The patient was initiated on therapeutic plasma exchange, hemodialysis, and intravenous methylprednisolone, followed by a tapering regimen of oral corticosteroids. Despite undergoing three sessions of plasma exchange and four sessions of hemodialysis ,

the patient remained anuric, with urine output persistently below 10 mL/day. In view of sustained anuria and biopsy-proven TMA, the patient was counselled regarding complement blockade therapy with eculizumab. She was administered her first dose of eculizumab 900 mg intravenously. Maintenance hemodialysis was continued during this period. The patient received a second dose of eculizumab after one week. By Day 15 following the initial dose, her urine output improved to 1500 mL/day, and hemodialysis was discontinued.
• After complete recovery she was started on 2 cycles of VCD chemotherapy following which she was taken for autologous HSCT.
• Conditioning-- melphalan 140 mg/m2.
• Complications during transplant- Grade 2 Mucositis and febrile neutropenia but there was no further episodes of TMA.
• Neutrophil engraftment on D+ 10
• Platelet engraftment on D +10.
She was successfully discharged after D+13 post autologous BMT.

Conclusions: TMA represents a potentially fatal clinical entity that necessitates prompt recognition and immediate therapeutic intervention to mitigate mortality risk.

Disclosure: There is no conflict of interest.

P302

OUTCOMES OF SECOND AUTOLOGOUS STEM CELL TRANSPLANTATION AS RESCUE THERAPY IN RELAPSED MULTIPLE MYELOMA PATIENT, WITHOUT CRYOPRESERVED CD34. CASE REPORT FROM TRANSPLANT CENTER IN VENEZUELA

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Background: Consolidation with Autologous Stem Cell Transplantation (ASCT) after induction therapy has shown a positive impact in Overall Survival (OS) and Event Free Survival (EFS) in patients with Multiple Myeloma (MM), however, the patients in Venezuela with Relapsed MM (RMM) where there is no access to: Anti-CD38-mAb, bi-specifics and cellular therapy (CAR-T), the only option therapeutic options is conventional therapy followed by a Second ASCT (2ASCT).

Methods: We conducted a retrospective study of all the patients with RMM who underwent a 2ASCT in the Bone Marrow Transplant Center "Dr Abraham Sumoza" in Venezuela from 2013 to 2025.

Results: Only one MMR patient underwent a 2ASCT, and it was the case of a 49year-old female diagnosed with MM ISS III in 2013, who was treated with Bortezomib, Thalidomide and Dexamethasone for 8 cycles achieving a Very Good Partial Response (VGPR), then proceeded to ASCT; a total of 4.5x106cell/kg granulocyte colony-stimulating factor (GCSF)-mobilized Peripheral Blood (PB) stem cells were collected and infused at that time, no remaining CD34+ cellular product was cryopreserved for future purposes, the conditioning regimen was Melphalan 180mg/m2, showing signs of engraftment by day 10. Complete Response was achieved by day 120 post-ASCT, and she received maintenance therapy with thalidomide for 2 years.
8 years after the first ASCT, the patient suffered a relapsed and received treatment with Cyclophosphamide, bortezomib, and dexamethasone for 8 cycles, obtaining a VGPR, she underwent a 2ASCT; using fresh collectedGCSF-mobilized PB stem cells as source, a total of 2x106cells/kg CD34 cells was obtained, the conditioning regimen of choice was Melphalan 200mg/m2 (Mel200). Evidence of neutrophile and platelet recovery was on days 13 and 15, respectively. The patient did not present any infection or need for platelet or red blood cell transfusion during the aplastic period. Currently, she has been on Lenalidomide as maintenance therapy for the last 2 years. After 3years of follow-up, she still has VGPR, with no signs of second malignancies or hematologic disorders.
The results presented in the study can be compared with other retrospective studies, where the authors concluded that a VGPR before a 2ASCT, a time between the first ASCT and the start of therapy for RMM of at least 2 years, and the use of Lenalidomide as maintenance therapy after 2ASCT, have a positive impact on OS and EFS.

Conclusions: A 2ASCT in an RMM patient had low toxicity and was associated with a good OS and EFS in our patient. The use of Melphalan as a conditioning regimen in previous ASTC had no impact on a second mobilization and collection of GCSF-mobilized PB stem cells. A VGPR before proceeding to a 2ASCT is key for a better outcome; however, we need more data to statistically prove our results. Therefore, we concluded that a 2ASCT is a feasible treatment for patients with RMM in our institution.

Disclosure: Nothing to declare.

Myelodysplastic Syndromes

OS01-07

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN HYPOPLASTIC MYELODYSPLASTIC SYNDROME FROM A LATIN AMERICAN MULTICENTER STUDY

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Background: The hypocellular Myelodysplastic Syndromes (h-MDS), a rare subtype accounting for 10–15% of Myelodysplastic Syndromes (MDS) patients, that is defined by reduction of ≤25% bone marrow cellularity, age adjusted according to WHO-2022. These patients are typically younger and characterized by more severe cytopenias, higher transfusion dependence and lower blast percentages as compared to normo/hypercellular MDS (n-MDS). The objective of this study is to describe the clinical characteristics and transplantation outcomes of patients with h-MDS compared to those with n-MDS, based on data from the Latin American Registry.

Methods: This is a retrospective study with 458 patients undergoing HCT at diagnosis. Clinical data were obtained from the transplant registry of 38 centers in Latin America (LA) between January 2000 to June 2025. Survival curves were performed the Kaplan-Meier method, and log-rank test. The statistical program used was SPSS v.23.1 $p<0.05$ were considered statistically significant.

Results: Among a total of 458 patients, 69 (15.07%) were diagnosed with h-MDS, while 389 (84.93%) had n-MDS. The median age was 52 years in the h-MDS cohort and 57 years in the n-MDS cohort. In the h-MDS group, 39 patients (56,52%) were male, with a mean age of 57.0±20.3 years, According to the IPSS-R, (53.85%) of patients were classified as intermediate risk, (25.64%) as low/very low risk, (15.38%) as high risk, and (5.13%) as very high risk. Most received grafts from compatible related donors (62,32%) and peripheral blood stem cells (55,07%) using myeloablative conditioning (68,12%). Death occurred in 31.88% of patients with MDS-h, post-transplant complications were observed in (75.36%) of patients and most patients did not relapse (98.25%) (Table 1). Compared with patients with n-MDS, those with h-MDS were younger (<65 years; $p=0.017$) and more frequently classified in the IPSS-R Low and Intermediate risk categories ($p=0.017$). They were also more likely to have received prior chemotherapy ($p=0.030$) and reduced-intensity conditioning regimens ($p=0.030$). In addition, h-MDS patients had a significantly lower relapse rate compared with n-MDS patients (p=0.023) (Table 1). No statistically significant difference in overall Survival (OS) was observed between patients with h-MDS and n-MDS undergoing allo-HCT, both at 5 years ($p=0.07$; Figure 1A). At 5-years, progression-free survival (PFS) patients with h-MDS had a significantly lower risk of relapse or death compared to n-MDS after allo-HCT (HR=0,63; CI 95%=0,40-0,99; p=0,046; Figure 1B). The Non-relapse mortality (NRM) at 5 years after allo-HCT did not differ significantly between patients with h-MDS and n-MDS ($p=0.392$; Figure 1C). In the univariate analysis, IPSS-R very high-risk was associated with an increased risk of mortality (HR=2.18; 95%CI:1.33–3.59; $p=0.002$). In the multivariate analysis, male sex (HR=1.36; 95% CI:1.00–1.85; $p=0.047$) and IPSS-R very high-risk (HR=2.85; 95% CI: 1.69–4.81; $p<0.001$) remained significant independent predictors of worse survival.

Figure 1: Overall survival (OS), Progression Free-Survival (PFS) and Non-relapse mortality (NRM) at 5 Years After Allo-HCT in Patients with (h-MDS) and (n-MDS) (n=458).

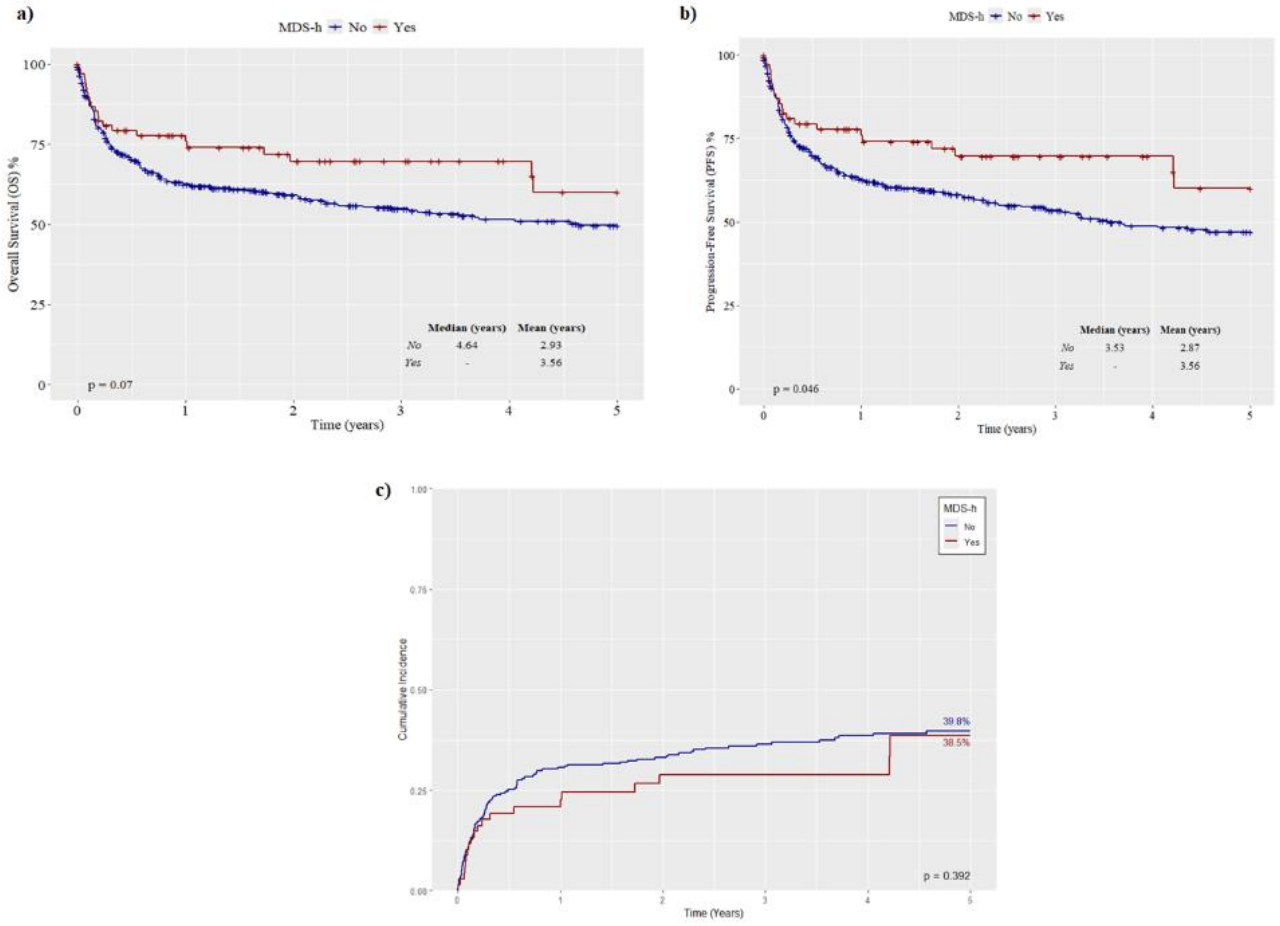

Table 1: Patient characteristics (N=458).

Variable	Group		
	MDS-h (n = 69)	MDS-n (n = 389)	*p*
Age Group			

Table 1: Patient characteristics (N=458).

< 65 anos	63 (92,65%)	316 (81,87%)	**0,042** [a]
65 years or older	5 (7,35%)	70 (18,13%)	
IPSS-R b			
Very Low Risk	0 (0%)	2 (0,87%)	**0,017**[b]
Low	10 (25,64%)	31 (13,54%)	
Intermediate	21 (53,85%)	81 (35,37%)	
High Risk	6 (15,38%)	84 (36,68%)	
Very High Risk	2 (5,13%)	31 (13,54%)	
Conditioning regimen			
Reduced-intensity	22 (31,88%)	99 (25,45%)	**0,030**[b]
Myeloablative	47 (68,12%)	263 (67,61%)	
Non-Myeloablative	0 (0%)	27 (6,94%)	
Relapse			
Yes	1 (1,75%)	44 (13,21%	**0,023**[a]
No	56 (98,25%)	289 (86,79%)	

Note: p-value a. Fisher Exact Test b: Chi-Square Test.*Bacterial infections, including multidrug-resistant bacterial infections, and fungal infections. Abbreviations: GVHD: graft-versus-host disease; HLA: Human Leucocyte Antigen; HCT: Hematopoietic Cell Transplantation; R-IPSS: Revised International Prognostic Scoring System.

Conclusions: We found that h-MDS was associated with distinct clinicobiological characteristics, as evidenced by significant differences in survival and IPSS-R risk category distribution. These findings reinforce the biological heterogeneity between subgroups and its impact on prognosis, which may influence decisions regarding HCT.

Disclosure: Nothing to declare

B414

IMPACT OF CONCURRENT GENETIC ALTERATIONS ON OUTCOMES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH TP53-MUTATED AML/MDS: A MULTI-CENTER COHORT STUDY

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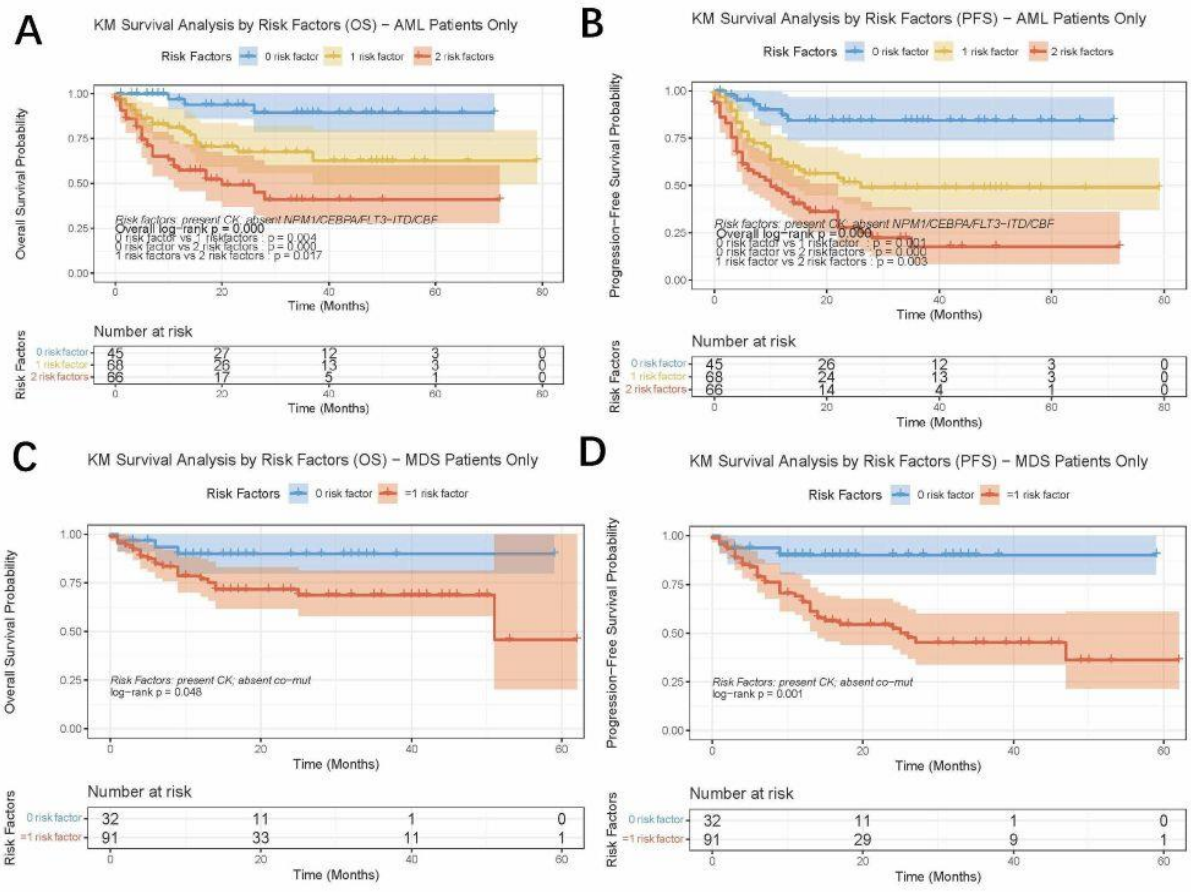
Background: TP53 mutations are associated with poor prognosis in acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS), even after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Discrepancies in the criteria used to define TP53 mutation status across professional societies and landmark studies, coupled with limited access to comprehensive TP53 allelic state assessment, have led to inconsistent clinical interpretations of outcomes in this population. While complex karyotype (CK) is a well-established adverse prognostic factor in TP53-mutated myeloid neoplasms, the impact of other coexisting genetic alterations on prognosis remains incompletely understood.

Methods: This multi-center, retrospective study analyzed 303 consecutive patients with TP53-mutated AML or MDS who underwent first allo-HSCT between January 2018 and December 2023. All patients had TP53 mutation confirmed by next-generation sequencing. Endpoints included overall survival (OS), progression-free survival (PFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM). Univariate and multivariate Cox models were used to identify prognostic factors. Subgroup and combined risk factor analyses evaluated the integrated impact of cytogenetic and molecular profiles.

Results: The cohort included 179 AML and 124 MDS patients. A complex karyotype was present in 133 (43.9%) patients, and 47 (15.5%) had chromosome 17p deletion. The median number of co-occurring myeloid mutations was 1; 180 (59.4%) patients had ≥1 co-occurring mutation, and 122 (40.2%) had ≥2. The overall burden of co-occurring somatic mutations was significantly higher in AML patients than in MDS patients (median 2 vs. 0, $p<0.001$). The most frequently co-mutated genes in the entire cohort included *TET2* (14%), *ASXL1* (9%), *DNMT3A* (7%), *RUNX1* (6%), and *FLT3-ITD* (4%). With a median follow-up of 21 months, the 3-year OS, PFS, CIR, and NRM rates for the entire cohort were 68%, 50.4%, 32.8%, and 17.6%, respectively. Univariate analysis identified CK as a significant predictor

for inferior OS (HR=2.813, 95% CI: 1.613–4.905, p<0.0001) and PFS (HR=2.745, 95% CI: 1.762–4.276, p<0.0001). In AML patients, the presence of specific concurrent genetic alterations (SCGAs)—CBF fusion genes, NPM1, FLT3-ITD, or CEBPA mutations—was associated with significantly improved OS (HR=0.157, 95% CI: 0.056–0.435, p<0.0001) and PFS (HR=0.198, 95% CI: 0.095–0.412, p<0.0001). Integration of CK and SCGA status enabled stratification of AML patients into three distinct prognostic tiers (favorable: 0 risk factors; intermediate: 1 factor; adverse: 2 factors) for both OS and PFS (all p<0.0001) (**Figure 1A-B**). In MDS, the presence of any co-occurring myeloid mutation (≥1) was a favorable factor for PFS (HR=0.457, 95% CI: 0.230–0.911, p=0.023). We therefore established a model that categorized patients based on the presence of at least one adverse risk factor (either CK positivity or the absence of any co-mutation). This model effectively stratified patients into two distinct risk tiers, with significant differences observed in both OS (p = 0.048) and PFS (p < 0.001) (**Figure 1C-D**).



Conclusions: For patients with TP53-mutated AML/MDS undergoing allo-HSCT, integrating complex karyotype, co-mutation burden, and specific fusion gene status provides significant prognostic information. These findings suggest the potential utility of a comprehensive genetic risk stratification model to guide clinical decision-making for this high-risk population.

Disclosure: Nothing to declare.

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A NOVEL TARGETED NGS ASSAY FOR TP53 LOH DETECTION FACILITATES ROUTINE MULTI-HIT CLASSIFICATION AND REFINES RISK STRATIFICATION IN MYELOID NEOPLASMS

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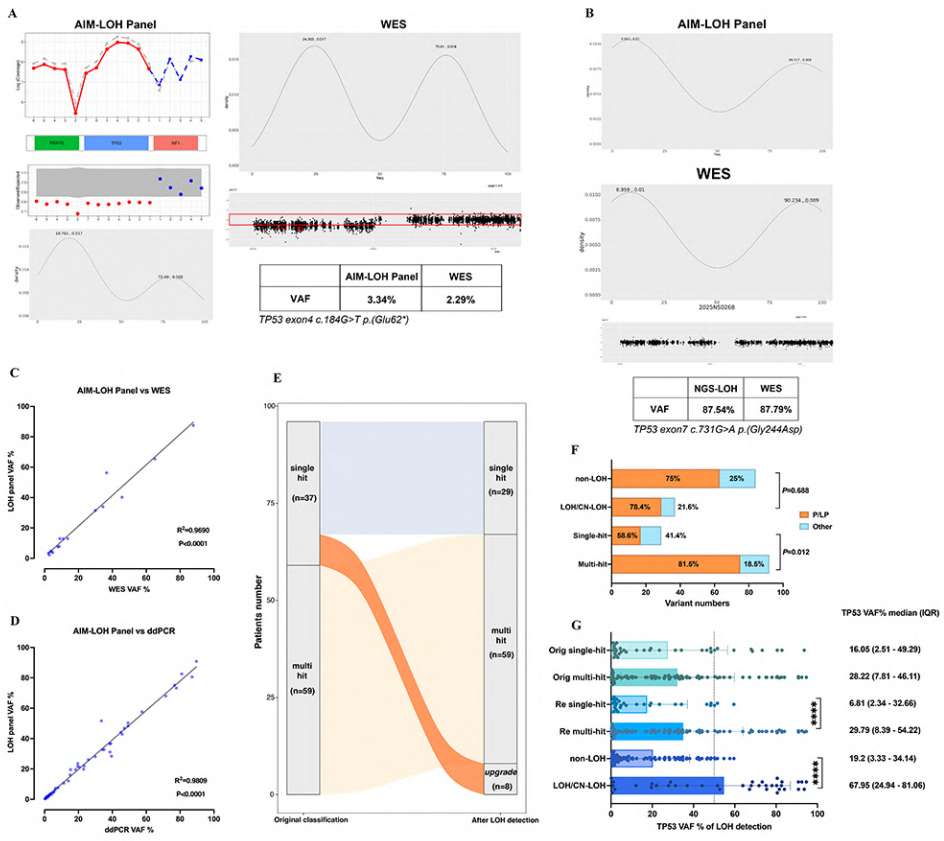
Background: TP53 mutations occur in around 10% of de novo AML or MDS and are frequently accompanied by copy-neutral loss of heterozygosity (CN-LOH), leading to biallelic TP53 inactivation and an intrinsically adverse prognosis. Current LOH detection relies on costly and time-consuming WGS/WES or SNP arrays, hindering routine clinical application and consequently leading to the misclassification of some multi-hit patients as single-hit. To address this gap, we established a novel targeted NGS-based assay for the direct detection of TP53 LOH/CN-LOH, validated its concordance with WES, and assessed its clinical significance.

Methods: A targeted SNP panel spanning the TP53 exonic region and ±500 kb flanks were designed (AIM-LOH Panel). Genomic DNA was sequenced on an Illumina NovaSeq platform, followed by quality control and alignment. A depth-matched reference was generated by dynamically selecting control samples with similar coverage profiles. Copy-number states across the target region were inferred using DECoN and categorized as deletion, neutral, or duplication. Variant allele frequencies (VAFs) at informative heterozygous loci were modeled using kernel density estimation (KDE) and were integrated with CNV calls to distinguish CN-LOH from LOH with deletion. The assay was applied to 96 TP53-mutated patients; 14 samples were cross-validated by WES. The association between biallelic status, upgraded by the LOH assay, and clinical outcomes was investigated.

Results: Bone marrow samples were obtained at diagnosis or pre-transplant during non-remission (61 MDS, 33 AML, 2 CMML/MPN). TP53 multi-hit at diagnosis was defined as: (i) ≥2 TP53 mutations, (ii) a single TP53 mutation with VAF >55%, or (iii) a single TP53 mutation with del(17)/del(17p). At diagnosis, 60.4% (59/96) were classified as multi-hit. AIM-LOH Panel detected LOH events in 34.4% (33/96) of patients (9 LOH, 24 CN-LOH) and

reclassified 8 patients from single-hit to multi-hit ("upgrade multi-hit"). VAFs were higher in reclassified multi-hit cases and in LOH-positive cases (P<0.0001). LOH events were fully concordant with WES (7 LOH/CN-LOH, 7 non-LOH), with strong VAF correlation (R^2=0.9590, P<0.0001). VAFs of ddPCR in 53 samples also showed high concordance with NGS-LOH (R^2=0.9809, P<0.0001). Notably, multiple TP53 mutations were more frequent in the non-LOH group than the LOH/CN-LOH group (33.3% vs 12.1%, P=0.024) and were inversely associated with LOH in multivariable analysis (adjusted OR 0.22, P=0.015). Patients were stratified as single-hit (n=29), multi-hit (n=59), or upgrade multi-hit (n=8). The single-hit group had higher 1-year OS than the multi-hit group (77.8% vs 57.4%, P=0.0215). Among 78 transplanted patients, post-transplant outcomes did not differ significantly across groups. In the entire cohort, HSCT independently predicted improved OS (HR=0.34, P=0.0043) and PFS (HR=0.49, P=0.034).



Factors associated with TP53 LOH	Univariate HR (CI95)	p.value	Multivariate OR (CI95)	p.value
CK/MK	1.5 (0.63-3.7)	0.366	1.99 (0.79-5.29)	0.154

TP53 >1 mutations	0.27 (0.075-0.82)	0.0308	0.22 (0.057-0.68)	0.0149
Age (per 10 years)	1.39 (0.99-2.05)	0.0726	1.46 (1.03-2.17)	0.0426
Factors influenced OS in whole cohort	**Univariate HR (CI95)**	**p.value**	**Multivariate HR (CI95)**	**p.value**
CK/MK	1.93 (1.02-3.67)	0.044	1.78 (0.88-3.61)	0.1108
Received HSCT	0.33 (0.16-0.67)	0.002	0.34 (0.16-0.71)	0.0043
LOH	1.33 (0.68-2.58)	0.401	NA	NA
Multi-hit	2.21 (1.1-4.44)	0.026	1.45 (0.62-3.38)	0.3954
>1 mutations	1.45 (0.77-2.72)	0.252	1.14 (0.56-2.29)	0.7205
Factors influenced PFS in whole cohort	**Univariate HR (CI95)**	**p.value**	**Multivariate HR (CI95)**	**p.value**
CK/MK	1.26 (0.75-2.13)	0.377	NA	NA
Received HSCT	0.46 (0.24-0.86)	0.016	0.49 (0.26-0.95)	0.0338
LOH	1.26 (0.72-2.23)	0.418	NA	NA
Multi-hit	1.52 (0.88-2.6)	0.132	1.38 (0.8-2.4)	0.2498
>1 mutations	1.2 (0.68-2.1)	0.527	NA	NA

Conclusions: This AIM-LOH Panel demonstrated complete concordance with WES at lower cost and shorter turnaround time. It reclassified 8 patients from single-hit to multi-hit, suggesting that LOH inference based on karyotype and VAF may misassign multi-hit. LOH was more common in older patients and those with a single TP53 mutation, and HSCT associated with improved outcomes. Limitations include the small sample size and the lack of validation in samples with low VAF. Overall, this method may facilitate risk stratification and support timely clinical decision-making.

Disclosure: Technical support was provided by Shanghai Tissuebank Biotechnology Co., Ltd. (Shanghai, China). The authors declare no conflicts of interest.

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COMPARATIVE OUTCOMES OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION IN MYELODYSPLASTIC/MYELOPROLIFERATIVE NEOPLASMS AND OTHER MYELODYSPLASTIC SYNDROMES: BRAZILIAN SBTMO/CIBMTR REGISTRY ANALYSIS

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Background: Myelodysplastic/Myeloproliferative neoplasms (MDS/MPN) are heterogeneous category of myeloid malignancies characterized by overlapping pathological and molecular features of both Myelodysplastic Syndrome (MDS) and Myeloproliferative neoplasms (MPN). Chronic myelomonocytic leukaemia (CMML), MDS/MPN with neutrophilia, MDS/MPN with SF3B1 mutation and thrombocytosis, and MDS/MPN, not otherwise specified (NOS) forms. These disorders often present with varying degrees of cytopenias and cytoses, and their prognosis remains poor despite advances in treatment. The objective of this study is to describe the clinical characteristics and transplantation outcomes of patients with MDS/MPN

who underwent allo-Hematopoietic Cell Transplantation (HCT) in Brazil and compare their outcomes with those of patients with other MDS.

Methods: This retrospective registry based-study included all consecutive 570 patients who received their first allo-HCT from any donors for MDS/MPN between 2012 and 2024, and reported to the Brazilian Registry of the Hematopoietic Cell Transplantation and Cell Therapy (RBTCH-TC), a partnership between the Brazilian Society of Hematopoietic Cell Transplantation and Cellular Therapy (SBTMO-CT) and the Center for International Blood & Marrow Transplant Research Registry. Categorical variables were compared using the Chi-square test or Fisher's Exact Test were conducted. Survival probabilities were estimated by the Kaplan-Meier method ($p<0.05$). Multivariable analysis was performed using Cox proportional hazards regression with a, stepdown approach, ($p<0.1$), using R Software (V. 4.2.1).

Results: Of 570 included patients, 94 (16.5%) had MDS/MPN and 476 (83.5%) had other MDS classifications (MDS). Among the 94 patients with MDS/MPN, the most frequent types were unclassifiable (60.6%) and CMML (29.8%). In the MDS/MPN group, 48.9% of patients were aged ≥60 years, 60.6% were male, most received grafts from haploidentical donors (47.9%), the majority had HCT-CI scores of 0 (57.4%), the mobilized peripheral blood was the predominant graft source (69.1%), and conditioning regimen was myeloablative in 50% of cases. MDS/MPN patients were significantly older ($p<0.001$) and more frequently had Karnofsky performance status (KPS) ≤80% ($p=0.004$) compared with MDS patients (Table 1). At 25 months, overall survival (OS) was significantly lower in MDS/MPN patients (41.9%) compared to those with MDS (59.7%, $p=0.03$; Figure 1a). Relapse-free survival (RFS) was also inferior in MDS/MPN patients (39.2% vs. 56.6%, $p=0.003$; Figure 1b), while non-relapse mortality (NRM) showed no statistically significant difference between groups ($p=0.331$; Figure 2C). In univariate analysis, MDS/MPN was associated with inferior OS (HR=1.44, 95%CI 1.03–2.00, $p=0.031$) and RFS (HR=1.58, 95%CI 1.16–2.14, $p=0.003$). In multivariable analysis, MDS/MPN remained an independent risk factor for inferior RFS (HR=1.35, 95%CI1.03–1.88; $p=0.0079$). The main limitation of this study was the heterogeneous patient characteristics.

Table 1: Patient and transplant characteristics of the study cohort (N=570).

Characteristics	MDS (n = 94)	MDS/MPN (n = 476)	P value
Age at transplant, median years (range)	50 (23-62)	59 (45.5-65.8)	**< 0.001***
Patient sex, n (%)			0.30
• Female	215 (45.2)	37 (39.4)	

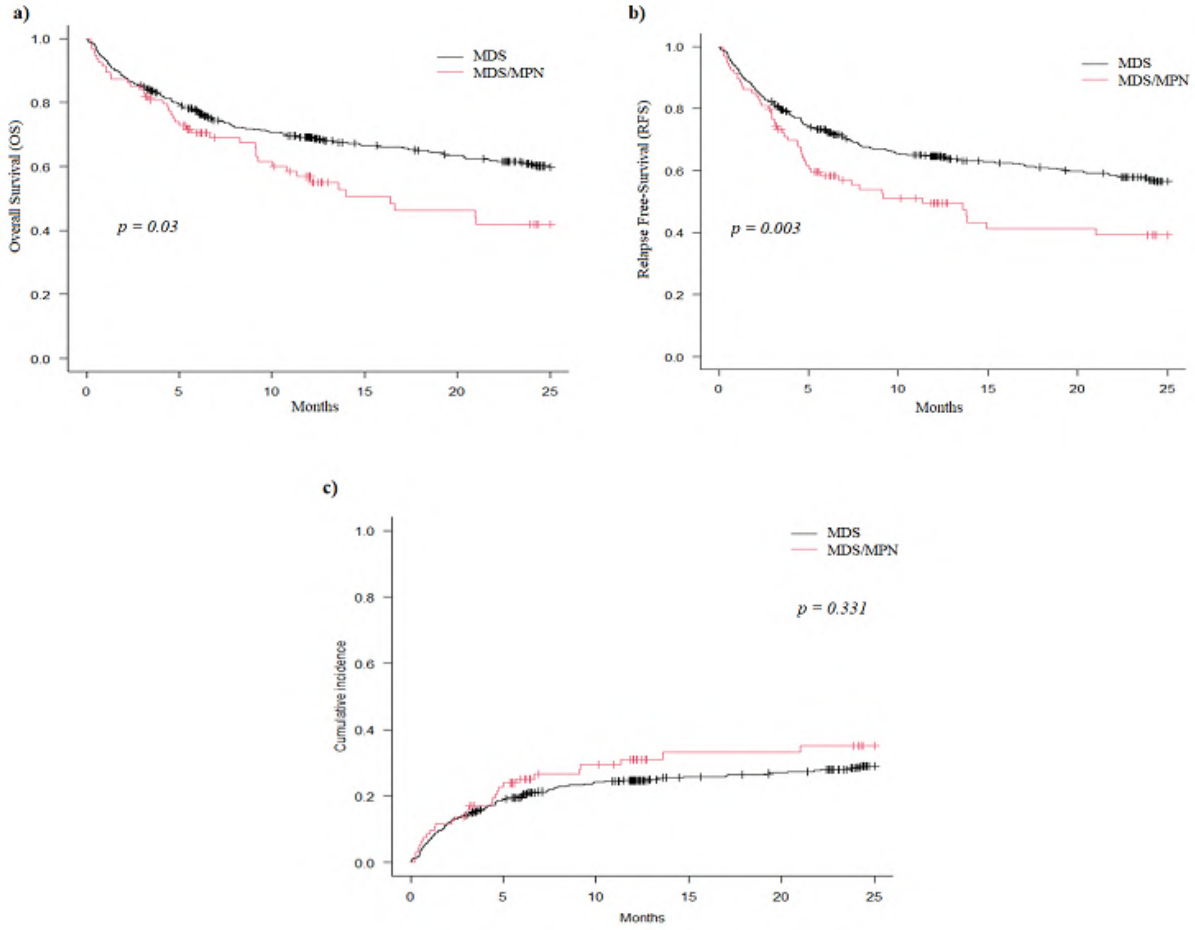
Table 1: Patient and transplant characteristics of the study cohort (N=570).

• Male	261 (54.8)	57 (60.6)	
HLA donor type, n (%)			0.243
• Matched Related	153 (32.1)	22 (23.4)	
• Matched Unrelated	119 (25)	27 (28.7)	
• Mismatched (Haploidentical)	204 (42.9)	45 (47.9)	
Graft cell source, n (%)			0.23
• Mobilized peripheral blood	284 (59.7)	65 (69.1)	
• Bone marrow	188 (39.5)	29 (30.9)	
Karnowfsky Performance Status at transplant, n (%)			**0.004***
• 100-90	383 (80.5)	65 (69.1)	
• ≤80	86 (18.1)	23 (24.5)	
Survival Status, n (%)			0.244
• Alive	284 (59.7)	50 (53.2)	
• Dead	192 (40.3)	44 (46.8)	
Note: p-value Chi-square test, *p<0.05. Abbreviations: HLA, Human Leukocyte Antigen;			

Table 1: Patient and transplant characteristics of the study cohort (N=570).

MDS: myelodysplastic syndromes; MDS/MPN: Myelodysplastic/myeloproliferative neoplasms.

Figure 2: Overall Survival, Relapse-Free Survival (RFS) and Non-relapse mortality (NRM) after First Allogeneic HCT in Patients with MDS (N=476) versus MDS/MPN (n=94). (A) The survival estimates at 25 months were 59.7% (95% CI, 54.7-64.4) for patients with MDS (black line), and 41.9% (95% CI, 29.3%-53.9%) for patients with MDS/MPN (red line). (B) The survival estimates at 25 months were 56.5% (95% CI, 51.5-61.2) for patients with MDS (black line), and 39.2% (95% CI, 27.5%-50.7%) for patients with MDS/MPN (red line). (C) The cumulative incidence of relapse estimates at 25 months were 29% for patients with MDS (black line), 35.2% for patients with MDS/MPN (red line).



Conclusions: In conclusion, patients transplanted for MDS/MPN were older, had poorer performance status, and experienced inferior OS and RFS compared with patients transplanted for other MDS subtypes. These findings confirm the adverse prognosis of MDS/MPN and underscore the need for further studies aimed at optimizing conditioning

strategies, donor selection, and post-transplant management to improve curative outcomes for this challenging patient population.

Disclosure: Nothing to declare

B420

OUTCOME OF UNRELATED AND HAPLOIDENTICAL HSCT AMONG CHILDREN WITH MYELODYSPLASTIC SYNDROME

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Background: Myelodysplastic Syndrome (MDS) in children is a rare hematologic disorder, characterized by dysregulation of hematopoiesis and a high risk of progression to acute myeloid leukemia. Despite significant advances in the diagnosis and treatment of MDS in adults, there remains a need in pediatric practice to accumulate clinical experience and analyze outcomes.

Methods: 36 patients with MDS received allogeneic hematopoietic stem cell transplantation (HSCT). 16 patients were treated using the αβ T-cell depletion platform, 17 patients were treated using post-transplant cyclophosphamide (PTCy), 3 – with conventional CNI-based GVHD prophylaxis (group characteristics, table 1).
All patients had cytopenia: transfusion dependence, leukopenia with neutropenia moderate to severe, 5 patients had progression to acute myeloid leukemia (AML).
17 cases had germline condition predisposing to MDS: 2 - Shwachman-Diamond syndrome (SDS), 2 - Severe Congenital Neutropenia, 2 unspecified primary immune deficiency, 1 patient due to Diamond-Blackfan anemia, 2 patients had Down syndrome, 1 patient had Noonan syndrome. Eight patients (22.2%) were found to have SAMD9/SAMD9L (all had monosomy 7), 1 patient had GATA1 (Down syndrome), 1 patient had GATA2, and 1 patient had CHECK2. Cytogenetic characteristics of MDS: monosomy 7 was detected in 14 patients (38.9%), trisomy 8 in 2 patients (5.5%), and 20 patients (55.6%) had no cytogenetic rearrangements.
27 patients (75%) did not receive chemotherapy before HSCT. 5 patients with AML received various courses of hypomethylating agents.
Preparative regimen included treosulfan 42 gr/m^2, fludarabine 150 mg/kg, thiotepa 10 mg/kg or melphalan 140 mg/m^2. Thymoglobulin 5mg/kg or ATGAM 100 mg/kg and rituximab 200mg/m^2 were used in a proportion of cases.
Post-transplant GVHD prophylaxis included for αβ T-cell depletion tacrolimus until day 180. In the PTCy group ruxolitinib 10 mg/m² until day +90, vedolizumab 10 mg/kg on days 0, +14,

+28, +60, abatacept 10 mg/kg on days +5, +14, +28, +60, +90 and PTCy on days +3, +4. For PBSC grafts were depleted of TCRαβ and CD19 cells with CliniMACS device. For PTCy unmanipulated bone marrow was used.

Group characteristics, table 1

Sex, male/female	16/20
Age, median at HSCT, years	8.7 (0.96-16.92)
Median time from diagnosis to HSCT, years	0.69 year (0.07-11.12)
Type of donor	
Haploidentical/ unrelated matched (MUD)/ matched related (MRD)	18/17/1
Graft characteristics	
αβT-CD	
CD34, *10^6/kg	7.15 (2.76-13.2)
T cells, *10^6/kg	13.35 (4.3-23.03)
PTCy	
CD34, *10^6/kg	5.03 (2.51-6.49)
T cells, *10^6/kg	29 (0.3-61.48)

Results: Cumulative incidence (CI) of engraftment were 0.917 (95% CI 0.83–1) for all patients. αβ T-cell depletion: the median 13 (9-26) days for white blood cells (WBC); 13 (9-29) days for platelets, PTCy: the medians 24.5 (15-33) days for white blood cells (WBC); 23.5 (13-256) days for platelets.
CI rejection was 0.26 (95% CI 0.14-0.48), 1 patient (competing events – 3 patients with no engraftment, 8 patients died). Eight patients died: 4 from TRM (1 patient with no engraftment, 1 patient with rejection, 2 patients from severe infection), 4 from progression (3 patients with AML, 1 patients with SDS). A median follow-up is 3.6 (0.29-13.43) years for all patients. Event–free survival was 66% (95% 49.5-82.8), respectively. Overall survival is 72.5% (55.8-89.2)

Conclusions: Significant proportion of pediatric MDS are associated with PID and inherited predisposition syndromes. Haploidentical and MUD HSCT provide a good chance of survival in pediatric MDS. Both key modern platforms of GVHD prevention, αβ T-cell depletion and PTCy, ensure acceptable outcome, although non-relapse mortality remains a problem.

Disclosure: Nothing to declare.

P303

IMPACT OF ALCOHOL CONSUMPTION AND SMOKING HISTORY ON OUTCOMES AFTER ALLO-HCT IN PATIENTS WITH MDS-RELATED DISEASES

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Background: Several studies have suggested associations between alcohol consumption, smoking, and the development of myelodysplastic syndromes (MDS), as well as disease prognosis. However, the impact of these lifestyle factors on outcomes after hematopoietic stem cell transplantation (HCT) in patients with MDS-related diseases remains unclear. We conducted a single-center retrospective study to evaluate the effects of alcohol consumption and smoking history before diagnosis on post-transplant outcomes.

Methods: We retrospectively analyzed 112 adult patients with MDS, acute myeloid leukemia with myelodysplasia-related changes (AML-MRC), or MDS/myeloproliferative neoplasm who underwent HCT between 2010 and 2024. Stem cell sources included bone marrow (n=57), peripheral blood stem cells (n=33), and cord blood (n=22).
Alcohol history was classified as drinkers (n=55) and non-drinkers (n=57) and further stratified into heavy (n=16) and light drinkers (n=32) according to the Japanese Ministry of Health recommendations, excluding missing data. Smoking history was categorized as ever-smokers (n=60) and never-smokers (n=52); ever-smokers were subdivided into current (n=15) and former smokers (n=45). Pack-years were used as a quantitative smoking index. Overall survival (OS), relapse rate (RR), and non-relapse mortality (NRM) after HCT were analyzed. Multivariable Cox proportional hazards models were constructed after confirming acceptable multicollinearity using variance inflation factors, adjusting for age, diagnosis, HCT-CI score, and IPSS-R.

Results: Drinkers showed inferior OS compared with non-drinkers (1-year OS, 55.2% vs 80.3%, P=0.005). Among drinkers, heavy drinkers demonstrated markedly worse OS than non-drinkers (1-year OS, 21.9%, P<0.001) and were identified as a strong adverse prognostic factor (HR 4.85, 95% CI 2.40–9.80, P<0.001). Drinkers tended to have higher early relapse rates than non-drinkers (1-year RR, 34.5% vs 15.8%, P=0.06), while heavy drinkers had a significantly higher relapse rate (1-year RR, 50.0%, P=0.005). NRM was numerically higher among heavy drinkers, although no statistically significant difference was observed.
Smoking history was not significantly associated with OS, although ever-smokers showed a trend toward inferior survival. No dose-dependent association with pack-years was identified. In contrast, ever-smokers had a significantly higher early relapse rate than never-smokers (1-year RR, 35.0% vs 13.5%, P=0.013), while NRM did not differ by smoking history.
In multivariable analyses, heavy alcohol consumption remained independently associated with inferior OS together with age and AML-MRC (HR 3.20, 95% CI 1.29–7.97, P=0.01). Neither alcohol consumption nor smoking history was independently associated with relapse

after adjustment, whereas IPSS-R high risk was the only significant predictor of early relapse.

Conclusions: In patients with MDS-related diseases undergoing HCT, heavy alcohol consumption was strongly associated with inferior overall survival and increased relapse in unadjusted analyses and remained an independent adverse prognostic factor for OS after multivariable adjustment. Smoking history was associated with higher relapse rates, although this effect was attenuated after adjustment. These findings suggest that alcohol consumption represents an important modifiable factor influencing post-transplant outcomes.

Disclosure: Nothing to declare

P304

CASE REPORT: CLEARANCE OF TP53 MUTATION POST ALLOGENEIC STEM CELL TRANSPLANT IN THE SETTING OF CHRONIC GVHD, WITH SUBSEQUENT TP53 MYELOID SARCOMA

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Background: *TP53* mutations in myeloid malignancies are well documented as adverse-risk genetic aberrations with extremely poor prognosis. Allogeneic haematopoietic stem cell transplant (allo-HSCT) is a potential curative therapy for *TP53-mutated* myeloid malignancies but outcomes remain poor in this population.

Methods: A 21-year-old male underwent a reduced intensity conditioning sibling HLA matched allo-HSCT (fludarabine and melphalan) in October 2021 for *TP53* (VAF 26%)-mutated myelodysplastic syndrome with marrow fibrosis and excess blasts in the context of Swachman-Diamond Syndrome (SDS). A female sibling was HLA matched and was identified as a heterozygous carrier of the pathogenic SDBS variant. The *TP53* (pTyr220) mutation was confirmed somatic.

Results: This TP53 variant was tracked using next generation sequencing (NGS) on post allograft samples and remained detected at VAF of 3% on day +30 despite full donor chimerism. During ciclosporin wean, the patient developed chronic GVHD of the mouth, eyes and liver. cGVHD was managed with topical steroids and intermediate dose oral prednisolone. As cGVHD developed, there was evident clearance of the TP53 mutation.
TP53 was sequenced at the following time points:

- Day+30 TP53 pTyr220 VAF 3%
- Day +100 TP53 pTyr220 <1% VAF
- Day +180 TP53 pTyr220 not detected
- Day +360 TP53 pTyr220 not detected
- 13 months post allo-HCT confirmed relapse with myeloid sarcoma

12 months post stem cell transplant (December 2022) the patient was diagnosed with relapsed *TP53*-mutated myeloid malignancy (CD13/CD33/CD34/CD117/HLA-DR+ and MPO weak) as myeloid sarcoma in the right shoulder and left paravertebral space. This was despite active cGVHD and no *TP53* mutation detectable on bone marrow biopsy one month prior. At the time of relapse, the bone marrow demonstrated 100% donor chimerism by XY FISH. Biopsy sample of the sarcoma was sent for next generation sequencing and identified *TP53* (pTyr220), *RUNX1* (pPro 325) and *NRAS* (pGln61) mutations The *TP53* and *RUNX1* mutations were detected on the initial diagnostic marrow in 2021 but the *NRAS* mutation was new. Despite salvage therapy the patient died due to progressive myeloid sarcoma.

Conclusions: Somatic mutations in acute myeloid leukaemia can be monitored as minimal residual disease (MRD) markers pre and post allograft. TP53 is not currently recognised as a valid MRD marker. Typically, persistence of MRD early post-transplant is highly associated with imminent relapse and few cases have described clearance of somatic mutations in the setting of developing cGVHD. The myeloid sarcoma was found to have a new *NRAS* mutation as well as the ancestral TP53 and RUNX1 variants. RAS pathway mutations are enriched in myeloid sarcoma and monocytic malignancies, which are known to have a predilection for sarcoma development.

Disclosure: Nothing to declare.

P305

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN LOW-RISK MYELODYSPLASTIC SYNDROME: A CASE SERIES OF SINGLE-CENTER EXPERIENCE

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Background: The indication for allogeneic hematopoietic stem cell transplantation (HSCT) in patients with lower-risk myelodysplastic syndrome (MDS) is controversial. Here we report the outcome of allogeneic HSCT in patients with low-risk MDS.

Methods: A total of 275 allogeneic stem cell transplantations (HSCT) were performed at Ege University Adult Bone Marrow Transplantation Unit in Turkey from January 2016 to November 2025. Six of them had undergone allogeneic HSCT with a low-risk MDS diagnosis. Medical records were evaluated retrospectively.

Results: Three of 6 patients were female and median age of diagnosis was 56.5 (28-69). Five of the six patients were diagnosed with MDS with low blasts, and one was diagnosed with MDS with low blasts and ring sideroblasts. Three patients had an ECOG score of 1 and three had a score of 0. The median ferritin level before transplantation was 1318 µg/L (140-6199). The median time to transplantation was 527.5 days (281- 2096) and the infused median stem cell count was 5.15 × 10^6/kg (range: 4.2– 8.25). The median donor age was 31 (range 20-52), and 4 donors were male and 2 were female. All patients and donors were

CMV positive. There was one major and one minor blood group incompatibility between recipients and donors. All transplants were performed using reduced-intensity conditioning. The median neutrophil and thrombocyte engraftment time were 24.5 (12-30) and 18 (12-27) days, respectively. Severe HSOS developed in 2 patients. CMV reactivation occurred in 1 patient and treated successfully. Acute GVHD (grade 1-2) developed in the gastrointestinal system in 1 patient. Median overall survival was 56 months (11-85.5). Median disease free survival was 12.75 months (1-68). At the last follow-up, 3 patients had died while 3 patients were healthy. Two patients died within the first 100 days because of severe HSOS.

Table 1: Characteristics of case series

Patients	Sex	Age at HSCT	R-IPSS	Risk Factors	Time to HSCT (days)	HCT-CI	Donor type	Conditioning regimen	HSOS	TRM	Alive
1	M	61	Low	Failure to erythropoietin, Severe neutropenia, > 2 U erythrocytes transfusion per month	2096	0	Haploidentical	Bu-Flu-TBI	Yes	Yes	No
2	F	44	Low	Failure to erythropoietin, > 2 U erythrocytes transfusion per month	527	0	MRD	Bu- Flu-AraC	No	No	Yes
3	F	29	Low	Severe thrombocytopenia	478	1	MMUD	Bu- Flu-AraC	No	No	Yes
4	M	70	Int	Poor cytogenetics, Severe thrombocytopenia	281	4	MMUD	Bu-Flu-ATG	No	No	No
5	F	59	Int	Severe thrombocytopenia	528	1	MUD	Flu-Cy-ATG	No	No	Yes
6	M	64	Int	Failure to erythropoietin	616	4	MUD	Bu-Flu-ATG	Yes	Yes	No

*R-IPSS: revised international prognostic score, Severe thrombocytopenia (<20 x 10^9/L), Severe neutropenia (<10 x 10^9/L), HCT-CI: Hematopoietic cell transplantation - specific comorbidity index, MUD: Matched unrelated donor, MMUD: Mismatched unrelated donor, MRD: Matched related donor, Bu: Busulfan, Flu: Fludarabine, TBI: Total body irradiation, ATG: Anti-thymocyte globulin, AraC: Cytarabine, HSOS: Hepatic sinusoidal obstruction syndrome, TRM: transplant related mortality.

Conclusions: In this small retrospective case series, we demonstrated the success of early allogeneic transplantation in patients with young, fully matched, related or unrelated donors. Thus, selecting an appropriate donor and promptly performing allogeneic transplantation appears to increase the success rate for low-risk MDS patients with risk factors.

Disclosure: Nothing to declare.

Myelofibrosis, Chronic Myeloid Leukaemia and Other Myeloproliferative Disorders

OS01-01

ROLE OF GENETIC ALTERATIONS IN PATIENTS TRANSPLANTED FOR CMML: AN ANALYSIS OF A FRENCH COHORT, ON BEHALF OF THE SFGM-TC

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Background: HSCT is the only potential curative therapy in CMML. The aim of our study is to analyze risk factors in transplanted CMML patients.

Methods: All adult patients transplanted in the SFGM-TC registry between 2010 and 2023 for CMML were included. In univariate analyses, estimates were given at 24 months and used the log-rank test for overall survival (OS), and Progression-free Survival (PFS); and Gray's test for cumulative incidence outcomes (relapse incidence (RI), non-relapse mortality (NRM), graft-versus-host (GVH)). Multivariable analyses used Cox proportional hazards models for OS, PFS and cause-specific Cox models for competing risk endpoints.

Results: 516 patients were included. Among patients with available data, 249 (62.7%) and 148 (37.3%) were classified as CMML-1 and 2, respectively, and 223 (55.6%) were considered as proliferative CMML at diagnosis. Cytogenetic risk according to CPSS was high, intermediate or low in 81 (17.5%), 51 (11%) and 332 (71.6%), respectively. 165 (62.5%), 58 (36.5%), 70 (44%), and 26 (18.4%) were mutated for *ASXL1*, *NRAS*, *RUNX1*, and *SETBP1*, respectively. The conditioning regimen was reduced intensity in 410 (79.6%). Donor type was matched sibling donor in 117 (22.7%), unrelated in 305 (59.1%) and mismatched related in 94 (18.2%).
Median age at HSCT was 62.52 years [IQR: 57.4-66.3]. In the entire cohort, 24-months OS and PFS were 55% (95% CI: 51-60) and 45% (95%CI:41-50) respectively. NRM and RI were 21% (95% CI: 18-25) and 33% (95% CI: 29-37). Grade II-IV and III-IV acute GVHD incidences were 32% (95%CI:28-36) and 12% (95% CI: 10-15), respectively. Extensive chronic GVHD incidence was 31% (95% CI: 27-35).
In univariate analysis, an HLA mismatched donor (OS 48% vs. 59% for matched donor, p=0.004), and red blood cell transfusion before SCT (OS 48% vs 66%, p<0.001) increased the risk of death. Thrombocytopenia <100x10^9/l at SCT increased the risk of relapse (38% vs. 26%, p=0.0084) or death (OS 51% vs. 62%, p=0.028). An HLA mismatch donor (31% vs. 17%, p<0.001) and sex mismatch (female donor to male recipient, 27% vs. 20% for other gender match, p=0.0114) increased the risk of NRM. Regarding genetic alterations, cytogenetic risk was not significantly associated (p=0.06) with OS (45%, 52%, 59%, in high, intermediate and low risk, respectively) PFS or NRM but was associated with RI (44%,

40%,29%, respectively, p=0.0397). After adjustment (Table 1), cytogenetic risk was confirmed as a risk factor for RI and OS. Univariate analysis highlighted *ASXL1* mutation as a risk factor for worse OS, PFS and NRM but not RI. *N-RAS* and *SETBP1* mutations were risk factors for PFS, while *RUNX1* mutation increased the risk of mortality. After adjustment (Table 1), *ASXL1* and *NRAS* mutations were significant predictors for OS or PFS while no mutation predicted RI. *ASXL1* mutation was strongly associated with NRM.

			95.0% CI		
		HR	Inferior	Superior	p
OS	***ASXL1* mutation**	**2.41**	**1.41**	**4.12**	**0.00133**
	NRAS mutation	1.64	0.93	2.88	0.0864
	RUNX1 mutation	1.23	0.66	2.27	0.512
	SETBP1 mutation	1.33	0.56	3.15	0.518
	Karyotype CPSS intermediate vs. high	**0.54**	**0.3**	**0.98**	**0.0417**
	Karyotype CPSS low vs. high	0.73	0.52	1.05	0.0869
PFS	*ASXL1* mutation	1.54	1	2.39	0.0511
	***NRAS* mutation**	**1.81**	**1.09**	**3.01**	**0.0227**
	RUNX1 mutation	0.89	0.52	1.52	0.661
	SETBP1 mutation	1.59	0.8	3.16	0.186
	Karyotype CPSS intermediate vs. high	0.66	0.38	1.12	0.124
	Karyotype CPSS low vs. high	0.79	0.57	1.1	0.167
RI	*ASXL1* mutation	1.04	0.61	1.77	0.885
	NRAS mutation	1.23	0.66	2.27	0.512
	RUNX1 mutation	1	0.52	1.92	0.996
	SETBP1	1.49	0.62	3.62	0.376
	Karyotype CPSS intermediate vs. high	0,8	0,43	1,48	0,469
	Karyotype **CPSS low vs. high**	**0.64**	**0.42**	**0.97**	**0.0375**
NRM	***ASXL1***	**3.45**	**1.48**	**8.03**	**0.00413**
	NRAS	2.03	0.79	5.24	0.142
	RUNX1	0.7	0.26	1.88	0.473
	SETBP1	1.94	0.65	5.83	0.236
	Karyotype CPSS intermediate vs. high	0.4	0.13	1.2	0.101
	Karyotype CPSS low vs. high	1.08	0.62	1.87	0.796

Conclusions: This registry study showed that more than half of patients were alive and free of their disease 2 years after HSCT. Cytogenetic risk is useful in predicting relapse in these patients. While *ASXL1* mutation is the strongest predictor for OS and NRM, none of the mutations predict risk of relapse.

Disclosure: Yves Chalendon has received consulting fees for advisory board from MSD, Novartis, Incyte, BMS, Pfizer, Abbvie, Roche, Jazz, Gilead, Amgen, Astra-Zeneca, Servier, Takeda, Pierre Fabre, Medac all via the institution; Travel support from MSD, Roche, Novartis, Pfizer, BMS, Gilead, Amgen, Incyte, Abbvie, Janssen, Astra-Zeneca, Jazz, Pierre Fabre, Sanofi all via the institution.
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OS01-02

COMPARISON OF GVHD PROPHYLAXIS STRATEGIES IN MYELOFIBROSIS PATIENTS UNDERGOING ALLOGENEIC CELL TRANSPLANTATION FROM MATCHED RELATED DONORS: A STUDY BY THE EBMT CHRONIC MALIGNANCIES WORKING PARTY

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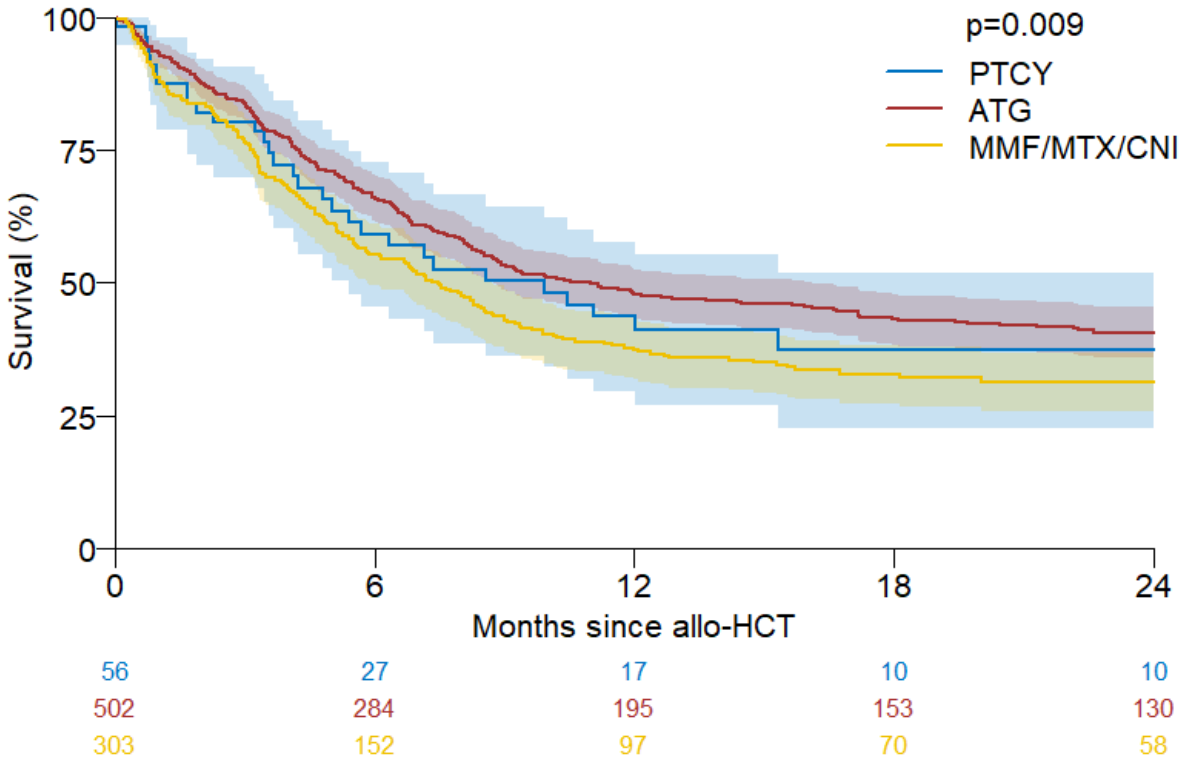
Background: Post-transplant cyclophosphamide (PTCy)-based prophylaxis has been successfully extended to matched related donor (MRD) allogeneic hematopoietic cell

transplantation (allo-HCT), although limited data are available on its efficacy and safety compared to conventional approaches in myelofibrosis (MF) patients undergoing MRD allo-HCT. We hereby present the outcomes of PTCy vs other GvHD prophylaxis regimens in MF patients transplanted with MRD, using data from the EBMT registry.

Methods: A total of 902 MF patients undergoing their first allo-HCT with a MRD between 2014 and 2022 across 227 participating centers, received either PTCy-based, ATG-based, or conventional prophylaxis (CP) with MMF/MTX/CNI without PT-CY or ATG. Patients with history of leukemic transformation were excluded. Primary endpoint of the study was GRFS.

Results: Overall, with a backbone of CNI prophylaxis, 58 patients received PTCy (35 with MMF), 526 received ATG-based prophylaxis (246 with MMF and 185 with MTX) and 318 received CP (126 with MMF and 165 with MTX). Baseline characteristics of the three groups were comparable, except for a higher proportion of patients with HCT-CI>3 in the PT-CY group (41% vs 21% and 23%). Busulfan-based conditioning regimen was used in the majority of pts across all three cohorts.
GRFS at 2 years was 37% (PTCy), 41% (ATG), and 31% (CP) (p=0.009), being significantly higher for ATG compared to CP, while no statistically significant difference was found comparing PTCy and ATG (p=0.4) (Fig.1). Neutrophil engraftment by day +28 was significantly better with ATG and CP as compared to PTCy (88% vs 89% vs 77%, p=0.012), platelet engraftment at day +100 was similar into the three groups (72%, 76%, 75%, p=0.17). With a median follow-up of 36.9 months, 2-ys OS rates were 67% (PTCy), 71% (ATG), 63% (CP), p=0.3.
The 2-yr PFS was 56% (PTCy), 56% (ATG), 58% (CP), p=0.7. The 2-yr cumulative incidence of relapse (CIR) was 29% with PTCy, 22% with ATG and 15% with CP, with no significant difference between PTCy and ATG (p=0.4), while a significantly higher rates of relapse was associated to PTCy and ATG as compared to CP (p=0.038 and p=0.006, respectively). There was no significant difference in 2-yr non relapse mortality (NRM) rates across the 3 groups: 15% in PTCy, 22% in ATG and 27% in CP. CI of Grade II-IV aGvHD was 14% for PT-CY, 18% for ATG, 29% for CP with significantly differences observed between PTCy and CP (p=0.011) and between ATG and CP (p<0.001). CI of extensive cGvHD at 2-yr was 23% for PT-Cy, 22% for ATG, 33% for CP with statistically significant differences between ATG and CP (p<0.001).



Conclusions: These results suggest that in the setting of MRD-HCT for MF, PTCy and ATG-based prophylaxis result in similar outcomes, although the hematologic recovery appears slower with PTCy. Both strategies are associated with lower rates of grade II-IV aGVHD and extensive cGVHD compared with CP, but they are associated with an increased relapse risk. While no differences in overall survival were observed across the three groups, the 2-yr GRFS with PTCY or ATG was slightly higher than with CP.

Disclosure: Nothing to declare

OS01-03

PHASE II SINGLE-CENTER PROSPECTIVE STUDY OF RUXOLITINIB ADMINISTERED BEFORE, DURING AND AFTER STEM CELL TRANSPLANTATION IN PATIENTS WITH MYELOFIBROSIS

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Background: Risk factors specific to myelofibrosis (MF) patients considering hematopoietic cell transplantation (HCT) include splenomegaly associated poor graft function and relapse, decreased performance status due to constitutional symptoms, bone-marrow fibrosis creating a poor environment for stem cell engraftment, and portal and pulmonary hypertension-associated non-relapse mortality (NRM). Use of pre-HCT ruxolitinib (Rux) has ameliorated many of these factors resulting in improved HCT outcomes. However, high rates of acute (71% Grade II-IV) and chronic graft-vs-host disease (GVHD) (55% at 3 years (44% moderate/severe)) in MF patients at our Center with standard tacrolimus and methotrexate GVHD prophylaxis remain an issue, and post-HCT Cytoxan is difficult to tolerate in older patients and those with organ dysfunction.

Methods: We conducted a Phase II single-center prospective study of peri-HCT Rux in patients with primary and secondary MF with a primary endpoint of grade II-IV acute GVHD powered to detect a 20% decrease (90% at a one-sided significance level of .05) compared to historical controls. Patients had to have at least Dynamic International Prognostic Staging System (DIPSS) Intermediate I stage disease, not have received prior HCT, and not transformed to AML. Patients were treated with at least 8 weeks of planned Rux prior to conditioning chemotherapy (cyclophosphamide 120 mg/kg and targeted 4-day busulfan, or fludarabine 150 mg/m2, and melphalan 140 mg/m2). Rux was then tapered to 5mg BID by Day -4 pre-HCT and could be increased up to 10mg BID after post-HCT Day +28 if tolerated. In addition to Rux, GVHD prophylaxis included tacrolimus (Tac) (target level 5-10) and MTX 10mg/m2 on Days 1, 3, 6 and 11; Tac was tapered starting at Day +100 over 4 months and Rux was scheduled to taper between 9-12 months post-HCT.

Results: Forty-five patients median age 63 (range 42-71) received HCT between 2021-2025. The majority had primary MF (56%), were JAK2 mutated (60%), had intermediate-2 or high-risk DIPSS (78%) disease and had at least 1 high-risk molecular mutation (51%). Most had unrelated donors (87% (25% HLA 9/10) and received fludarabine/melphalan conditioning (67%). Patients received Rux for a median of 5.2 (2.6 - 35.8) months prior to conditioning and were continued until a median of 14.5 months post-HCT. All patients engrafted at median Day 18 (range 13 – 43). Acute GVHD grade II-IV was diagnosed in 31% (n = 14), and grades III-IV in 4% (n = 2) patients respectively. The estimated probability of all grades chronic GVHD at one year was 22% (95% CI: [11%, 35%]); 1-year CI for moderate-to-severe chronic GVHD was 7.1% (95% CI: [1.8%, 17%]. Kaplan-Meier estimates of survival at 1 year and 2 years were 95% (95% CI: [89%, 100%]) and 86% (95% CI: [76%, 98%]), respectively. The estimated probability of relapse and NRM at one year were 6.9% (95% CI: [1.8%, 17%]) and 2.5% (95% CI: [0.19%, 12%]), respectively.

Conclusions: Compared to MF patients given standard tacrolimus and methotrexate GVHD prophylaxis at our Center, the incidence of acute GVHD was 40% lower and moderate/severe chronic was < 10% at 1-year evaluation. A multivariate matched comparison analysis is ongoing.

Clinical Trial Registry:

- **Primary ID** RG1006507
- **Secondary IDs** NCI-2020-01626
- **ClinicalTrials.gov ID** NCT04384692

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OS01-04

THE RECENT DEVELOPED AND MULTI-CENTER VALIDATED CONCISE OBJECTIFIABLE RISK EVALUATION (CORE) SCORE PREDICTS NRM RISK PRIOR TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN MYELOFIBROSIS PATIENTS

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Background: The CORE score was recently established in a large, single-center cohort and validated in a multi-center cohort (Weise et al, Cancers 2024, BMT 2025) for prediction of non-relapse mortality (NRM) after allogeneic hematopoietic stem cell transplantation (allo-HCT). This study sought to confirm its ability to predict NRM risk in myelofibrosis patients.

Methods: Three hundred sixteen (316) consecutive adult patients who had undergone allo-HCT for myelofibrosis between 2013 and 2025 at our center, were analysed in regards to NRM (with relapse as competing risk). Of these 208 were diagnosed with primary myelofibrosis, whereas the remaining 108 patients had either post-essential thrombocythemia (ET, n=58) or post-polycythemia vera (PV) myelofibrosis (n=50). Patients with secondary acute leukemia were excluded. 71 patients who had been included in the initial cohort used for the development of the CORE score were excluded from the analysis. HLA-matched unrelated donors were used in 66%, followed by HLA-matched related donors (12%). Haplo-identical related and other HLA-mismatched related donors were used in 5% and 16% of cases, respectively. Myeloablative conditioning was performed in 30%, while reduced intensity conditioning was used for the remaining 70% of patients.
A comparison between CORE score and HCT-CI was conducted using the area under the receiver operating characteristics (ROC) curve and the findings are presented as c-statistics with the corresponding confidence interval (CI). All reported p-values are two-sided and p-

values <0.05 were considered statistically significant. Statistical analysis was performed using RStudio (version 2024.04.1) and SPSS (version 27).

Results: Among 182 patients, for whom full data were available and did not contribute to the development of the CORE score, with a median follow-up for NRM of 711 days, low-risk and intermediate- risk groups accounted for 46% and 49% of the patients with 10 and 28 observed events, respectively. Only a very small population of 9 patients (5%) were high-risk with 4 observed events. The corresponding 2-year NRM rates after allo-HCT were 11% for the low-risk group, 27% for the intermediate-risk group and 44% for the high-risk group (p=0.002). OS rates at 2 years posttransplant were 85%, 65% and 56%, respectively (p<0.001). The CORE score did not significantly impact relapse incidence (p=0.128) (figure 1 and table 1).
In direct comparison, the CORE score performs superior to the HCT-CI score with c-statistics of 0.617 (CI 0.51-0.73) compared to 0.461 (CI 0.35-0.58) for the HCT-CI and 0.484 (CI 0.37-0.6) for the age adjusted HCT-CI. Furthermore, the HCT-CI as well as the age adjusted model fails to predict NRM risks in our cohort with 2-year NRM rates of 24%, 27% and 16% for the low-, intermediate-, and high-risk group, respectively (p=0.614), and 2-year NRM rates of the age adjusted model of 24%, 24% and 21% for the intermediate-, high-, and very-high-risk group, respectively (p=0.939), while the low-risk group contained only one patient without an event.

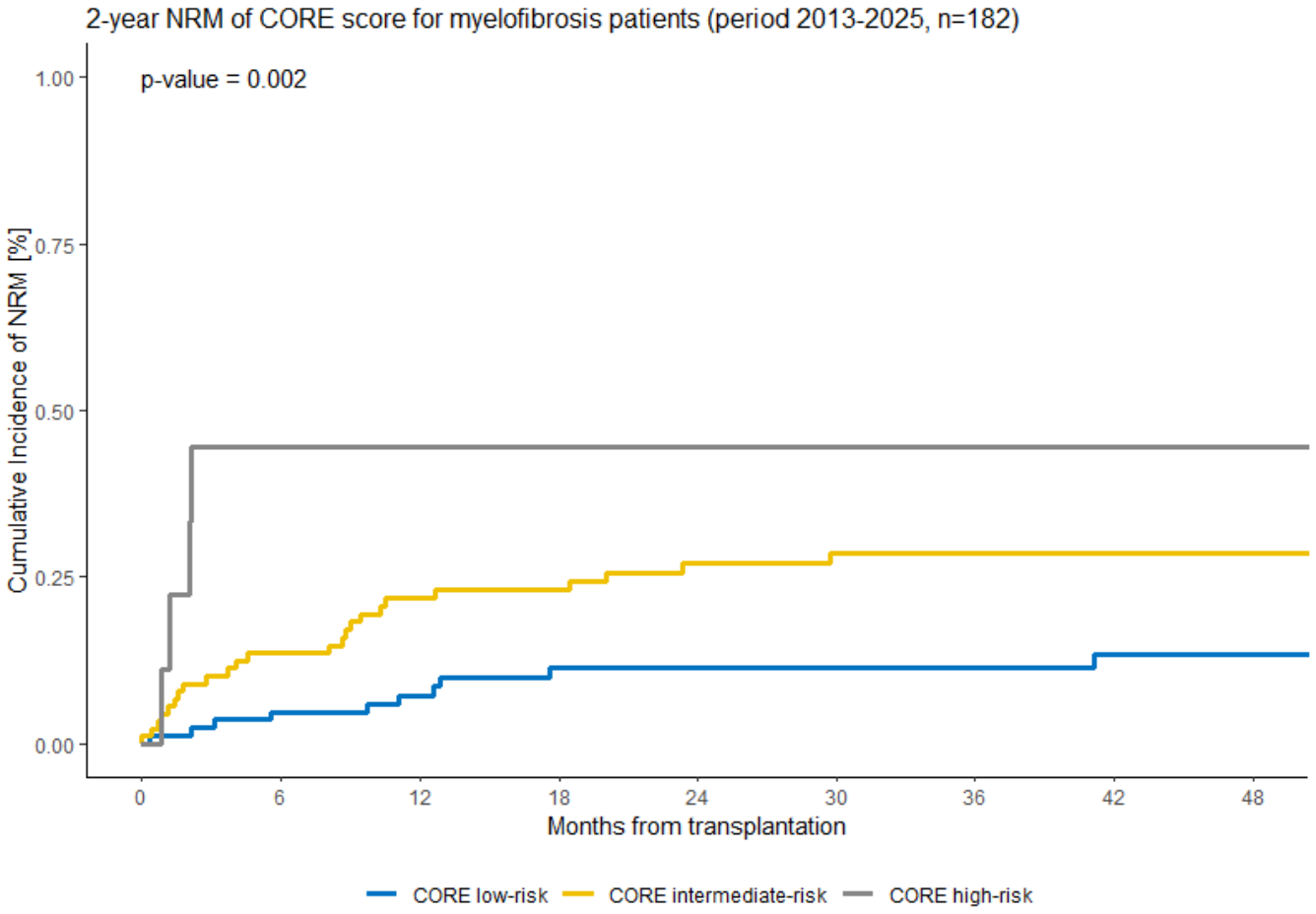

Table 1: CORE risk score prediction for non-relapse mortality, overall survival and relapse in myelo

	NRM			OS			R
Score	HR (95% CI)	P (%)	2-y (%)	HR (95% CI)	P (%)	2-y (%)	HR (95% CI)
Total		0.002			<0.001		
0-1	reference		11	reference		85	reference
2-4	2.94 (1.4-6)	0.003	27	2.79 (1.7-4.6)	<0.001	65	2.13 (1-4.6)
≥5	5.36 (1.5-19.5)	0.011	44	5.39 (2.3-12.6)	<0.001	56	1.83 (0.5-7)
N=182							

Conclusions: The CORE score is a multi-center validated, concise and objectifiable risk evaluation tool which offers improved predictive capability compared to the HCT-CI with regards to the risk of NRM and OS prior to allo-HCT in myelofibrosis patients.

Disclosure: Nothing to declare.

OS01-05

OLVEREMBATINIB-MEDIATED DEEP REMISSION IMPROVES ALLOGENEIC STEM CELL TRANSPLANTATION OUTCOME IN PATIENTS WITH BLAST CRISIS CHRONIC MYELOID LEUKEMIA: THE FIRST REAL-WORLD PRACTICE

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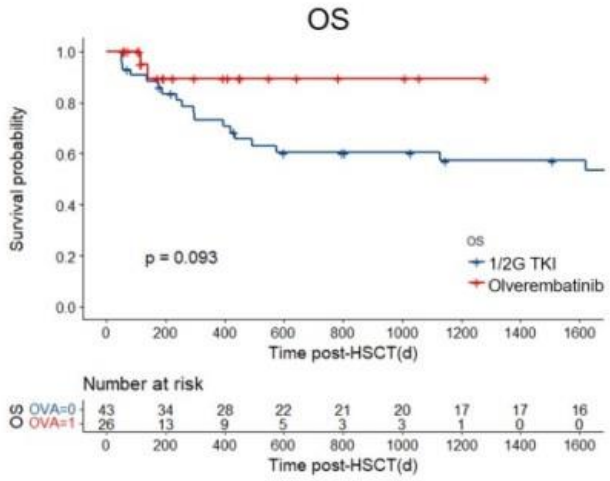
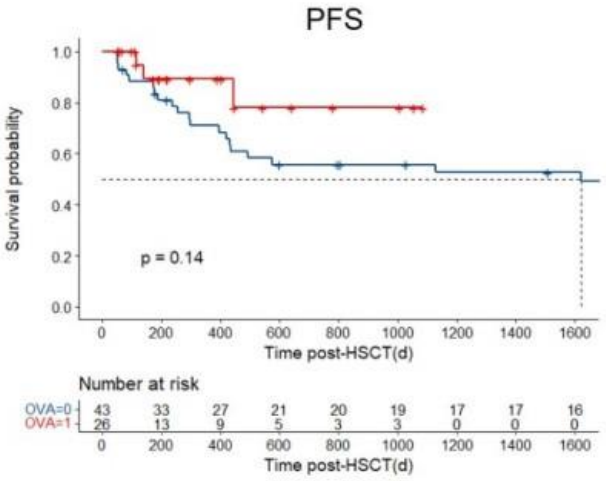
Background: Despite therapeutic advances, blast crisis chronic myeloid leukemia (BC-CML) remains poor outcomes. Long-term survival depends on achieving a second chronic phase (CP) followed by allogeneic hematopoietic stem-cell transplantation (allo-HSCT). We aimed to investigate whether the novel tyrosine-kinase inhibitor (TKI) olverembatinib improves responses and optimizes allo-HSCT outcomes compared to the first-/second-generation TKIs (1/2G-TKIs) in BC-CML.

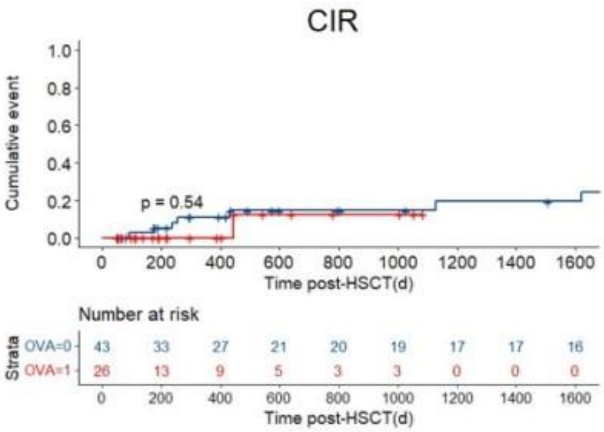
Methods: This real-world practice analysis captured data from consecutively enrolled BC-CML patients aged ≥14 years undergoing allo-HSCT at the Institute of Hematology and Blood Diseases Hospital Chinese Academy of Medical Sciences between November 2021 and July 2025, including both *de novo* and chronic phase-transformed cases. Collected data included demographic and clinical characteristics, treatment responses and transplant-related outcomes. Cumulative incidences of complete cytogenetic response (CCyR), major molecular response (MMR), and complete molecular response (CMR) were calculated using the Fine-Gray test. Categorical variables were analyzed by Fisher's exact test, continuous variables by Mann-Whitney U test. Overall survival (OS) and progression-free survival (PFS) were calculated according to Kaplan Meier. Institutional Review Board (IRB) approval was obtained in accordance with the Declaration of Helsinki.

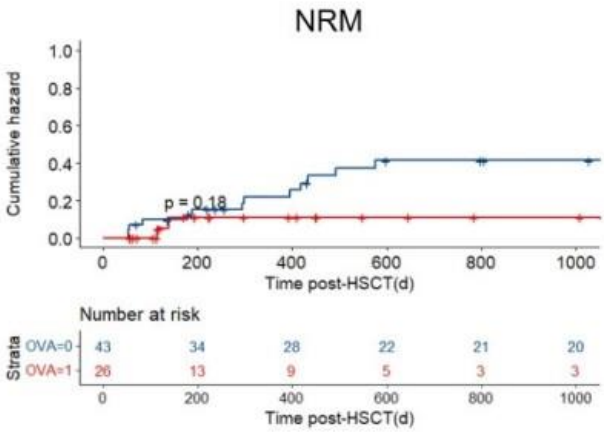
Results: A total of 69 patients with BC-CML receiving pre-transplant TKIs treatment were included in the study (median age 33 years, range 14–61). At BC diagnosis, 40.6% (n=28) exhibited additional cytogenetic abnormality, including 20 complex karyotype. Twenty-one patients (30.4%) harbored ABL1 mutations, predominantly E255K and Y253K. T315I was seen in 6 cases. Thirty-five (50.7%) patients carried additional genetic mutations, including myeloid neoplasm-associated mutations (e.g., ASXL1, RUNX1) and IKZF1 deletions. All patients received TKIs+chemotherapy before transplantation and were stratified by pre-transplant TKIs exposure: 1/2G-TKI cohort (n=43, imatinib, nilotinib, flumatinib or dasatinib) versus olverembatinib (n=26). The olverembatinib cohort demonstrated advanced pre-

transplantation treatment responses: higher hematologic remission rates (100% vs 81%, p<0.05) and CCyR rate (80.8% vs 55.8%, p=0.041). Notably, olverembatinib achieved significantly improved molecular remission at transplantation: MMR 53.8% vs 16.3% (p<0.001) and CMR 23.1% vs 4.7% (p<0.05).
Haploidentical transplants were the predominant HSCT type (olverembatinib 80.8% vs control 58.1%) with no graft failure documented. Both cohorts showed a high incidence of grade II-IV aGVHD (57.7% vs 79.1%) and infections (23.1% vs 65.1%). Olverembatinib cohort showed improved survival: the one-year OS (89% vs 70.8%), and PFS (78% vs 68%), lower NRM (10.6% vs 23%), and reduced relapse incidence (12.5% vs 14.6%).


OS
Survival probability
p = 0.093
OS
1/2G TKI
Olverembatinib
Time post-HSCT(d)
Number at risk
OS
OVA=0 43 34 28 22 21 20 17 17 16
OVA=1 26 13 9 5 3 3 1 0 0
Time post-HSCT(d)


PFS
Survival probability
p = 0.14
Time post-HSCT(d)
Number at risk
OVA=0 43 33 27 21 20 19 17 17 16
OVA=1 26 13 9 5 3 3 0 0 0
Time post-HSCT(d)


CIR
Cumulative event
p = 0.54
Time post-HSCT(d)
Number at risk
Strata
OVA=0 43 33 27 21 20 19 17 17 16
OVA=1 26 13 9 5 3 3 0 0 0
Time post-HSCT(d)


NRM
Cumulative hazard
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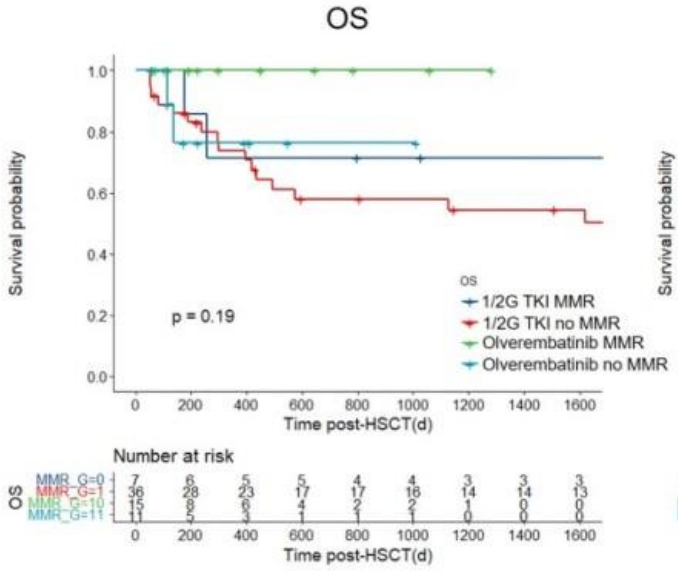
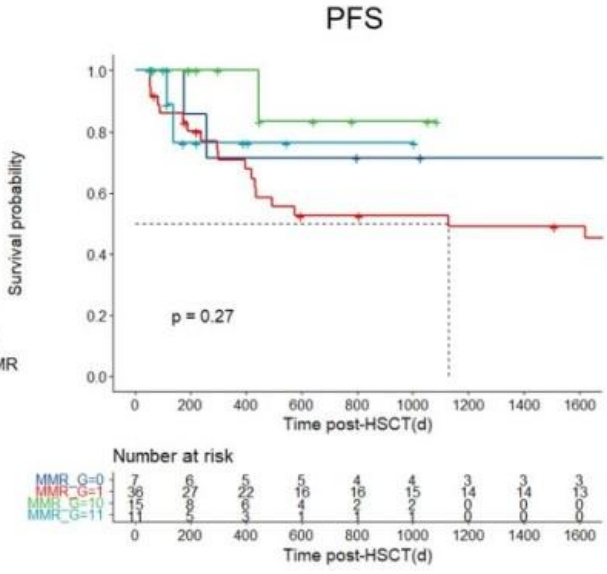
Time post-HSCT(d)
Number at risk
Strata
OVA=0 43 34 28 22 21 20
OVA=1 26 13 9 5 3 3
Time post-HSCT(d)


OS
Survival probability
p = 0.19
OS
1/2G TKI MMR
1/2G TKI no MMR
Olverembatinib MMR
Olverembatinib no MMR
Time post-HSCT(d)
Number at risk
OS
MMR_G=0 7 6 5 5 4 4 3 3 3
MMR_G=1 36 28 23 17 17 16 14 14 13
MMR_G=10 15 8 6 4 2 2 1 0 0
MMR_G=11 11 5 3 1 1 1 0 0 0
Time post-HSCT(d)


PFS
Survival probability
p = 0.27
Time post-HSCT(d)
Number at risk
MMR_G=0 7 6 5 5 4 4 3 3 3
MMR_G=1 36 27 22 16 16 15 14 14 13
MMR_G=10 15 8 6 4 2 2 0 0 0
MMR_G=11 11 5 3 1 1 1 0 0 0
Time post-HSCT(d)

Conclusions: This real-world analysis provides the first clinical evidence supporting the efficacy and safety of olverembatinib in transplant-eligible BC-CML. Olverembatinib significantly enhances pre-transplant molecular responses, compared to 1/2G-TKIs, associating with improved survival after transplantation. With a manageable safety profile, olverembatinib represents a promising bridging strategy prior to allo-HSCT, potentially redefining frontline management of BC-CML.

Disclosure: Nothing to declare.

OS01-06

COMPARING THE MTSS AND MYELOFIBROSIS ALLORISK STRATIFIER SCORES FOR PREDICTING EARLY MORTALITY AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION: A SINGLE-CENTER EXPERIENCE

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Background: Early transplant-related mortality (TRM) remains a major barrier to the use of allogeneic hematopoietic stem-cell transplantation (allo-HCT) in patients with myelofibrosis (MF). Although several prognostic scoring systems guide candidate selection based on biological disease risk, few tools are specifically designed to estimate TRM, such as the Myelofibrosis Transplant Scoring System (MTSS), which nonetheless presents several limitations. More recently, EBMT has proposed the machine-learning–based AlloRisk Stratifier as a dynamic AI-driven tool to improve the prediction of early TRM.

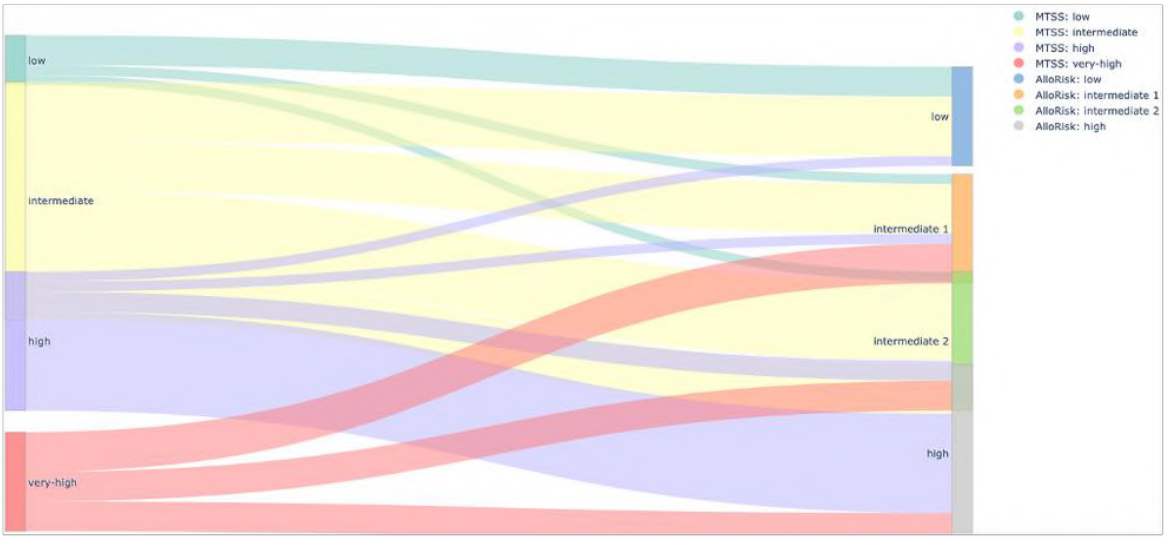
Methods: We retrospectively analyzed 54 consecutive patients with MF who underwent allo-HCT at San Raffaele Hospital (Milan, Italy) between January 2013 and November 2024, with a minimum follow-up of 12 months (with 80% of HCT performed in the past five years). Patients transplanted in blastic phase, undergoing a second transplant, or diagnosed with MPN/MDS overlap were excluded. Donor selection and the management of transplant-related complications followed international standards. MTSS scores were assigned according to Gagelmann et al., while AlloRisk categories were derived using the EBMT open-access calculator. Statistical analyses included Fisher's exact test for group comparisons and Harrell's concordance index (C-index) to evaluate discriminative performance.

Results: Among the 54 patients, 63% were older than 57 years and 80% had a Karnofsky performance status >80%. JAK2V617F mutations were present in 65%, ASXL1 in 44%, and ≥2 additional high-risk mutations in 41% of evaluable cases. According to MTSS, 9%, 45%, 26%, and 20% of patients were classified as low, intermediate, high, and very-high risk, respectively. Most patients (96%) received reduced-toxicity conditioning, including dose-adjusted treosulfan–thiotepa–fludarabine (52%) and treosulfan–melphalan–fludarabine

(24%). PTCy-based GvHD prophylaxis was used in 96% of cases. Donor types included matched unrelated (30%), mismatched unrelated (36%), and haploidentical donors (11%).After a median follow-up of 20.5 months, overall survival was 63%, with 20 deaths (37%), predominantly transplant-related. The 1-year cumulative incidence of non-relapse mortality was 25.9%, with relapse treated as a competing event. MTSS-defined 1-year mortality rates were 20%, 16%, 35%, and 27% across increasing risk categories (p = 0.35). In contrast, the AlloRisk Stratifier assigned 19%, 20%, 26%, and 35% of patients to low, intermediate-1, intermediate-2, and high-risk groups, with corresponding 1-year mortality rates of 0%, 9%, 29%, and 47% (p = 0.085) (Figure 1). Patients classified as high-risk by AlloRisk showed significantly higher 1-year mortality compared with all other categories combined (9/19 vs 5/35; p = 0.02) (Table 1). Discrimination for 1-year mortality was superior for the AlloRisk Stratifier (C-index 0.726) compared with MTSS (0.587).

MTSS Risk-category	Total	1-year deaths	1-year mortality rate	AlloRisk Stratifier category	Total	1-year deaths	1-year mortality rate
Low	5	1	20%	Low	10	0	0%
Intermediate	24	4	16%	Intermediate-1	11	1	9%
High	14	6	35%	Intermediate-2	14	4	29%
Very-high	11	3	27%	High	19	9	47%
Global p-value			0.35 (NS)				0.085 (trend)
Higher vs others p-value			0.13 (NS)				0.02 (sig)

Conclusions: In this homogeneous single-center cohort uniformly treated with contemporary conditioning and PTCy-based prophylaxis, the EBMT AlloRisk Stratifier outperformed the MTSS in predicting early NRM. The model showed a clear risk gradient, with no deaths in the low-risk group and progressively increasing mortality across categories, whereas MTSS displayed limited discriminatory ability. The AlloRisk Stratifiermay serve as a pragmatic aid for pre-transplant decision-making, particularly in centers using modern allo-HCT platforms.



Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

OS01-08

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PEDIATRIC CHRONIC MYELOID LEUKEMIA IN THE TKI ERA: AN EBMT PEDIATRIC DISEASES WORKING PARTY ANALYSIS

Meinolf Suttorp[1], Jacques-Emmanuel Galimard[2], Mouad Abouqateb[2], Marc Ansari[3], Caroline Besley[4], Arnaud Dalissier[2], Ali Alahmari[5], Malek Benakli[6], Brigitta Versluys[7], Iwona Dachowska-Kałwak[8], Renata Formankova[9], Tariq Ghafoor[10], Marta Gonzalez Vicent[11], Jolanta Gozdzik[12], Rawad Rihani[13], Charlotte Jubert[14], Katharina Kleinschmidt[15], Ludmila Zubarovskaya[16], Markus Metzler[17], Stephan Mielke[18], Frederic Millot[19], Caroline Furness[20], ***Herbert Pichler***[21]*, Samppa Ryhanen[22], Stephanie Sembill[17], Jerry Stein[23], Emel Unal[24], Jacek Wachowiak[25], Marco Zecca[26], Krzysztof Kalwak[27]*

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Center, Ammann, Jordan, [14]CHU Bordeaux Groupe Hospitalier Pellegrin-Enfants, Bordeaux, France, [15]Department of Pediatric Hematology, Oncology and Stem Cell Transplantation University of Regensburg, Regensburg, Germany, [16]RM Gorbacheva Research Institute, St. Petersburg, Russian Federation (the), [17]Dept. of Pediatric Oncology & Hematology, Univ. Hospital, Erlangen, Erlangen, Germany, [18]Karolinska Univ. Hospital, Stockholm, Sweden, [19]INSERM - CHU de Poitiers, Poitiers, France, [20]Royal Marsden Hospital, London, United Kingdom of Great Britain and Northern Ireland (the), [21]St. Anna Children's Hospital, Department of Pediatrics and Adolescent Medicine, Medical University of Vienna, Vienna, Austria, [22]Children's Hospital, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, [23]Schneider Children`s Medical Center of Israel, Petah Tikva, Israel, [24]Univ. of Ankara, Ankara, Turkey, [25]Department of Pediatric Oncology, Hematology and Transplantology, University of Medical Sciences, Poznan, Poland, [26]San Matteo Pavia Transplant Programme, Pavia, Italy, [27]Department of Pediatric Hematology, Oncology and BMT, Wroclaw Medical University, Wroclaw, Poland

Background: Since the introduction of tyrosine kinase inhibitors (TKIs), allogeneic hematopoietic stem cell transplantation (HSCT) is no longer first-line therapy for chronic myeloid leukemia (CML) in chronic phase (CP). However, HSCT remains indicated for pediatric CML (pCML) patients with failure of multiple treatment lines. We analyzed HSCT outcomes in pCML over the last two decades.

Methods: This retrospective registry-based analysis used data from the EBMT Pediatric Diseases Working Party. Patients younger than 18 years at the time of HSCT, with pCML at any disease stage, transplanted between 2006 and 2022, and with sufficient data available were included.

Results: A total of 209 patients were analyzed (55.5% male). Median age at diagnosis was 11.3 years (range, 0.2–17.3) and at HSCT 12.6 years (range, 1.6–17.9). First-line TKI therapy was administered in 82% of patients. Molecular remission following first-line TKI (n=179) was reported in 24.0% of patients (26.9% in CP1, 10.7% in ≥CP2, and 23.8% in ≥accelerated phase [AP]). A second treatment line was given to 35.1% of patients, predominantly TKIs (62/72), achieving molecular remission in 29.5% (25.0% in CP1, 33.3% in ≥CP2, and 40.0% in ≥AP). After third-line TKI therapy (n=23 of 27 receiving third-line treatment), molecular remission was achieved in 28.6%.
At HSCT, disease status was CP1 in 72.2%, CP2 in 14.4%, >CP2 in 1.0%, and advanced phases in 12.4% of patients. Over time, disease stage at HSCT shifted significantly toward more advanced phases (p=0.002).
Conditioning regimens were total body irradiation (TBI)-based in 16.8% of patients. The remaining patients received BuCy (50.5%), BuFlu (4.8%), BuFluThio (4.8%), TreoFluThio (4.3%), FluMelThio (13.0%), or other combinations (5.8%). Stem cell sources were bone marrow (55.0%), peripheral blood (39.7%), or cord blood (5.3%). Donors were HLA-identical siblings (47.0%), other matched relatives (2.9%), mismatched relatives (2.9%), or unrelated donors (47.3%). Ex vivo T-cell depletion was performed in 7.7% of grafts. Cumulative incidence of acute GVHD grade II–IV was 33.5% by day 100. With a median follow-up of 8.9 years, chronic GVHD at 8 years occurred in 30.2%, with extensive disease in 18.1%. Overall survival (OS) at 8 years was 82.5% and declined with more advanced disease stage (CP1: 85.5%; ≥CP2: 77.2%; AP/BP: 71.3%). Compared with CP1, hazard

ratios for OS were 2.55 (p=0.04) for >CP2 and 2.15 (p=0.09) for AP/BP. Progression-free survival and relapse incidence at 8 years were 68.6% and 19.6%, respectively, and both worsened with advanced disease. Non-relapse mortality was 11.9% at 8 years and was not associated with disease stage. Compared with busulfan-based conditioning, FluMelThio and FluMelTreo-based regimens were associated with superior OS (HR 0.18; p=0.02), with FluMelThio showing 100% OS at 2 years and no NRM at 8 years. Compared with busulfan-based regimens, TBI-based conditioning was associated with improved PFS (HR 0.37; p=0.03).

Table 1. Outcomes according to conditioning regimen

Variable	Regimen	2-year OS (%)	8-year PFS (%)	8-year RI (%)	8-year NRM (%)
Regimen	Bu-based (n=133)	78.0 [69.7–84.3]	62.0 [52.8–69.9]	22.5 [15.5–30.3]	15.5 [9.8–22.3]
	TBI-based (n=29)	88.4 [72.0–95.5]	82.7 [65.4–91.8]	14.5 [5.2–28.4]	2.9 [0.2–12.9]
	FluMel-based (n=30; 27/30 with thiotepa)	100	89.7 [71.3–96.5]	10.3 [2.5–24.6]	0
	Other (n=11)	77.9 [35.4–94.2]	51.9 [16.3–79.0]	26.0 [2.8–60.1]	22.1 [2.5–53.8]
	P value	0.04	0.02	0.56	0.03

Conclusions: HSCT remains an important therapeutic option for pCML patients with inadequate response to TKI therapy. While the optimal conditioning regimen according to disease status requires further clarification, FluMelThio appears to be a particularly promising approach.

Disclosure: Nothing to declare.

B422

PELABRESIB PLUS RUXOLITINIB AS BRIDGING THERAPY TO HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN MYELOFIBROSIS: INSIGHTS FROM MANIFEST AND MANIFEST-2 STUDIES

Claire Harrison[1], Raajit Rampal[2], Alessandro Maria Vannucchi[3], Vikas Gupta[4], Andrew Kuykendall[5], Moshe Talpaz[6], Jean-Jacques Kiladjian[7], Ruben Mesa[8], Prithviraj Bose[9], Marina Kremyanskaya[10], ***Michael Loschi***[11]*, Grace Cleary[12], Rajendra Jinwal[13], Soorya Surendran[14], Claudia Gorcea-Carson[15], John Mascarenhas[10]*

[1]Guy's and St. Thomas' NHS Foundation Trust, London, United Kingdom of Great Britain and

Northern Ireland (the), [2]Memorial Sloan Kettering Cancer Center, New York, United States of America (the), [3]Azienda Ospedaliera-Universitaria Careggi, University of Florence, Florence, Italy, [4]Princess Margaret Cancer Centre, Toronto, Canada, [5]Moffitt Cancer Center, Tampa, United States of America (the), [6]University of Michigan, Ann Arbor, United States of America (the), [7]Hôpital Saint-Louis, Université Paris Cité, Paris, France, [8]Wake Forest University, Winston-Salem, United States of America (the), [9]The University of Texas, Houston, United States of America (the), [10]Tisch Cancer Institute, New York, United States of America (the), [11]Nice University Hospital, Nice, France, [12]Novartis Ireland Limited, Dublin, Ireland, [13]Novartis Pharma AG, Basel, Switzerland, [14]Novartis Pharmaceuticals Corporation, Hyderabad, India, [15]Novartis Pharmaceuticals UK Limited, London, United Kingdom of Great Britain and Northern Ireland (the)

Background: Myelofibrosis (MF) is a progressive myeloproliferative neoplasm with limited curative options, where haematopoietic stem cell transplantation (HSCT) remains the only potentially curative therapy. However, eligibility for HSCT is often restricted by disease severity, symptom burden, and other comorbidities. Pelabresib (PELA), a bromodomain and extra-terminal inhibitor, in combination with ruxolitinib (RUX), has demonstrated deep and durable spleen volume reductions and symptom improvement in the MANIFEST and MANIFEST-2 studies. This analysis aims to evaluate the impact of PELA+RUX on clinical parameters relevant to HSCT eligibility in Janus kinase inhibitor (JAKi)-naïve patients with MF enrolled in MANIFEST and MANIFEST-2.

Methods: Data from the open-label Phase 2 MANIFEST study arm 3 (NCT02158858) and Phase 3 global randomised double-blind active control MANIFEST-2 study (NCT04603495) were analysed in a post-hoc analysis to identify patients who underwent HSCT after treatment with either PELA+RUX or placebo (PBO)+RUX and assess the timing of HSCT and clinical response to study treatment. Key endpoints included: spleen volume reduction of 35% from baseline (SVR35), total symptom score improvement by 50% (TSS50), and time to HSCT eligibility.

Results: As of the Week 96 data cutoff for MANIFEST-2, 15/214 (7.0%) patients in the PELA+RUX arm and 18/216 (8.3%) patients in the PBO+RUX arm were eligible for, or received, HSCT. In this subgroup, patients' baseline characteristics were similar to the full population (Rampal RK, et al. *Nat Med*. 2025;31:1531–1538). In the PELA+RUX arm, 6/15 patients had haemoglobin levels of ≤10 g/dL versus 10/18 in the PBO+RUX arm. Haemoglobin response was achieved by 3/15 and 3/18 patients in the PELA+RUX and PBO+RUX arms, respectively. PELA+RUX demonstrated notable improvements in spleen volume reduction, with 66.7% SVR35 (10/15) versus 16.7% (3/18), and greater improvement of symptoms, with 53.3% TSS50 (8/15) versus 38.9% (7/18) in the PBO+RUX arm at Week 24. Median time from treatment start to HSCT was similar between arms, with 344.0 and 343.5 days in the PELA+RUX and PBO+RUX arms, respectively. As of 9 January 2025, in arm 3 of the MANIFEST study (PELA+RUX in JAKi-naïve MF), 13/84 patients underwent HSCT with 69.2% SVR35 (9/13) and 66.7% TSS50 (8/12) at Week 24. In arm 3, median time from treatment start to HSCT was 395.0 days.

Conclusions: PELA+RUX enabled a subgroup of JAKi-naïve MF patients to undergo HSCT, demonstrating significant reductions in spleen volume and notable improvements in

symptoms, indicating potential as a bridging therapy to HSCT in MF and supporting broader clinical utility.

Clinical Trial Registry: NCT02158858 (MANIFEST, https://www.clinicaltrials.gov/study/NCT02158858); NCT04603495 (MANIFEST-2, https://clinicaltrials.gov/study/NCT04603495)

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Moshe Talpaz has received support/funding from Novartis/Sumitomo/BMS.
Jean-Jacques Kiladjian has received support/funding from Novartis/AbbVie/GlaxoSmithKline/AOP Health/BMS; served on DSMB/Advisory Boards for Incyte.
Ruben Mesa has received support/funding from MorphoSys/CTI/BMS/Genentech, Inc./AbbVie/Incyte/GlaxoSmithKline/Novartis.
Prithviraj Bose has received support/funding from Incyte/BMS/CTI/MorphoSys/Sumitomo/Karyopharm/Kartos/Telios/Ionis/Disc/Ajax/Geron/Janssen/Merck/Blueprint/Cogent/Incyte/GSK/Abbvie/Takeda/Pharma Essentia/Jubilant/Morphic/Novartis/Raythera/Cogent.
Marina Kremyanskaya has received support/funding from Incyte/Celgene/BMS/MorphoSys/Protagonist/Ionis/Silence Therapeutics/Kura Oncology/Incyte/AbbVie.
Michael Loschi has received support/funding from Janssen/Abbvie/Alexion/BMS/Gilead/GlaxoSmithKline/Incyte/Jazz/Kartos/Mallinkrodt/Novartis/Roche/Sanofi/Takeda.
Grace Cleary, Rajendra Jinwal, Soorya Surendran, and Claudia Gorcea-Carson are employed by Novartis; Grace Cleary, Rajendra Jinwal, and Claudia Gorcea-Carson hold Novartis stock/options.
John Mascarenhas has received support/funding from Incyte/Novartis/Geron BMS/AbbVie/CTI/Sobi/Karyopharm/Disc

Medicines/Ajax/PharmaEssentia/Kartos/MorphoSys/GlaxoSmithKline/Novartis/Roche/Merck/Pfizer/Geron/Blueprint Medicines/Keros/Galecto/Sumitomo; served on DSMB/Advisory Boards for Galecto and Incyte.
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B424

HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR PATIENTS WITH MYELOFIBROSIS: A CHINESE MULTICENTER RETROSPECTIVE STUDY

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Background: Despite the emergence of Janus kinase (JAK) inhibitors, allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only curative treatment for

myelofibrosis (MF). Haploidentical HSCT (Haplo-HSCT) expands access to transplantation for patients lacking an HLA-matched sibling donor or matched unrelated donor. However, data on Haplo-HSCT for MF are currently scarce. This study aimed to evaluate the real-world outcomes of Haplo-HSCT in the treatment of MF in China.

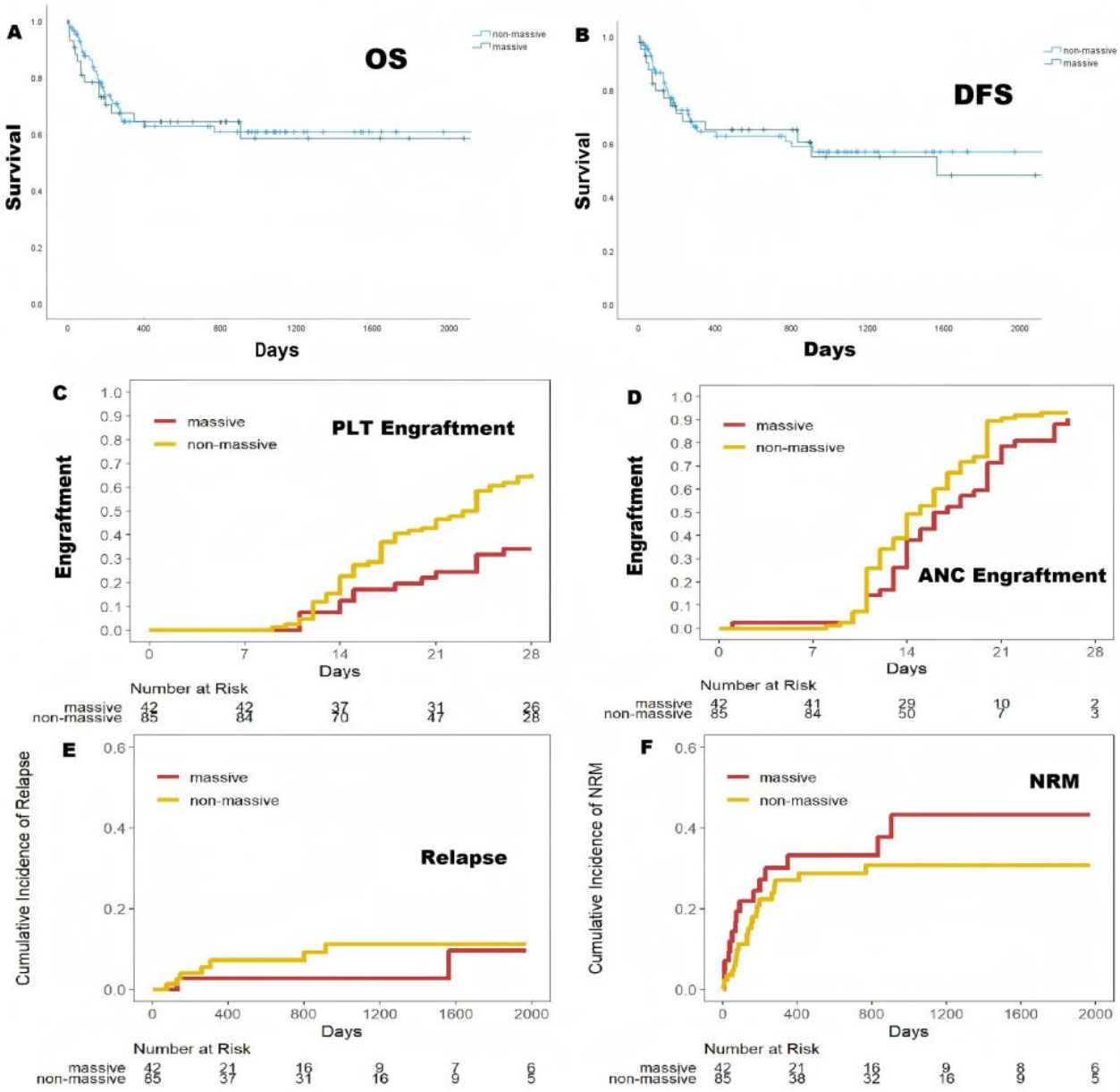
Methods: This study retrospectively analyzed clinical data of 127 MF patients who underwent haplo-HSCT at 32 hematology centers in China between December 2008 and December 2024. Kaplan-Meier survival analysis and competing risk models were used to calculate the 1-year and 3-year overall survival (OS), disease-free survival (DFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM) rates post-transplantation. Competing risk models were also applied to estimate the incidence of graft failure (GF) and engraftment. Competing risk regression analysis was performed to identify factors associated with GF. The adjusted probabilities of OS and DFS were estimated using the Cox proportional hazards model, with adjustment for other significant clinical variables included in the final multivariate models.

Results:

Characteristics	Value
Age, Median (Range)	53 (13-69)
Sex	
Male, n (%)	76 (59.8)
Female, n (%)	51 (40.2)
Diagnosis	
PMF, n (%)	83 (65.4)
Post-PV/ET MF, n (%)	16 (12.6)
MF-AML, n (%)	28 (22)
Risk (DIPSS-plus)	
Int-1 risk, n (%)	12 (9.5)
Int-2 risk, n (%)	108 (85)
High risk, n (%)	7 (5.5)
Pretransplant splenomegaly	
No splenomegaly	19 (15)
Mild splenomegaly	66 (52)

Massive splenomegaly	42 (33)
MNC, Median (Range)	11.83 (2.62-157.25)×10^8/Kg
CD34, Median (Range)	6.33(1-23.64)×10^6/Kg

Among the 127 patients, 83 were diagnosed with primary myelofibrosis (PMF), 16 with post-essential thrombocythemia/polycythemia vera MF (post-ET/PV MF), and 28 with MF transformed into acute myeloid leukemia (MF-AML). The last follow-up date was December 31, 2024. The neutrophil engraftment rate at day 28 was 92.9% and the platelet engraftment rate at day 100 was 62.5%. The 60-day good graft function (GGF) rate was 62.5%. Graft failure occurred in 17 patients (14 primary, 3 secondary), corresponding to an incidence of 13.2%. Splenomegaly negatively affected GGF rates (non-massive splenomegaly: 71.4%, massive splenomegaly: 44.1%; P = 0.008) and increased the incidence of GF (non-massive splenomegaly: 8.8%, massive splenomegaly: 21.8%, P = 0.038). The incidences of Epstein-Barr virus (EBV) infection and cytomegalovirus (CMV) infection were 25.2% and 20.5%, respectively. The incidences of acute graft-versus-host disease (GVHD, grades II–IV) and chronic GVHD (moderate to severe) were 44% and 25%, respectively.
With a median follow-up duration of 830 days, the 3-year OS and DFS rates were 60.3% and 56.7%, respectively, with a CIR of 8.45% and an NRM of 34.3%. In univariate analysis, only massive splenomegaly was associated with OS (hazard ratio [HR] = 2.924; 95% confidence interval [CI], 0.993–8.605; P = 0.051) and DFS (hazard ratio [HR] = 2.431; 95% confidence interval [CI], 0.893–6.617; P = 0.082). Pre-transplant white blood cell count, hemoglobin level, platelet count, MF grading, Hematopoietic Cell Transplantation-Comorbidity Index (HCT-CI), donor-specific antibodies, graft mononuclear cell count, and CD34+ cell count were not associated with survival, engraftment, GVHD, or infection.



Conclusions: Haploidentical HSCT (Haplo-HSCT) is a feasible curative option for patients with MF. However, the relatively high incidences of NRM and GF compromise the efficacy of Haplo-HSCT, particularly in patients with massive splenomegaly. These findings highlight the importance of pre-transplantation management.

Disclosure: All authors declare no conflict of interest.

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ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR MYELOFIBROSIS: PATTERNS AND OUTCOME AFTER RELAPSE AND LONG-TERM FOLLOW UP

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Background: Allogeneic hematopoietic stem-cell transplantation (HSCT) is the only potentially curative approach in patients with myelofibrosis. However, data on long-term outcome after HSCT are relatively limited.

Methods: This is a retrospective analysis of HSCT outcomes of patients with myelofibrosis following HSCT in a single institution, between 2002 and 2025. Patients who had transformation to AML before HSCT were not included.

Results: The study included 102 patients, median age 60 years (range, 27-74). The donor was an HLA- matched sibling (n=37), matched-unrelated (n=50) or mismatched unrelated/ haploidentical (n=15). The conditioning regimen was fludarabine and reduced dose intravenous busulfan (FluBu, total 6.4-8 mg/kg, n=25); fludarabine, thiotepa, busulfan (TBF, n=61) or other regimens (n=16). GVHD prophylaxis included cyclosporine and methotrexate or mycophenolate and ATG (grafalon).
With a median follow-up of 5.6 years (range, 0.1-22 years), 56 patients are alive and 46 have died, 30 of non-relapse causes and 16 of relapse. The estimated 10-year overall survival (OS) is 48% (95%CI, 35-60). The estimated 10-year non-relapse mortality (NRM) and relapse mortality was 34% (95%CI, 24-48) and 18% (95%CI, 11-29), respectively. 10-year OS tended to improve in more recent years ($\geq$2015), 61% (95%CI, 49-74) compared to earlier years of HSCT, 36% (95%CI, 20-53), respectively (P=0.16). 10-year OS also tended to improve with TBF conditioning, 63% (95%CI, 50-76) compared to FluBu conditioning, 28% (95%CI, 10-45), respectively (P=0.15).
A total of 32 patients were alive and disease-free 5-years after HSCT. Six patients subsequently relapsed 5.3 to 18.9 years after HSCT and 1 of them died. Four patients had late NRM, 2 second malignancies, 1 chronic GVHD and 1 cardiovascular event. For patients who were alive and disease-free 5 years after HSCT, the estimated subsequent 5-year OS and disease-free survival were 77% (95%CI, 56-98) and 56% (95%CI, 33-78), respectively. In all, 26 patients relapsed after HSCT, estimated 5-year and 10-year rate 22% (95%CI, 15-32) and 31% (95%CI, 21-45), respectively. Median time to relapse was 1.2 years (range, 0.2-18.9). Ten patients are alive, a median of 1.3 years (range, 0.3-18.1) and estimated 5-year OS 30% (95%CI, 9-51) after relapse. There were 3 patterns of relapse with different outcomes. Four patients relapsed as Polycythemia-Vera (PV). One achieved CR with DLI and is in CR for more than 18 years. The 3 others progressed again to myelofibrosis 38, 64 and 156 months later and are all alive, a median of 9.6 years (range, 5.3-18.1). Thirteen patients relapsed as myelofibrosis in chronic phase. Five are alive and 8 died, median survival 2.4 years (range, 0.2 to >7.5) after relapse. Nine patients relapsed as MDS/ AML, only one is alive, median survival of 0.8 years (range, 0.1-1.5).

Conclusions: Allogeneic HSCT can allow long-term survival and possible cure in myelofibrosis. However, long-term survivors are at continuous risk for late relapse and late NRM. For those who are not cured, HSCT may reset the pattern of progression of the myeloproliferative process. Patients who relapse as PV or chronic phase myelofibrosis can achieve long-term survival after relapse, while patients relapsing as MDS/ AML have dismal prognosis.

Disclosure: Nothing to declare.

B426

ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR MYELOFIBROSIS USING POST-TRANSPLANT CYCLOPHOSPHAMIDE: PRELIMINARY RESULTS FROM THE GETH-TC CLINICAL PRACTICE PROTOCOL

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Background: Post-transplant cyclophosphamide (PT-Cy) is increasingly being adopted as a universal platform for GvHD prophylaxis, regardless of donor type. However, specific challenges in myelofibrosis (MF), such as higher risks of graft failure and poor graft function, require a careful evaluation of PT-Cy in this disease. Reducing PT-Cy dose to improve tolerability is under investigation, particularly in HLA-matched transplants, and may be particularly relevant for MF patients.

Methods: In January 2023, a clinical practice protocol was developed under the auspices of the GETH-TC (Grupo Español de Trasplante Hematopoyético y Terapia Celular) to harmonize transplant procedures for MF across centers in Spain. The core elements of the protocol included the use of PT-Cy at either standard (50 mg/kg on days +3 and +4, for HLA-mismatched transplants) or reduced dose (30 mg/kg on days +3 and +4, for HLA-matched transplants) combined with calcineurin inhibitors or rapamycin +/- mycophenolate. JAK inhibitor treatment was discontinued prior to stem cell infusion. The recommended conditioning regimens were based on combinations of thiotepa (T), busulfan (BU), and

fludarabine (Flu). The reduced intensity conditioning regimen was T5Flu120BU2 for HLA-matched transplants and T5Flu150BU2 for HLA-mismatched transplants, whereas the myeloablative regimen consisted of Flu120BU4 for HLA-matched transplants and T10Flu150BU3 for HLA-mismatched transplants. Here, we present preliminary results of the protocol, including overall survival (OS), engraftment, relapse, non-relapse mortality (NRM), and acute and chronic GvHD.

Results: Fifty-seven adult patients with MF in chronic (n=55) or accelerated phase (n=2) who underwent allo-HCT between January 2023 and October 2025 in 11 centers were included. Main deviations from the protocol were: use of treosulfan instead of BU (n=3), standard-dose PT-Cy with an HLA-matched donor (n=7), reduced-dose PT-Cy with an HLA-mismatched donor (n=2), and addition of ATLG to reduced-dose PT-Cy (n=9, all from a single center). Median interval from diagnosis to allo-HCT was 21.1 months. The main characteristics of the series are shown in Table 1.

Table 1. Main characteristics at transplantation in 57 myelofibrosis patie

Age at transplant, year	Median (Interquartile range)
Sex	Male
Myelofibrosis type	Primary myelofibrosis
Genotype	JAK2
	CALR
	MPL
	Triple negative
High molecular risk	Mutation in ASXL1, SRSF2, IDH1, IDH2, U2A
Splenectomy	Yes
Prior JAKi treatment	Yes
Spleen irradiation	Yes
Karnofsky performance status	<90
Hematopoietic Cell Transplant-specific Comorbidity Index	High (>=3)
Conditioning regimen	Myeloablative
Stem cell source	Peripheral blood
Donor type	MRD / MUD / MMUD / Haplo / MMRD, other

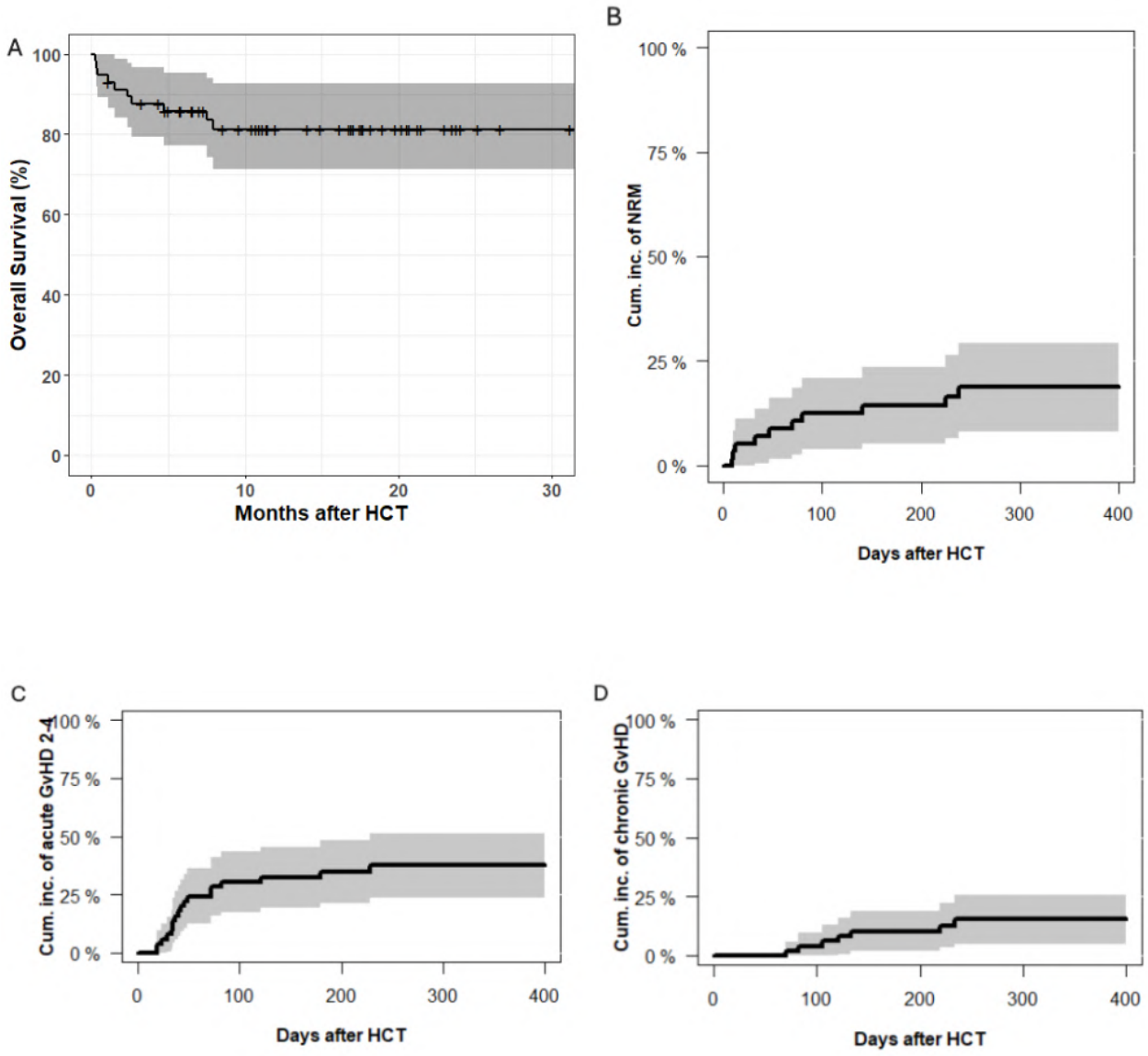
Table 1. Main characteristics at transplantation in 57 myelofibrosis patie

Post-transplant cyclophosphamide	100 mg/kg / 80 mg/kg / 50-60 mg/kg

MRD: matched related donor. MMRD: mismatched related donor (one allelic diference). MUD: matched unrelated

Three patients developed sinusoidal obstructive syndrome. One patient experienced primary graft failure. Median time (95% CI) to neutrophil and platelet engraftment was 19 days (17-20) and 27 days (23-30), respectively. Twenty patients (35%) had poor graft function, two of whom received a CD34+ cell boost. Two patients had disease relapse. Incidence of acute GvHD grades II-IV and III-IV at 120 days and moderate/severe chronic GvHD at 12 months were 37% (95% CI: 23-52), 16% (95% CI: 4-28), and 15% (95% CI: 5-26), respectively (Figure 1, C-D). After a median follow-up of 16.8 months from transplant, the estimated 2-year OS rate and NRM rate were 81% (95% CI: 70-92), and 19% (95% CI: 8-29), respectively (Figure 1, A-B). Causes of death were GvHD (n=5) and infection (n=5). The estimated 2-year OS rates were 84%, 83%, 91%, and 53% for transplants from MRD, MUD,

MMUD, and haploidentical donors, respectively (p=0.40).



Conclusions: This preliminary analysis shows an encouraging 2-year OS with our protocol, with NRM being the main cause of treatment failure. Poor graft function constitutes a common complication. Cohort expansion, longer follow-up, and harmonization of molecular monitoring are underway.

Disclosure: Nothing to declare

B427

MTSS PREDICTS OUTCOME OF HAPLO-SCT IN MYELOFIBROSIS

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Background: Allo-SCT is the only potential curative option for pts with primary or secondary myelofibrosis (MF). Outcome after allo-SCT is affected by several factors, including the selection of an appropriate donor. Matched related (MRD) and matched unrelated (MUD) donors are the preferred donor source in MF. The introduction of PTCy has extended the option of allo-SCT to patients with only haploidentical donor options and substantially improved the outcome after haplo-transplant in hematological malignancies. However, data on the use of haploidentical donors in pts with MF are limited, and were not included as an independent risk factor in the Myelofibrosis Transplant Scoring System (MTSS). We aimed to estimate the prognostic impact of the haploidentical donor source in the context of different conditioning regimen and other risk factors we took advantage of a large multicenter cohort.

Methods: We performed a retrospective analysis of patients with MF, who received first haploidentical allo-SCT at nine transplant centers between 2015 and 2024. Uni- and multivariate analyses were performed to determine variables which are associated with overall survival (OS), relapse, non-relapse mortality (NRM), neutrophil engraftment and GvHD.

Results: One hundred pts (54% primary/46% secondary MF) with a median age of 60 years (range, 29-78) received a haplo-SCT after RIC (47%) or MAC (53%) using PB (73%) or BM (27%) stem cells. MIPSS70 was low, int and high in 1%, 55% and 44% respectively, while MTSS was low, int, high and very high in 2%, 24%, 32% and 42%. With a median follow-up of 5.9 years, the OS, relapse and NRM at 6 years for the entire cohort was 46%, 21% and 34%, while aGvHD grade 3/4 and cGvHD were observed in 11% and 29% of pts. Patients with MTSS low/intermediate, high and very high-risk group demonstrated 6-yr OS of 66%, 48%, 33% and NRM of 18%, 31%, 46% respectively. Furthermore, in univariate analysis Flu-Bu-based conditioning was significantly associated with lower relapse probability and higher engraftment rate compared to TBI-based and Flu-Mel-based conditioning. In multivariate analyses the presence of a portal vein thrombosis before allo-SCT was significantly associated with adverse outcomes for OS (p=0.001, HR 4.17), relapse (p=0.02, HR 2.07) and NRM (p=0.03, HR 3.88), while triple-negative MF was an independent adverse risk factor for decreased OS (p=0.005, HR 4.54).

Conclusions: In this multicenter cohort primarily NRM seems to limit outcome after haplo-SCT in MF pts. While haploidentical transplant may be the only donor source for some patients with MF, careful consideration should be paid to risk factors including the MTSS before recommending this donor source.

Disclosure: Nothing to declare.

B428

LONG-TERM MINIMAL RESIDUAL DISEASE MONITORING BY DIGITAL DROPLET PCR AFTER ALLOGENEIC STEM CELL TRANSPLANTATION IN MYELOFIBROSIS IS PREDICTIVE OF RELAPSE: A RETROSPECTIVE AND PROSPECTIVE STUDY

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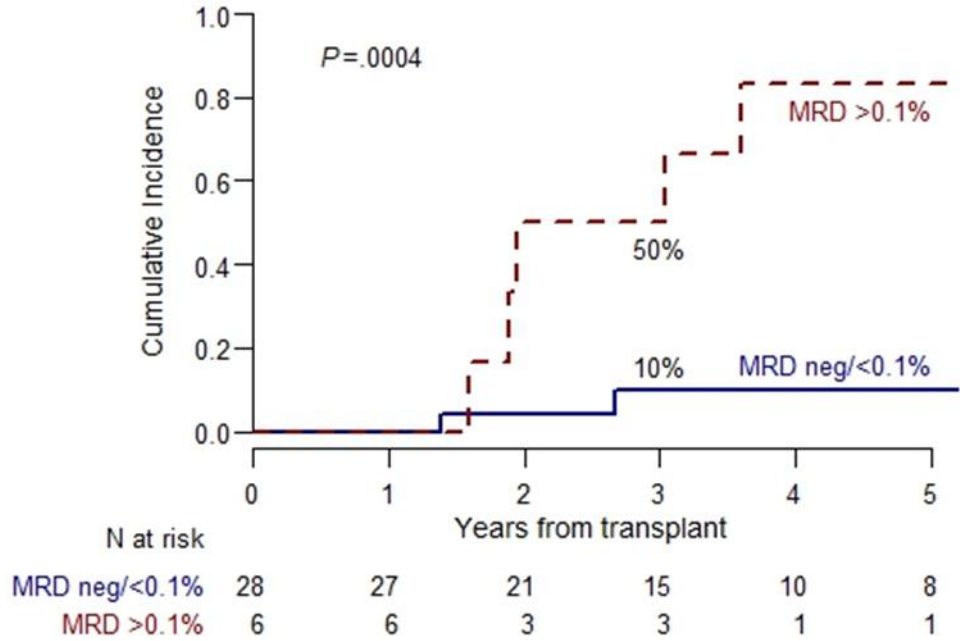
Background: Relapse is one of the leading causes of transplant failure in myelofibrosis (MF), and post-transplant molecular monitoring of the driver mutation is recommended. Achieving minimal residual disease (MRD) negativity at days 30, 100, and 180 post-HCT appears to be associated with improved transplant outcomes. However, little is known about the clinical significance of long-term (beyond 12 months) MRD positivity.

Methods: This is an ambispective analysis of consecutive patients with primary or secondary MF who were transplanted between 2007 and 2025 at our institution. MRD monitoring was performed using digital droplet PCR (ddPCR) in patients carrying *JAK2V617F* mutations, *MPL* mutations or alternative mutations in triple-negative patients, with a sensitivity of at least 0.05%. Patients with *CALR* mutation were excluded, as they are not currently evaluable by ddPCR. All patients had molecular characterization before transplant by a next-generation sequencing (NGS) panel including 30 myeloid genes.

Results: Of 83 MF patients evaluated, 51 (61%) patients were assessable for MRD monitoring by ddPCR. Median age at transplant was 59 years (range 42-68). Very high-risk cytogenetic abnormalities were found in 9 (19%) patients. Seven patients (14%) experienced blastic evolution before transplant. The donor type was matched unrelated (57%), haploidentical (17%), mismatched unrelated (16%) and HLA-identical sibling (10%). The driver mutation was *JAK2V617F* in 40 (78%) patients and *MPL* in 10 (20%) patients. One patient was triple negative but had a *ZRSR2* mutation, which could be monitored by ddPCR. NGS analysis revealed at least one HMR (high molecular risk) mutation in 21 (48%) patients. The most frequent additional mutations were *ASXL1* (41%), *DNMT3A* (16%), *TET2* (11%), *SF3B1* (11%) and *EZH2* (9%).
After a median follow-up of 2.3 years (range 0.1-15.5), the 3-year overall survival (OS),

progression-free survival (PFS), cumulative incidence of relapse (CIR), and non-relapse mortality (NRM) were 70%, 57%, 29%, and 14%, respectively. MRD positivity was detected in 62%, 45%, and 28% of patients at day +30, +90, and +180 after transplant, respectively. An MRD-positive status at day +90 was significantly associated with an increased risk of relapse (HR 1.79, 95% CI, *p=0.04*).
Thirty-four patients were alive at 1 year after transplant and were evaluable for MRD status. Ten patients were identified as MRD-positive during long-term follow-up (≥ 1 year after transplant), with 4 showing very low levels of positivity (< 0.1%).
Long-term detection of MRD positivity > 0.1% was significantly associated with a lower PFS (HR 7.77, 95% CI, *p=0.005*) and a higher CIR (HR 12.24, 95% CI *p=0.002*) compared to patients MRD-negative or with a very low level (<0.1%) of MRD positivity. The 3-year CIR for patients with long-term MRD positivity > 0.1% was 50%, compared to 10% for those MRD-negative or with MRD levels below 0.1% (95% CI, *p=0.004*; Figure 1).
Univariate analysis suggested *JAK2V617F* mutation (HR 3, 95% CI, *p=0.3*) and HMR mutations (HR 3.25, 95% CI, *p=0.1*) as risk factors for persistent long-term MRD positivity, though not statistically significant.



Conclusions: This study reinforces the value of MRD monitoring after transplant and underscores the importance of ongoing surveillance during long-term follow-up.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

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HAPLOIDENTICAL STEM CELL TRANSPLANTATION USING NOVEL PROTOCOL DEMONSTRATED EXCELLENT OUTCOMES FOR PATIENTS WITH MYELOFIBROSIS

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Background: Allogeneic stem cell transplantation (allo-HSCT) is the only curative option for myelofibrosis (MF). For patients without a matched sibling (MSD) or unrelated donor (MUD), haploidentical donors are a valid alternative. However, there are relatively few reports of haplo-HSCT for MF, partly due to high graft failure and non-relapse mortality (NRM). Our previous study suggested pre-transplant massive splenomegaly as the main risk factor of graft failure after haplo-HSCT (*Bone Marrow Transplant. 2025 Nov 25. doi: 10.1038/s41409-025-02746-4.*). Therefore, we recently developed a novel protocol based on the pre-transplant spleen size (Fig. 1A). And this prospective study aims to evaluate the efficacy of this novel transplant protocol in MF.

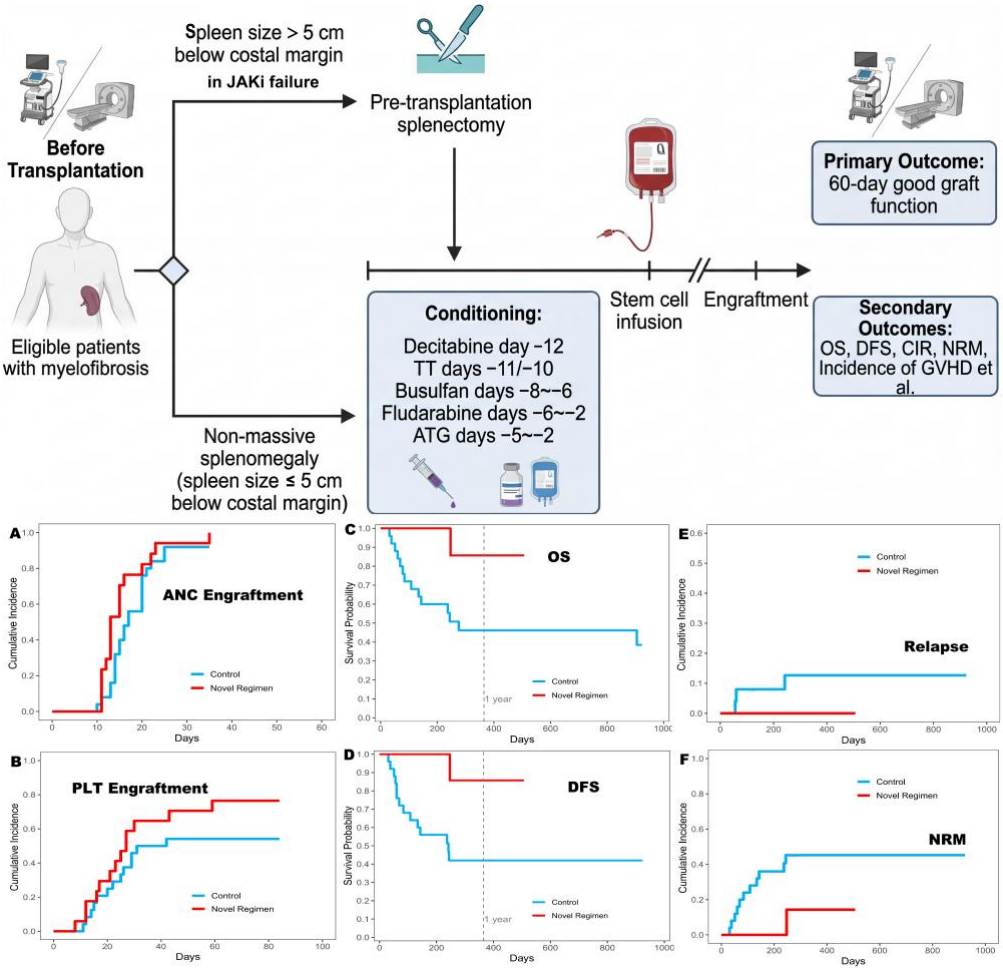
Methods: This was a prospective single-center study performed at Peking University People's Hospital. MF patients (primary or secondary to polycythemia vera/essential thrombocythemia) was eligible if they had no MSD/MUD but an available haploidentical donor. Patients with active infection or ECOG score > 2 or estimated survival＜30 days were excluded. The pre-transplant spleen size-based stratification strategy and the novel DTBFA conditioning regimen was described in Fig 1. The primary endpoint was good graft function (GGF) at day 60 which was defined engraftment of both neutrophil and platelet. Secondary endpoints include overall survival (OS), disease free survival (DFS), cumulative relapse incidence (CIR), non-relapse mortality (NRM), graft versus host disease (GVHD), immune reconstitution. This study was registered on Clinical trial (NCT06674382).

Results:

Characteristics	**Cohorts**	
	Novel regimen(n=17)	**Conventional regimen(n=25)**
Age, Median (Range)	55 (33-69)	51(22-61)
Sex		
Male, n (%)	9 (52.9)	14(56)
Female, n (%)	8 (47.1)	11(44)

Diagnosis		
PMF, n (%)	11(64.7)	15(60)
Post-PV/ET MF, n (%)	5(29.4)	6(24)
MF-AML, n (%)	1(5.9)	4(16)
GIPSS		
Int-2 risk, n (%)	2(11.8)	6(24)
High risk, n (%)	15(88.2)	9(36)
Not available, n (%)	0(0)	10(40)
Pretransplant splenomegaly		
Non-massive splenomegaly	9 (53.0)	8(32)
Massive splenomegaly	3 (17.6)	13(52)
Splenectomy	5 (29.4)	4(16)
MNC, Median (Range)	9.28 (1.04-15.95)×10^8/Kg	9.35 (6.21-16.36)×10^8/Kg
CD34, Median (Range)	8.32(0.97-13.71)×10^6/Kg	4.12(1-11.89)×10^6/Kg

This was an Interim Result of the Prospective Study. During January 2024-September 2025, seventeen MF patients were prospectively enrolled. The last follow-up was November 30, 2025 with a median 351 days (Table 1). The 60-day GGF was 82.4%. The engraftment of neutrophil and platelet was 100% and 82.4%, respectively. The grade II-IV acute GVHD and moderate/severe chronic GVHD was 33.3% and 11.9%, respectively. The 1-year OS, DFS, CIR and NRM was 85.7%, 82.4%, 0% and 14.3%, respectively (Fig.1). All patients had significant myelofibrosis regression(≥1 WHO MF grade reduction) within 3 months post-transplant. The median time of significant myelofibrosis regression was 1 month post-transplant.
Furthermore, 25 MF patients who received haplo-HSCT at our center during December 2008–2023 were treated as historical controls. Patients in novel regimen group demonstrated a trend of improved 60-day GGF (82.4% vs 56%, P=0.13), ANC engraftment (100% vs 92%, P=0.088), PLT engraftment (82.4% vs 56%, P=0.13), better survival (1-year OS: 85.7% vs 46.2%, P=0.015; DFS: 85.7% vs 42.0%, P=0.007;) and lower NRM (14.3% vs 45.2%, P=0.027).



Conclusions: Haplo-HSCT using a novel protocol based on pre-transplant spleen size demonstrated promising outcomes in patients with MF. However, this should be further validated in multicenter study.

Disclosure: All authors declare no conflict of interest.

B430

THE EFFICACY AND SAFETY OF PD-1 MONOCLONAL ANTIBODY IN THE TREATMENT OF HEMOPHAGOCYTIC SYNDROME：SYSTEMATIC REVIEW

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Background: Hemophagocytic lymphohistiocytosis (HLH), also known as hemophagocytic syndrome (HPS), is a life-threatening hyperinflammatory syndrome characterized by immune dysregulation. While standard protocols (HLH-1994/2004) utilizing glucocorticoids and etoposide are effective for many, patients with refractory or relapsed (r/r) HLH face poor prognoses. Recently, Programmed cell death protein-1 (PD-1) monoclonal antibodies have emerged as a potential targeted therapy, particularly for Epstein-Barr virus (EBV)-associated HLH, by reversing T-cell exhaustion. This study retrospectively analyzed the clinical efficacy, and safety profile of PD-1 inhibitors in the treatment of HLH.

Methods: A comprehensive search of the case reports, retrospective studies, and clinical trial data was conducted on PubMed, Web of Science, and Embase, up to July 2025. Data regarding the efficacy and safety of PD-1 monoclonal antibodies used (such as sintilimab, nivolumab, camrelizumab, and tislelizumab) in both pediatric and adult patients with HLH were included.

Results: A total of 12 studies were involved，covering with Epstein-Barr virus-associated hemophagocytic lymphohistiocytosis (EBV-HLH) and related malignancies. In pediatric patients (aged 3–7 years) with CAEBV and r/r EBV-HLH, sintilimab (3mg/kg, once every 3-4 weeks, monotherapy or combined with L-DEP regimen (pegaspargase, liposomal doxorubicin, etoposide, and high-dose methylprednisolone)) induced partial or complete clinical remission and significantly reduced plasma EBV-DNA levels (>50%), successfully serving as a bridge to allogeneic hematopoietic stem cell transplantation (HSCT) in some cases. Regarding adult patients, A retrospective study of seven R/R EBV-HLH patients (aged 15–36 years) treated with nivolumab reported positive outcomes, with a 16-month overall response rate (ORR) of 85.7% and a complete response (CR) rate of 71.4%. Some studies have reported that, sintilimab salvage therapy effectively restored complete donor chimerism and eradicated viral loads in patients who received allo-HSCT due to EBV-HLH/CAEBV.
In terms of combination therapies, regimens integrating PD-1 inhibitors with chemotherapy or targeted agents showed superior outcomes. A comparative study involving 98 patients with extranodal NK/T-cell lymphoma-associated HLH revealed that adding PD-1 monoclonal antibody to chemotherapy significantly improved overall response rates (73.3% vs. 45.5%) and survival compared to chemotherapy alone. Furthermore, novel combinations with ruxolitinib, venetoclax, or thalidomide achieved rapid clinical remission in EBV-HLH. Safety assessments indicated that PD-1 blockade following HSCT was associated with a high risk of graft-versus-host disease (GVHD, incidence up to 55%). Rapid immune reactivation triggered by PD-1 inhibitors may paradoxically exacerbate cytokine storms, necessitating vigilant monitoring.

Table 1 Efficacy and Safety Characteristics of the included studies

Author, year	Diagnose	Age	Interventions	Sample size	Outcomes
Song et al. 2025	Refractory EBV-HLH	53 years old; 28 years old	Patients were treated with a combination of the BCL-2 inhibitor venetoclax (100 mg	2 patients	All patients achieved comp remission.

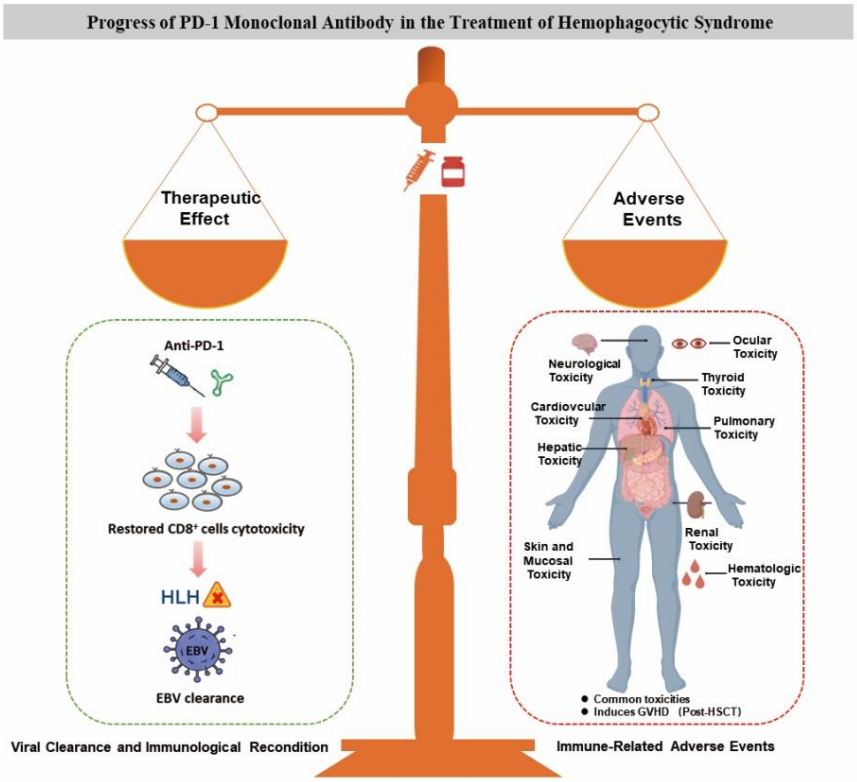
			daily) and Sintilimab (200 mg every 3 weeks).		
Cheng et al. 2024	r/r EBV-HLH	72 years old	The patient was treated with the sintilimab (200 mg every 3 weeks) combined with thalidomide (100 mg daily) maintained for 5 courses.	1 patient	After initiating the combina related indicators quickly r within 3 days, and comple achieved. The patient expe recurrence of HLH during a No drug-related adverse re
Guo et al. 2024	r/r EBV-HLH	Median age of 6.5 years (range: 3–10 years).	sintilimab as mono-therapy (3 mg/kg every 3–4 weeks) or sintilimab (2 mg/kg) combined with the L-DEP regimen.	4 patients	Clinical Response: All four to PD-1 inhibitors and achi response (PR) and success allo-HSCT. Serious side eff including increased liver en
Song et al. 2024	Refractory EBV-HLH	29 years old	Patient was treated with the PD-1 inhibitor camrelizumab (200 mg) followed by emapalumab (100 mg twice a week) combined with continuous renal replacement therapy (CRRT), dexamethasone, intravenous immunoglobulins, ruxolitinib, and etoposide.	1 patient	Patient experienced rapid Body temperature normali emapalumab administratio markers, liver enzymes, an improved significantly with Adverse Events: The patie infusion reactions (chills an inhibitor administration lea deterioration and multi-org
Chen et al. 2023	CAEBV, EBV-HLH	aged 4 years 2 months, 6 years 2 months, and 12 years 6 months.	sintilimab (3 mg/kg every 3–6 weeks with 13-30 cycles) combinated with antiviral drugs, glucocorticoids, and immunosuppressants.	3 patients	All patients achieved a com response (clinical CR) or p response (clinical PR).
Zhu et al. 2023	EBV-HLH with T and B lymphocyte involvement.	17 years old	Camrelizumab was continued as maintenance therapy combined with rituximab (to target infected B cells) and ruxolitinib (to inhibit inflammation).	1 patient	The patient achieved comp remission.
Xu et al. 2023	EBV-HLH	22 to 68 years old	Initial treatment: sintilimab （200 mg every 2–3 weeks ） combined with ruxolitinib (10–15 mg twice daily). Maintenance therapy: two weeks after achieving	12 patients	All 12 patients responded (resolution of fever). 9 pat complete response (CR), a partial response (PR) but n week.

			clinical remission, ruxolitinib was discontinued and sintilimab was continued at intervals of 3 weeks.		Minor adverse reactions in gastrointestinal discomfort
He et al. 2022	Extranodal NK/T-cell lymphoma-associated hemophagocytic lymphohistiocytosis (NK/T-LAHS).	Median age was 42 years (range 7–77 years).	The study compared two groups: nti-HLH and anti-ENKTL chemotherapy (ChT) alone and ChT plus anti-PD-1 mAb (median dose 200 mg every 3 weeks).	98 patients (43 in the ChT + anti-PD-1 mAb group, 55 in the ChT only group).	The overall response rate significantly higher in the mAb group (73.3%) comp group (45.5%). The ChT + group had a higher rate of vs. 70.2%). Immune-relat anti-PD-1 group included rash (5.0%), and hypothy some grade 3-4 cases.
Pi et al. 2022	Relapsed EBV-HLH after allo-HSCT	22 years old	The patient was treated with the sintilimab (2 mg/kg on day 104 post-transplant, with an additional cycle on day 118) after failure of other interventions like CsA reduction, rituximab, ruxolitinib, DLI, and DEP chemotherapy.	1 patient	Fever, cytopenia, elevated increased serum ferritin/s DNA levels in PBMCs and returned to normal ranges injection. Adverse Events: The patie occasional skin rashes, gas infections, and pneumonia which were controlled with anti-infective drugs.
You et al. 2022	CAEBV with HLH, relapsed with mixed donor chimerism after allo-HSCT.	33 years old.	The patient received sintilimab as salvage therapy (two doses of 200 mg, on day +69 and on day +84 post-transplant respectively) after the failure of other interventions like withdrawal of immune suppression, multiple donor lymphocyte infusions (DLI) and so on.	1 patient	Following the PD-1 inhibito DNA load in both plasma a negative by day +97; The chimerism (DC) halted and complete donor chimerism onwards. The patient developed gra +90, manifested by skin r liver function, which were immunosuppressants.
Yu et al. 2021	Refractory retroperitoneal Epstein-Barr virus-positive diffuse large B-cell lymphoma (EBV-positive DLBCL)	19 years old.	The patient received tiririzumab (200 mg every 3 weeks). Following partial response to PD-1 blockade, the patient received a single infusion of anti-CD19 CAR-T cells co-expressing PD-1	1 patient	A complete response was metabolic tumor volume o after treatment. Plasma EB completely eradicated.

	with secondary HLH.		decoy receptors (2×10^6 cells/kg).		
Liu et al. 2020	r/r EBV-HLH	Median age of 25 years (range 15-36 years).	Induction therapy: nivolumab monotherapy (100 to 200 mg every 3 to 4 weeks). Maintenance therapy: nivolumab (100 mg every 3 months) was administered for up to 1 year upon undetectable plasma EBV-DNA.	7 patients	All 5 clinical CR patients re for >40 weeks with a med months. Adverse Events: Persistent observed in 4 responders Transient worsening of cyt increased ferritin/sCD25 w patients (pseudoprogressio pruritus and depigmentatio patient during maintenanc

Conclusions: PD-1 monoclonal antibodies demonstrate significant therapeutic potential as salvage therapy for r/r EBV-HLH, effectively reducing viral loads and inducing remission. However, immune checkpoint inhibition acts as a double-edged sword; while it reactivates immune function, it carries risks of aggravating hyperinflammation and inducing severe GVHD in transplant recipients. Clinical application requires careful risk-benefit assessment, particularly regarding dosage and timing relative to the inflammatory peak. Further large-scale clinical trials are needed to establish standardized protocols.

Graphical abstract



Disclosure: Nothing to declare.

B431

INCIDENCE, CLINICAL OUTCOME, AND THERAPEUTIC IMPLICATIONS OF RELAPSE AFTER ALLOGENIC STEM CELL TRANSPLANTATION FOR PH-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents the only potentially curative option for myelofibrosis (MF) and blast-phase myeloproliferative neoplasms (BP-MPN), but its effectiveness is limited by a substantial risk of disease recurrence, ranging from 10% to 45% depending on disease phase.

Methods: We conducted a retrospective, single-center study to evaluate the incidence and clinical outcomes of relapse in MPN patients undergoing allo-HSCT. Molecular relapse (MR) was defined as reappearance of a driver mutation (*JAK2*, *CALR*, or MPL) without evidence of hematologic disease; hematologic relapse (HR) was defined as overt clinical recurrence (e.g., leukocytosis, new/worsening cytopenias, peripheral blood [PB] blasts).

Results: The study included 47 patients who underwent allo-HSCT for either MF (n=35; 74%) or BP-MPN (n=12; 26%) between 2013 and 2024. Median age was 59.8 years (range, 41.9-69.6), 18 (38%) were female. All patients received PB stem cells as graft source. Donor was HLA-matched unrelated in 29 (62%), haploidentical in 11 (23%), and identical sibling in 6 (13%). Reduced-intensity conditioning was used in 40 (85%) patients.
After a median follow-up of 3.5 years (95% CI, 1.2-4.5), 10 (21%) patients experienced disease recurrence (6 MF; 4 BP-MPN). Cumulative relapse incidence at 1, 3, and 5 years was 19%, 35% and 35%, respectively. Driver mutation status included mutant *JAK2* (m*JAK2*) in 5 patients, m*CALR* in 3, m*MPL* in 1, and a triple-negative profile in 1.
Molecular relapse occurred in 8 (17%) patients at a median of 6.3 months (range, 1.6-32.9) after allo-HSCT (6 MF; 2 BP-MPN). All MR cases were accompanied by decline in donor chimerism. Driver mutation distribution was m*JAK2* in 4 (50%) patients, m*CALR* in 3 (38%), and m*MPL* in 1 (12%). Most MRs (n=6/8) occurred within the first year after transplantation. Three patients relapsed while receiving calcineurin-inhibitor (CNI) prophylaxis/therapy; in all cases, CNI discontinuation did not induce molecular remission.
Besides CNI discontinuation, therapeutic management of MR included donor lymphocyte infusion (DLI) in 7 of 8 patients (mean administrations number, 2 [range, 1-3]; dose range, 1×10^6/Kg-1×10^7/Kg). Four patients developed graft-versus-host disease (GVHD), prompting DLI discontinuation. Three patients failed to clear their mutation and progressed to HR, whereas 4 achieved molecular remission and remained in sustained MR-free status. Among responders, 1 (25%) carried m*JAK2*, 2 (50%) m*CALR* (type-1/like), and 1 (25%) m*MPL*. Non-responders had m*JAK2* (n=2) or m*CALR* type-2/like (n=1).
Finally, HR occurred in 5 (11%) patients at a median of 21.4 months (range, 2.7-53.9) post-transplant (2 MF; 3 BP-MPN). Three had preceding MR and are currently managed as lower-risk MF. The remaining 2 patients relapsed with aggressive BP-MPN and died shortly thereafter.

Conclusions: Post-transplant relapse remains relatively frequent and clinically challenging. DLI demonstrates meaningful activity in MR, particularly in patients with *CALR*- or *MPL*-mutated disease, which is associated with better post-transplant outcomes and may potentially exert an "antigenic activity". These findings gain relevance with emerging targeted therapies—such as anti-mCALR monoclonal antibodies—that could expand therapeutic options also for managing post-transplant relapse. Limitations include the retrospective design and small cohort, underscoring the need for larger studies.

Disclosure: Nothing to declare.

B432

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REDUCED-INTENSITY HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION WITH POST-TRANSPLANT CYCLOPHOSPHAMIDE IN PATIENTS WITH ADVANCED MYELOFIBROSIS

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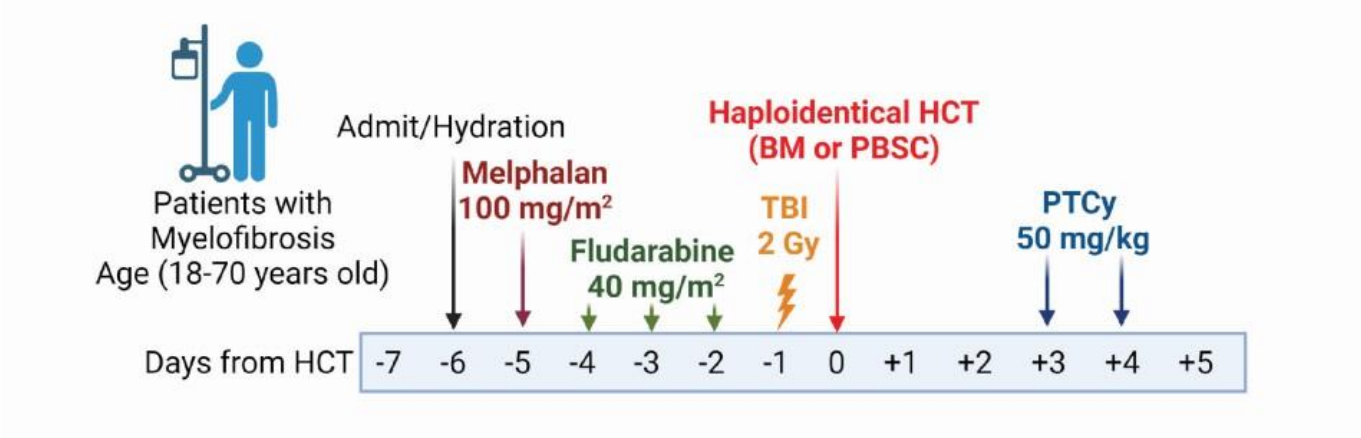
Background: Allogeneic hematopoietic cell transplantation (HCT) remains the only curative therapy for myelofibrosis (MF); however, many patients—particularly older adults—lack a suitable HLA-matched donor. The development of HLA-haploidentical transplantation (HaploHCT) using post-transplant cyclophosphamide (PTCy) has significantly expanded donor availability. We conducted a pilot study (NCT03118492) to evaluate the safety and feasibility of a reduced-intensity conditioning (RIC) regimen integrating fludarabine with Melphalan (FM100) and low-dose TBI (2 Gy) prior to HaploHCT in patients with advanced MF.



Methods: Twenty-two patients were enrolled across two sequential cohorts. After observing early toxicity in the first four patients (CH-1), eligibility was refined to exclude those with accelerated-phase disease, significant pulmonary hypertension, and to implement strict fluid management in the subsequent 18 patients (CH-2). The primary endpoint was safety, defined as the incidence of unacceptable toxicity (UT), including any Bearman grade 3–4 regimen-related toxicity, prolonged grade 4 neutropenia, or death. Secondary endpoints included rates of cytokine release syndrome (CRS), acute and chronic GVHD, engraftment, progression-free survival (PFS), and overall survival (OS).

Results: Median age was 59 years (Range= 48-70), with 55% male, 59% primary MF, and 32% high risk disease. The median interval from MF diagnosis to HCT was 1052 days (range: 27-7651). Two of four patients in CH-1 experienced UTs (persistent grade 3 anorexia; acute kidney injury and prolonged neutropenia), prompting protocol modification. In CH-2, only 1 of 16 patients experienced a UT (acute kidney injury).
A total of 20 patients (3 in CH-1 and 17 in CH-2) had neutrophil engraftment with median

time to engraftment of 20 days in CH-1 and 21 days in CH-2. All patients achieved complete donor chimera (>95%) by day 100. A total of 18 patients (2 in CH-1 and 16 in CH-2) had platelet engraftment with median time to engraftment of 53 days in CH-1 and 36 days in CH-2. With median follow up of 24 months (range: 12-25), 2-year OS and PFS for the entire cohort were 77% (95% CI, 53–90) and 59% (95% CI, 33–77), respectively. CH-2 demonstrated markedly improved outcomes versus CH-1, with 2-year OS of 83% vs 50% and 2-year PFS of 60% vs 50%, respectively. No patients experienced relapse at 1 year, and cumulative incidence (CI) of relapse was 18% in year 2. NRM was also improved in CH-2, with 100 day- and 2-year NRM of 6% and 18%, respectively, versus 25% and 50% in CH-1. Day 100 CI of Grade 2-4 and 3–4 acute GVHD was 32% and 5%, respectively. At 2 years, moderate/severe chronic GVHD CI was 5% in the entire cohort.

Patient and Transplant Characteristics

	CH-1 (N=4)	CH-2 (N=18)	Total (N=22)
Age at HCT, years Median (Range)	60 (48-68)	59 (50-70)	59 (48-70)
Gender Female Male	 2 (50%) 2 (50%)	 8 (44.4%) 10 (55.6%)	 10 (45.5%) 12 (54.5%)
Race/Ethnicity Non-Hispanic White African American Asian Hispanic	 2 (50%) 0 (0%) 1 (25%) 1 (25%)	 3 (16.7%) 6 (33.3%) 3 (16.7%) 6 (33.3%)	 5 (22.7%) 6 (27.3%) 4 (18.2%) 7 (31.8%)
HCT Comorbidity Index 0 1-2 3+	 1 (25%) 2 (50%) 1 (25%)	 12 (66.7%) 4 (22.2%) 2 (11.1%)	 13 (59.1%) 6 (27.3%) 3 (13.6%)
Karnofsky Performance Status 70 80 90 100	 1 (25%) 2 (50%) 1 (25%) 0 (0%)	 0 (0%) 4 (22.2%) 9 (50%) 5 (27.8%)	 1 (4.5%) 6 (27.3%) 10 (45.5%) 5 (22.7%)
Days from Diagnosis to HCT Median (Range)	1067 (449-2500)	798 (27-7651)	1052 (27-7651)

Patient and Transplant Characteristics

MF Type			
Primary	1 (25%)	12 (66.7%)	13 (59.1%)
Secondary	3 (75%)	6 (33.3%)	9 (40.9%)
MF Risk			
High	2 (50%)	5 (27.8%)	7 (31.8%)
Intermediate II	2 (50%)	13 (72.2%)	15 (68.2%)

Conclusions: This pilot study demonstrates that RIC HaploHCT using FM100 TBI200 and PTCy based GvHD prophylaxis is safe and feasible for patients with advanced MF, with low rates of NRM, relapse, and severe acute or chronic GVHD—particularly when performed early before progression or development of significant pulmonary hypertension. These results support HaploHCT as an effective and accessible curative option for MF patients, including those from racial and ethnic minority backgrounds who lack HLA-matched donors.

Clinical Trial Registry: NCT03118492

Disclosure: Monzr M. Al Malki: Ossium Health, Inc., Gilead, Gamida Cell, Jazz Pharma, Incyte, TScan Therapeutics, CareDx, Tr1X, Inc.
Idoroenyi Amanam: BMS, GSK, Incyte
Guido Marcucci: Patents concerning aspects of BN-CD38 technology
Stephen Forman: Allogene
Ryotaro Nakamura: Omeros, Pfizer, Ono Pharmaceutical, Sanofi, Blue Bio, Miyarisan Pharmaceutical
Haris Ali: GSK, Karyopharm, PharmaEssentia, Sobi, Incyte

B433

INFLUENCE OF HLA-DPB MATCHING ON OUTCOMES AFTER ALLO-HSCT FOR MYELOFIBROSIS

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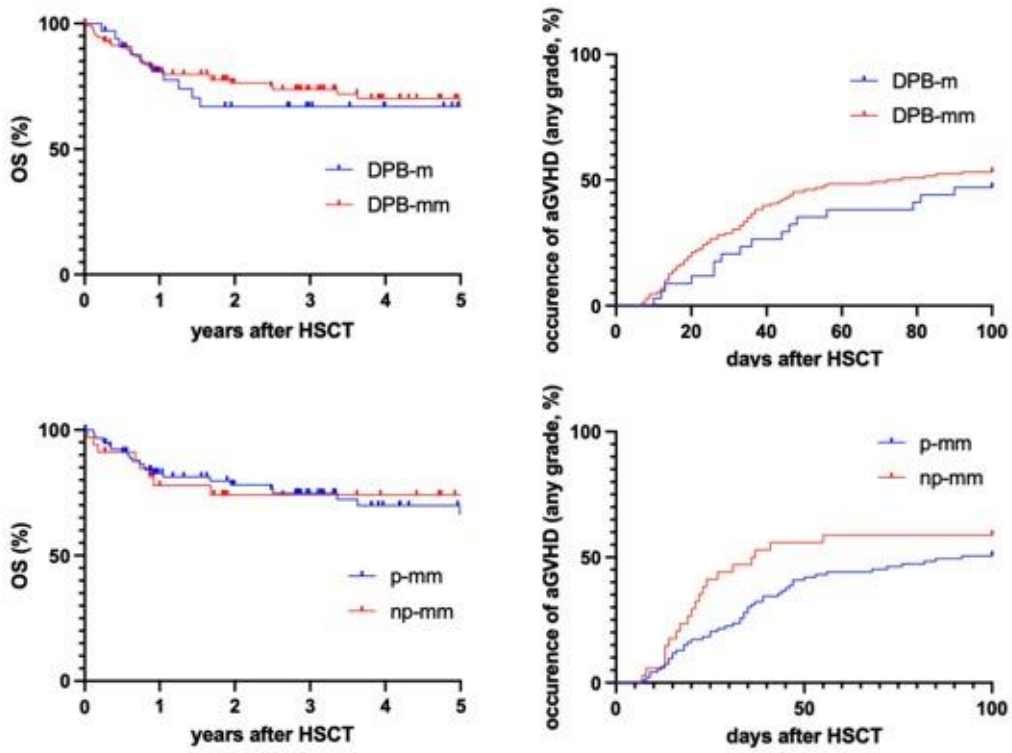
Background: Donor selection for allogeneic hematopoietic stem cell transplantation (alloHSCT) is an important factor influencing post-transplant outcomes. Especially HLA-matching determines overall survival, treatment-related mortality, disease-free survival, and the occurrence of acute and chronic graft-versus-host-disease (aGvHD and cGvHD). In recent

years, the discovery of the DPB-system as part of the HLA class II antigens has introduced a new factor for donor selection. Retrospective data showed a significant influence of HLA-DPB mismatch on transplant outcome depending on their T-Cell Epitope (TCE) group. Whether the described influence is relevant for alloHSCT in myelofibrosis remains unknown.

Methods: A total of 163 patients undergoing alloHSCT for myelofibrosis in a single center from 2017 to 2025 with available data for HLA-DPB were included in this retrospective analysis. The median follow-up time was 1147 days (3.14 years). There was no statistical difference in diagnosis (PMF; postET-MF, postPV-MF), risk score, or conditioning regimen between the groups. TCE group and subsequently permissivity of mismatch was defined as reported in Lancet Oncology (2012) 13:366-74. Survival functions were calculated using the Kaplan-Meier estimator. Statistical curve comparison was performed using the log-rank test for Overall Survival (OS), Disease-free Survival (DFS), Transplant-related Mortality (TRM) and occurrence of aGvHD. Hazard-ratios (HR) are given as a pike estimator.

Results: Our exploratory analysis showed no difference in OS among all compared groups. Comparing DPB-matched (DPB-m) and DPB-mismatched (DPB-mm) groups, disregarding TCE groups or permissivity, the HR for OS was 1.09 (95%CI:0.52 to 2.24) with no difference between the curves (p=0.80). The HR comparing permissive-DPB-mismatches (p-mm) and non-permissive-DPB-mismatches (np-mm) was 0.90 (95%CI: 0.41 to 1.98).
Comparing the TRM of DPB-m to DPB-mm yielded similar results, with a HR of 1.46 (95%-CI: 0.55 to 3.83) and no significant difference between the curves (p=0.39).
When looking at DFS, no difference was found regarding HLA-DPB-matching. Comparing DPB-m to DPB-mm, the calculated HR was 1.32 (95%CI: 0.6910 to 2.549) with a p-value of 0.36 for curve comparison. Similarly, when looking at permissive vs. non-permissive mismatches within the DPB-mm group, no statistical difference was found. HR for DFS comparing p-mm and np-mm was 1.08 (95%CI: 0.5426 to 2.179), while the curve comparison p-value was 0.82.
Analysis for the occurrence of aGvHD showed a small trend favoring the DPB-matched cohort. HR for aGvHD between DPB-m and DPB-mm was 0.70 (95%CI: 0.4517 to 1.094) with curve comparison missing statistical significance with a p-value of 0.12. Surprisingly, the same could be observed between p-mm and np-mm with a HR of 0.71 (95%CI: 0.4051 to 1.243) and a p-value of 0.17.



Conclusions: In this retrospective dataset, there is a trend towards a higher rate of aGvHD for the DPB-mismatched cohort, while not reaching statistical significance in this small patient sample. No difference is found in OS, DFS, and TRM regarding HLA-DPB-matching for patients undergoing alloHSCT for myelofibrosis.
To further delineate the relevance of HLA-DPB-matching for patients suffering from myelofibrosis, more data is needed beyond this exploratory analysis.

Disclosure: Mathias Schäfersküpper: Neovii Biotech - Travel expenses.

B435

POOR GRAFT FUNCTION FOLLOWING ALLOGENIC STEM CELL TRANSPLANTATION FOR PH-NEGATIVE MYELOPROLIFERATIVE NEOPLASMS: INCIDENCE, RISK FACTORS, AND PROGNOSTIC IMPLICATIONS FROM A SINGLE-CENTER EXPERIENCE

*Giacomo Coltro[1], Giulia Borgi[2], **Edoardo Simonetti**[1], Chiara Camerini[1], Ilaria Cutini[1], Antonella Gozzini[1], Mirella Giordano[1], Gaia Mirabella[2], Paola Guglielmelli[1,2], Alessandro M. Vannucchi[1,2], Chiara Nozzoli[1]*

[1]Azienda Ospedaliera-Universitaria Careggi, Florence, Italy, [2]University of Florence, Florence, Italy

Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only potentially curative treatment for myelofibrosis (MF) and blast phase myeloproliferative neoplasm (BP-MPN). However, it is burdened by substantial risks, including graft failure (GF) and poor graft function (PGF), both major determinants of post-transplant morbidity and mortality.

Methods: This retrospective, single-center study aimed to determine the incidence of PGF, its clinical implications, and potential risk factors; PGF was defined using both the EBMT definition (Bone Marrow Transplant. ;2024;59(6):832–837) and the criteria by Alchalby H. *et al.* (Bone Marrow Transplant.;2016;51(9):1223-7).

Results: Forty-eight patients undergoing allo-HSCT for MF (n=36; 75%) or BP-MPN (n=12; 25%) were included. Median age was 59.9 years (interquartile range [IQR], 9.6); 30 (63%) were male. All patients received peripheral blood stem cells as graft source. Most had HLA-matched unrelated donors (n=30; 63%), followed by haploidentical donors (n=11; 23%). Reduced-intensity conditioning was used in 41 patients (85%), whereas myeloablative conditioning was used in 7 (15%).
The cumulative incidence of leukocyte engraftment was 91%. The median time to leukocyte and platelet engraftment was 19 days (IQR, 6.5) and 25 days (IQR, 23), respectively. A total of 9 (21%) patients fulfilled the EBMT criteria for PGF with a cumulative incidence of 17%.
In univariate logistic regression analysis, pre-transplant factors associated with increased risk of PGF at day +100 (PGF^{100}) included severe splenomegaly (palpable >10 cm) (odds-ratio [OR], 14.7; 95%CI, 2.5-43.8; p=.0057), mutant *EZH2* (m*EZH2*) (OR, 10.5; 95%CI, 1.3-49.7; p=.0262), and *m*ASXL1 (OR, 5.8; 95%CI, 1.1-36.4; p=.0441). Conversely, non-*CALR*/*MPL* driver genotype was associated with reduced risk of PGF^{100} (OR, 0.03; 95%CI, 0-0.26; p=.0005). Upon multivariate Firth's logistic regression analysis, severe splenomegaly (OR, 8.2; 95%CI, 1.3-33.2; p=.0399) and non-*CALR*/*MPL* genotype (OR, 0.04; 95%CI, 0-0.39; p=.0134) remained significantly associated with a higher and lower risk of PGF^{100}, respectively.
Subsequently, by applying the definition provided by Alchalby H. *et al.*, 9 (21%) patients fulfilled the criteria. Univariate Cox proportional hazards analysis identified severe splenomegaly (hazard-ratio [HR], 12.1; 95%CI, 3.1-47.1; p=.0003), pre-transplant JAK-inhibitor therapy (HR, 5.6; 95%CI, 1-45.2; p=.0457), m*EZH2* (HR, 6.1; 95%CI, 1.6-23.1; p=.0069), m*ASXL1* (HR, 5.7; 95%CI, 1.2-27.5; p=.0152), and m*U2AF1* (HR, 5.1; 95%CI, 1.1-24.8; p=.0425) as significant risk factors for PGF. Conversely, non-*CALR*/*MPL* genotype was confirmed to be associated with a lower risk of PGF (HR, 0.04; 95%CI, 0-0.36; p<.0001). Upon multivariate analysis, severe splenomegaly (HR, 4.3; 95%CI, 1.1-17.1; p=.0099) and non-*CALR*/*MPL* genotype (HR, 0.07; 95%CI, 0-0.57; p=.0022) remained independent predictors of PGF. Figure 1 displays the unadjusted cumulative incidence curves of PGF for the two indipendent prognostic factors.
Finally, PGF did not significantly affect overall survival, non-relapse mortality, disease relapse/progression, or graft-versus-host disease incidence, although the limited sample size may constrain interpretability.

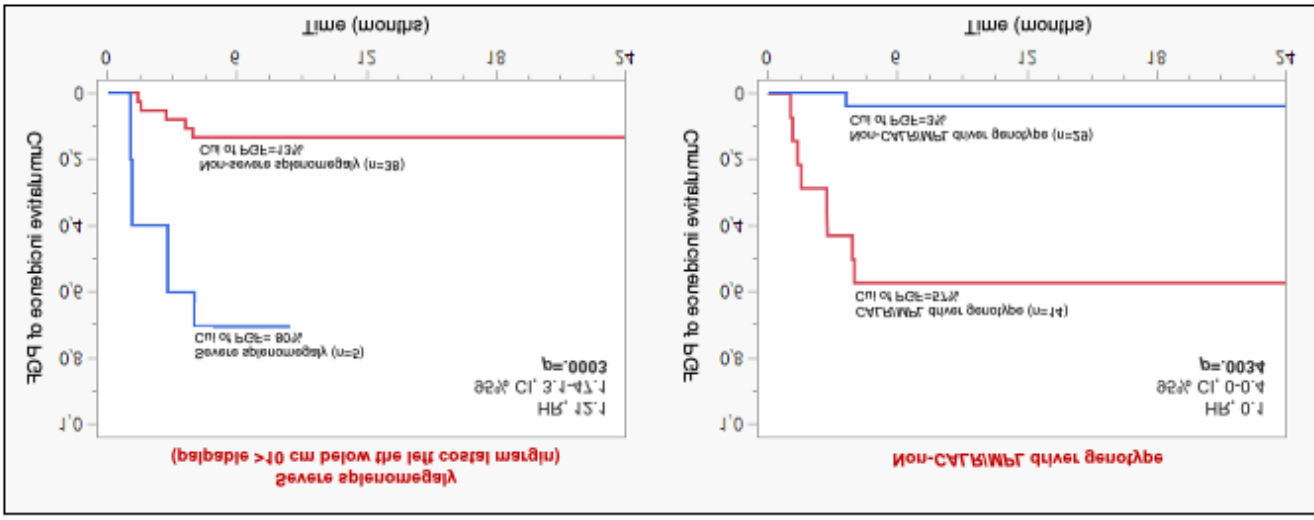


Figure 1. Unadjusted cumulative incidence (CIR) of poor graft function (PGF) according to the independent predictive factors identified in multivariable analysis

Conclusions: In our cohort, PGF emerged as a frequent post-transplant complication. Both severe splenomegaly and non-*CALR*/*MPL* driver genotype were independently associated with higher PGF risk, suggesting a shared pathogenic continuum. Although high molecular risk (HMR) mutations did not retain independent significance, their association with PGF in univariate models supports a potential biological role in compromising hematopoietic recovery and niche reconstitution.

Disclosure: Nothing to declare.

P306

IMPACT OF SPLENIC RADIOTHERAPY BEFORE HAEMATOPOIETIC STEM CELL TRANSPLANT ON ENGRAFTMENT AND TRANSFUSION NEEDS IN PATIENTS WITH MYELOFIBROSIS

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Background: Splenomegaly at the time of haematopoietic stem cell transplant for myelofibrosis is associated with a risk of graft failure and poor survival. Splenic radiotherapy before transplant may be beneficial and this has been offered in our centre since 2020. We report on the safety, efficacy and outcomes of splenic radiotherapy before transplant and compare these against those who have not had splenic radiotherapy.

Methods: Splenic radiotherapy (5Gy in 5 fractions) was given a week before transplant conditioning. Survival was analysed using Kaplan-Meier methods. Engraftment, transfusion independence, serial blood count and donor lymphocyte infusion (DLI) were assessed between radiated and not radiated groups.

Results: Thirty-four patients underwent transplant for myelofibrosis. Median follow-up was 35.1 months. Of which, 21 received pre-transplant splenic radiotherapy (median age 63.5) and 12 did not (median age 62.0). Of the radiated group, 12 (57.1%) had primary myelofibrosis, the median DIPSS score was 3 and the median Charlson co-morbidity index was 4. Ruxolitinib therapy before radiotherapy was reported in 16 (76.2%).
The median spleen size prior to radiotherapy was 22.0cm. The median spleen reduction post-radiotherapy was 3.0 cm (15%, 95% CI: 10-28%), with no difference between previous ruxolitinib exposure and non-exposure (median 3.0 vs 3.25 cm, p=0.51). Radiotherapy-related toxicities occurred in 61.9%, mostly nausea and vomiting. One patient developed tumour lysis syndrome.
The median overall survival was not reached in either group (HR=0.95, 95% CI: 0.31-2.89, log-rank *p*=0.90). Engraftment times were similar (neutrophils 19 vs 17 days, platelets 22 vs 19 days, p>0.05). Chimerism remained comparable at day +30 (94.3% vs 94.5%, p=0.97), day +60 (89.0% vs 94.5%, p=0.36) and day +100 (92.8% vs 95.1%, p=0.86).
The radiated group required fewer red cell transfusions per inpatient day (0.62 vs 0.82, p=0.047). Platelet transfusion rates were similar (0.98 vs 1.03 bag/day, p = 0.96). Kaplan-Meier analysis similarly suggested a trend toward earlier transfusion independence among radiated patients (log-rank p=0.07, HR = 2.11, 95% CI: 0.91-4.89). At day +100, haemoglobin was higher among radiated patients (97.5 vs 87 g/L, p=0.027) but other counts were similar. DLI requirement (33.3% vs 23.1%, p = 0.70) and GvHD incidence (52.4% vs 61.5%, p = 0.73) did not differ.
On univariate analysis of the radiated cohort, only higher DIPSS score predicted poorer survival (HR = 7.71, p=0.043).

Conclusions: We report less transfusion needs whilst in patient and a trend toward faster transfusion independence post-transplant in those who received splenic radiotherapy. Splenic radiotherapy was not associated with inferior survival, engraftment kinetics, chimerism, GvHD or DLI incidence.

Disclosure: Nothing to declare

P308

ALLOGENEIC STEM CELL TRANSPLANTATION IN MYELOFIBROSIS: SINGLE CENTRE EXPERIENCE

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Background: Allogeneic stem cell transplantation (AHSCT) is the only potentially curative treatment for myelofibrosis, achieving overall survival rates between 40-60%, transplant-related mortality of 30% and relapse rate of 25%.

Methods: We conducted a single-center, retrospective study including 15 patients with primary and secondary myelofibrosis who underwent AHSCT between January 2000/June 2025. All transplants used peripheral blood as stem cells source and received antifungal and antiviral prophylaxis (letermovir for CMV-seropositive since available), as well as graft-versus-host disease (GVHD) prophylaxis with different regimens.

Results: Table and image 1: patients and transplants' main characteristics.

Patient	Age (years)	Year	Type of myelofibrosis	Driver mutations	Additional genetic abnormalities	DIPSS/ DIPSS+	Exposure to JAK inhibitors (ruxolitinib) and response	Splenomegaly (cm)	Spleen treatment
1	53	2000	Primary	-	-	Int-2	No	Yes (24)	No
2	58	2003	Primary	-	-	Int-2	No	Yes (21)	Radiotherapy
3	55	2005	Primary	-	-	High	No	Yes (15)	No
4	55	2005	Primary	-	-	Int-1	No	Yes (16)	No
5	46	2007	Primary	-	-	Int-2	No	Yes (-)	No
6	61	2012	Secondary (ET)	-	-	High	No	Yes (20)	No
7	57	2012	Primary	-	-	Int-2	No	Yes (20)	Radiotherapy
8	52	2017	Secondary (ET)	CALR	-	Int-2	No	No	No

9	61	2019	Primary	CALR	-	Int-2	Yes (no response)	Yes (22)	Radiotherapy
10	37	2021	Secondary (ET)	JAK2	-	Int-2	Yes (no response)	Yes (15)	No
11	58	2022	Secondary (PV)	JAK2	-	Int-1	Yes (no response)	Yes (30)	Radiotherapy Splenectomy
12	52	2023	Secondary (ET)	CALR	-	Int-1	Yes (response)	Yes (20)	No
13	50	2023	Primary	MPL	-	Int-2	Yes (no response)	No	No
14	56	2024	Secondary (ET)	JAK2	ASXL1, NRAS, SRSF2, TP53	Int-2	Yes (lost response)	Yes (22)	Splenectomy
15	43	2025	Secondary (ET)	CALR	SF3A1	Int-1	Yes (switch to momelotinib)	Yes (21)	No

Table 1

Proportion of primary and secondary myelofibrosis was 54% vs 46%, the latter secondary to essential thrombocytemia (ET) in 6 patients and to polycythemia vera (PV) in one. JAK2 and CALR were the most frequent driver mutations. No available molecular alterations before 2017. One patient had high-risk mutations ASXL1 and TP53. All but 4 patients had intermediate-2 or high risk DIPSS and DIPSS-plus score.
All patients but 2 (86%) presented splenomegaly at diagnosis. Median spleen size: 20.5 cm. Four received radiotherapy and 2 splenectomy.
Seven patients received pre-transplant ruxolitinib; two responded to treatment: one had initial response that later lost, and the other one switched to momelotinib because of secondary anemia.

Patient	Donor (HLA)	Conditioning regimen	HCT-CI	Infused cell dose (CD34+x10⁶/kg)	GVHD prophylaxis	Leukocyte graft (days)	Platelet graft (days)	Complications	Graft function	Survival (months)
1	MRD (id)	BuCy	2	12.1	CsA + MPD	-	-	- VOD - Died pre-engraftment	Primary graft failure	Dead (1)
2	MRD (id)	FluMel	4	6.7	CsA + MTX	14	25	cGVHD	Poor graft function	Alive (268)
3	MRD (id)	FluBu	2	3.8	CsA + MMF	13	19	- CMV reactivation - cGVHD	Poor graft function Secondary graft failure	Dead (9)
4	MRD (id)	FluBu	2	4.5	CsA + MMF	16	13	cGVHD	Poor graft function	Alive (246)
5	MRD (id)	FluBu	1	5	CsA + MMF	31	36	Patient declined second transplant	Poor graft function Secondary graft failure	Dead (54)
6	MRD (id)	FluBu	5	5	CsA + MTX	22	33	- CMV reactivation - Second transplant	Poor graft function Secondary graft failure	Dead (3)
7	MUD (11/12)	FluBu + ATG	3	-	CsA + MTX	21	-	Died during transplant	Leukocyte engrafment	Dead (1)
8	MUD (11/12)	FluBu + ATG	2	3.3	CsA + MTX	15	12	CMV reactivation	Poor graft function	Alive (103)
9	Haplo	FluBu	3	6.1	CsA + MMF + Cypost	30	41	cGVHD	Poor graft function	Alive (73)
10	MUD (11/12)	TBF	1	5	CsA + Cypost	24	53	- aGVHD - CMV reactivation	Normal	Alive (55)
11	MUD (10/12)	TBF	3	6.2	CsA + MMF + Cypost	17	19	- CMV reactivation - cGVHD - Relapse	Normal	Alive (37)
12	MUD (11/12)	TBF	2	6.3	CsA + MMF + Cypost	32	41	- CMV reactivation - cGVHD	Normal	Alive (29)
13	MUD (9/10)	TBF	3	5.7	CsA + MMF + Cypost	28	28	- aGVHD - CMV reactivation	Normal	Alive (29)
14	MUD (id)	FluBu	2	4.7	CsA + Cypost	24	53	aGVHD	Normal	Alive (22)
15	MUD (id)	TBF	3	6	CsA + MMF + Cypost	25	55	VOD	Poor graft function	Alive (6)

Image 1: Transplants' main characteristics. MRD: matched related donor. MUD: matched unrelated donor. Id: identical. Haplo: haploidentical donor. FluBu: fludarabine-busulfan. TBF: thiotepa, busulfan and fludarabine. BuCy: busulfan-cyclophosphamide. FluMel: fludarabine-melphalan. aGVHD: acute graft-versus-host-disease. cGVHD: chronic graft-versus-host-disease. CsA: cyclosporine A. MTX: methotrexate. MMF: mycophenolate mofetil. MPD: methylprednisolone. VOD: veno-occlusive disease.

Regarding donor type: 40% (6/15) were from matched related donors, 40% (6/15) mismatch unrelated, 13.3% (2/15) matched unrelated and 6.6% (1/15) haploidentical. Most commonly conditioning regimen was fludarabine-busulfan. Four patients received TBF (thiotepa, busulfan and fludarabine) and the rest other regimens (BuCy, FluMel).
For GVHD prophylaxis, cyclosporine A was mainly used in combination with other immunosuppressants (methotrexate, mycophenolate mofetil). Since 2019, post-transplant cyclophosphamide was widely used in haploidentical or unrelated donor transplants.
Median time to leukocyte engraftment was 23 days and 33 days to platelet engraftment. Eight patients experienced poor graft function, with slow recovery. Additionally, 3 patients suffered graft loss, 2 of them secondary to CMV reactivation. Of these patients, one experienced adequate hematopoietic recovery after CMV treatment, another underwent second allo-transplant, and the third one declined second transplant. Only one patient had primary graft failure and donor cell-boost was infused.
CMV reactivation was frequent (7/15); none of these were under letermovir prophylaxis at the time of reactivation. Chronic GVHD was also common in 6/15. Two patients suffered veno-occlusive disease.
Survival rate was 66% (10/15). Causes of death: primary graft failure in 1 patient, hepatic and pulmonary cGHVD in another, secondary graft failure in 2 patients; one patient died during pre-engrafment period. To date, alive patients remain in complete remission with a

median follow-up of 46 months, except for one patient who relapsed 34 months after transplant.

Conclusions: Our cohort supports that AHSCT in myelofibrosis can be curative, with high survival rate. Changes in management of these patients over the years can be observed, with trend toward improved transplant outcomes, partially explained by introduction of JAK inhibitors, molecular monitoring and post-transplant cyclophosphamide. Poor graft function and graft failure remain relevant complications representing main causes of post-transplant mortality. Further studies are needed to improve management of these complications and patient prognosis.

Disclosure: Nothing to declare.

P309

ASCIMINIB AS BRIDGE TO ALLOGENEIC-HEMOPOIETIC STEM CELL TRANSPLANT (ALLO-HSCT) IN A MULTICENTER CHRONIC MYELOID LEUKEMIA (CML) PATIENTS' COHORT

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Background: In the last decades, major molecular response (MMR) achieved by tyrosine kinase inhibitors (TKIs) in CML patients has significantly reduced the indication for allo-HSCT. However, a small percentage of patients are resistant or intolerant to multiple TKI lines, resulting in worse outcome and subsequent indication for allo-HSCT. Asciminib, a selective BCR::ABL1 allosteric inhibitor, has recently been approved for chronic-Phase (crP) CML with resistance or intolerance to at least two previous TKIs. Therefore, the safety and efficacy of Asciminib as bridge therapy before allo-HSCT is still an unexplored issue.

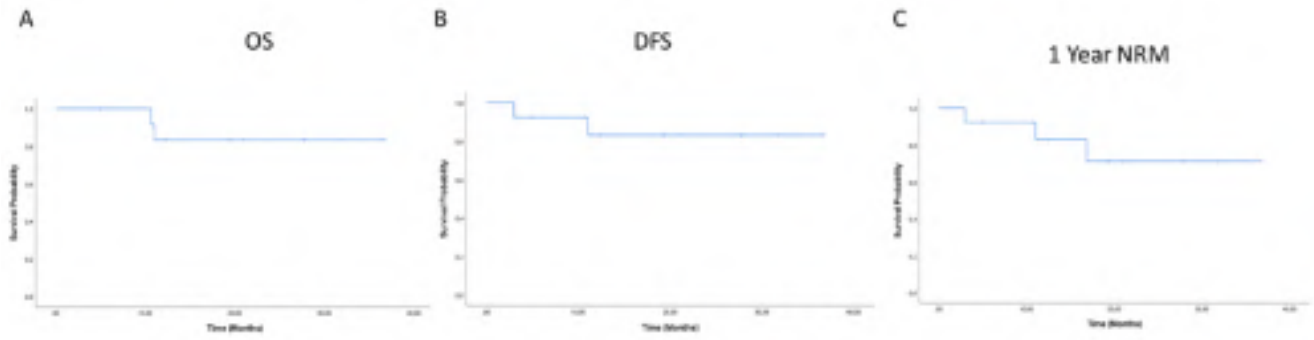
Methods: Therefore, we retrospectively collected data of 13 CML patients treated with Asciminib and allo-HSCT, across 9 Italian allo-HSCT Programs. Baseline clinical characteristics of patients are summarized in Table 1. Median follow-up time, Overall survival (OS), Disease Free Survival (DFS) and 1-Year Non-Relapse Mortality (NRM) have been estimated with Kaplan Meier method.

Total number of patients	13

Age: Years, median (range)	56 (20-70)
Sex: Male, number (%)	7 (54)
Additional genetic alteration: Number of patients, (%)	4 (31)
State of Disease pre allo-HSCT:	
Active chronic disease, number (%)	6 (46)
Active accelerated/blastic disease, number (%)	1 (8)
CHR and CcyR, number (%)	5 (38)
MR3, number (%)	1 (8)

Results: In our heavily pre-treated cohort, median TKIs lines before Asciminib was 4, among which 11/13 were previous Ponatinib exposed. Reason to start Asciminib was resistance, intolerance or both to others TKIs in, respectively, 8, 3 and 2 out of 13 patients. About safety, 7/13 patients discontinued the therapy due to grade 3/4 Adverse Events, followed by a definitive stop in 3/13 of them. At 3 months, Complete Hematological (CHR), cytogenetic (CcyR), Molecular (MMR) and no response were observed in 3, 2, 1 and 6 patients, respectively, out of 12 evaluable patients.
Median time between Asciminib start and allo-HSCT was 6.77 months (range: 3.1-21.3). All patients but one underwent allo-HSCT in crP, state of disease before allo-HSCT is detailed in Table 1. Donors were MRD, MUD, mMUD, haploidentical and from multiples Cord blood in 5, 3, 1, 3 and 1 patients, respectively. Conditioning intensity accordig to EBMT 2018 was intermediate in 3 cases and high in 10 cases. All patients engrafted as PMN and PLTS. At 90 days after allo-HSCT, all crP patients showed a full donor chimerism and a deep molecular response, while the patient in accelerated phase (aP) had a mixed chimerism and did not reach any response. Cumulative incidence of aGVHD was 23% but no patients developed grade 3-4 aGVHD nor cGVHD. Molecular relapse after allo-HSCT occurred in two cases, treated with Asciminib and Ponatinib, obtaining an MMR. Two transplant related side effects, consisting in Pure Red Cell Aplasia and thrombotic microangiopathy, were observed and successfully treated. With a median follow up of 20.64 months from allo-HSCT, OS, DFS and 1 year NRM were respectively 84%, 77% and 7% (Figure 1, A, B and C). Overall, 2 patients died: one for persistence of aP disease and one for encephalitis.

Figure 1



Conclusions: In conclusion, in TKIs resistant CML, allo-HSCT remains the best clinical option, with excellent results in terms of deep molecular response and limited incidence of complications. In our cohort of advanced-lines patients, the use of Asciminib seems to be a potential bridge strategy for allo-HSCT, although the discrete incidence of related adverse events. Further studies in larger cohorts are warranted in order to confirm these results and drive clinical decisions.

Disclosure: Nothing to declare.

P310

ALLOGENEIC HSCT IN A 7-YEAR-OLD GIRL WITH ADULT-TYPE PRIMARY MYELOFIBROSIS: A RARE CASE REPORT

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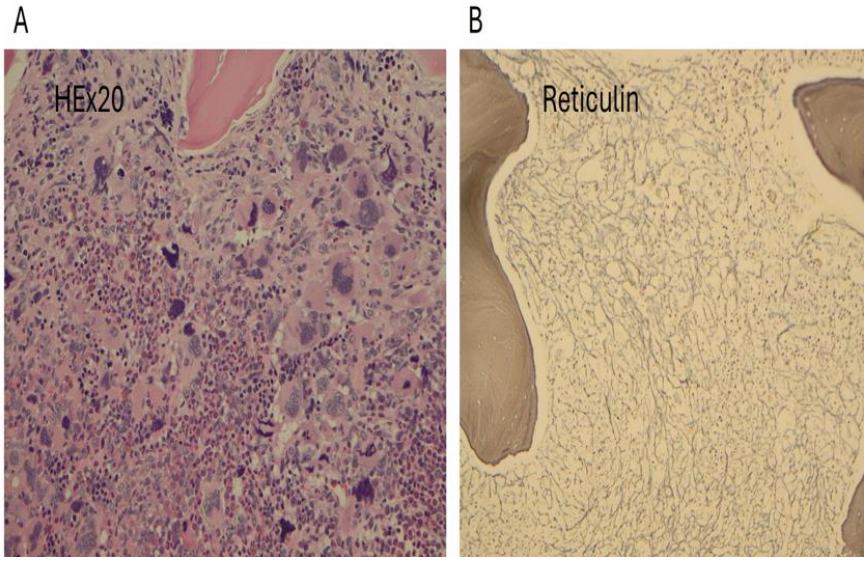
Background: Primary myelofibrosis (PMF) is a myeloproliferative neoplasm characterized by clonal proliferation of myeloid cells, leading to reactive bone marrow fibrosis, progressive marrow failure, hepatosplenomegaly, and extramedullary hematopoiesis. Driver mutations such as *JAK2*, *CALR*, or *MPL* are common, while triple-negative disease is associated with a more aggressive clinical course. PMF is extremely rare in children and may present as a reactive, often reversible secondary form, which differs substantially from the adult disease. In contrast, adult-type PMF in children exhibits the same clinicopathological features as adult PMF, including megakaryocytic atypia with reticulin or collagen fibrosis, splenomegaly, and constitutional symptoms. This form is typically more severe, and although JAK inhibitors have shown promising results in reducing symptom burden, allo-HSCT remains the only curative therapy, yet historically associated with a high risk of graft rejection.

Methods: **Case presentation:** A previously healthy 7-year-old girl presented in December 2024 with a one-month history of abdominal pain, headache, fatigue, and weight loss.

Results: Blood tests showed leukocytosis with neutro- and monocytosis, thrombocytosis, elevated LDH, and 3% blasts. Bone marrow biopsy revealed a hypercellular marrow with atypical megakaryocytic proliferation, reticulin fibrosis grade II–III, collagen fibrosis, and osteosclerosis, consistent with PMF (Figure 1). Karyotype was normal, and extended NGS and whole-genome sequencing detected no somatic or germline variants.



Follow-up showed persistent leukocytosis (30 ×10⁹/L), thrombocytosis (891 ×10⁹/L), elevated LDH (1600 U/L), and splenomegaly, but no blast excess. EWOG board review in February 2025 confirmed triple-negative adult-type PMF. A two-month watch-and-wait approach showed no improvement in bone marrow pathology, supporting the indication for HSCT. Bridging therapy with the JAK inhibitor ruxolitinib was given for 30 days to facilitate engraftment with tapering prior to conditioning.

In May 2025, the patient underwent allo-HSCT from a matched sibling donor using EWOG-MDS–based conditioning with busulfan (AUC 75 mg·h/L), cyclophosphamide (120 mg/kg), melphalan (140 mg/m² ×1), and ATG Grafalon (30 mg/kg). GvHD prophylaxis consisted of tacrolimus and methotrexate. Neutrophil engraftment occurred on day +21.

Early post-transplant complications included acute skin GvHD stage 3 (overall grade II) on day +14, responding promptly to steroids, and prolonged dysuria and hematuria. At day +84, the patient developed dyspnea and a restrictive pulmonary function pattern consistent with cryptogenic organizing pneumonia—a non-infectious pulmonary complication—diagnosed radiologically and treated with pulse steroids (15 mg/kg ×3 for three courses), resulting in clinical recovery and near-normal lung function. Full donor chimerism was achieved by day +35, but a four-week period of cytopenia occurred from day +70, which resolved spontaneously. At day +180, the patient maintains full donor chimerism with normal hematologic recovery and a CD4+ T-cell count of 128 cells/µL. Tacrolimus is maintained at 4–6 µg/L due to the risk of graft rejection, with gradual tapering planned.

Conclusions: Adult-type primary myelofibrosis in childhood is extraordinarily rare, with only very few pediatric cases described, leaving no evidence-based guidelines for transplant management. This case adds clinical experience for HSCT decision-making in such patients. Despite significant post-transplant complications, the patient achieved full donor chimerism and remains clinically well six months post-transplant.

Disclosure: Nothing to declare.

P311

ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PATIENTS WITH PRIMARY MYELOFIBROSIS

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Background: Primary myelofibrosis (PMF) is a rare Philadelphia chromosome–negative myeloproliferative neoplasm with a heterogenous clinical course, with a poor prognosis. JAK inhibitors improve symptoms without providing a cure. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative option, reserved for young and high-risk patients (pts). We report the outcomes of a series of 15 pts who underwent this procedure over a period of 257 months.

Methods: From May 2002 to December 2024, an HLA-identical allogeneic HSCT was performed in 15 pts with PMF, including 3 pts in leukemic transformation and 3 pts with post-essential thrombocythemia myelofibrosis (post-ET MF). Median age at transplantation was 45 years (37–59) and a sex ratio (M/F) of 1.1. The median interval between diagnosis and transplantation was 35 months (5–108). Molecular analysis identified the JAK2 mutation in 3/13 pts, CALR in 4/5 pts and MPL in 1/1 pt. According to the DIPSS prognostic score: intermediate-1 in 1 transfusion-dependent pt, intermediate-2 in 9 pts, and high-risk in 5 pts. Pre-transplant management was heterogeneous due to the long study period: transfusion program in 5 pts, Hydroxyurea alone or combined with Interferon in 5 pts, splenectomy in 2 pts, and splenic irradiation in 6 pts. Two conditioning regimens were used sequentially: Busulfan–Fludarabine (4 pts), and Busulfan–Fludarabine combined with antithymocyte globulin (11 pts). GVHD prophylaxis consisted of Cyclosporine and Methotrexate. A peripheral blood stem cell graft was used for all pts, with a mean CD34+ cell dose of 8.9 × 10^6/kg (5.9–12.5). As of July 31, 2025, follow-up ranged from 8 to 276 months.

Results: The mean time to neutrophil recovery was 17 days (13–57). One primary graft failure occurred in a pt with 73% donor chimerism, corrected with a CD34+ cells boost. Early complications (all with favorable outcomes) included 1 case of VOD, 1 case of TMA, and 1

case of hemorrhagic cystitis. Acute GVHD occurred in 1 pt (7%), grade III, and extensive chronic GVHD was observed in 6 pts (46%) after a mean delay of 5 months (4–9). CMV reactivation occurred in 3 pts (21%). Three pts (21%) relapsed, two of whom received donor lymphocyte infusion (DLI). Seven pts (46%) are alive after a median follow-up of 26 months (7–71), and 8 pts (53%) died (early infection: 1, pulmonary aspergillosis: 2, GVHD: 4 pts, relapse: 1 pt). Overall survival (OS) and event-free survival (EFS) at 23 years were 47% and 45%, respectively.

Conclusions: Allogeneic HSCT is currently the only curative treatment for primary or secondary MF in eligible pts with intermediate-2/high-risk DIPSS scores or unfavorable mutations. Reduction of splenomegaly (with JAK2 inhibitors or splenic irradiation) is essential to improve engraftment and reduce transplant-related mortality.

Disclosure: Nothing to declare

P312

THIRD-LINE TREATMENT OF CHRONIC MYELOID LEUKEMIA WITH TKI IN THE POST-BMT SETTING IN PATIENT WITH POSITIVE MRD

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Background: Since incorporation of TKI, progression to accelerated phase of CML rarely occurs. Nevertheless, progression to blast phase contemplates a very poor prognosis with overall survival of 9 to 12 months. In this setting BMT has a key role associated to TKI maintenance in cases of positive MRD. Third and forth generation TKI are of great importance in refractory cases, often associated with drug related toxicity. In our settings, there are financial and access boundaries.

Methods: We present a clinical case that illustrates the benefits in this clinical scenario.

Results: 32 year old man, with no clinical records. Presents with 3 months of weight loss, malaise and feverish feeling. Palpable spleen 20 centimeters under costal margin. At diagnosis: Hb: 8.8 WBC: 90.100 Blast: 5% Eosinophils: 13% Basophils: 25% Platelets: 69.000; RT-PCR BCR-ABL p210: detected. Bone marrow flow citometry: Myeloid blasts: 4% Lymphoid blasts: 1%. Configures diagnosis of Chronic Myeloid Leukemia of high risk (by Sokal, Hasford and ETLS). Starts on Dasatinib 100 mg per day, after one year only achieves complete hematologic response (CHR), remaining qPCR BCR-ABL: 72%^{IS}; T315I mutation by PCR: undetected. Switch of therapy with Nilotinib 800 mg per day with no molecular response in 6 months (qPCR BCR-ABL: 44%^{IS}). There was a petition to starts third generation TKI, delayed for financial reasons.
Evolves with loss of hematologic response and progression to accelerated phase; in this context starts on Ponatinib 45 mg per day with CHR but no molecular response (qPCR BCR-ABL: 16,7%^{IS}) and Ponatinib was discontinued due to hematologic toxicity grade 3.
Intense chemotherapy was conducted with 7+3 protocol, resumes Ponatinib 45 mg every

other day. TKI was stopped due to cardiological toxicity. Allogenic BMT was performed with related identical donor with RIC conditioning (BuFlu2). Hematologic recovery by day 16, resumes TKI with Ponatinib 15 mg every other day by day 46. Does not achieve Major Molecular Response (MMR) by day 90 (qPCR BCR-ABL: 0,138%^{IS}). Ponatinib was again discontinued due to hematologic toxicity.
Starts oh Asciminib by day 124, achieving MR 4.0 by day 195 which is maintained by day 395.

Conclusions: This clinical case shows that there still cases of chronic myeloid leukemia resistant to second generation TKI, even with early initiation at diagnosis. Toxicity is often associated with resistance. In our case, starting Ascminib as maintenance treatment post BMT, instead of Ponatinib due to hematologic and cardiologic toxicity, had a major impact on response achieving MR 4.0 sustained with no toxicity associated.

Disclosure: No potential conflict of interest.

P313

IMPACT OF DOSE-ESCALATION STRATEGIES ON CLINICAL OUTCOMES OF ROPEGINTERFERON ALFA-2B IN POLYCYTHEMIA VERA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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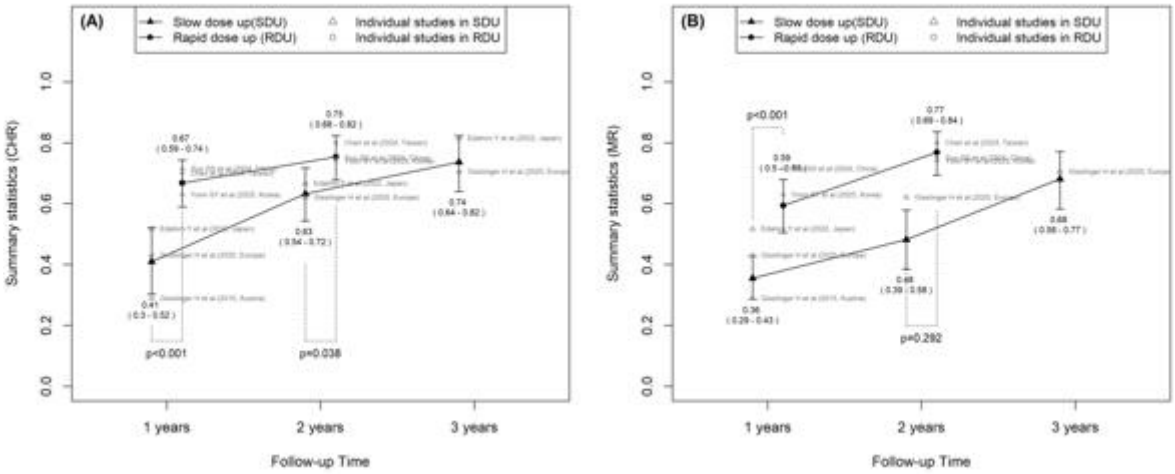
Background: Ropeginterferon alfa-2b is a long-acting interferon increasingly used for cytoreduction and molecular response in polycythemia vera (PV), yet the impact of different dose-escalation strategies on efficacy and safety remains unclear.

Methods: A systematic review and meta-analysis was performed according to PRISMA guidelines. PubMed, Embase, and the Cochrane Library were searched through September 24, 2025 for studies evaluating ropeginterferon alfa-2b in adult patients with PV. Eligible studies reported at least one clinical outcome, including complete hematologic response (CHR), molecular response (MR), *JAK2* V617F allele burden, adverse events (AEs), treatment discontinuation, thrombosis, or disease transformation. Randomized trials and non-randomized interventional or cohort studies were included. Studies were categorized by dose-escalation strategy into slow dose-up (SDU), starting at 50–100 µg with gradual increases, and rapid dose-up (RDU), initiating at 250–350 µg with early escalation to 500 µg. Random-effects meta-analyses were conducted using restricted maximum likelihood estimation. Subgroup analyses compared SDU and RDU strategies at 1-, 2-, and 3-year follow-up intervals. Risk of bias was assessed using RoB 2 and ROBINS-I tools according to study design.

Results: Nine studies met inclusion criteria. At 1 year, the pooled CHR proportion across all studies was 0.59 (95% CI, 0.47–0.71) with substantial heterogeneity. Subgroup analysis

demonstrated significantly higher CHR rates with RDU compared with SDU (0.67 vs. 0.41; p < 0.001). This difference persisted at 2 years, with CHR proportions of 0.75 for RDU and 0.63 for SDU (p = 0.038). At 3 years, CHR data were available only for SDU-treated patients, yielding a pooled proportion of 0.74. Molecular response analysis at 1 year showed a pooled MR proportion of 0.40 (95% CI, 0.28–0.53). MR was significantly higher in the RDU group than in the SDU group at 1 year (0.59 vs. 0.36; p < 0.001). At 2 years, MR proportions increased in both groups (0.77 for RDU and 0.48 for SDU), although the between-group difference was no longer statistically significant (Figure). Five studies reported quantitative changes in *JAK2* V617F allele burden at 1 year, demonstrating a significant pooled mean reduction of −22.2%. Safety analyses including all nine studies showed low pooled incidences of thrombosis (4.0%), serious adverse events (5.0%), treatment discontinuation (7.0%), and disease transformation (1.0%), with no consistent signal of increased toxicity associated with rapid dose escalation.



Conclusions: Ropeginterferon alfa-2b is an effective and well-tolerated treatment for PV. Rapid dose-escalation strategies are associated with earlier and higher hematologic and molecular response rates without compromising safety, suggesting that titration speed is a clinically relevant factor in optimizing early treatment outcomes.

Disclosure: Nothing to declare.

Solid Tumours

B436

SEQUENCE ORDER IN BU MEL CONDITIONING FAILS TO PREDICT SURVIVAL: PK AND OUTCOME DATA FROM A PEDIATRIC NEUROBLASTOMA AND EWING SARCOMA COHORT

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Background: Busulfan (Bu)–melphalan (Mel) conditioning was historically standard for autologous transplantation in high-risk neuroblastoma, though less common in the era of tandem transplants. The optimal sequence (Bu-Mel vs. Mel-Bu) remains unclear, as sequence-related pharmacokinetic (PK) interactions may influence drug exposure, sinusoidal obstruction syndrome (SOS), and overall survival (OS).

Methods: To retrospectively assess whether conditioning sequence affects Bu or Mel PK, SOS risk, and OS in 36 children (0.7–16.8 years) undergoing autologous HSCT between 2010–2024 for solid tumours (30 neuroblastoma, 6 Ewing's sarcoma) at a single centre. Methods: Conditioning comprised Bu (3.2–5.65 mg/kg daily ×4) and Mel (140 mg/m²). Twenty-one patients received Bu-Mel, fifteen Mel-Bu. First dose Bu area-under-the-concentration-versus-time curve (AUC0-∞, trapezoidal rule) was available for all patients; in 27 full 4-day Bu PK enabled calculation of cumulative AUC (cAUC) by summation. The Bu dose was not PK-adjusted, though one patient had a dose omitted for elevated AUC. Mel PK data was available for 18 patients (5 Bu–Mel, 13 Mel–Bu). First-dose Bu and Mel clearance (CL) were compared using the Mann-Whitney test. Associations of Bu cAUC above/below median (72.4mg/L·h) and Mel AUC above/below median (9.0mg/L·h) on SOS incidence were assessed using the Friedman test, and on OS with Kaplan–Meier and multivariate Cox regression. Additional covariates assessed in multivariate models included disease relapse/progression, moderate/severe SOS, age and glomerular filtration rate.

Results: Pharmacokinetics
First day Bu and Mel clearance did not differ between the Bu-Mel and Mel-Bu groups (median Bu CL 4.9 versus 4.1 L/h , median Mel CL 8.6 versus 10.6 L/h, respectively), indicating no sequence effects on Bu or Mel disposition. In the four-day Bu PK data, Bu clearance declined significantly over successive treatment days in both groups ($p<0.05$, Friedman test), consistent with metabolic saturation. Median Bu cAUC was 72.4 (IQR:59.2– 79.5) mg/L.h, with no difference between sequence groups.
Toxicity
SOS occurred in 44% of patients; 28% were classified as moderate–severe. SOS incidence did not differ between Bu-Mel(43%) and Mel-Bu(47%), $p>0.05$. Neither elevated Bu or Mel exposure, nor total mg/kg Bu dose predicted SOS severity.
Survival

Sixteen patients have died; disease relapse/progression was the leading cause of death. Bu cAUC >72.4mg/L.h was associated with a trend toward longer OS (mean 11.0 versus 6.8 years, p=0.14); similar mean survival times were observed for the Mel-Bu and Bu-Mel groups (9.9 and 9.0 years, respectively, p=0.35). In the multivariate analysis, only disease relapse/progression was significantly associated with mortality: HR 367.5 (95% CI 1.1–117106; p<0.05).

Conclusions: The Bu-Mel and Mel-Bu conditioning sequences produced equivalent PK, SOS risk, and survival outcomes. Bu clearance declined daily regardless of sequence. A trend toward improved survival with higher cumulative Bu exposure was noted. Disease progression was
the sole independent predictor of OS, underscoring the dominance of neuroblastoma biology over conditioning optimisation. These findings support flexibility in sequencing Bu-Mel conditioning and highlight the need to focus on post-transplant disease control strategies. Larger multicenter studies are needed to evaluate whether refined exposure targets can improve disease outcomes without increasing toxicity.

Disclosure: Nothing to declare.

OTHER TOPICS

Data management

P315

MULTI-MISMATCH SEARCHES IN HAP-E SEARCH

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Background: In the context of allogenic human stem cell transplantations (HSCT) so called matching algorithms are used to identify the best matching donors for a patient.

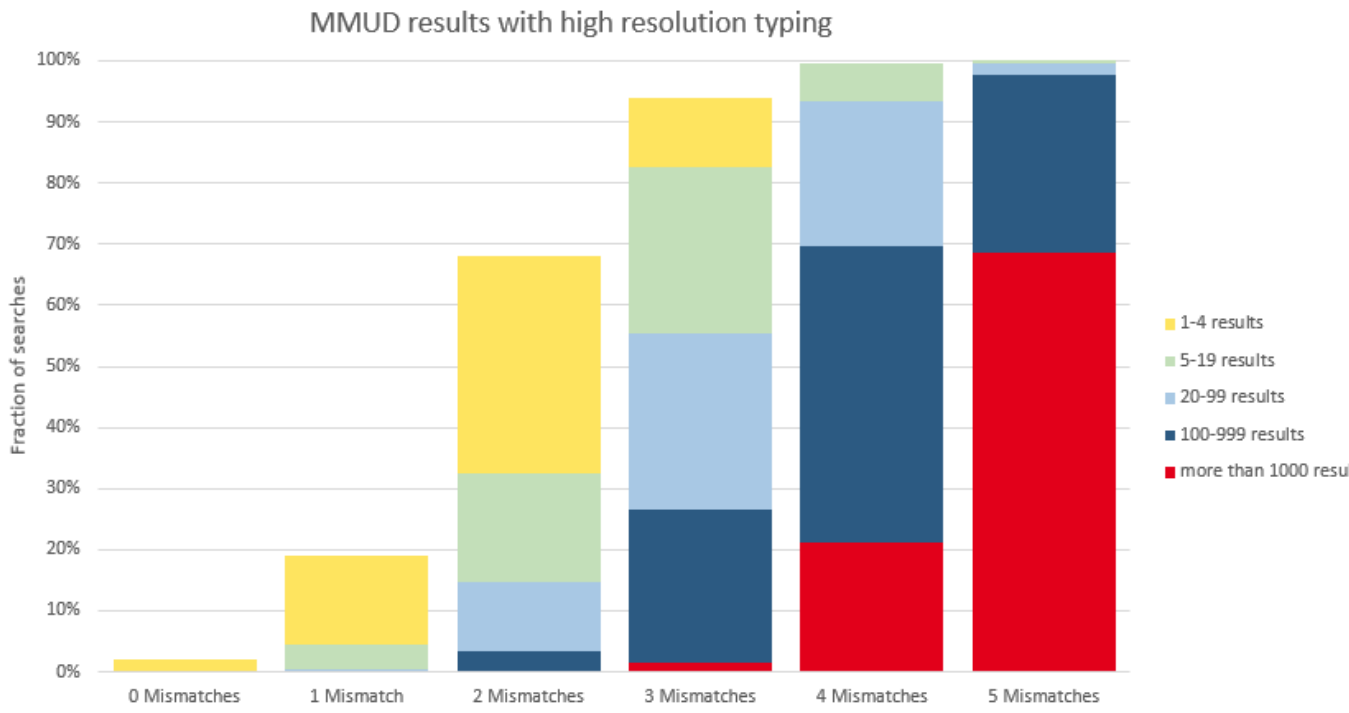
Methods: As clinical practice evolves, the requirements for donor–recipient matching algorithms must likewise adapt. To address the increasing use of mismatched unrelated donors (MMUD) in transplantation, we extend Hap-E Search to support higher-level multi-mismatch searches. In the context of this work, a MMUD search is defined as one that returns donors with match grades down to 4/8 (A, B, C, DR) or 5/10 (A, B, C, DR, DQ). Such MMUD searches are meant to complement the already existing standard mismatch searches. To improve performance and reduce data volume while focusing on clinically meaningful results, we introduced the following constraints for MMUD searches:
• MMUD searches are performed only for patients with high-resolution HLA typing at the

relevant search loci (A, B, C, DR for 4/8; A, B, C, DR, DQ for 5/10).
• Only donors with high-resolution HLA typing at the corresponding search loci are included.

- We call an HLA typing "high resolution" if all contained alleles fall into the same "g" group. "g" grouping combines alleles with identical DNA sequences over exons 2 and 3 (including null alleles) with alleles that show synonymous mutations n this region.

• With these restrictions in place, match-probability calculations are no longer required.

Results: With these MMUD searches, a high number of donors can be found even for challenging searches when the number of allowed mismatches exceeds two (see figure 1), justifying our approach. Including donors with non-high resolution or incomplete typing would only result in extensive lists of search results, the majority of which would possess negligible matching probabilities.
This behavior can already be seen in standard mismatch searches in Hap-E Search which allow for match grades as low as 4/6 (A, B, DR), 6/8 (A, B, C, DR), and 8/10 (A, B, C, DR, DQ), including matching probability calculations without imposing resolution requirements on either donors or patients. For example, up to ~500,000 potential donors in an 8/10 search for a high resolution patient have been seen with very low (<1%) probabilities of achieving an 8/10 match.
We have evaluated our MMUD search approach on a cohort of one million donors, whose HLA typing distribution is representative for the WMDA donor pool. Our new MMUD search, down to a match grade of 5/10, was conducted for 184 challenging patient typings, for which standard mismatch searches (8/10) yielded no or only a very limited number of matching donors. Median search duration for all MMUD searches was one minute.



Conclusions: Rising global demand for MMUD transplantation increases the urgency for robust, scalable matching tools. Hap-E's new MMUD capability provides a practical, technically efficient new feature that, combined with the standard (mismatch) search, provides a comprehensive search result list focusing on clinically relevant results.

Disclosure: Nothing to declare.

P316

EVALUATING 2.5 YEARS OF OMOP IMPLEMENTATION IN THE EBMT REGISTRY: APPROACH, CHALLENGES AND OUTCOMES

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Background: In its transition to a new database, the EBMT has replaced the original relational database structure with the Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) for its analytical database.

Methods: In August 2023, the new EBMT Registry went live. The system is a successor to ProMISe, and a migration of legacy data was carried out. We evaluate the results of the implementation of OMOP CDM in the EBMT Registry based on the following criteria: 1) suitability of the available dictionaries for EBMT data collection, measured by the percentage of custom concepts, 2) suitability of the model for the EBMT Registry, assessed by experiences preparing data using OMOP, and 3) adoption by end-users, which could only be evaluated by feedback received from EBMT study unit staff and external database users.

Results: OMOP is a well-known and commonly used CDM, but it lacks haematology- and oncology-specific terminology. In the 2.5 years since go-live, the EBMT Registry team has mapped all data to the OMOP CDM and used it as a basis for exports. Out of 5012 mapped concepts, 48.5% are custom concepts, making our OMOP implementation substantially different from a more standard OMOP CDM. This difference, together with a lack of standardised definitions for key concepts, can impair the reproducibility of studies across different OMOP CDMs. Attending to the particularities of the EBMT Registry data, the Registry relies on: i) relationships between different questions to explain an event, ii) the capture of absence of events, and iii) the usage of longitudinal data; none of which are reflected by OMOP. On one hand, EBMT has tried to work around the absence of an event hierarchy in OMOP using the fact-relationship tables and visit occurrence details. On the other hand, capturing negatives is important for outcome analysis, as the absence of a positive response in the EBMT Registry does not necessarily mean an event did not happen. The only method to get longitudinal data from OMOP is by generating separate tables, which has been done by the Registry IT team. Finally, regarding the adoption by users, both internal and external users of the EBMT Registry, covering data managers, clinical data specialists, and statisticians across Europe and outside, are not responding positively to the OMOP implementation. They prefer a wide-format dataset with variables for studies and statistical analysis. Despite all the aforementioned drawbacks, the EBMT Registry IT team has managed to build a library of robust OMOP-based reports end users are satisfied with.

Conclusions: Although it is possible to work with the OMOP data model and adapt it to accommodate EBMT's needs, its usability and user-friendliness remain debatable. The EBMT has managed to build a repository of study-ready data based on OMOP information. Still, the time and expertise required for such transformations set a high entry barrier for adoption. Furthermore, the necessary adjustments to the model to ensure it adapts to different research needs lead to slight differences between organisations' OMOP models, complicating the model's data-sharing objective.

Disclosure: Nothing to declare

P317

HLA: A MICROSCOPIC MARVEL CREATING A MACROSCOPIC CHALLENGE IN HSCT DATA MANAGEMENT - UNDERSTANDING THE STRUGGLE AND THE CASE FOR AUTOMATION

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Background: HLA data is critical for HSCT outcomes, yet its complexity presents persistent and significant challenges for Data Management Staff (DMS) responsible for entering it into the EBMT Registry. Despite the EBMT HLA manual, released September 2024, HLA training remains inconsistent, and mismatch entry is particularly problematic. Discontinuation of the BSBMTCT Data Registry (BSBMTCT-DR) HLA data entry service in February 2025 further increased difficulties for UK and Republic of Ireland (UK&ROI) DMS. Due to HLA entry requirements of the EBMT Registry, the BSBMTCT-DR assessed DMS experience, confidence, consistency and completeness with HLA entry, and further examined barriers hindering accurate and complete entry.

Methods: A two-pronged approach was employed to assess HLA data entry by UK&ROI DMS:
1. Survey of DMS
An online survey was sent to 31 allograft centres in the UK&ROI targeting DMS responsible for HLA data entry. The survey assessed experience, confidence and barriers to consistent and accurate HLA data entry.
2. Registry HLA Data Analysis
EBMT provided an export of HLA typing and mismatch entry counts. Analysis focused on June 2024 to September 2025 (inclusive), covering the introduction of mismatch fields in the Registry and the last full month of data before export. Completeness of typing and mismatch data was assessed across all loci. Data migrated from ProMISe were excluded.

Results: Survey:
Twenty-two DMS from 20 centres participated. The majority of respondents were Data Managers (82%), others included Quality Managers and Data Coordinators. There was variable HLA data entry experience (32% of respondents ≥5 years, 23% <6 months). Before February 2025, 40% relied on BSBMTCT-DR for HLA entry. The HLA manual delivered clear benefit, boosting confidence for nearly a third of users for typing and mismatch entry. While 86% of respondents always entered HLA typing, only 73% consistently recorded mismatches. Barriers to HLA data entry included:

- HLA complexity and insufficient confidence
- Time-constraints
- Registry useability issues
- Perceived low priority
- Inconsistent access to pre-calculated mismatch data
- Difficulty in calculating mismatches

- HLA training deficiencies

Registry HLA Data Analysis:
EBMT export data highlighted that molecular HLA typing entries dominated per locus (2,077–2,428), while serology entries were minimal (20–81), particularly for donors.
Mismatch entries were far lower indicating incomplete data entry; 1,050-1,078 molecular entries per locus, 15-17 serology entries per locus. No single locus was systematically neglected.
Approximately 46% of fully typed molecular pairs had corresponding mismatch records, compared with 83% for serological typing.
Examining missing HLA data, 23% of allografts had no HLA typing and 47% had no mismatch data regardless of whether HLA typing had been entered.

Conclusions: HLA data entry, particularly mismatches, remains a major challenge for DMS due to complexity, workload, and insufficient training. While enhanced training, improved Registry usability, and wider adoption of the HLA manual can support accurate HLA data entry, manual entry is still inherently inefficient and error-prone. Automated solutions, like direct report uploads and autocalculation of mismatches, offer a more sustainable and reliable approach. Without automation, incomplete or inaccurate HLA data will persist compromising research quality and HSCT outcomes, now and in the future.

Disclosure: Nothing to declare.

P318

A STRONGER EUROPEAN VOICE TO SUPPORT GENE AND CELL THERAPIES: EUROGCT AS A COMMON TOOL

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Background: Gene and cell therapies (GCTs) face various communication and comprehension challenges when transitioning from bench to bedside. These challenges include complex science, regulation, and ethics, impacting clinical adoption and the GCTs sector. Moreover, the challenges are often exacerbated by misinformation and voices dominated by AI-mediated search platforms owned by tech giants.

Methods: The EuroGCT consortium was built through connecting 47 European partner organisations including academic institutions, learned societies, national centres of excellence, and patient organisations. Funded by the European Commission, the consortium has created a network of expertise and an online information hub that focusses on the pivotal role of science communication in navigating the complexities of therapy development and public comprehension. It is dedicated to demystifying GCTs as it extends beyond the

laboratory and enters the realms of broader societal impact.
We began from the position that digital spaces – particularly search engines like Google – create the backbone of the informational environments that inform non-expert interactions. Through targeted science communication initiatives, building and updating our information hub at www.eurogct.org, we explore the significance of engaging with diverse stakeholders, including patient advocacy groups, regulators, clinicians, developers, media, bioethicists, social scientists, artists, computer scientists, and the public at large. By fostering two-way dialogue and disseminating accessible information including explainers, factsheets, films, and educational material, we empower these stakeholders as they search for high quality referential information online. Through implementing self-developed, research-led search engine optimisation and metadata enhancements, we improve EuroGCT resources' visibility in search engines and generative AI searches.
By fostering engagement, promoting transparency, and advocating for collaborative resource development, EuroGCT endeavours to realise the full potential of these transformative treatments to improve health outcomes while contributing to a fair and equitable society.

Results: EuroGCT is a common information hub for pre-competitive, international and interdisciplinary collaboration to address pressing concerns faced by our research community as well as the patients and publics.
To empower the public and patient stakeholders to actively and effectively participate in shaping the trajectory of GCT development, we have developed accurate and accessible information explaining the science, the ethical and social impact in the Discover section of the hub.
To help stakeholders interested in developing GCTs navigate the complex pathways bringing therapies from lab to patients, the Research Pathways section facilitates their access to information on practical steps needed at each stage of product development.
Our results extend beyond the boundaries of public facing information to address key considerations in all stages of therapy development, such as regulatory frameworks, accessibility, and equitable access. Website traffic and search engine (including AI search) integration demonstrate EuroGCT's success in achieving its objectives.

Conclusions: The EuroGCT consortium's work underscores the critical importance of collective science communication in driving responsible and inclusive translation of gene and cell therapies beyond the laboratory through accessible information. EuroGCT's information hub is an established common tool for all European stakeholders.

Disclosure: The authors have no conflict of interest to declare.
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P319

PBMT DATA MANAGEMENT GROUP: BUILDING FOUNDATIONS AND FOSTERING NATIONAL COLLABORATION

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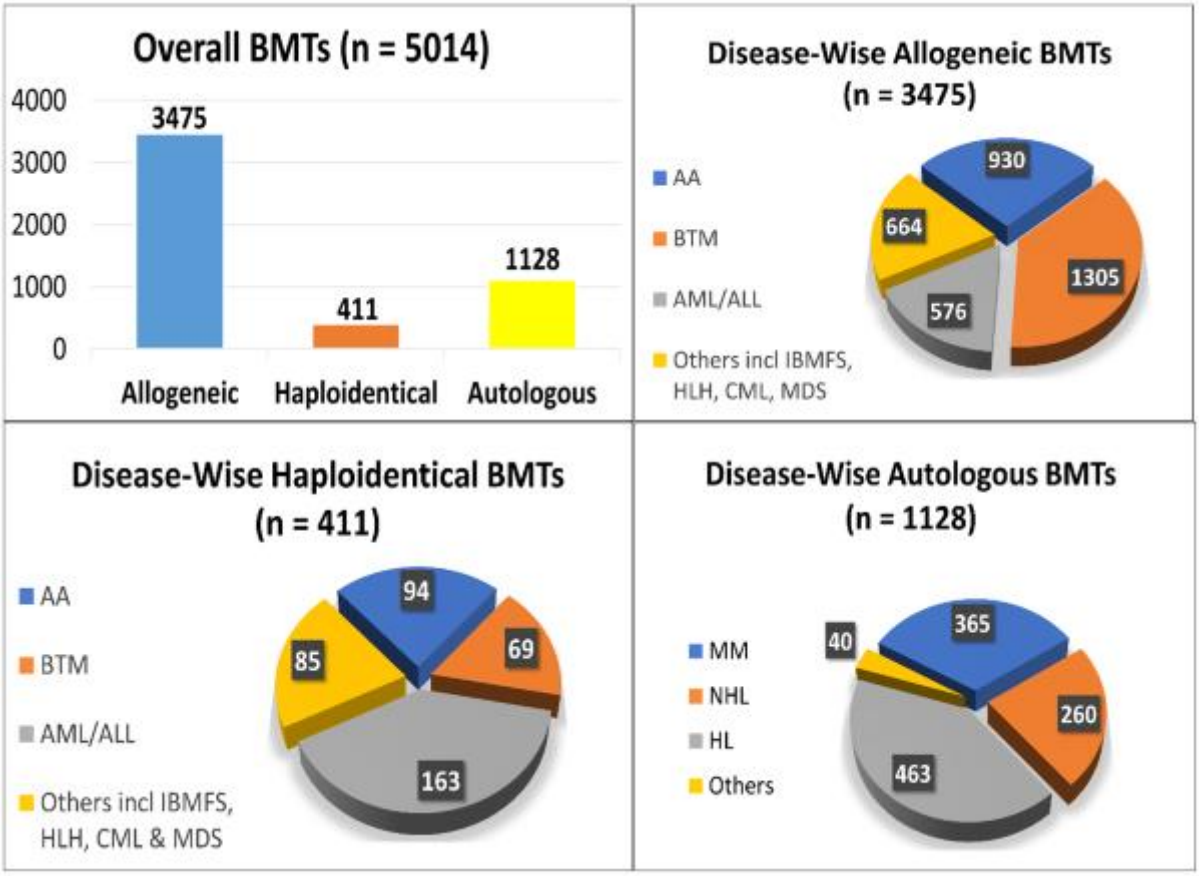
Background: Hematopoietic stem cell transplantation (HSCT) services in Pakistan have expanded rapidly, with multiple centers established between 1999 and 2024. To support this growth and ensure standardized national reporting, the Pakistan Blood & Marrow Transplant Group (PBMT) Data Management Group (DMG) was established as a central coordinating body for HSCT data governance and oversight. The PBMT is currently undergoing registration with the Islamabad Capital Territory Administration (ICTA), Government of Pakistan, under the applicable Societies Registration Act. Through coordinated efforts, the PBMT DMG has strengthened national collaboration in bone marrow transplantation, hematology-oncology, and emerging areas such as cellular and gene therapies, promoting research and evidence-based clinical practice.
The PBMT DMG has implemented a unified HSCT data collection framework across affiliated centers, aligned with international standards set by the CIBMTR and EBMT. To sustain national HSCT growth, there is a critical need to enhance capacity building, accelerate digital transformation, and further institutional collaboration. This study summarizes national HSCT activity, identifies existing gaps, and outlines outcome-driven DMG initiatives for 2024–2025, with particular emphasis on developing a comprehensive strategy for digitizing the national data center. A key milestone was the structured review of the 2024 national survey to improve alignment of local reporting with international registry requirements.

Methods: Annual survey data were collected from 14 PBMT-affiliated centers, capturing cumulative transplant numbers, transplant modalities (autologous, fully matched allogeneic, and haploidentical), and primary disease indications. National and international collaboration was assessed by documenting center participation in CIBMTR, EBMT, and WBMT activities.

Results: As of June 2025, a total of 5,014 HSCT procedures have been performed nationally. The highest transplant activity was reported by AFBMTC (n=1,849), followed by NIBD & BMT (n=803), SIH (n=594), AKU (n=559), and SKMCH&RC (n=428), with additional contributions from other centers. Allogeneic HSCTs constituted the majority of procedures, with beta thalassemia major, aplastic anemia, and acute leukemias (AML/ALL) being the most common indications. Detailed transplant-specific analyses are presented in Figure 1. National collaboration remains strong, with five centers contributing to CIBMTR, three to EBMT, and all 14 centers participating in WBMT reporting through the PBMT platform.



Conclusions: The PBMT Data Management Group has established a robust foundation for nationwide HSCT data collection and effective integration with the global transplant community. However, reliance on predominantly paper-based systems limits efficiency, data quality, and timely research output. Transitioning to a fully digital infrastructure is essential to maximize the value of national HSCT data. Adoption of REDCap is recommended as a scalable, secure, and internationally recognized platform to formalize the national data center and support the sustainable development of HSCT services in Pakistan.

Disclosure: Nothing to declare.

P321

THE STRATEGIC ROLE OF BRAZIL IN THE INTERNATIONAL SUPPLY OF STEM CELLS: THE CONTRIBUTION OF REDOME TO LATIN AMERICA AND THE WORLD

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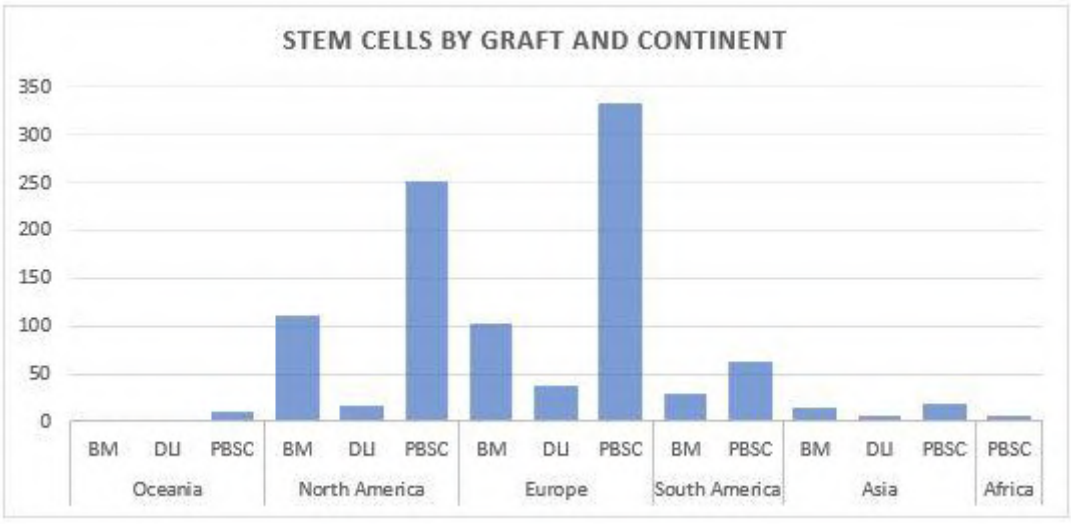
Background: Access to a diverse and extensive pool of unrelated hematopoietic stem cell donors is critical for successful allogeneic transplantation. While global collaboration is the cornerstone of donor searches, the geographic distribution of registries is marked by strong geographic asymmetry. Brazil hosts the third-largest bone marrow donor registry globally (REDOME), with over 6 million potential donors, establishing itself as the largest repository of genetic diversity in Latin America. This analysis aims to quantify Brazil's role in providing cellular products such as Bone Marrow (BM), Peripheral Blood Stem Cells (PBSC), and Lymphocytes for international transplantation, with a focused assessment of its strategic importance for Latin America, a region with limited national registry infrastructure.

Methods: We conducted a retrospective, observational study of all international requests for cellular products facilitated by Brazil's registry from January 2013 to December 2024. Data on product type (BM, PBSC, Lymphocytes), recipient location (by continent and country), and request outcomes were extracted from the REDOME database. The analysis included descriptive statistics that were used to analyze donation volumes, temporal trends, and geographic distribution of recipients.

Results:



Between 2013 and 2024, Brazil provided 999 cellular products for international transplantation. PBSC was the predominant graft source (68.2%, n=681), followed by BM (25.7%, n=257) and donor lymphocytes (6.1%, n=61; note: some donations may involve multiple products). Europe was the primary recipient continent (47.3%, n=473), followed by

North America (37.8%, n=378), South America (9.2%, n=92), Asia (3.7%, n=37), Oceania (1.2%, n=12), and Africa (0.7%, n=7). Within the Americas, a detailed analysis reveals that Latin American and Caribbean nations received 20% of all international Brazilian donations, underscoring a vital regional partnership. Notably, this support is channeled to a concentrated group of countries with formal donor registries: Argentina (leading recipient in the region), Chile, Uruguay, Paraguay, and Mexico. The remaining donations within the Americas were for the United States and Canada.

Conclusions:
This analysis solidifies Brazil's position as a foundation of the global donor registry network and the undisputed central pillar for hematopoietic stem cell provision in Latin America. The consistent, decade-long support for South American nations underscores a successful model of regional health cooperation showcasing REDOME's strategic impact on the international donation ecosystem. The significant potential for expanding these partnerships is evident. Strategic initiatives should include: 1) Formalizing and streamlining collaborative frameworks with registries in Argentina, Chile, Uruguay, Paraguay, and Mexico; 2) Developing shared logistical and financial mechanisms to further reduce access barriers; and 3) Leveraging Brazil's expertise to support the development of nascent registries in other Latin American and Caribbean countries. Strengthening this regional network is paramount to expanding equity in transplant access and building a more cellular therapy ecosystem more integrated, sustainable and self-sufficient in Latin America.

Disclosure: Nothing to declare

P322

STRENGTHENING NATIONAL TRANSPLANT INFRASTRUCTURE THROUGH INTERNATIONAL COLLABORATION: LESSONS FROM THE DKMS EXPERIENCE IN COLOMBIA

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Background: Access to unrelated stem cell transplantation in Latin America remains limited by regulatory, logistical, and infrastructural constraints. DKMS's operational experience in Chile, where it supported multiple transplant centers and helped strengthen donor-related workflows, provided strategic insights for shaping a collaborative model in Colombia. These insights guided the partnership with the Colombian Bone Marrow Donor Registry of IDCBIS "Dar Células" and national transplant centers to improve operational readiness, enhance knowledge transfer, and strengthen national transplant capabilities.
Objectives: To describe the operational context, early outcomes, and transferable practices arising from collaboration between DKMS, IDCBIS, and Colombian transplant centers.

Methods: Key challenges in the Colombian unrelated HSCT landscape were identified and addressed through the development of a complementary model between IDCBIS and DKMS Registry. Under this model IDCBIS led domestic donor recruitment and public outreach initiatives, while DKMS Registry provided centralized search coordination and product procurement. Transplant centers were supported through access to affordable high-resolution patient HLA typing, domestic and globally registered unrelated donors via Hap-E Search, and extensive training on search and request procedures aligned with WMDA standards. A bilingual working environment was adopted to enhance engagement and facilitate communication across teams. Early outcomes and outreach impact were analyzed using operational data (2022-2025) from donor search requests, match identification (global and IDCBIS donors), and product procurement and deliveries timelines.

Results: Prior to the collaboration, only one transplant center actively conducted unrelated donors and searches and performed transplants from this source. Following implementation, active participation increased to 13 transplant centers, indicating substantial national engagement. Standardized communication pathways, unified search workflows, structured criteria for assessing donor suitability, and a bilingual working language enhanced process consistency and faster case handling. Access to affordable high-resolution HLA typing and WMDA-aligned training further improved search quality. Colombia's cohesive hematology and oncology community also supported the rapid adoption of the hybrid search and request support program.
Between 2022 and 2025, IDCBIS registered more than 11,000 local donors successfully. In 2024, donor listing on Hap-E Search began, and 10,330 Colombian donors are currently accessible in the system, enhancing match options for Colombian patients, particularly those from ethnic minorities.. During the overall time period 449 unrelated donor searches were coordinated, resulting in 56 matched unrelated donor transplants, with cellular products collected through DKMS or partner registries.

Conclusions: Leveraging lessons from Chile and adapting them to Colombia's context has strengthened national transplant capacity and long-term sustainability. Expanding equitable access to stem cell transplantation in Latin America requires intentional knowledge transfer, structured cooperation, and strong partnerships with transplant centers. Every patient deserves access to unrelated HSCT, and collaboration is key to breaking down barriers. By supporting transplant centers in countries where unrelated donor transplantation in still emerging, DKMS helps expand access to life-saving therapies and brings hope closer to patients. The collaboration between an international operator and a local organization illustrates how internationally supported yet locally driven capacity building can enhance national transplant infrastructure and improve patient access across Latin America.

Disclosure: Nothing to declare.

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DETERMINANTS AND TRENDS IN UNRELATED ALLOGENEIC HSCT CANCELLATIONS: A 10-YEAR SINGLE-CENTER ANALYSIS

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Background: Cancellations of allogeneic hematopoietic stem cell transplantation (HSCT) remain a significant clinical and operational challenge, adversely affecting patient outcomes, donor engagement, and healthcare resource utilization. These challenges are particularly pronounced in unrelated voluntary donor settings, where donor availability, medical suitability, and logistical constraints critically determine whether a planned transplant proceeds. Although international donor registries, enhanced supportive care, and improved coordination networks have expanded access to transplantation, a substantial proportion of scheduled procedures remain uncompleted. Understanding the determinants of cancellations—especially donor-related factors—is essential for optimizing donor selection, enhancing patient management, and improving the robustness of transplant programs.

Methods: We conducted a retrospective analysis of 659 planned unrelated allogeneic HSCTs at a single donor center from February 2015 to mid-December 2025. 498 transplants were successfully completed, while 161 (24.4%) were cancelled. Cancellations were classified as patient-related, donor-related, or center/logistics-related. Donor-related cancellations were further subclassified into medical unsuitability, personal reasons, professional conflicts, pregnancy, travel abroad, and "graft-source mismatch" (donor offers peripheral blood cells instead of the requested bone marrow). COVID-19–related operational disruptions were included under center/logistics-related factors. Descriptive statistics quantified the distribution and temporal trends of cancellation determinants.

Results: Of the 161 cancellations, 70 (43.5%) were patient-related, 78 (48.4%) donor-related, and 13 (8.1%) center/logistics-related. Patient-related cancellations were primarily due to clinical deterioration: disease relapse happened in 9 cases (5.6%), rapid deterioration in 20 cases (12.4%), and pre-transplant mortality in 18 cases (11.2%). Three patients (1.9%) declined transplantation, and two patients (1.2%) achieved a response which made HSCT clinically unnecessary. Additionally, 18 procedures (11.2%) were cancelled following center decisions to proceed with alternative donors based on dynamic clinical reassessment. Donor-related cancellations were the most common category, slightly exceeding patient-related cancellations. Medical unsuitability accounted for 29 cases (18.0%), personal reasons for 26 cases (16.1%), and professional commitments for 12 cases (7.5%). Donor travel abroad contributed to four cancellations (2.5%), and four donors (2.5%) were willing to donate only peripheral blood, inconsistent with the transplant indication. Pregnancy occurred in three cases (1.9%). These findings underscore the multidimensional vulnerability of unrelated donor pathways, shaped by donor health, availability, personal commitments, and practical considerations.
Center- and logistics-related cancellations totaled 13 cases (8.1%). Eleven (6.8%) were attributable to collection-center delays, and two (1.2%) were due to COVID-19–related operational disruptions. Notably, six patients from the cancelled cohort received

haploidentical related donor transplants, illustrating the clinical utility of alternative donor strategies. Temporal trends indicated that donor-related cancellations were driven by health and personal factors, whereas patient-related cancellations consistently reflected disease progression and pre-transplant mortality throughout the decade.

Conclusions: Unrelated HSCT cancellations arise from a complex interplay of patient instability, donor limitations, and logistical inefficiencies. Donor-related factors represented the most frequent category, highlighting the importance of early donor evaluation, enhanced donor engagement, and systematic backup donor planning. Patient-related cancellations emphasize the need for optimized disease control and timely activation of transplantation. System-level barriers, including collection-center delays and pandemic-related disruptions, highlight opportunities for organizational improvement. Strengthening these domains will reduce preventable cancellations and enhance the efficiency of HSCT programs.

Disclosure: Nothing to declare

P324

MONITORING OF BKV DNAEMIA AND HEMORRHAGIC CYSTITIS AFTER ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Hemorrhagic cystitis (HC) is a frequent complication after allogeneic HCT. Irradiation, drug toxicity and polyomavirus BK (BKV) infection are the main causes of HC. The diagnosis of BKV-HC is based on the triad: detection of BKV reactivation, macroscopic hematuria and urinary symptoms. Currently, the management of BKV-HC is mainly based on the use of uroprotective medications and bladder irrigation, since available antivirals have not proven effective. BKV monitoring has not been recommended for a long time. However, recent data show an increase in HC, likely reflecting the rise in the use of PTCy, beyond haploidentical HCT. In this study, we revisit the characteristics of BKV-HC and BKV DNAemia, as well as their risk factors and impact on non-relapse mortality (NRM) and overall survival (OS).

Methods: Single-center, retrospective cohort study based on review of electronic medical records of allo-HCT recipients from 2020–2024. BKV DNAemia was monitored weekly by quantitative PCR. HC grade III and IV were considered severe. The cumulative incidences (CI) of BKV DNAemia and HC, and the variables associated with their occurrence were determined by Fine-Gray proportional hazard regression using the R software. Overall survival was estimated using the Kaplan-Meier method.

Results: 310 allo-HCT were included: 96 (30,9%) MRD, 145 (46,8%) haploidentical and 69 (22,3%) MUD. The median age was 31.6 (2-73) years, 24.8% of the patients (pts) were

children. During monitoring, 154 pts presented BKV DNAemia (CI=49.7%), at a median of 38 (3-423) days post-HCT. Median viral load at reactivation was 599 (599-27,715) copies/mL DNAemia lasted from less than 7 to 140 (median 35) days. Variables associated with BKV DNAemia were haploidentical or unrelated mismatch donor (mMUD). 113 (74%) patients were asymptomatic at DNAemia detection, 19 (12%) developed urinary symptoms before and 22 (14%) concurrently with DNAemia. BKV-HC was diagnosed in 27 patients for a CI of 8.7% (7% MUD, 8% MRD and haplo, 25% mMUD; p=0.23). No variable was associated with the occurrence of BKV-CH. The 2-year overall survival (OS) was 67.4%. Lower OS was observed in haploidentical (p=0.009), mMUD HCT (p=0.002), performance status ≤80% (p=0.015), and non-myeloablative/reduced intensity conditioning (p=0.03). Non relapse mortality (NRM) at 2 years was 20.4%, significantly higher in pts with NMA/RIC conditioning (p<0.0001) and severe BKV-HC (p=0.005). The positive and negative predictive values of DNAemia for the development of HC was 14.9% and 95.5%, respectively.

Conclusions: In this series, BKV-DNAemia was frequently detected in haploidentical and mMUD HCT. Although frequent, BKV-DNAemia did not precede symptoms of hemorrhagic cystitis. Most patients (74%) were asymptomatic, and some developed urinary symptoms before or concurrently with virus detection in the blood. Therefore, our data confirm that monitoring for BKV post-allo-HCT is irrelevant. The cumulative incidence of BKV hemorrhagic cystitis was 8.7%, and in severe cases, it affected NRM, without impacting OS.

Clinical Trial Registry: 79118724.4.0000.5434

Disclosure: Nothing to declare.

P325

IMPLEMENTATION OF THE BRAZILIAN SOCIETY OF CELLULAR THERAPY AND BONE MARROW TRANSPLANTATION EDUCATIONAL PLATFORM: PRELIMINARY RESULTS AND CHALLENGES

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Background: Continuous education is essential to sustain high-quality standards in hematopoietic cell transplantation (HCT) and advanced cellular therapy. To address the national need for structured, accessible, and standardized training, the Brazilian Society of Cellular Therapy and Bone Marrow Transplantation (SBTMO) developed a digital educational platform aimed at centralizing resources and supporting multidisciplinary capacity building across Brazil.

Methods: Beginning in November 2023, alignment meetings were conducted to define the target audience, access structure , and priority educational needs. The implementation process included planning, technical assessment, customization, and pilot testing to determine qualification criteria, functional requirements, and security standards for platform selection. Following proposal refinement in November 2024, the contract was approved in January 2025. Platform customization included visual identity development, user self-registration settings, standardized data fields, and certificate templates. In April 2025, pilot testing began with the migration of existing materials, starting with the Portuguese version of a Data Manager Manual, thus focusing on data management content as a foundation for broader educational expansionstandardized workflow for handling training-content requests was also introduced to organize and prioritize demands from the SBTMO community. Platform usage metrics were then descriptively analyzed to guide ongoing improvements.

Results: A total of 150 professionals from Brazilian transplant centers registered during the first year. Platform analytics recorded 369 cumulative accesses/views (57 in 30 days, 114 in 90 days, 146 in 180 days, and 152 in 365 days), demonstrating sustained engagement (Figure1). Key educational materials included three versions of the Data Manager Manual; the 5th edition of the Summary Slides of the Brazilian HCT and Cellular Therapy Registry (RBTCH-TC 2025), accessed by 45 institutions (22 downloads; 49% completion rate for automated certificate generation); and two video lectures on WBMT/LABMT data reporting (104 total enrolments, with completion rates still in progress). Preliminary feedback emphasized the relevance, clarity, and accessibility of the content. Identified challenges included regional disparities in internet connectivity, limited institutional time allocated for training, and the need for continuous content updating to reflect the rapid advances in cellular therapy and evolving data-quality standards. Addressing these challenges will be critical for scalability and long-term success; however, early findings indicate strong feasibility and the platform’s potential to improve national standardization and data management competency across Brazilian HCT programs.

Conclusions: The SBTMO educational platform represents a significant milestone in nationwide capacity building for HCT and cellular therapy in Brazil. Preliminary results demonstrate its feasibility, acceptance, and early impact on professional training and data-quality practices. Future developments will expand content beyond data management, reinforcing multidisciplinary education and promoting national standardization.

Disclosure: No conflicts of interest to declare

P326

BUILDING THE LOCAL EVIDENCE BASE: DEMOGRAPHIC PROFILE OF DLBCL PATIENTS IN WALES

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Background: Real-world data (RWD) are increasingly important for informing healthcare planning and supporting evidence-based decision-making. Understanding local patient demographics is particularly relevant in Diffuse Large B-Cell Lymphoma (DLBCL), where age is widely recognised as a key determinant of treatment eligibility and tolerance, with older adults remaining underrepresented in clinical trials. International datasets such as SEER (SEER-21, 2018-2022) report that approximately 50% of DLBCL patients are <65 years, 25% are 65–74, and 25% are ≥75 years at diagnosis. However, real-world local demographic data for Wales remain limited. Wales comprises seven Health Boards, with tertiary haemato-oncology and cellular therapy services centralised at Cardiff and Vale University Health Board (CVUHB) for six of these seven, equating to ~80% of the Welsh population.
By characterising the demographic profile of patients diagnosed with DLBCL at CVUHB, this study provides a foundation for reliable local RWD and intelligence to support service planning. The final aim is to expand analyses to an all-Wales dataset.

Methods: This retrospective observational study included all CVUHB residents diagnosed with DLBCL between 1 January 2015 and 31 December 2023. Cases were identified using ICD-10 code C83.3, with patient lists obtained from central databases including Digital Health and Care Wales (DHCW) and Cancer Network Information System Cymru (CaNISC). Coded data were validated, anomalies and discrepancies removed, and diagnoses confirmed using Welsh Clinical Portal (WCP). Demographic data were extracted from WCP, Cardiff and Vale Clinical Portal, and ChemoCare Electronic Chemotherapy Prescribing System. Variables included age, sex, patient residence at diagnosis and year of diagnosis. Descriptive analyses were performed to identify trends in age and sex distribution over time.

Results: Table 1: Annual age-specific case numbers from 2015 to 2023

Years	0-64 (n)	65-74 (n)	75+ (n)	All ages (n)
2015	6	8	20	34
2016	7	13	11	31
2017	8	12	10	30
2018	13	11	13	37
2019	10	9	14	33
2020	5	13	7	25
2021	12	5	7	24
2022	6	11	8	25
2023	13	5	13	31
TOTAL n (%)	80 (30%)	87 (32%)	103 (38%)	270 (100%)

A total of 270 people were identified, with a median age of 71 years (range 21–93). Overall age distribution was 30% <65 years, 32% 65–74 years, and 38% ≥75 years. Fifty-six per cent of patients were male, with sex distribution consistent over the nine-year period. Previous studies suggest that male patients with DLBCL may have slightly worse survival than females, highlighting the clinical relevance of this distribution. Table 1 shows yearly variation in age distribution, with fewer case numbers during 2020–2022, likely reflecting COVID-19–related impacts on diagnosis and healthcare access.

Conclusions: DLBCL patients in Wales were diagnosed at an older age than the US SEER dataset, with a median age of 71 compared to 66 and with 38% aged ≥75 years versus ~25%, respectively, suggesting a larger proportion may be ineligible for intensive therapies. Real-world demographic data are essential for understanding local populations, anticipating treatment needs, guiding treatment planning, and informing resource allocation. Characterising these demographics supports data-driven decision-making, highlights unmet needs, and underpins development of tailored protocols for older or high-risk patients.

Disclosure: Nothing to declare

P327

LEVERAGING MACHINE LEARNING TO PREDICT POST-TRANSPLANT COMPLICATIONS IN ALLOGENEIC HSCT

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Background: Allogeneic hematopoietic stem cell transplantation (Allo-HSCT) is a potentially curative therapy for hematologic malignancies. Despite its effectiveness, patients remain at risk for serious post-transplant complications, including non-relapse mortality (NRM), relapse, graft rejection, acute graft-versus-host disease (aGvHD), and chronic GvHD (cGvHD). Accurate early prediction of these outcomes can support clinical decision-making and improve long-term outcomes.
Objectives: To develop and evaluate machine learning models for predicting the probability of NRM, relapse, rejection, aGvHD, and cGvHD within one-year post-Allo-HSCT.

Methods: We used pre-transplant clinical data from 16,427 French adult patients who received Allo-HSCT for malignant hematologic diseases between 2013 and 2023, recorded in the European Society for Blood and Marrow Transplantation (EBMT) registry. Following a systematic literature review, six machine learning algorithms were selected: logistic regression, decision tree, random forest, XGBoost, elastic net, and a stacking ensemble model. Predictive variables were chosen based on both clinical relevance and literature evidence. Model performance was evaluated using the Area Under the Receiver Operating Characteristic Curve (AUC) and accuracy. SHapley Additive exPlanations (SHAP) were used to interpret model predictions and identify key variables influencing each outcome.

Results: Of the 16,427 patients included, 59% were male. Patients aged ≥55 years represented 52% of the cohort; 28% were aged 40–55, and 20% were under 40. The most frequent diagnosis was acute leukemia (58.4%), followed by myelodysplastic syndromes (13.2%), lymphoma (11.8%), and myeloproliferative disorders (7.0%). One-year post-transplant outcomes were as follows: NRM occurred in 25.0% of patients, relapse in 19.0%, rejection in 7.8%, aGvHD in 60.0%, and cGvHD in 38.9%. Among tested models, the stacking ensemble showed the best overall performance in terms of AUC and accuracy across most outcomes, except for cGvHD.

- For rejection, the most influential predictors were treatment period, HLA matching, performance status, and conditioning regimen.
- For relapse, treatment period, Disease Risk Index (DRI), conditioning regimen, and Thiotepa based conditioning were key variables.
- For aGvHD, treatment period, donor type, and HLA matching ranked highest.
- For cGvHD, main predictors included treatment period, performance status, Thiotepa based conditioning, CMV match, and HLA matching.
- For NRM, top predictors were patient age, Thiotepa based conditioning, and treatment period.

Conclusions: Machine learning models, particularly ensemble approaches, demonstrated strong predictive performance and could serve as valuable tools to support clinical decision-making in the management of Allo-HSCT patients. The predictive performance of the stacking ensemble model was superior to that of the logistic regression model alone. These findings highlight the potential of data-driven approaches to improve individualized risk stratification and post-transplant care.

Disclosure: Nothing to declare.

Health Economics and Technology Assessment

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TEN YEARS OF POST-ALLOGENEIC HSCT HEALTHCARE UTILIZATION IN FRANCE: A NATIONWIDE POPULATION-BASED STUDY (2013–2023)

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) remains the treatment of choice for many malignant and non-malignant hematologic disorders. However, the post-transplant period is often marked by intensive and specialized healthcare needs, which remain insufficiently described and poorly quantified.
Objective: To describe the patterns and evolution of healthcare resource utilization in adult patients during the post-allogeneic HSCT period between 2013 and 2023, using French national health insurance claims data (SNDS), with a minimum follow-up of one-year post-transplant.

Methods: We conducted a retrospective, population-based cohort study including all adults who underwent allogeneic HSCT in France from 2013 to 2023. Data were extracted from the French National Health Data System (SNDS), covering sociodemographic and clinical characteristics, inpatient care and outpatient care.

Results: A total of 17,203 patients were included, with males representing 52% of the cohort. Regarding age distribution, 38% were over 59 years, 51% were between 30 and 59 years, and 11% were under 30. The most frequent indication for HSCT was acute myeloid leukemia (38.4%), followed by acute lymphoblastic leukemia (10.5%). At the end of the study period, 60% of patients were alive. The use of outpatient clinic (OC) visits peaked during the first six months post-transplantation, totaling 183,253 visits, and remained stable across the study period. More than half of clinical follow-up and rehabilitation hospitalizations

also occurred within the first six months, a consistent trend over time. A similar distribution was observed for hospitalizations involving intensive care, 57% of which occurred within the first year.
Over time, care utilization patterns evolved, with a marked decline in early mortality: among patients transplanted in 2013, 18% died within six months compared with 13% in 2023. The number of OC visits decreased progressively, reaching 16,357 in year 5. Conversely, the median duration of clinical follow-up and rehabilitation hospitalizations during the first year increased from 13 days in 2013 to 29 days in 2023. Hospitalizations involving intensive care maintained a stable median length of stay throughout the study period.
Beyond hospital care, community-based care played a key role. General practitioner visits represented the majority of consultations and showed steady growth over time. The most frequently consulted specialties were hematology and ophthalmology. Physiotherapy sessions increased by 30% between 2013 and 2023

Conclusions: Our results show a steady increase in post-transplant healthcare needs over the past decade, particularly in rehabilitation services. This study provides a comprehensive overview of post-HSCT healthcare utilization and its evolution over time, which is essential for assessing healthcare provision and adapting to evolving clinical practices. This is a preparatory analysis before matching the current cohort data with data for the same patients from the EBMT registry.

Disclosure: Nothing to declare.

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M-CSF–STIMULATED ALVEOLAR MACROPHAGES SAFEGUARD FROM INVASIVE ASPERGILLOSIS

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Background: Invasive pulmonary aspergillosis poses a life-threatening complication in immunocompromised individuals, including recipients of allogeneic hematopoietic cell transplantation (allo-HCT). By contrast, immunocompetent individuals are usually protected against infection with *Aspergillus fumigatus,* the causative agent of aspergillosis. The mechanisms underlying pulmonary innate immune protection remain poorly understood.

Methods:

We employed super-resolution and dynamic confocal microscopy to investigate the impact of cytokines—primarily M-CSF and IL-34—on the phenotype and migratory behavior of primary alveolar macrophages (AMs) in vitro. In addition, we performed functional in vitro assays to assess AM phagocytic activity.

To evaluate the effects of exogenous cytokine stimulation on the pulmonary immune response in vivo, we used mouse models of allo-HCT (8 Gy total body irradiation, C57BL/6 → BALB/c) and invasive intratracheal *A. fumigatus* infection. Mouse survival and clinical performance were monitored, and local host–pathogen interactions were analyzed using flow cytometry and three-dimensional light-sheet fluorescence microscopy.

Results:

We identified alveolar macrophages (AMs) as key players in pulmonary antifungal defense. In immunocompromised mice, AMs conferred protection against lethal invasive aspergillosis by day 6, but not by day 4, post–allo-HCT. AMs exhibited the highest frequency, proliferation, and phagocytic activity in the lung compared with neutrophils and monocytes, suggesting that tissue-resident AMs are primarily responsible for protecting mice from *A. fumigatus* infection. This observation was confirmed by selective AM depletion, which rendered mice susceptible to uncontrolled infection.

To enhance AM function at the earlier time point, we tested cytokine-based interventions and found that M-CSF—but not IL-34—both of which bind the CSF-1 receptor, promoted greater migratory activity (0.52 vs. 0.30 µm/min, respectively), increased versatility (diffusion coefficient of 0.78 vs. 0.60 µm²/min, respectively), enhanced phagolysosomal function, and improved fungal killing in murine tissue-resident AMs. Notably, similar results were observed in human primary tissue-resident AMs.

In allo-HCT recipient mice, M-CSF locally expanded tissue-resident AMs by 1.5-fold. Furthermore, M-CSF enhanced AM killing capacity and protected 90% of HCT recipients from lethal *A. fumigatus* infection on day 4 post-HCT. This M-CSF–mediated protective effect was abrogated by AM depletion. Moreover, M-CSF treatment preserved lung tissue integrity and reduced serum levels of pro-inflammatory cytokines.

Conclusions: Our findings demonstrate a critical role of tissue-resident AMs in pulmonary antifungal immunity and suggest that therapeutic modulation of AM activity via M-CSF may offer a promising strategy to combat severe fungal infections in immunocompromised patients.

Disclosure: Nothing to declare.

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THE USE OF EFFICIENCY ANALYSIS TO EVALUATE UNRELATED BONE MARROW DONOR REGISTRIES

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Background: Hematopoietic stem cell (HSC) transplantation is a standard treatment for malignant and non-malignant blood diseases, and selecting a matched donor is essential to achieving good results. To increase the probability of eligible donors, unrelated donor registries were created worldwide. In 2025, around 45 million donors were distributed among registries of 57 countries. The high cost of adding donors and the expenses associated with donor procurement are the main challenges for registries, impacting public and private health systems. The Brazilian Bone Marrow Donors Registry (REDOME) was created in 1993, and it is the only registry of bone marrow donors in the country, maintained exclusively by public resources.
This project has the primary objective of examining and evaluating the efficiency of REDOME compared to other bone marrow donor registries on a global scale, and analyzing its role in this context.

Methods: Using data collected by WMDA in 2022 (Global Trend Reports) and public registries' reports with financial data, production indexes, and an efficiency scale, an efficiency scale was created using Data Envelopment Analysis (DEA). DEA is a non-parametric linear programming technique used to evaluate the relative efficiency and productivity of a set of comparable entities, often called Decision-Making Units (DMUs). This strategy analyzes the efficiency of organizations based on inputs and outputs. To compare registries, the selected inputs were the total of voluntary donors registered on 01/01/2022 and the expenses of the registries. The selected outputs were new donors registered in 2022, HSC collected from national patients, and HSC collected from international patients.

Results: Considering the total number of hematopoietic progenitor cell (HPC) products obtained from REDOME for national and international patients (425 and 77, respectively), REDOME ranks 11th and 18th, respectively. However, the number of cell products collected relative to the number of samples requested for confirmatory typing indicates that REDOME is only in position 66 among 70 analyzed registries, suggesting inefficiency throughout the process. The DEA analysis was performed using data from 18 registries, and the efficiency score indicated that REDOME presented an intermediate score (0,89), confirming the inefficiency of operational processes (Table 1). The most efficient organizations include the two largest registries - NMDP-National Marrow Donor Program (USA) and DKMS Registry gGmbH (Germany) – but also more minor, well-established registries, like Anthony Nolan,

DKMS Chile, Tobias Registry, indicating that the number of donors is not associated with the efficiency itself.

DMU	DEA Score	DMU	DEA Score
NMDP - National Marrow Donor Program (USA)	1	Tobias Registry (Sweden)	1
DKMS Registry gGmbH (Germany)	1	Verein Geben für Leben (Austria)	1
Anthony Nolan (UK)	1	National Bone Marrow Donors Registry named after Vasya Perevoshchikov (Russia)	1
Registro de Donantes de Médula Ósea (REDMO - Spain)	1	Austrian Bone Marrow Donor Registry	0,964787
Fundacja DKMS (Poland)	1	National Registry of Hematopoietic Stem Cells Voluntary Donors	0,907484
Matchis Foundation (Netherlands)	1	REDOME - Registro Brasileiro de Doadores Voluntarios de Medula Ossea	**0,890617**
DKMS United Kingdom	1	Gift of Life Marrow Registry (USA)	0,830797
Australian Bone Marrow Donor Registry	1	Singapore BMDP	0,676276
Fundación de Beneficencia Pública DKMS (Chile)	1	DKMS United States of America	0,243936

"Table 1: DEA Analysis for 18 registries. Results equal to 1 indicate the highest level of efficiency."

Conclusions: The complexity and the high costs associated with unrelated donor registry activities make efficiency analysis a priority for these organizations. The use of specific strategies can highlight opportunities for improvement, and the DEA created an "efficient frontier" among 18 registries, stimulating benchmarking among the registries. The REDOME results indicate the need to identify and seek best practices. These data can support decision-making, strengthen registries, and enhance international cooperation, thereby improving outcomes for patients who need a HSC transplantation.

Disclosure: Nothing to declare.

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CAR-T COST CONSTRAINTS IN GERMANY: BUDGET IMPACT, PATIENT ACCESS, AND EASYGEN'S POTENTIAL FOR COST-DRIVEN INNOVATION

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Background: CAR-T cell therapies provide transformative outcomes for patients with hematologic malignancies and are increasingly explored for severe autoimmune diseases. However, high upfront costs raise concerns regarding long-term affordability for healthcare systems. Transparent estimates of current and future budget impact are needed to guide innovation aimed at cost reduction.

Methods: Within the EU-funded EASYGEN project, Germany served as the initial case study. We quantified the share of German healthcare expenditures attributable to CAR-T therapies in 2024 and modelled a 10-year scenario reflecting growth in hematologic indications and potential expansion to autoimmune diseases, illustrating the need for cost-reducing innovation and the role of the EU EASYGEN public–private partnership. Inputs included German 2024 macro-expenditure data and CAR-T activity figures: total healthcare spending €538 billion[1]; ~1,068[2,3] patients treated with CAR-T; and an average hematologic CAR-T product price of €291,674 (products only[4]) plus an estimated ~15% additional treatment-related costs (apheresis, conditioning chemotherapy, CAR-T infusion, hospital stay, and post-treatment monitoring[5]), totaling €338,000 per patient. For autoimmune indications, only product costs (€291,674) were applied. According to a recent IQVIA report[6], only 17% of eligible patients in Germany currently receive CAR-T driven not only by tmanufacturing constraints. But also by limited referral pathways, center capacity, and system-level readiness challenges.
We developed a simplified 10-year projection with the following assumptions: (a) minimum hematologic scenario: 1,068 patients in 2024, increasing by 15% annually to ~4,321 patients in 2034; (b) maximum epidemiology-driven scenario: assuming an annual demographic growth rate of 0.2%[7] ; (c) autoimmune expansion (minimum case): by year 10, autoimmune CAR-T patients equal the minimum hematologic case (4,321), calculated using product-only costs; (d) constant real prices; and (e) healthcare expenditures growing at 3% annually. Economies of scale were not applied, as autologous cell therapies are inherently individualized and do not benefit from conventional bioprocess scaling efficiencies[8].

Results: In 2024, CAR-T expenditures were €361 million (1,068 × €338,000), representing 0.067% of total German healthcare spending. Over 10 years, hematologic CAR-T use increases to 4,321–6,409 patients (1,068 patients in 2024, rising to ~6,409 by 2034), depending on uptake assumptions. Assigning an equal number of autoimmune CAR-T patients in the minimum expansion scenario, total CAR-T use in 2034 reaches 8,642–10,730 patients. Corresponding annual expenditures range from €2.7 to €3.4 billion, with hematologic indications accounting for €1.5–2.2 billion and autoimmune indications for approximately €1.3 billion. With total healthcare spending projected to reach ~€723 billion, CAR-T therapies represent ~0.38–0.47% of total expenditures, corresponding to a 7.5–9.5-fold increase in absolute spending and a ~5.6–7.0-fold increase in budget share compared with 2024.

Conclusions: Although CAR-T therapies currently account for a small fraction of German healthcare expenditures, projected clinical expansion implies a substantial future budget impact. This underscores the need for innovation in manufacturing, logistics, and cost-efficient delivery to enable sustainable access. The EASYGEN consortium is strategically positioned to support such innovation by standardizing CAR-T processes, reducing per-patient costs, and facilitating scalable access across oncology and autoimmune indications.

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The authors declare no conflicts of interest.

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THE ECONOMIC BENEFIT FOR PATIENTS AND CAREGIVERS OF EXPANDING CAR-T CENTRES IN SPAIN

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Background: Travel to a qualified hospital to receive advanced therapies represents a significant financial burden for patients diagnosed with hematological cancer and their caregivers. This study aims to quantify the direct non-healthcare cost savings experienced by patients and their caregivers as a result of enhanced geographical accessibility to CAR-T cell therapies.

Methods: A geoeconomic model was developed to simulate the territorial distribution of hospitals and patients' home location and caregivers to estimate the travel costs in two scenarios: CAR T management and administration in 29 hospitals (current situation) vs. hypothetical expansion of CAR T access to all 65 hospitals that currently perform autologous stem cell transplants in Spain. Distribution was carried out based on the nearest available treatment center within each region, where possible. A cohort of 3,094 patients with potential indication for CAR T-cell therapy was constructed based on clinical and epidemiological data. Geographic data (latitude and longitude) were used to measure the distance between the hospital and the patient's home location. The distribution of the Spanish population was assumed to represent the patients' addresses. Patients were distributed according to the frequency of use of different means of transport, distinguishing between urban and rural areas. The costs included public and private transportation, accommodation and meals, all derived from public rates. The results were obtained by comparing the distances from the patients' home location to the nearest hospital in each of the scenarios and applying the costs associated with traveling.

Results: The hypothetical expansion of CAR T access from 29 to 65 hospitals was associated with a 76% reduction in the total cost for the entire cohort of patients and caregivers (from €2,218,460 to €535,283). The average cost per patient in the 29-hospital scenario was €717 compared to €173 in 65-hospital scenario, generating a potential saving of €544 per patient. The difference between the 29 and 65 hospitals scenarios in the cost of accommodation was −€1,305,063, followed by the cost of meals (-€300,207) and transportation (−€77,907). The hypothetical expansion of centres reduced the percentage of patients and caregivers requiring accommodation by 14% (18% vs 4%).

Conclusions: Hypothetical expansion of authorised CAR-T centres in Spain reduced the financial burden on patients and caregivers, especially in regions with lower hospital coverage. These potential savings could improve equity of access and represent an opportunity to optimise the efficiency of the healthcare system in the implementation of advanced therapies.

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Raimundo García Boyero has participated in a speakers’ bureau for Abbvie, has provided consulting or advisory role by Gilead and had traveled accommodations or other expenses by Abbvie, Servier and Roche.
Dunia Miguel Llorente: Nothing to declare
Teresa Olave Rubio: has participated in a speakers’ bureau for J&J, Roche, BeOne, AstraZeneca, Jazz, and Abbie; has provided consulting or advisory role by J&J, Roche, BeOne, AstraZeneca, Jazz, and Abbie and had traveled accommodations or other expenses by BeOne, AstraZeneca, Jazz, and Abbie.
Raquel Domínguez-Hernández is employee of PORIB and received fees for their consultancy services in relation to the development of this work.
Carlos Pardo: currently employed at Gilead Sciences, Spain
Victoria Martín-Escudero: currently employed at Gilead Sciences, Spain
Ana Margarita Redondo Izal: Nothing to declare

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ANALYSIS AND OPTIMIZATION POTENTIALS OF CURRENT CAR-T CELL THERAPY MANAGEMENT: A PROCESS MANAGEMENT PERSPECTIVE

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Background: Cell and gene therapies are among the most expensive therapies within the healthcare sector. Systematic reviews of economic evaluations of CAR-T therapies for cancer treatment show that CAR-T therapies tend to be more costly, but also more effective than their comparator treatments. As their use increases and large numbers of new advanced cell therapies are developed, the CAR-T therapy management process needs to be optimized in order to reduce the diagnosis to treatment time (turnaround process). This reduces therapy manufacturing time and associated costs, facilitating better access for patients.

Methods: We conduct eleven semi-structured expert interviews with clinicians, pharmacists, nurses, and coordinators with a CAR-T cell background from Germany, Ireland and Spain. Based on the interview results, we map the CAR-T cell therapy process using Business Process Model and Notation (BPMN) and identify the optimization potentials.

Results: Based on the interviews, we map the entire CAR-T cell therapy process and derive 12 challenges with potential for optimization:

1. Indication - deciding on the right cancer therapy regimen for the individual patient
2. High response rate vs. low long-term remission rate of CAR-T therapies
3. Adverse events - resulting in a revolving door effect between outpatient care and hospitalization in the CAR-T center
4. Poor patient health before or after apheresis
5. Patient access – e.g. due to limited number of CAR-T cell centers patients must travel great distances to receive treatment and be monitored
6. High drug manufacturing cost due to centralized manufacturing and long production time
7. No standardization in terms of contracting between CAR-T manufacturing partners
8. High variety of CAR-T product specifications (different premedication, thawing procedures, treatment of side effects) requires extensive training and process management
9. Highly complex process management including logistics and coordination due to multi-stakeholder involvement
10. High staff workload due to continuous neurological testing
11. Limited number of beds at CAR-T and local centers - increased availability required for the expected scaling of CAR-T therapies
12. Complex regulation on regional, national and European levels

Conclusions: The presented findings lay important groundwork for the definition of an optimized CAR-T cell therapy management process. The project EASYGEN aims to enable an automated, modular manufacturing platform for CAR-T cell production at the point-of-care and thereby reduce treatment cost by 50%, reduce manufacturing time significantly, broaden eligibility for new European patient groups and enable seamless integration of CAR-T cell manufacturing into routine hospital workflows.

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FEASIBILITY OF SYSMEX XN-1000 HEMATOPOIETIC PROGENITOR CELL COUNTS FOR REAL-TIME MONITORING OF ALLOGENEIC STEM CELL COLLECTION

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Background: Background: In allogeneic hematopoietic stem cell (HSPC) collection, the optimal CD34 dose is 6-8 x106/kg, real time monitoring of CD34+ cell yield is critical to avoid excessive collection, which can result in unnecessary splitting and cryopreservation of surplus products. Flow cytometry is the gold standard for CD34+ enumeration, but its turnaround time of at least 45 minutes delays decision-making, during which additional CD34+ cells continue to be collected. The Sysmex XN-1000 provides a rapid, automated hematopoietic progenitor cell (HPC) count that could serve as a surrogate for real-time monitoring. This study aimed to assess the feasibility of using Sysmex XN-1000 HPC counts to estimate the collected CD34+ dose in midway apheresis samples, compared to flow cytometry.

Methods: Forty-two midway apheresis samples from allogeneic HSPC donors were analyzed concurrently using the Sysmex XN-1000 for HPC counts and FACS Canto-II flow cytometry for CD34+ enumeration. Correlation between the two methods was evaluated using Pearson and Spearman coefficients. Agreement was assessed by Bland-Altman analysis.

Results: Sysmex HPC counts showed a moderate positive correlation with flow cytometry CD34+ counts (Pearson $r = 0.612$, $p < 0.001$). Bland-Altman analysis demonstrated a mean bias of +74.2, with wide 95% limits of agreement (-1033 to +1181), indicating that the two methods are not directly interchangeable.

Conclusions: The Sysmex XN-1000 HPC count offers a rapid and practical screening tool for real-time monitoring of HSPC collections, enabling earlier estimation of the collected CD34+ dose compared to flow cytometry. This may help prevent over-collection and reduce the need for splitting and cryopreservation of surplus stem cell doses. However, due to proportional bias and wide limits of agreement, Sysmex XN-1000 could either overestimate or underestimate the $CD34^+$ cell count by a clinically significant margin. Such discrepancies may lead to premature termination or unnecessary prolongation of apheresis, resulting in either insufficient stem cell collection requiring an additional apheresis session—thus exposing the donor to extra procedural risks—or overcollection necessitating further product processing and cryopreservation. Therefore, confirmatory flow cytometry remains necessary for final clinical decision-making.

Clinical Trial Registry: Not applicable

Disclosure: I have no conflict of interest to declare.

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MEASUREMENT OF COST IN A VALUE-BASED PERSPECTIVE: COMPARATIVE ANALYSIS OF ONLINE AND OFFLINE EXTRACORPOREAL PHOTOPHERESIS (ECP) MODALITIES IN SPAIN

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Background: Extracorporeal photopheresis (ECP) is an established immunomodulatory therapy for conditions such as cutaneous T-cell lymphoma, graft-versus-host disease (GVHD), and organ transplant rejection. ECP can be delivered via two modalities: offline (multi-stage) and online (integrated). Understanding the resource utilization and cost implications of each modality is essential for optimizing healthcare delivery.

Methods: An independent assessment was conducted at University Hospital Virgen de la Arrixaca (Murcia, Spain) using Time-Driven Activity-Based Costing (TDABC) methodology. Twenty ECP procedures (10 online, 10 offline) were mapped and analyzed for resource consumption, staff time, and direct costs. Patient experience was also assessed via questionnaire.

Results:

- Procedure Time: Online ECP sessions were significantly shorter, averaging 76 minutes less than offline (218.9 vs. 295.0 minutes; $p < 0.001$). The largest time savings were observed in the treatment phase, with offline procedures requiring 88% more time.
- Cost Analysis: The mean total cost per session was €2,053.5 for online and €2,157.8 for offline ECP, a modest difference that did not reach statistical significance (p =

0.191). Personnel costs were significantly higher for offline procedures (€167.5 vs. €114.5; p = 0.035), driven by increased nursing time. Consumable costs were higher for online ECP, while indirect costs (facilities, equipment) were higher for offline.
- Patient Experience: Patients reported high satisfaction with both modalities, with no significant differences in perceived comfort, staff competence, or self-reported health status. Transportation and hospital waiting times were identified as the main burdens.

Conclusions: Online (integrated) ECP offers substantial operational advantages, with significantly reduced procedure times and lower personnel costs, though total cost differences are modest and context-dependent, they are slightly in favor of Online (integrated) ECP. The findings support the adoption of integrated ECP systems in high-volume centers seeking efficiency gains, but highlight the need for granular local cost structure analysis. Patient satisfaction remains high regardless of modality. Future research should incorporate larger samples, clinical outcomes, and broader societal costs to inform comprehensive value assessments between different ECP modalities.

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Quality Management and JACIE

QM1-4

A WORKFLOW-INTEGRATED DIGITAL PLATFORM FOR PROCEDURE PLANNING AND REAL-TIME CAPTURE OF JACIE-REQUIRED KPIS IN APHERESIS UNITS AND CELL THERAPY PROCESSING AND CRYOPRESERVATION LABORATORIES

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Background: Joint Accreditation Committee ISCT-Europe & EBMT (JACIE)-certified centers must report an increasing number of key performance indicators (KPIs) to meet accreditation and quality requirements. In many centers, these metrics are not consistently captured through standardized, workflow-integrated data entry and are instead recorded across multiple data sources, leading to duplicate documentation and manual data compilation for KPI reporting.

Methods: Accordingly, from October 2024 to July 2025, a process improvement project was conducted in the Hematology Service of Ramón y Cajal University Hospital, applying the Lean Six Sigma DMAIC (Define–Measure–Analyze–Improve–Control) framework. Workflows in the Apheresis Unit and the Cell Therapy Processing and Cryopreservation Laboratory were mapped and analyzed to characterize process steps, roles, handovers, information flows, and activity volumes. Based on this assessment, functional requirements were defined for the development of a digital platform within the hospital's institutional digital environment. The solution was designed to (i) align real-time capture of JACIE-required KPIs with operational workflows through standardized electronic forms and (ii) provide a unified workspace for planning and scheduling, structured data entry, and real-time operational monitoring, enabling end-to-end traceability of all procedures.

Results: The platform was deployed in August 2025, providing web and mobile access with real-time procedure status updates. It is embedded in routine practice with 22 direct and 15 indirect users, including physicians, nurses, and laboratory technicians. Since deployment, the platform has supported monthly planning and coordination of more than 100 procedures for more than 80 patients. Core functionalities include (i) a color-coded operational calendar displaying procedures by day, type, and status, enabling monitoring of occupancy rates and workload distribution; (ii) workflow-embedded standardized documentation to ensure end-to-end traceability; (iii) real-time capture of JACIE-required KPIs; (iv) an integrated calculator estimating donor blood volume for hematopoietic progenitor cell collections based on donor/recipient parameters and target cellular dose; and (v) automated, exportable reports providing audit-ready KPI summaries and real-time performance monitoring. The platform manages a broad procedure portfolio, including leukapheresis, lymphocytapheresis, extracorporeal photopheresis, and cellular therapy product infusions. Standardized data capture has generated a structured database supporting analyses of patient cohorts, procedural performance, and resource utilization, informing ongoing protocol optimization and evidence-based capacity planning.

Conclusions: Lean Six Sigma provides a robust framework to redesign complex clinical workflows and embed quality management into routine operations. In this project, DMAIC enabled integration of JACIE requirements into daily practice through a unified digital platform, strengthening traceability and improving process efficiency while reducing administrative burden and supporting greater clinical focus on patient care. Systematic, real-time KPI capture with audit-ready reporting enables continuous performance monitoring and data-driven decision-making. Beyond its local impact, this initiative demonstrates a scalable, cost-efficient approach that can be transferred to other centers seeking to standardize apheresis and cell therapy workflows within existing institutional digital environments, supporting digital transformation while maintaining alignment with international quality standards.

Disclosure: Nothing to declare.

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QM EXPERIENCE OF THE ROME TRANSPLANT NETWORK (RTN): OPTIMIZING AND HARMONIZING QUALITY, CONSISTENCY, AND DONOR–PATIENT SAFETY ACROSS A METROPOLITAN PROGRAM

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Background: Rome Transplant Network (RTN) is a JACIE accredited Metropolitan HSC Transplant Program established in Rome from 2006 as a cooperative alliance among 6 centers (Policlinico Tor Vergata, San Giovanni Addolorata, Isituto Regina Elena, Policlinico Campus Biomedico, S. Eugenio e S. Andrea Hospitals) for a total of 13 Clinical Units, Cell Collection and Cell Processing Facilities with the partnership of 2 further certificated ACF and PF (San Camillo Forlanini and Policlinico Umberto I Hospitals).The introduction of the new EUSoHO Regulation 2024/1938 and the alignment with JACIE standards highlighted the urgency of implementing harmonized procedures, interoperable traceability systems, and shared donor–patient safety strategies. Ensuring consistency of processes and documentation across multiple centers became essential to guarantee compliance, efficiency and equitable quality of care for donors and recipients. Goals are to implement and evaluate a structured, network-wide QP aimed at harmonizing critical pathways, improving regulatory and accreditation readiness, enhancing donor/patient protection, and establishing a sustainable, collaborative quality culture across a multi-center transplant program.

Methods: From January to October 2025, RTN performed seven inspections across transplant programs of the member hospitals. These assessments were performed by certified JACIE inspectors and qualified QMS assessors and were structured as full accreditation-style visits. This approach ensured rigorous evaluations and enabled the early identification of systemic gaps, risks, and areas requiring standardization.In addition, RTN organized tree multidisciplinary meetings—two on stem cell processing and one on clinical transplant pathways—structured as scientific conferences where each hospital presented its practices, challenges, and performance indicators. A third network-wide meeting, focused on apheresis, is scheduled for early 2026. These meetings were designed not only to share expertise but also to ensure uniform training and alignment of staff competencies and procedures across the network. Furthermore, three operational boards—clinical, apheresis, and processing—hold monthly remote meetings to discuss updates on regulatory requirements, process variations, CAPA and quality indicators. This continuous governance model enables real-time communication, problem solving, and progressive harmonization of workflows across the entire network.

Results: Cross-inspections identified recurrent issues such as variability in donor consent documentation, incomplete ISBT-128 implementation, partial harmonization of cryopreservation workflows, and heterogeneous QMS documentation. Following implementation of the RTN Quality Program, significant goals were achieved: alignment of SOPs and traceability procedures across facilities; adoption of a unified donor–patient pathway through the IAAPP platform; strengthened compliance with SoHO Articles on coding, traceability, and vigilance; improvement in the completeness and reliability of apheresis documentation; creation of a shared audit schedule and a quantitative competency matrix; reduction of inter-center variability in cryopreservation QC monitoring; standardization of vigilance and adverse event reporting through a common RTN form; enhanced communication and shared decision-making through remote board meetings.

Conclusions: The RTN QP strengthened harmonization, donor/patient safety, and regulatory compliance across a multi-center transplant network. By integrating accreditation-style inspections, structured multidisciplinary meetings, and continuous shared governance, the program established a sustainable framework for quality improvement. This model provides a scalable, replicable approach for a metropolitan networks aiming to achieve high levels of consistency, operational resilience, and readiness for SoHO implementation and JACIE certification.

Disclosure: Nothing to declare

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IMPROVING JACIE INSPECTOR EDUCATION WEBINAR ATTENDANCE THROUGH STRUCTURED PERFORMANCE IMPROVEMENT

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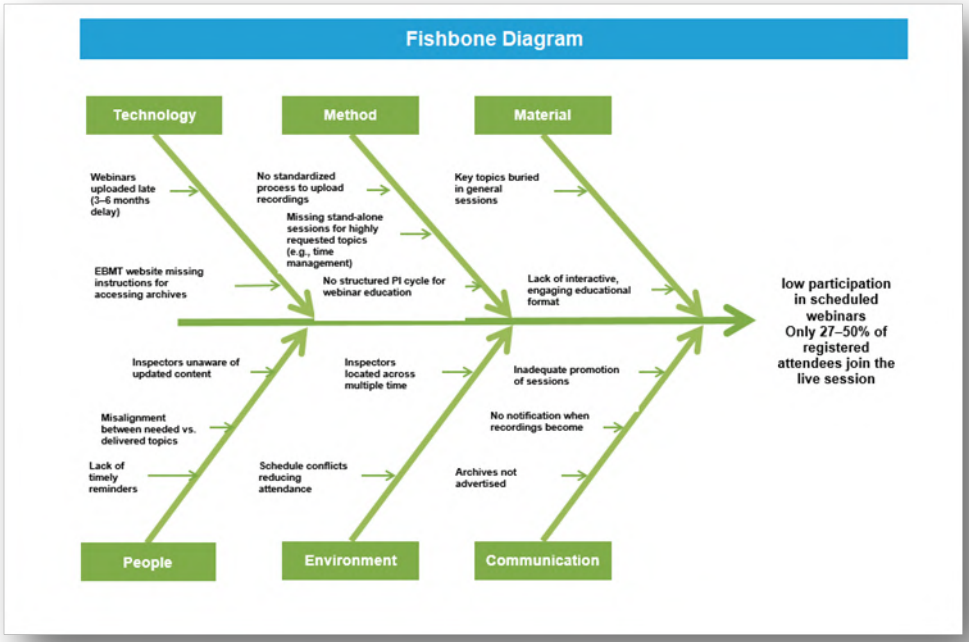
Background: The JACIE Inspector Committee delivers 5–6 educational webinars per year to ensure inspectors remain updated, competent, and confident in conducting inspections. Despite having **348 active inspectors**, webinar attendance averaged **only 35 participants** per session (Jan 2024–May 2025).
Our aim - Increase inspector webinar participation by **at least 50%** and improve access/visibility of recorded sessions by implementing targeted PI interventions by Q2 2026.

Methods: The team used **three investigative streams:**

- Feedback – Analysis of post inspection surveys
- Archives – the content and accessibility of the current archives
- Awareness/ advertising – how we make our inspectors aware of the webinars and the archives

We applied **quality tools** to identify root causes and improvement opportunities. Evidence was retrieved from post-inspection surveys, website review, and webinar registration data.



FISHBONE (ISHIKAWA) DIAGRAM Problem: LOW WEBINAR ATTENDANCE - between 27-50% of those registered went on to attend the webinar

Technology

- Webinars uploaded late (3–6 months delay)
- EBMT website missing instructions for accessing archives

Methods:

- No standardized process to upload recordings
- Missing stand-alone sessions for highly requested topics (e.g., time management)
- No structured PI cycle for webinar education

Materials:

- Key topics buried in general sessions
- Lack of interactive, engaging educational format

People:

- Inspectors unaware of updated content
- Lack of timely reminders

- Misalignment between needed vs. delivered topics

Environment:

- Inspectors located across multiple time zones
- Schedule conflicts reducing attendance

Communication:

- Inadequate promotion of sessions
- No notification when recordings become available
- Archives not advertised

5 WHYS ANALYSIS - Problem: *Low attendance at JACIE inspector webinars.*

Why?
Because inspectors do not join live sessions.
➞ *Why?* They may not find the topics relevant or aligned with needs.

Why?
Because key requested topics—time management, labels, validation—were not highlighted or positioned as targeted sessions.
➞ *Why?* Time management had **not been delivered as a stand-alone webinar** despite being the most requested topic

Why?
Because inspectors who miss live sessions do not watch recordings.
➞ *Why?* Archived webinars were delayed by **3–6 months** before being uploaded, making them inaccessible

Why?
Because inspectors were unaware of where or how to access recordings.
➞ *Why?* The EBMT website did not provide clear instructions on accessing the e-learning recordings.

Why?
Because communication and advertising strategies were insufficient.
➞ *Why?* Registered attendees were not notified when recordings became available, and archives not promoted.

Results:

1. **Scheduled a Time Management webinar**—addressing the No.1 inspector request.
2. **Added a clear paragraph to the EBMT website** explaining how to access recordings.
3. **Revamped consent/approval process** to accelerate uploading webinars.

4. **Communicated that all webinars will be uploaded**—reducing pressure to attend live.
5. **Notified registrants when recordings become available.**
6. **Promoted archive improvements** and initiated **EBMT 2026 abstract submission** to increase visibility.

Results (Early Impact) - Although early in the PI cycle, the interventions are expected to deliver:

- Increased attendance through better topic alignment.
- Faster access to recordings (reduced upload delays).
- Improved inspector satisfaction/preparedness.
- Higher engagement through clearer communication and promotion.

Conclusions: **Next Steps:**

- **Monitor attendance trends quarterly**
- **Automate reminders & follow-up emails**
- **Develop KPI dashboard:**

  - Attendance %
  - Recording access rate
  - Timeliness of uploads
  - Post-webinar satisfaction

Disclosure: Nothing to declare

P343

THROUGH THE EYES OF A QUALITY MANAGER: MANAGING THE REGULATORY AND INSPECTION BURDEN OF MULTIPLE INSPECTIONS IN A STEM CELL TRANSPLANT CENTER

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Background: The Clinical Haematology service at Imperial College Healthcare NHS Trust (ICHT) in London, UK boasts a large stem cell transplant (SCT) centre, undertaking 207 autologous and allogeneic transplants in financial year 2023-24 and 191 in 2024-25.
The centre offers treatment with cellular therapies including stem cell and other advanced therapeutic medicinal products (ATMPs) such immune effector cells and gene-modified therapies.
SCTs such as ICHT operate within a highly regulated environment and are routinely subject to multiple inspections, sometimes concurrently, from national and international bodies such as JACIE, HTA, MHRA in addition to mandatory external audits by cell therapy manufacturing

companies as well as internal audits.
Maintenance of certification and monitoring of compliance requires an intensive, rolling quality management programme to ensure organisational adherence against all inspection standards. Some bodies have in excess of 200 standards (JACIE has >900 standards). While these inspections aim to ensure patient safety and compliance, they often create significant operational challenges, including duplication of effort, resource strain, and staff fatigue. Quality managers play a pivotal role in coordinating these processes in applying practical strategies to ensure a comprehensive inspection experience.

Methods: Adopting a qualitative approach, drawing on the experience of a Quality Manager in a large UK stem cell transplant center over a three-year period to assess effective ways of mitigating the burden and coordination of multiple inspections. Data sources during the preparation period included:

- Inspection schedules, and reports from JACIE, HTA, external and internal audits.
- Process mapping and gap analysis identifying areas of risk requiring corrective action as well as highlighting regulatory requirements through utilising matrices and trackers (via Excel).
- Comprehensive communication mechanisms to ensure staff are fully onboarded including inspection preparation material such as staff FAQs and interview practice.

Staff feedback collected through structured interviews and post-inspection debriefs. A thematic framework was applied to categorise strategies that improved efficiency and reduced burden.

Results: Between 2022 and 2025, the center underwent seven major inspections and audits. Inspection preparation time ranged from 8-12weeks based on the nature of the review and inspections notification lead-time. Key findings include:

- Duplication of documentation contributed to preparation workload increase.
- Staff stress and fatigue was affected during consecutive inspections. However, staff felt well supported by inspection readiness material and clear communications particularly when the inspectors provided clear instructions.
- Implementation of a centralised compliance matrix streamlined tasks and reduced workload duplication.
- Inspection compliance and readiness dashboard improved preparedness and reduced last-minute corrective actions.
- Having a reliable document control system which can also act as a key organisation tool through its function as a central evidence depository.

Conclusions: Managing multiple inspections in a SCT requires a proactive, integrated approach. While the burden of inspection can pose a risk to SCTs, implementing strategies such as centralised documentation systems, effective team communication mechanisms, and continuous readiness monitoring helped to reduce regulatory burden and improve staff well-being. Quality managers are uniquely positioned to lead this transformation, ensuring compliance without compromising patient care. Future work should explore digital solutions and collaborative models across centers to further streamline inspection processes.

Disclosure: N/A

P344

ATMP MANUFACTURING INSIDE A JACIE-ACCREDITED FACILITY: MISSION IMPOSSIBLE OR THE NEW STANDARD?

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Background: Many academic centres build separate GMP facilities for ATMP manufacturing. At the stem cell laboratory, Karolinska University hospital, we successfully overlaid GMP manufacturing onto the existing JACIE-accredited cell processing laboratory within the same grade C cleanroom suite.

Methods: To highlight differences between GMP manufacturing and JACIE processing, a comparison was made between the procedure for GMP manufacturing of virus-specific T cells (VSTs) and the JACIE-accredited minimal manipulation method for depletion of TCRα/β+ and CD19+ cells.
All cell therapies were prepared in closed systems in a grade C cleanroom with allogenic leukapheresis products as starting material. VSTs were GMP manufactured on the fully automated CliniMACS Prodigy system by virus-specific peptide stimulation followed by antibody-based identification of IFN-γ-secreting cells that were enriched using magnetic bead separation. Depletion of TCRα/β+ and CD19+ cells was conducted by manual antibody labelling and washing of cells followed by magnetic separation on the CliniMACS plus automated system.
GMP manufacturing at the JACIE-accredited facility was achieved by using risk evaluated segregation, extensive GMP batch documentation, validation, enhanced environmental monitoring, and aseptic processing in a single quality management system.

Results: Authorization for GMP manufacturing under the hospital exemption was achieved during autumn 2024. Since then, ATMP batches have been successfully manufactured alongside uninterrupted JACIE cellular processing.

	JACIE	**GMP**
Product	Depletion of TCRα/β+ and CD19+ cells	Virus-specific T cells
Regulatory framework	8th JACIE edition Swedish legislations	EudraLex vol 4 part IV HSLF-FS 2025:1*
Manufactured batches**	11	4

Simultaneous cleanroom activities	Routine in one cleanroom entity	Routine in separate cleanroom entities
Total controlled documents	~7	~36
Documentation system	JACIE SOPs	GMP SOPs and batch records
Production time	12 h	30 h
Number of staff needed	3	7
Staff roles	Combined	Defined for production, QC and QA
Product release by	Clinician	QP
Aseptic process simulation	Not applicable	Process validation and operator validation
Environmental monitoring during production	Air pressure (particle counting and microbial monitoring performed routinely)	Air pressure Continuous particle counting Settle plates Contact plates Glove sampling
Cleanroom	C grade	C grade
Cleanroom classification	Annual external classification Internal environmental monitoring	Annual external classification Internal environmental monitoring
Release assays	TNC Total T cells TCRα/β+ cells B cells Stem cells Viability Viral testing Biosafety testing	TNC Total T cells IFN-γ+ T cells Viability Viral testing Biosafety testing Environmental monitoring
Biosafety testing	Validated clinical sterility	Sterility EP 2.6.1 Endotoxin EP 2.6.14 Mycoplasma EP 2.6.7

*Swedish medicinal product agency authorization for hospital exemption.
**Between October 2024 and November 2025.

Conclusions: JACIE standards set the foundation for manufacturing by establishing robust quality systems, cleanroom operations, and clinical processing expertise in transplant centres. Overlaying EU GMP ATMP manufacturing onto an established JACIE-accredited laboratory is complex but achievable. The approach is safe, enables GMP quality, preserves clinical context, and accelerates patient access to advanced cellular therapies. With the 9th edition JACIE standards and EU GMP guidelines increasingly aligned, this integrated model is enabling a pragmatic standard for hospital transplant centres delivering both hematopoietic grafts and innovative ATMP cell therapies.

Disclosure: Nothing to declare.

P345

JOINT INSPECTIONS FOR INSTITUTIONAL AND JACIE CERTIFICATIONS: THE ITALIAN EXPERIENCE

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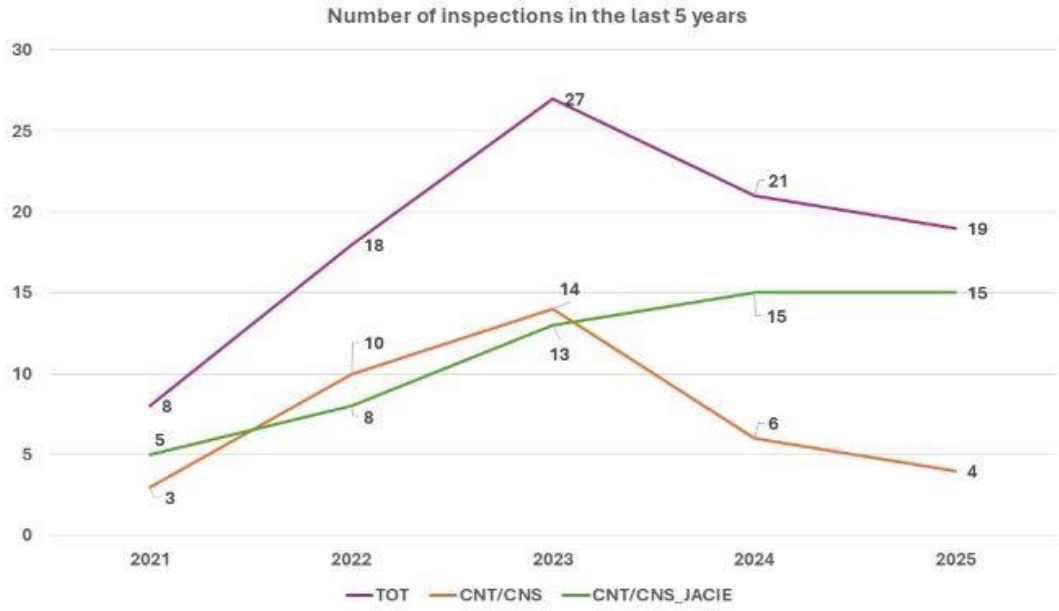
Background: Since 2007, the National Transplant Centre (CNT), in collaboration with the National Blood Centre (CNS), has conducted inspection activities aimed to monitoring italian Transplant Programs (TPs) compliance with national regulations laid down by European directives on tissue and cells (D. Lgs. 191/2007, D. Lgs. 16/2010) and blood (D.M. 2/11/2015).
In parallel, from 2004, the Joint Accreditation Committee–ISCT–EBMT (JACIE) operates as a voluntary professional certification, designed to evaluate the quality of clinical, collection, and processing procedures for hematopoietic stem cell transplantation (HSCT). Over the years, the Italian Competent Authorities (CNT/CNS) and JACIE have collaborated in order to avoid multiple inspections for the TPs.
Following an introduction of a new Italian regulation (ASR No. 49/2021) this collaboration has intensified with the aim of optimising resources and carrying out joint inspections.

Methods: The Italian model integrates two parallel and complementary inspection pathways:

- Institutional inspection by CNT/CNS, based on mandatory requirements derived from European Directives and national Legislative decrees.
- JACIE inspection, focused on professional excellence standards and on the quality management of clinical, collection, and processing units.

Joint inspections involve an inspection team with dual qualification, assessing compliance both with national regulatory requirements and with JACIE standards.

Results: Between 2021 and 2025 the CNT/CNS and JACIE performed joint inspection in 56 full program HSC autologous, allogeneic, adult and paediatric centres in Italy (18% with more than 2 Clinical, Collection or Processing Units, sometimes placed in different Hospitals), involving 211 inspectors.
From 2023, the joined inspections incresead from 50% to 79% in 2025, demonstrating an alignment among institutional inspection and JACIE accreditation programme (fig. 1).



The alignement comes from a strict collaboration between inspection coordinators CNT and JACIE, involved in the organization, that includes:

- Scheduling joint inspections over the year;
- First contact by CNT to propose to the TP a date for inspection;
- First contact by CNT with CNT/Jacie inspectors to define the composition of the inspection team;
- Confirmation by the JACIE office that the TP meets the JACIE requirements for the inspection;
- Organisation of the logistics by CNT and JACIE e.g. number of inspectors, and inspection duration and the inspection schedule;
- Completion of the inspection;
- Completion of reports and outcomes as per institutional procedures.

In addition, in 2025a JACIE Inspector training course was carried out in Italy with the aim to increase the number of inspectors with double qualification. This goal was achieved and to date the 90% (70/78) of the italian CNT/CNS inspectors are also JACIE inspectors.

Conclusions: The Italian experience shows that joint CNT/CNS–JACIE inspections represent an effective model for resource optimisation reducing redundancies. This is useful for a future unified inspection program aimed at mutual recognition between institutional certification and JACIE certification.
This model could be replicable, particularly in view of the application of REGULATION (EU) 2024/1938, which promotes cooperation among Member States, ensuring quality, safety, and consistency in HSCT pathways. The harmonisation of inspection criteria, the independence of assessors, and the potential integration of international standards into institutional requirements are key elements of an increasingly synergistic certification system.

Disclosure: Nothing to declare.

P346

A PATIENT-CENTERED, END-TO-END DIGITAL PLATFORM FOR HSCT AND CAR T-CELL THERAPY: A PROCESS-ENGINEERING APPROACH

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Background: Hematopoietic stem cell transplantation (HSCT) and CAR T-cell therapy pathways are complex, multi-step processes requiring coordination across multiple teams, information systems, and decision points. In many centers, transplant and cell therapy committee coordination, procedural planning, longitudinal patient follow-up, and the capture of clinical and quality indicators are still managed through fragmented tools and manual workflows, limiting standardized end-to-end traceability of the patient journey. In addition, currently available commercial solutions are largely product-centered, focusing on cellular product traceability from collection to infusion, and often fail to provide a patient-centered, end-to-end view of HSCT and CAR T-cell therapy pathways.

Methods: At Ramón y Cajal University Hospital, more than 120 HSCT and CAR T-cell therapy procedures are performed annually, while a larger number of patients are evaluated without completing all phases of the pathway. To address this operational complexity, a process and software development project was undertaken using an agile Scrum methodology. A multidisciplinary team, including a process engineer, (i) mapped the as-is HSCT and CAR T-cell therapy patient journey, (ii) conducted gemba walks in clinical and laboratory areas to directly observe workflows, handovers, and information flows, and (iii) performed patient-pathway simulations to test typical and exceptional scenarios and to derive and prioritize functional requirements.

Results: Guided by these analysis, a modular web-based prototype platform was developed within the hospital's institutional digital environment, providing a patient-centered view of the HSCT and CAR T-cell therapy pathway. The platform comprises five main modules: (i)

transplant and cell therapy committee request and assessment, (ii) HSCT management, (iii) CAR T-cell therapy management, (iv) related donor evaluation, and (v) unrelated donor search management. Through a single real-time interface, users access an end-to-end record of each case, including patient and donor status within the circuit, planned and pending activities, and the responsible areas at each step, as well as information on pre-transplant planning, cell collection and cryopreservation, admission to the transplant unit, infusion, post-transplant follow-up, comorbidity scores, and associated clinical documentation. In addition, a shared status dashboard, task lists, and automated alerts support coordination and workflow management for the transplant and cell therapy committee. The data model incorporates fields for key clinical variables and quality indicators aligned with JACIE standards, enabling consistent data capture across HSCT and CAR T-cell cases and facilitating the generation of quality reports.

Conclusions:

This process-engineering–driven platform unifies patient-centered coordination, clinical documentation, and quality-indicator capture within a single end-to-end system. Its implementation at Ramón y Cajal University Hospital has demonstrated feasibility for centralizing patient data, improving traceability, and generating a homogeneous dataset that underpins a high-value clinical repository for quality monitoring, research, outcome analysis, and evaluation of therapeutic strategies. This scalable approach may serve as a model for other centers seeking integrated pathway management solutions in complex cell therapy programs.

Disclosure: Nothing to declare.

P347

SMART, SIMPLE, STREAMLINED: USING MS FORMS TO IMPROVE COMPETENCY MONITORING IN A BUSY BMT UNIT

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Background: As a large bone marrow transplant (BMT) unit, up-to-date staff clinical competencies is essential to adhere with regulatory compliance (such as the JACIE standards, section B in particular) and patient safety. Assessments historically relied heavily on a paper-based system where competencies were handed out and completed by hand. These were then marked manually by the assessors who also had the task of tracking the competencies across several departments and staffing levels. Email reminders were often sent, paper forms would go missing and the assessor would have to start the cycle again. This was time consuming and inefficient.
To address this, the quality team decided on Microsoft (MS) Forms as they provided a streamlined simple process and would reduce the administrative burden. It's a platform accessible by all. Following Covid the Trust encouraged a 'paper-light' approach to documentation, therefore this approach met the goal.

Methods: The process to switch to MS forms for competency distribution and assessment was done over 2 phases. Phase 1 was the planning phase. The quality team had focus meetings to discuss processes and workload. This followed by converting all competency assessments into MS forms and automating the marking scheme.
Phase 2 was the implementation phase. Initially this was trialled out by the quality team to ensure that all the fields and options were functioning well and that the marking scheme was consistent. Once happy, this was rolled out to all clinical staff when they were due to complete a competency assessment. Support was always made available from the quality team.

Results: The switch from paper competency assessment forms to MS forms has proved to be very successful. Staff reported that they have found it much easier completing the assessments online and therefore not worrying about misplacing the form or finding time to bring it to the quality team.
Assessors reported a more streamline process, less administrative work, faster results as they were now marked electronically as well as a better storage capability as the results were automatically stored with the option to have them available via an excel sheet for overall reviewing and data collecting.

Conclusions: The decision to adopt MS forms for competency assessments in our BMT unit proved to be very beneficial for both staff and assessors. It has enhanced the efficiency, speed and reliability of the process. The changeover addressed many of the previous challenges such as the manual collection, marking and document loss. It provided a centralised location for the forms to be sent out as well as be stored and monitored easily. The project demonstrated that the change to an online platform for clinical competency assessments and monitoring improved the process for the assessor and staff completing them. As the team grows and as the speciality expands an online solution is the best way forward as long as its user friendly, adaptive and staff support is always available.

Disclosure: Nothing to declare

P348

IMPLEMENTING JACIE QUALITY STANDARDS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE MANDATORY AUDIT OF EARLY OUTCOMES

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Background: The Joint Accreditation Committee ISCT-Europe & EBMT (JACIE) accreditation framework represents the international benchmark for quality, safety, and outcome-driven practice in hematopoietic stem cell transplantation (HSCT) and cellular therapy programs. Paediatric HSCT Centres face distinct challenges due to the complexity of indications, high-risk patient profiles, and the need for robust multidisciplinary coordination. The Paediatric

Stem Cell Transplantation Program at King Faisal Specialist Hospital and Research Centre (KFSH&RC), Riyadh, Saudi Arabia, established a structured, outcomes-based clinical audit program as part of its JACIE accreditation and continuous quality improvement strategy. This audit focused on key early post-transplant indicators, that includes engraftment outcomes, to assess clinical performance and compliance with JACIE quality management standards.

Methods: A retrospective clinical audit was conducted to evaluate engraftment outcomes among all pediatric patients who underwent hematopoietic stem cell transplantation HSCT at the study center between 1STJan 2021 and 31ST Dec 2024. Eligible cases were identified through Data Unit of the center. Audit indicators were selected in alignment with Joint Accreditation Committee ISCT-EBMT (JACIE) quality management standards and the institution's key performance indicators to ensure consistency with internationally accepted benchmarks. The primary outcome of interest was engraftment performance. Neutrophil engraftment was defined as the first of three consecutive days with an absolute neutrophil count (ANC) ≥0.5 ×10^9/L. Platelet engraftment was defined as achieving a platelet count ≥20 ×10^9/L sustained for at least seven consecutive days in the absence of platelet transfusion support. Secondary outcome measures included the time to neutrophil and platelet engraftment, calculated from the date of stem cell infusion (day 0) to the date on which engraftment criteria were first met. Data were analyzed descriptively to assess engraftment patterns and performance over the audit period.

Results: Between 2021 and 2024 audit cycle, a total of 589 pediatric allogeneic and autologous hematopoietic stem cell transplants were performed, of which 578 cases were analyzable respectively for engraftment. Patients who died before day +28 post-transplant were excluded from engraftment analysis. During 2021,137 transplants were performed, with 134 analyzable cases; neutrophil and platelet engraftment were achieved in 98% of these patients, with a (median time to neutrophil engraftment of 18,19,20 days and platelet engraftment of 20, 21, 22 days. In 2022, 145 transplants were conducted, 143 were analyzable, and 95% reached successful engraftment (median neutrophil 18,19,20 days; platelet 21, 22, 23 days. In 2023, 151 transplants were performed with 148 analyzable cases, among which 96% achieved engraftment (median neutrophil 19, 20, 21 days; platelet 22, 23, 24 days. Finally, in 2024, 156 transplants were carried out, 153 were analyzable, and 97% achieved (median neutrophil 19, 20, 21 days; platelet 22, 23, 24 days.

Conclusions: This JACIE-aligned clinical audit of the Pediatric Stem Cell Transplantation program demonstrates that annual monitoring of engraftment outcomes through existing governance and CAPA processes enhances accreditation readiness, transparency, and ongoing quality improvement. The findings underscore the value of continuous, outcomes-driven audits in maintaining JACIE compliance and ensuring safe, high-quality transplant care.

Disclosure: Nothing to declare.

P349

IMPLEMENTING A MULTI-LEVEL DASHBOARD TO IMPROVE QUALITY, TRACEABILITY AND COMPLIANCE IN CELLULAR THERAPY PROCESSES: A BLOOD BANK'S EXPERIENCE

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Background: Structured, comprehensive, and timely data management is a fundamental requirement for ensuring quality, traceability, and regulatory compliance within Tissue Establishments (TE).
To meet this need, a "*Cruscotto*" was developed—based on Project Management principles and aligned with JACIE and CNT Standards—using Microsoft Excel as an operational database designed to collect, organize, and analyse in real time all information related to cellular manipulations performed in our TE.
The tool supports both daily operational activities and serves as a reference platform during audits and inspections.
This dashboard is structured across three interconnected decision-making levels, each oriented toward specific objectives:

- Strategic Level (Leadership): aimed at assessing long-term sustainability and the competitive position of the service. The "*Cruscotto*" enables monitoring of the aggregated non-conformity rate, analysis of key performance indicators, audit success rates, and satisfaction metrics from affiliated Centers. These elements reinforce decision-making related to service expansion, resource allocation for innovation, and the maintenance of high regulatory standards.
- Tactical Level (Management and Analysis): supports operational efficiency and medium-term risk management. The system integrates analysis of process times, deviations from activity-related KPIs, distribution of root causes of non-conformities, and monitoring of critical stock levels. This allows managers to identify workflow bottlenecks, adjust personnel training investments, and implement targeted corrective actions to prevent operational issues.
- Operational Level (Daily Execution): ensures real-time verification of manipulation activities and correct application of procedures, guaranteeing immediate traceability and prompt intervention in the event of critical deviations.

Methods: Structurally, the "*Cruscotto*" includes dedicated worksheets for the main procedure categories (HPC-AUTO, HPC-ALLO, HPC-M, CAR-T, Extracorporeal Photopheresis), each designed to collect more than 40 clinical and technical variables: donor/patient data, collection parameters, quantitative outputs (CD34+, viability, WBC count), manipulation details, adverse events, and process-specific quality indicators. This organization ensures both daily operational oversight and the creation of a consistent, longitudinal database suitable for retrospective analysis and performance comparisons over time.

Results: Between 01/01/2025 and 30/11/2025, a total of 671 procedures were recorded (see Table 1), resulting in a significant improvement in data completeness and enhanced

ability to monitor collection and manipulation efficiency, operator performance, and procedural outcomes.

Jan-Nov 2025	HPC-AUTO	HPC-ALLO family	HPC-ALLO registry	CAR-T	ECP	HPC-Marrow family	HPC-Marrow Registry
number of procedures	93	31	48	29	464	2	4

Conclusions: The implementation of the "Cruscotto" proved fully compliant with regulatory and excellence standards, improving traceability, documentation consistency, data verification speed, and continuous monitoring of activities. Its flexibility allows ongoing updates, integration of new indicators, automated calculations, and graphical summaries. Moreover, it has become a central tool in preparing documentation for audits and inspections, as well as in generating quarterly reports.
In conclusion, the "Cruscotto" is not merely a data aggregator, but a transformative tool that ensures Tissue Establishments operate with maximum safety, efficiency, and full regulatory compliance.

Disclosure: None

P350

JACIE QUALITY COORDINATION IN A ADULT/PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION AND CELL THERAPY PROGRAM

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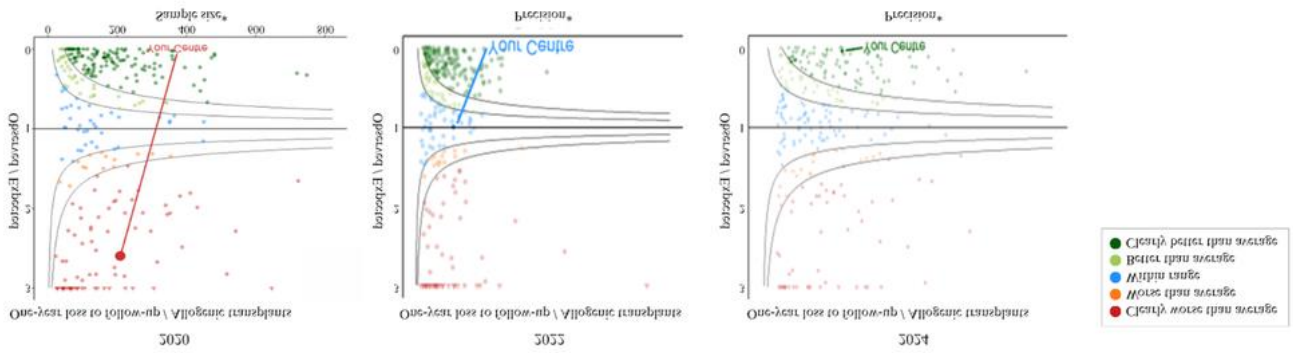
Background: The Joint Accreditation Committee ISCT/EBMT (JACIE) ensures that Hematopoietic Stem Cell Transplantation and Cell Therapy (HSCT-CT) programs meet established quality standards and best clinical practices. Its accreditation provides academic, professional, and managerial recognition for HSCT-CT units.
The objectives of this work are to present the experience and evolution of quality coordination toward achieving JACIE accreditation, to improve the quality management of the HSCT-CTP through the involvement of institutional leadership, and to obtain and maintain JACIE accreditation.

Methods: Compliance with JACIE standards: Hematopoietic Cellular Therapy – Accreditation Manual. Two key roles were identified: the Quality Manager (QM) and the Data Manager (DM). The QM is responsible for establishing and maintaining systems for reviewing, modifying, and approving quality policies and operational procedures aimed at monitoring and ensuring compliance with program standards. The QM must also receive ongoing training

in both cell therapy and quality management.
The DM must have sufficient staffing to collect the required data for the specific forms of the EBMT (European Society for Blood and Marrow Transplantation) international registry, as well as participate in annual specialized training.
Changes in the performance of the QM role between 2012 and 2022 were analyzed: from a position initially requiring a hematology specialist, or other (medical or non-medical) disciplines, and currently being held by nursing staff. The position evolved from part-time to full-time, merging the QM and DM roles into a single individual.

Results: As of 2025, all re-accreditations of the adult program have been maintained, CAR-T accreditation (HSCT-CT) has been achieved, the pediatric HSCT program has been accredited, and accreditation of bone marrow harvesting is ongoing.
A full update of all treated patient records has been completed in the EBMT registry. The centre's standing in the EBMT Benchmarking Report has improved substantially, rising from markedly below the average to clearly above it. (Figure1).



In addition, the progressive implementation of quality standards has permeated the entire clinical programme, strengthening multidisciplinary engagement and fostering a shared culture of continuous improvement. This has been translated into greater team confidence and reassurance, enhanced institutional positioning, strengthened document control, comprehensive and timely registry completion, systematic outcome monitoring, and sustained compliance with administrative authorisations. These gains have been accompanied by challenges, including the need for substantial investment in personnel, ongoing training, and potentially the acquisition of a dedicated document management system.

Conclusions: Achieving JACIE accreditation is not only essential to ensure high-quality care but also to avoid being at a disadvantage or risk the loss of administrative authorization to continue the HSCT-CT program.
Moreover, the combined QM–DM role has proven to be a cornerstone of the program, ensuring consistency, traceability, and integration between clinical practice quality, and data management activities. This hybrid figure has become essential for sustaining accreditation and continuous improvement.

Disclosure: No disclosure.

P351

DEVELOPING EXCELLENCE: HOW A STRATEGIC QUALITY FRAMEWORK LAUNCHED A CUTTING-EDGE CELL COLLECTION CENTRE

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Background: The safe establishment of the Anthony Nolan Cell Collection Centre (CCC) required a coordinated and innovative quality framework aligned with regulatory approval (Human Tissue Authority and Care Quality Commission) and development towards JACIE accreditation.

Methods: A phased validation strategy was implemented to commission the CCC, initially focusing on Donor Lymphocyte Collections (DLCs) to prioritise donor safety. Validation was conducted across the three core processes the CCC had to implement;

1. medical assessment and clearance,
2. DLC procedures and laboratory processes, and
3. Peripheral Blood Stem Cell (PBSC) collections.

Regulatory compliance with the Human Tissue Authority (HTA) and Care Quality Commission (CQC) formed the foundation of the quality management system (QMS). Equipment underwent installation, operational and performance qualifications (IQ/OQ/PQ). Staff training required development of a competency-based framework supported by an electronic QMS. Deviations, incidents, audits, supplier qualification, and risk management were managed under established QMS governance.

Results: 42 medical assessments from volunteer donors, 26 DLCs, and 3 PBSC collections were completed for the validation of the CCC processes, which started in March 2025. To minimise donor burden throughout validation, all DLCs were conducted as reduced collections. All critical clinical and laboratory equipment, including Spectra Optia, Sysmex XN-550, BD FACS Lyric, and BD BACTEC FX®, were successfully validated during this process. Core clinical and laboratory staffing achieved full operational competency enabling the CCC to 'go live.' Donor feedback demonstrated high satisfaction with staff professionalism and environment, directly informing service improvements. The CCC was granted a HTA satellite licence for procurement and testing following a planned site visit in February 2025. CQC registration was also achieved on target. A few low-risk outstanding actions (e.g., PBSC G-CSF cold-chain validation and formal CVC service agreement) were mitigated and did not prevent operational 'go live'. The centre opened safely for both DLC and PBSC collections for allogeneic donors in July 2025.

Conclusions: A structured, phased quality management approach enabled the safe, compliant and timely opening of the new CCC while maintaining donor safety as Anthony Nolan's primary focus. Key lessons learned included the need to build in sufficient time for developing high-quality documentation, SOPs, training material and ensuring adequate time

to test these in the unique clinical and laboratory environment. This early investment in robust documentation and process testing was critical to a successful operational launch. Our audit programme and continuous improvement strategy now refine these processes further, supporting the delivery of a consistently safe donor experience and high-quality cell products for patients. This approach positions the CCC to progress effectively toward JACIE accreditation and provides a replicable model for establishing new cell collection services within a resilient and quality-driven framework.

Disclosure: Nothing to declare.

P352

VALIDATION OF EXTRACORPOREAL PHOTOPHERESIS USING THE THERAKOS™ CELLEX™ PHOTOPHERESIS SYSTEM: A MULTICENTER EUROPEAN PROJECT

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Background: Extracorporeal photopheresis (ECP) is a well-established therapeutic option for cutaneous T cell lymphoma (CTCL), acute and chronic graft-versus-host disease (GvHD) and solid organ transplant rejection. ECP is an apheretic procedure that involves collecting peripheral blood leukocytes, inducing apoptosis using 8-methoxypsoralen (8-MOP) and UVA irradiation, and then returning the treated cell mixture to the patient by intravenous infusion. The growing need to ensure uniform quality standards across ECP programs underscores the importance of having a validated and reproducible process to support accreditation pathways. This study aimed to develop and evaluate a standardized validation protocol for care providers intending to validate ECP procedures performed using the THERAKOS™ CELLEX™ instrument.

Methods: This multicenter project was conducted across 6 centers in 4 European countries. An expert panel developed a comprehensive Validation Masterplan consistent with GMP and FACT–JACIE requirements, defining standardized procedures for sample collection, shipment, and laboratory testing. A total of 43 paired untreated (pre-ECP) and 8-MOP/UVA-treated (post-ECP) apheresate samples were collected using the THERAKOS™ CELLEX™ Photopheresis System. 37 patients with varying clinical indications (GvHD, systemic sclerosis, localized scleroderma or lung transplant rejection) provided samples that were shipped overnight (<24 h) to a central laboratory for harmonized analysis. Automated hematology counts and flow cytometry (Annexin-V/7-AAD staining) were used to assess product composition and apoptosis rates in $CD45^+$ leukocytes, $CD3^+$ T cells, $CD33^+$ myeloid cells, and

CD14⁺ monocytes at 0 h and 22 h. Data were evaluated with repeated-measures ANOVA, paired t-test or correlation analyses.

Results: The expert panel defined and approved the Validation Masterplan, establishing robust protocols for sample shipping and centralized analysis of photopheresates. Samples analysed upon arrival showed that early apoptotic CD3⁺ T cells predominated on day 1 (12.81±5.09 % vs. 2.35±1.95 %; p<0.0001; n=43; Fig. 1A), while late apoptotic T cells increased over 22 h culture (47.41±13.38 % vs. 12.81±5.09 %; p<0.0001; n=43; Fig. 1B). Post-ECP samples showed significantly reduced viability in CD45⁺ leukocytes (7.33±5.25 % vs. 34.84±18.06 %; p<0.0001; n=43) and CD3⁺ T cells (6.77±7.33 % vs. 57.51±27.28 %; p<0.0001; n=43) after culture for 22 h compared to pre-ECP samples. After 22 h culture, the frequency of late apoptotic T cells was significantly higher in post-ECP samples across all centers (47.41±13.38 % vs. 15.67±13.74 %; p<0.0001; n=43). Apoptosis induction in myeloid cells after 22 h culture was less consistent (viability pre-ECP: 11.55±11.84 %; viability post-ECP: 6.96±8.04 %; p=0.0039; n=43). Assay reproducibility was confirmed by strong correlation (R^2 = 0.94) between repeated samples. Variability in viability rates

appeared patient-specific rather than assay-related.

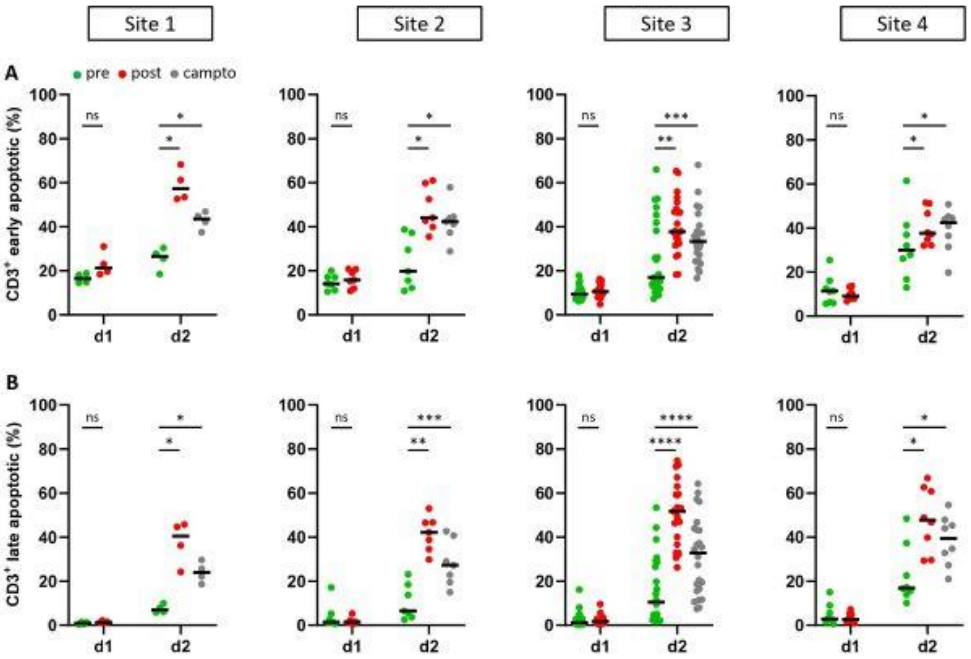

Figure 1 *8-MOP-treated and UVA-irradiated CELLEX samples contain significantly higher frequencies of late apoptotic cells.* ECP samples were stained for flow cytometry analysis before (d1) and after (d2) 22 h cell culture. Frequencies of early (A) and late (B) apoptotic T cells were determined in untreated pre (green dots) and in 8-MOP/UVA treated post samples (red dots). Camptothecin treated pre samples (grey dots) were used as positive control (results are shown as individual values (dots) and median (line); n=4 for Site 1 n=7 for Site 2, n=24 for Site 3 and n=8 for Site 4; statistical analysis was performed using RM one-way ANOVA with Geisser-Greenhouse correction and Tukey's multiple comparisions test; p values are indicated as ns=p>0.05, *=p<0.05, **=p<0.005, ***= p<0.001 and ****= p<0.0001).

Conclusions: This multicenter European validation study confirms that ECP performed with the THERAKOS™ CELLEX™ device reliably induces apoptosis in patient-derived leukocytes across a range of clinical indications. While patient-related factors and sample handling variations may influence apoptotic profiles, the validation protocol proved robustness and reproducibility, supporting its use for standardizing ECP validation procedures.

Disclosure: This study was sponsored and funded by Therakos UK Limited. Support for third-party assistance in development of the Validation Masterplan and oversight of the study was provided by ICMED and funded by Therakos UK Limited.
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P353

SUSTAINING QUALITY IN A COMBINED JACIE-ACCREDITED CENTRE: TWO DECADES OF CONTINUOUS IMPROVEMENT INCLUDING IEC ACCREDITATION

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Background: Our combined adult haematopoietic stem cell transplantation and cell therapy centre initiated preparations for JACIE (Joint Accreditation Committee ISCT-Europe & EBMT) accreditation twenty years ago. The centre is accredited for all activities except paediatric transplantation since 2008 and, at the latest reaccreditation in 2024, successfully included immune effector cell (IEC) therapy. Over time, JACIE standards have shaped not only our compliance processes but also our institutional culture of quality and safety.

Methods: A retrospective evaluation of quality management activities was performed covering the period 2004–2024. Data from internal audits, adverse event reporting, risk assessments, corrective and preventive actions (CAPA), staff education, and key performance indicators (KPIs) were analysed across clinical, collection, processing, and IEC programmes. Trends over successive accreditation cycles were compared to assess the sustainability of quality standards.

Results: Audit compliance rates remained consistently above 80%. Over the last five years, 135 deviations and adverse events were analysed using structured root cause and risk analysis, resulting in 35 corrective and 30 preventive actions. The number of high-risk events decreased by 42% compared with the previous cycle. Regular risk reviews enabled early identification of process gaps and improvement of traceability. Multidisciplinary engagement, continuous training, and strong leadership commitment proved essential for maintaining quality performance.

Conclusions: Two decades after initiating JACIE preparations, our experience confirms that sustained excellence requires embedding quality culture into everyday clinical practice. The integration of systematic risk and adverse event analysis enhanced patient safety and process reliability. The inclusion of IEC activities further strengthened our comprehensive and forward-looking quality management framework.

Disclosure: nothing to declare

P354

DISPOSAL OF HEMATOPOIETIC STEM CELLS IN A PEDIATRIC TRANSPLANT UNIT OVER 10 YEARS IN ARGENTINA: A QUALITY MANAGEMENT OPPORTUNITY FOR PROCESS OPTIMIZATION

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Background: Cryopreservation of hematopoietic stem cells (HSC) is an essential practice in both autologous and allogeneic transplant programs. However, a significant proportion of the collected units remain stored unused or are ultimately discarded, posing ethical, logistical, and economic challenges. This study analyzes a decade of experience at a public pediatric transplant center, describing the magnitude and causes of discarded stem cell units (SCU) , with the aim of providing national evidence for the design of rational storage and disposal policies.

Methods: A retrospective study was conducted at a public pediatric center in Argentina, analyzing cryopreserved SCU between November 2014 and November 2024. The relationship between stored, infused, and discarded units, distribution by type of hematopoietic stem cell transplantation (HSCT), reasons for discarding, and storage duration were described.
Because the indications and kinetics of HSC use are different between autologous and allogeneic transplantation, they will be described separately.
Since 2017, our policy has been to keep backup doses for a year; however, the duration of storage for cryopreserved HSCs is a subject of debate.

Results: Over a 10-year period, 204 units corresponding to 84 patients were cryopreserved. 34.3% were discarded, predominantly in the unrelated allogeneic transplant group (54.4%), followed by autologous transplants (19%) and related haploidentical transplants (14%).

Table 1.Distribution of SCU by type of HSCT

TYPE OF HSCT	**Patients**		**Cryopreserved SCU**	**Infused** SCU	**Discarded SCU**	**Discard %**
Autologous	**37**		**107**	**85**	**20**	**18.7**
Haploidentical	**5**		**7**	**6**	**1**	**14.2**

URD	**42**		**90**	**24**	**49**	**54.4**
Total	**84**		**204**	**115**	**70**	**34.3**

HCT: Hematopoietic Cell Transplant SCU:Stem Cells Units URD: Unrelated Donor

In this 10-year retrospective series from a public pediatric transplant unit, approximately one-third of the cryopreserved units were discarded. Discarding was concentrated mainly in the unrelated transplant group, due to the practice of cryopreserving backup units that are ultimately not used. In autologous transplants, discarding was associated with disease progression or death, while in haploidentical transplants it was low.
In pediatric centers like ours, which perform allogeneic transplants with unrelated adult donors, it is common to receive apheresis products with a cellularity higher than needed to meet the target dose for the pediatric recipient. This weight difference between adult donor and pediatric recipient leads to the generation of more than one cryopreserved unit per patient. This can result in an unintentional increase in the number of units stored.
Except in cases where the patient has died, the decision to discard a cryopreserved unit is difficult to make.
Strategies for improvement include defining strict criteria for cryopreservation of backup units, establishing storage periods, and implementing disposal policies.

Conclusions: Over a 10-year period, 34% of cryopreserved units were discarded, with unrelated donor units predominating. The main reasons were: non-use of backup units, disease progression, and recipient death. Our findings are consistent with international reports and underscore the need for standardized storage and discard policies in order to optimize resources.

Disclosure: Nothing to declare

P355

THE REGULATION OF CLINICAL TRIALS WITH HEMATOPOIETIC STEM CELL PREPARATIONS: CHALLENGES AND PERSPECTIVES IN THE CONTEXT OF REGULATION (EU) NO. 536/2014

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Background: The regulation of clinical trials involving hematopoietic stem cell preparations (HSCPs) is complex because it involves both European and national legal requirements.

While the EU Clinical Trials Regulation (CTR, Regulation (EU) No. 536/2014) seeks to harmonize clinical trial procedures, HSCPs are excluded from its scope since they are classified as tissue products under Directive 2004/23/EC. This creates significant regulatory differences among EU Member States, complicating the planning and execution of multinational clinical trials. The lack of harmonization particularly hinders academic research and the development of innovative cell-based therapies in Europe, a significant locational disadvantage.

Methods: A qualitative research design was used, systematically analyzing relevant European and national legal frameworks, along with conducting expert interviews. The legal analysis focused on Germany and selected EU member states, examining requirements for safety, quality, and ethics in clinical trials with HSCPs. Expert interviews with clinicians, legal professionals, and regulatory experts provided practical insights into the challenges of implementing these regulations in multinational studies.

Results: The legal framework in Germany differs significantly from that of other European countries and has notably strict rules for clinical trials involving HSCPs. These trials are classified as medicinal products under the German Medicines Act (AMG), which requires extensive manufacturing authorization, GMP compliance, and thorough documentation. In contrast, many other EU countries categorize HSCPs as tissue products, which only require ethical review for clinical trials. This difference creates substantial administrative burdens and causes delays in multinational studies, as seen in the T-Haplo for SCD trial (NCT04201210), which faced divergent regulatory pathways in Germany, Austria, and Italy. Experts confirm that the lack of harmonization poses major barriers to academic research and international collaboration. The upcoming EU SoHO Regulation (2024/1938) aims to improve harmonization, though uncertainties remain about how it will be implemented nationally and whether national regulations and laws will continue to overrule EU regulations such as SoHO.

Conclusions: Current regulatory frameworks for clinical trials with HSCPs in Europe are fragmented, with significant differences in legal classification, approval procedures, and quality requirements. Germany's particularly restrictive approach limits academic research and complicates multinational studies. Harmonization at the European level—especially through clear criteria for classifying cell preparations and streamlined approval processes—is urgently needed. The implementation of the SoHO Regulation offers an opportunity to reduce regulatory barriers, but its success will depend on consistent application across Member States and avoiding additional bureaucratic hurdles. Targeted support for academic research, including simplified procedures for low-risk studies and centralized guidance, is necessary to promote international studies and strengthen academic research.

Disclosure: Nothing to declare

P357

WHO IS CURRENTLY OCCUPYING THE BMT QUALITY MANGER CHAIR, MULTI-CENTER DESCRIPTIVE USING LINKEDIN® WEBSITE

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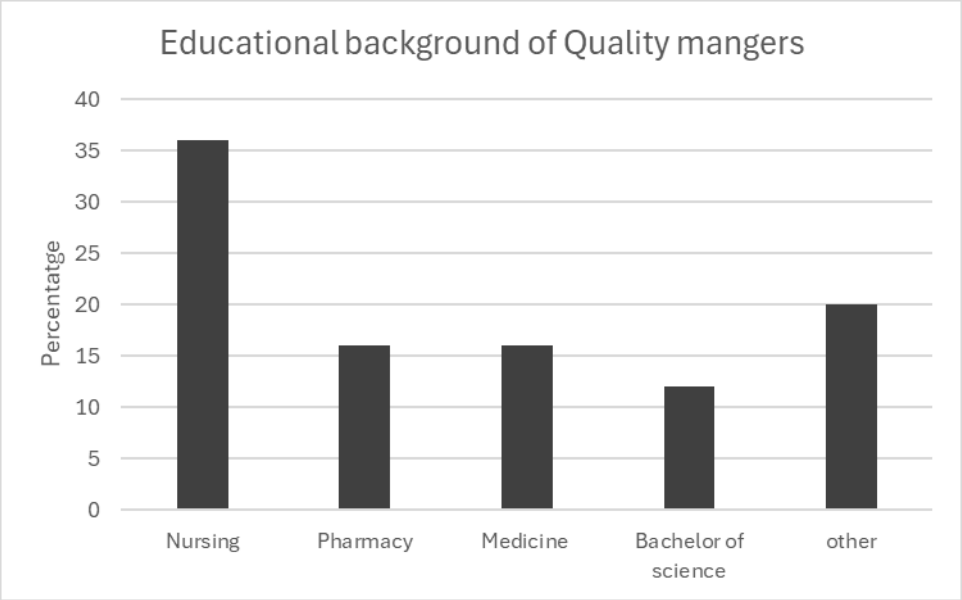
Background: The FACT–JACIE HSCT Standards provide only a broad description of the qualifications required for a cellular therapy quality manager. According to the 9th Edition, the role may be fulfilled by "an individual with an undergraduate degree or equivalent in health or biological sciences, accompanied by training or experience in quality management". This broad definition allows considerable variation in the educational backgrounds of quality managers, despite their carrying out similar functions across centers operating under the same standards. The objective of this analysis is to determine the educational backgrounds of individuals currently serving as quality managers and to assess the extent of diversity in the educational qualifications of those performing quality management functions in cellular therapy and bone marrow transplantation.

Methods: A list of JACIE- and FACT-accredited centers was obtained from the respective websites. Centers were selected to achieve broad geographic representation, with up to five centers included per continent. Availability of publicly accessible information identifying the quality manager was an additional inclusion criterion. LinkedIn searches were performed to determine the educational background of cellular therapy and bone marrow transplant quality managers/ Quality assurance officers. The proportion of each educational background was calculated by dividing the number of quality managers with the same educational background by the total number of centers analyzed, multiplied by 100. For example, the percentage of nurses' representation was calculated by dividing the number of quality managers with Bachelor of Nursing, which is nine, by the total number of centers which is 25 accordingly the percentage of nurses was (9/25) *100= 36%. Diversity within each continent was calculated by dividing the number of distinct educational backgrounds by the total number of centers, multiplied by 100.

Results: A total of twenty-five centers were included in the analysis, and the educational backgrounds of their quality managers or quality assurance officers were identified. Eight distinct educational backgrounds were observed across the cohort. Notably, three quality managers held non-healthcare degrees, all of whom were senior professionals with more than 20 years of experience. Nursing was the most common educational background, followed by pharmacy and medicine, as illustrated in the accompanying graph below. The lowest diversity in educational backgrounds was observed in North America, while the highest diversity was seen in Africa, likely influenced by the smaller number of centers included from that region



Continent	%Diversity
Africa	100
Asia	80
Europe	80
Australia	75
South America	75
North America	40

Conclusions: Nurses appear to be the most common healthcare professionals assuming the quality management role, particularly in North America. As bone marrow transplantation and cellular therapy continue to advance and evolve, there is a growing need to strengthen the qualifications of quality managers and reduce variability in their educational backgrounds. Future studies are warranted to determine the most appropriate educational profile for this role and to define the certifications or requirements that should be considered essential for the position.

Disclosure: Nothing to declare.

P358

BUILDING A COST-EFFICIENT, JACIE-ALIGNED GMP FACILITY FOR CAR-T MANUFACTURING WITH SCALABLE EXPANSION TO CELL AND GENE THERAPIES IN AN LMIC SETTING: EXPERIENCE FROM CARTOGENE THERAPEUTICS

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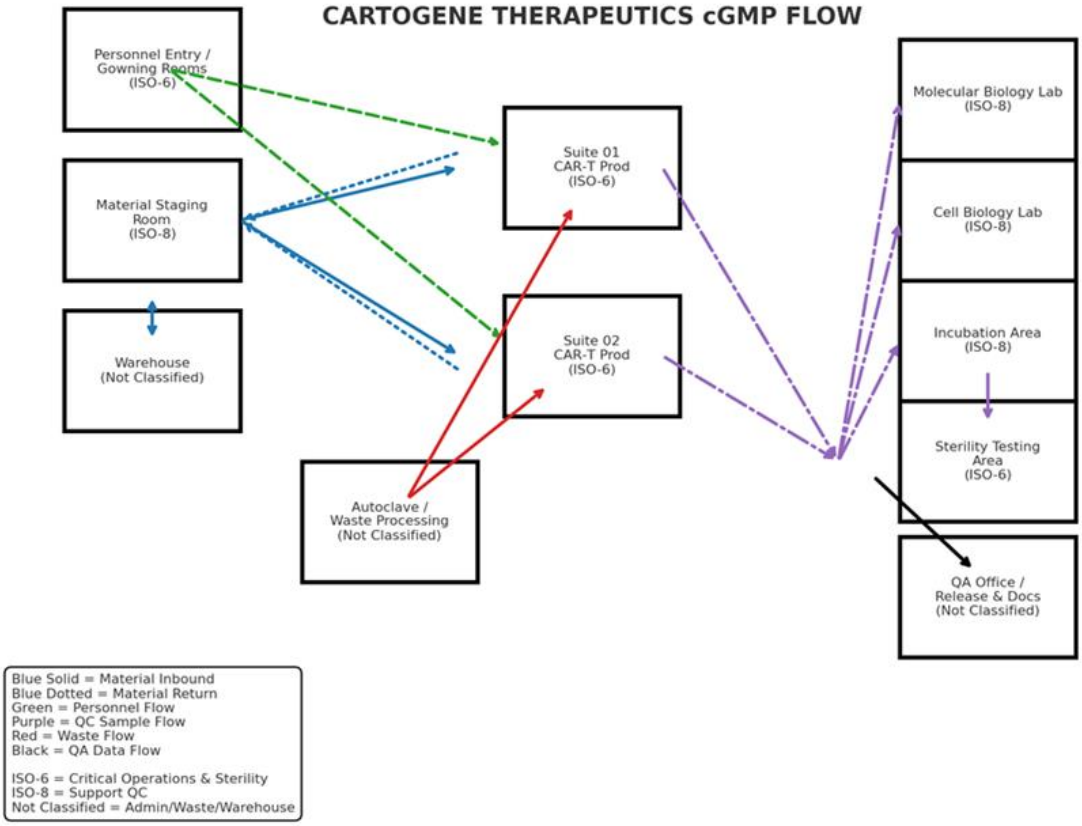
Background: CAR-T cell therapy has demonstrated curative potential in relapsed/refractory B-cell malignancies; however, access remains limited in low- and middle-income countries (LMICs), where treatment costs can exceed 10–20× the average annual income. A primary barrier is the lack of domestic GMP-compliant manufacturing aligned with recognised international accreditation frameworks such as JACIE. To sustainably expand access, infrastructure must be designed to balance global quality expectations with affordability, streamline workflows to reduce operational complexity, and incorporate modularity for future cell and gene therapy (CGT) expansion. Cartogene Therapeutics has developed a cost-optimised GMP in India to enable affordable CAR-T production and establish a scalable pathway for subsequent CGT modalities.

Methods: A manufacturing of ~3500 sq. ft. was developed using value-engineered construction principles, reducing infrastructure-related expenditure by an estimated **40–50%** relative to comparable facilities in high-income countries. The manufacturing environment includes:

- **Two independent CAR-T manufacturing core suites (ISO-6)** are designed for autologous and adaptable for other workflows.
- **Closed-system processing**, minimising open handling and controlling environmental exposure for all critical steps
- **Segregated functional areas,**including:
    1. Primary and secondary gowning zones **(CLASS-B, ISO-8 → ISO-6)**
    2. Process staging and fill-finish **(ISO-6)**
    3. Warehousing with physical separation of raw, in-process, and finished goods
    4. Defined hazardous waste handling pathways
    5. Dedicated block for Cell biology, Molecular biology, Incubation **(ISO-8**) and Sterility area **(ISO-6)**

Material and personnel movements were engineered to eliminate cross-contamination risks using independent airlocks, labelled directional flow pathways, and **dedicated dynamic pass boxes.**
A **unidirectional waste management system** ensures that all generated biohazard materials are sealed, transferred into a segregated warehouse pathway, and sterilised before removal by licensed biomedical waste handlers.
Manufacturing cleanrooms utilise **PUF-filled modular partitions**, smooth powder-coated finishes, epoxy flooring, and coving at all junctions to enable high cleanability. **Dedicated AHUs** and pressure cascade zoning provide contamination-risk-aligned environmental control and reduce downtime for maintenance.

The integrated warehouse enables centralised material control for the entire organisation while maintaining GMP segregation through a **material staging room** that prevents cross-flow between clinical and non-clinical inventory.



Results: The facility successfully meets cGMP principles and is architecturally aligned with JACIE accreditation requirements for cellular therapy facilities. Key operational outcomes include:

- **Streamlined personnel workflow,** lowering gowning-related nonproductive time and reducing facility occupancy burden while ensuring contamination prevention.
- **>30% operational manpower efficiency** achieved through simplified logistics, pass-box-driven movement.
- **Improved manufacturing**, supporting tighter vein-to-vein timelines.
- **Initial production capacity for ≥700 therapies per year**, with scalability option.
- **Robust segregation of material states**, preventing mix-ups and enabling operational excellence metrics critical for regulatory audits.
- **Cost-reduction enablement** through localised supply chain development and optimised OPEX models — positioning CAR-T as a more sustainable alternative.

The design supports **future-ready transformation**, with pathway adaptations already mapped for CGT.

Conclusions:

Cartogene Therapeutics has established a cost-efficient, globally aligned CAR-T manufacturing facility tailored for LMIC constraints without compromising quality or scalability. This JACIE-aligned infrastructure not only supports the immediate deployment of accessible autologous CAR-T programs in India but also lays the foundation for regional growth in advanced cell and gene therapies. This model offers a reproducible blueprint for LMIC healthcare readiness in next-generation biologics.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

P359

MICROBIAL CONTAMINATION OF CELLULAR THERAPY PRODUCTS: A DECADE OF SUCCESS OF SINGLE CENTER EXPERIENCE IN THE MENA REGION

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Background:

Aseptic technique is critical in Cellular Therapy Processing laboratories to ensure the safety, purity, and efficacy of cellular therapy products (CTPs). Hematopoietic stem cell products (HPSCs), used in bone marrow transplantation (BMT), are administered to immunocompromised patients who are highly vulnerable to infections. Even minimal microbial contamination can lead to severe complications, including sepsis, graft failure, and increased clinical interventions. Therefore, strict adherence to Good Manufacturing Practices (GMP) and contamination control is essential to protect patient outcomes and meet regulatory standards. Since the initiation of our BMT program in 2015, our facility has consistently maintained a 0% microbial contamination rate (bacteria and fungi) in CTPs sourced from apheresis or bone marrow harvest (BMH) and processed in a cGMP-compliant cleanroom. This study highlights the effectiveness of our comprehensive control measures implemented before, during, and after CTP processing.

Methods: Our control measures are based on Good Manufacturing Practices (GMP), JACIE standards, and our own expertise. Key measures include:

- **Access Control:** Prior authorization, controlled access, use of tacky mats and shoe covers, and limiting the number of staff in cleanrooms.
- **Personnel Hygiene:** Daily bathing, wearing clean clothes, and prohibiting smoking, makeup, nail polish, hair gel, body lotions, and accessories.

- **Personal Protective Equipment (PPE):** Use of sterile cleanroom garments.
- **Cleaning Protocols:** Regular cleaning of biosafety cabinet, processing devices and stations, with monthly deep cleaning by specialized personnel.

- **Environmental Monitoring:** Continuous surveillance of temperature, pressure, and humidity, scheduled AHU and HEPA filter changes, and monthly air sampling and particle counting.
- **Microbial Testing:** Staff finger dabs pre- and post-processing, strict aseptic techniques, and particle counting during processing.
- **Processing**: using close system under Grade A and by using strict aseptic techniques

A retrospective analysis of sterility testing was conducted on 1,603 samples, using BACTEC pediatric blood culture bottles at various stages of CTP processing. Cultures were monitored for 10 days for bacterial or fungal growth.

Results: Of the 1,603 samples analyzed, none tested positive for bacterial or fungal contamination, yielding an observed contamination rate of 0% (95% CI: 0–0.19%). Compared to the internal benchmark contamination rate of 2%, this result was highly significant (exact binomial test, $p < 0.0001$).

Conclusions: The stringent control and aseptic measures implemented at cGMP-CTL-DLMP-HMC have proven highly effective in preventing microbial contamination, achieving a 0% contamination rate compared to an internal benchmark of 2-3%. Our decade-long experience provides a reproducible model for other institutions aiming to improve safety in Cellular Therapy Processing, reduce infection risk, and optimize outcomes for immunocompromised patients undergoing BMT.

Disclosure: Nothing to declare

P360

REGULATORY MODELS FOR CAR-T CENTER QUALIFICATION IN ITALY AND SWITZERLAND: IMPLICATIONS FOR CLINICAL RESPONSIBILITIES AND QUALITY GOVERNANCE

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Background: The implementation of commercial CAR-T therapies requires transplant programs to fulfill specific authorization, quality and organizational requirements. Italy and Switzerland apply distinct frameworks regarding center qualification, JACIE accreditation,

GMP responsibilities and the role of national authorities. Misinterpretations—particularly concerning Swissmedic's scope and the status of JACIE in Switzerland—can significantly affect program design.

Methods: Comparative analysis of national documents:
• Italy: State-Regions Agreement 5/5/2021, AIFA provisions for commercial CAR-T, CNT requirements;
• Switzerland: Swissmedic regulations for cell manufacturing and handling activities, SBST criteria for center recognition, LAMal provisions for reimbursement;
• FACT–JACIE standards, 8th edition.
The analysis was supplemented with direct observations regarding the qualification of CAR-T centers and transplantation in the two contexts.

Results: Italy.
In Italy, for commercial CAR-T products, qualified centers must have regional authorization identifying the centers authorized for CAR-T reimbursement, possess CNT certification, JACIE accreditation for allogeneic transplantation (clinical unit, collection, processing), and availability of intensive care. The production and handling of commercial CAR-T is carried out exclusively by pharmaceutical companies holding AIC (Novartis, Gilead, BMS, J&J), which retain GMP responsibility for the process. Hospitals are qualified for clinical management, patient care, and complications, but not as GMP sites for collection and handling.
Italian legislation does not go into detail on the requirements for non-commercial CAR-T/IEC (academic trials, compassionate use), which are not limited to allogeneic JACIE accreditation, allowing greater regulatory flexibility for trials.
Switzerland.
Swissmedic does not require centers administering commercial CAR-T to have a full GMP license, as production remains industrial, similar to Italy. Swissmedic authorizations only come into play when a center performs activities defined as manufacturing steps.
The crucial difference compared to Italy concerns JACIE: in Switzerland, it is mandatory in practice, because LAMal reimbursement of transplant activities (including CAR-T as part of the same clinical-organizational pathway) requires the center to be recognized as a transplant program.
Recognition is verified by the SBST (Swiss Society for Stem Cell Transplantation), which checks compliance with JACIE requirements and communicates the center's suitability. Without this recognition, services are not reimbursable.
SBST and Swissmedic have completely separate roles: SBST is responsible for clinical quality and eligibility for reimbursement; Swissmedic is responsible for the regulation of medicines.

Conclusions: The two models differ on key aspects.
In Italy, there is a clear separation between industrial responsibility (company holding the AIC) and clinical responsibility (hospital center).
In Switzerland, on the other hand, the system structurally links the quality of programs (JACIE) to the reimbursement of services through LAMal, with SBST as the national control body.
Misinterpretations of Swissmedic's role and the nature of GMP requirements in Switzerland can lead to an overestimation of the regulatory obligations of clinical centers. A thorough understanding of the differences is essential for designing efficient CAR-T programs, clearly defining responsibilities, and harmonizing European quality models.

Disclosure: Nothing to declare.

P361

30 YEARS OF THE NHS CORD BANK - MAINTAINING A STABLE INVENTORY

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Background: The NHS Cord Bank has been operational since 1996 and will celebrate both it's 30th anniversary and the provision of 1000 cord blood transplants in 2026. More than 20,000 cords with diverse HLA types have been donated to the bank since it opened. The median number of years in storage for cords provided for transplant is just under 8 years and the oldest cord issued had been in storage for over 20 years. It is of utmost importance to maintain a stable inventory and to evidence this stability as part of an accreditation programme and to maintain the confidence of transplant centres. We are building the statistical model and will present the stability data from the NHS Cord Bank and the engraftment data for cords that have been transplanted.

Methods: Data was extracted from our laboratory management system and cleaned by statisticians. The data set comprised 938 records of cords issued between 1999 and 2023, which had been donated and banked between 1996 and 2021. To analyse outcomes, a dataset was built from single cord tranplants using days to neutrophil engraftment as the primary measure of engraftment. This data was obtained from the Eurocord data, providing the main cohort of cases and all clinical outcome variables.
The effect of cord age/time in storage on viability was assessed by considering the following quality variables:
CD34+ count ($\times 10^6$): pre-freeze and post-thaw
Percentage of Viable CD34+: pre-freeze and post-thaw
TNC ($\times 10^6$): pre-freeze and post-thaw

Results: The final cohort size was 880 after data cleaning with a median storage time of 4.6 years prior to transplant and a maximum storage time of 21.8 years. Preliminary analysis has shown no statistically significant decline in CD34+ viability or TNC post-thaw related to duration in storage. The statistical model is being refined to consider changes in CD34+ enumeration and the data will be re-evaluated for CD34+ counts. Looking at patient outcomes, no evidence of difference in time to engraftment or one-year overall survival was seen based on the age of the cord.

Conclusions: This work builds on an earlier analysis of the effect of time in storage on quality parameters with a larger cohort of transplanted cords and a longer median storage time as well as cords that had been in storage over 20 years. Our initial analysis of outcomes

related to duration of storage does not indicate any difference in time to engraftment. All cords undergo thorough release testing on post thaw samples prior to release to ensure that the requested dose for the patient is available as well as viability and potency.of the cord. Cords that do not meet the release criteria are very few in number but will be included in a further analysis to determine whether there is any relationship to duration of time in storage. Our results indicate that quality parameters are unaffected regardless of the time in stable, cryogenic storage and should not be a barrier to selection.

Disclosure: Nothing to declare

P362

DISPOSAL OF AUTOLOGOUS HEMATOPOIETIC STEM CELL ALIQUOTS: A REGULATORY AND ETHICAL ANALYSIS FROM THE SAN GIOVANNI ADDOLORATA PROCESSING FACILITY

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Background: The disposal of hematopoietic stem cell (HSC) products represents a critical but often overlooked phase within the lifecycle of Substances of Human Origin (SoHO). While regulatory and clinical attention traditionally focus on donor selection, collection, processing, cryopreservation, and infusion, the final step—safe, justified, and traceable disposal—has gained importance under EU Regulation 2024/1938. Disposal practices are regulated by EDQM guidelines, JACIE Standards, and the Italian CNT Guidelines, which define safety, traceability, and ethical requirements for human-derived materials. At the San Giovanni Addolorata Hospital, the transplant program serves adult patients affected by multiple myeloma, lymphomas, and acute myeloid leukemia, for whom stem cell collection and storage are integral to therapeutic pathways. In general, disposal may occur due to quality issues, loss of indication, incomplete traceability, container damage, or time-based criteria such as storage exceeding ten years. Although such thresholds exist, no time-based criterion was applied in this experience. Disposal was required only following the confirmed death of the patients.

Methods: An evaluation of disposal workflows was conducted at the SGA Processing Facility. The regulatory framework included EU Regulation 2024/1938, EDQM Guidelines, JACIE Standards and the Italian CNT Guidelines. Process mapping described each operational step from the decision to eliminate an aliquot to its final destruction, including documentation flows, biosafety procedures, authorization pathways, and record validation. An ethical assessment ensured responsible stewardship of human-derived material. A central methodological component was the use of the Regional Electronic Prescription Platform (SISMED), which enabled verification of patient vital status, retrieval of official death certificates, and the ability to trace patients who had been lost to follow-up after discharge, ensuring accurate long-term outcome confirmation. All disposal documentation, including

these certificates, was reviewed, verified, and formally validated by the Transplant Program Director and the Processing Facility Director, ensuring complete regulatory, ethical, and traceability compliance. SOPs, disposal records, biovigilance data, and staff interviews were analyzed to evaluate workflow adherence and training adequacy.

Results: in 2025 a total of 58 aliquots were eliminated, consisting of 30 stored internally and 28 stored externally at a contracted third-party facility. Disposal concerned material belonging exclusively to deceased patients. In every case, the only indication for disposal was the confirmed death of the patient; no time-based storage criterion, including thresholds beyond ten years, was applied. For each disposal event, documentation—including the death certificate—was verified and signed by the Transplant Program Director and the Processing Facility Director, guaranteeing appropriate authorization and complete traceability. Eliminating these aliquots resulted in a significant reduction in cryostorage burden, generating measurable savings in storage space and associated costs, particularly for externally stored material

Conclusions: In the SGA Transplant Program, disposal of HSC aliquots was required only due to patient death, underscoring the need for rigorous documentation, ethical oversight, and strict regulatory compliance. Adherence to EU Regulation 2024/1938, EDQM and JACIE standards, and the Italian CNT 2014 Guidelines, combined with regional information platforms such as SISMED capable of long-term patient tracing, ensures respectful, transparent, and justified disposal practices. Continuous monitoring promotes responsible stewardship and alignment with evolving European regulatory expectations.

Disclosure: Nothing to declare

P363

GLOBALIZING PSIRF

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Background: **What is PSIRF:** The Patient Safety Incident Response Framework (PSIRF) provides a structured approach to developing and maintaining effective systems and processes for responding to patient safety incidents, with the overarching goal of facilitating learning and driving continuous improvement in patient safety.
PSIRF was introduced by NHS England in August 2022 and implemented by The Cellular Therapy Program in March 2024.
Strategic Aims of PSIRF:
• Compassionate engagement and involvement of key staff members and patients affected by patient safety incident
• Proportionate responses to identify learning from patient safety incidents
• System-based approach to action plans and quality improvement following patient safety incidents

• Effective governance and oversight focused on strengthening response processes and systems

Methods: **PSIRF from the lens of SEIPS:** PSIRF uses SIEPS (System Engineering Initiative for Patient Safety) as a system-based approach from learning from patient safety incidents.
What does PSIRF involve:
Cultural change
Transition from the Serious Incident Framework, towards promoting a proportionate and learning focused approach to responding to patient safety incidents.
This shift has led to:
• Change in incident management systems
• Change in incident management processes and governance
• Policy update and staff training
• Change in communication, engagement and overall approach

Results: **Outcome of PSIRF Implementation**
• There has been an increase in the number of incidents reported since the introduction of PSIRF. This is viewed as a positive outcome, demonstrating that staff feel empowered to speak up when things go wrong or nearly go wrong
• Various learning responses have been implemented, leading to improvements in the program's systems, processes, and policies, with less emphasis on individual blame and more focus on systemic change.
• Confidence and satisfaction among our patient safety partners have increased, particularly due to the program's engagement with patients and next of kin (NoKs) involved in incidents. This includes fulfilling Duty of Candour obligations, providing timely feedback to queries and complaints, sharing findings from investigations, and outlining action plans to prevent recurrence.
• The quality strategy, aligned with the program's objectives, has contributed to improvements in patient safety, experience, treatment, and care. These enhancements have been driven by learning from incidents and near misses.

Conclusions: **Cellular Therapy Program Quality Strategy in-line with PSIRF:**
Quality Strategy 2026: To improve patients' health outcomes through continuous quality improvement.
Our objectives:
• Detect and review adverse events and risks across all program areas.
• Carry out system-wide learning by implementing quality improvement projects across the program.
• Implement effective actions derived from lessons learned across various quality domains.
• Monitor, evaluate, and refine processes to sustain improvements in patient safety and experience.
• Ensure adherence to established quality metrics and regulatory standards.
We aim to achieve this by:
• Maximising the utilisation of our resources (policies, processes, and systems) to support effective care delivery.
• Ensuring accountability for actions through an evidence-based approach.

• Driving continuous monitoring and improvement, supported by data-driven insights and analysis.

Disclosure: No conflict of interest.

P364

GAPP-PRO JOINT ACTION: LATEST UPDATE

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Background: The Joint Action *Piloting GAPP Model Approach for Assessing and Authorising Novel Substances of Human Origin Preparation Processes* (GAPP-PRO) was launched in February 2024 (https://gapp-pro.eu).
The GAPP-PRO Joint Action builds upon the previous European initiative GAPP, bringing together national Competent Authorities (CAs) and other stakeholders involved in the authorisation of preparation processes for Substances of Human Origin (SoHO).

Methods: A survey to collect updated information on SoHO preparation processes in Europe, categorised by different risk levels — including bedside preparations — was carried out. This survey was addressed to all European CAs.
In parallel, joint country and cross-country assessments are being conducted within pilot authorisation processes for different types of SoHO: blood, blood components, tissues, cells, reproductive cells, breast milk, and faecal microbiota. The main goal is to properly evaluate, through a set of indicators, the applicability of the GAPP methodology (https://www.gapp-ja.eu), which includes the application of a Preparation Process Dossier (PPD) as common approach.
In addition, interviews with the SoHO entities that prepared the PPDs, as well as with the experts and CAs involved in the evaluations, are planned to gather relevant insights for further consideration.

Results: The survey results will form the basis of the SoHO Preparation Compendium, which will be incorporated into the SoHO Platform as outlined in the Substance of Human Origin Regulation (Regulation (EU) 2024/1938).
The pilots using real PPDs, along with the indicators and interview findings, will support the evaluation and refinement of the GAPP methodology for different types of SoHO. The involvement of all relevant stakeholders will contribute not only to the validation of the tool, but also to the development of a harmonised procedure endorsed by both SoHO entities and CAs.
The new SoHO Regulation establishes that CAs must provide guidelines and templates for submitting applications for preparation process authorisation, as well as for designing clinical

outcome monitoring plans. The updated GAPP-PRO Guideline will be aligned with this new Regulation.

Conclusions: The GAPP-PRO Guideline will offer SoHO entities a standardised methodology for requesting authorisation of preparation processes, and provide CAs with a common framework for reviewing and approving these processes. This will enhance mutual recognition across the European Union.

Clinical Trial Registry: Not applicable.

Disclosure: No conflict of interest.

Psychological Issues

PSY4-3

A PROTOCOL FOR ASSESSING PSYCHOLOGICAL READINESS FOR HEMATOPOIETIC STEM CELL TRANSPLANT AND GENE THERAPY IN SICKLE CELL DISEASE

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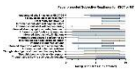
Background: Recent advances in hematopoietic stem cell transplant (HSCT) and gene therapy (GT) offer increasing access to transformative therapies for sickle cell disease (SCD). These treatments offer potential life-changing benefits but also carry psychological implications. Guidance on evaluating readiness for therapy is limited. We describe our protocol for evaluating patient readiness for HSCT and GT in pediatric SCD and report characteristics of a novel patient-reported questionnaire measuring self-appraisals of readiness.

Methods: Youth with SCD ages 8-24 years being considered for HSCT or GT completed a psychological evaluation consisting of a clinical interview and brief cognitive assessment. Patients also completed a 16-item readiness survey. Respondents used a visual analog scale (range=0-10) to rate self-perceptions of knowledge and readiness for BMT or GT, with higher scores reflecting greater subjective readiness.

Results: Fifteen patients were evaluated: the mean age was 14.64 years (SD=4.55) and 60% were female. Eight patients (53%) were evaluated for a nonmyeloablative HSCT, 6 (40%) for gene therapy, and 1 (7%) for a myeloablative HSCT. Evaluations occurred 0.10-5.07 months prior to treatment (M=1.88; SD=1.32) following a median of 3 consults with the transplant team (IQR = 2-4). All patients were diagnosed with HbSS and previously

treated with hydroxyurea. Mean IQ was 99.73 (SD=19.19).
The clinical assessment involved a semi-structured interview evaluating social, emotional, academic, medical, and family histories as well as patient knowledge of and expectations for the planned treatment. Questions spanned transplant logistics, treatment trajectory, potential complications, and medication, isolation, diet, and follow-up requirements, as well as personal experiences and past coping with medical symptoms, treatments, hospitalizations, and adherence. At the conclusion of each evaluation, patients and caregivers were provided information about the availability of psychological support and recommendations to enhance readiness. Recommendations were also relayed to the medical team to incorporate into treatment planning.
Internal consistency of the readiness survey was good (Cronbach's alpha=.84). The mean composite score on the readiness survey was 6.38 (SD=1.83, range 0-10). The two highest rated items included: "How ready do you feel for transplant?" (M=8.07, SD=2.55) and "How informed do you feel about the length of time you might be in the hospital for your transplant?" (M=7.93, SD=2.43). The two lowest rated items included: "How informed do you feel about the foods you can/cannot eat during or after transplant?" (M=4.53, SD=4.03) and "How informed do you feel about the problems that might come up during transplant?" (M=4.93, SD=3.56). IQ was not significantly correlated with perceived readiness or number of consults, but older age was correlated with subjective ratings of understanding of the reason for transplant and feeling in control of the decision to pursue treatment (r=.69, CI=.27-.89 and r=.72, CI=.33-.90, respectively).



Conclusions: Patient psychological readiness is a critical component of preparation for HSCT and GT and has the potential to meaningfully enhance treatment outcomes. We described a protocol for assessing readiness that could be replicated at other institutions and reported psychometric properties and results of a novel patient-reported readiness questionnaire. Such efforts hold promise for improving patient readiness for transformative therapies as access widens globally.

Disclosure: Nothing to declare.

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PSYCHOSOCIAL WELL-BEING IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (ALLO-HSCT) AND THEIR CAREGIVERS: A PROSPECTIVE STUDY

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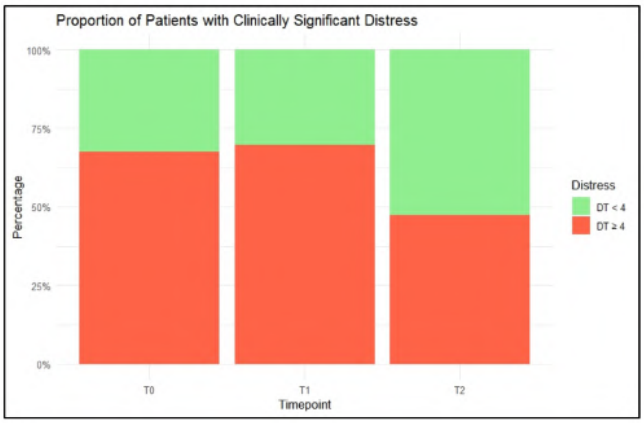
Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) can be curative for many hematologic malignancies but places a substantial psychological and emotional burden on patients and caregiver. This study assessed distress, quality of life (QoL), and unmet needs in allo-HSCT patients over 12 months using a variety of validated psychometric tools.

Methods: In this single-center, prospective study, between February 2020 and January 2024, 115 out of 143 screened patients were enrolled after meeting eligibility criteria, including informed consent, language comprehension, and absence of untreated psychiatric diseases. Assessment was performed at baseline (T0), 6 (T1), and 12 months after allo-HSCT (T2), using validated tools: Distress Thermometer (DT), Psychological Distress Inventory (PDI), Short Form Health Survey (SF-36), Needs Evaluation Questionnaire (NEQ), and the Family Strain Questionnaire–Short Form (FSQ-SF) for caregivers. The Psychosocial Assessment of Candidates for Transplantation (PACT) questionnaire was submitted at baseline. Repeated-measures and linear mixed-effects models were used to evaluate change over time.

Results: The median age at transplant was 56 years (IQR 48.5 -65.0), with a male-to-female ratio of 69:46. Acute Myeloid Leukemia was the most frequent diagnosis (57/115 patients, 50%), followed by Myelodysplastic Syndrome (14%), and Myelofibrosis (12%).Of the 115 enrolled patients', only 80 (70%) performed the PACT questionnaire following the initial psychological assessment. The median score was 38 (IQR 32 – 40); only 9% had a low PACT score (<29). Among them, 1 patient scored between 0-19, 2 patients between 20-24, and 6 patients between 25-29. At baseline, 67% of patients reported clinically significant distress (DT ≥ 4), increasing at 6 months (69%) and significantly decreased at 12 months (47%; p=0.0012) (Fig. 1A). PDI scores showed a similar pattern, peaking at 6 months (median: 31.4) and returning near baseline at 12 months (median: 28.5) (Fig. 1B). Female reported higher psychological distress than male at baseline (p=0.044) and 6 months (p=0.002), with the difference attenuating at 12 months.
SF-36 scores demonstrated significant improvements over time in multiple subscales, particularly between 6- and 12-months post-transplant. Notable improvements were observed in physical functioning (T0-T1 p=0.0014; T1-T2 p=0.0019), energy/fatigue (T0-T1 p=0.0007; T1-T2 p=0.0136), emotional well-being (T0-T1 and T1-T2 p=0.0382), social functioning (T1-T2 p=0.00015), pain (T1-T2 p=0.0289), and general health (T0-T1 p=0.011; T1-T2 p=0.0058).
Unmet needs assessed by NEQ were higher at 6 and 12 months than at baseline, especially regarding information clarity, future expectations, and communication with medical staff, with significant improvements over time in several items (adjusted p<0.01). Sex and age influenced perceived needs, with greater changes reported by female and younger patients (<48 years).
Regarding caregivers, moderate–high burden decries over time, while a small but persistent proportion experienced severe burden (Fig. 1C).

1A



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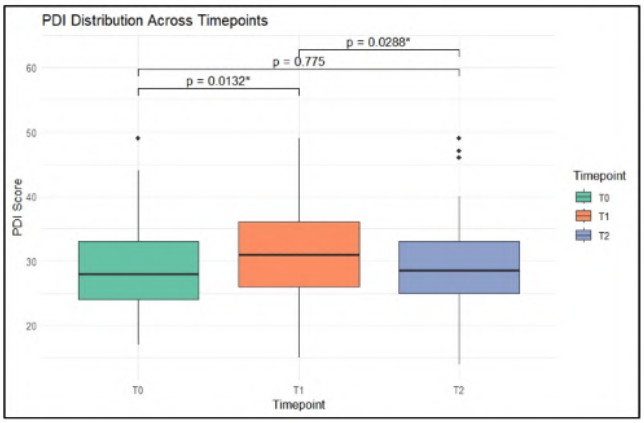

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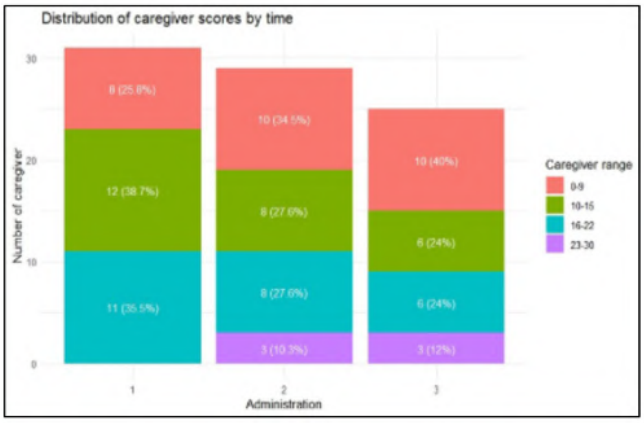

Conclusions: This study underscores the dynamic course of psychological distress in allo-HSCT patients, with a peak at 6 months post-transplant and declines by 12 months, alongside improvements in quality of life and unmet needs. Sex- and age-related differences support personalized, time-sensitive psychological care, and integrated longitudinal assessment, underscores the value of psycho-oncology services and caregiver support into HSCT care models, with the of improving clinical outcomes.

Disclosure: Nothing to declare.

P376

LEVEL 1 PSYCHOLOGICAL SKILLS TRAINING FOR HSCT STAFF

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Background: Psychological support within cancer care and HSCT services in the UK is currently understood in line with a four-level model (NICE, 2004), where support at Levels 1 and 2 is provided by healthcare professionals from a range of non-psychological professional backgrounds, and support at Levels 3 and 4 is provided by psychological specialists. Level 2 psychological skills training is widely recognised and delivered within the majority of cancer and HSCT services, with a clear consensus of what this training should cover and who should deliver it (Association of Clinical Psychologists UK, 2025). Level 1 training, on the other hand, is less developed, even though the majority of care in the aforementioned services is provided by level 1 professionals.

Methods: To address this gap, psychological specialists at Great Western Hospital have developed a half-day psychological skills package, which has been mapped against the ACCEND capabilities for the 'Supportive Workforce'. The training is provided by psychological specialists and covers:
1. Recognition of emotional distress (includes types of distress and the impact of this).
2. Responding to emotional distress (includes exploration strategies, trauma-informed care and onward referral).
3. Self-care.
Twenty-five members of staff, consisting mainly of staff nurses and healthcare assistants, have attended the training. At the end of each training session, attendees filled out an evaluation form, which enquired into the extent to which the training had been helpful and added confidence and skills in a variety of areas. Both qualitative and quantitative feedback was collected.

Results: Descriptive statistics indicated that the level 1 training increased attendees' confidence, knowledge and ability to support people with cancer who experience psychological distress. Most attendees (>82%) rated this increase at the highest possible level.
Further qualitative analysis identified 4 themes:
- '**Sufficiency of Training Conten**t': Training had met expectations and relevant comprehensive.
- '**Clinical Communication and Interpersonal Skills**': The training had improved emotional awareness and empathy for patients.
- '**Wellbeing, Emotional Awareness and Resilience**': Attendees had developed greater awareness of stress, boundaries and self-care.
- '**Applying Learning; Intentions, Challenges and Support'**. While the attendees stated that they had strong intentions to implement their learning from the training, they also identified barriers in the form of time and confidence.

Conclusions: This evaluation demonstrates the value of delivering a structured Level 1 psychological skills training package for HSCT clinical staff. Although the four-level psychological support model is well established, Level 1 training has remained underdeveloped for the workforce that provides most direct patient care. Findings from this pilot indicate that a brief, specialist-delivered programme can enhance staff confidence,

knowledge, and perceived capability in recognising and responding to distress. Quantitative feedback showed consistently high benefit, complemented by qualitative analysis which highlighted improved communication skills, greater emotional awareness, and increased recognition of the importance of self-care. Attendees also noted barriers to applying their learning, particularly limited time and confidence. These insights emphasise the need for organisational support and opportunities for ongoing skill consolidation. Overall, the training package offers a promising foundation for strengthening psychologically informed care across cancer and HSCT services.

Disclosure: None

P379

COMBINING VIRTUAL NATURE EXPOSURE AND HYPNOSIS TO IMPROVE QUALITY OF LIFE IN PATIENTS UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION: FEASIBILITY AND EFFICACY OUTCOMES

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Background: Hematopoietic cell transplantation (HCT) is widely used to treat hematological malignancies but is associated with substantial adverse effects, including a reduced quality of life (QoL) exacerbated by prolonged protective isolation. There is therefore an urgent need for tailored interventions to improve patients' psychosocial well-being and QoL immediately after transplant. Nature exposure is a promising approach to support well-being. Its effects are explained by attentional mechanisms: nature facilitates the restoration of attentional resources and promotes focus on positive elements. However, protective isolation prevents direct nature exposure.
In this context, we developed a virtual reality (VR) intervention that brings natural environments (forest, beach) into the hospital room through immersive audiovisual stimuli. Given the effects of nature exposure are mediated by attentional processes, we combine it with hypnosis, a technique aiming at enhancing focus on positive elements. Following a processual methodology for the development of non-pharmacological interventions, we conducted a feasibility study including patient recommendations.

Methods: Participants were offered autonomous use of the intervention for two weeks between from Day 7 to Day 21 (±3 days) after HCT. Frequency of use, cybersickness symptoms, and compliance were monitored. Semi-structured interviews were conducted in 8 users to explore patients' suggestions for improvement. The study also included a pilot evaluation of efficacy, assessing QoL before and after the intervention using the Functional Assessment of Cancer Therapy – Bone Marrow Transplantation (FACT-BMT). Secondary outcomes included self-reported pain, anxiodepressive symptoms, and fatigue.

Results: Among the 60 participants initially approached, 18 declined participation prior to effective inclusion, citing lack of interest in hypnosis, perceived complexity of VR, or absence

of perceived need for support. Ultimately, 42 participants were included (22 control, 20 experimental group). In the intervention group, 18 underwent allogeneic HCT and 2 autologous HCT. Feasibility outcomes revealed a relatively low retention rate (60%), heterogeneous use of the headset (1 to 7 sessions), and low cybersickness. Patient feedback highlighted a preference for supervised, time-limited sessions rather than autonomous use. The pilot efficacy analysis showed no significant change in QoL between pre- and post-intervention assessments.

Conclusions: Our work represents one of the first interventions for patients undergoing HCT developed using a structured framework for non-pharmacological interventions. The absence of significant effects of the intervention on QoL may be explained by feasibility factors, including low retention, variability in VR exposure, and autonomous use of the intervention. Based on those findings and participants recommendations, we revised the protocol to design a feasible randomized controlled trial aimed at evaluating the efficacy of this non-invasive and cost-effective intervention to preserve QoL in HCT patients. The inclusion of participants started on the November 1st, 2025. To date, 9 patients (5 control and 4 intervention; all allogeneic HCT) have been included and enrolled, and preliminary results from the first 20 patients will be presented at time of the conference.

Clinical Trial Registry: NCT06817759

Disclosure: Nothing to declare

P380

PIONEERING PSYCHOSOCIAL SUPPORT FOR BONE MARROW TRANSPLANT PATIENTS: A DESCRIPTIVE CROSS-SECTIONAL SURVEY STUDY AT ABU DHABI BONE MARROW TRANSPLANT PROGRAM, CENTER OF EXCELLENCE

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Background: Psychosocial support is increasingly recognized as a critical component of comprehensive care for individuals undergoing hematopoietic stem cell transplantation. Support groups provide structured environments for patients to share lived experiences, receive emotional validation, strengthen coping strategies, and reduce the isolation commonly associated with prolonged and intensive treatment. At Abu Dhabi Stem Cell Center (ADSCC) and Yas Clinic Khalifa City (YCKC), a pioneering in-person support group for bone marrow transplant (BMT) patients was developed to address these needs. Patients are introduced to the group during their first psychosocial consultation with the clinical social worker and are encouraged to continue participation throughout their treatment journey. The group convenes monthly for two hours, with the first hour dedicated to educational content and facilitated peer discussion, followed by a second hour centered on wellness-focused

activities such as yoga, sound healing, salon pampering, cake-decorating workshops, and vision-board exercises.
Given the novelty of this program within the United Arab Emirates where there are limited psychosocial support offering to BMT patients, objective of this study was to assess participant satisfaction with the current support group structure and to collect patient perspectives on potential areas for improvement.

Methods: A descriptive cross-sectional survey was conducted using an electronic questionnaire developed through Microsoft Forms. Confidentiality was ensured through fully anonymous response collection, with no names or email addresses recorded. The survey was administered in English, as all participants were fluent in the language. A four-point Likert scale was used for multiple-choice items, and an open-ended question was included to capture suggestions on how the support group could better meet patient needs. The survey assessed the extent to which the support group met participant's need, the appropriateness of the time allocated to educational speakers versus group discussion, and participant satisfaction with the activity component of the sessions.

Results: A total of 20 participants completed the survey, with ages ranging from 19 to 65 years. Overall satisfaction was high across all program components. Detailed results are presented in the table below. Qualitative feedback highlighted opportunities to enhance the program by incorporating hybrid (virtual + in-person) participation options, improving logistical arrangements, increasing caregiver involvement, and expanding wellness focused content activities.

Table 1: Participant Satisfaction with Support Group (N = 20)

Survey Question	Response Options	N (%)
How well do you feel the support group is meeting your needs?	Extremely satisfied	19 (95%)
	Somewhat satisfied	1 (5%)
How would you rate the breakdown of time spent with speakers vs. group discussion?	Sufficient time	19 (95%)
	Need more time in group discussion	1 (5%)
How satisfied have you been with the activity session?	Very satisfied	19 (95%)
	Dissatisfied	1 (5%)

Conclusions: This initiative represents the first in-person BMT support group program in the UAE. Findings demonstrate high levels of patient satisfaction and underscore the value of a multifaceted psychosocial support model for BMT patients. The program's success led to its adoption as a hospital-funded service, with dedicated financial and manpower resources allocated for expansion in 2026. Future studies should evaluate the cost-effectiveness of this intervention and its broader impact on patient quality of life and psychosocial outcomes.

Disclosure: Nothing to declare

P381

CHRONIC FATIGUE SYNDROME AND PSYCHOSOCIAL FACTORS IN ADULT PATIENTS BEFORE HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The relevance of this study is due to the high prevalence of chronic fatigue syndrome (CFS) in oncology practice and the need to identify key factors influencing its development and implementation effective rehabilitation programs. The aim of the study was to analyze the relationships between CFS severity and a number of psychological, demographic, and clinical parameters in cancer patients.

Methods: A single-center study was conducted from February to November 2025 at the Gorbacheva Research Institute of Oncology, Cancer Research, and Traumatology. Seventy-five cancer patients (37 women, 38 men) aged 19 to 68 years (mean 40.8, median 40.1) participated in the study before HSCT. The majority of patients were diagnosed with acute leukemia (n = 54, 72%), followed by chronic myeloid leukemia (n = 10, 13.3%), and other diagnoses (n = 11, 14.6%). The average disease duration in the sample was 24.5 months (median 11.5). At the time of the study, 52 patients were in remission from their underlying disease.
Structured questionnaires were used to collect data: the HADS (anxiety and depression) scale, the MMAS-8 to assess treatment adherence, and the FACIT-F questionnaire (severity of CFS). Clinical and anamnestic parameters were also recorded: duration of cancer treatment in months, body mass index (BMI), degree of protein-energy malnutrition (PEM), and the status of the underlying disease. Statistical analysis was performed using nonparametric Spearman correlation analysis (ρ). The level of statistical significance was set at $p < 0.05$.

Results: The study found that the mean CFS score for the sample was 124.5 points (median 127.1). We identified 56% (n=42) of subjects scored above the mean, while 44% (n=33) scored below. According to the FACIT-F questionnaire, the lower the score, the more severe the CFS, with the maximum score being 160 points. Correlation analysis revealed statistically significant moderate inverse relationships between the severity of chronic fatigue syndrome and psychological indicators: the higher the anxiety ($p < 0.001$) and depression ($p < 0.001$), the more severe the CFS. The relationship between CFS severity and treatment adherence (MMAS-8) was weak and did not reach statistical significance ($\rho = 0.205$, $p = 0.077$). None of the clinical and anamnestic parameters demonstrated a significant linear relationship with the severity of CFS.

Conclusions: The data obtained indicate the important role of the psychological component in the pathogenesis and clinical presentation of chronic fatigue syndrome in cancer patients. This highlights the need to include screening and treatment of anxiety and depressive disorders in comprehensive rehabilitation and maintenance therapy programs to reduce the severity of CFS. The results indicate a predominant association between chronic fatigue syndrome and the psychoemotional state of patients in this group of patients. The identified correlations confirm the importance of a bio-psycho-social approach in oncology and the need for multidisciplinary patient management.

Disclosure: Nothing to declare.

P382

CELL THERAPIES AND PSYCHOLOGICAL WELLBEING: ASSESSING IMPACTS AND IMPROVING SUPPORT IN THE UK

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Background: Cellular therapies are transformative treatments that offer hope to patients facing life-threatening conditions, but their psychological burden can be profound and pervasive. This study aimed to summarise the psychological impact and stressors patients and those close to them experience, identify any unmet needs and gaps in support provision in the UK, and understand policy interventions that could address these gaps.

Methods: We conducted a literature review of peer-reviewed journals and clinical guidelines from the last five years to understand what's already known about psychological needs and support in transplant care and gaps in UK service provision.
Using purposive sampling, we conducted semi-structured interviews with patients, caregivers, related stem cell donors and healthcare professionals about their experiences and priorities for psychological care. This was supplemented by previous survey results about patients' and carers' experiences of the financial impact of treatment and the support they were offered.
Data was coded using a thematic analysis. Emerging themes were clarified through discussion with the research team and a lived experience focus group.

Results: In total, we spoke to eight patients and carers, three stem cell donors and five healthcare professionals. Additionally, we received 48 survey responses and reviewed 40 research articles.
Patients reported feelings of anxiety, depression and PTSD, as well as struggling with their identity and social relationships throughout treatment and recovery. These effects could by exacerbated by long periods of protective isolation, the financial burden of illness and treatment, uncertainty about outcomes and relapse, and disruption to family and social lives. Children may also miss out on developmental and social milestones.
Family members and carers are also negatively impacted, reporting stress, fatigue and anticipatory grief. Financial strain and separation from other children and family members,

particularly for parents, were common stressors for poor mental health in carers.
Finally, experiences of family and sibling donors can vary greatly, with some feeling pride and gratitude, while others can feel anxiety and fear, a responsibility to donate, and guilt about unsuccessful outcomes.
While there are examples of excellent care, access to specialist psychological support is inconsistent across the UK. Participants reported that mental wellbeing support is treated as optional throughout the treatment pathway, with the biggest gaps existing in support for patients with non-malignant indications, for family members, family donors and carers, and for outpatients during post-transplant care.

Conclusions: This study reflects the intense, all-encompassing impact cell therapy can have on patients and loved ones.
Our results suggest that embedding specialist psychologists into multi-disciplinary teams can offer a lifeline to patients in their treatment journey and that, in the absence of specialist support, all patient-facing staff should be adequately trained to spot the signs of poor mental health and take appropriate action to secure support for the patient. Psychosocial support should also be extended to families and family donors.
By investing into workforce training and specialist psychologist roles, and integrating psychological care into long-term follow-up, the UK can lead the way in creating a truly holistic model of care for cell therapy patients and their families.

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P383

PSYCHOLOGICAL RISKS AND SUPPORT NEEDS IN HSCT: PILOT STUDY FINDINGS

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Background: Hematopoietic stem cell transplantation (HSCT) is the only curative option for many severe oncological, hematological, and immunological diseases. However, it is an extremely aggressive procedure with significant toxicity, prolonged isolation, and demanding recovery. Most patients reach HSCT after multiple relapses, already experiencing physical and psychological strain. Under these conditions, assessing anxiety and adjustment disorders becomes critical for maintaining treatment adherence and improving outcomes.

Methods: The pilot phase of the project to develop and implement a method for the medical prevention of anxiety and adaptation disorders (F41, F43) in patients undergoing

hematopoietic stem cell transplantation was conducted at the Transplantation Department of the Republican Scientific and Practical Center for Pediatric Oncology, Hematology, and Immunology in close collaboration with specialists from the Republican Scientific and Practical Center for Mental Health. Clinical-psychopathological, clinical-biographical, experimental-psychological, and statistical research methods were used.

Results: In 2024-2025, the pilot project involved 43 transplant patients (26 boys, 17 girls) aged 3 to 27 years (median age 12.7 years) with cancer (neuroblastoma), oncohematological (acute lymphoblastic leukemia, acute myeloid leukemia, acquired aplastic anemia, anaplastic large cell lymphoma), hematological (myelodysplastic syndrome, Blackfan-Diamond anemia), and immunological (primary immunodeficiency) diseases, as well as the legal representatives of minor patients. To ensure an accurate comparison between the clinical and psychological studies, the patients were divided into three age subgroups: 3 to 7 years (9 patients), 8 to 17 years (26 patients), and 18 to 35 years (8 patients). To assess distress severity in patients before and after HSCT, the NCCN Distress Thermometer was administered. Symptom severity in patients before and after HSCT was evaluated using the Children's HSCT Symptom Questionnaire. Depression severity was assessed using the Children's Depression Questionnaire. A visual analog scale (VAS) was used to evaluate pain intensity before and after HSCT. Changes in quality-of-life indicators were assessed using the PedsQL 4.0 questionnaire.
Based on the analysis of these tests, data confirmed that severe distress in patients is a risk factor for reduced treatment adherence. Uncorrected distress during HSCT procedures is an additional risk factor for anxiety and adjustment disorders.
It was also shown that most parents of patients lack coping strategies to support their children during HSCT; intolerance of uncertainty (fear of death and loss of a child) is closely associated with anxiety symptoms and helplessness. The primary concern is the uncertain prognosis for survival after HSCT and the overall course of the disease.

Conclusions: These results demonstrate a high incidence of distress and adaptation disorders in patients undergoing HSCT and their immediate families. These conditions have a significant impact on treatment adherence and overall quality of life. The need for early psychoprophylactic intervention aimed at correcting anxiety disorders and supporting patients' families has been identified. The development and implementation of psychological support programs are essential for improving the effectiveness of comprehensive transplant care.

Disclosure: Nothing to declare.

P384

ASSESSING PSYCHOSOCIAL NEEDS OF RELATED STEM CELL DONORS: STAFF PERSPECTIVES FROM A UK REGIONAL STEM CELL CENTRE

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Background: Related stem cell donors may experience complex psychosocial and relational pressure; psychosocial wellbeing is critical to safe and effective donation. While psychological assessment is well established in UK renal living donor pathways, practice within stem cell donor assessment is less clearly defined.
Aim: To establish a baseline understanding of current practice, staff confidence, and perceived need for psychology input when assessing and supporting the psychosocial needs of related stem cell donors within a UK regional centre.

Methods: An exploratory online survey was distributed to medical staff involved in related donor assessment over a one-month period. Questions focused on current psychosocial assessment practices, confidence in identifying risk, and views on additional psychological support.

Results: Three responses were received. Psychosocial concerns were recognised and in some cases acted upon, including declining donation on mental health or relational grounds. However, approaches varied and largely relied on individual clinical judgement rather than structured tools or agreed pathways. Respondents expressed an appetite for clearer guidance, training, and enhanced access to specialist psychology support to enhance consistency, confidence and care.

Conclusions: This small scoping exercise suggests that psychosocial assessment of related donors is occurring but variable, with staff interest in strengthening psychosocial support. Aligning practice more closely with established UK renal living donor psychology guidance may support staff, improve consistency, and strengthen donor-centred care. Planned developments include targeted training, practical resource materials, and a psychological advice or consultation pathway. Future developments include exploration of donors psychosocial needs and experiences, and the donor-recipient dyad.

Disclosure: No conflicts of interest.

Pharmacology

Pharm2-2

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ENABLING MODEL INFORMED PRECISION DOSING OF BUSULFAN IN HSCT PATIENTS: AN EXTERNAL MODEL EVALUATION

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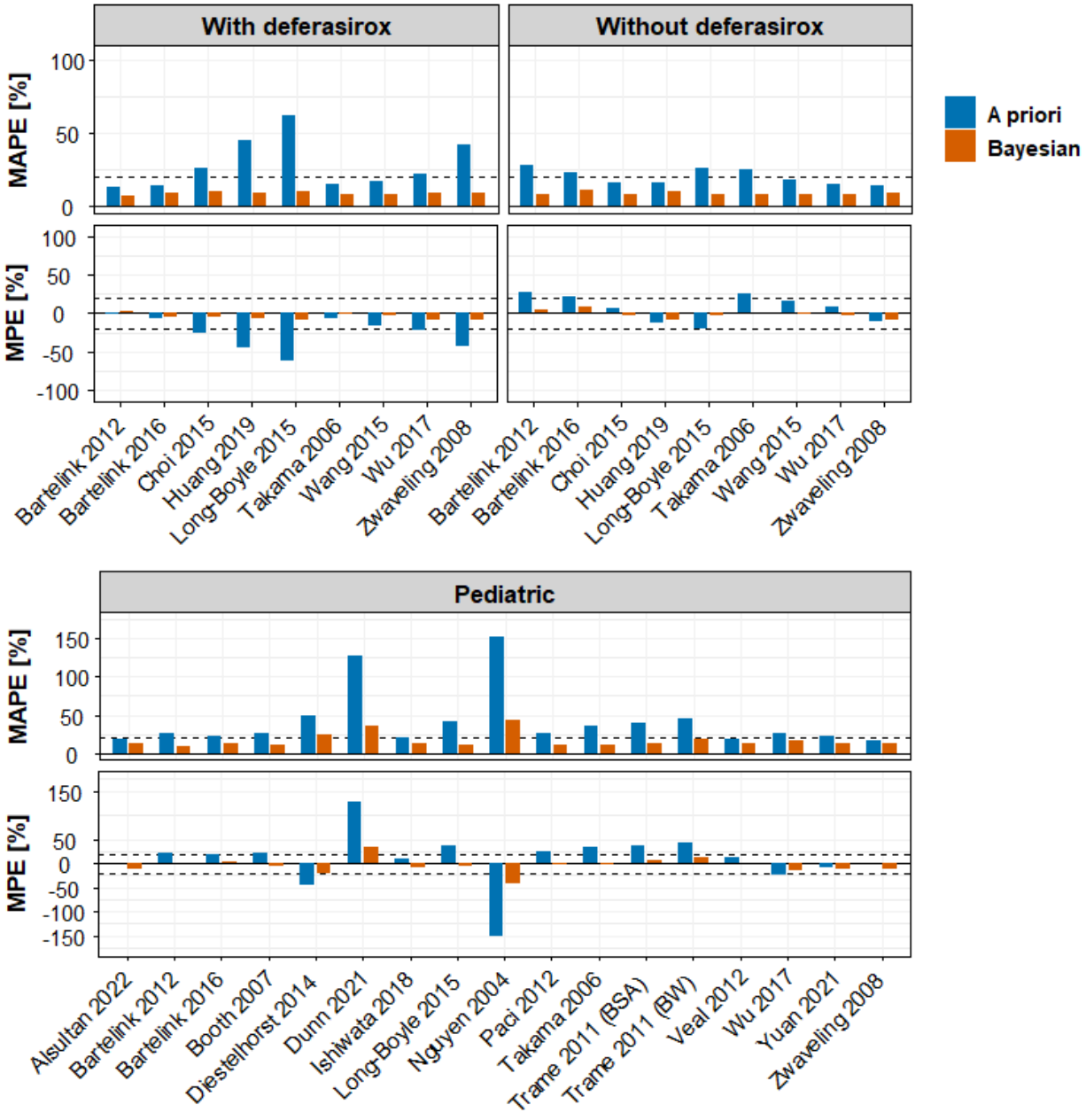
Background: Busulfan is commonly used in conditioning regimens prior to allogeneic hematopoietic stem cell transplantation (allo-HSCT), however its narrow therapeutic index and high interindividual variability in patient pharmacokinetics (PK) presents clinical challenges [Seydoux et al., 2022]. The need to balance adequate busulfan exposure with the risk of toxicity has motivated progress in the adoption of therapeutic drug monitoring (TDM) for busulfan [Domingos et al., 2024; Palmer et al., 2016]. Model informed precision dosing (MIPD) leverages a mathematical model and statistical framework to integrate patient data to precisely estimate individual PK profiles and is therefore recognized as gold standard for calculating a personalized busulfan dose [Shukla et al., 2020]. However, to reliably implement a MIPD workflow, a robust external evaluation of existing population pharmacokinetic (popPK) models is necessitated. The aim of the present study was thus to assess individual model performance in both pediatric and adult patients. Additionally, model performance was compared in adults with and without deferasirox co-medication, an iron chelator indicated to decrease busulfan clearance, to identify best performing models in distinct patient subpopulations [Essmann et al, 2022].

Methods: Retrospectively collected, anonymized PK data from 419 allo-HSCT patients (81 pediatric, 338 adult) with deferasiox co-medication administered in 101 adult patients. A total of 23 published popPK models were processed in NONMEM® (version 7.5) to perform an external model evaluation. Model performance was stratified according to patient population (adult vs. pediatric) and deferasirox co-medication. Models were applied according to the population age group for which they were originally developed. Performance was assessed using *a priori* prediction of the first dosing interval and Bayesian forecasting of the second dose based on prior observations collected during TDM. PK data for a second dose were available for 246 patients. Evaluation metrics included median absolute prediction error (MAPE) and median prediction error (MPE).

Results: The models evaluated in our study varied considerably in their predictive performance in the *a priori* scenario. Bayesian forecasting substantially improved predictive performance, yielding MPE or MAPE values within ±20%, with the exception of two models for the pediatric subpopulation. Within adult patients, the deferasirox co-medication showed an effect on predictive performance in the *a priori* scenario, where the presence of the comedication resulted in predominantly underpredictions (MPE: -62.4 to 1.24%; MAPE: 12.97 to 62.4), compared to the non-deferasirox subgroup (MPE: -19.4 to 27.6%; MAPE: 14.1 to 27.8%). For children, *a priori* predictions varied more notably (MPE: -151.1 to 128.0%; MAPE: 16.5 to 151.1%).
Bayesian forecasting yielded higher accuracy and precision for adult patients with deferasirox co-medication (MPE: -8.36 to 2.71%; MAPE: 7.03 to 10.5%) and in those without the co-medication (MPE: -9.0 to 8.57%; MAPE: 7.73 to 10.9%). Performance was also improved for

children (MPE: -42.2 to 35.0%; MAPE: 9.53 to 42.5%).



Conclusions: Several models demonstrated acceptable model performance overall. As expected, *a priori* predictions were less adequate in the deferasirox co-medication subgroup; however, Bayesian forecasting minimized the impact, potentially attributed to disparities in subgroup sizes. Reliable MIPD implementation necessitates further model evaluations and a popPK model incorporating the effect of deferasirox.

Disclosure: Nothing to delcare.

Pharm2-3

HIGHER INFLIXIMAB EXPOSURE IS ASSOCIATED WITH IMPROVED RESPONSE IN PEDIATRIC STEROID-REFRACTORY GRAFT-VERSUS-HOST DISEASE: DO WE NEED THERAPEUTIC DRUG MONITORING?

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Background: Steroid-refractory acute graft-versus-host disease (SR-aGvHD) after allogeneic hematopoietic stem cell transplantation (HSCT) is associated with considerable morbidity and mortality. Infliximab (IFX), a monoclonal antibody directed against tumor necrosis factor alpha, is a widely used off-label therapeutic option in SR-aGvHD. This study aims to evaluate the impact of IFX exposure on remission and survival of SR-aGvHD in a pediatric HSCT population.

Methods: This retrospective dual-center cohort study included consecutive children treated with IFX for grade II-IV SR-aGvHD between November 2012 and May 2024. IFX was initiated as standard of care according to national guidelines at 10mg/kg intravenously once weekly. Trough levels were routinely obtained and used to adjust dosing or skip administrations. For this study, IFX exposure (area under the curve; AUC) per patient was estimated using all measured concentrations and a pediatric population pharmacokinetic (popPK) model for IFX. To minimize bias in estimating the true effect of IFX, exposure was restricted to the first 28 days ($AUC_{0\text{-}28}$). The primary outcome was overall response rate (ORR; any improvement in GvHD severity) at day 28. Secondary outcomes were overall survival (OS) and event-free survival (EFS). Cox proportional hazard models and Fine-Gray competing risk analyses were used.

Results: Forty-one patients (19 female, 46.3%) with a median age at HSCT of 8 years (IQR 3.0-11.5) were included. Median follow-up among survivors was 76.5 months (IQR 45-109.3). Malignancy was the most common HSCT indication (19/41, 46.3%). Median time from HSCT to aGvHD and to IFX initiation was 33 days (IQR 25-49) and 45 days (IQR 35-102), respectively. In total, 205 IFX concentrations were available (median 3 per patient); with a median IFX $AUC_{0\text{-}28}$ of 2387 mg*days/L (IQR 1577-3143).
Twenty-five of 41 patients (61%) achieved OR by day 28, with a median time to response of 14 days (IQR 10-18.5). Although, evaluation of the log relative hazard (log HR) against $AUC_{0\text{-}28}$ showed that an $AUC_{0\text{-}28}$>2400 mg*day/L was not associated with higher response rates (figure 1a) in univariable analysis (p=0.12, figure 1b), a significant association was observed in multivariable analysis (log HR 1.015, 95% confidence interval [CI] 1.0033-1.028 for every 100 units in $AUC_{0\text{-}28}$, p=0.013). Higher IFX exposure was also associated with improved overall survival (log HR 0.93; 95%CI 0.87-0.99 for every 100 units in AUC,

p=0.036), and improved EFS (log HR 0.27, 95%CI 0.088-0.85, p=0.025 for those with AUC >2400 mg*day/L).

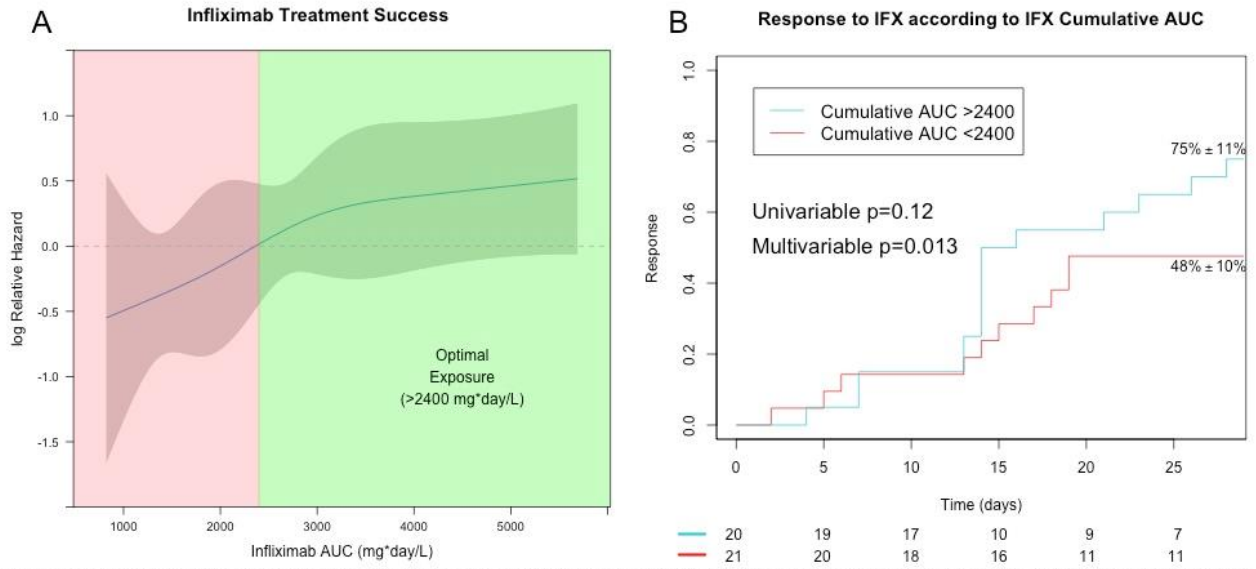

Figure 1: Panel A: Log-relative hazard for overall response rate for acute graft-versus-host-disease plotted against the area under the curve for infliximab from 0-28 days, demonstrating a positive hazard ratio with AUC 0-28 above 2400 mg*day/L. Panel B: Cumulative incidence curve of overall response rate within 28 days after startof infliximab in those with an area under the curve for infliximab from 0-28 days under and over 2400 mg*day/L.

Conclusions: This study suggests that higher IFX exposure is associated with better GvHD response, as well as improved EFS and OS in children with SR-aGvHD, within the first 28 days. These findings support a potential role for therapeutic drug monitoring (TDM) to optimize IFX AUC dosing in this population. Future prospective trials comparing TDM-guided dosing with standard care are needed to confirm these observations.

Disclosure: Nothing to declare

Pharm2-4

EVALUATING THE EXPOSURE-RESPONSE AND EXPOSURE-TOXICITY RELATIONSHIP OF RUXOLITINIB IN STEROID-REFRACTORY ACUTE GRAFT-VERSUS-HOST DISEASE

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Background: One of the leading causes of morbidity and mortality following allogeneic hematopoietic stem cell transplantation (HSCT) is steroid-refractory acute graft-versus-host disease (SR-aGVHD). High-dose steroids are the mainstay of treatment for GVHD; which makes SR-aGVHD life-threatening. Ruxolitinib, a Janus Kinase (JAK) inhibitor, is a critical second-line therapeutic agent for the management of SR-aGVHD, especially in a country like India, where there is limited access to advanced cellular therapies. There are certain

limitations such as baseline cytopenia, variability in patients' plasma concentration and concomitant use of azole antifungal drugs causing drug-drug interactions, may influence therapeutic outcomes in HSCT patients. Thus, this study was planned to evaluate the relationship between the plasma concentration of ruxolitinib with its clinical response and toxicity in patients with SR-aGVHD.

Methods: This was a prospective and observational study conducted at a tertiary care hospital with HSCT centre over a duration of three years. Adult patients aged 18 years or above with grade II-IV SR-aGVHD, being treated with ruxolitinib were included. The drug dose was 5-10 mg 12 hourly. Dose was modified based on drug-drug interactions and cytopenia. Liquid chromatography-mass spectrometry assays were done on days 7, 14 and 28 to measure the steady-state trough plasma concentration of drug. The primary endpoint was overall response rate (ORR) at day 28. The secondary endpoints included incidence of grade ≥3 haematologic toxicities (thrombocytopenia, neutropenia) and incidence of documented infections as well as non-relapse mortality (NRM) and overall survival (OS) at six months. For analysis, patients were categorised based on ruxolitinib trough concentration. Mann-Whitney U test and Fisher's exact test was used for group comparisons. Kaplan-Meier survival analysis was used for estimation of OS and NRM. Factors associated with overall response were identified using multivariate logistic regression models. P-value < 0.05 was considered significant statistically.

Results: Total 86 patients were included in the study. The mean age of participants was 37.53 ± 4.86 years. 63.41% patients had grade III-IV aGVHD. 76.32% patients were on concomitant azole antifungal. The median tough concentration of ruxolitinib was 57.8 ng/mL. The ORR at day-28 was 65.53%, with 33.26% patients showing complete response. Patients with higher trough concentrations (> 70 ng/mL) had significantly higher ORR compared to those with trough concentrations below 70 ng/mL (78.13% vs 53.09%, P = 0.01). Similarly, the incidence of grade ≥ 3 thrombocytopenia was more in higher exposure patients as compared to lower exposure group (28.18% vs 13.96%, P = 0.03). Overall, incidence of infection was 25.69%, the most common being viral infections (56.41%). OS at six months was 59.85% and NRM was 24.69%.

Conclusions: Thus, higher plasma concentration of ruxolitinib showed improved response rates in patients with SR-aGVHD; but also increased incidence of hematologic toxicities. Individualised dose regimens and therapeutic drug monitoring can help optimize ruxolitinib therapy by minimizing drug-drug interactions and incidence of cytopenia in susceptible patients.

Disclosure: There is no conflict of interest to declare.

P385

OPEN WIDE: EXPLORING SALIVA AS A NON-INVASIVE TOOL FOR POSACONAZOLE LEVELS IN CHILDREN

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Background: Therapeutic drug monitoring (TDM) is essential for optimising triazole antifungal therapy in immunocompromised children. Frequent blood sampling, however, is invasive and distressing, particularly for children undergoing intensive cancer treatment or haematopoietic cell transplantation (HCT). Non-invasive TDM methods, such as saliva sampling, offer a promising alternative due to ease of collection and suitability for home use. Emerging evidence supports salivary monitoring for agents such as voriconazole, but there are no published data for posaconazole despite its increasing use in children. This study aimed to determine whether posaconazole can be reliably detected in the saliva of paediatric oncology and HCT patients.

Methods: We conducted a 2-year prospective pharmacokinetic study (2023 to 2025) at The Royal Children's Hospital Melbourne. Children aged 1 to <18 years receiving posaconazole during inpatient care were eligible; those with oral mucositis, bleeding, or infection were excluded. Paired posaconazole serum levels at steady-state (5 to 7 days after initiation) and unstimulated saliva samples were collected within 15 minutes of each other using both an oral synthetic swab and passive drool (0.5–2 mL, Salimetrics®). Samples were analysed via ultra-performance liquid chromatography–tandem mass spectrometry in positive electrospray ionisation mode. Ethics approval was obtained (HREC 81867).

Results: Ten children (median age 14.1 years, range 8.1–17.8) were enrolled. A median of two serum (range 2–5) and two saliva (range 2–5) samples per child were collected, with a median sampling interval of 5 minutes (range 0–10). Posaconazole concentrations were undetectable (<0.05 mg/L) in 25/26 (96%) saliva samples, despite majority of the samples reported as therapeutic (median 1.4 mg/L, range 0.1–5.0). Only one saliva sample had detectable posaconazole (0.06 mg/L) with a paired serum concentration of 5.0 mg/L. Correlation between plasma and saliva concentrations could not be calculated.

Conclusions: This is the first prospective study assessing salivary detection of posaconazole in children. Our findings indicate that saliva sampling is unsuitable for posaconazole TDM in immunocompromised children. The minimal detection is possibly related to its high protein binding (>98%) similar to itraconazole and in contrast to voriconazole (~58%) and fluconazole (~10%), which have demonstrated reliable salivary penetration. Future work should focus on agents with proven salivary penetration, such as fluconazole and voriconazole, to reduce the burden of invasive sampling in this population.

Clinical Trial Registry: NA

Disclosure: Nil to disclose

P386

ANTIFUNGAL PROPHYLAXIS PATTERNS AND INVASIVE FUNGAL INFECTIONS OUTCOMES IN PAEDIATRIC ALLOGENIC HCT: A MULTICENTRE COHORT STUDY

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Background: Invasive fungal infections (IFIs) remain a significant complication after paediatric haematopoietic stem cell transplant (HCT). Evidence guiding antifungal prophylaxis selection in children is limited, particularly regarding the most appropriate mould-active strategies for children who develop IFI early post HCT. This study aimed to determine antifungal prophylaxis use and associated IFI incidence across a multicentre paediatric HCT cohort.

Methods: We conducted a retrospective review of children undergoing first allogenic HCT at two large Australian HCT centres; The Royal Children's Hospital (RCH) and Perth Children's Hospital (PCH) between 2016 and 2022. Patients who received a second HCT were excluded. Antifungal prophylaxis use was divided into two time periods based on the timing of engraftment; a pre-engraftment period (start of conditioning to Day 30) and a post-engraftment period (Day 31–100). Choice of antifungal prophylaxis was classified as non–mould-active (fluconazole), mould-active (including micafungin, liposomal amphotericin B, voriconazole and posaconazole), or mixed (both non-mould active and mould active agents). Clinical data obtained included patient demographics, transplant indication, donor type, antifungal stop date, and development of IFI defined as; proven, probable or possible IFI.

Results: A total of 239 allogeneic HCT episodes were analysed (RCH 84%; PCH 16%). Median age at day 0 was 6.9 years (IQR 3.1–12.8), and 59% of patients were male. Twenty-five patients had a history of IFI prior to HCT (10.5%); these children were older (11.5 vs 6.7 years) and more often had malignant disease (72% vs 57%), particularly AML (61% vs 29%) compared to children without a history of IFI pre-HCT. Donor types were similar between both groups.
Among children without prior-IFI pre-HCT, pre-engraftment antifungal prophylaxis used most frequently was fluconazole in 71.96% (154/214), with mould-active agents used in 21.96% (47/214) and mixed regimens in 6.07% (13/214). Children with prior-IFI pre-HCT were more likely to receive secondary prophylaxis with a mould-active agent in 60% (15/25) and fluconazole was rarely prescribed alone (2/25, 8%).
Regarding post-engraftment prophylaxis, fluconazole remained the most common in the no prior-IFI pre-HCT group (96/214, 44.85%), with mould-active (62/214, 28.97%) and mixed regimens (56/214, 26.16%) also used. Prior-IFI pre-HCT patients continued to favour mould-active (16/25, 64%) and mixed prophylaxis regimens (6/25, 24%).
IFI incidence overall occurred infrequently, in 10.46% (2+23/25+214) of the total cohort. IFI incidence was lower (2/25, 8%) in children with prior-IFI pre-HCT, compared to (23/214, 10.75%) in those with no history of IFI pre-HCT. All IFIs in prior-IFI pre-HCT patients occurred pre-engraftment (1 probable and 1 possible).
In children without prior-IFI pre-HCT, IFIs occurred more frequently in the post-engraftment

period (14/23, 60.9%) compared to pre-engraftment (9/23, 39.1%). Importantly, all proven IFIs (2/2) occurred on fluconazole monotherapy. Probable IFIs (9/23, 39.1%) occurred across fluconazole monotherapy, mould-active and mixed regimens.

Conclusions: Antifungal prophylaxis in paediatric allogenic HCT was strongly risk-adapted, with increased mould-active use in patients with prior history of IFI. IFIs occurred across all prophylaxis strategies, with all proven IFIs occurring in patients on fluconazole monotherapy. Most IFIs arose post-engraftment, highlighting the need for consistent, risk-based escalation to mould-active prophylaxis in immunosuppressed children.

Disclosure: Nothing to declare

P387

A UK RETROSPECTIVE ANALYSIS OF THE USE OF BELUMOSUDIL IN THE MANAGEMENT OF CHRONIC GRAFT VERSUS HOST DISEASE

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Background: Chronic Graft versus Host Disease (cGvHD) is the leading cause of late morbidity and mortality following allogeneic stem cell transplantation. Belumosudil is licensed in the UK for the treatment of cGvhD after two or more systemic treatments. This study retrospectively assessed the delivery of Belumosudil and the available outcome data.

Methods: All UK allograft centres were invited to submit data to the UKBMT Pharmacists Group. All patients commenced on Belumosudil from July or December 2023 in Scotland, England or Wales were included, according to Scottish Medicines Consortium and NICE approvals respectively.

Results: 179 patients were included from 10 UK centres during the study period (June to November 2025 dates). Table 1 shows baseline data and prior treatments delivered.
129 (72%) of patients received Belumosudil 200mg once a day, where 20 (16%) received concomitant PPI. In contrast, 94% (46) of the 49 patients who received Belumosudil twice a day received PPI.

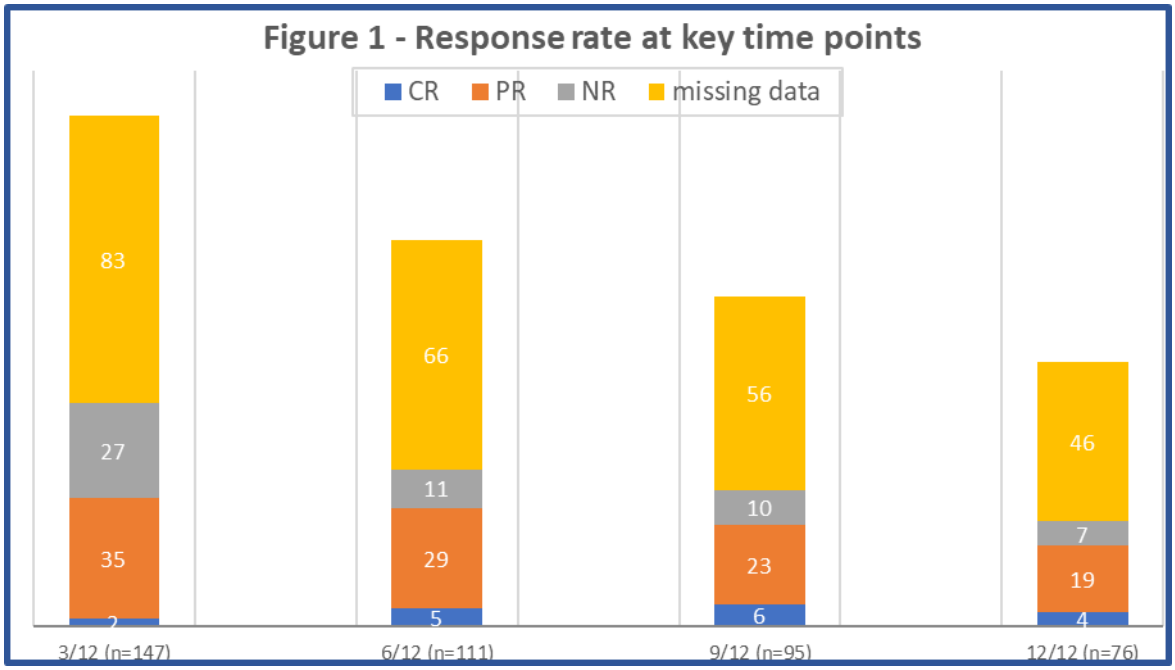
Table 1	n=179 (%)
Gender	
Male	112 (63%)
Female	67 (37%)

Transplant Intensity	
Reduced Intensity Conditioning (RIC)	104 (58%)
Myeloablative Conditioning (MAC)	73 (41%)
Data unavailable	2 (1%)
Previous acute GvHD	
Yes	127 (71%)
No	44 (25%)
Data unavailable	8 (4%)
Chronic GvHD grade at start of belumosudil treatment	
Mild	7 (4%)
Moderate	60 (34%)
Severe	67 (37%)
Data unavailable	45 (25%)
Number of organs involved at baseline	
1 organ	44 (25%)
2 organs	57 (32%)
3 organs	38 (21%)
4 organs	25 (14%)
5 organs	9 (5%)
6 or more organs	4 (2%)
Data unavailable	2 (1%)
Number of lines of prior therapy	
2 Lines	72 (40%)
3 Lines	61 (34%)
4 Lines	22 (12%)
5 Lines	15 (8%)
6^{+} Lines	7 (4%)
Data unavailable	2 (1%)
Therapies exposed to prior to initiation of belumosudil	
Steroids	166 (93%)
Calcineurin inhibitor	81 (45%)
Extracorporeal Photopheresis (ECP)	109 (61%)
Ruxolitinib	46 (26%)
Imatinib	18 (10%)
Mycophenolate Mofetil	53 (30%)
Rituximab	4 (2%)
Sirolimus/ mTOR inhibitor	7 (4%)
Etanercept	4 (2%)
Other	27 (15%)
Data unavailable	2 (1%)
Dose of belumosudil (n=179)	
200mg OD	129 (72%)

Concomitant PPI	20 (16%)
Not on PPI	84 (65%)
Data unavailable	25 (19%)
200mg BD	49 (27%)
Concomitant PPI	46 (94%)
Not on PPI	2 (4%)
Data unavailable	1 (2%)

149 patients had received Belumosudil for at least 3 months to permit assessment of response. After excluding patients with missing NIH response data (n=71), the best overall response rates were as follows (n=78): CR = 9 patients (11.5%), PR = 45 patients (57.7%) and NR = 24 patients (30.8%). Response rates at specific time points are presented in figure 1.

Lee Symptom scoring was only undertaken in 3 centres and both baseline and follow-up scores were only available for 19 patients in total. 12/19 patients (63.2%) reported a clinically significant improvement in Lee symptom score (defined as a reduction in total score of at least 7 points) at some point during belumosudil treatment. When comparing baseline scores with scores at last follow-up, 7/19 patients (36.8%) reported an improvement.



Steroid reduction is an important measure of treatment efficacy. 92 (51%) patients were in receipt of steroids when starting belumosudil (33 (18%) unknown). Data recorded at 90 days for 58 of these patients shows 40 reduced their steroid dose (12 fully tapered) within 90 days. Of the 42 patients still taking belumosudil at 6 months 28 (67%) had decreased steroid doses where a further 10 (24%) tapered fully.

Belumosudil was stopped in 64 (36%) of patients over the course of the study. 5 patients

(8%) had a complete response in their cGvHD. 14 (22%) had progressive cGvHD, 15 (23%) stopped due to adverse effects, and 23 (36%) stopped due to death. 3 (5%) patients chose to stop belumosudil (3 (3%) unknown). Adverse effects included hepatotoxicity (5, 33%), Oedema (2, 13%), CNS related (4, 27%), other 4 (27%).

Conclusions: This study highlights the challenges in reporting and collecting real-world data retrospectively for cGvHD, where there can be significant missing data in response criteria and patient reported outcome measures. Where data was available, the combined overall response rate of 69.2% is comparable to that reported in the prospective ROCKstar trial, as were the reported rates of adverse events. This exemplifies the need for a dedicated prospective UK GvHD database and registry for future real-world studies.

Disclosure: FK has received honoraria and speaker fees from Incyte, Sanofi, Therakos, and Jazz. Advisory board to Incyte, Vertex, and Sanofi. Research funding from Gilead.
SS has received conference funding from Medac
ND has received speaker fees from Novartis and Abbvie. Advisory board to Novartis and Sanofi

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EVALUATING THE IMPACT OF A DEDICATED OUTPATIENT PHARMACY CLINIC ON MEDICATION SAFETY AND TRANSITIONS OF CARE FOR PATIENTS UNDERGOING HAEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Medication-related problems are common in haematopoietic stem cell transplantation (HSCT) due to complex polypharmacy, frequent dose adjustments, narrow therapeutic index medicines, and multiple care transitions. Dedicated transplant pharmacists play a vital role in improving medication safety and streamlining transitions of care, but evidence for outpatient pharmacy clinic models is limited. We established an outpatient HSCT pharmacy clinic service in May 2025 and evaluated its impact over the first six months (30th of May to 30th of November 2025). The aims were to describe services delivered, quantify pharmacist interventions and assess early process outcomes.

Methods: A prospective service evaluation was conducted for all patients attending the pharmacist-led outpatient clinic between 30th of May and 30th of November 2025. The clinic aimed to review patients 7–10 days prior to planned transplant admission and 7–14 days after discharge, each consultation was allocated 30 minutes. During each visit, the pharmacist reviewed the upcoming conditioning chemotherapy protocol, discussed key side

effects, documented allergies, completed a full medication history and medication reconciliation, identified drug interactions, reviewed relevant drug levels, screened for adherence issues, and assessed tolerability issues with prior chemotherapy. The clinic operated using trained HSCT pharmacists, aligned with FACT–JACIE standards for pharmacist competence, quality management, and record keeping. Data were obtained from the electronic medication management record and the cancer centre operational dashboard, capturing the number of visits, patient demographics, medication reconciliation activity, allergy documentation, and the number and type of pharmacist-led interventions. Interventions were categorised into four domains relevant to quality and safety: cessation or modification of inappropriate or interacting medicines, medication additions required to meet protocol-based recommendations, therapeutic drug monitoring (TDM)-guided dose changes, and chemotherapy dose optimisation based on patient-specific parameters. Descriptive statistics were used to summarise the clinic activity.

Results: Over the six-month period, 52 patients (13 autologous and 39 allogeneic transplant recipients), attended 76 outpatient visits, with 43 pre-transplant and 33 post-transplant consultations. Medication reconciliation and allergy documentation clarification were completed for all 52 patients, resulting in standardised medication lists that were directly accessible to inpatient teams. A total of 109 pharmacist interventions were recorded, of which 91 (83%) were accepted by the transplant team. This equated to an average of 2.1 interventions per patient, and 1.4 interventions per visit. The most frequent interventions involved cessation or modification of inappropriate or interacting medicines (n=57). Suggested medication additions as per transplant protocol (n=24), TDM-guided dose-change recommendations (n=20), suggested chemotherapy dose adjustments (n=8).

Conclusions: During the first six months of operation, the implementation of the outpatient pharmacy clinic enhanced medication safety, improved the accuracy and consistency of medication reconciliation and allergy documentation, and strengthened transitions of care. The high proportion of accepted pharmacist interventions highlights meaningful clinical impact, opportunities for deprescribing, and strong multidisciplinary collaboration. Ongoing data collection will focus on broader quality indicators, including reducing time to chemotherapy charting and ordering, patient and clinician satisfaction data, and reductions in readmission rates to further evaluate and quantify the clinic’s contribution to overall transplant program quality.

Disclosure: Nothing to declare

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POSACONAZOLE IN PAEDIATRICS: ARE WE HITTING THE MARK OR MISSING THE TARGET?

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Background: Invasive fungal infections (IFIs) pose a significant risk to immunocompromised children undergoing cancer treatment or haematopoietic cell transplantation (HCT). Posaconazole is widely used for prophylaxis and treatment, but paediatric data on optimal dosing remain limited. This study evaluates posaconazole dosing, therapeutic drug monitoring, and clinical outcomes of prophylaxis and treatment in children.

Methods: This 8-year retrospective audit included children (≤18 years) receiving cancer therapies or HSCT at the Royal Children's Hospital, Melbourne. Data on posaconazole dosing, serum concentrations, efficacy, and adverse effects were collected. The non-parametric Mann–Whitney U-test test was used to compare continuous variables. Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 29.0 (IBM Corp., Armonk, NY, USA).

Results: Eighty children (median age 12.8 years) received 106 posaconazole courses: two-thirds were for prophylaxis, and the remainder were for IFI treatment. The majority had haematological malignancies (71%), with 36% undergoing allogenic HCT. Therapeutic concentrations (prophylaxis ≥0.7µg/mL; treatment ≥1.0µg/mL) were achieved in 92% and 76% of courses, respectively. The IV formulation achieved target concentrations in all patients with a median dose of 7 mg/kg/day. For the delayed release tablet, 97% (median dose 7mg/kg/day) and 83% (median dose 10mg/kg/day) achieved the prophylaxis and treatment target, respectively. While for oral suspension, only 67% of prophylaxis courses (median dose 7mg/kg every 8 hours) and 29% of treatment courses (median dose 8 mg/kg every 8 hours) achieved target concentrations. Children receiving oral suspension via a nasogastric tube had a lower success rate compared patients receiving doses orally (median 0.9 µg/mL, range 0.4-2.2 vs. 0.6 µg/mL, range 0.1-1.2, $p < 0.05$). Treatment of proven/probable IFIs was successful in all cases (median trough concentration 1.7µg/mL). Adverse events occurred in 21% of patients with hepatotoxicity occurring in 16%.

Conclusions: Posaconazole is effective in preventing and treating IFIs in children but requires higher than recommended doses to achieve therapeutic targets for treatment.

Clinical Trial Registry: NA

Disclosure: Nil to disclose

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AN EVALUATION OF COMPLIANCE WITH A VACCINATION PROGRAMME FOR PATIENTS WHO HAVE UNDERGONE ALLOGENEIC STEM CELL TRANSPLANTATION OR CAR T-CELL THERAPY

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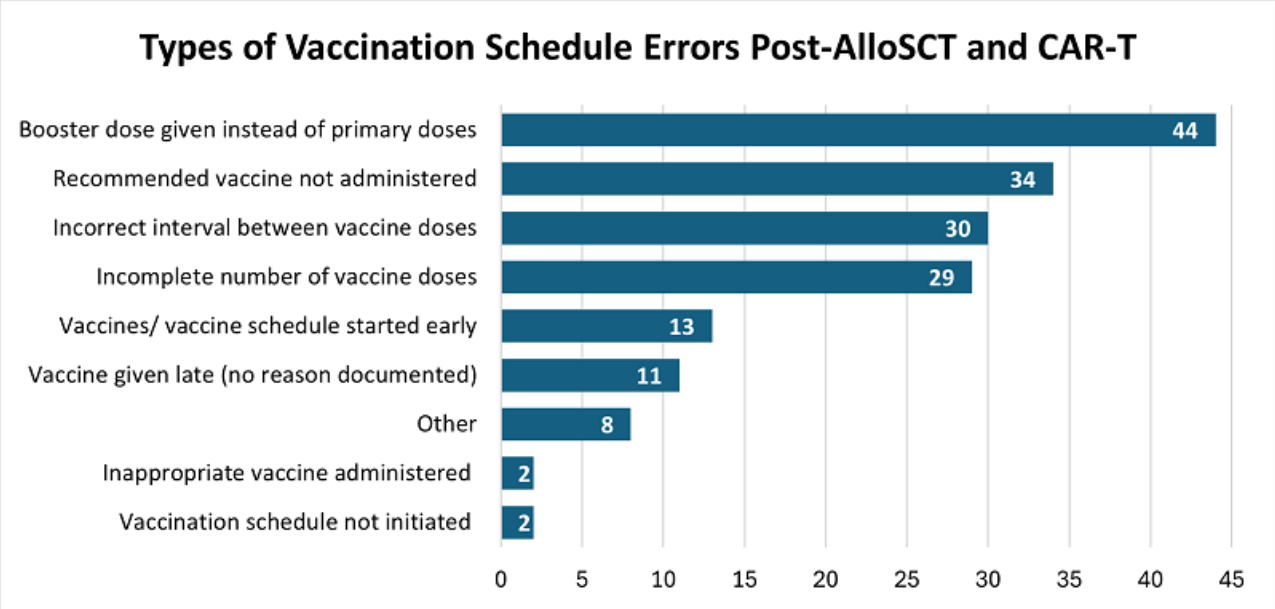
Background: Patients undergoing stem cell transplantation (SCT) or CAR T-cell therapy experience profound and prolonged immunosuppression, increasing the risk of severe and life-threatening infections. Additionally, there is a decline in antibody levels to vaccine-preventable diseases post-treatment, therefore patients should be considered never vaccinated. Consequently, patients should be re-vaccinated to restore antibody levels and mitigate infection-related mortality. National and international guidance recommend commencing vaccination relatively early post-treatment. Inactive vaccinations are typically advised from 3-6 months, while live vaccines are generally considered safe after two years has elapsed. Local practice at our hospital (a large tertiary haematology centre) is to ask the general practitioners (GP) of our patients to deliver the vaccination programme based on a printed schedule that we provide.
We conducted a retrospective evaluation of vaccination practices. Our primary aims were to assess compliance with the vaccine schedule and to identify common errors.

Methods: Patients who received an allogeneic SCT (AlloSCT) between January-December 2024 or CAR-T therapy between June 2019-March 2025 were eligible for inclusion. Patients who died or relapsed within 6 months, or were experiencing complications following treatment necessitating postponement of vaccinations (e.g. GvHD) were excluded. Primary Care (GP) records and clinic letters were reviewed to identify vaccine administration or documented reasons for omission. Compliance was assessed by comparing vaccine initiation and details of recorded vaccinations (including vaccine brands) with the schedules issued to patients and their GPs. Data was inputted into Microsoft Excel, and descriptive analysis was conducted.

Results: In total, 147 patients (62 AlloSCT and 85 CAR-T) were included in the evaluation. 58.5% (40 AlloSCT and 46 CAR-T) of patients were non-compliant with at least one part of their vaccination schedule. Overall, a total of 173 errors were identified, with a median of one error per patient (range 0-5). These errors were classified into nine categories, as shown in Figure 1.



The most common reason for non-compliance was booster doses given instead of the primary vaccine(s) (n=44), this included COVID-19 boosters given instead of primary doses (n=30) and Pneumovax 23® (designed to be given as a booster) being given instead of Prevenar13® (n=13). Other reasons include omission of recommended vaccinations (most commonly shingles or Pneumovax 23® vaccine) (n=34), receiving the incorrect number of vaccinations (n=29), and incorrect vaccine intervals (n=30). We found no major differences in errors between the AlloSCT and CAR-T subgroups.

Conclusions: This retrospective service evaluation has highlighted significant non-compliance with the vaccination schedule post AlloSCT and CAR-T, with 58.5% of patients identified as non-compliant. Reasons were not directly investigated but are likely to be multifactorial e.g. delayed or missing vaccine paperwork, unfamiliarity with the procedure amongst GPs or vaccine unavailability. The non-compliance issues identified could potentially lead to inadequate vaccine responses, leaving patients vulnerable to vaccine-preventable infections. To improve compliance, we introduced a vaccine passport in July 2025 which is now given to all eligible patients. We believe that enhanced communication and education, along with continued close monitoring of compliance, will be essential to optimize vaccine adherence and reduce infection-related complications in this vulnerable population.

Clinical Trial Registry: n/a

Disclosure: Vaishali Dulobdas: sponsorship to attend conferences, speaker- Kite/Gilead and AbbVie, project grant (fellowship)- Kite/Gilead.
Simran Dhadda: Speaker fee- Pfizer.
Nick Duncan: Speaker fee- Novartis and AbbVie, adboard- Sanofi.
Donna Walsh: Travel support- Roche and Kite/ Gilead, Honoraria- Vertex Pharmaceuticals and AbbVie.

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A PROSPECTIVE STUDY EVALUATING THE ROLE OF NOVEL PLATELET-DERIVED MICRORNAS IN MEGAKARYOCYTE DIFFERENTIATION

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Background: Extracellular vesicles (EVs), derived from platelets, containing bioactive molecules, such as, proteins, lipids, and microRNAs (miRNAs) have emerged as critical mediators of intercellular communication. Recent evidence has suggested key influence of platelet-derived miRNAs in the fate and function of other haematopoietic cells, the role of miRNAs in megakaryocyte differentiation is not fully established. Identifying and characterising the specific miRNAs and their regulatory pathways can help reveal novel potential therapeutic targets for platelet-related disorders and bone marrow failure syndromes. Hence, this study was planned with an aim to identify and evaluate the functional role of platelet-derived miRNAs in regulating thrombopoiesis.

Methods: This was a prospective, observational study conducted at a tertiary care hospital. For the study, platelets were obtained from healthy donors after taking written informed consent. Nanoparticle tracking analysis and CD63/CD41 flow cytometry was used to characterise EVs. Next-generation sequencing (NGS) was used for global miRNA profiling after extracting total RNA from EV. Quantitative real-time polymerase chain reaction (qRT-PCR) was used to validate the candidate miRNAs with highest differential expression. Primary human megakaryocytes were co-cultured with platelet-derived EVs with identified miRNAs to evaluate their effects. Proplatelet formation, flow cytometry and immunofluorescence were conducted. CRISPR/Cas9-mediated knockout megakaryocyte progenitors were used for further exploration of specific miRNAs. Comparisons between treated and control groups were made using unpaired two-tailed t-tests or one-way ANOVA with post hoc Tukey's test where appropriate. Data were expressed as mean ± standard deviation (SD). $P<0.05$ was considered statistically significant.

Results: Platelets from 60 donors was collected. The most significantly upregulated miRNAs on NGS were miR-223-5p and miR-126-3p with fold changes of 3.8 ± 0.6 and 4.5 ± 0.7, respectively ($P \leq 0.001$) compared to control group. This was confirmed by qRT-PCR. Co-culture of megakaryocytes with EVs showed significant upregulation of CD41+ and CD42b+ cells ($P < 0.001$). There was a significant ($P < 0.01$) enhancement of proplatelet formation in megakaryocytes treated with miR-223-5p (68.7 ± 5.2) and miR-126-3p (74.2 ± 6.1) compared to untreated control (32.4 ± 4.5). The knockout experiment revealed a significant reduction in thrombopoietic potential and impaired formation of proplatelet in vitro.

Conclusions: Platelet-derived EVs act as carriers of regulatory miRNA species that influence hematopoietic cell development in a paracrine manner. miR-223-5p and miR-126-3p were identified as critical platelet-derived miRNAs enhancing thrombopoiesis. These findings provide a basis for exploring miRNA-based therapeutic strategies in thrombocytopenic disorders such as ITP and aplastic anaemia.

Disclosure: There are no conflict of interest to declare.

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IMPACT OF LOW DOSE ANTI-T-LYMPHOCYTE GLOBULIN ON CLINICAL OUTCOMES IN THE ERA OF POST-TRANSPLANT CYCLOPHOSPHAMIDE

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Background: Post-transplant cyclophosphamide (PT-Cy) and Anti-T-Lymphocyte Globulin (ATLG) are effective strategies for graft-versus-host disease (GVHD) prophylaxis, and are increasingly used in combination. While emerging evidence suggests association between absolute lymphocyte count (ALC) and ATLG clinial outcomes, this relationship has not yet been evaluated in the specific setting of PT-Cy-based prophylaxis. Therefore, we conducted a single-centre study to analyse the effect of the ATLG dose and ALC count on clinical outcomes in patients receiving PT-Cy.

Methods:

Patients who underwent allogenic hematopoietic stem cell transplantation (allo-HSCT) between May 2024 and October 2025 and received combined GVHD prophylaxis with pre-transplant ATLG (Grafolon®) and PT-Cy (days +3/+4, total 60-100 mg/kg) were included. Our center's protocol utilized a lower-dose ATLG regimen (cumulative <10 mg/kg). Pre-treatment ALC (cell/µL) was recorded on the day of first ATLG infusion. ATLG doses were assessed as total mg and mg/kg. Overall survival (OS), progression-free survival (PFS), Graft-versus-host-disease (GVHD)- free survival, cytomegalovirus (CMV) reactivation-free survival, and BK virus event- free survival, neutrophil, platelet, lymphocyte engraftment days were analysed. Survival probabilities were calculated using the Kaplan–Meier method (Log-rank test for comparisons). The impact of key variables, including ATLG dose and ALC, was assessed using Cox proportional hazards regression models (HR and 95% CI), with variables categorized by median cut-off. Pearson coefficients were calculated in correlation analyses with engraftment days. Statistical significance was defined as $p < 0.05$. Analyses were performed using SPSS and MedCalc (version 23.2.0)

Results: A total of 25 patients (60% female) with a median age of 53 years (range: 21–69) were included in the retrospective analysis. The demographic, clinical, and transplant characteristics of patients are listed in Table 1. The median follow-up period was 127 days (13-403). A total ATLG dose of ≥480 mg was significantly associated with a higher hazard of CMV reactivation (HR: 3.60; 95% CI: 1.29–10; p=0.01) compared to lower doses. The incidence of CMV reactivation was not significantly influenced by ALC levels or the ATLG dose when analyzed by mg/kg (p>0.05). Additionally, patients with lower ALC (<140/ µL) had significantly lower BK virus event-free survival (p=0.007). No statistically significant correlation was found between the ATLG dose (mg/kg or total mg) or the ALC and the time to neutrophil, platelet, or lymphocyte engraftment (p>0.05). Neither the ALC nor the weight-based ATLG dose (mg/kg) showed a statistically significant association with other survival endpoints.

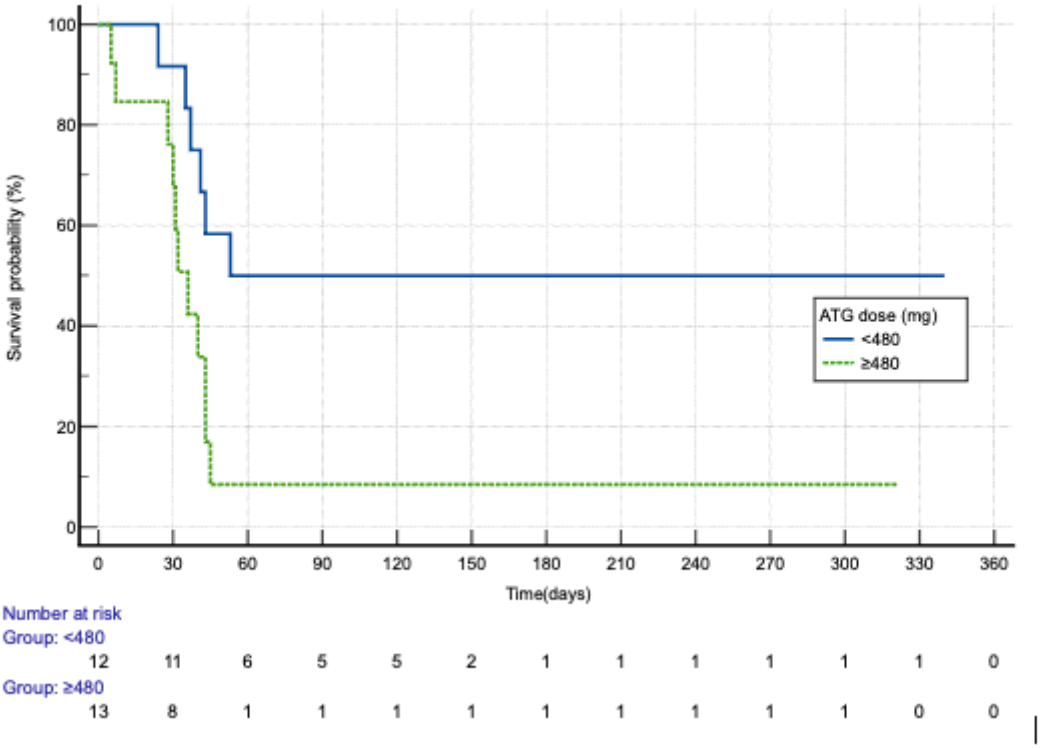
Table 1. Distribution of demographic, clinical, and transplant characteristics of patients who underwent allogeneic hematopoietic stem cell transplantation

		Total Number n=25(100)	**Median(Min-Max)**
Year			53(21-69)
Weight (kg)			70(45-122)
Gender Female Male		 15(60) 10(40)	
Disease AML Others		 21(84) 4(16)	
HLA Match Compatiblity 10/10 9/10 Haploidentifical		 4(16) 16(64) 5(20)	
Conditioning regimen MAC NMA and RIC		 10(40) 15(60)	
MRD +		10(40)	
aGVHD		6(24)	
Disease progression		3(12)	
Death		5(20)	
CMV Reactivation		17(68)	
ATLG Dose <6.27 (mg/kg) ≥ 6.27 (mg/kg) <480 (mg) ≥480 (mg)		 13(52) 12(48) 12(48) 13(52)	

ALC <140/µL ≥ 140/µL		11(44) 14(56)	0.14(0-4.70)
Engrafmant days Neutrophil engraftment Platelet engrafment ALC engrafment			15(11-32) 18(11-33) 30(16-125)

AML: Acute myeloid leukemia, HLA: Human leukocyte antigen, MAC: Myeloablative conditinoing, NMA: Non-myeloabletive, RIC: Reduced intensity conditioning, MRD: Minimal residual disease, aGVHD: acute graft-versus-host-disease,
CMV: Cytomegalovirus, ATLG:Anti-T-lymphocyte globulin, ALC: Absolute lymphocyte count

Figure 1. CMV reactivation-free survival



Conclusions: Our study demonstrates that higher cumulative ATLG doses significantly increases the hazard of CMV reactivation, and ALC serve as a risk marker associated with BK virus event-free survival in patients receiving combination of PT-Cy and ATLG.
Overall, these findings, when used in combination with PT-Cy, highlight the importance of careful ATLG dose optimization rather than fixed weighted dose and support the need for

larger-scale studies to further clarify exposure-response relationships and improve personalized prophylaxis strategies.

Disclosure: No conflict of interest.

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ANTICIPATION OF PHARMACOTHERAPEUTIC PROBLEMS PRIOR TO ALLO HEMATOPOÏETIC CELL TRANSPLANTATION IN PATIENTS WITH CO-MORBIDITIES: A TWO YEARS EXPERIENCE REVIEW

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) frequently involves patients with multiple co-morbidities and then polymedication. This increases the risks of complications during the transplant procedure, either through the mechanism of action, the adverse reaction profile or the risk of pharmacological interactions. Since more than 2 years, some cases are discussed between an hematologist and a clinical pharmacist in order to anticipate any problem related to the patients' pharmacotherapy.
This study aimed to describe the decisions issued before the transplant procedure.

Methods: This is a monocentric and descriptive study. From January 1st, 2023 to April 30th, 2025, patients eligible to allo-HSCT were selected by a senior hematologist on the base of predetermined risks of complications. For each patient, we recorded all their medications 7-15 days before admission. As the engraftment protocol was known, the risks related by the whole pharmacotherapy were screened, leading to shared therapeutic decision before hospitalization and summarized in the patients' medical electronic file.
Pharmaceutical interventions (PI) were based on an adapted version of the Act-IP classification [1] consist in: continuing, adding, stopping or substituting drugs, dose adaptation or therapeutic drug monitoring (TDM). New PIs consist in requiring expertise from a specialist physician and anticipating a risk occurrence during hospitalization. Comparisons involved Student t test; correlations involved Kendall tau test (a=5%).

Results: The 104 patients included (55.8±11.5 years-old; gender ratio = 1.21) received allo-HCT principally for AML (47.1%), MDS (20.2%) and ALL (17.3%). Conditioning was mainly no MAC regimen (69.2%).The most frequent co-morbidities were hypertension (34.6%), dyslipidemia (21.2%) and T2 diabetes (13.5%). Most patients have more than 3 comorbidities (48.0%).
Prior to admission, patients had 5.60±2.32 medications with 3.79±2.21 for comorbidities. 294 PI were formulated (i.e. 2.82±1.30 PI/patient). Most PIs concern drug stop (29.9%, e.g. hypolipemiants, oral antidiabetics or platelets antiaggregating agents); drug maintenance (23.1%, e.g. sartans, betablockers) and prevention of drug iatrogeny (14.6%, e.g. preventing drug-drug interactions with antiepileptics such as valproate and meropenem).

There is a correlation between the number of PI and the total number of drugs (tau = 0.404; p < 0.0001) or the number of drugs for comorbidities (tau = 0.410; p < 0.0001). At the end, the number of drugs out of allo-HCT protocol is statistically different: 4.09 ± 2.21 (p < 0.0001).

Conclusions: Some drugs are inappropriate for allogeneic transplant patients. Physicians and clinical pharmacists must remain vigilant about the risk of complications during allo-HCT procedures due to co-morbidities medications.
Recommendations were recently published by the French bone marrow and cell therapy society (i.e. SFGM-TC) [2]. Further studies will confirm the clinical benefit for patients receiving allo-HCT.

Disclosure: There is no disclosure.

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TACROLIMUS C/D RATIO–BASED METABOLIZER PHENOTYPE: A POTENTIAL PREDICTOR OF ACUTE KIDNEY INJURY IN HEMATOPOIETIC CELL TRANSPLANTATION RECIPIENTS

Luiz Carlos da Costa-Junior[1,2], *Rita de Cássia Barbosa da Silva Tavares*[2], *Marina Izu*[2], *Simone Cunha Maradei*[2], *Maria Claudia Rodrigues Moreira*[2,3], *Marta Colares Nogueira*[2], *Décio Lerner*[2], *Teresa de Souza Fernandez*[4], *Paulo Caleb Júnior Lima Santos*[1,5]
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Background: Tacrolimus (TAC) is a calcineurin inhibitor (CNI) widely used for prophylaxis of graft-versus-host disease (GVHD) following allogeneic hematopoietic cell transplantation (HCT). Its pharmacokinetics exhibit substantial interindividual variability that affects both immunosuppressive exposure and toxicity. The concentration-to-dose (C/D) ratio provides a practical surrogate of intrinsic metabolic capacity, enabling patient stratification into fast and slow metabolizers. Because acute kidney injury (AKI) is a frequent early complication with major clinical impact, early identification of individuals at increased risk may support more tailored immunosuppressive management.

Methods: We conducted a retrospective single-center cohort study including allogeneic HCT recipients treated with TAC between 2014 and 2023 who had therapeutic drug monitoring available during the first 21 days of therapy. TAC was administered as a continuous 24-hour infusion (0.01–0.05 mg/kg/day) and adjusted to maintain trough concentrations of 5–15 ng/mL. The C/D ratio was calculated as follows: C/D ratio (ng/mL per mg/kg) = TAC trough concentration (ng/mL) ÷ [daily TAC dose (mg) ÷ body weight (kg)]. Patients were classified

as median: fast (<420 ng/mL·mg^{-1}·kg) or slow metabolizers (≥420). AKI was defined using KDIGO 2012 criteria, with baseline creatinine established as the lowest stable pre-TAC value over ≥5 consecutive days. Statistical analyses included chi-square or Fisher's exact tests, Mann–Whitney U tests, and cumulative incidence estimation using 1–Kaplan–Meier with comparisons by log-rank test up to day +21.

Results: Seventy-one HCT recipients were evaluated (mean age 21 years; 35.2% pediatric; 50.7% male). Fast and slow metabolizers were evenly distributed (49.3% vs. 50.7%). Underlying diagnoses included acute leukemias (52.2% collectively), bone marrow failure syndromes (22.5%), and myelodysplastic/myeloproliferative neoplasms (12.7%). Donor types (31.0% related, 36.6% haploidentical, 32.4% unrelated), graft sources (62.0% bone marrow, 38.0% peripheral blood), conditioning intensities (47.9% myeloablative), and GVHD prophylaxis regimens were similarly distributed between groups. AKI occurred in 38.0% of recipients by day +21, and 23.9% developed stage 2–3 injury. Stage 2–3 AKI was more frequent among slow metabolizers (36.1%) compared with fast metabolizers (11.4%, p = 0.015). In time-to-event analysis, slow metabolizers had a significantly increased hazard of moderate-to-severe AKI (HR 3.71; 95% CI 1.21–11.39; p = 0.0136). Slow metabolizers also required fewer TAC dose increases (50.0% vs. 96.8%) and more dose reductions (50.0% vs. 3.2%) compared with fast metabolizers.

Conclusions: The tacrolimus concentration-to-dose (C/D) ratio reliably identified metabolic variability in hematopoietic cell transplantation recipients. Slow metabolizers, characterized by higher C/D ratios, showed an independently increased risk of stage 2–3 acute kidney injury in the early post-transplant period. They also required fewer dose escalations and more dose reductions compared with fast metabolizers. These findings support the C/D ratio as a practical and accessible tool for early risk stratification and individualized tacrolimus management. By enabling early identification of patients with increased susceptibility to renal toxicity, this pharmacokinetic parameter strengthens its role as a potential predictor to guide more proactive and safer immunosuppressive strategies.

Clinical Trial Registry: Not applicable. This study is not a clinical trial.

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CLINICAL, LABORATORY, AND PHARMACOLOGICAL FACTORS INFLUENCING CALCINEURIN INHIBITOR PLASMA LEVELS IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: Calcineurin inhibitors (CNIs), particularly cyclosporine (CSA) and tacrolimus (TAC), are essential for graft-versus-host disease (GVHD) prophylaxis after allogeneic hematopoietic cell transplantation (HCT). However, both agents exhibit substantial inter- and intra-individual pharmacokinetic variability, despite standardized dosing and routine therapeutic drug monitoring (TDM). Such variability may compromise the maintenance of therapeutic ranges required for effective GVHD prevention. Identifying clinical, laboratory, and pharmacological factors that influence CNI exposure is therefore critical, especially if these determinants are predictable or modifiable. Additionally, whether CSA and TAC differ in their susceptibility to these influences remains incompletely understood. Understanding these patterns could improve individualized dosing and early post-transplant pharmacological management.

Methods: This retrospective single-center cohort included allo-HCT recipients transplanted between 2002 and 2023, excluding umbilical cord blood grafts. Clinical, laboratory, demographic, and pharmacological data were extracted from electronic medical records. Intravenous CSA and TAC were administered according to institutional protocols with daily through monitoring. All measurements obtained from day 1 to day 21 after CNI initiation were analyzed. Separate linear mixed-effects models (LME) were developed for CSA and TAC to evaluate associations between plasma levels and key covariates: age, sex, race, body weight, creatinine, AST/TGO, ALT/TGP, albumin, hematocrit, antifungal exposure (fluconazole, micafungin, voriconazole), and day since CNI initiation. Patient unique identifier (matricula) was included as a random intercept to account for repeated observations. Models were fitted using lmer() (lme4), with Satterthwaite-adjusted inference via lmerTest. Complete case analyses were performed for each CNI group. This report presents preliminary findings; additional patients are currently being incorporated. The study was approved by the institutional ethics committee in accordance with the Declaration of Helsinki.

Results:

Table 1. Full Mixed-Effects Model Results for CSA and TAC.

	CSA				**TAC**		
Variable	β	SE	*p*		β	SE	*p*
Intercept	83.73	52.3	0.111		4.28	4.61	0.354

Day since CNI initiation	*3.36*	*0.8*	*3.06e-05*		*0.31*	*0.063*	*7.98e-07*
Antifungal: Fluconazole	9.31	16.18	0.566		1.27	1.14	0.269
Antifungal: Micafungin	16.27	26.49	0.54		*4.41*	*1.67*	*0.0086*
Antifungal: Voriconazole	6.29	17.01	0.712		0.21	1.1	0.845
Age (years)	0.016	0.352	0.963		*-0.068*	*0.026*	*0.0089*
Body weight (kg)	*1.06*	*0.286*	*0.00025*		*0.057*	*0.02*	*0.0047*
Sex (Male)	-5.7	10.64	0.593		*-1.93*	*0.887*	*0.03*
Race: Parda	-10.24	10.8	0.344		1.42	0.886	0.11
Race: Black	-2.66	15.62	0.865		1.38	1.17	0.238
Creatinine	-10.3	7.74	0.184		-0.64	0.841	0.446
AST (TGO)	0.022	0.165	0.892		0.0063	0.0042	0.133
ALT (TGP)	-0.074	0.114	0.516		*-0.012*	*0.0053*	*0.0229*
Albumin	-1.24	11.98	0.918		-1.4	0.881	0.112
Hematocrit	*5.43*	*1.576*	*0.000656*		0.216	0.134	0.108

A total of 634 HCT recipients were identified in the institutional cohort. Among them, 291 CSA users and 70 TAC users had complete clinical, laboratory, and pharmacological covariates available for mixed-effects modeling, contributing 1,401 CSA and 350 TAC trough measurements between days 1 and 21 after CNI initiation. For CSA, higher levels were independently associated with later days after CNI initiation (β = +3.36/day; p < 0.001), greater body weight (β = +1.06/kg; p < 0.001), and higher hematocrit (β = +5.43; p < 0.001). No antifungal agent or hepatic biomarker showed a significant association with CSA levels. For TAC, several variables significantly influenced exposure: later days after initiation (β = +0.31/day; p < 0.001), micafungin use (β = +4.40; p = 0.009), younger age (β = −0.068; p = 0.009), male sex (β = −1.93; p = 0.030), higher body weight (β = +0.057; p

= 0.005), and lower ALT (β = −0.012; p = 0.023). Full results for all covariates are presented in Table 1.

Conclusions: CNI plasma levels are influenced by drug-specific patterns involving clinical, laboratory, and pharmacological factors. CSA exposure was primarily shaped by weight and hematocrit, whereas TAC demonstrated additional associations with age, sex, hepatic function, and micafungin use, reflecting its more complex metabolism. These findings suggest that part of the variability in CNI levels is predictable and occasionally modifiable, supporting refined, individualized TDM strategies to optimize GVHD prophylaxis.

Clinical Trial Registry: Not applicable. This study is not a clinical trial.

Disclosure: The authors declare no conflicts of interest. This study was supported by Brazilian governmental research funding agencies (FAPESP, CAPES, CNPq, and FAPERJ).

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IMPACT OF ANTIBIOTIC PROPHYLAXIS ON GRAM-NEGATIVE INFECTION RATES IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Bloodstream infections (BSIs) remain a major cause of morbidity and mortality in children undergoing hematopoietic stem cell transplantation (HSCT). Fluoroquinolone prophylaxis has been used to prevent infectious complications; however, its overall impact remains controversial due to concerns regarding antimicrobial resistance, potential drug-related toxicities and inconsistent efficacy data.

Methods: We conducted a retrospective cohort study of pediatric HSCT recipients transplanted between October 2020 to June 2025. Patients were divided into two groups based on exposure to quinolone prophylaxis: those transplanted between October 2020–October 2022 (prophylaxis group) and those transplanted between November 2022–June 2025 (no-prophylaxis group). Demographic and clinical variables collected included sex, underlying diagnosis, age at transplant, type of HSCT, donor type and cell source. The primary outcome was the incidence of gram-negative infections within the first six months post-transplant. For each infectious episode, site of infection and causative microorganism were recorded. Data were obtained from electronic medical records. Group comparisons were performed using χ^2 or Fisher's exact test for categorical variables.

Results: A total of 42 pediatric HSCT recipients were included, with 21 patients in the prophylaxis group and 21 in the no-prophylaxis group. The cohort had a mean age of 8.73 years at the time of HSCT and 23 patients (55%) were male. Underlying diagnoses included acute lymphoblastic leukemia (ALL) in 23 patients (55%), acute myeloid leukemia (AML) in 8

patients (19%) and other conditions (non-malignant diseases) in 11 patients (26%).
In the prophylaxis group, 7 of 21 patients (33%) developed at least one gram-negative bacterial infection within the first six months post-transplant; three of these patients experienced two infectious episodes. Similarly, in the no-prophylaxis group, 7 of 21 patients (33%) developed gram-negative infections, with three patients experiencing two episodes. In the prophylaxis group, infections included 3 bloodstream infections and 4 urinary tract infections, whereas in the no-prophylaxis group, 5 bloodstream infections and 2 urinary tract infections were observed. Comparisons between groups were performed using Fisher's exact test. No statistically significant differences were observed in the incidence of gram-negative infections between groups.
Overall, the most frequently isolated microorganisms were *Klebsiella pneumoniae* (n = 5) and *Pseudomonas aeruginosa* (n = 3), followed by *Escherichia coli* (n = 2) and *Stenotrophomonas maltophilia* (n = 2). Less frequently identified pathogens included *Campylobacter jejuni* (n = 1) and *Proteus mirabilis* (n = 1).

Conclusions: In this cohort of pediatric HSCT recipients, quinolone prophylaxis was not associated with a reduction in the incidence of gram-negative infections during the first six months post-transplant. Infection rates were comparable between patients who received prophylaxis and those who did not. Although differences in infection localization were observed between groups, no statistically significant differences were identified and no clear clinical benefit of prophylaxis was demonstrated. Larger, prospective studies are needed to better define the role of antibacterial prophylaxis in preventing gram-negative infections in pediatric HSCT patients.

Disclosure: Nothing to declare.

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VANCOMYCIN PROPHYLAXIS IN PAEDIATRIC UMBILICAL CORD BLOOD TRANSPLANTS: A SINGLE CENTRE SERVICE EVALUATION

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Background: Umbilical cord blood (UCB) transplants offer many advantages, including expanding access. Delayed engraftment, lack of transferred immunity and incidence of acute graft versus host disease (GvHD) increases risk of infectious complications in this cohort. Despite bacterial prophylactic regimens, the value of prophylaxis targeting a wider range of gram-positive pathogens is unknown. Experiences and reports in literature note that *Streptococcus Viridans* has accounted for a high rate of bacteraemia events in neutropenic paediatric patients. Vancomycin, a glycopeptide antibiotic with broad gram-positive coverage, is included in local institutional guidelines for UCB transplant recipients during neutropenic phase, starting at D+1. The aim of this project was to evaluate safety and appropriateness of this regimen including analysis of target level range for prophylaxis.

Methods: All patients who received a transplant using UCB as stem-cell source between January 2021 and December 2024 were included. Patient's demographics (including age and weight), treatment details (conditioning regimen, date and dose of vancomycin initiation and completion) and laboratory results (including first vancomycin levels, positive blood cultures and acute kidney injury warnings linked to creatinine) were retrospectively collected using electronic prescribing system, collated and analysed.

Results: A total of forty-nine cord blood recipients were recorded. Median age was 4.6 years (range 0-12years). Eleven patients (22%) were excluded from data collection due to contraindications to vancomycin prophylaxis (reasons including already being on treatment dose or a recorded allergy to vancomycin). Median starting dose for vancomycin was 16mg/kg BD (range 10.2 – 21.5mg/kg).
Timing to first level varied from 1 to 9 days from initiation (average 3.3 days). Average first level value was 4.6mg/L (aiming for a trough level of less than 10mg/L as per trust guideline for prophylaxis). Flags for acute kidney injury due to raise in creatinine were monitored in first week of initiation. One patient required discontinuation of prophylaxis due to high-levels (11.8mg/L) and AKI stage 3. Average duration of prophylaxis was 9.5 days (range 2-21 days). Most common reason for cessation was change to vancomycin treatment regimen due to persistent fever spikes in 61% of patients (n=23). Ten patients received vancomycin prophylaxis until Neutophils >0.2 as per policy.

Conclusions: Despite adherence to current trust policy, a large variation in time to first level and levels reported between ages outlines need for clearer guidance and needs to incorporate patient factors. In view of large proportion of patients pre-emptively moving to treatment regimens due to fever spikes, patient numbers optimally adhering to proposed prophylactic regimen were small. A previous single centre publication has outlined the safety of vancomycin prophylaxis in neutropenic Acute Myeloid Leukaemia patients, but clear guidance on dosing and target strategies in UCB transplants remain limited. Therapeutic drug monitoring for vancomycin remains essential to prevent further toxicity (particularly in early acute transplant phase), but further work is required to outline optimal strategy for prophylaxis.

Disclosure: No disclosures

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RETROSPECTIVE REVIEW OF LETERMOVIR FOR CYTOMEGALOVIRUS PROPHYLAXIS IN PAEDIATRIC ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Cytomegalovirus (CMV) infection remains one of the most clinically significant complication following allogeneic haematopoietic stem cell transplantation (alloHSCT). Since

its approval in 2017, letermovir prophylaxis has become standard practice in adults CMV seropositive recipients (R+). Letermovir usage in paediatrics was previously limited to retrospective case series. Recently in February 2025, the European Medicines Agency (EMA) extended the approval of letermovir to paediatrics based on pharmacokinetics and safety data from phase 2b study. At KK Women's and Children's Hospital (KKH) in Singapore, letermovir was first used in a paediatric HSCT patient for secondary prophylaxis of CMV in July 2024. We have since expanded the use of letermovir for primary prophylaxis. This review analyses letermovir usage in paediatric HSCT patients at KKH to-date.

Methods: Paediatric alloHSCT patients at KKH who received letermovir prophylaxis from July 2024 to September 2025 were included in this retrospective review. Data on letermovir indication, duration, efficacy and safety were analysed. Clinically significant CMV infection (CS-CMVi), defined as CMV disease or viraemia leading to pre-emptive treatment (PET), was used to assess efficacy of letermovir prophylaxis. Patients were dosed according to EMA label. Letermovir tablets were cut, crushed and diluted in water for paediatric administration.

Results: A total of 14 patients, median age 7.6 years (2.8 – 12.8 years), were included in this review. The median follow-up duration was 237.5 days (110-512 days).
Letermovir was used as primary prophylaxis in 12 patients, with majority (10/12) being CMV R+. Two patients who were CMV D-R- were initiated on letermovir prophylaxis—patient 3 developed detectable low copies of CMV DNAemia (<500 copies/ml) on day -3, while the haploidentical donor for patient 5 was found to be CMV IgM positive (CMV PCR and CMV IgG negative) during pre-transplant screening. Letermovir was given as secondary prophylaxis in 2 patients—patient 1 had multiple episodes of CMV reactivations requiring extended treatment with ganciclovir or foscarnet over 3 months, while patient 4 was started on letermovir after initial PET for CMV reactivation peri-engraftment.
2/14 patients developed CS-CMVi during letermovir prophylaxis. Patient 7 was started on letermovir primary prophylaxis on D+65 and was treated with 1-week course of ganciclovir when her CMV viral load increased to log 3.5 on D+70, fulfilling the criteria for CS-CMVi. She continued letermovir after PET without further episodes of CMV reactivation. In retrospect, patient 7 likely experienced a CMV blip while on letermovir prophylaxis which may not have warranted initiation of ganciclovir PET. Patient 9 developed CS-CMVi 46 days after stopping letermovir prophylaxis on D+100.
Letermovir was initiated at a median of D+14, with median duration 133 days. Reasons for extended duration of letermovir in 10 patients beyond 100 days included poor graft function, delayed immune reconstitution, multiple immunosuppressants for graft-versus-host disease treatment. Letermovir was well-tolerated without significant attributable side effects. No patients discontinued letermovir due to adverse effects.

Table 1. Clinical characteristics and outcome of paediatric patients who received letermovir prophylaxis at KK Women's and Children's Hospital.

Patient no.	Age (years)	Type of alloHSCT	Donor/ recipient CMV serostatus	Indication of letermovir	Letermovir initiation day	Letermovir duration (days)	CS-CMVi

Table 1. Clinical characteristics and outcome of paediatric patients who received letermovir prophylaxis at KK Women's and Children's Hospital.

1	4.0	1st: T-deplete haplo 2nd: T-replete haplo	D+R+	Secondary prophylaxis	D+102	211	Nil
2	5.7	T-deplete haplo	D-R+	Primary prophylaxis	D+7	182	Nil
3	9.8	MUD	D-R-	Primary prophylaxis for recipient CMV PCR detectable at <500 copies/ml on D-3	D+1	171	Nil
4	10.2	MUD	D-R+	Secondary prophylaxis	D+22	182	Nil
5	7.0	T-replete haplo - cord vaccine transplant	D-R-	Primary prophylaxis for haplo donor CMV IgM+	D-1	112	Nil
6	2.3	T-deplete haplo	D-R+	Primary prophylaxis	D+7	194	Nil
7	12.7	MSD - T-replete haplo vaccine transplant	D+R+	Primary prophylaxis	D+65	164	Yes
8	12.8	MUD	D-R+	Primary prophylaxis	D+14	82	Nil
9	8.1	T-deplete haplo	D+R+	Primary prophylaxis	D+9	91	Yes

Table 1. Clinical characteristics and outcome of paediatric patients who received letermovir prophylaxis at KK Women's and Children's Hospital.

10	10.8	T-deplete haplo	D+R+	Primary prophylaxis	D+31	68	Nil
11	6.9	T-replete haplo - cord vaccine transplant	D+R+	Primary prophylaxis	D+7	119	Nil
12	10.5	T-deplete haplo	D+R+	Primary prophylaxis	D+14	147	Nil
13	7.1	MUD	D-R+	Primary prophylaxis	D+14	86	Nil
14	2.8	1st: T-deplete haplo 2nd: T-replete haplo	D+R+	Primary prophylaxis	D+14	118 (ongoing)	Nil
	median: 7.6				median: D+14	median: 133	

Abbreviations: alloHSCT, allogeneic haematopoietic stem cell transplant; CS-CMVi, clinically significant CMV infection; haplo, haploidentical haematopoietic stem cell transplant; MSD, matched sibling donor; MUD, matched unrelated donor.
Note: KK Women's and Children's Hospital uses TCRαβ CD45RA depletion for T-deplete haplo.

Conclusions: Letermovir prophylaxis appears to be safe and effective in our series of paediatric alloHSCT patients. Further research is needed to better define CMV viral load thresholds for initiating PET while on letermovir prophylaxis.

Disclosure: Nothing to declare.

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SUBTHERAPEUTIC CYCLOSPORINE CONCENTRATIONS DESPITE STANDARD DOSING IN HSCT PRACTICE

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Background: Cyclosporine remains a cornerstone of graft-versus-host disease (GVHD) prophylaxis following allogeneic hematopoietic stem cell transplantation (HSCT). Although current guidelines recommend an initial dose of 3 mg/kg/day, a substantial proportion of patients at our institution fail to achieve the target trough concentration of 150–250 ng/mL. Therefore, evaluating whether this standard dosing strategy provides adequate therapeutic exposure is clinically important.

Methods: This single-center, prospective observational study included patients who underwent allogeneic HSCT between January 2023 and December 2024 (NTUH REC approval number 201810058RIND). Standard GVHD prophylaxis consisted of cyclosporine 3 mg/kg/day divided twice daily, in combination with an anti-metabolite agent. Cyclosporine was dosed based on ideal body weight or total body weight, whichever was lower (the lower body weight). Steady-state trough concentrations obtained under the 3 mg/kg/day regimen were analyzed. The primary endpoint was the proportion of transplantation cases achieving the target trough concentration of 150–250 ng/mL at the first measurement.

Results: A total of 97 patients were enrolled; two patients underwent multiple allogeneic HSCTs during the study period, yielding 100 transplantation cases for analysis. The median age was 53 years (range, 20–74), and 54 patients (55%) were male. The median initial cyclosporine trough concentration was 83 ng/mL (range, 15–170). Dose adjustments were made in 70% of cases based on early drug levels. Fifty-two cases met the definition of overweight (BMI >24) and 7 were underweight (BMI <18.5). There was no significant difference in levels among patients receiving empirical dosing across body weight categories, with mean concentrations of 82.7 ng/mL in the overweight group, 86.5 ng/mL in the underweight group, and 90.2 ng/mL in those with normal body weight. ($p>0.05$)
Drug–drug interactions were identified in 21 cases receiving concurrent antifungal therapy (6 on voriconazole, 12 on isavuconazole, 3 on fluconazole). Empirically, cyclosporine was reduced by 50% when co-administered with voriconazole, whereas the standard 3 mg/kg dose was maintained with isavuconazole or fluconazole. Only 1 case (8.3%) with isavuconazole met target level.
Cyclophosphamide was included in the conditioning regimen for 96 patients; the remaining four cases involved second or later transplants, limiting the ability to assess the contribution of cyclophosphamide to cyclosporine clearance. Only 5 patients (5.2%) achieved the target concentration on initial measurement; all five involved conditioning regimens containing cyclophosphamide, with patient BMI ranging from 22–30.

Conclusions: The standard cyclosporine dose of 3 mg/kg/day frequently fails to achieve target therapeutic concentrations in HSCT patients. Despite a wide distribution of BMI in the cohort, no clear association between body size and achieving therapeutic levels was observed

when dosing was based on lower body weight. This finding suggests that using lower body weight for dosing is appropriate. Drug-drug interactions with cyclophosphamide also unlikely contribute to reduced cyclosporine exposure. However, we found that current dosing recommendations of 3 mg/kg/day may be insufficient, and early dose adjustment or higher initial dosing should be considered to optimize GVHD prophylaxis. Further studies are warranted to determine the optimal cyclosporine dosing strategy in patients undergoing HSCT.

Clinical Trial Registry: NTUH REC approval number 201810058RIND

Disclosure: Nothing to declare.

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RISK VS BENEFIT: CIPROFLOXACIN PROPHYLAXIS IN HIGH DOSE MELPHALAN AUTOLOGOUS SCT - A SINGLE CENTRE EXPERIENCE

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Background: Fluoroquinolone prophylaxis (FQP) is recommended in adult patients with expected neutropenia ≥7 days, aiming to reduce mortality, febrile episodes and Gram negative blood stream infections (BSI), however should be balanced against potential harmful effects. Recent UK recommendations and incidence of colonization with multi-drug resistant (MDR) bacteria, such as ESBL producing Gram negatives and vancomycin resistant enterococci in our Unit, led to a trial of discontinuing routine ciprofloxacin prophylaxis in patients undergoing high dose melphalan autologous stem cell transplant.

Methods: Retrospective review: Twenty patients (January-June 2024) receiving FQP (Group 1) were compared to 20 patients (January–June 2025) not treated with FQP (Group 2). Data obtained via hospital patient records. Patient characteristics, hospital acquired infections and antibiotic use during hospital admission was reviewed. Length of hospital stay (LoS), serious adverse reactions (SAE) to antibiotics and acquisitions of MDR bacteria detected on routine screening were also recorded.

Results: Both groups were comparable in baseline characteristics, with the exception of more transplants being commenced in the ambulatory setting in group 2, admitted to hospital in the neutropenic phase. All patients required broad spectrum antibiotics for neutropenic fever/suspicion of BSI at least once following transplant. There was no significant difference in the number of episodes of neutropenic fever in either group. There was higher incidence of BSI (twice the rate of Gram negative BSI) in the no FQP group, although no significant difference in antibiotic course length. There were no *Clostridium difficile* infections, representative of our local epidemiology.
Double the number of patients on FQP required a second course of antibiotics but patient numbers are extremely small. The total number of antibiotic days was longer in the FQP

group, 3 patients in this group required ICU admission – one for piperacillin/tazobactam anaphylaxis, one for potential infection/bleeding and one non-infection related. No patients required ICU admission in the no FPQ group. There were no deaths, all patients were discharged from hospital, with only one re-admission which was not infection related. There was no difference in ESBL Gram negative isolation – one BSI in each group. The Gram negative BSIs in the no FQP group were, largely not MDR, with the exception of one ESBL *Klebsiella*. Gram positive infections occurred in both groups which would not be prevented by ciprofloxacin prophylaxis.

	Group 1 FQP (N=20)	**Group 2 no FQP (N=20)**
Gender Male Female	 14 6	 15 5
Median Age	60	62
Diagnosis: Myeloma AL amyloidosis POEMS	 20 0 0	 18 1 1
Median Length of stay (range)	18 days (10-39)	19 days (10-27)
Hospital readmission rate within 30 days	1 (unrelated to infection)	0
Escalation of care to Intensive Care Unit (ICU)	3 (1 airway obstruction, 1 penicillin anaphylaxis, 1 ?infection/?bleed)	0
VRE Acquisition (N) CPE acquisition (N) C. *difficile* infection	4 0 0	4 0 0
BSIs (N)	6 (*E. coli* x 2 *Streptococcus mitis/oralis* x 2 *Niallia circulans* x 1 *Rothia mucilaginosa* x 1)	*9* *(E.coli x 2* *VRE x 2 (Vancomycin resistant Enterococcus faecium)* *Streptococcus mitis/oralis x 1* *Streptococcus infantarius x 1* *Pseudomonas aeruginosa x 1* *Klebsiella pneumoniae x 1* *Streptococcus gallolyticus x 1*

Patients received a single course of antibiotics (N) Patients received 2 courses of antibiotics (N)	18 2	19 1
Total antibiotic exposure (days)	227	203
SAEs	Penicillin anaphylaxis	N/A

Conclusions: Our results mirror previous studies, FQP was associated with lower rate of Gram negative BSI, higher rate of BSI including Gram negative BSI in the non FQP group, but no difference in outcome in particular mortality between the two groups.
There was no impact on LoS, broad spectrum antibiotic treatment or VRE acquisition. Gram negatives in our non FQP group were in the main, not MDR. The study involves small patient numbers therefore more data is required to draw any firm conclusions, other than the increase in BSI rate including Gram negatives in the non FQP group, but the majority were susceptible to empirical antibiotics and no patients in the no FQP group required escalation of care to ICU. It is important to consider local antimicrobial resistance epidemiology.

Disclosure: Nothing to declare

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AWARENESS OF EXTRAVASATION MANAGEMENT FOR CYTOSTATIC AND NON-CYTOSTATIC DRUGS AMONG HEMATOLOGISTS IN THE CZECH REPUBLIC

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Background: Extravasation of intravenous drugs remains a significant clinical challenge with potentially severe consequences for patient outcomes. While awareness of extravasation caused by cytotoxic agents is well established, substantial knowledge gaps persist regarding non-cytostatic drugs and the appropriate selection of antidotes among practicing hematologists—an issue that warrants urgent attention.

Methods: A cross-sectional survey using an anonymous questionnaire (Microsoft Forms) was conducted among hematologists at two major Czech centers (University Hospital Hradec Králové and Institute of Hematology and Blood Transfusion, Prague) to assess their knowledge of extravasation prevention, recognition, and management.
The 14-item questionnaire covered demographics, clinical experience, risk factors, symptom

recognition, extravasation management knowledge, high-risk agents, and awareness of antidote availability. Data were analyzed using descriptive statistics.

Results: A total of 25 hematologists completed the survey (17 from University Hospital Hradec Králové, 8 from the Institute of Hematology and Blood Transfusion).
A striking paradox emerged: although 17 out of 25 respondents (68%) had more than 10 years of clinical experience, the same proportion (68%) rated their own knowledge as merely basic—a concerning self-assessment.
Critical gaps were identified: only 15/25 (60%) were aware of institutional protocols covering both cytostatic and non-cytostatic drugs, and alarmingly, 10/25 (40%) could not identify where antidotes were stored. Knowledge of specific antidotes was inconsistent: 20/25 (80%) correctly identified DMSO 99% for anthracyclines, but only 12/25 (48%) knew the appropriate treatment for vinca alkaloid extravasation (hyaluronidase with heat compresses), while 9/25 (36%) incorrectly chose cold application. For propofol, 15/25 (60%) provided the correct answer (hyaluronidase with cold compresses), and for radio/x-ray contrast agents, 20/25 (80%) answered correctly (cold compresses).
Only 8/25 participants (32%) were able to identify all risk factors predisposing patients to extravasation and furthermore, only half of respondents 14/25 (56%) accurately recognized the clinical manifestations of extravasation. Notably, only 3/25 participants (12%) correctly classified all agents belonging to the group of vesicants. These findings highlight persistent gaps in comprehensive knowledge regarding extravasation risk assessment and management among experienced clinicians.

Conclusions: Significant and unexpected knowledge gaps persist among experienced hematologists regarding extravasation management protocols, antidote accessibility, and treatment procedures for specific agents. These findings represent a critical patient safety concern and underscore the urgent need for targeted, continuous education to standardize clinical practice and prevent potentially irreversible tissue damage.

Disclosure: Nothing to declare.

P403

RISK ASSESSMENT OF HERPESVIRUS REACTIVATION IN CHILDREN UNDERGOING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION WITH PROPHYLACTIC USE OF LETEMOVIR: A RETROSPECTIVE SINGLE CENTER OBSERVATIONAL STUDY

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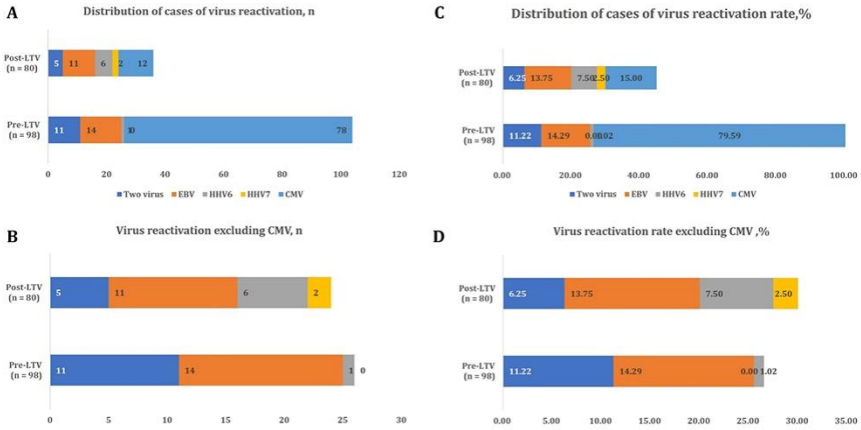
Background: Virus reactivation after allogeneic hematopoietic stem cell transplantation is a common complication that seriously affects patient prognosis. Letermovir (LTV), a novel drug for preventing cytomegalovirus (CMV) infection, significantly reduces the need for broad-spectrum antiviral drugs such as ganciclovir and foscarnet. This broad-spectrum antiviral also

exhibit inhibitory activity against other herpesviruses, such as HHV-6. Studies in adults suggest that LTV use may be associated with reactivation of HHV6. The immune reconstitution process, viral infection spectrum, and response to LTV in children may differ from those in adults. Currently, there is a lack of information on the reactivation patterns and clinical outcomes of herpesviruses in pediatric HCT patients in the context of LTV use.

Methods: A single-center retrospective study was established and approved by the Ethics Committee of Children's Hospital of Soochou University (2025CS136). Patients' data were extracted from the electronic medical record system from September 2022 to March 2024. They were divided into two groups based on whether they received LTV prevention or not. Patient demographic information was collected, including age, sex, primary disease, donor type, stem cell source, pre-treatment regimen, GVHD prevention regimen, LTV usage, and virus monitoring data.

Results: A total of 98 patients were included in the Pre-LTV group, with 80 patients in the Post-LTV group. The proportion of CMV reactivation in the Post-LTV group was significantly lower than that in the Pre-LTV group (36.2% vs 70.4%, $p < 0.001$), whereas the proportion of HHV6 and HHV7 reactivations in the Post-LTV group was higher than that in the Pre-LTV group (8 cases vs 1 case, $p < 0.015$). The neutrophil engraftment time in the Post-LTV group was longer than that in the Pre-LTV group(13.0 ± 3.5 vs. 12.2 ± 1.8 days, $p = 0.046$) (Fig 1). In addition, according to the grouping of HHV6/7 activation and without HHV6/7 activation, there was no different in neutrophil engraftment time between cases with and without HHV6/7 activation. However, the platelet engraftment time was longer in cases with HHV6/7 activation than in those without activation, at No active 13.0 ± 5.6, HHV6 27.2 ± 31.3, HHV718.0 ± 1.4 days, respectively, $p < 0.001$. No HSV-1/2, VZV was detected in all cases.

Figure1 Number and proportion of reactivated viruses



Conclusions: Prophylactic use of LTV in pediatric transplant patients can significantly reduce the risk of CMV reactivation, but these patients also experience an increased risk of HHV6 and HHV7 reactivation due to the weakened "bypass" inhibitory effect of broad-spectrum antiviral drugs, which may prolong platelet engraftment.

Disclosure: Nothing to declare.

Patient Advocacy: Patients' Reported Outcome and Expectations

P365

VARIANCES IN PATIENT EXPERIENCES WITH SHARED DECISION-MAKING BY TREATMENT IN PATIENTS WITH LBCL: ANALYSIS OF LYMPHOMA COALITION'S 2024 GLOBAL PATIENT SURVEY ON LYMPHOMAS AND CLL

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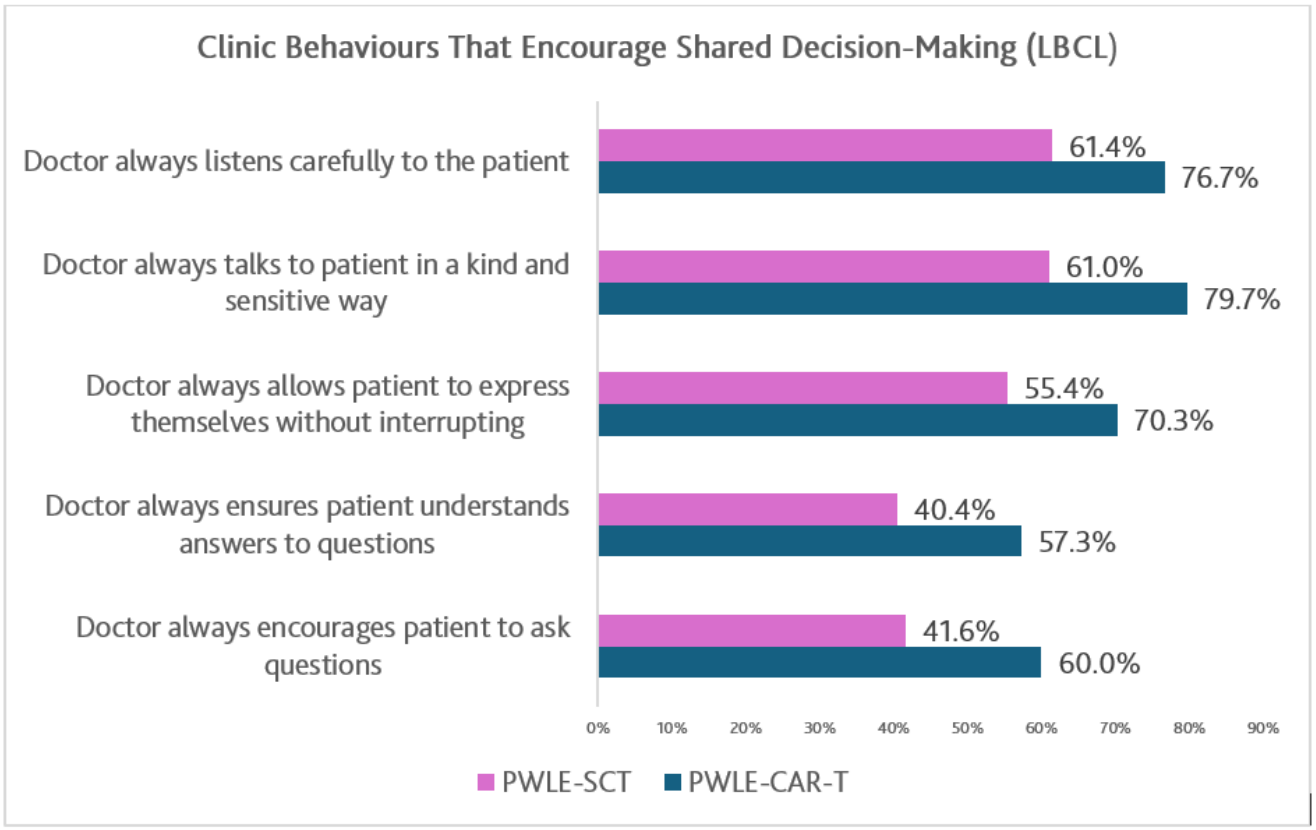
Background: Shared decision-making (SDM) is a key aspect of patient-centred care for patients with large B-cell lymphoma (LBCL), requiring patient inclusion in care decisions and healthcare providers (HCPs) understanding preferences and needs of patients. In relapsed/refractory (R/R) or high-risk LBCL, guidelines recommend stem cell transplant (SCT) or CAR-T therapy. This study investigates variances in SDM by these therapy classes.

Methods: A cross-sectional, anonymous online global survey for patients with lymphoma was deployed in 2024. This analysis focuses on people with lived experience (PWLE) with LBCL, exploring questions regarding SDM including treatment goals, perceived involvement in care decisions and patient-HCP communication. Responses were categorised by last treatment (CAR-T, SCT) for descriptive analysis and comparison of SDM experience.

Results: The study included 178 PWLE-LBCL (R/R or high-risk) from 23 countries, categorised by last treatment received: CAR-T (42.1%, n=75) or SCT (57.9%, n=103). While the CAR-T cohort was slightly older and the overall sample included more females, most patients were in remission (CAR-T: 50.7%; SCT: 61.2%).
A significant gap persists in SDM. Nearly all patients desired high involvement (CAR-T: 100%; SCT: 97%), but far fewer felt adequately involved (CAR-T: 62.5%; SCT: 49.5%). Most preferred collaborating with their doctor on decisions (around 58% in both groups), emphasising the vital need for clinic integration of SDM.
Treatment goals differed: Remission was very important to a higher proportion of PWLE-SCT (97.3% vs. 76.9% CAR-T), as was improved quality of life (80.6% vs. 66.7% CAR-T).
CAR-T patients consistently reported more positive interactions related to productive SDM clinic behaviours. They were more likely to feel their HCP always encourages questions (60.0% vs. 41.6% SCT), routinely checks understanding (57.3% vs. 40.4% SCT), experienced fewer interruptions (70.3% vs. 55.4% SCT), and perceived greater clinician kindness/sensitivity (79.7% vs. 61%) and attentive listening (76.7% vs. 61.4%).
Treatment choice was limited, particularly for SCT patients (CAR-T: 46.7% offered a choice; SCT: 27.8%). Subsequently, far more SCT patients wished they had received a different

therapy (29.5%) due to its impact of the treatment on their QOL, compared to CAR-T patients (14.6%).



	PWLE-CAR-T (n=75)	PWLE-SCT (n=103)
Biological sex	Female 57.3%	Female 68.9%
Average age	59.7 years [range 25-87]	53.5 years [range 27-76]
Patient definitely involved in care decisions as much as they want to be	62.5%	49.5%
Patient would like SDM with doctor	59.2%	57.0%
Patient would like to make care decisions alone	15.5%	15.0%

	PWLE-CAR-T (n=75)	PWLE-SCT (n=103)
Patient would like doctor to make care decisions alone	25.4%	24.0%
Factors very important to treatment choice		
Cure	78.8%	86.8%
Improved/longer survival	75.5%	89.2%
Bring about a remission or response	76.9%	97.3%
Improved quality of life	66.7%	80.6%
Fewer side effects / more tolerable side effects	35.3%	35.1%
Duration of treatment	21.2%	29.7%
Certainty of available treatment data/results	46.2%	40.5%
Patient was given a therapy choice prior to most recent treatment	46.7%	27.8%
In hindsight, patient would have chosen a different treatment option due to impact on quality of life	14.6%	29.5%

Conclusions: Suboptimal SDM persists for all PWLE-LBCL and improvements are needed for all patients. While most patients desire high involvement, just over half achieve it. Crucially, SDM is more successful in the CAR-T cohort (higher involvement, better communication, more options). This highlights the need for proactive, targeted SDM efforts to close the significant engagement gap in the SCT patient group.

Disclosure: Lymphoma Coalition was sponsored by Astra Zeneca, Eli Lilly, Incyte, Kite, a Gilead Company, Johnson & Johnson Innovative Medicine, Novartis, Regeneron, F. Hoffmann-La Roche Ltd, SERB Pharmaceuticals, Sobi - Swedish Orphan Biovitrum, Takeda Pharmaceuticals. None of the authors benefited personally from the research.
Natacha Bolanos has consulted with Ipsen, Novartis, Roche, Sobi and Takeda. Any funds received for this work were paid to Lymphoma Coalition.
Lorna Warwick has consulted with BMS, Ipsen, Novartis, Regeneron, Roche, and Takeda. Any

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Kathryn Perry has consulted with Ipsen and Takeda. Any funds received for this work were paid to Lymphoma Coalition.

P366

EXPLORING DEATH, GRIEF AND BEREAVEMENT AT ANTHONY NOLAN: THE IMPORTANCE OF STRUCTURED INVOLVEMENT TO IMPROVE SUPPORT FOR BEREAVED LOVED ONES

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Background: Death after stem cell transplant is a common reality: around half of patients do not survive beyond five years. Research shows that bereavement experiences in this community can be distinct and severe, affecting a wide range of individuals including patients' families and even unrelated donors, who may feel sadness, grief, and helplessness. Parents bereaved after a child's transplant often report higher levels of depression, anxiety, and traumatic grief than those whose children received other treatments. Despite this, bereavement support specific to stem cell transplant is limited, fragmented, and reactive, leaving staff uncertain and emotionally strained when supporting families. We wanted to know where Anthony Nolan's work and support currently sits within this, and what we could do differently and better. This led to us thinking how to best involve bereaved loved ones in such a sensitive project.

Methods: We used the Design Council's double diamond framework for involvement. We conducted 12 1 on 1 interviews with people who had been bereaved after their loved one had a stem cell transplant. We then convened as a working group to review and find themes. A survey was then created that included those themes and asked for feedback and further insight. 29 people responded to the survey, and a small group of these people are continuing their involvement, for example with user testing new resources.

Results: We found seven themes:

1. Grief is unique, even within families grieving the same person. This is connected to the next theme.

2. Isolation after isolation: the bereaved experience of isolation is compounded and connected, by them, to their loved one's experience of being in isolation for treatment.

3. Participants experience guilt about their perceived incorrect decisions, inaction or own stem cells in the case of sibling donors.

4. Bedside manner: the way the death is dealt with within healthcare teams is different and not as well received by the bereaved.

5. The gap for CYP support is larger than for adults, leading to inequality within the support of families.

6. Family dynamics change following a death, and the role of next of kin influences this.

7. This was all underpinned with an overarching theme of a need for more support in both professional intervention and peer support.

Conclusions: As we were able to carry out meaningful involvement, we have an enriched set of outcomes that are directly connected to what loved ones told us about their experience. We were able to see there is unmet need in this area, and Anthony Nolan are well placed to provide supportive interventions such as improved health information, working with healthcare professionals to provide information materials at the right time for the bereaved. We also believe that stem cell and CAR-T informed counselling services that can cater to families would address some of the need for emotional support. We will explore working with relevant organisations and loved ones to deliver peer support. All these outputs continue with involvement at the forefront of this continuing significant project.

Disclosure: Nothing to declare

P368

THE NEW EU REGULATION ON SOHO: STRENGTHENING THE PROTECTION OF DONORS, RECIPIENTS AND OFFSPRING

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Background: The European Union (EU) regulation 2024/1938 on standards of quality and safety for Substances of Human Origin (SoHO) intended for human application was adopted on 13 June 2024 in order to solve issues that were not (sufficiently) addressed by the previous EU directives on blood (Directive 2002/98/EC) and tissues and cells (Directive 2004/23/EC). Among them, an extensive evaluation of the EU legislation led by the European Commission highlighted that they were avoidable risks for donors and for children born from donated gametes, and that patients were not fully protected from avoidable risks.

Methods: This study is based on an analysis of the preparatory documents and of the final adopted version of the EU regulation on SoHO regarding the protection of SoHO donors, recipients and offspring. It combines legal and biomedical sciences approaches as well as fundamental and practical analysis in order to clarify and discuss the new EU legal measures targeting the protection of SoHO donors, recipients and offspring.

Results: The EU regulation on SoHO strengthens the protection of SoHO donors, recipients and offspring through the introduction of two dedicated chapters with detailed binding rules. First, the fundamental principles of the protection of donors are anchored within the

provisions of the EU regulation on SoHO. Not only these principles are recognised and key notions such as compensation and consent are legally defined, but conditions for their implementation are provided, especially regarding voluntary and unpaid donation of SoHO and consent.
Second, minimum standards are established and increased to ensure a high level of safety and protection of health of SoHO donors, SoHO recipients and offspring from medically assisted reproduction. It implies the data collection from SoHO donors and the mandatory use of SoHO living donors' registries to monitor their health after SoHO donation. It also implies a positive benefit/risk balance for SoHO recipients and offspring and mitigation of risks of communicable and non-communicable disease transmission (including the transmission of serious genetic conditions and cancer), and of any other avoidable risk to the health. Those risks include those: related to the protection of dignity, resulting from cross-contamination between SoHO, arising from microbial contamination of SoHO from the environment, the personnel, the equipment and the materials coming into contact with SoHO, linked to the addition or contact with any reagents and solutions, linked to the changes of the inherent properties of SoHO, and to human error.
Third, the implementation of particular standards to protect SoHO donors, recipients and offspring shall comply with additional binding rules adopted by the European Commission. In their absence and upon demonstration of relevance to SoHO competent authorities, SoHO entities shall take into account guidelines published by the ECDC, the EDQM, the Member States, or guidelines or technical methods considered compliant with EU law standards by the inspectors of SoHO establishments.

Conclusions: The EU regulation on SoHO operates a major shift from the quality and safety of SoHO to the wider protection of SoHO donors, recipients and offspring which is either strengthened or newly covered.

Disclosure: *Aurélie Mahalatchimy and Valentin Roby have no conflict of interest to declare. Christian Chabannon has received speaker honoraria and consulting fees from BMS, Gilead/Kite, Novartis, Jazz Pharmaceuticals, Janssen/J&J and Miltenyi Biotec.*
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P369

DESIGNING LIFE AFTER CAR-T: EXPLORING PATIENT UNCERTAINTY AND EDUCATION NEEDS IN POST-CAR-T THERAPY LIFE

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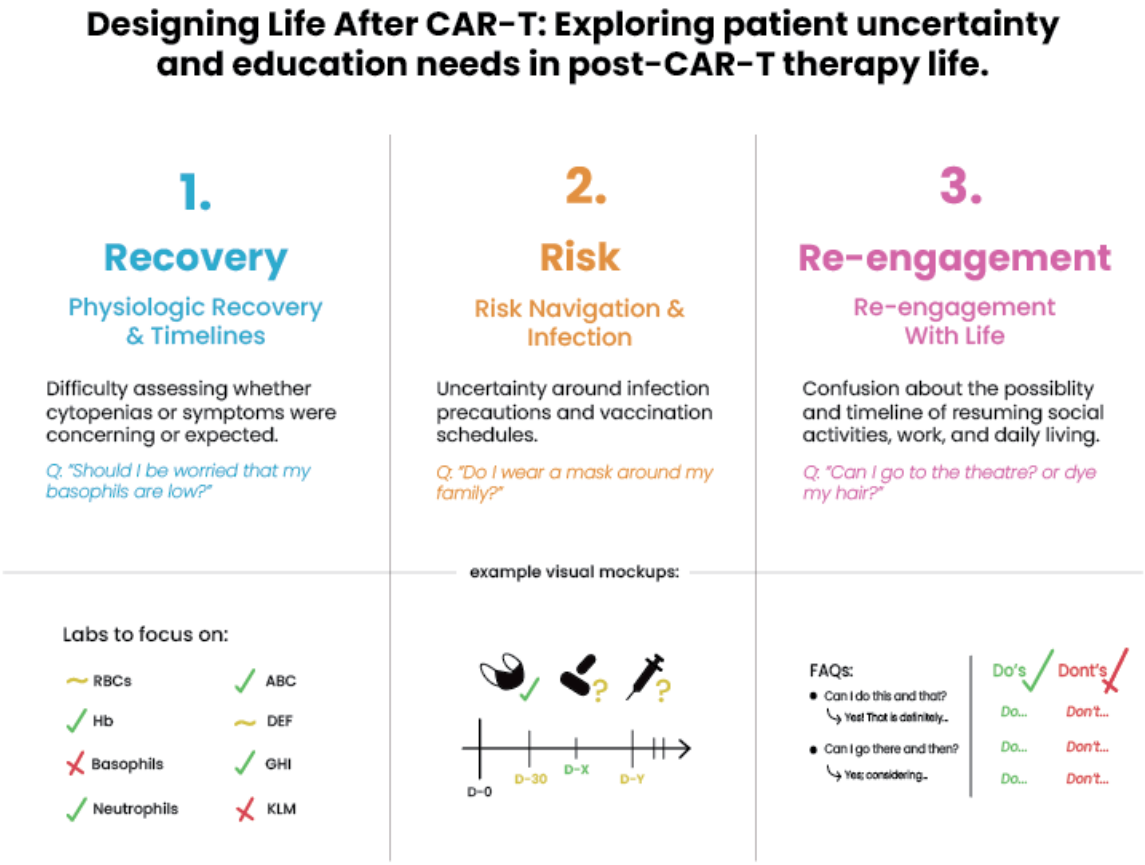
Background: CAR-T therapy patient education resources are often comprehensive when it comes to pre-treatment education; yet, far less emphasis is placed on the post-CAR-T period: when patients leave a highly-monitored inpatient environment and face confusing symptoms, fluctuating lists of lab values, and an uncertainty on their readiness for returning

to daily life. In practice, these uncertainties manifest as questions such as "Should I be worried that my basophils were low?, "Can I go to the theatre?", or "Can I swim at my family's pool party?".

Methods: This reflective analysis integrates on-the-ground clinical observations in patient encounters (focusing on recurrent questions and concerns voiced by patients during follow-up) and thematic insights from patient-reported experience literature. A design-thinking approach was then used as a lens to identify unmet needs, map out thematic domains of patient uncertainty, and translate them into proposed solutions.

Results:

Three domains emerge to represent the core categories of uncertainty that were observed and appear to influence patient confidence, behaviors, and emotional well-being: recovery, risk, and re-engagement.
Recovery (Physiologic Recovery & Timeline): Patients exhibited difficulty assessing whether changes such as fluctuating cytopenias or certain symptoms represented concerning developments or expected recovery patterns. Patient questions included "Should I be worried that my basophils are low?", and "I saw that my RBC count is low?".
Risk (Risk Navigation): Uncertainty about infection precautions, including masking, exposures, and vaccines, was a major driver of anxiety. Patient questions included "Do I wear a mask with my family?", and "What about the flu vaccine?".
Re-engagement (Re-engagement With Life): Patients expressed confusion and worry about the possibility and the timeline of resuming social activities, work, and other daily functions. Patient questions included "Can I go to the theatre?", and "So I was wondering if I could dye my hair?".
A visual post-CAR-T life guide is proposed to address these domains purposefully: incorporating simplified explanations and structured time lines to address Recovery, stratified precautions tied to immune milestones to address Risk, and scenario guidelines and FAQs to address Re-engagement.



Conclusions: Major themes of uncertainty in post-CAR-T life were recovery timelines, risk navigation, and re-engagement with daily life. This structured understanding can then inform the creation of purposeful and accessible patient education tools. Iterative design-thinking, alongside visual graphic design, emphasize clarity, usability, and co-creation: appropriate for an education tool that must be well-suited for the cognitive and emotional demands of the post-CAR-T period, and that may reduce patient anxiety, improve communication efficiency at follow-up visits, and enhance quality of life during early survivorship. Collaborative development with clinicians and patients will then support future feasability of pilot testing and implementation - whether that be as a student-led project, a clinic-based initiative, an academic center program, or a broader organizational rollout.

Disclosure: Nothing to declare.

P370

CAREGIVERS' PROXY ASSESSMENTS OF HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH HEMATOLOGIC MALIGNANCIES

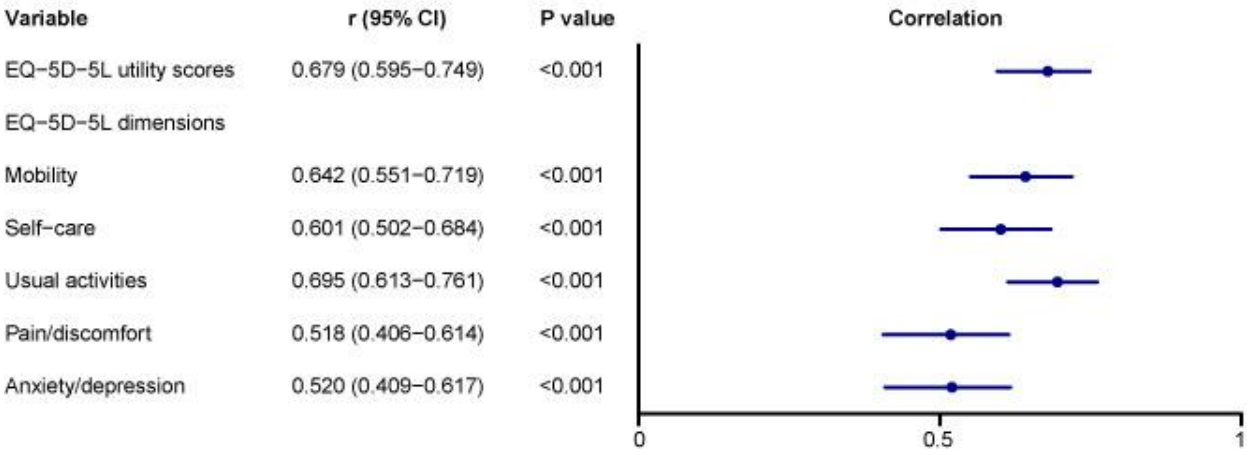
Wei Qin[1], Fenfang Tong[1], Cong Zeng[1], ***Yajing Xu***[1]
[1]*Xiangya Hospital, Central South University, Changsha, China*

Background: Patients with hematologic malignancies are commonly burdened by the disease itself as well as treatment-related side effects, which makes it difficult for them to complete the health-related quality of life (HRQoL) assessments. We aimed to investigate the reliability and influencing factors of caregivers as proxies in measuring HRQoL for patients with hematologic malignancies.

Methods: 203 patients with hematologic malignancies and their caregivers were enrolled. Both patients and caregivers independently completed the EuroQol 5-Dimensions 5-Levels questionnaire to collect patient self-rated HRQoL and caregiver proxy-rated HRQoL. Additionally, caregivers completed the Generalized Anxiety Disorder 7-Item Scale, Patient Health Questionnaire-9, and Family APGAR Index to evaluate their anxiety symptoms, depression symptoms, and perceptions of family functioning.

Results: The caregiver proxy-rated HRQoL exhibited strong correlations with patient self-rated HRQoL, in both EQ-5D-5L utility scores (r = 0.679, P < 0.001) and EQ-5D-5L dimensions (correlation coefficients from 0.518 to 0.695, all P < 0.001). Exact agreements between caregiver proxy-ratings and patient self-ratings ranged from 66.5% to 84.2% across EQ-5D-5L dimensions. Caregivers' demographic characteristics and perceptions of family functioning had no impact on the accuracy of proxy assessments, while greater anxiety symptoms (r = 0.408, P < 0.001) or depression symptoms (r = 0.288, P < 0.001) among caregivers were significantly associated with their overestimation of patients' symptom burden.

Qin et al. Figure 1



Conclusions: Caregivers are reliable proxies for assessing HRQoL in patients with hematologic malignancies. However, the anxiety or depression symptoms of caregivers may increase their overestimation in patients' symptom burden.

Disclosure: Nothing to declare.

P371

QUALITY OF LIFE TRAJECTORIES IN THE YEAR FOLLOWING ALLOGENEIC STEM CELL TRANSPLANT: A MIXED-METHODS STUDY

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[1]*Anthony Nolan, London, United Kingdom of Great Britain and Northern Ireland (the),* [2]*Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom of Great Britain and Northern Ireland (the)*

Background: Allogeneic haematopoietic cell transplantation (allo-HCT) offers curative potential for many haematological disorders; however, patients often face physical and psychosocial challenges which affect quality-of-life (QoL). This study prospectively examined QoL trajectories and patient perspectives about change in wellbeing in the first year following allo-HCT.

Methods: This multicentre prospective cohort study used a convergent mixed-methods design. Adult (≥18 years) allo-HCT recipients from three UK centres completed questionnaires at baseline (pre-transplant), day 0, day 28, day 100, and day 365 (one-year follow-up). QoL was assessed at each timepoint using the 29-item Patient-Reported Outcomes Measurement Information System (PROMIS-29) which evaluates physical function, fatigue, sleep disturbance, anxiety, depression, pain interference, social participation, and pain intensity. Descriptive statistics were used to summarise cohort characteristics. PROMIS T-score trajectories were analysed using the Friedman test with Bonferroni-adjusted Wilcoxon post-hoc comparisons. Semi-structured interviews conducted at one-year follow-up explored patient experience of recovery and how symptom burden influenced QoL after transplant. Qualitative data were analysed using framework analysis and integrated with quantitative findings using a joint display.

Results: Sixty patients were enrolled (median age 56 years, range 21–74). Most participants were male (70%), White British (80%), and married or in civil partnerships (58%). The majority had acute myeloid leukaemia (53%) and received a matched unrelated donor transplant (67%). Over half held higher or degree-level education (57%), and most lived in the least deprived areas (upper IMD quartile, 8–10; 47%).
Physical function scores declined from baseline (45.9 ± 9.2) to day 28 (36.8 ± 8.1; $p<0.001$, $r=0.81$, 95% CI 0.72–0.86) with partial recovery by day 100 (43.5 ± 9.4; $r=0.68$, 95% CI 0.48–0.84). Fatigue scores increased from baseline (52.1 ± 9.8) to day 28 (63.6 ± 9.3; $r=0.83$, 95% CI 0.75–0.87). Social participation declined (36.4 ± 6.7; $r=0.73$, 95% CI 0.58–0.84), and sleep disturbance rose between day 0 (47.9 ± 5.1) and day 28 (53.1 ± 8.0;

r=0.72, 95% CI 0.57–0.84), all p<0.001 (Bonferroni-adjusted). Anxiety scores peaked on day 0 (57.9 ± 10.2), while depression scores were highest on day 100 (53.0 ± 10.5). By one year, most QoL domains had recovered to baseline levels, though few patients achieved population normative values.
Interviews with ten participants contextualised these trends. Five themes were identified: (1) initial decline, slow improvement, but never the same; (2) health first, social life second; (3) learning to live with fatigue; (4) evolving anxiety; and (5) the long-term burden of isolation. Participants described initial recovery as physically and emotionally demanding, characterised by weakness, fatigue, and restricted social contact leading to isolation and reduced confidence. At one year post-HCT, participants described ongoing challenges with energy, physical stamina, and anxiety about relapse and long-term health.

Conclusions: Recovery after allo-HCT is characterised by early decline and gradual, sometimes incomplete improvement in QoL during the first year. Integrating patient perspectives with PROs helps capture the real experience of recovery and guide survivorship care that better supports long-term wellbeing.

Disclosure: This study is sponsored and funded by Anthony Nolan. Additional funding to support this study has been received from NIHR (205434) and Therakos.

P372

SUPPORTING PATIENTS WITH LIMITED OR NO ENGLISH TO PARTICIPATE IN RESEARCH: A NATIONAL SURVEY OF LANGUAGE AND TRANSLATION SUPPORT IN UK ALLOGENEIC TRANSPLANT CENTRES

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Background: Patients with limited or no English often face barriers to accessing health information and opportunities to participate in research. The purpose of this study was to investigate i) which languages other than English are most spoken by UK cell therapy patients and ii) what translation and interpretation services are available to support patients with limited or no English to participate in research.

Methods: A cross-sectional survey was distributed to health care professionals working within UK adult allogeneic transplant centres (June–September 2025). The survey captured: i) which languages other than English are most spoken; (ii) the availability and perceived quality of interpretation and written translation services; (iii) local NHS trust policies on translation and interpretation; and (iv) perceived barriers to engaging patients with limited or no English in research. Descriptive statistics were used for closed-ended questions, while inductive thematic analysis was applied to free-text responses.

Results: A response was received from 58 health professionals across 22/23 (95%) of UK adult allogeneic transplant centres. Respondents were predominantly nurses (n=38, 66%) or doctors (n=8, 14%). All respondents reported caring for patients with limited or no English.

60% of respondents reported that >5% of their patient population had limited English. There was widespread variation between respondents from different transplant centres about which languages other than English were most spoken. However, Arabic, Urdu and Polish emerged as the most frequently encountered languages nationally. There was a relatively even split between the use of in-person and video or telephone interpretation services (48% vs 52%). 36% of respondents reported that access to an interpreter often affected their ability to recruit patients to research studies. Availability of written translated materials was limited. Only one respondent could name a current study at their centre that provided translated materials for participants. 90% of respondents were unaware of, or reported the absence of, a local NHS trust policy or guideline for including patients with limited or no English in clinical trials and research studies. Within free-text comments respondents highlighted that it was often difficult to ensure patients with limited or no English fully understand study information, that taking informed consent was challenging, and that reliance on family members as informal interpreters was common.

Conclusions: This survey highlights that UK transplant centres consistently care for patients with limited or no English, yet there is limited structured translation or interpretation services to support these patients to participate in research. The findings underscore the need for language support to be included in broader strategic initiatives designed to improve diversity and inclusion in clinical research. To inform evidence-based guidance and policy recommendations, future research should seek to work directly with patients with limited or no English to understand their experience care and using translation and interpretation support.

Clinical Trial Registry: N/A

Disclosure:

Nothing to declare:

- The survey was conducted as part of routine work at Anthony Nolan
- There was no commercial funding
- No author has personal financial conflicts related to translation services or vendors

P373

SCALING SOCIOECONOMIC AND QUALITY OF LIFE DATA COLLECTION AMONG HAEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS IN THE UK: SEQOL STUDY PROGRESS AND SAMPLE SIZE FORECAST

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Background: The purpose of the SEQoL study is to scale the collection of socioeconomic and quality of life data among allogeneic haematopoietic cell transplant (HCT) recipients. Data from the SEQoL study will be linked with clinical outcome data and used to investigate the effect of social determinants on patient outcomes and quality of life. This abstract presents the current recruitment progress and the sample size forecast.

Methods: Within the SEQoL study, adult (>18 years) allogeneic HCT patients are invited to complete a brief demographic and quality-of-life questionnaire before conditioning, on the day of their transplant, on days 28 and 100, and at 6, 9 and 12 months post-transplant. Outcome measures include the MacArthur Ladder, The Functional Assessment of Cancer Therapy - Bone Marrow Transplantation (FACT-BMT), and Lee Symptom Scale for chronic graft-versus-host-disease. Transplant centres are responsible for participant recruitment and consent, but outcome data collection and follow-up are managed by the research team at Anthony Nolan. Each transplant centre has received a tablet computer to facilitate e-consent and electronic data collection at baseline. Patient consent to link patient-reported outcome data from the SEQoL study with clinical outcome data held by national registries is obtained at enrolment.

Results: Recruitment to the SEQoL study opened in August 2024, since then >480 patients (as of December 2025) have enrolled in the study. There are 23 NHS transplant centres in the UK which provide allogeneic HCT to adults. The SEQoL study is open in 19 of these transplant centres, the remaining centres are planned to open in 2026. To ensure sufficient statistical power to detect even small effect sizes between socioeconomic predictors and patient outcomes following HCT, an estimate of the required sample size based on an 80% power threshold and a 5% significance level was produced. Given the inclusion of up to 10 socioeconomic variables in multivariable models and accounting for an anticipated 30% dropout rate by 12 months post-transplant, it is estimated that a minimum of 1175 participants are required to retain adequate power for the final analysis. The SEQoL study recruits on average 10 new patients per week. It is forecast that 1175 patients will be recruited by March 2027 after which data linking with clinical outcomes will begin. Consistent with the pilot study, capacity and workload at transplants centres has influenced the SEQoL study recruitment rate. The research team are working with transplant centres to streamline study processes related to study monitoring to overcome issues related to workload and are actively encouraging centres to involve health professionals in the co-ordination of the study via the NIHR, Associate Principle Investigator (PI) Scheme.

Conclusions: The SEQoL study will enable investigation into the temporal change in quality-of-life outcomes post-transplant and the effect of subjective and objective socioeconomic status on patient outcomes. Without this data there is limited understanding of how a stem cell transplant affects patient quality-of-life, and the impact of social determinants of health on clinical outcomes.

Disclosure: This study is sponsored and funded by Anthony Nolan. Additional funding to support this study has been received from NIHR (205434) and Therakos.

P374

CLINICAL PROFILE AND HEALTHCARE RESOURCE UTILIZATION IN PATIENTS WITH SICKLE CELL DISEASE WHO RECEIVED HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTS IN THE UNITED STATES

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Background: Sickle cell disease (SCD) is a genetic blood disorder that causes red blood cells to become abnormally shaped (sickle-shaped), leading to vaso-occlusive crises (VOCs), hemolysis, and end-organ damage. Haploidentical hematopoietic stem cell transplant (haplo-HSCT) is a type of allogeneic hematopoietic stem cell transplant (allo-HSCT). It uses stem cells from a half-matched donor, most often a close family member like a parent or sibling. It is a potential curative treatment option for patients with SCD. The use of haplo-HSCT has increased in the last decade; however, its risks such as graft-versus-host disease (GvHD), graft failure, and death can be significant. This study aims to characterize the clinical profile and healthcare resource utilization (HCRU) among patients with SCD who received haplo-HSCT in the United States (US).

Methods: This retrospective observational cohort study utilized the TriNetX Dataworks-USA National EHR Network Database. Patients with SCD were identified based on ≥1 inpatient or ≥2 outpatient records with an SCD diagnosis between June 1, 2010, and October 24, 2023 (patient identification period). Given the lack of specific ICD-10 codes for haplo-HSCT, an algorithm for patient identification was recommended by medical experts: ≥1 record of allo-HSCT on or after the first SCD diagnosis, receiving thiotepa as part of the conditioning regimen and cyclophosphamide as part of the GvHD prophylaxis care plan. Physician notes in a subset of patients were reviewed to confirm the use of haplo-HSCT. The index date was the date of the first record of haplo-HSCT procedure. Demographics were assessed on the index date. Mortality, transplant-related complications, treatments, and HCRU were summarized in the follow-up periods post haplo-HSCT.

Results: Thirty-five patients with SCD who underwent haplo-HSCT were identified. The mean age was 17.9 (SD: 7.9) years and 45.7% were female. The mean follow-up from the index date was 2.8 [SD: 1.7] years. Four patients (11.4%) died: one died during the first 100 days post haplo-HSCT and three died within 16 months after haplo-HSCT. Many patients experienced transplant-related complications: graft rejection or failure (17.1%), acute GvHD (17.1%), and/or chronic GvHD (20.0%). During the follow-up period after the first 100 days post haplo-HSCT, 76.5% of patients were prescribed opioids. About two thirds of patients (64.7%) had an emergency room (ER) visit, with an average of 2.2 (SD: 5.2) ER visits per-patient-per-year (PPPY); the mean number of inpatient visits PPPY was 3.3 (SD: 8.6) and the mean number of outpatient visits PPPY was 45.0 (SD: 31.2).

Conclusions: The results of this study demonstrate the risks and burden associated with haplo-HSCT in patients with SCD. There is a notable 11.4% mortality rate, and many patients experience burdensome complications and require enduring HCRU following haplo-HSCT. Despite advancements in transplant conditioning regimens leading to reduced graft rejection/failure rate and GvHD prevention, haplo-HSCT still poses considerable risks, highlighting the need for innovative therapies that deliver curative potential without the risks inherent to haplo-HSCT.

Disclosure: Arie Barlev, Amy Li, Duncan Brown, Suzan Imren, Aric Parnes, and Sara Rodrigues are current or former employees of Vertex Pharmaceuticals, Inc. and may own stock or stock options in that company. Kinwei Arnold Chan, Amanda Moore, Gina Giase, and Bridget Nolan are employed by TriNetX, LLC.

NURSES TOPICS

Care of the Carer (Healthcare Team and Caregiver)

NG12-04

THE CURRENT SITUATION OF STRESS AND MENTAL HEALTH INTERVENTION OF HEMATOPOIETIC STEM CELL TRANSPLANT CAREGIVERS

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Background: **Objective:** This study systematically analyzes the current stress levels and influencing factors among HSCT caregivers, exploring mental health intervention strategies to improve caregivers 'psychological well-being, thereby enhancing treatment outcomes and family functioning.

Methods: A prospective longitudinal design was employed, with 100 pairs of HSCT patients and their primary caregivers (daily accompaniment ≥4 hours) planned for inclusion. Follow-up surveys were conducted at key time points: pre-transplantation, alogenic anemia phase, post-donor phase, and 3 months post-transplantation. The caregivers' psychological status was assessed using standardized scales, including:
1. Stress Levels: The Caregiver Stress Index (CSI) was used for qualitative screening of stress presence; 2. Burden Degree: The Zarit Caregiver Burden Inventory (ZBI) and Caregiver Burden Inventory (CBI) were employed to quantify physical, emotional, and social burdens; 3. Psychological Reactions: Negative and positive feelings were analyzed through the Caregiver Response Assessment Scale (CRA). The study combined questionnaire surveys, clinical data, and social support indicators (e.g., financial pressure, family relationships) to analyze key factors influencing psychological status using a multivariate regression model.

Results: 1. Current Stress Status: Financial Burden: 43% of families need to sell assets or borrow money, with annual out-of-pocket medical expenses exceeding 50% of household income. Caregiver Intensity: 61% of caregivers require professional nursing skills, 72% experience sleep deprivation, and postoperative daily caregiving time ≥10 hours for 3 months. 2. Psychological Issues: Anxiety (30%), depression (60%), and post-traumatic stress symptoms (PTSS, 20%-30%) significantly higher than general population; family relationship tension rate reaches 38%,83% of caregivers go out for entertainment <5 times annually. 3. Influencing Factors: Patient Factors: Allogeneic transplantation and complications (e.g., GVHD) significantly increase stress; 4. Caregiver Factors: Young age, low education level, and negative coping styles correlate with higher anxiety; 5. Social Support: Financial

pressure, information opacity, and insufficient family support exacerbate psychological burdens.

Conclusions: HSCT caregivers universally face multidimensional stress, and their mental health status directly impacts patient recovery and family stability. Future interventions should focus on: 1. Long-term monitoring: Establish a comprehensive psychological assessment system covering the entire transplant cycle, with particular attention to high-risk phases (e.g., acute phase and complication phase); 2. Personalized support: Develop digital psychological platforms (e.g., online consultation, peer support communities) and integrated intervention programs (e.g., cognitive behavioral therapy, mindfulness training); 3. Family and social support: Provide economic assistance guidelines, family communication tools, and enhance professional guidance for caregivers by medical teams. This study provides empirical evidence for optimizing mental health interventions for HSCT caregivers, emphasizing the need to integrate caregiver support into the overall management framework of hematologic disease treatment.

Disclosure: Nothing to declare.

NP24

MONITORING STRESS AND WORKLOAD IN PRIMARY CAREGIVERS OF PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC PROGENITOR CELL TRANSPLANTATION: A ONE-YEAR SINGLE-CENTER EXPERIENCE

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Background: Allogeneic Hematopoietic Progenitor Cell Transplantation (allo-HSCT) is the only curative treatment for various malignant and non-malignant hematological diseases. It is a highly complex procedure with high morbidity in the early stages; therefore, the role of the primary caregiver is essential. The reviewed literature shows that these caregivers experience high levels of stress and burden, which negatively affect their quality of life.

Methods:

An observational, descriptive, cross-sectional study was designed at the University Hospital of Salamanca, conducted from July 2024 to July 2026. Caregivers were recruited in the allogeneic transplant nursing clinic during the pre-transplant assessment. All caregivers were included except those with physical or psychological disabilities and/or healthcare training.

Participants completed the Perceived Stress Scale (PSS-10), the Gijón questionnaire, and the Zarit Caregiver Burden Scale at the time of study inclusion, one month after the allogeneic transplant, at three months, and at one year. The PSS-10 questionnaire is scored from 0 to 40 points, with higher scores indicating higher stress levels. The Zarit scale ranges from 22

to 110 points and is stratified as follows: 22–46 "no burden," 47–55 "mild burden," and 56–110 "severe burden."

Clinical variables related to the patient's disease and treatment will be extracted from medical records. Statistical analysis will be performed using the SPSS v.25. Results will be presented using descriptive statistics, with frequency distributions and percentages for qualitative variables, and measures of central tendency and dispersion for quantitative variables.

Results:

39 caregivers have been recruited. All participants (100%) completed the baseline assessment and the one-month follow-up, 87% (n=34) completed the three-month follow-up; and 39.5% (n=15) completed the one-year follow-up. Six caregivers (15.4%) withdrew from the study due to the death of their relatives. Table 1 shows the characteristics of these caregivers and the mean scores on the administered scales.

Age (mean)	57,57 years (30-72)
Sex	Female: 31 (79.5%) Male: 8 (20.5%)
Caregiver's highest level of education	Primary Education: 11 (28.2%) Secundary Education: 2 (5.1%) High School: 3 (7.7%) University Degree: 8 (20.5%) Post-University Degree: 5 (12.8%) Profesional Education: 9 (23.1%) No answer: 1 (2.6%)
Caregiver's employment status at baseline	Full-time work: 12 (30.8%) Part-time work: 2 (5.1%) Household duties: 8 (20.5%) Unemployed: 8 (20.5%) Retired: 5 (12.8%) Others: 4 (10.3%)
Caregiver/patient relationship	Partner: 25 (64.1%) Sibling: 3 (7.7%) Son/Daughter: 3 (7.7%) Mother/Father: 8 (20.5%)
Living with the patient	Yes: 33 (84.6%) No: 6 (15.4%)

Other dependents under the care of the same caregiver	Yes: 10 (25.6%) No: 28 (71.8%) No answer: 1 (2.6%)
Possibility of alternating with another caregiver	Yes: 25 (64.1%) No: 14 (35.9%)
Patient and caregiver residence	Salamanca: 9 (23.1%) Castilla y León: 16 (41%) Extremadura: 12 (33.3%) Others: 1 (2.6%)
Mean baseline stress scale score Mean stress scale score at 1 month after allo-HSCT Mean stress scale score at 3 months after allo-HSCT	18.24 points (7–30) 19.25 points (7–33) 18.79 points (0–32)
Mean baseline Zarit scale score Mean Zarit scale score at 1 month after allo-HSCT Mean Zarit scale score at 3 months after allo-HSCT Mean Zarit scale score at 1 year after allo-HSCT	40.64 points (22–69) 40.44 points (26–65) 41.93 points (23–71) 40.71 points (25–59)

Table 1.

As shown in Table 1, the mean stress score remains high throughout the process due to its complexity, but it is lower during the first month while the patient is hospitalized, which may be related to the fact that care responsibilities fall mainly on healthcare professionals. Stress increases at three months, when the patient usually presents greater fragility and dependence for basic activities of daily living and decreases again at one year, as patients begin to regain part of their life prior to allo-HSCT. Regarding the Zarit scale, scores remain constant throughout the year, around 42 points, indicating an absence of caregiver burden.

Conclusions:

After one year of follow-up, we observed that caregivers of our patients experience consistently high levels of stress throughout the process; however, they do not exhibit significant caregiver burden. This finding should be interpreted with caution, as the impact of hospitalizations due to complications on caregiver burden requires further investigation. Additionally, potential bias may arise when patients complete questionnaires under stress or pressure.

Based on these findings, the next step would be to evaluate the impact of hospitalizations on caregiver burden and to determine the effectiveness of psychological interventions for caregivers.

Disclosure: No disclosure.

NP38

PSYCHOSOCIAL ASSESSMENT OF PATIENTS AND CAREGIVERS UNDERGOING AUTOLOGOUS HAEMATOPOIETIC STEM CELL TRANSPLANTATION AT HOME

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Background: Haematopoietic Stem Cell Transplantation (HSCT) is a procedure that has increasingly demonstrated the benefits of home-based treatment over hospitalization. In order to offer this option to patients who live far from the hospital, we collaborate with the Asociación Española Contra el Cáncer (AECC), which provides us with apartments close to the hospital.
This programme also requires the patient to have a caregiver throughout the process. The caregiver plays a crucial role in the HSCT home programme. Despite their critical role, their needs and wellbeing are often overlooked.
Currently, a psychosocial assessment of the patient is recommended to identify the most vulnerable individuals, as well as an assessment of the caregiver's wellbeing.
This study analyses, for the first time at the national level, the psychosocial risk of patients undergoing home-based HSCT using the Gijón Socio-Family (GSF) scale and the level of adverse effects on the quality of life of the primary caregiver using the Family Reported Outcome Measure (FROM-16) scale. The results of these measurements significantly help to implement holistic clinical practice.

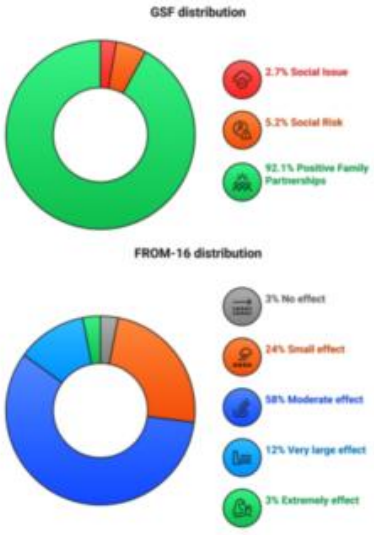
Methods: Data were collected retrospectively from March 2021 to November 2025 from all patients and their caregivers undergoing home-based HSCT in a tertiary hospital. Patients were assessed in person and systematically using the GSF, and caregivers were assessed using the FROM-16.
Statistical analyses were performed using SPSS software.

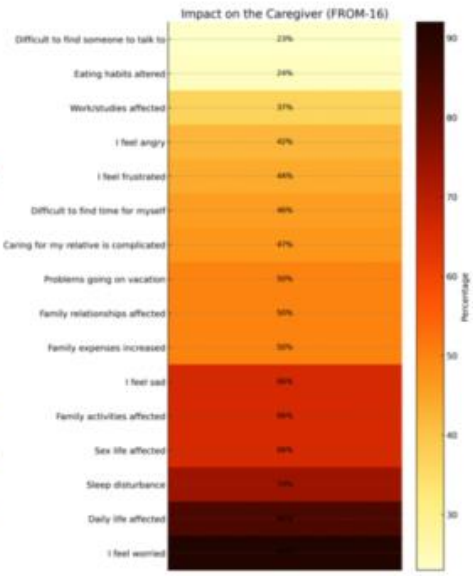
Results: Patients with data for both GSF and FROM-16 were analysed. Of a total of 46 patients transplanted at home between March 2021 and November 2025, only 38 patients and 38 caregivers could be analysed (Table 1). The GSF shows that 92.1% of patients have a

good socio-family assessment; likewise, FROM-16 shows that the home-based HSCT process has a moderate effect on the primary caregiver in 58% . Additionally, FROM-16 shows that, on an emotional level, 92% of caregivers report being somewhat or very concerned about the situation, while 66% feel sad and 42% feel angry. Only 23% find it difficult to talk about their thoughts with someone. On a personal and social level, 84% of caregivers see their daily lives as somewhat or very affected. Furthermore, 74% of them report having sleep disturbances. On the other hand, 37% of caregivers report that their work or studies have been affected and 50% report an increase in their family expenses. 47% of caregivers consider caring for their family member to be complicated. And 66% say that their sex life is affected (Image 1).Finally, the relationship between both scales and different transplant complications such as fever, diarrhoea, mucositis, and readmission was analysed, showing no direct association with them.

Table 1. Patient characteristics

Patients, n	38
Age, median (range)	55 (21-71)
Man/Female, n (%)	19 (50) /19 (50)
Caregiver, n (%)	
Couple	24 (63)
Mother/Father	6 (16)
Brother/Sister	3 (8)
Son/Daughter	3 (8)
Others	2 (5)
Primary disease, n (%)	
Multiple myeloma	22 (58)
Lymphoma	9 (24)
Cancerous tumours	7 (18)
Age-adjusted Sorror, n (%)	
0-1	11 (29)
2-3	17 (45)
4-7	10 (26)
Location HSCT, n (%)	
Patient's home	28 (74)
AECC apartment	10 (26)
Readmission, n (%)	10 (26)





Conclusions: Most patients with access to the home transplant programme are in a good socio-familial situation. Furthermore, it is clear that this transplant modality has a moderate effect on caregivers, without this affecting the outcome of the transplant. Measures need to be implemented to help minimise this effect on caregivers, with the support of professionals. The AECC has enabled us to perform this type of transplant in 26% of our patients.

Disclosure: Nothing to declare.

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NP106

DIGESTIVE AND SYSTEMIC PROPHYLAXIS IN HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): A NATIONAL SURVEY IN FRANCE

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Background: Infectious prevention in pediatric hematopoietic stem cell transplantation (HSCT) remains a critical issue. Historically, prophylactic oral digestive decontamination (PDD) aims to reduce the risk of bacterial translocation, but its effects on microbial diversity and the emergence of multidrug-resistant bacteria (MDR) are controversial. In the context of increasing antibiotic resistance and ongoing research in the prevention and treatment of acute and chronic graft-versus-host disease (GVHD), we conducted a multicenter survey to map the practices of digestive prophylaxis and empirical antibiotic therapy in pediatric allogeneic HSCT in France.

Methods: A structured questionnaire was sent to 12 French pediatric transplant centers. The collected data covered: (1) the use of PDD, (2) oral care practices, (3) microbiota surveillance, (4) nutritional modalities (oral, enteral, and parenteral), (5) antibiotic and antifungal prophylaxis, and (6) the use of fecal microbiota transplantation (FMT). Centers also estimated the annual frequency of gastrointestinal GVHD by grade.

Results: PDD practices were highly variable: one center used it systematically, two used it conditionally, while the majority did not use it. Oral care was universal but heterogeneous in composition, ranging from antifungals and/or antibiotics to simpler formulations like bicarbonate or Caphosol® (calcium phosphate). Exclusive oral nutrition was rare (<25% of patients in all centers), leading to frequent use of enteral (>50% in 4 centers) or parenteral nutrition (>50% in 3 centers). Empirical antibiotic therapy in febrile aplasia primarily relied on third-generation cephalosporins alone (50% of centers), sometimes combined with an aminoglycoside (25% either systematically or conditionally). FMT was reported in 4 centers (33.3%), exclusively for severe gastrointestinal GVHD. All centers reported an incidence of gastrointestinal GVHD grade 3–4 of less than 25%.

Conclusions: This survey represents the first national multicenter analysis describing digestive and nutritional prophylactic practices in pediatric allogeneic HSCT in France. The marked variability observed, particularly regarding PDD, nutrition, and antibiotic prophylaxis, highlights the lack of consensus and the empirical adaptation of strategies. The low reported incidence of severe gastrointestinal GVHD does not allow for a causal link to be inferred but strengthens the hypothesis of a protective role of the microbiota when preserved. These results call for prospective pediatric studies incorporating microbiological data and clinical outcomes to define harmonized recommendations.

Disclosure: Nothing to declare

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NP96

IMPACT OF SWITCHING FROM SODIUM CITRATE AND TAUROLIDINE TO 4% TETRASODIUM EDTA AS A CATHETER LOCK SOLUTION IN HEMATOLOGY PATIENTS

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Background: Central venous catheters (CVCs) are essential for patients undergoing autologous or allogeneic transplantation and chimeric-antigen T-cell therapy. Catheter-related infections and lumen cause treatment interruption, increased healthcare costs, and are a significant cause for morbidity. Both 4% tetrasodium EDTA and the combination of 4$ sodium citrate with taurolidine exhibit antimicrobial and anticoagulant properties and inhibit biofilm formation. Additionally, 4% tetrasodium EDTA can eradicate established biofilm.

Methods: We performed a retrospective analysis of medical records from July to October 2025. A total of 92 hematological patients requiring CVCs were included and divided into two groups, 52 patients in the citrate + taurolidine group, and 40 patients in the 4% tetrasodium EDTA group.
The group that utilized citrate+taurolidine consist of:
-20 Autotransplant
-5 MUD
-1 Sibling
-3 Haploidentical transplant
-21 Stem Cell Collection
-2 CAR-T administration.
The group in which 4% Tetrasodium EDTA was used, consists of:
-18 Autotransplant
-5 MUD
-2 Sibling
-3 Haploidentical transplant
-10 Stem Cell Collection
-2 CAR-T administration.
Statistical analysis was performed using IBM SPSS Statistics. Chi squared test was used to assess differences between groups.

Results: Switching from citrate + taurolidine to 4% EDTA resulted in a marked clinical improvement. Catheter-related infections decreased from 23.08% (n=12) to 5.00% (n=1) (p=0.017) (Figure 1a). CVC occlusions decreased from 26.92% (n=14) to 2.5% (n=1) (p=0.002) (Figure 1b).

Conclusions: Compared with other lock solutions, 4% tetrasodium EDTA significantly reduced CVC-related infections and improved CVC patency. Its superior antimicrobial and antibiofilm activity translated into meaningful clinical benefits and potential cost savings for hematology patients requiring central venous access.

Disclosure: Nothing to declare.

Donor Care

NG12-01

CLOSING THE GAP IN DONOR CARE: A RETROSPECTIVE AUDIT OF RELATED STEM CELL DONOR FOLLOW-UP

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Background: Haematopoietic Cell Transplant (HCT) practices are highly regulated, yet clear standards for post-donation care of related stem cell donors are lacking (Sanchez et al, 2023). Kisch et al (2017, 2025) emphasise the need for systematic, early, and individualized follow-up for addressing physical symptoms, psychological well-being, and social or relational factors. Anecdotal feedback from our related donors highlighted unmet needs and a sense of abandonment. In response, we implemented a related-donor follow-up telephone clinic, modelled on an unrelated-donor registry framework, safely providing structured personalised care throughout recovery. Donors are contacted by telephone 5 times (day +2, +7, month 1 ,6 and 12) after each donation (PBSC – peripheral blood stem cell or DLC-donor lymphocyte collection) regardless of recipient outcome. Each call includes structured assessment of physical psychological, and social/ relational well-being with escalation of concerns as required.

Methods: We conducted a retrospective audit of related PBSC and DLC donors attending our follow-up telephone clinic between January 2023 and November 2025. Data included donor demographics, donation type (PBSC or DLC), and follow-up outcomes (physical symptoms and emotional well-being) and were analysed using descriptive statistics.

Results: We reviewed 86 donation follow-up episodes from 71 related donors (median age 43, range 16-70; 38 male, 33 female). There was 15 additional collections (6 second PBSC, 9 DLC) from donors whose first donation was also in the audit window (n=71). Most were siblings (n=57), with parents (n=7) and children (n=7) also donating. HLA matched donors accounted for 50 relatives while the remaining 21 were haploidentical.
Of 430 scheduled follow-up calls, 114 were not completed (period of staff shortages), largely impacting the 6 and 12 month follow-up. Physical symptoms were reported in 70 of the 86 donation episodes: most commonly tiredness (n=45), bone pain (n=31), headache (n=20), and line site bruising (n=16). Most resolved within one month; though persistent adverse effects (AE) were reported after 13 donations at one month (tiredness and abnormal blood results) with AEs from 7 of these exceeding one month, largely attributable to pre-existing conditions. All were triaged and received medical review (transplant centre or general practitioner). Central venous catheter insertion (femoral line) was required for 10 collections with no associated complications reported.

Emotional recovery varied: full recovery was reported after 52 donations, with reports of feeling worse (n=7) mainly due to concern for the recipient (4/7) or feeling better (n=7) due to satisfaction in supporting their family.

Characteristic	Number of Donors (n=71)	Total donations (n=86)
Median age years (Range)	43 (16-70)	
Gender Male Female	 38 33	
Relation to recipient Sibling Parent Children	 57 7 7	
Degree HLA match Full Match Haploidentical	 50 21	
Type of Donation PBSC - Second Donation DLI - Second Donation	 67 4 	 73 6 13 9
Follow-ups (D2, D7, W4, 6M, 12M) Total follow-ups (86 donation × 5 timepoints) Completed Follow-ups Follow-ups not completed Follow-up ongoing D+2 Follow-up • Completed • Not completed D+7 Follow-up • Completed		430 245 114 63 78 8 71 15 57 26

• Not completed		
1 Month Follow-up		27
		32
• Completed		
• Not completed		12
		33
6 Months Follow-up		
• Completed		
• Not completed		
12 Months Follow-up		
• Completed		
• Not completed		
Physical Symptoms		
Infection at donation site		0
Palpitations		4
Insomnia		5
Night Sweats		6
Stiffness		7
Pain at donation site		7
Fever or Chills		8
Muscular Pain		8
Rashes		9
Nausea/Vomiting		11
Dizziness		13
Loss of Appetite		14
Other		14
Bruising at donation site		16
Headache		20
Bone Pain		31
Tiredness		45
Incidence of symptoms		
1 or more physical symptoms		70
reported		16
No physical symptoms reported		
Emotional recovery		
Feeling normal		52
Feeling better than usual		7
Feeling worse than usual		7
-Recipient Alive		3

-Recipient Deceased Not Documented		4 20
Late side Effects At 1 month post donation >1 month post donation		 13 7
Lines at Donation IVC Femoral Lines Not documented		 66 10 10
Lines related side effects Infection - Femoral Line - IVC Pain - Femoral Line - IVC Bruising - Femoral Line - IVC		 0 0 0 7 1 6 16 3 12

Conclusions: This audit underscores the value of a systematic related-donor follow-up clinic in ensuring safe, effective care. While minor gaps exist due to staffing, overall compliance and donor feedback are positive. Persistent 1-month symptoms suggest a 2-month follow-up may be beneficial. Beyond tracking physical and psychological symptoms, the clinic provides emotional support and regular contact, particularly important when recipients face transplant complications, allowing timely additional support for donors.

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Disclosure: Nothing to declare

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NG27-08

A FAIR MATCH? AUDIT OF GEOGRAPHIC INEQUITY IN RELATIVES TISSUE TYPING TIMELINES

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Background: Timely identification of related stem cell donors is critical in haematopoietic stem cell transplantation (HCT). Anecdotal reports suggest that HLA typing of non-UK resident (non-UK-R) related donors is frequently delayed, potentially affecting transplant decision making. Delays may arise from logistical barriers including customs clearance, incomplete documentation, shipping costs, and visa requirements, sometimes necessitating donation overseas. This audit examined whether these challenges represent isolated events or recurring systemic issue affecting transplant timelines and contributing to potential inequity for patients and their non-UK-R donors.

Methods: A 2-year retrospective audit (January 2024–December 2025) examined HLA typing and donation requests for non-UK resident (non-UK-R) related donors, with UK-resident (UK-R) donors as a comparator. Data were extracted from transplant centre records, typing centre correspondence, and electronic systems, including donor demographics, relationship to recipient, country of origin, and key timelines from typing pack dispatch to HLA report issue and sample validity. Descriptive statistics were used for analysis.

Results: A total of 122 tissue-typing packs were sent to 93 non-UK-resident (non-UK-R) and 122 to 110 UK-resident (UK-R) potential related donors. In the UK-R relative group, 52/110 were male and 58/110 female; ages 17-75; siblings (74/110), parents (9/110), children (26/110) other relative (1/110). In the non-UK-R group, 45/93 were male, 48/93 female, age 17 to 75; siblings (87/93), parents (2/93), children (2/93), other relative (3/93).
Pack receipt confirmation was lower for non-UK-R donors (99/122 vs 109/122), mainly due to address omissions and customs delays. Packs were sent to 33 countries, with recurring issues in USA (9/23), Pakistan (8/8), Nigeria (7/11), Spain (4/5), Albania (3/6), Nepal (3/4), Kenya (2/2), South Korea (2/2), Bolivia (2/2) and Brazil (2/2).
Sample return rates were also lower for non-UK-R donors (69/99 vs 96/109), often due to border controls (8/30) and dispatch costs (5/30). Median transit time was longer for non-UK-R donors (5 vs 2 days; range 2-21 vs 1-11 days), contributing to lower sample validity (53/69 vs 90/96); 17/69 non-UK-R sample dates were lacking. Failed DNA testing was the predominant reason for invalid samples; labelling errors were rare (3 vs 3).
HLA results were broadly comparable (full match UK-R 11/90 vs non-UK-R 10/53; haplo-identical 62/90 vs 31/53; not matched 17/90 vs 11/53). However, 8 UK-R donors have proceeded to cell collection, while no non-UK-R donors did, due to alternative donors, donor health, travel constraints, or pending transplant decisions. highlighting ongoing barriers and potential inequity for patients with non-UK-R related donors.

Characteristics (Non-UK-R)	**Packs Non-UK (n= 122)**	**Packs UK (n=122)**	**Relatives non-UK (n= 93)**	**Relatives UK (n=110)**
Age (years), median (IQR) • Range Gender • Male • Female			51 (38-59) (17-75) 45 48	45.5 (33-59.3) (17-75) 52 58
Relationship • Sibling • Parent • Child • Aunt • Cousin			87 2 2 3	74 9 26 1 0
Sample type • Blood • Buccal	23 98	83 39		
Journey packs packs received • Test completed HLA testing lab received Travel turnaround (days), median (IQR)	99 86 69 5 (2-6)	109 96 96 1.5 (1-2)		
Overall success rate Sample tested	53	90		

successfully **Result):** **FULL MATCH** **HAPLO** NOT A MATCH	 **10** **31** 11	 **11** **62** 17		
Proceed with cell collection With matched relative With alternative Donor (VUD or UK-R)	 0 27	 8 18		
Countries sent: Albania Algeria Bangladesh Bolivia Brazil Canada Denmark Dubai Equador France Germany Ghana Israel Italy Kenya Lagos Latvia Libreville Moldova Nepal New Zealand Nigeria Pakistan Poland Dominican Republic South Africa South Korea Spain Sweden	 6 (3 issues) 3 (0 issues) 1 (0 issues) 2 (2 issues) 2 (2 issues) 9 (2 issues) 4 (1 issues) 2 (1 issue) 1 (1 issue) 3 (0 issues) 6 (2 issues) 1 (0 issues) 2 (1 issue) 3 (1 issue) 2 (2 issues)			

Thailand Uganda United Arab Emirates USA	3 (0 issues) 1 (0 issues) 1 (1 issue) 1 (0 issues) 4 (3 issues) 2 (0 issues 11 (7 issues) 8 (8 issues) 1 (0 issues) 2 (2 issues) 4 (2 issues) 2 (2 issues) 5 (4 issues) 3 (1 issue) 1 (0 issues) 2 (2 issues) 1 (0 issues 23 (9 issues)			

Conclusions: This audit highlights significant geographic inequity in tissue typing timelines for non-UK-R relatives and the challenges faced by all stakeholders in identifying suitable donors. Notably, none of the 10 matched non-UK-R relatives in this audit sample were invited to donate, with transplants proceeding using alternative donors. These findings reveal a systematic disadvantage for non-UK-R related donors potentially limiting donor utilisation and timely patient access and exposing clear inequities in current HCT pathways. Some deficiencies, such as customs delays and courier costs, could be addressed but this requires coordinated action among transplant teams, overseas registries, government bodies and international courier providers.

Disclosure: Nothing to declare

NP12

APPLICATION OF LONG PERIPHERAL CANNULA IN DONOR APHERESIS - EXPERIENCE OF ONE CENTER

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Background: Allogeneic peripheral hematopoietic cell (PBSC) collections place high demands on venous access while maintaining the comfort and safety of the donor. The assessment of peripheral venous access is the responsibility of the apheresis nurse. Fixed 16G and 17G (PVC) dialysis peripheral cannulas are used as standard. In case of poor quality of peripheral veins in both limbs of the donor, we insert short-term central dialysis cannulas (CVC). Since 9/2024, we have started using long peripheral venous cannulas (LPC), which are introduced under ultrasonographic control. They are used in donors who have only one good venous access on the forearm and are at risk of central dialysis catheter (CVC) insertion. The aim of this work is to present the first experiences with this access and compare them with the period before its implementation.

Methods: A retrospective single-center analysis of all allogeneic PBSC collections was performed in the period 09/2023–09/2025. The data analysis was divided into two sets: Period without LPC use 09/2023–09/2024 and period with LPC use 09/2024–09/2025. The frequency of use of individual venous accesses, flow stability during apheresis and the total duration of the collection were evaluated. When using LPC, a peripheral metal dialysis needle (PVC) was used for the collection line, and the return line was run through a long peripheral cannula (LPC). Data were drawn from the internal documentation of the apheresis center.

Results: In total, the set includes 176 allogeneic PBSC collections, of which 91 collections in the period without LPC use and 85 in the period after the insertion of LPC. Three types of venous access were compared - PVCs, CVCs, and LPCs. In the period before LPC insertion, 78% of collections were performed using PVC (71/91) and 22% using CVC (20/91). In the period after LPC insertion, 83% of collections were performed using PVC (70/85) and 8% (7/85) using CVC. LPC was used in 9% of apheresis (8/85), which represents a 65% reduction in the need for CVC. When using PVC, flow rate (72 (86-50) vs. 72 (83-50) ml/min) and collection time (235 (261-167) vs. 242 (274-197) min.) did not differ between the two periods. When using CVC, flow rate (71 (88-52) vs. 78 (83-63) ml/min) and collection time (222 (250-155) vs. 220 (229-121) min.) did not differ in both periods. When using LPC, the flow rate was (70 (73-58) ml/min.) and the collection time was (254 (259-204) min.). Compared to PVC, comparable flow rate is achieved with a discretely longer collection time.

Conclusions: Implementation of LPC led to a reduction in the need for CVC without a negative impact on flow rates or collection time. A key element is careful assessment of

venous access by the nurse during the pre-collection examination, which will allow safe and effective apheresis planning.
Given the size of the analyzed set, the results should be interpreted with some caution, however, the available data show a stable course of apheresis and support the continuation of data collection and further development of the use of LPC in clinical practice.

Disclosure: No conflict of interest.

NP73

COUNT THEM IN: RECOGNISING DUFFY NULL NEUTROPENIA IN AFRO-CARIBBEAN POPULATION WITH THE AIM TO BROADEN DONOR INCLUSION. CASE REVIEW OF A NEUTROPAENIC DONOR

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Background: In allogeneic stem cell transplants, a well-matched Human Leukocyte Antigen (HLA) donor is critical for optimal outcome. However, the likelihood of finding a suitable unrelated donor is unequal across ethnic groups. Potential donors must undergo strict medical assessments, and an unexpected blood result, like neutropaenia, might cause the donor to be placed on hold or cancelled.
Racial neutropenia is disproportionately common among people of Black and Asian backgrounds – the very groups already struggling to find well matched donors. This is associated with the Duffy Null Antigen, which is expressed by 66% of African Americans and 80% of West Africans.
The Duffy antigen, encoded by the *ACKR1* gene, gives rise to the Duffy blood group system and acts as a chemokine receptor. The Duffy null phenotype (Fy(a-) Fy(b-)) leads to abnormal neutrophil regulation and a low neutrophil count but no functional or pathological abnormality
This case involves a patient of West African background with no suitable unrelated donor but a fully matched sibling with an unexplained neutropenia during donor medical assessment.

Methods: Case Description: A West African patient, diagnosed with hepatitis associated aplastic anaemia required an allogeneic stem cell transplant. Unrelated donor search found no suitable matches, but a sibling was fully HLA-matched.
At the sibling's donor medical, she was found to be neutropaenic, with neutrophil count of 0.91 x 10^9/L. This was concerning for her own health and also the viability of using her as a donor.
Haploidentical transplant from a parent was considered, but both parents expressed donor specific antibodies (DSA) against the patient, ruling them out. With limited alternative options, the case of the matched sibling donor was revisited.
The team considered performing a bone marrow biopsy to rule out malignancy but chose to test for the Duffy Null phenotype. Blood samples were sent to NHSBT, Birmingham and the results confirmed *Duffy null* status therefore confirming the neutropaenia as racial and not

pathological. The team proceeded with her as the donor.
The sibling donor received 5 days of GCSF injections for mobilisation, followed by two days of harvesting.

Results: A CD34+ harvest dose of 7.85 x10^6/kg was obtained and patient went into transplant receiving the full dose. He engrafted on day +12 (neutrophil count of 2.1 x 10^9/L) and discharged on day +16 (neutrophil count of 2.3 x 10^9/L).

Conclusions: This case highlights the role Duffy null biomarker can play in stem cell donor selection and how lack of awareness can lead to unfair exclusion of potential donors. With Duffy null highly prevalent among the populations who are underrepresented on the global stem cell register, it is crucial that potential donors from Black/Asian background that have unexplained neutropaenia at donor medicals will be probed further by having Duffy antigen testing and not simply ruled out. 'Let us count them in'.

Disclosure: Nothing to declare.

NP87

PSYCHOLOGICAL IMPACT OF LAST MINUTE SCHEDULING CHANGES ON RELATED DONORS

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Background: The Christie acts as a collection centre for registries, and for related donors. When looking at related and unrelated pathways, related donors may be identified and required to proceed to donation at very short notice, receiving less structured support. Dates can frequently change in response to the recipient's clinical condition. This unpredictability can create significant emotional and psychological strain for related donors. Related donors experience intensified stress and anxiety due to the emotional responsibility of donating to a sibling. Time pressures and uncertainty add to the psychological burden. Last minute changes can disrupt personal, professional, and family commitments, impacting donor wellbeing and overall donor experience.

Methods: We aim to highlight how last-minute changes can impact related donors experience and the psychological impact this causes. If matched its discussed in MDT. Donors are contacted to attend for medical assessment, followed by donation as soon as identified. Dates are calculated carefully with patient timeline and donor preferences.
Design: Reflecting on case studies we aim to improve future donor experience in relation to psychological impacts. Both donors were aware that donation is voluntary.
Donor 1: 20-year-old female, studying full time in Exeter (approximately 240 miles away). Initially not planned to be used as donor but due to her siblings unrelated donor withdrawing last minute, she was contacted with two day's notice to attend for a medical. Donation planned for two weeks later; however confirmatory typing was not complete. This resulted in two possible donation dates being communicated to donor considering a delay with

confirmatory typing. The donation process also coincided with the donor's 21st birthday. The short notice caused disruption to academic and personal commitments and caused long distance travel last minute. The uncertainty caused significant stress and anxiety, highlighting the psychological impact of last-minute donor scheduling.
Donor 2: 53-year-old female in full time employment. Donating for sibling. Due do pharmacy issue with patients conditioning treatment donation had to be postponed the day before the donor was due to start GCSF. No dates could be confirmed initially causing uncertainty for donor. The short notice cause stress and worry for donor. The donor had to rearrange work schedule and a family holiday that had already been postponed due to donation.

Results: Both donors donated for their siblings. However, both experienced last minute changes to plans and dates. This resulted in additional psychological burden and disruption to donor's everyday life and life events; on top of the emotional worry and sense of responsibility already associated with donating to a sibling.

Conclusions: Both donors donated to help their siblings despite the initial plan changing. As a collection centre undertaking donor medicals and harvests, we always aim to manage expectations and minimise disruption to donors. However, unforeseen last-minute changes can significantly increase the psychological burden. Ensuring clear and consistent communication between donors and the clinical team is essential in providing support throughout the process. Signposting donors to support services such as peer groups at Maggie's Centre could help further improve the donor experience.

Disclosure: Nothing to declare

Impact of New Therapies on Patient Care

NP26

FOSCARNET SODIUM ENEMA FOR REFRACTORY CMV GASTROENTERITIS AFTER HAPLOIDENTICAL HSCT: A CASE SERIES

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Background: Cytomegalovirus (CMV) gastroenteritis is a severe complication following allogeneic hematopoietic stem cell transplantation (allo-HSCT). When systemic antiviral therapy fails to effectively alleviate intestinal symptoms or clear viral loads, effective alternative management strategies are urgently needed.

Methods: We report two cases of haploidentical HSCT recipients diagnosed with CMV gastroenteritis characterized by intractable diarrhea and positive stool CMV-DNA. Following a suboptimal response to systemic antiviral regimens, both patients received foscarnet sodium retention enemas as salvage or adjunctive therapy. Clinical outcomes were longitudinally

monitored, including changes in stool/blood viral loads and improvement in gastrointestinal symptoms.

Results: Case 1 (36-year-old female, AML) presented with severe diarrhea and elevated stool CMV-DNA despite systemic treatment. Following the initiation of foscarnet sodium enema on day +63 post-transplantation, stool CMV-DNA turned negative within 5 days, accompanied by significant symptom relief. Case 2 (60-year-old female, CMML) developed severe enteritis with high viral loads on day +61. After receiving combined intravenous and rectal foscarnet therapy, stool CMV-DNA cleared by day +70, and clinical symptoms improved significantly. Both patients tolerated the local therapy well, with no observed mucosal injury or systemic toxicity.

Conclusions: Foscarnet sodium enema represents a promising, non-invasive adjunctive therapy for refractory CMV gastroenteritis after allo-HSCT. It can effectively reduce local viral burden and accelerate symptom resolution when systemic drug penetration is insufficient.

Disclosure: Nothing to declare.

NP29

IMPACT OF THE ETAPES-ONCO PEER SUPPORT PROGRAM ON THE NEEDS OF HEMATOLOGY-ONCOLOGY PATIENTS WHO HAVE UNDERGONE CELLULAR THERAPY: PRELIMINARY RESULTS

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Background: In Canada, hematological cancers represent roughly 10% of all cancer cases. Although their incidence is growing each year, survival rates of hematological cancer are also on the rise. The recent therapeutic advances, particularly hematopoietic stem cell transplantation (HCT) and CAR-T cell therapy, are playing a big role in the survival outcomes. However, these therapies are complex and have the potential to generate side effects as well as creating isolation, uncertainty, and emotional distress: they often create unmet needs in patient's lives. Peer-support programs have shown promise in oncology, but none have been specifically designed for hematology-oncology patients undergoing cellular therapies in Canada. To address this gap, the ETAPES-Onco project was developed to create a structured peer-support program tailored to their needs. This poster aims to present preliminary findings on the perceptions of patients with hematological cancer who underwent cellular therapies and were paired with a patient partner through the ETAPES-Onco peer-support program, focusing on how this support addressed their needs.

Methods: For this study, a qualitative descriptive approach was adopted (Thorne, 2016). We are currently recruiting patients over 18 years old who have undergone cellular therapies (allograft or CAR-T) and agreed to be paired as part of the study. Individual interviews are planned three months after peer pairing, using an interview guide based on a supportive care framework (Fitch, 2008) and a conceptual peer support framework (Dennis, 2003). Qualitative data analysis is ongoing and is being conducted using a three-step iterative content analysis approach, which includes data condensation, data display, and conclusion drawing (Miles et al., 2014).

Results: The preliminary findings (3 interviews on 10) inform that peer support addressed seven main domains of patient needs (emotional, informational, psychological, physical, informational, practical and spiritual), with the greatest positive impact perceived on emotional, psychological, and informational needs. The results also highlight that peer support helps motivate and reassure patients, making them feel valued and more secure throughout their care trajectory. Data collection and analysis are still ongoing.

Conclusions: This study has potential to highlight the key role that patient partners can play in reducing unmet needs among patient undergoing cellular therapies. The insights can inform nursing practice and support the broader implementation of structured peer support pathways in oncology care.

Disclosure: Nothing to declare.

NP39

EFFICACY OF ACUPOINT APPLICATION COMBINED WITH HERBAL FUMIGATION AND WASH IN PREVENTING DIARRHEA AND PERIANAL INFECTION IN PATIENTS WITH ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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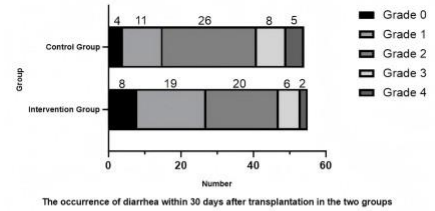
Background: Diarrhea is a common and serious complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT), often leading to perianal infection, severity of hemorrhoidal disease, systemic complications, and impaired recovery. While current treatments focuses on symptomatic management, mucosal repair, infection prevention, and electrolyte balance, its preventive efficacy remains limited. Traditional Chinese medicine (TCM), guided by holistic and syndrome differentiation principles, has shown potential in regulating intestinal immunity, reducing inflammation, and protecting mucosal integrity. This randomized controlled trial aimed to evaluate whether these TCM interventions could reduce diarrhea duration, prevent perianal infection, and improve quality of life in allo-HSCT patients.

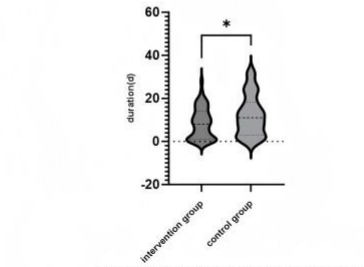
Methods: In this single-center, randomized, controlled, open-label trial, 116 patients scheduled for allo-HSCT were randomly assigned to either the intervention group (n=61) or

the control group (n=61) from March to August in 2025. The intervention group received daily herbal fumigation of the perianal area twice daily starting 24 hours before conditioning, along with acupoint application at Shenque (CV8), Tianshu (ST25), and bilateral Zusanli (ST36) for 4 hours daily. The control group received povidone-iodine warm water fumigation of the perianal area twice daily. The primary endpoints were the incidence of diarrhea and perianal infection within 30 days post-transplant. Secondary endpoints included diarrhea duration, the severity of hemorrhoidal disease within 30 days after transplantation, incidence of intestinal aGVHD, non-relapse mortality (NRM) within 100 days, and patient-reported symptom burden and quality of life.

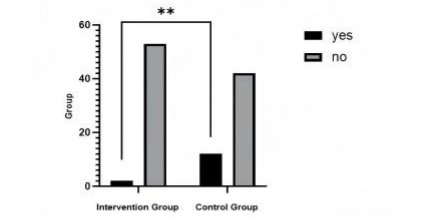


The occurrence of diarrhea within 30 days after transplantation in the two groups

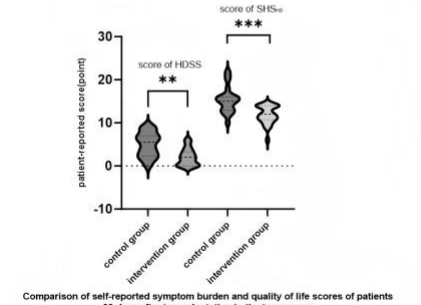
Grade 0: No diarrhea
Grade 1: 2–3 loose stools per day above baseline
Grade 2: 4–6 loose stools per day above baseline
Grade 3: 7–9 loose stools per day above baseline
Grade 4: ≥10 loose stools per day above baseline with dehydration or requiring parenteral nutrition



Comparison of the number of days with persistent diarrhea within 30 days after transplantation in the two groups



Comparison of new perianal infections within 30 days after transplantation in the two groups



Comparison of self-reported symptom burden and quality of life scores of patients 30 days after transplantation in the two groups

HDSS:Hemorrhoidal Disease Symptom Score
SHS-e:Short health scale adapted for hemorrhoidal disease

Results: A total of 109 patients (57 male, 52 female) completed the study (54 in the intervention group, 55 in the control group). There was no significant difference in the overall incidence of diarrhea between the two groups. However, the incidence of diarrhea with grade ≥2 in the intervention group was significantly lower than that in the control group (50.9% vs 72.2%,P=0.023). The duration of diarrhea in the intervention group(IQR:3,13) was significantly shorter than that in the control group(IQR:3,22) (P =0.038).
The new perianal infection rate within 30 days post-transplant was significantly lower in the intervention group (3.6% vs 22.2%, p=0.004).
No significant differences were observed between groups in the severity of hemorrhoidal disease within 30 days after transplantation (P=0.414), 100-day incidence of intestinal aGVHD (P=0.115) or NRM (P=0.494).
Patient-reported symptom burden (P=0.006) and quality of life (P<0.0001)were significantly better in the intervention group based on patient self-reports.

Conclusions: The combination of herbal fumigation and acupoint application significantly reduce the incidence of diarrhea with grade ≥2 and shortened diarrhea duration and reduced perianal infections in allo-HSCT patients. These TCM interventions were safe, well-tolerated,

and associated with improved patient-reported quality of life. This integrative approach may serve as a supportive strategy to mitigate diarrhea-related complications and enhance recovery in transplant recipients, demonstrating the potential of TCM external therapies to enhance standard supportive care protocols and improve patient recovery outcomes.

Clinical Trial Registry: NCT06912347

Disclosure: Nothing to declare

NP109

NURSE-LED INITIATIVE SKIN CARE GUIDELINE TO MINIMIZE TREOSULFAN RELATED SKIN TOXICITY AMONG PAEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT IN NATIONAL UNIVERSITY HOSPITAL, SINGAPORE

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Background: Treosulfan-based conditioning regimens are commonly used in pediatric allogeneic hematopoietic stem cell transplantation (HSCT). However, they can cause significant skin toxicity, including erythematous patches, hyperpigmentation, and erosions. A skin care guideline (Treosulfan) was formulated in year 2020 to minimize these effects.

Methods: The guideline included twice daily showers (hypoallergic bath oil), regular moisturizer application (3 times a day), loose-fitting clothing, frequent diaper changes (every 2 hourly), specific central line care (cleaning solution as sterile non-alcohol based povidone iodine, follow by 0.9% normal saline and covered with non-occlusive dressing), and eye care (tear natural eye drop 4 times a day). Nursing assessments documented skin changes using CTCAE Grading for rashes and Lund and Browder chart was used to calculate body surface area. Skin assessment was performed per shift and documented on electronic medical record.

Results: From year 2020 to 2025, 47 patients (median age 8.27 years) received Treosulfan-based conditioning. Treosulfan skin care regime was delivered to all the 47 patients. Grade 1-2 erythematous rashes were commonly observed in skin folds and diaper areas. Pruritus and rashes peaked between days 9-14 post-transplant and resolved by day 21. None of the child age>10 years old do not have grade 2 skin toxicity. Hyperpigmentation persisted up to 60 days post-transplant. No patients required dermatologist referral for skin excoriation or dressing for skin excoriation.

Conclusions: Skin toxicity related to Treosulfan can be significantly reduced through increased shower frequency, moisturizer application, frequent diaper changes, avoiding thick clothing, and using non-occlusive dressings. This guideline appears effective in minimizing severe skin complications associated with Treosulfan-based conditioning in paediatrics HSCT patients.

Disclosure: Nothing to declare.

NP115

PLATELET-RICH GEL PROMOTES RAPID WOUND HEALING IN SEVERE CUTANEOUS GRAFT-VERSUS-HOST DISEASE

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Background: Graft-versus-host disease (GVHD) remains a major cause of morbidity and mortality following allogeneic haematopoietic stem cell transplantation. Chronic GVHD is a frequent long-term complication, with cutaneous manifestations being the most common sign. Skin lesions are often associated with pain, risk of infection, and a significant reduction in quality of life. Skin complications include ulcerations and scleroderma, typically associated with pruritus, dysesthesia, and pain. Despite the burden on patients, caregivers, and the healthcare system, there is still a gap in evidence-based guidelines for wound management in these cases.
Platelet-rich plasma (PRP) has emerged as a promising regenerative therapy. The theoretical basis is that PRP accelerates the repair process by providing platelet and protein concentrations above physiological levels. Moreover, reinforcement of the fibrin mesh supports healing by maintaining the viability and sustained release of bioactive molecules.

Methods:

- Comprehensive skin assessment: evaluation of skin integrity and wound dimensions.
- Implementation of regenerative therapy**,** using **Platelet-Rich Gel (PRG)** on persistent, non-healing ulcerated lesions after standard topical treatments failed.
- Serial weekly applications of PRG, combined with appropriate cleansing and protection of the perilesional skin.

Results: Overall improvement in skin lesions on the lower limbs was achieved, along with a notable reduction in pruritus, dryness, and pain, allowing better mobility and comfort.
Lesion 1: After 5 applications, wound size reduced from 15mm to 3mm, indicating accelerated tissue regeneration.
Treatment was extended onto 2 additional lesions. Lesions 2 & 3: In just 5 weeks the diameter decreased from 38mm to 6mm, showing a faster granulation process and wound closure.
No treatment-related adverse effects were reported. Consequently, a rehabilitation program could be successfully started.

Conclusions: Familiarity with the National Institutes of Health (NIH) assessment criteria for chronic GVHD is highly recommended.

The inclusion of Platelet-Rich Gel in the multidisciplinary management of cutaneous GVHD proved effective in reducing wound size and promoting healing in extensive and complex ulcerations.
It is vital to identify and implement evidence-based practices, such as advanced wound care therapies, to provide symptom relief and promote effective healing, ultimately improving functional outcomes and quality of life in patients with severe cutaneous GVHD.

Disclosure: Nothing to declare

NP116

COMPLEXITIES IN GENE THERAPY- MANUFACTURING DELAYS AND THE IMPACTS OF THIS ON THE PATIENTS AND THEIR FAMILIES

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Background: Royal Manchester Children's Hospital is a centre at the forefront of gene therapy research and treatment. Here, we offer both licensed treatments and conduct several clinical trials, treating a vast patient caseload that ranges from rare metabolic conditions to haemoglobinopathies. The successes of these new treatments are groundbreaking and exciting; however, all new medicines come with their own challenges. We have looked at the ranging complexities of these gene therapy treatments and how the delays in manufacturing and treatment have impacted patients and their families both physically and emotionally.

Methods: We looked at all factors leading to delays and complications, and how this impacted the patient. The biggest reasons for delays included poor mobilisation and stem cell collection counts, issues with manufacturing itself, as well as the availability of manufacturing slots and long wait times for manufacturing the final product.
We reviewed patient data from neurocognitive assessments from our metabolic patients and clinical treatment requirements from our haemoglobinopathy patients, such as additional red cell transfusions and red cell exchanges. We collected qualitative data through speaking to patients and their families to try to understand the first-hand experiences of these treatments and how the delays have impacted their patient journey. With the majority of these treatments, we receive patient referrals globally, and so the burden of treatment is already exponential for families coming to our site.

Results: We reviewed our clinical data as well as direct patient experiences to conclude our findings. We have looked at the neurocognitive testing in our metabolic patients and have seen with some patients a decrease in this whilst waiting for treatment. This has meant a decrease in the development of the patient, potentially reducing the efficacy of the treatment being offered.
The emotional impacts of families were also looked at. With our hemoglobinopathy gene therapy patients, the difficult mobilisation regimes were identified as a challenge for both

patients and families, especially sickle cell patients, due to the multiple cell cycles requiring hospital admissions, extra central line access and vigorous pain management plans.
It was found that being open and honest with the realistic timeframes of treatment helped families prepare themselves for the expected burden. Psychology input and frequent meetings with the consultants and specialist nurses, both virtually and face-to-face, have also helped with understanding the complex treatment journey.

Conclusions: We are hoping that with more experience in gene therapy, delays and manufacturing times will be minimised, which will contribute to the overall experience of the patient and their family.
It has become apparent that, as nurses, we often have no control over the delays identified; however, we can have a direct impact on the patient and family experience going forward, despite the challenges faced as highlighted above.

Clinical Trial Registry: Not applicable

Disclosure: Nothing to declare

NP126

SIDE EFFECTS AND LONG-TERM EFFECTS – THE EXPERIENCES OF PATIENTS WITH CAR T-CELL THERAPY. A SCOPING REVIEW

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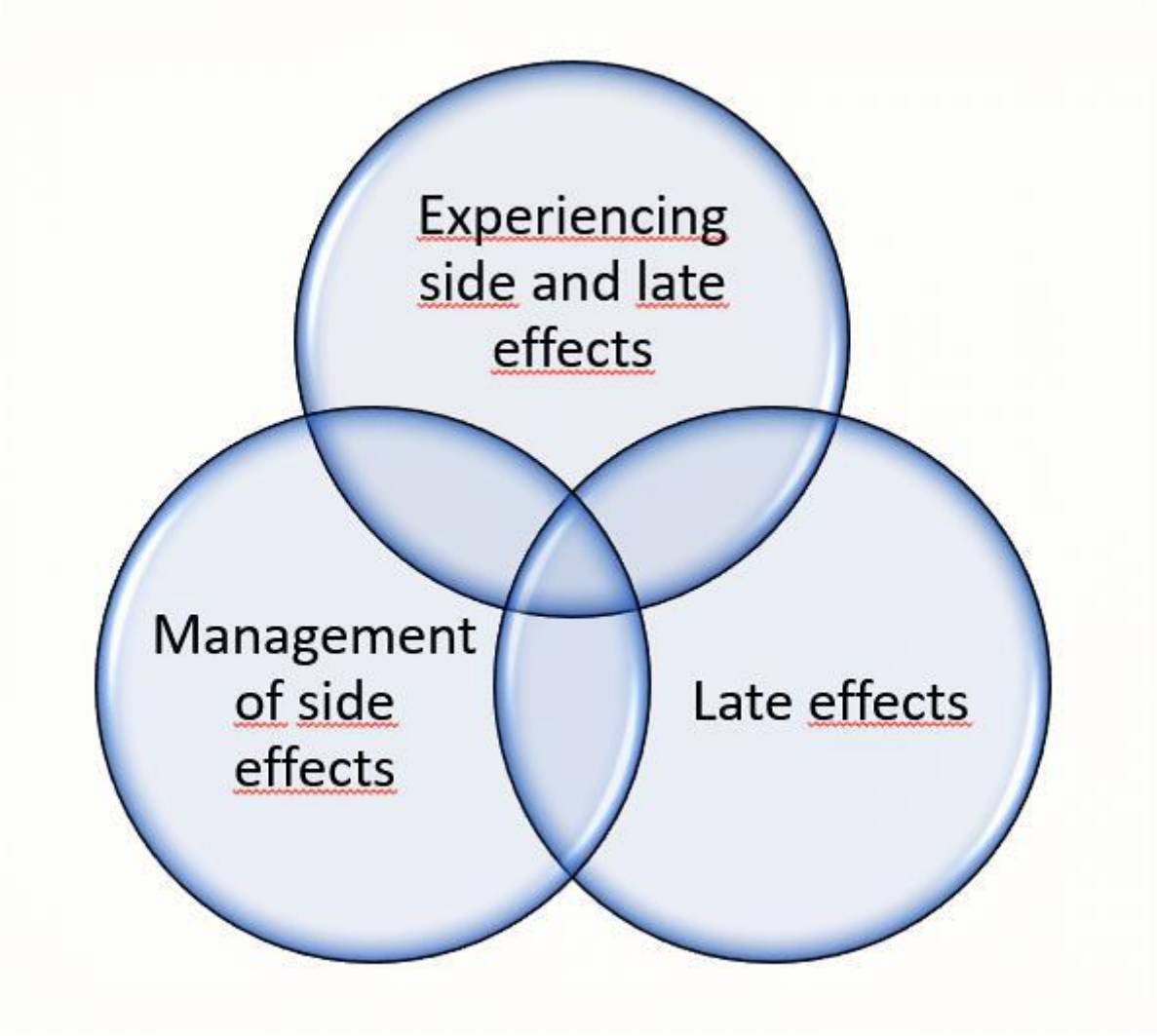
Background: Worldwide, the number of people with cancer is increasing. For patients with haematopoietic/oncological cancers, CAR T-cell therapy offers new chances of surviving their disease. The potentially life-threatening side effects of CAR T-cell therapy, such as cytokine release syndrome and neurotoxicity, require close monitoring of patients. Persistent cytopenia and delayed neurotoxicity may occur after CAR T-cell therapy. These symptoms present challenges for patients and nurses in the provision of care. The aim of the scoping review was to provide an overview of the current esearch regarding the side effects and long-term effects of CAR T-cell therapy in order to identify research gaps. The review focused on how patients experience the side effects and long-term effects and how they are managed by nurses.

Methods: A scoping review was carried out according to Arksey and O'Malley (2005) and the recommendations of the Joanna Briggs Institute for Scoping Reviews (Peters et al, 2020). The databases PubMed, CINAHL, LIVIVO, Cochrane Library and Web of Science were searched using keywords. The study selection was performed independently by both researchers.

Results: The search led to 15 publications that were included in the final analysis (see table 1). A majority of the included publications were scientific articles on the management of side effects and long-term effects, a smaller group were qualitative studies on patient experiences, and one was a quantitative study on the occurrence of long-term effects. The

following result categories were identified: 'Experience of side effects and late effects', 'Management of side effects' and 'Late effects' (see Figure 1). Regarding the management of side effects, the studies indicated a consensus on the importance of monitoring patients in order to be able to react quickly when side effects occur. Patients experienced CAR T-cell therapy as safe and felt prepared for the side effects, while they were often unaware of possible long-term effects.



Authors, Year	Country	Study Design	Aim	Study Population
Baer et al., 2019	USA	Scientific article	Current recommendations for the care of	Non applicable

			patients with CRS and ICANS	
Beaupierre et al., 2019	USA	Scientific article	Patient care during CAR T-cell therapy	Non applicable
Bixby et al., 2023	USA	Qualitative study	To identify the patients' experiences	18 patients after CAR T-cell therapy
Buitrago et al., 2019	USA	Scientific article	Overview of CAR T-cell therapy late effects	Non applicable
Delforge et al., 2023	USA	Qualitative study	Long-term patient experience after CAR T- cell therapy	45 patients with multiple myeloma after CAR T-cell therapy
Halton et al., 2017	USA	Scientific article	Development of standards for the care of patients during CAR T-cell therapy	Non applicable
He et al., 2023	China	Qualitative study	Skills of nurses caring for patients during CAR T-cell therapy	15 nurses
McConville et al., 2017	USA	Scientific article	Education of patients and their caregivers by nurses during CAR T-cell therapy	Non applicable
Neelapu, 2019	USA	Review	Monitoring and management of CRS + ICANS	Non applicable
Puckrin et al., 2023	Canada	Review	Management of long-term late effects of CAR T-cell therapy in adults	Non applicable

Ruark et al., 2020	USA	Quantitative study	Examination of neuropsychiatric and other long-term effects after CAR T-cell therapy	40 patients after CAR T-cell therapy
Shah et al., 2022	USA	Qualitative study	Patients' experiences with CAR T-cell therapy	47 patients before and 58 after CAR T-cell therapy
Stenson et al., 2023	UK	Qualitative study	Patients' and caregivers' experiences with CAR T-cell therapy	10 patients and 4 caregivers
Tang et al., 2023	China	Case study	Role of nurses in the early detection of side-effects	One patient during CAR T-cell therapy
Taylor et al., 2019	USA	Scientific article	Overview of CAR-T cell therapy and side-effects management and nurses training	Non applicable

Conclusions: Nurses play an important role in the care of patients before, during and after CAR-T cell therapy. So far, there has been little research on how patients experience the side effects and long-term consequences. Studies in which CAR-T cell therapy is examined in the context of the patients' life world can provide more in-depth insights.

Disclosure: The authors have nothing to disclose.

NP74

NEW THERAPIES, NEW DEMANDS: A NURSING PERSPECTIVE ON PATIENT CARE TRANSFORMATION

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Background:

The rapid introduction of novel therapies including cellular therapies (notably CAR-T), targeted small molecules and reduced-intensity conditioning regimens are reshaping delivery of care across all forms of hematology services. Nurses are central to safe implementation of these new therapies, yet the practical implications for workflows, patient education, toxicity monitoring and health-service organization are incompletely described in the literature. Our objective was to synthesize how recent therapeutic advances affect patient care delivery, nursing workload, patient outcomes and to identify priority areas for nursing practice development.

Methods:

A structured literature synthesis was performed (2018–2025) using guideline documents, systematic reviews, narrative reviews and original studies addressing cellular therapies, targeted agents and conditioning changes.

Results:

Three consistent impacts emerged. 1. Increased clinical complexity. Novel agents produce characteristic toxicities (cytokine-release and neurotoxic syndromes) requiring early recognition, standardized grading, rapid escalation pathways and placing high demands on bedside assessment and urgent multidisciplinary action. 2. Shifts in care settings. Accumulating experience supports outpatient and early-discharge models for some cellular therapies; these models improve patient experience and resource use but require robust ambulatory monitoring, clear escalation routes and integrated community links. 3. Workforce, education and governance implications. The literature highlights gaps in formal competency frameworks, the need for targeted training, revised staffing models and clear local protocols to maintain safety as application of therapies decentralizes and need for highly skilled nurses rises.

Conclusions:

Emerging therapies have shifted care in three key ways. 1. Increased clinical complexity. Novel agents produce characteristic toxicities (cytokine-release and neurotoxic syndromes) requiring early recognition, standardized grading, rapid escalation pathways and placing high demands on bedside assessment and urgent multidisciplinary action. 2. Shifts in care settings. Accumulating experience supports outpatient and early-discharge models for some cellular therapies; these models improve patient experience and resource use but require robust ambulatory monitoring, clear escalation routes and integrated community links. 3. Workforce, education and governance implications. The literature highlights gaps in formal competency frameworks, the need for targeted training, revised staffing models and clear local protocols to maintain safety as application of therapies decentralizes and need for highly skilled nurses rises.

Disclosure: Nothing to declare.

Education and Training

NG27-02

BRIDGING THE EDUCATIONAL GAP: A NATIONAL, NURSE-LED ONLINE APHERESIS COURSE TO ENHANCE QUALITY IN HSCT AND CELLULAR THERAPY

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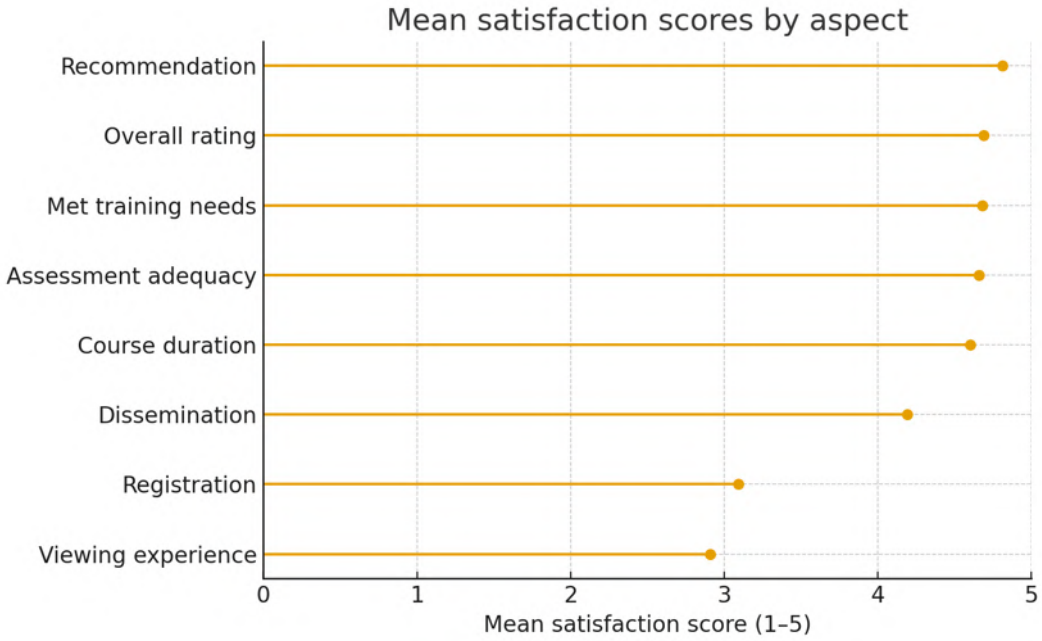
Background: Apheresis is the essential first step for cell collection, directly influencing treatment success and patient safety. Traditionally, nurse training relied on informal mentorship and fragmented courses, lacking consistency and depth. This gap compromises quality across the hematopoietic stem cell transplantation (HSCT) and cellular therapy chain—including emerging therapies such as chimeric antigen receptor T-cell (CAR-T) therapy. To overcome this, the Nurses Apheresis Group from the Spanish Group for Hematopoietic Transplantation and Advanced Therapies (GETH-TC) developed a comprehensive free online program.

Methods: group of 20 apheresis nurses representing ten hospitals from across Spain developed a curriculum of 17 topics organized into four modules:
(1) fundamentals of apheresis and vascular access;
(2) hematopoietic stem cell collection, photoapheresis, CAR-T lymphocyte apheresis, and quality systems;
(3) therapeutic procedures such as erythroapheresis, platelet/leukocyte depletion, and plasma treatments; and
(4) pediatric apheresis. Content was delivered through the GETH-TC Virtual Campus, an accessible e-learning platform, via short pre-recorded videos (max 20 minutes each), enabling flexible, self-paced learning over six months. Participants were required to achieve ≥60% on multiple-choice assessments, with two attempts available for each exam. At the end of the course, participants completed a mixed-methods evaluation survey (eight Likert-scale items and three open-ended questions) to assess satisfaction, relevance, and areas for improvement.

Results:

In its first edition, 189 nurses enrolled. Quantitative data showed high overall satisfaction, with a mean rating of 4.2/5. The highest scores were observed for overall course quality and recommendation to peers (Figure 1), whereas registration and viewing experience received slightly lower ratings, highlighting areas for future improvement. Thematic analysis of over 200 qualitative comments emphasized key strengths: expert nurse-led teaching, clinical relevance, and inclusion of real cases, including pediatric scenarios. Suggested improvements included downloadable materials (PDFs/slides), technical platform refinements, more dynamic video formats, expanded content on advanced topics (CAR-T, central lines), and interactive elements such as forums or live Q&A sessions.



Conclusions: The first national standardized apheresis course in Spain—created by nurses for nurses—successfully established a standardized, accessible, and highly valued training program that strengthens the foundation of HSCT and cellular therapy care in Spain. By equipping nurses with consistent, evidence-based competencies in apheresis—a pivotal procedure for cell collection—the course enhances quality and safety in this rapidly evolving field. The model is scalable and reproducible for other regions and offers a framework for continuous professional development. Future editions will integrate participant feedback, focusing on downloadable.

Disclosure: Nothing to declare

NP01

GLOBAL COLLABORATION AND AI-ENHANCED ONLINE EDUCATION FOR UKRAINIAN HCT NURSES IN WARTIME

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Background: Hematopoietic cell transplantation (HCT) capacity in Ukraine has continued to expand despite nearly four years of full-scale war. National transplant activity increased from 223 in 2022 to 404 in 2024, with 343 procedures performed by September 2025. The number of transplant centers rose from 9 to 11, and pediatric HCT volume nearly doubled (31 to 59).
A well-prepared nursing workforce is essential for further HCT advancement, as nurses play a crucial role in patient management and care. In high-income countries, nurses routinely undertake patient education, psychological support, transplant coordination, quality management, and infection control. In contrast, Ukrainian nursing education does not address the unique requirements of HCT, and limited English proficiency restricts access to international guidelines and training. These factors, combined with the psycho-social burden of war, place HCT nurses among the most vulnerable members of the healthcare workforce in our country.
To respond to these gaps, the Ukrainian Professional Society for Pediatric Oncology and Hematology (UkrPSPOH) and the Ukrainian Association for Blood and Marrow Transplantation (UABMT), in collaboration with the Worldwide Network for BMT Nurses Group (WBMT-NG), launched a national hybrid educational course.

Methods: Preparatory work began in 2023 with a survey assessing skills and educational needs among HCT nurses at the National Specialized Children's Hospital. Results revealed strong demand for competency improvement and identified language barriers as a major limitation. In 2024, UkrPSPOH and UABMT requested WBMT-NG support in developing a national training initiative.
Curriculum development involved more than 15 WBMT-NG contributors. 5 modules program covered HCT fundamentals, donor selection, apheresis, GVHD, complications, supportive therapy, and quality management. In total 540 minutes of English-language educational content was produced, translated and voice-dubbed into Ukrainian using open-access artificial intelligence (AI) and natural language processing tools, with expert post-review ensuring accuracy. This helped reduce production costs approximately 4.5-fold, allowing redirection of funds toward the hands-on workshop.
Between April and June 2025 each module was delivered weekly via Zoom plus one in-person simulation workshop on central venous line care in Kyiv. Modules were moderated by HCT hematologists, while a messenger group supported communication and peer networking. Session recordings were uploaded to an open-access YouTube channel, ensuring

continuous access despite wartime disruptions and after course completion.
Enrollment was open to all healthcare professionals, requiring only a 42-item pre/post Multiple-Choice Question test on HCT topics alongside with a brief self-assessment survey.

Results:

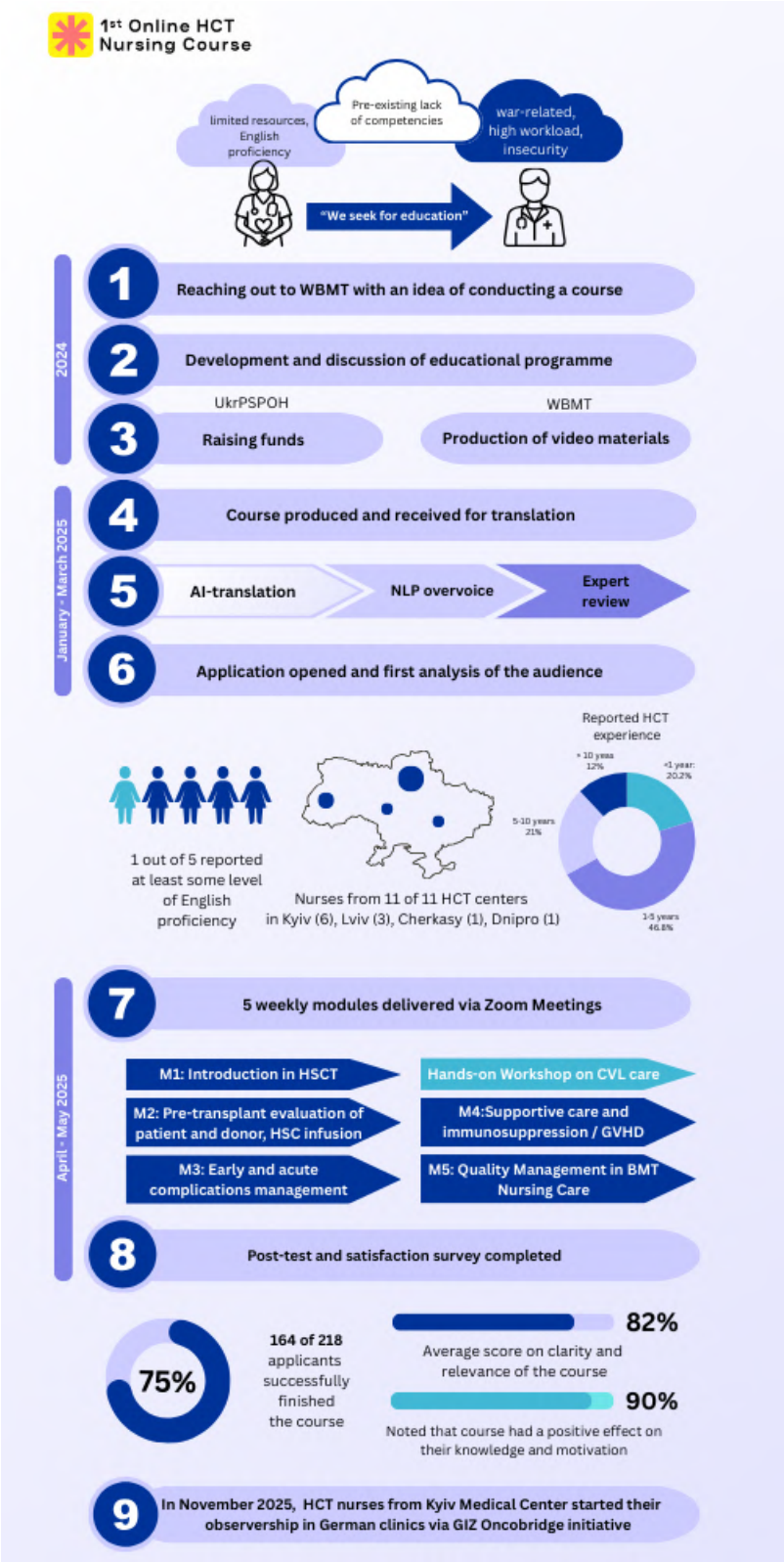
Course outcomes and metrics described in the table.

Parameter	Enrolled	Completed
# HCT centers represented	11	11
# of applicants (%)	218	164 (75,2%)
# of nurses (%)	181 (83%)	153 (93%)
# of interns, physicians, non-medical (%)	37 (17%)	11 (7%)
# of correct answers on a test (mean)	33 / 42 (78,6%)	39 / 42 (92,9%)

Satisfaction with the AI-translated course remained high: clarity (mean 4.2/5), relevance (4.3/5), and accessibility (4.7/5). 154 (90%) participants noted that course had a positive effect on their knowledge and motivation.

Conclusions:

This initiative demonstrates a major unmet need for structured HCT nursing education. Despite Ukraine's UMIC status, wartime conditions restrict opportunities for self-education and professional growth among nurses. By combining efforts with global network, expert-developed content with AI-assisted translation, this program offers a scalable model for expanding access to high-quality HCT education. The framework has been adapted by WBMT-NG for implementation in Mongolia and other countries with low or without HCT activities.


1st Online HCT Nursing Course
limited resources, English proficiency
Pre-existing lack of competencies
war-related, high workload, insecurity
"We seek for education"
2024
1 Reaching out to WBMT with an idea of conducting a course
2 Development and discussion of educational programme
UkrPSPOH
WBMT
3 Raising funds
Production of video materials
January - March 2025
4 Course produced and received for translation
5 AI-translation
NLP overvoice
Expert review
6 Application opened and first analysis of the audience
Reported HCT experience
1 out of 5 reported at least some level of English proficiency
Nurses from 11 of 11 HCT centers in Kyiv (6), Lviv (3), Cherkasy (1), Dnipro (1)
April - May 2025
7 5 weekly modules delivered via Zoom Meetings
M1: Introduction in HSCT
Hands-on Workshop on CVL care
M2: Pre-transplant evaluation of patient and donor, HSC infusion
M4:Supportive care and immunosuppression / GVHD
M3: Early and acute complications management
M5: Quality Management in BMT Nursing Care
8 Post-test and satisfaction survey completed
75%
164 of 218 applicants successfully finished the course
82%
Average score on clarity and relevance of the course
90%
Noted that course had a positive effect on their knowledge and motivation
9 In November 2025, HCT nurses from Kyiv Medical Center started their observership in German clinics via GIZ Oncobridge initiative

Disclosure:

The project concept and implementation were led jointly by the Ukrainian Professional Society for Pediatric Oncology and Hematology (UkrPSPOH), the Ukrainian Association for Blood and Marrow Transplantation (UABMT) and the Worldwide Network for Blood and Marrow Transplantation (WBMT). WBMT Nursing Group provided presentations and educational video materials free of charge. The offline component of the program, (the hands-on workshop), was funded by the Charitable Foundation "Tabletochki" (Ukraine), UkrPSPOH and National Specialized Children's Hospital "Okhmatdyt". The online component was supported by "SERVIER-Ukraine", LLC Biopharma Plasma (Ukraine), and L'Oréal Ukraine. The funders (except UkrPSPOH) had no role in the design, content development, data collection, analysis, or reporting of the project.

NP02

BUILDING A SKILLED AND CONFIDENT CAR-T NURSING WORKFORCE: ASSESSING THE IMPACT OF NURSE-LED CAR-T EDUCATION

Cassandra Abbott[1], *Pippin Ellis*[1], *Olivia Cook*[1,2], *Ty Simpson*[1], *Georgina Lea*[1], *Caitlin Wesols*[1], *Madeleine Sloane*[1], *Yumei Lew*[1], *Elli Foley*[1], *Aaron Hill*[1], *Christina Kazzi*[2,1], *Miriam Wronski*[2,1], *Katherine Ko*[2,1], *Elizabeth Cole*[2,1], *Akshay Bapat*[1], *Nermen Tawfik*[1], *Jian Li*[1], *Shu Min Wong*[1], *Shafqat Inam*[1], *Shevon Fernando*[1], *Michael Swain*[1], *Mastura Monif*[2,1], *Danielle Lee*[1], *Ellen Heywood*[1], *Constantine Tam*[1,2], *Andrew Spencer*[1,2]
[1]*Alfred Health, Melbourne, Australia,* [2]*Monash University, Melbourne, Australia*

Background: Chimeric Antigen Receptor T-Cell (CAR-T) therapy is a highly specialised treatment that re-engineers' patients' own immune cells to treat malignant and selected autoimmune diseases. While it can be highly effective, CAR-T therapy is associated with potentially life-threatening toxicities. A skilled and knowledgeable nursing workforce is critical for early recognition of patient deterioration and the delivery of timely and specialised care. To address this need, a comprehensive nurse-led CAR-T education program was developed specifically for nurses and other health professionals. The aim of this abstract is to evaluate the impact of a nurse-led CAR-T education day on participants' knowledge and confidence in caring for patients receiving CAR-T Cell therapy.

Methods: A multidisciplinary curriculum was developed to encompass the CAR T-Cell treatment pathway, from the initial patient assessment through to post-treatment recovery. Key topics included CAR-T mechanisms of action; leukapheresis and cell processing; clinical signs and management of Immune Effector Cell Associated Neurotoxicity (ICANS) and Cytokine Release Syndrome (CRS); emerging clinical trials; and medication management. A pre- and post-education survey design was used to assess changes in self-reported knowledge and confidence. Knowledge was rated on a 5-point Likert scale (1='Very poor understanding' to 5='Very good understanding') and confidence rated on a 10-point scale (0='Not at all confident'' to 10= 'Extremely confident'). Descriptive statistics were used to summarise participants' response, and independent samples t-tests were performed to compare pre- and post- education scores, with a statistical significance set at 0.05.

Results: Nine CAR-T education days were facilitated from March 2023 to November 2025, with a total of 255 participants. Pre-education surveys were completed by 239 participants, and post-education survey by 218 participants. Attendees included registered nurses (47.1%), clinical trial coordinators (21%), nurse managers (9.2%), clinical nurse specialists (6.2%), clinical nurse consultants (5%), nurse educators (2.5%), ICU liaison nurses (2.5%), scientists (1.5%), and others unspecified health professionals (5%).
An increase in self-reported knowledge and confidence scale after the education program were observed in all domains: CAR-T Cell mechanisms of action (median 3.04 to 4.49, $p<0.001$); patient eligibility criteria, workup, and apheresis (median 2.54 to 4.30, $p<0.001$); role of the cellular therapies unit (median 2.64 to 4.32, $p<0.001$); daily nursing care (median 3.17 to 4.53, $p<0.001$); CRS assessment and management (median 3.32 to 4.57, $p<0.001$); ICANS assessment and management (median 3.24 to 4.58, $p<0.001$); CAR-T medications (median 2.77 to 4.44, $p<0.001$); Discharge planning and patient education (median 2.73 to 4.39, $p<0.001$); and Outpatient nursing care (median 2.66 to 4.36, $p<0.001$). Confidence levels in caring for patients receiving CAR-T cell therapy improved significantly (median 5.20 to 8.18, $p<0.001$).

Conclusions: A structured, nurse-led CAR-T education program significantly improves nursing knowledge and confidence, directly supporting safe and effective CAR-T patient care. As CAR-T therapies continue to expand, ongoing specialised nursing education will be essential to optimise patient outcomes and maintain service excellence.

Disclosure: Cassandra Abbott has received conference travel support and speaker fees from Gilead.
Ty Simpson has received conference travel support and speaker fees from Gilead.
Mastura Monif has served on the advisory board for Merck and Alexion, and has received speaker honoraria from Merck, and her institution receives funding from Australian National Health Medical Research Council.
Constantine S Tam has received honoraria from AbbVie, BeiGene, Janssen, AstraZeneca, Novartis and Lilly

NP06

WHEN KNOWLEDGE AND ATTITUDES DO NOT TRANSLATE INTO PRACTICE: PILOT INSIGHTS FROM HEMATOLOGY AND HEMATOPOIETIC STEM CELL TRANSPLANTATION NURSES' SEXUAL HEALTH CARE

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Background: Sexual health is a critical yet often neglected component of survivorship care for patients with hematologic malignancies and those undergoing hematopoietic stem cell transplantation (HSCT). Despite their central role in holistic cancer care, hematology and HSCT nurses frequently encounter barriers such as cultural taboos, limited training, and the absence of clear clinical guidelines. To date, little is known about their attitudes, knowledge, and practices in this specialized field, underscoring the need for exploratory evidence. This

pilot study aimed to provide preliminary insights into the sexual health care attitudes, knowledge, and practices of hematology-oncology and HSCT nurses, to identify variations across demographic and professional characteristics, and to examine interrelationships among these domains.

Methods: A cross-sectional survey was conducted with 36 nurses working in hematology-oncology and HSCT units at a medical center. Validated instruments—the Sexual Health Care Attitudes Scale (SHC-A), Sexual Health Care Knowledge Scale (SHC-K), and Sexual Health Care Practice Scale (SHC-P)—were administered. Data were analyzed using descriptive statistics, independent-sample t-tests, one-way ANOVA, and Pearson's correlation coefficients.

Results: The mean SHC-A score was 32.9, and the mean SHC-K score was 43.4, both indicating relatively higher levels compared to previously reported ranges. The SHC-P score averaged 6.4, suggesting higher practice levels than in earlier studies, yet representing only 30.1% of SHC items implemented. Group comparisons showed that nurses with prior SHC-related training had significantly higher practice scores ($t = 2.07$, $p = .046$). Age was significantly associated with knowledge scores ($F = 5.01$, $p = .013$), and nurse professional role showed a borderline association with attitudes ($F = 3.28$, $p = .050$). Correlation analysis revealed a significant positive association between knowledge of consultation and documentation and overall attitudes scores ($r = 0.46$, $p = .004$). In contrast, negative associations emerged between attitude subdomain: concerns about colleagues' negative perceptions and practice in sexual and fertility preservation ($r = -0.42$, $p = .022$), as well as between practice in fertility preservation and knowledge of psychosocial aspects ($r = -0.38$, $p = .045$) and communication skills ($r = -0.39$, $p = .037$).

Conclusions: This pilot study highlights both the strengths and limitations in hematology-oncology and HSCT nurses' readiness to provide sexual health care. While nurses demonstrated relatively positive attitudes and knowledge, these were not consistently translated into practice, with less than one-third of care items implemented. The findings underscore the urgent need for targeted education, structured training, and institutional support to bridge the gap between knowledge, attitudes, and practice. Future studies should incorporate qualitative approaches to explore the underlying reasons for this disconnect—such as cultural taboos, workplace dynamics, and role boundaries—and conduct larger-scale surveys to validate these preliminary results. Strengthening sexual health care within survivorship models has the potential to enhance both the quality of care and the quality of life for patients undergoing hematologic malignancy treatment and HSCT.

Disclosure: Nothing to declare

NP16

IMPLEMENTING STRUCTURED EDUCATION IN APHERESIS: A COMPARATIVE EVALUATION OF TRAINING EFFICIENCY AND LEARNER PERCEPTIONS

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Background: Apheresis services require a highly skilled workforce capable of delivering complex procedures safely and efficiently. Historically, training within our unit followed an ad-hoc, sequential model where learners progressed through procedures as opportunities arose. Plasma exchange (PEX) and white cell depletion (WCD) training occurred only when suitable patients were available, and no dedicated study time was provided for theoretical learning. As a result, staff required an average of **62 weeks** to become fully competent, often reporting uncertainty when managing alarms or troubleshooting during complex procedures. These limitations highlighted the need for a structured, standardised education pathway to strengthen competency, improve confidence, and support service efficiency.

Methods: Two apheresis team leaders completed the Terumo Spectra Optia Expert Trainer Courses for TPE, MNC and CMNC, enabling them to design a comprehensive, competency-based education programme integrated with enhanced teaching on optimisation, troubleshooting and citrate management. The pathway incorporated protected study days, staged learning outcomes and supervised practical sessions, mapped directly to the Terumo MNC/CMNC, TPE and WCD programmes, and the Therakos ECP learning pathway. Structured feedback was collected at key points - after completion of Terumo and again after Therakos training, to evaluate clarity, pacing, readiness and confidence. Training duration, confidence and preparedness were compared across cohorts before and after pathway implementation.

Results: The first cohort (n=3), all with haematology experience, achieved full competency in a median of **25 weeks**, representing a **60% reduction** in training time. The buddy-based on-call model enabled earlier rota participation and enhanced clinical exposure. Staff reported that the structured sequence, theory/practice integration and stepwise development from machine components to optimisation supported confidence and knowledge retention. The second cohort (n=3), with only one member having haematology experience, achieved full competency in an average of **26 weeks**. A consolidation period (mean 17 weeks) between Terumo and Therakos training, supported knowledge embedding while accommodating capacity pressures.
Feedback from this cohort was consistently positive: learners valued instructor support, accessible materials, and the interactive nature of the training, as seen in evaluation forms from the Terumo and ECP programmes. Constructive feedback highlighted the need for pacing adjustments, ensuring uninterrupted consolidation, and limiting the number of concurrent Terumo trainees to preserve focus. Some learners felt more confident in the modality they trained on first, recommending sequencing refinement.

Conclusions: Implementing a structured apheresis education pathway substantially reduced training duration while improving learner confidence, competence and service

responsiveness. Faster sign-off enables earlier contribution to the on-call rota, supporting workforce capacity and meeting service demand. Enhanced theoretical grounding and optimisation skills have the potential to improve procedural quality, collection efficiency and, ultimately, patient outcomes.
Going forward, learner feedback will guide refinement of the programme. All new trainees will begin with ECP to provide a supportive introduction to the specialty; consolidation periods will be protected and paced according to individual progression; and assessment timelines will be adapted to ensure learners achieve competency within a structure that reflects their needs and supports safe, confident practice.

Disclosure: Nothing to declare Cara Cunningham
Nothing to declare Joanne Bird

NP28

IMPLEMENTATION OF A MENTORSHIP PROGRAMME FOR NEWLY HIRED NURSES IN ONCO-HEMATOLOGY AND BONE MARROW TRANSPLANT UNIT AT SAN RAFFAELE HOSPITAL, MILAN

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Background: Nurse turnover is a global issue, with a significant impact on the quality of care, organizational costs, and staff well-being. Young nurses and new hires are particularly vulnerable to the risk of leaving, especially in highly complex clinical settings such as the Hematology and Bone Marrow Transplant Unit (UOE-TMO). The stress associated with entering the professional world, feelings of inadequacy, gaps in training, and difficulties in managing complex clinical situations are documented risk factors. In this scenario, structured mentoring programs have proven effective in improving job satisfaction, promoting professional growth, and reducing turnover. In light of this evidence, the UOE-TMO at San Raffaele Hospital has developed a structured induction program for newly hired nurses, based on 1:1 mentoring with a clinical tutor and a mentoring program lasting up to six months.

Methods: A standardized operating procedure was implemented that defines roles, responsibilities, training tools, and evaluation methods for the induction program. The program consists of three main phases:

1. 1:1 Tutoring (first month): the clinical tutor accompanies the new hire for twelve hours shifts for a total of 12-14 days, helping them acquire the skills outlined in the job description and progressively monitoring their autonomy.
2. Mentoring (1st-6th month): the mentor guides the nurse in consolidating clinical, organizational, and interpersonal knowledge, tailoring the content to the mentee's training needs.

3. Pediatric tutoring (after at least 6 months): dedicated to the management of patients in the developmental age, with expert tutors and the progressive assignment of responsibilities.

The program is supported by structured tools such as: a theoretical-practical guide for new hires, mandatory distance learning courses, theoretical tests, skills assessment checklists, and periodic feedback meetings with mentors, tutors, and coordinators. Assessments are carried out at the end of the first month, the third month, and the sixth month, with dedicated interviews and the completion of formal tools.

Results: The adoption of the program has made it possible to structure a uniform, progressive, and personalized path for new hires, reducing the risk of overload and promoting the gradual acquisition of clinical and organizational skills. Direct tutoring ensured patient safety and facilitated on-the-job learning, while mentoring supported professional growth, critical thinking development, responsibility management, and team integration. The assessment tools allowed for the early identification of critical areas, supporting targeted training interventions. Greater continuity of care and better adaptation of new hires to the UOE-TMO context were observed, helping to strengthen their sense of belonging and job satisfaction.

Conclusions: The mentoring and coaching program for newly hired nurses in UOE-TMO is an effective strategy for supporting the transition from training to clinical practice in a highly complex setting. The structuring of clear roles, dedicated teaching tools, and assessment stages promotes autonomy, safety, competence, and professional well-being. The integrated clinical tutor-mentor approach is an organizational investment that can improve the quality of care, reduce turnover, and enhance the potential of the new generation of nurses.

Disclosure: Nothing to declare.

NP30

ESTABLISHING THE FIRST PEDIATRIC BONE MARROW TRANSPLANT NURSING PROGRAM IN THE UAE: A MODEL FOR COMPETENCY BASED EDUCATION AND INTERNATIONAL COLLABORATION

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Background: The Abu Dhabi Bone Marrow Transplant (AD-BMT) Program, a joint initiative between Abu Dhabi Stem Cells Center and Yas Clinic Khalifa City, was commissioned in 2021 to establish a national and regional benchmark for stem cell transplant care. In 2023, the program achieved Center of Excellence (COE) status for Bone Marrow Transplant, the first in

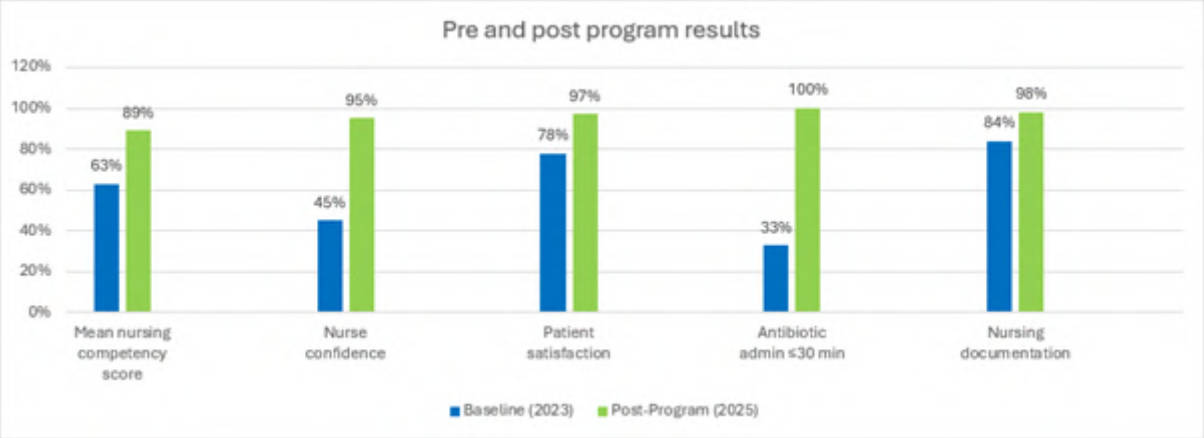
the UAE, and attained FACT accreditation in 2025, aligning with international quality and safety standards. Rapid program expansion highlighted the need to prepare newly hired nurses for the specialized pediatric BMT workforce. The aim was to create a sustainable framework for nursing excellence through structured education, competency validation, and mentorship. A three-year collaboration with Boston Children's Hospital (BCH) supported nursing education, competency assessment, policy development, mentorship, and program capacity building.

Methods: A multimodal nursing education program was developed and implemented across the pediatric BMT unit and inpatient hematology unit in collaboration with BCH and AD-BMT nursing educators. The program incorporated didactic instruction (30%), simulation-based training (25%), bedside mentorship (30%), and structured competency validation (15%). The APHON Chemotherapy and Biotherapy Provider Course was introduced to strengthen oncology nursing skills, targeting 100% completion for pediatric BMT nurses and 50% for inpatient nurses. The program educator achieved APHON Instructor status, enabling independent local and regional delivery of standardized oncology nursing education. BCH nurse experts conducted in-person visits every four months and monthly virtual meetings to evaluate competencies, identify practice gaps, guide policy alignment, and support implementation. Learning outcomes were assessed through pre- and post-tests, direct observation, and formal six-month revalidation cycles.

Results: Following implementation, significant improvements were observed across all measured indicators for the 30 participating nurses. Mean nursing competency scores increased from 63% to 89%, and self-reported confidence improved from 45% to 95%. Timely antibiotic administration within 30 minutes increased from 33% to 100%. Patient satisfaction rose from 78% to 97%, and nursing documentation accuracy improved from 84% to 98%. The central line associated bloodstream infection rate remained at zero per 1,000 catheter days throughout the program. Two APHON Courses were delivered. In the first course, 100% (n=13) passed the exam under BCH instruction. In the second locally delivered course, 100% (n=12) passed under the YCKC instructor, demonstrating sustainability and strengthening internal capacity. Qualitative feedback highlighted stronger communication between nurses and families, improved interdisciplinary collaboration, enhanced confidence in managing complex BMT cases, and greater autonomy in decision making. Establishing a locally APHON competent workforce and an in-country instructor created a sustainable framework for continued professional development and laid the foundation for a regional pediatric oncology nursing education hub.

Indicator	Baseline (2023)	Post-Program (2025)	Mean	Mean Difference	Std. Deviation
Nursing Competency score	0.63	0.89	0.76	26% ↑	0.427

Nurse Confidence	0.45	0.95	0.7	50% ↑	0.459
Patient Satisfaction	0.78	0.97	0.88	19% ↑	0.325
Antibiotic admin ≤30 min	0.33	1	0.67	67% ↑	0.471
Nursing documentation	0.84	0.98	0.91	14% ↑	0.286



Conclusions: Through structured education, mentorship, and capacity building, the AD-BMT Program established the UAE's first pediatric BMT nursing program, achieving COE and FACT accreditation within three years of inception. Collaboration with BCH and implementation of the APHON framework resulted in measurable improvements in competency, safety, and patient centered care. The development of local instructor capacity ensures sustainability, knowledge transfer, and scalability. This model provides a reproducible approach for advancing pediatric BMT nursing excellence in emerging healthcare systems across the world.

Disclosure: Nothing to declare

NP32

GLOBAL NURSING EXCHANGE: EXPERIENCES FROM THE "HOW DO YOU DO IT" ONLINE SESSIONS BY THE EBMT NURSES GROUP PAEDIATRIC COMMITTEE

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Background: In 2024, the EBMT Nurses Group Paediatric Committee initiated in 2024 a series of online, interactive sessions titled *"How Do You Do It…"* to facilitate the exchange of practical skills among paediatric nurses within and outside Europe. The aim of these sessions was to provide an accessible platform for sharing knowledge and clinical experiences, thereby contributing to improved quality of care. The online sessions also helped identify gaps and variations in nursing practices that may require further attention or harmonization. Since its launched, the committee organized 4 one-hour interactive online meetings using an digital tool for interactive presentations with real-time audience participation, addressing topics such as isolation rules, discharge after HSCT, central line care, and pain management. Summaries of each meeting were shared on the EBMT website in the form of infographics. An evaluation was conducted to understand the perceived value of these sessions and identify needs and collate topics for future sessions.

Methods: To evaluate participant experiences, a web-based survey was distributed by email in October and November 2025 to all those who had attended at least one session. One reminder was send after three weeks. The survey consisted of nine closed-ended and four open questions. Responses were collected using a five-point Likert scale ranging from "strongly agree" to "strongly disagree" and freetext. Results were analyzed using descriptive statistics.

Results: A total of 24 nurses from 14 countries responded to the survey (Europe 17, non-Europe 7). Seventy percent indicated that the content of the sessions was relevant to their daily practice. Approximately 55% reported learning about new practices or gaining ideas that could be implemented in their own centers. Several responders highlighted that the sessions provided valuable insights into new procedures, materials, and effective strategies to enhance clinical collaboration. Moreover, 75% believed that these sessions could contribute to the development of shared guidelines.
Most participants learned about the sessions through the EBMT website (27%), the EBMT newsletter (33%), or the paediatric committee's mailing list (27%). Overall, the online format was considered easy to access (69%), and 66% found the session duration appropriate. Around 75% reported that they would recommend the *How Do You Do It*

sessions to colleagues. Overall, participants enjoyed participation and comments included: *"It's not easy for us, nurses, to have a place to share. That's why I enjoyed it the most."* and *"Exchanging ideas with colleagues in other countries in a low-threshold format is very valuable."*
Up to three respondents disagreed on the closed-ended questions, although the survey did not provide sufficient information to identify the underlying reasons.

Conclusions: The EBMT Nurses Group Paediatric Committee's *"How Do You Do It…"* online sessions were generally perceived as a valuable means of sharing information, exchanging practical skills, and fostering connections among paediatric nurses within and outside Europe. Based on the positive evaluation, the committee will continue offering these sessions and will integrate suggested future topics such as gene therapy, GvHD, skin care, apheresis, and cultural differences.

Disclosure: None

NP119

DEVELOPMENT AND USABILITY TESTING OF A CAR-T THERAPY E-LEARNING RESOURCE FOR HEALTHCARE PROFESSIONALS: A QUALITATIVE THINK-ALOUD STUDY

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Background: As demand for CAR-T and other advanced cellular therapies increases, there is a growing need for healthcare professionals (HCPs) to receive the appropriate training and education on this topic. Scoping work led by the Cellular Therapy Clinical Nurse Specialist (CNS) at Anthony Nolan along with an established focus group, identified limited UK-focused, multi-professional educational resources on CAR T-cell therapy, particularly inclusive of paediatric care. A CAR-T e-learning resource was developed by Anthony Nolan. The aim of this project was to address this gap through the development, implementation and evaluation of a comprehensive e-learning resource. Alongside development, a qualitative usability study was embedded to formally evaluate user experience and learning design, recognising the importance of conducting research into digital education in this area.

Methods: HCPs were invited to take part in a qualitative think-aloud interview. During the first part of the interview HCPs were asked about their views on e-learning and their CAR-T education needs. During the second part of the interview, they completed the think-aloud task using the CAR-T e-learning resource as a prompt. Content analysis was conducted to identify emerging themes and topics. Findings from the interviews were incorporated into the development of the final e-learning resource. Participants were then sent a link to access the final resource and asked to complete it in their own time, as well as a feedback survey to share their thoughts on the entire e-learning resource.

Results: HCPs were positive about the use of e-learning due to its flexibility. Participants felt e-learning is most effective when the content is relevant to their role and when there is opportunity to contribute to Continuing Professional Development (CPD). However, participants shared that e-learning is not always accessible and barriers to its use include time, access to resources and funding. Participants stressed the importance of keeping education up to date with the rapidly evolving field of CAR-T therapy. HCPs want to feel educated on the entire CAR-T pathway, from patient eligibility through to late effects, with neurotoxicity and long-term effects being a key priority. Participants were positive about the content, design and usability of the e-learning resource developed by Anthony Nolan. Overall, they felt the content was detailed and relevant to HCPs with varying levels of knowledge on the CAR-T pathway. Participants felt the design of the resource was engaging and visually appealing and reported smooth navigation and accessibility. Small improvements suggested during user testing were implemented in the build of the final modules.

Conclusions: E-learning is viewed by health care professionals as a valuable and accessible resource for training, particularly in a rapidly evolving treatment such as CAR-T. The collaborative approach undertaken in the development of this resource and think aloud methodology utilised has ensured that the learning objectives have been clearly addressed for the workforce accessing the training and as such has provided a robust introduction into the CAR-T pathway for UK HCPs.

Disclosure: Nothing to declare

NP71

HAEMATOPOIETIC, CELL THERAPY AND TRANSPLANT PREPARATIVE TRAINING FOR REGISTERED NURSES IN SINGHEALTH, SINGAPORE

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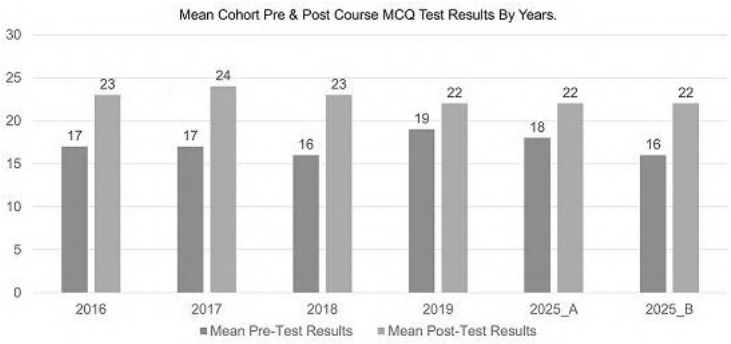
Background: SingHealth has the largest public Haematopoietic Stem Cell Transplant (HSCT) and cell therapy programme in Singapore. The adult service is provided in Singapore General Hospital (SGH) while the paediatric programme is housed off site at the KK Women's and Children's Hospital (KKH). Annually, close to 170 HSCTs and CAR-T cell treatments are performed across these two sites. The training and competence preparation of HSCT nurses were decentralized and organized independently prior to year 2015.

Methods: To standardize the HSCT preparative training of our nurses, the SingHealth HSCT course for Registered Nurses (RNs) was conceptualized in year 2016. The 35 hours in-person theoretical training curriculum was developed to conform with the standards of the 6th edition of the Foundation for the Accreditation of Cellular Therapy (FACT)-Joint Accreditation Committee ISCT-Europe & EBMT (JACIE) international standards for haematopoietic cellular therapy product collection, processing, and administration. The 5-day course enrolled RNs who had at least 2 years of working experience in the haemato-oncology units. The course

was taught by the staff members of the multi-disciplinary HSCT teams from both SGH and KKH. To ensure rigor for the course, assessment methodologies of pre-post course MCQ testing, case-based discussion and group presentations, stem cell infusion competency assessment, and individual post course reflective journaling were instituted.

Results: From year 2016 to 2025, a total of 8 runs of the HSCT course was conducted. A virtual edition was organized in year 2021 due to the COVID-19 pandemic restriction orders imposed in Singapore. A total of 132 participants (112 SingHealth nurses, 15 non-SingHealth nurses, and 5 HSC transplant coordinators) attended the course. Upon completion of the course, participants were presented with the certificate of completion and continuing nursing education points awarded by the Singapore Nursing Board. Paired pre and post course multiple choice questions (MCQ) tests were administered for 6 of the 8 cohorts. All 6 cohorts showed improvements in post course MCQ test results, reflecting the positive impact of the course curriculum.
Qualitative accounts from participants reported good satisfaction with the course curriculum. Two recurring themes that surfaced from participants were 'gaining confidence' and 'showing empathy'. Participants felt more confident and competent to care for these patients with their increased knowledge and understanding of HSCT management and treatment principles. Participants were better able to empathize and journey with these patients during their treatment.



Conclusions: The SingHealth Haematopoietic Stem Cell Transplant course continues to be the main HSCT preparative programme for registered nurses working within SingHealth group of hospitals and nurses working with the private stem cell transplant services in Singapore.
The course curriculum was revised in year 2020 and incorporated management and care of patients undergoing chimeric antigen receptor T cell therapy.

Clinical Trial Registry: Not Applicable

Disclosure: Nothing to declare.

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NP82

BUILDING INCLUSIVE CLINICAL CULTURES: SUPPORTING NEURODIVERSE STAFF IN A SPECIALIST HAEMATOLOGY AND TRANSPLANT SETTING

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Background: Transplant and cellular therapy is a dynamic and complex speciality that needs to nurture and support staff. Neurodiversity is an umbrella term, used to describe natural differences in how individuals' brains' think and process information. It's estimated that around 1 in 7 people in the UK have neurodevelopmental differences (Keeping Well, 2024) In 2023 the NHS published its first equality, diversity and inclusion (EDI) improvement plan. By recognising and valuing unique contributions of neurodivergent individuals, organisations can build stronger, more innovative and inclusive teams as people from different backgrounds bring different experiences, perspectives and skills.
The Clinical Educator team work closely with new staff, preparing them to care for transplant patients. During their induction, staff have disclosed they are neurodivergent or require additional learning support. Some of the established staff have also shared they are neurodivergent. Recognising an importance to adapt our teaching styles; we explored safe and non-judgemental ways that gave staff an opportunity to highlight any learning needs. "This is Us and You" was developed.

Methods: 'This is us and you' is intended to establish a setting for an inclusive and welcoming culture.
By providing the new staff member with a little information about each of us, we then invite them to tell us about themselves, including any information they think would be useful for us, as educators, to know.
Some staff have disclosed information using the document. However, the hope is that even if they do not feel comfortable disclosing via the document, they will feel the team is a welcoming, safe space where we aim to treat everyone as individuals and try to tailor the learning to them.

Results: Since September 2024, 45 new starters within the Haematology directorate have received the 'This is Us & You' document. It was completed by 19 members of staff and 2 disclosed learning needs or diagnoses within the document. 8 out of 19 informed us of their preferred style of learning.
It is important to emphasise that staff do not need a formal diagnosis to access support or reasonable adjustments. We aim to update our learning programme and materials, implementing learning approaches that are inclusive and therefore benefit all staff.
As an educator team, we are growing a culture to normalise and accept learning differences and encourage established staff to feel comfortable disclosing any issues that may be affecting them. We are developing confidence in our ability to provide inclusive education to all our haematology nursing staff.

Conclusions: So, What Now? Still lots to do!
It's the beginning of an extensive project involving the wider nursing team. One of the findings is lack of education and training to raise awareness of neurodiversity in the workplace. As educators, we found it difficult to access practical support and guidance in clinical practice.
Therefore, it's understandable why staff do not want to disclose their challenges to managers and colleagues for fear of being labelled. As a result, neurodivergent nurses can be seen as underperforming and requiring improvement plans.

Disclosure: Nothing to Declare.

NP94

IMPROVING DELIVERY AND DOCUMENTATION OF JACIE-REQUIRED EDUCATION AND COMPETENCIES IN AN ADULT AUTOLOGOUS TRANSPLANT SERVICE

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Background: High-quality care for patients undergoing autologous stem cell transplantation relies on a nursing workforce that is knowledgeable, competent, and fully compliant with JACIE Standards. Within our 10-bedded haematology unit, autologous transplant activity represents a small proportion of overall admissions, averaging approximately 16 patients per year. As a result, nurses did not perceive JACIE education requirements as integral to their clinical practice, and the implications of non-compliance were poorly understood. In addition, the service faced longstanding challenges with education delivery, inconsistent attendance at training sessions, and inadequate systems to evidence compliance and track competency renewal.
Historically, the service delivered supplementary JACIE training through evening sessions via Microsoft Teams. Attendance and presenter engagement were low, as staff were reluctant to undertake education in their personal time. Competency records were limited: documentation captured only the date of completion, with no mechanism to monitor or prompt renewal. Staff often overlooked expiring competencies, including critical haematology nursing skills, jeopardising compliance with JACIE and hospital-mandated nursing requirements.

Methods: A structured and sustainable intervention was therefore developed to redesign how JACIE-required education and competencies were delivered, monitored, and evidenced. Evening training was discontinued entirely. At the start of each year, a detailed education plan was created, aligning topics to relevant JACIE Standards and distributing content between face-to-face JACIE Away Days. All monthly education was pre-recorded, uploaded to YouTube, and accessible during protected work hours. On completion of the training staff received an attendance certificate; participation was logged on a central spreadsheet. Standard operating procedures were updated to embed the process, clarify expectations, and

outline consequences of non-compliance. Reminders were issued to staff who had missed required training, copied to nurse managers to reinforce accountability.
To address competency renewal, the existing matrix was redesigned to include an expiry date column with a red-amber-green status system: red for expired, amber for competencies due within three months, and green for those in date. Nurses received monthly reminders prompting them to schedule assessments well before expiry. A new end-of-year CPD record, signed by the Programme Director, further formalised individual accountability. Where training remained incomplete, a deviation was raised in accordance with the training SOP.

Results: The redesigned education model led to demonstrable improvements in compliance, engagement, and documentation. Pre-recorded content provided predictability and flexibility, while explicit links to JACIE Standards improved staff understanding of its importance. Knowledge quizzes strengthened learning, and attendance certificates supported appraisal and revalidation. By year end, all nurses achieved full compliance with required JACIE training, and 95% of clinical competencies were in date.

Conclusions: This initiative highlights the need for proactive, structured, and well-governed approaches to clinical education in transplant services. Embedding protected learning time, reminders, and clear accountability supports staff engagement and ensures ongoing compliance with JACIE and NMC requirements. Continuous review and involvement of frontline staff including a registered nurse and healthcare assistant in planning future training for 2026 will help ensure the programme remains relevant, engaging, and sustainable.

Disclosure: Nothing to declare

NP95

IN HOUSE EDUCATION PROGRAMME 15 YEARS LATER: WHERE ARE WE NOW?

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Background: In 2011 a weekly education programme was introduced within our haematology and transplant unit to support nurses and allied health professionals (AHPs) in maintaining competence and meeting regulatory requirements. Advances in medicine, treatments and evolving healthcare delivery demand continuous professional development. Evidence shows that structured education improves staff retention, job satisfaction, and patient care (Pashmena et al, 2024). JACIE standards further highlight the need for specialist education in haematology and transplant services, this includes maintaining evidence of competence and assessment in clinical skills such as cell infusion, line care and treatment delivery (EBMT, 2025). We have had to adapt our education provision due to the introduction of complex treatments such as CAR-T cell, gene therapy and new clinical trials. In addition, changes to workforce and overseas recruitment has led to additional hurdles such as

language barriers and varying standards of clinical skills and education.
Original objectives:

- Deliver regular, accessible transplant-focused education
- Provide informal, 30-minute sessions
- Offer attendance certificates for portfolios/revalidation
- Ensure compliance with JACIE standards
- Make resources available via platforms such as QPULSE
- Utilise multidisciplinary team expertise
- Share presentations on request

Methods: **Then:**

- 2011, weekly were sessions introduced, covering transplant and haematology topics
- 2013, appointment of a practice educator (3 days/week)- the practice educator ensured mandatory training and haematology/ transplant knowledge, skills and competency were maintained
- 2019, full time practice educator (5 days/week)
- 2022, expansion of the transplant unit
- 2022, dedicated education room established

Now:

- Weekly sessions continue to include:
  - Attendance registers and certificates
  - Evaluation forms for feedback and topic suggestions
  - 30-minute duration to maximize participation
  - Use of extended MDT to deliver teaching
- Additional initiatives introduced:
  - Appointment of additional practice educator to cover 7-day service
  - "Tiny Teaching" (10-minute sessions with tip sheets)
  - Daily handover quizzes
  - Biannual haematology study days with protected time
  - 1:1 patient-focused teaching
  - support staff to attend training days outside of the hospital

Results:

- 60 nurse questionnaires assessed barriers to education
- 60 evaluation forms reviewed for attendance and engagement
- Findings confirm sessions are relevant, well-received, and appropriately timed.
- Findings highlight reasons for non-attendance of sessions such as workload and staffing

Conclusions: The in-house education programme remains valuable and effective since introduction 15 years ago. Feedback suggests staffing pressures and limited protected time still hinder participation. To address these barriers, diverse educational formats have been implemented to ensure consistent access to updates and sharing of key messages. The practice educator team, now fully embedded, continues to grow and recognise that they

must be adaptable in their teaching style to meet the needs of the service and team whilst ensuring the department meet regulatory requirements. We plan to update and adapt our education pack to include a learning passport.
References: EBMT, 2025. FACT-JACIE standards for Hematopoietic cellular therapy (HCT) and Immune Effector cells (IEC), 9th edition. Retrieved from STS.5.2.051_HCT_Manual_9th_Ed_R1.pdf
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Clinical Trial Registry: N/A

Disclosure: nothing to declare

Outpatient Developments and Ambulatory Care

NP07

EXPERIENCES OF AT-HOME AUTOLOGOUS STEM CELL TRANSPLANTATION IN SPAIN: CURRENT OVERVIEW AND IMPROVEMENT AREAS

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Background: Management of Autologous Stem Cell Transplant (ASCT) in a Homecare Units (HCU) or an Ambulatory Setting (AS) is a growing trend. In Spain, the first experiences began before 2000; however, it was in the last decade that they started to expand. In 2023, the GETH Spanish Nurses Group (GETH-SNG), established the Homecare Group (HCG) with the following main objectives: 1. To have a general overview of the Spanish HCU, 2. To understand the impact of ASCT programmes 3.To identify common aspects to develop multicentre studies.

Methods: Nurses from various HCUs were identified through GETH-SNG and invited to participate in the HCG. A data base was created to collect information about: inclusion criteria, non clinical reasons for patients' exclusion, HCU models, resources, patients included (over the last 3 years), readmissions, other programmes for complex haematology patients and educational programmes to patients and caregivers. Methodologies related to

educational programmes were exposed in the regular HCG on-line meetings. Data were also collected from literature published by some of the units.

Results: Of the 9 HCUs invited, 8 had ASCT programmes, and 7 HCUs reported data. Across all units, the inclusion criteria were: ECOG ≤ 2, home-hospital distance of 30-60 min, a 24/7 caregiver and voluntary acceptance. The two main exclusion criteria for candidates who met the clinical conditions were long distance from the hospital and lack of a caregiver. Some hospitals reported alliances with foundations to help cover a part of these social needs.
All ASCT HCUs provided care 365 days a year during daytime hours, only one reported 24h availability of homecare. Most had a special circuit for managing emergencies at the hospital.
Between January 2023 and September 2025, a total of 1241 SCT patients were treated across 5 hospitals. The following table has the results for each hospital regarding the number of patients included, readmissions, reasons for readmission, patients who returned home to complete the process and alternative complex programmes for haematology patients. (table1)
All HCU reported educational programmes prior to discharge for patients and caregivers to ensure adequate management and safety at home. They also agreed on the importance of ongoing home-based training to support proper adherence to the recommendations, adapted to each patient's tools and abilities. None reported formal evaluations to measure the effectiveness of these interventions.

Table 1: HCU characteristics and activities Jan-2023 to Sep-25

Hospitals	**At-home Visits**	**HCU model (TASP)**	**1ST ASCT**	**N. SCT (2023-25)**	**N (%) ASCT (2023-25)**	**N (%) ASCT at HCU**	**N (%) Readmission Return home**	**Reassons**	**Port-folio Complex programs**
Clínic (Barcelona)	Nurse	Early discharge	Nov-2000	279	148 (53%)	108 (73%)	4 (3'7%) 0	Persistent fever	Early discharge: CAR-T, AL Total outpatient: CAR-T, AL, Bispecific therapy
Reina Sofía (Córdoba)	Nurse	Early discharge	Jan-2021	218	97 (44'5%)	63 (65%)	12 (19%) 7/12 (58%)	Fever, electrolyte replacement, caregivers' loss	Early discharge: CAR-T, Alo-SCT, AL

Hospitals	At-home Visits	HCU model (TASP)	1ST ASCT	N. SCT (2023-25)	N (%) ASCT (2023-25)	N (%) ASCT at HCU	N (%) Readmission Return home	Reassons	Port-folio Complex programs
Regional (Málaga)	Nurse	Early discharge: Linfoma Total Outpatient: MM	Mar-2020	382	153 (40%)	80 (52%)	1 (1,2%) 0	Central line complications	Early discharge: CAR-T, Alo-SCT, AL
Fundación Jiménez Díaz (Madrid)	Nurse	Early discharge	Mar-2021	150	81 (54%)	28 (35%)	10 (35'7%) 4/10 /40%)	Fever	Early discharge,
Marqués de Valdecilla (Santander)	Physician & Nurse	Early discharge	Jan-1997	nd	*795	*84 (10,6 %)	*10 (12%) 2/10 (20%)	*9 sepsis 1 family claudication	Early discharge, AL
Clínic (Valencia)	Nurse	Early discharge	Oct-2020	212	93 (44%)	52 (56%)	6 (11.5%) 6/6 (100%)	Fever Diarrea Mucositis	Early discharge: CAR-T, AL
Álvaro Cunqueiro (Vigo)	Nurse	No							Ramp up Venetoclax Chemotherapy.

*Results obtained of a published series between 1997 to 2019

Conclusions: Social resources are needed to improve equity and increase the recruitment to HCUs for all patients who meet the clinical criteria, despite the alliances with foundations. The number of patients attended and efficiency reported by the different HCUs are high, enabling the hospitals to increase the capacity to manage complex cases.
Accurate health training programmes are essential for managing ASCT patients prior to discharge and during at home follow-up. Formal evaluations to collect feedback on these interventions are needed in order to improve the programmes.

Disclosure: Nothing to declare.

NP11

TRANSPLANT @ HOME: A SINGLE CENTRE EXPERIENCE IN HOME-BASED CARE FOR AUTOLOGOUS STEM CELL TRANSPLANTATION

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Background: Autologous stem cell transplantation (ASCT) for multiple myeloma has traditionally been carried out in the inpatient setting. Post COVID-19, many centers globally have shifted to home-based transplantation with safe follow-up and comparable outcomes. However, data on healthcare economics, acceptability and safety of this care model in the Asian setting are lacking. In Singapore, the Hospital-at-Home (HaH) model has become mainstream in public healthcare institutions. Since 2024, we started a pilot program with HaH (NUHS@Home) to offer home-based ASCT for myeloma.
Our pilot program aimed to evaluate the safety, feasibility, and impact on patients' quality of life of a home-based ASCT strategy in Singapore.

BMT Coordinator Assessment & Education for Home Transplant		
This assessment is to be completed before patient is enrolled into the NCIS Home Monitoring & Treatment Program. This helps identify patients and caregivers, who meet both the clinical and home assessment criteria for the program. The assessment will ensure that the safety of patients, caregivers and healthcare professionals is maintained at every stage of the Home Transplant Program.		
Pre-Transplant Assessment		**Assessor's comments for transplant physician review**
Patient Assessment	Medical History assessed and reviewed ☐ Age <65 (if ≥65 years old but fit, for individual case basis consideration) ☐ ADL independent ☐ Availability of dedicated caregiver ☐ Patient has good understanding of treatment ☐ Patient has good history of compliance ☐ Organ functions within acceptable limits	Special mention ☐ Others
	Psychosocial assessment There are identified issues that needs special highlight to the referred MSW ☐ Yes [add remarks] ☐ NIL concerns	
	Home within reasonable distance ☐ YES, ≤ 45 mins by car from NUH ☐ NO, ≥ 45 mins by car from NUH	
	Home environment brief assessment Following area [ticked] that requires special mention to transplant physician and/or OT ☐ Bathroom/Toilet ☐ Pets ☐ Plants ☐ Young children ☐ Renovation in progress at home or nearby ☐ NIL concerns	Special mention ☐ Others
Caregiver Assessment	Identified caregiver screening Following eligibility criteria met ☐ Physically available 24/7 to provide care ☐ Able to remain contactable 24/7 ☐ Able to bring patient back for treatment ☐ Able and willing to learn subcutaneous injection technique ☐ Steadfast/ Observant/ Resilient	Special mention ☐ Others
Conclusion	Passed Assessment. ☐ YES, proceed to plan and engage for Home Transplant ☐ NO, will discuss with primary transplant physician [remarks]	
Additional Remarks		
Transplant Education		
Patient & Caregiver Education	Before and Throughout Transplant period up till D+100 ☐ Nutrition ☐ Intake-Output and Body weight self-charting ☐ Exercises/ Activities to prevent boredom ☐ Personal Hygiene, Oral care ☐ Fall Prevention (home environment risks) ☐ Infection Prevention measures ☐ Blood test monitoring (pancytopenia precautions) ☐ D0 preparation: ice cubes, soft chewy candies ☐ Daily video call with NUHS@Home and BMT team ☐ Vital signs frequency & reportable values ☐ Symptoms charting & reportable adverse events ☐ CVAD care ☐ Medication management - reinforce adherence ☐ Given Patient Information Leaflet ☐ Given Emergency contact information ☐ Route to ward 58HD/ Ward 8A – Patient walkabout	
	Upon Discharge, up till D+100 ☐ TCU compliance - short- and long-term follow-up ☐ Long-term recovery expectations ☐ Travelling clearance by transplant physician	
Additional Remarks		

Methods:

Suitable myeloma patients undergoing ASCT could enrol into the home transplant program based on eligibility criteria including patients' age, functional status, medical comorbidities, caregiver availability and social situation (Refer to Image). Eligible patients received pre-transplant conditioning and stem cell infusion in the outpatient setting then returned home under the care of the HaH team. Daily video consults involving the patient/ caregiver, transplant team and HaH team were conducted. The HaH team also conducted home visits on alternate days, including blood-taking. Patients and caregivers were trained to monitor vital signs, record intake and output, and administer subcutaneous granulocyte colony stimulating factor injections. Ad-hoc interventions, including intravenous hydration or

medications were provided as needed. Patients had access to a 24-hour emergency hotline, with protocols for an expedient return to hospital where necessary. For febrile episodes, patients were admitted directly to a pre-booked bed in the transplant ward for investigations and intravenous antibiotics. For transfusions, patients were transfused in the hospital before returning home. Clinical charts were reviewed for transplant outcomes, and quality of life (QoL) was assessed with the Functional Assessment of Cancer Therapy-Bone Marrow Transplant scale (FACT-BMT version 4) pre-transplant and Day 30 post-transplant.

Results: We report our initial experience with the first 12 patients in the pilot program from September 2024 to November 2025. Median age was 62 (range: 45-67) with 5 females and 7 males. No unexpected toxicities occurred. Eight patients were returned to hospital, as per a pre-planned workflow, on a median of day +8 of transplant (range Day +7 to +15). All patients who required a return to the hospital managed to do so expediently, within our predetermined cutoff of 45 minutes. There were no ICU admissions or deaths. A median of 12 bed-days was saved (9-21) per patient, totalling 172 bed-days saved.
Overall, the program was well accepted by patients and their caregivers, with positive feedback on exit interviews. Quality of life was well-preserved as assessed by FACT-BMT scores improving from a median of 99 at baseline (range 81-136) to 116 post-transplant (range 87-126), and all but 3 patients showing improved scores post-transplant.

Conclusions: Our pilot results suggest that with careful patient selection, and protocolized treatment workflows in close collaboration with HaH, home-based ASCT is safe, feasible and accepted by patients. Our model of care allows for significant bed-savings, while maintaining patients' QoL.

Disclosure: Nothing to declare

NP19

A NURSING ROLE IN IMPROVING OPERATIONAL EFFICIENCY IN CELLULAR THERAPY CLINICAL TRIALS

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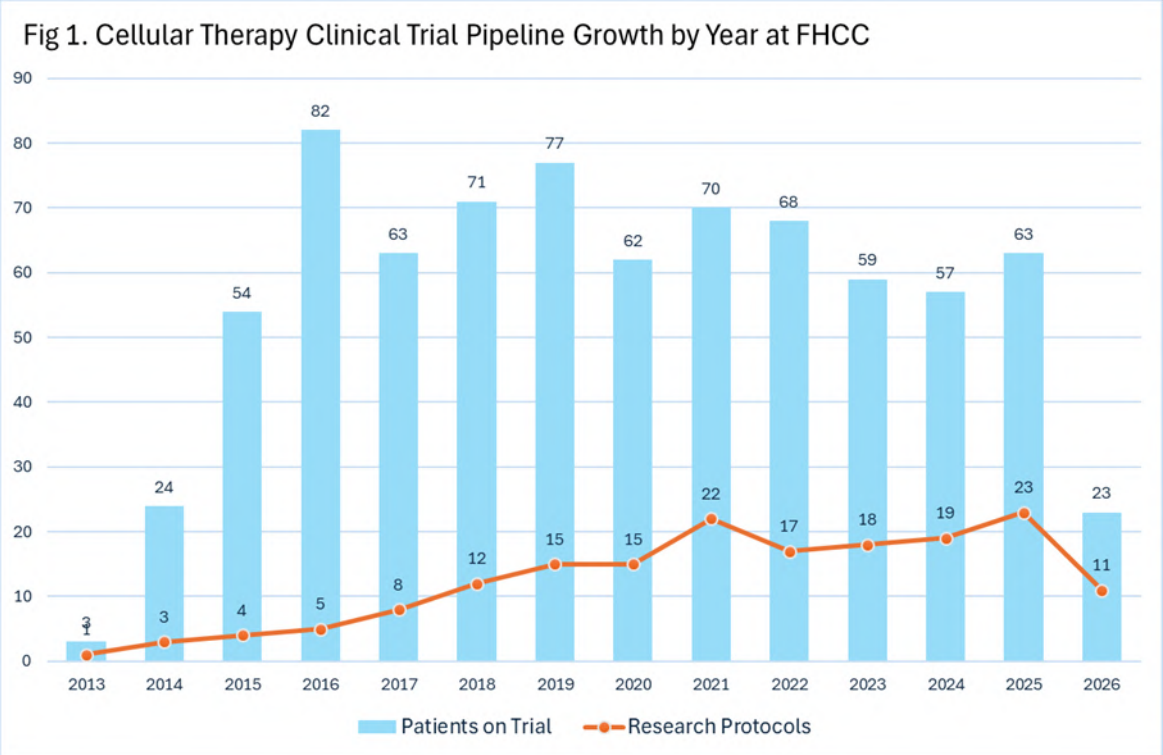
Background: Cellular therapies including chimeric antigen receptor T-cell (CAR-T), T-cell receptor (TCR), and tumor infiltrating lymphocytes (TIL) therapies have transformed cancer care. Clinical trials now span autologous, allogeneic and in-vivo constructs and are expanding into disease states beyond hematologic malignancies including solid tumors and autoimmune disorders. Translating these protocols into the clinic is complex and requires coordination across multiple disciplines. Despite having multidisciplinary teams with significant experience, planning and executing trials often reveal gaps between the research and clinical teams. While the clinical research nurse role is not new, they are often embedded within clinical research teams and support specific protocols. Here we describe a unique clinical trial coordinator research nurse (CTCRN) role supporting our cellular therapy clinical trial pipeline within a centralized cell therapy service (IMTX) with a rotational physician and advanced

practice provider model at Fred Hutchinson Cancer Center (FHCC) in Seattle, Washington, USA.

Methods: The CTCRN role was introduced in 2017. We identified stakeholders and key elements supported by the CTCRN. We analyzed quality metrics from patients who received cellular therapy from July 2013 through October 2025 at FHCC.

Results: As of October 2025, we have treated 1260 patients with cellular therapy products at FHCC IMTX, of which 776 patients were treated on a clinical trial protocol. The FHCC IMTX clinical trial pipeline has grown from one research protocol to 56 unique clinical trial protocols that accrued patients with a range of 1- 195 patients per study. The number of protocols that accrued patients by year ranged from 1 to 23 protocols. Prior to 2017, there were a maximum of 5 protocols that accrued patients per year. Fig. 1 shows program growth over time.



We identified 14 stakeholders supported by the CTCRN role across several multidisciplinary teams from planning through trial activation and accrual. Key elements supported by the CTCRN role included clinical trial planning, education, and clinical support and are described in Table 1.

Table 1. Key Elements Supported by CTCRN Role Span Planning, Education and Clinical Support

Key Elements	Details
Clinical Trial Operations Planning	• Supports Feasibility of Operations Meetings • Clinical Research Protocol Roadmap Review • Patient Journey Review • Validation of Clinical Order Sets • Sponsor Site Initiation Visit (SIV)
Education	• Coordinates Clinical In-Service with PI and Clinical Trial RN – recorded and curated as on-demand enduring content • OnCore (Clinical Trial Management System) • Creates Clinical Trial Fact Sheets (high level overview of clinical trial flow)
Clinical Team Support	• Validated Order Sets and EMR (EPIC) Checklists • Clinical scheduling guidelines per protocol • Coordinates dissemination of protocol updates and amendments • Maintains high level reference for open protocols ("Cellular Immunotherapy Snapshot") • Creation of job aids for highly complex studies • 1:1 Clinical support for first-patient-in per protocol, and as needed

Conclusions: There is high added value in a clinic focused CTCRN role in an expanding centralized cell therapy service administering both investigational products and commercial therapies concurrently. We have been able to expand our clinical research portfolio and have supported >60% of patients treated at FHCC IMTX on a clinical research protocol. Focused surveys are planned to measure staff perspectives on key elements supported by the CTCRN role to identify gaps and further improve clinical trial integrity at FHCC.

Disclosure: Nothing to declare

NP22

CONTINUOUS CARE UNIT: A FEASIBLE MODEL TO OPTIMIZE URGENT MANAGEMENT IN HAEMATOLOGICAL MALIGNANCIES, TRANSPLANTATION AND CAR-T PATIENTS

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Background: The increasing number of patients undergoing active treatment, coupled with improved survival rates and growing therapeutic complexity, has led to a rise in acute complications among cancer patients, resulting in greater utilization of emergency departments (ED). In hematologic malignancies, the rapid management of febrile neutropenia remains particularly critical. Effective triage, early symptom recognition, and timely implementation of evidence-based clinical algorithms are essential to optimize patient outcomes.
We aimed to describe the utilization of a Continuous Care Unit (CCU) by haematology patients. A secondary objective was to analyse CCU use among hematopoietic stem cell transplant (HSCT) and CAR-T recipients.

Methods: Prospective data were collected from haematology patients requiring CCU care between November 13, 2023, and November 14, 2024. The CCU operates from 9:00 a.m. to 5:00 p.m., staffed by two internists and one nurse, with five beds dedicated to urgent care. Outside these hours, patients follow standard care pathways. A descriptive analysis of clinical and demographic variables was performed.

Results: The CCU received 2,454 cancer-related evaluation requests, of which 2,189 (89%) were accepted; the main reason for non-acceptance was lack of capacity (11%). Among accepted cases, 629 (29%) involved haematological malignancies (mean age 60.4 years, SD 17.3). The most frequent diagnoses were lymphoproliferative disorders (42%), HSCT recipients (17%), and multiple myeloma (16%). Fifty-four CAR-T patients (9%) were attended. Triage classified 49% of haematology patients as urgency level 3 and 40% as level 4. For HSCT patients, level 3 predominated (61%), while CAR-T patients were mainly level 4 (36%). Infections were the leading reason for consultation across all groups: haematology (50%), HSCT (63%), and CAR-T (50%). Disease-related symptoms accounted for 29% of HSCT visits, while 31% of CAR-T patients required management of infusion reactions. Hospital admission was necessary for 58 haematology patients (9%), and 19 (3%) received home hospitalization. Among HSCT patients, 6.5% were hospitalized and 4% managed at home; for CAR-T patients, 6% were hospitalized and one received home care. After discharge, 58% of haematology patients continued routine follow-up, while 29% required CCU re-evaluation within 24–48 hours. Similar patterns were observed in HSCT (45% routine follow-up; 41% re-evaluation) and CAR-T patients (72% routine follow-up; 20% re-evaluation), respectively.

Conclusions: A part-time CCU significantly improves urgent care for haematology patients, providing timely, specialized management and reducing ED burden. The high acceptance rate and predominance of intermediate triage levels highlight its role in optimizing care for immunocompromised patients. This model is safe, feasible, and enhances continuity of care through protocol-driven management, the knowledge and skills of specialist nurses and structured ambulatory follow-up.

Disclosure: Nothing to declare.

NP62

REDUCING INPATIENT BED UTILISATION BY DELIVERING CAR-T LYMPHODEPLETION CHEMOTHERAPY IN AN AMBULATORY SETTING AT SHEFFIELD TEACHING HOSPITALS

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Background: Chimeric Antigen Receptor T-cell (CAR-T) therapy normally requires hospitalisation for lymphodepletion chemotherapy due to the intensity of treatment and the need for close monitoring. Increasing demand for cellular therapies has placed pressure on inpatient beds, prompting exploration of safe outpatient approaches. In January 2024, Sheffield Teaching Hospitals (STH) introduced ambulatory delivery of lymphodepletion for eligible CAR-T patients to reduce inpatient stay and enhance patient experience. STH has a well-established emergency assessment and admission pathway for haematology patients. Any patient developing symptoms or complications during ambulatory lymphodepletion are reviewed immediately in the day unit by experienced haematology staff, with direct admission to the haematology ward when required. This supports rapid clinical assessment, continuity of specialist care, and minimised treatment delays.

Methods: A multidisciplinary working group, comprising haematology nurses, medical staff, and ambulatory care teams implemented a pathway enabling CAR-T patients to receive lymphodepletion chemotherapy (Day −5, −4, −3) in the ambulatory unit. Patients were then permitted to rest at home or in ambulatory accommodation (Day −2, −1) before returning on Day 0 for their CAR-T infusion and subsequent planned inpatient admission for post infusion monitoring. Eligibility criteria included patient preference, proximity to hospital, and availability of a home carer or access to ambulatory flats.

Results: Between January 2024 and the time of reporting, 24 patients received lymphodepletion chemotherapy via the ambulatory pathway. Within this group, four patients required admission during lymphodepletion, primarily due to fevers or hypotension. A further three patients were managed as inpatients from Day −5 because a home carer was not available. These three were not included in the 24 ambulatory cases.
The ambulatory pathway saved 100 inpatient bed nights, averaging approximately four days saved per ambulatory patient. Four patients used ambulatory accommodation, while the remainder returned home between treatments. Patients reported valuing the shorter hospital stay, increased comfort, greater independence, and positive effects on mental and physical wellbeing.
There were no unplanned admissions and no complications beyond those expected, indicating that the pathway is feasible and functions effectively when supported by established emergency assessment processes. At the time of reporting, five additional patients were preparing for ambulatory lymphodepletion, demonstrating continued sustainability and confidence in the model.

Conclusions: Introducing ambulatory lymphodepletion chemotherapy for CAR-T patients significantly reduced inpatient bed usage while maintaining effective clinical care and improving patient experience. This innovative model supports more efficient use of hospital resources, shortens inpatient stays, and aligns with wider efforts to expand outpatient cellular therapy care. The pathway is reproducible for other centres seeking to optimise capacity while maintaining high quality patient centred care.

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Nick Morley: Support to attend conferences - Takeda
Nick Morley: Speaker fess - AMGEN
Bethany Colton: Speaker fee & support to attend conferences - Kite Gilead
Bethany Colton: Roche - Speaker fee

NP65

CHALLENGES OF LAUNCHING AN AT-HOME HOSPITALIZATION PROGRAM: THE "SANT PAU A CASA" HOSPITAL-AT-HOME EXPERIENCE

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Background: At-home hospitalization (AHH) is an increasingly used care model for selected hematological patients. Accurate estimation of census and enrollment is essential for its successful implementation. Furthermore, because a proportion of patients develop complications requiring urgent hospital transfer, dedicated pathways must be established to ensure timely management. We aimed to assess the challenges encountered during the implementation of a new single center AHH program and to describe the process involved.

Methods: Since April 2024, all consecutive adults undergoing autologous stem cell transplantation (ASCT) were evaluated for potential eligibility in the AHH program. Inclusion criteria were defined as follows: ECOG ≤ 2, travel time from home to the hospital within one hour by public transportation, availability of a suitable 24-hour caregiver, adequate cultural level and cognitive capacity to collaborate with the nursing team, and a suitable home environment. Exclusion criteria were: refractoriness to platelet transfusion, decompensated psychiatric disorders, and previous infection from multi-drug resistant organisms. In case of urgent transfers, a dedicated protocol was established in collaboration with the Barcelona Emergency Medical Service. Patients were instructed to contact the on-call hematologist or AHH physician if they experienced warning symptoms. Non-urgent transfers were arranged through the standard ambulance services coordinated by the AHH team.

Results: Since the program started, 15/81 (18’52%) consecutive patients assessed as potential referrals were enrolled. Diagnosis among enrolled patients included Multiple Myeloma (n=5), non-Hodgkin Lymphoma (n=8) and Hodgkin Lymphoma (n=3).
Among the 65 ineligible pts, reasons included: lack of a 24-hour caregiver (n=24, 30%), living >1h from the hospital (n=17, 21%), comorbidities (n=13, 16%), inadequate cultural level (n=1, 1%) and the temporary program closure in August (n=10, 12%). One patient discontinued the program on day+1 due to severe early toxicity.
Among the 15 enrolled patients, the median age was 54 years (range 27-71) and 67% were male. A total of 2 patients (13’3%) received 3 red blood cell transfusions and 6 patients (40%) 9 platelet transfusions at home, none of which were associated with transfusion reactions.
Five (33’3%) patients were discharged from AHH without complications after a median of 14 days (range 11-16). Ten patients required readmission (HL n=2, NHL n=5, MM n=3), most commonly due to fever (9/10), including one case of influenza A and one case of *Giardia intestinalis* colitis; one patient was readmitted for atrial fibrillation. Barcelona Emergency Medical Service activation was required in 7 cases (35%), while conventional transfers were used in 13 occasions (65%). Readmitted patients remained hospitalized for a median of 8 days (range 1-17), and one subsequently returned to AHH without complications.

Conclusions: Our initial experience with the AHH program in ASCT recipients highlights that a minority were eligible. Some barriers, such as the need for a 24-hour caregiver or living far from the hospital, could be mitigated with additional social resources. While several patients completed the program successfully, readmissions-mainly due to infections- were common. Close coordination with emergency services and thorough patient and caregiver education are essential for safe program implementation.

Disclosure: Nothing to declare.

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NG07-02

VITAMIN D MONITORING AND REPLACEMENT IN HAEMATOPOIETIC STEM CELL TRANSPLANTATION: A CLINICAL AUDIT OF PRACTICE AGAINST REGIONAL GUIDELINES

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Background: Vitamin D deficiency is highly prevalent among haematopoietic stem cell transplantation (HSCT) recipients, driven by prolonged hospitalisation, limited sunlight exposure and treatment-related factors. Increasing evidence suggests that suboptimal vitamin D status is not only common but clinically significant, being linked with poorer bone health, delayed immune recovery and a greater risk and severity of graft-versus-host disease (GvHD) (Mancin et al., 2024). As a modifiable factor, vitamin D represents an important yet under-recognised aspect of supportive transplant care. The South East London (SEL) Clinical Guideline for the Management of Vitamin D Deficiency and Insufficiency in Adults (2023) recommends routine screening and treatment using defined loading and maintenance regimens. This audit evaluated local practice against these standards to identify gaps and opportunities to improve patient outcomes.

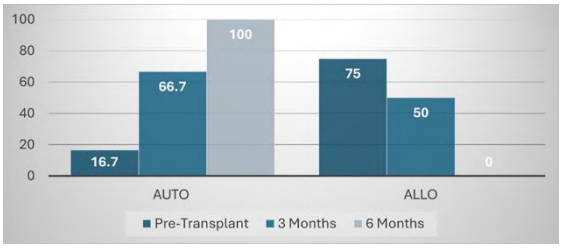
Methods: A retrospective review was undertaken of all patients who underwent HSCT between October 2023 and October 2024 at King's College Hospital. Of 255 patients, 10 who died within six months post-transplant were excluded, leaving 245 evaluable cases (151 autologous, 94 allogeneic). Patient age ranged from 17 to 75 years (mean 55.2). Data were extracted from the electronic patient record (EPIC) at three timepoints: pre-transplant, three months and six months post-transplant. Vitamin D status was classified as deficient (<25 nmol/L), insufficient (25–50 nmol/L) or sufficient (>50 nmol/L). Prescribing of loading or maintenance vitamin D was compared with SEL guideline recommendations.

Results: Vitamin D was tested in 18.3 % of patients pre-transplant, 15.6 % at three months, and 16.0 % at six months, well below the ≥90 % target for high-risk populations. Among those tested, 62.8 % were deficient or insufficient pre-transplant, 55.2 % at three months and 45.0 % at six months. Of the total cohort, 50.6 % received any vitamin D prescription, but prescribing was largely empirical and often unrelated to measured status. Among 20 patients with confirmed deficiency, only 9 (45 %) received an appropriate loading dose. Of 36 patients with insufficiency, 15 (42 %) received maintenance supplementation. Allogeneic recipients were marginally more likely to be tested (20.2 % vs 17.2 % autologous) but were less consistently treated at six months, when none of 3 deficient patients received a loading dose.

Table 1. Vitamin D testing and Deficiency Rates by Timepoint

Timepoint	Patients tested n (%)	Deficient n (%)	Insufficient n (%)
Pre-transplant	45 (18.3)	10 (23.3)	17 (39.5)
3 months	38 (15.6)	5 (10.5)	17 (44.7)
6 months	39 (16.0)	5 (12.5)	13 (32.5)

Figure 1. Appropriate Vitamin D Loading-Dose Prescription in Deficient HSCT Patients



Conclusions: Vitamin D monitoring and replacement in HSCT patients at our centre are inconsistent and substantially below guideline recommendations. Testing occurred in fewer than one in five patients, and only 45 % of those with deficiency received the recommended loading regimen. These results reflect international variation in practice (Ros-Soto et al., 2019; Kenny et al., 2019) and highlight a need for systematic improvement.
Following presentation of these findings to the haematology consultant group, work is underway to introduce automatic vitamin D testing at defined HSCT milestones and implement a standard operating procedure (SOP) for supplementation. A re-audit is planned within 12 months to evaluate improvement in compliance and patient outcomes.

Disclosure: Nothing to declare

NG27-07

PREPPING WITH PREHAB: A PHYSICAL ACTIVITY FOCUSED "PREHABILITATION" PILOT WITHIN THE ALLOGENEIC BMT PATHWAY

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Background: To enhance the care pathway for patients undergoing allogeneic Bone Marrow Transplant (BMT), the Physiotherapy (PT) and Occupational Therapy (OT) team piloted an improvement project to enhance the existing pre-transplant assessment. This initiative aligns

with current evidence supporting early intervention and prehabilitation to improve patient outcomes and Quality of Life (QoL).

Methods: Fifty-nine patients were screened within the pilot, between April and November 2025. 35 completed the "prehabilitation" process, and 29 were admitted for transplant. Patients completed Outcome Measures (OM's)(see Table 1.) during a pre-assessment video consultation and were stratified into Specialist, Targeted, or Universal pathways for tailored follow-up over a six-week period (pre-transplant). OM's were repeated on admission, and functional performance (30-second chair stand test (30s CST)) was reassessed at discharge. Results were compared to those from a 2016–2018 project (N=148) where a virtual pre-transplant assessment was introduced without follow-up. Hospital length of stay (LOS) was used as a secondary OM. The pilot was conducted within the PT/OT team, though it was largely PT-led. As part of standard care, patients also received input from the wider Multi-Disciplinary Team (MDT), including dietetics and psychology.

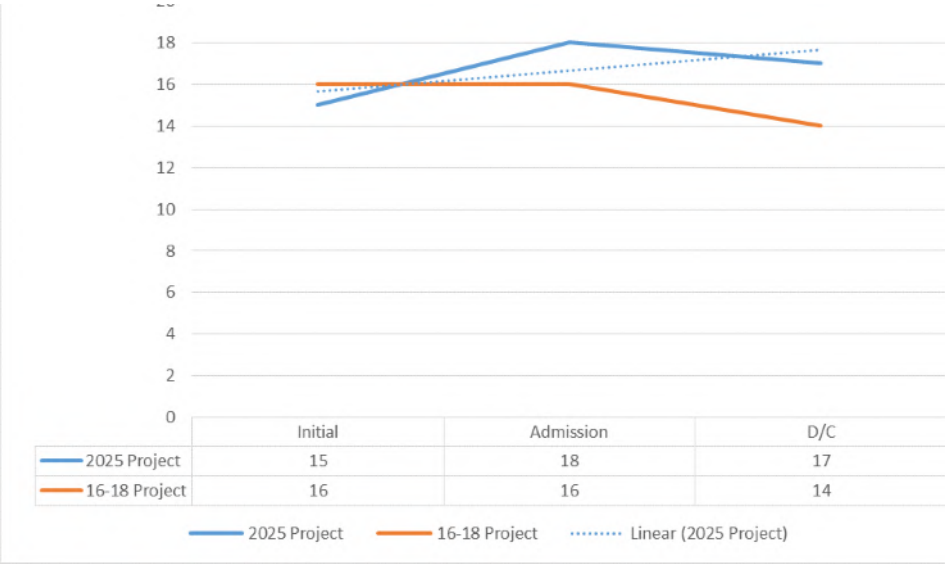
Table 1. Outcome Measures

Time Point	Primary Outcomes	Secondary Outcomes
Pre-transplant Assessment (Initial)	EORTC QLC-C30 30-Second Chair Stand Test Godin Leisure-Time Exercise Questionnaire	-
Hospital Admission for Transplant (Admission)	EORTC QLC-C30 30-Second Chair Stand Test Godin Leisure-Time Exercise Questionnaire	-
Hospital Discharge (Discharge)	30-Second Chair Stand Test	Length of Stay

Caption: *Outcome measures collected at three key time points: pre-transplant assessment, hospital admission, and discharge. Primary outcomes included quality of life (EORTC QLQ-C30), functional performance (30-Second Chair Stand Test), and physical activity (GLTEQ). Secondary outcome of length of stay was recorded at discharge.*

Results: Over half of patients (54%) required Specialist PA support. Functional outcomes improved significantly from initial assessment to discharge (30s CST, $p = 0.0018$), with Universal patients showing the greatest relative gains and Specialist patients showing meaningful improvement from a lower baseline. Targeted patients declined slightly despite similar baseline scores to the Universal group. PA levels increased significantly, with inactivity dropping from 48% to 16% and mean GLTEQ scores rising from 17 to 37 ($p < 0.05$). QoL domains showed no statistically significant change, though physical and role function showed positive trends. Mean LOS was 4 weeks, shorter than the typical 4–6 weeks, with 68% discharged within 4 weeks.

Graph 1. 30s CST Change



Caption: *Physical activity scores improved in the 2025 Project from initial assessment (15) to admission (18), with a slight decline at discharge (17), indicating sustained benefit. In contrast, the 16–18 Project showed minimal change at admission (16) and declined to 14 at discharge, suggesting reduced long-term impact.*

Conclusions: Introducing a PA based prehabilitation approach to the allogeneic BMT pathway shows promise for improving functional outcomes, with improvements maintained throughout treatment. Targeted patients demonstrated the least functional improvement and may require an adapted approach. QOL scores did not demonstrate significant change which could suggest the need for further OT and wider MDT involvement. Although there is some evidence correlating with reduced LOS, further investigation is required to evaluate this and explore associated cost-effectiveness.

Clinical Trial Registry: N/A

Disclosure: N/A

NP14

GUIDING NURSING-LED STRATEGIES TO PREVENT CATHETER-RELATED BLOODSTREAM INFECTIONS DURING ALLOGENEIC HSCT: INFLUENCE OF CATHETER TYPE AND TIMING

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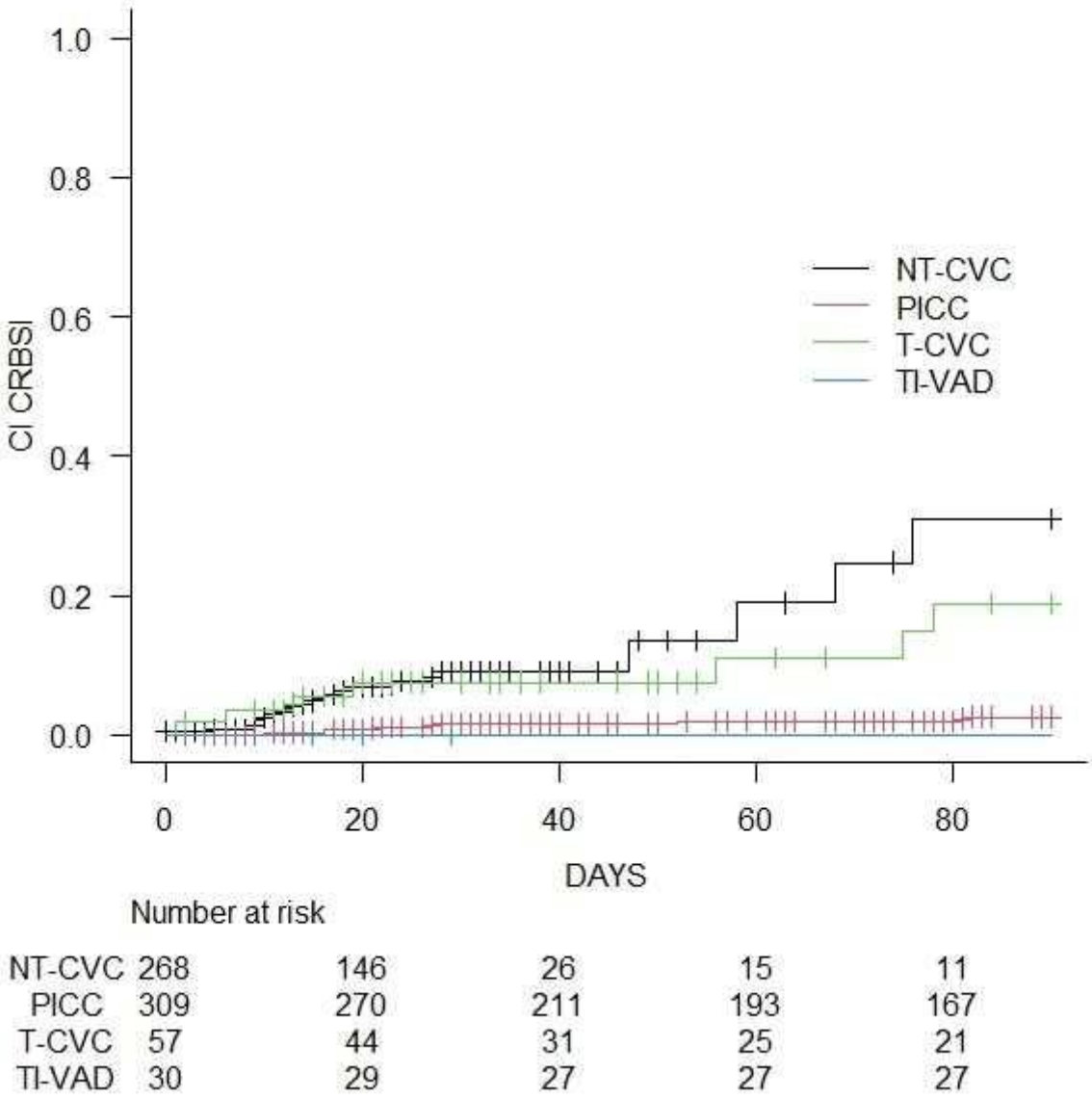
Background: Catheter-related bloodstream infections (CRBSI) during allogeneic transplantation (Allo-HSCT) represent a critical factor influencing patient morbidity and mortality. Proper use and maintenance of central venous catheters (CVC) throughout the transplantation process are essential to minimize infection risk. There are only a few reports describing how catheter type and timing influence CRBSI incidence and how this information can guide nursing interventions. This study aims to evaluate it, providing insights into their chronological development and potential preventive strategies.

Methods: We performed a single-center, retrospective, descriptive study of patients who underwent Allo-HSCT at our institution between 2015 and 2024. The catheters included in the analysis were: PICC (peripherally inserted central catheter), NT-CVC (non-tunneled central venous catheter: jugular, subclavian, and femoral), T-CVC (tunneled central line catheter), and TIVAD (totally implantable venous access device). Catheter-related infections were defined according to the EBMT IDWP 2025. Cumulative incidences (CI) were calculated from catheter insertion to removal.

Results: We analyzed 432 patients. The median age was 56 years, and 62.3% of the patients were male. The most frequent diagnoses were AML (37.5%).
A total of 694 catheters were reported. Of these, 32% (n=225) were the first catheter for a patient, 35% (n=241) were the second, and 33% (n=228) were third or subsequent. The most frequent catheter types were PICCs (44%; n=311), NT-CVCs (39%; n=271), T-CVCs (8%; n=58), TIVADs (6%; n=42), and unspecified CVCs (2%; n=12).
Median catheter durations were: PICCs 98 days (IQR 33–175), NT-CVCs 21 days (IQR 13–27), T-CVCs 51 days (IQR 20–180), and TIVADs 654 days (IQR 298–981). We identified 190 bacteremia episodes in 132 patients, of which 47 were classified as definite CRBSI. Among these, 68% (n=32) were caused by Gram-positive cocci, 23% (n=11) by Gram-negative bacilli, and 9% (n=4) by other pathogens. The most commonly identified species was *S. epidermidis* (38%; n=18).
Median time to CRBSI was 88 days (IQR 29–160) for PICCs, 21 days (IQR 14–27) for NT-CVCs, 32 days (IQR 15–109) for T-CVCs, and 685 days (IQR 218-981) for TIVADs. The CI of CRBSI at days 7, 15, 30, and 90 was 1% / 2.4% / 4.7% / 8%. CI at days 7, 15, and 30 for PICCs was 0 / 0.3% / 1.5%, for NT-CVCs 0.8% / 4.3% / 8.9%, for T-CVCs 3.5% / 5.4% /

7.5%, and no CRBSI was observed at day 30 for TIVADs (p<0.01). (Figure 1).



Conclusions: Time to infection varies by catheter type, emphasizing the need for nursing-led monitoring and preventive interventions to reduce infection risk.
T-CVCs and NT-CVCs present the highest early risk of infection, reinforcing the need for intensive monitoring during the first weeks after insertion. In our center, PICCs are the preferred catheter for Allo-HSCT due to their safety and ease of use, although their infection risk increases over the long term, underscoring the importance of ongoing vigilance. TIVADs

remain the safest option for prolonged use.
Infections occur predominantly due to Gram-positive cocci, particularly *S. epidermidis*, highlighting the critical role of strict hand hygiene and aseptic handling by nursing staff.

Disclosure: No disclosure.

NP23

HEALTHCARE PROFESSIONALS' AND MANAGERS' EXPERIENCES AND PERCEPTIONS OF IMPLEMENTING CHANGE – IN THE CONTEXT OF ALLOGENEIC STEMCELL TRANSPLANTATION

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Background: A successful introduction of new work practices and them becoming routine work depends on the context, healthcare professionals' response to the intervention and the prevailing culture and climate. Therefore assessing the organisation's readiness for change early in the process is crucial to create a sustainable implementation. This knowledge can inform implementation strategies, support that the new way of working remains over time at the site, as well as guidance for future implementations in other contexts. The aim of this study was to investigate the organisations' readiness for change and prerequisites for implementing a new way of working in a highly specialised hospital care setting.

Methods: A cross-sectional survey with 94 participating health care professionals (HCP) and mangers from two centres for allogeneic hematopoietic stem cell transplantation (allo-HCT) in Sweden was employed to investigate their experiences of working with change and organisational readiness for change (ORC). HCPs' and mangers' experiences of working with change and readiness for change was further investigated through nine individual and four focus group interviews at the two centres. The ORC instrument has four factors with sum scores *Motivation for change, Resources, Staff Attributes* and *Organisational climate.* The four factors are made up by twenty subscales and in total 113 items, with responses on a Likert scale and sum scores ranging between 10-50. A score of 30 is considered a neutral midpoint, reflecting neither overall agreement nor disagreement. Scores closer to 50 reflect strong agreement, and scores closer to 10 reflect strong disagreement.

Results: The overall organisational readiness for change scored a neutral average (36.6), with the four factors mean sum scores ranging between 32.59 – 41.75 and subscale mean

sum scores ranging from 31.16-43.68 (Table 1), indicating that no area requires major development before implementing new practices. While staff generally reported good working climate, trust, leadership, and openness to change, time constraints and stress were significant barriers (50% lacked time; 90% reported stress). Most staff felt capable of adapting to change, though 67% expressed concern about future workplace conditions. There was a significant positive association between being a woman and the factor *Motivation for change,* with women being more likely to have higher scores for motivation to change (B=5.30; CI: 1.19-9.42; p=0.01). The interviews supported the findings from the quantitative data and indicated that HCPs and managers perceive change initiatives as complex, often shaped by previous experiences where projects were launched, but failed to achieve long-term impact. Preference was expressed for bottom-up approaches, and the importance of communication, preparation, and a clear purpose. Barriers included time and resources; facilitators included ambassadors, leadership, and support. The context allo-HCT was posed as highly specialised oncology care characterised by high workload.

Table 1. Results for the four factors of organisational readiness for change

FACTOR	SUBSCALES (Factor)	Mean sum score (SD)*	Range
Motivation for Change	Program needs	32.98 (8.41)	12-47
	Training needs	32.26 (7.15)	10-50
	Pressures for change	31.89 (6.06)	13-45
Resources	Workplace	33.42 (11.50)	10-50
	Staffing	31.16 (6.50)	17-43
	Training	35.22 (6.32)	20-48
	Equipment	38.84 (4.75)	27-47
	Internet	43.62 (3.64)	35-50
Staff Attributes	Growth	38.13 (7.97)	12-50
	Efficacy	43.68 (4.79)	30-50
	Influence	43.31 (5.32)	30-50
	Adaptability	40.98 (4.36)	30-50
	Satisfaction	41.99 (5.85)	25-50
Organisational climate	Mission	34.29 (7.29)	18-50
	Cohesion	38.90 (6.56)	15-50
	Autonomy	35.84 (3.61)	28-48
	Communication	36.67 (6.56)	16-48
	Stress	38.03 (7.42)	20-50
	Change	35.81 (4.33)	26-44
	Leadership	35.34 (4.75)	24-46

*A score of 30 is considered a neutral midpoint, reflecting neither overall agreement nor disagreement. Scores closer to 50 reflect strong agreement, and scores closer to 10 reflect strong disagreement.

Conclusions: In the context of specialised allo-HCT care, the organisation demonstrates moderate readiness for change; however, successful implementation of new work practices will depend on balancing workload demands with adequate resources. Findings from ORC surveys and staff interviews provide critical insights to guide planning and support prior to integrating new interventions into routine practice.

Disclosure: Nothing to declare.

NP31

IMPLEMENTATION OF NEUTROPENIA PATHWAY TO IMPROVE ANTIBIOTIC TURNAROUND TIME IN PEDIATRIC BMT PATIENTS AT ABU DHABI BONE MARROW TRANSPLANT PROGRAM, CENTER OF EXCELLENCE (UAE)

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Background: Pediatric patients undergoing bone marrow transplants are highly immunocompromised and at significant risk for life-threatening infections due to intensive chemotherapy, conditioning regimens, and prolonged neutropenia. Fever is often the earliest sign of sepsis or bacteremia, and even brief delays in empiric antibiotic therapy can lead to rapid deterioration. Early antibiotic administration is consistently linked to reduced morbidity and mortality. Historically, our center in the United Arab Emirates lacked a standardized neutropenia pathway, resulting in variable clinical responses and delayed antibiotic initiation. To address this, the pediatric BMT team implemented a quality improvement project to develop a standardized pathway aimed at improving the timeliness and consistency of antibiotic administration while aligning care with international standards. The primary aim was to reduce the mean antibiotic turnaround time from physician order to medication administration by 30 minutes or less for febrile neutropenic pediatric BMT.

Methods: A multidisciplinary team of physicians, nurses, and pharmacists developed and implemented the neutropenia pathway, outlining clear step by step actions with defined nursing and pharmacy responsibilities. Education was central to rollout, with nursing staff receiving targeted training through in-service sessions, case-based discussions, unit huddles, electronically distributed materials, and ongoing competency validation to ensure adherence. Operational changes were also introduced to support timely antibiotic administration, including stocking key empiric antibiotics on the unit to eliminate pharmacy dispensing delays and requiring all antibiotics to be ordered as STAT in the electronic medical record to ensure prioritization. Following implementation, an audit was conducted to assess nursing compliance through a retrospective chart review of 40 febrile neutropenic episodes over a 10-month period in pediatric BMT. Three timepoints were collected for each episode: fever identification, antibiotic prescription, and antibiotic administration. Antibiotic turnaround time (TAT) was defined as the interval in minutes between prescription and administration. Compliance was calculated as (episodes with TAT ≤ 30 minutes ÷ total analyzed episodes) × 100, and monthly performance trends were assessed using mean, median, and interquartile range (IQR).

Results: The quality improvement project was Initiated in January 2025 until October 2025. Compliance improved steadily, reaching 100% by July and was maintained up to October.

Across all audited episodes, the mean TAT was above 30 minutes between February and April which improved May forward. Monthly trends demonstrated early delays, with the highest mean TAT in February (76.7 minutes), followed by progressive improvement beginning in May (26.0 minutes), and the lowest mean TAT achieved in September (7.5 minutes).

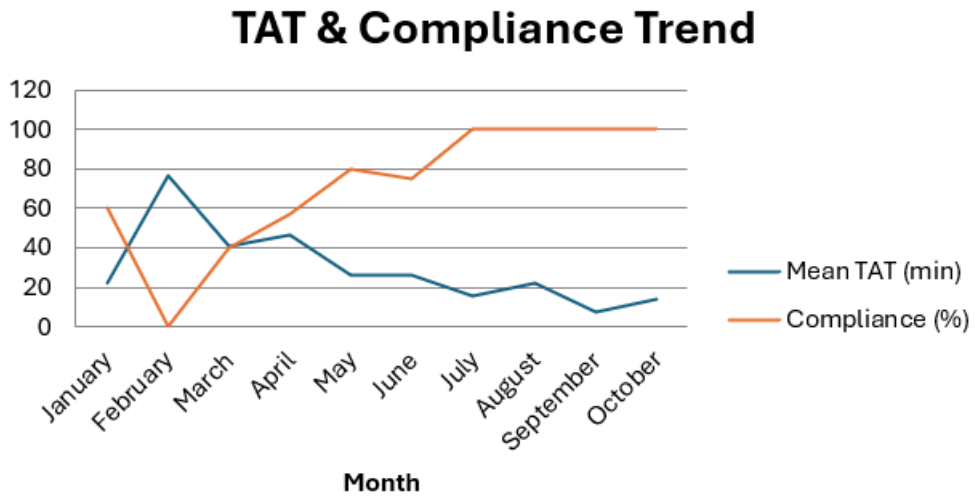

Table1.Monthly Antibiotic Turnaround Time (TAT) Performance, Jan-Oct.2025

Month	Total Episodes (n)	Mean TAT (min)	Median (min)	TAT ≤30 min (n=episodes)	Compliance (%)
January	5	21.8	21.0	3	60%
February	3	76.7	71.0	0	0%
March	5	40.8	47.0	2	40%
April	7	46.9	29.0	4	57%
May	5	26.0	26.0	4	80%
June	4	26.0	28.5	3	75%
July	5	15.6	15.0	5	100%
August	3	22.3	20.0	3	100%
September	2	7.5	7.5	2	100%
October	1	14.0	14.0	1	100%

OVERALL	40	32.0	25.5	27	67.5%

Conclusions: The developed neutropenia pathway significantly improved timely antibiotic administration in febrile neutropenic paediatrics BMT. Enhanced nursing compliance, interdisciplinary communication, and reduced care variability were achieved through structured workflow. Sustained improvement demonstrates the value of structured clinical pathways in promoting patient safety and optimizing outcomes.

Disclosure: Nothing to declare

NP41

READINESS FOR DISCHARGE – HOLISTIC UNDERSTANDING OF THE PATIENT JOURNEY FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Allogeneic stem cell transplantation (allo-SCT), a life-saving treatment for multiple hemato-oncological patients, is characterized by a complex hospitalization and discharge process. The post-transplant transition from hospital to home is a critical stage associated with increased risk of morbidities, particularly, infections, and the development of acute graft-versus-host disease (aGVHD), all requiring hospital readmissions. Therefore, thorough and structured discharge preparation, encompassing patient education for self-management and timely recognition of early signs of complications, is essential and should be initiated early during the inpatient phase. SCT coordinators and nursing staff, providing continuous clinical patient-centered support throughout the transplantation course, play a pivotal role in planning, implementation, and optimization of the discharge process. The current study, conducted by the multilingual SCT nursing team at a tertiary-care medical center, aimed to identify the principal determinants of patients' discharge readiness and to establish the basis for targeted, evidence-based interventions, designed to improve patient safety, ensure care continuity, and reduce post-transplant complications and hospital readmissions.

Methods: In this quantitative observational study, validated questionnaires in Hebrew, Arabic, and Russian were used to evaluate patient's discharge readiness in key domains, including illness perception, language and communication barriers, compliance to treatment, medication management and discharge instructions comprehension. The questionnaires were distributed by nurses on the discharge day with request to be completed within the next 24-48 hours. Independent samples t-tests and Pearson correlation coefficients were applied to examine relationships between language characteristics, illness perception, treatment compliance, and discharge readiness. SPSS was used.

Results: The study included 60 post-allo-SCT patients [65% males, median age 54.1 (range, 20-77) years]. The study population was multicultural (46.7% Muslim, 40.0%

Jewish, 8.3% Christian, 5.0% Druze), showing substantial linguistic diversity (40% native Hebrew and 40% Arabic speakers, 10% Russian speakers, 10% speakers of other languages). A total of 83% of participants preferred receiving medical information and instructions in their native language. Approximately one-third of patients indicated low/insufficient proficiency in Hebrew. While oral explanations were provided by multilingual nurses, written discharge recommendations were given in Hebrew (primary official language). Overall discharge readiness levels were moderate to high (mean 3.1, SD=0.89), but varied significantly: highest for Hebrew-speakers (median 3.32) and lowest for Russian-speakers (median 2.28). Statistically significant differences were revealed in instructions comprehension ($p < 0.001$) and medication management ($p=0.005$). Significant positive correlations were found between discharge readiness and illness perception ($r=0.353$, $p < 0.01$), Hebrew proficiency ($r=0.470$, $p < 0.01$), and treatment compliance ($r=0.483$, $p < 0.01$). While overall readiness did not differ by the native language, native Hebrew speakers showed significantly higher readiness regarding medication management [$t(58) = -2.558$, $p=0.013$].

Conclusions: Post-allo-SCT discharge readiness is found to be influenced not only by clinical parameters, but also by psychological and communicative factors, illness perception, comprehension of instructions and treatment compliance. These findings highlight the need to incorporate culturally and linguistically tailored education into discharge planning. The study supports the development of a holistic, ward-based model emphasizing adaptive illness perception, patient-centered communication, and individualized preparation for home care, with the potential to reduce complications, prevent readmissions, and promote health equity.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare.

NP103

ADMINISTRATION OF GRAFALON® (ATLG) WITH A GRADUALLY INCREASING INFUSION RATE: IMPACT ON TOLERABILITY IN PEDIATRIC PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

Giulia Pessina[1], Cyriaque Ndayishimiye[1], Raffaella Garbarino[1], Evelina Olcese[1], Alessia Salvatore[1], Tiziana Pastorino[1], Benedetta Pezza[1], Sonia Bianchi[1], ***Simona Calza***[1]*, Maura Faraci[1]*
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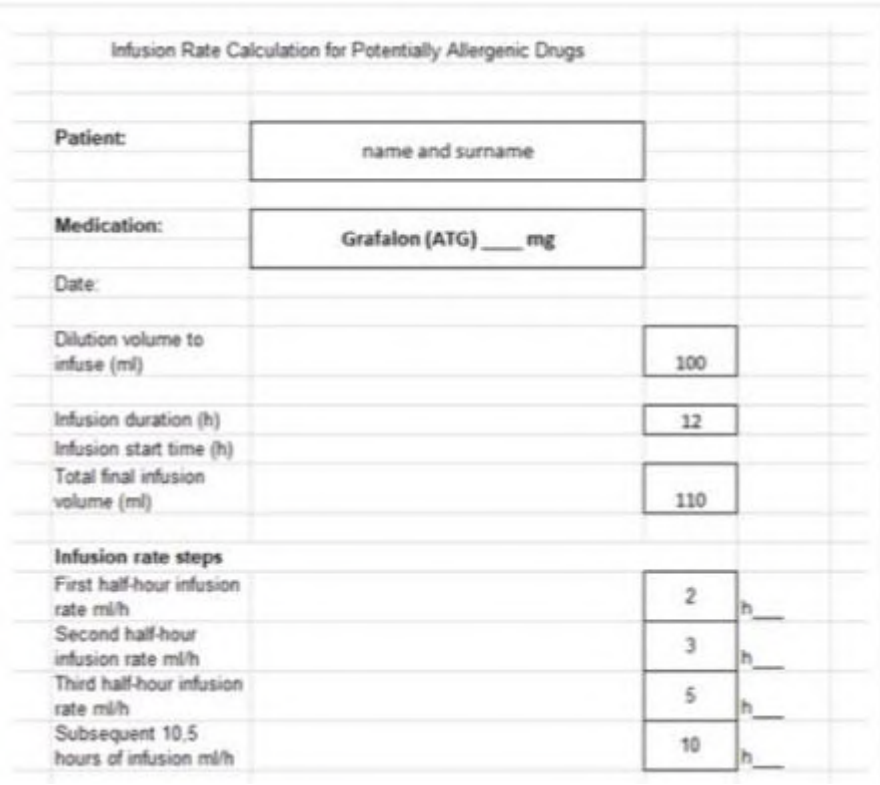
Background: Grafalon® (ATLG, anti-T-lymphocyte globulin) is a polyclonal immunoglobulin widely included in the preparatory regimen before allogeneic hematopoietic stem cell transplantation (HSCT), aimed at preventing graft rejection and graft-versus-host disease (GvHD). However, infusion-related reactions are frequent adverse events, potentially dependent on dose or infusion duration. At our HSCT unit, a procedure involving a

progressively increasing infusion rate was introduced to improve drug tolerability and reduce the severity of infusion reactions.



Infusion Rate Calculation for Potentially Allergenic Drugs

Patient:	name and surname	
Medication:	**Grafalon (ATG) ____ mg**	
Date:		
Dilution volume to infuse (ml)		100
Infusion duration (h)		12
Infusion start time (h)		
Total final infusion volume (ml)		110
Infusion rate steps		
First half-hour infusion rate ml/h		2 h___
Second half-hour infusion rate ml/h		3 h___
Third half-hour infusion rate ml/h		5 h___
Subsequent 10,5 hours of infusion ml/h		10 h___

Methods:

A retrospective observational study was conducted on 69 pediatric patients who received allogeneic HSCT at Istituto G.Gaslini, between April 2019 and May 2023. Data were collected on demographic characteristics, underlying disease, conditioning regimen, GvHD prophylaxis, Grafalon® dosage, and infusion modality and reactions. The drug was administered in 12 hours according to a gradually increasing infusion rate (Figure 1) with increments every 30 minutes for the first 1.5 hours until reaching the final rate, maintained for the remaining hours. All infusion reactions, management strategies, and infectious complications (CMV reactivation) were recorded.

Results: A total of 39 patients (56.5%) experienced at least one reaction during Grafalon® infusion, most commonly fever (n=31), chills or malaise (n=13), and tachycardia (n=11). Among these, 11 patients (28.2%) developed a second reaction and 2 (5.1%) a third, all of which were successfully managed through temporary suspension and supportive therapy, without requiring permanent discontinuation. The average infusion duration in cases with multiple reactions was prolonged (up to 14 hours), but overall tolerability was good. CMV reactivation occurred in 26 patients (37.7%), consistent with expected rates in the transplant population.

Conclusions: The adoption of a progressively increasing infusion rate for Grafalon® administration proved effective in reducing the severity of infusion reactions, ensuring better

tolerability and treatment continuity. This experience highlights that a standardized and shared nursing protocol for drug administration and monitoring represents a safe and reproducible strategy, with potential benefits for the quality of care in pediatric HSCT patients.

Clinical Trial Registry: not apply

Disclosure: NOTHING TO DECLARE

NP50

AN OBJECTIVE PATIENT NEEDS-BASED ACUITY TOOL FOR THE STEM CELL TRANSPLANT PATIENT POPULATION

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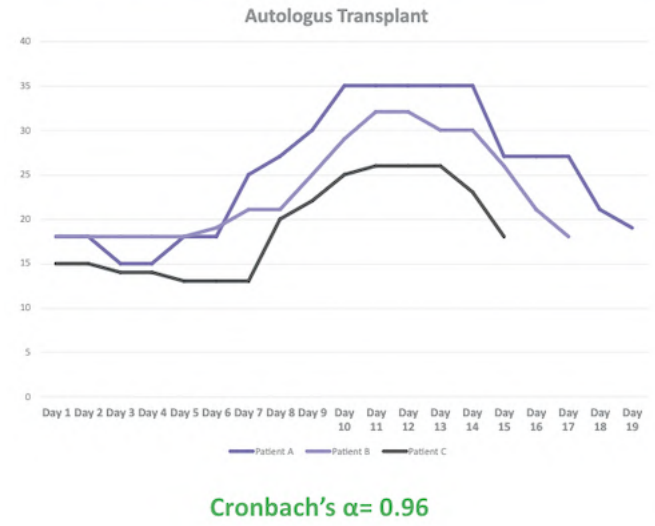
Background: Correctly identifying patient care needs per shift and equally balancing nursing workload increases nurse satisfaction and optimizes resources needed to provide appropriate levels of care on an inpatient stem cell transplant (SCT) unit. There also is not a standardized objective acuity tool for the SCT patient population and literature supports the use of tailored acuity tools for speciality patient populations. Since the SCT patient population comes with its own specific set of needs that creates complexity in care, it is vital that they are accurately represented to provide the safest and highest quality nursing care.

Methods: Observation and pre-implementation feedback on the existing process supported the need for a defined grading approach. Utilizing the DMAIC (Define, Measure, Analyze, Improve, Control) methodology, an objective acuity tool was designed to the needs of the SCT population through literature search and staff input. Each nurse filled out one acuity tool per shift, turned it into the charge nurse, and the total acuity number for each patient was utilized to equally balance workload between all nurses. When determining the reliability and accuracy of the tool, the acuity sheets were collected from day shift and night shift across a 4 month period. Patients were randomly selected from different time frames to determine acuity trends from time of transplant to discharge. This data was then streamlined into a spreadsheet and the data was graphed for visual trends in the different stem cell transplant types. Cronbach's alpha was calculated utilizing the data and scores that were input into the spreadsheet.

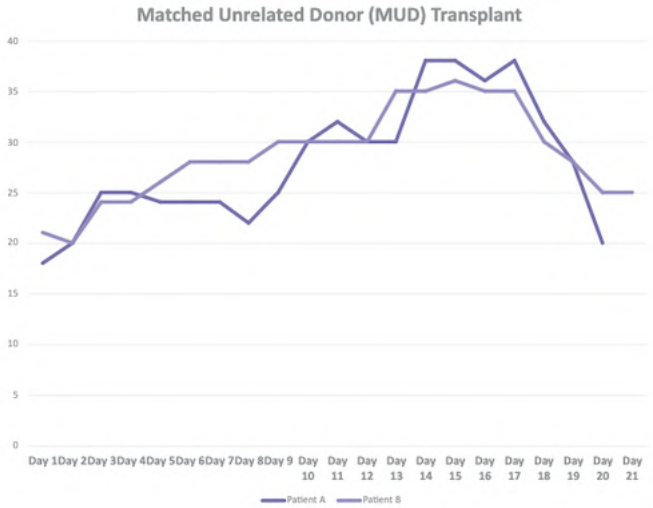
Results: The development and implementation of the objective acuity tool was successful, with a 61% increase in accurately grading patient acuity, a 48% increase in balanced nursing workloads, and a 45% increase in satisfaction with patient acuity in nursing assignments. The tool is reliable with **α=**0.93, and 97% of staff feel the implementation was beneficial.

Results



Cronbach's α= 0.96

Cronbach's α= 0.91



Conclusions: Overall, the development and implementation of an objective patient needs-based acuity tool has been successful on the SCT unit at a large urban academic medical center. The consensus from the nurses on the unit is that the implementation of the tool has been beneficial, and staff have noticed a more balanced workload between each nurse on shift. The nursing staff also feel that the tool accurately reflects the care their patients are requiring per shift, helping them to better identify their total patient acuity and nursing workflow. This tool can be adopted and adapted to other institutions' needs as well as when novel treatments arise, which may warrant new categories to be added utilizing the reliable basic framework of the tool to improve quality of nursing and patient care.

Clinical Trial Registry: Not a clinical trial

Disclosure: Nothing to declare

NP59

CENTRAL VENOUS CATHETER MANAGEMENT AND REMOVAL PATTERNS IN ALLOGENEIC HSCT: INSIGHTS FOR NURSING PRACTICE

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Background: Central venous catheters (CVCs) are fundamental in allogeneic hematopoietic stem cell transplantation (Allo-HSCT), providing access for treatment and supportive care. Nursing staff play a key role in catheter management and complication detection. This study evaluates the reasons for catheter removal and aims to identify areas for improvement.

Methods: We performed a single-center, retrospective, descriptive study of patients who underwent Allo-HSCT at our institution between 2015 and 2024. The catheters included in the analysis were of the following types: PICC (peripherally inserted central catheter), NT-CVC (non-tunneled central venous catheter), T-CVC (tunneled central venous catheter), and TIVAD (totally implantable venous access device).
The reasons for catheter removal were recorded, including catheters placed during the transplant or those already in place at the time of transplantation. Subsequent catheters per patient were also included.

Results: We analyzed 432 patients. The median age was 56 years, and 62.3% were male. The most frequent diagnoses were AML (37.5%) and MDS (13.4%).
A total of 694 catheters were analyzed. The most frequent catheter types were PICCs (44%; n=311), NT-CVCs (39%; n=271), T-CVCs (8%; n=58), TIVADs (6%; n=42), and unspecified CVCs (2%; n=12).
Median catheter duration varied by type: NT-CVCs 22 days (IQR 13–28), T-CVCs 51 days (IQR 20–180), PICCs 98 days (IQR 33–175), and TIVADs 654 days (IQR 298–981).
Catheter removal occurred in 97% of cases. The indications for removal were end of treatment (49% n=335), exitus (13% n=93), persistent fever (10% n=70), signs of local infection (9% n=58), persistent bacteremia (5% n=36), pathogen-directed removal (4% n=27), sepsis/septic shock (3% n=19), thrombosis (1% n=7) and other or unknown reasons (6% n=49).
When indications for catheter removal were analyzed by catheter type, a relevant proportion of infection-related withdrawals was observed, particularly in NT-CVCs (37%, n=100). Within this group, subclavian CVCs showed the highest proportion of infection-related removals (44%, n=26). Infection-related withdrawal was also observed in T-CVCs (34%, n=20), PICCs (25%, n=77), and TIVADs (17%, n=7). In contrast, removal due to end of treatment was the most frequent indication for PICCs (69%, n=215), NT-CVCs (56%, n=152), T-CVCs (35%, n=60), and TIVADs (48%, n=20). Thrombosis was an uncommon indication across all catheter types.
A total of 210 catheters were removed for infection-related reasons (persistent fever, signs of local infection, persistent bacteremia, pathogen-directed removal and sepsis/septic shock).

Regarding catheter tip, 44 (21%) were not sent for culture. The remaining 166 tips (79%) were analyzed, of which 115 (55%) were negative. Details of catheter tip culture submissions are shown in Table 1.

Reason for removal (suspected infection related to catheter)	PERSISTENT FEVER n=70	SIGNS OF LOCAL INFECTION n=58	PERSISTENT BATEREMIA n=36	INDICATED BY PATHOGEN n=27	SEPSIS/SEPTIC SHOCK n=19
Catheter tip not sent	15 (21%)	14 (24%)	11 (31%)	2 (7%)	2 (11%)
Catheter tip sent	55 (79%)	44 (76%)	25 (69%)	25 (93%)	17 (89%)
Cultive negative	48 (69%)	28 (48%)	17 (47%)	11 (41%)	11 (58%)

Conclusions: Most catheter removals in this Allo-HSCT cohort were planned, while infection-related withdrawals were less frequent. Non-tunneled central venous catheters, particularly those placed in the subclavian vein, showed a higher proportion of infection-related removals.
Among the catheters removed at our center, a proportion of catheter tips were not sent for culture. Implementing a protocol to encourage systematic submission of catheter tip samples at the time of removal may help improve monitoring of catheter-related infections.

Disclosure: Nothing to declare.

NP66

A NURSING LED QUALITY IMPROVEMENT INITIATIVE SUSTAINING ZERO CLABSI IN A ABU DHABI BONE MARROW TRANSPLANT PROGRAM, CENTER OF EXCELLENCE IN THE UNITED ARAB EMIRATES

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Background: Central line associated bloodstream infections (CLABSIs) remain among the most serious yet preventable complications in hematopoietic stem cell transplant (HSCT) recipients. Profound immunosuppression in bone marrow transplant (BMT) patients necessitates strict adherence to evidence-based infection prevention practices to reduce morbidity, mortality, and healthcare burden. Between 2023 and 2025, a series of nursing led CLABSI prevention interventions were implemented in the BMT Unit under the Abu Dhabi BMT (AD-BMT) Program. This initiative was aligned with FACT/JACIE accreditation

requirements and CDC/NHSN surveillance standards to support safe, high-quality care for an expanding adult and pediatric transplant population.

Methods: This observational quality-improvement study assessed CLABSI rates, adherence to central line care bundles, and key nursing performance indicators in the BMT Unit from January 2023 to October 2025. A total of 190 BMT patients were managed by 30 BMT nurses, with 4,335 central line days recorded through retrospective chart review from line insertion date to removal.
CLABSI surveillance followed CDC/NHSN laboratory-confirmed BSI definitions, and central line days were counted by NHSN methodology. The CLABSI rate was calculated as the number of CLABSI events divided by the total number of central line days, multiplied by 1,000; during the study period, zero CLABSI events over 4,335 central line days resulted in a CLABSI rate of 0 per 1,000 central line days
A multidisciplinary infection prevention framework was implemented in response to increased patient volume. The intervention included standardized central line insertion and maintenance bundles aligned with CDC, INS, and ONS guidelines. All patients received the full central line care bundle, and 100% of nurses completed structured onboarding and annual competency validation covering aseptic technique, hub disinfection, dressing change protocol, catheter access procedures, and maintenance of sterility.
Daily line necessity audits, real-time adherence monitoring, hand hygiene surveillance and daily safety huddles supported continuous quality assurance. Simulation-based training, bedside coaching, and a one-to-one preceptorship model were used to reinforce nursing practice. Patient and family engagement was integrated into central line education to promote shared accountability in infection prevention.
Performance data including Central line bundle compliance, hand hygiene adherence, and line-days were reported to the ADBMT program Quality Department and the Department of Health (DOH) for validation and regulatory KPI reporting.

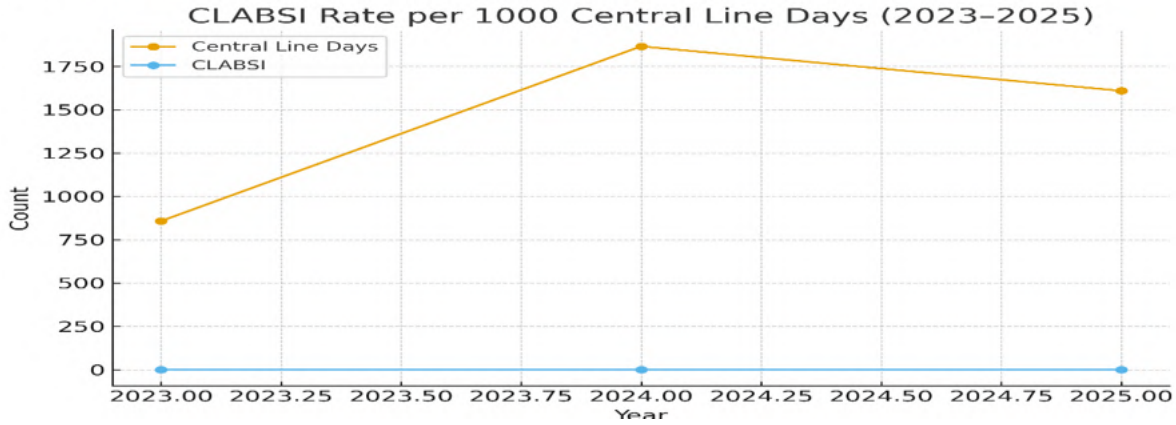
Results: From January 2023 to October 2025, the BMT Unit sustained a CLABSI rate of 0 infections per 1,000 central line days despite high central line utilization rates among BMT patients. Central line care bundle adherence remained at 100%, verified through real-time audits and 100% yearly validation of competencies for all BMT Staff

Table1: CLABSI Performance Indicators in the BMT unit

Indicator	Result	FACT/JACIE Relevance
Study period	January 2023 – October 2025 (34 months)	Continuous quality monitoring
HSCT patients (adult & pediatric)	190	Program activity volume
Specialized BMT nurses	30	Qualified staffing
Total central line days	4,335	NHSN surveillance denominator

CLABSI rate	0 per 1,000 central line days	Infection prevention outcome
Central line utilization rate	100%	High-risk population
Central line bundle adherence	100%	Evidence-based practice compliance
Nursing competency validation	100% annually	FACT/JACIE competency standards
Hand hygiene compliance	100%	Infection control KPI
Patient & family education	100% participation	Patient engagement standard

Figure 1. CLABSI Rate per 1,000 Central Line Days (Jan 2023 – Oct 2025)



Conclusions: Sustaining zero CLABSI over nearly three years in a high-risk BMT population demonstrates the effectiveness of nursing-led, evidence-based practice supported by interdisciplinary collaboration and a robust safety culture. This quality initiative highlights AD-BMT program as a regional leader in infection prevention and reinforces the critical role of nursing leadership in meeting FACT/JACIE standards, advancing patient safety, and achieving sustained quality outcomes. These findings confirm that zero CLABSI is achievable and maintainable through structured education, continuous monitoring, and strong clinical governance.

Disclosure: Nothing to declare

NP77

IMPLEMENTATION OF THE INCIDENTS NEWSLETTER "LEARNING SHARE TO IMPROVE CARE" IN HAEMATOLOGY AND DAY UNIT TRANSPLANT (HTDU) AND IN AMBULATORY CARE/ WITHINGTON WARD (WW)

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Background: Incident reporting is a cornerstone of patient safety and it's widely recognised as an important method for improving safety in healthcare (Leistikow et al, 2016). Effective incident reporting, coupled with systematic learning from incidents are essential components of patient safety and quality improvement (Macrae,2025). Sharing incidents with staff - alongside feedback, learning and solutions – not only prevents recurrence of the same or similar incidents, but also fosters an environment for open reporting, learning and improvement (Care Quality Commision, 2016). As part of the Christie CODE Quality Scheme, incidents should be reviewed timely, feedback and learning shared with staff and celebrating success implemented in the units. So, in January 2025, a monthly incident newsletter titled Learning Share to Improve Care was implemented in HTDU and Ambulatory Care/ WW. Designed as concise, one-page resource, the newsletter idea was focused on learning together from incidents, sharing knowledge and improving the nursing care to haematology patients, including patients pre and post autologous and allogenic haemopoietic stem cell in both units. By May 2025, the incident newsletter was formally adopted within the Christie CODE Quality Scheme as a model across the Trust to disseminate learning and reinforce safety culture.

Methods: It is used a qualitative investigation, employing the qualitative content analysis approach. Data collected from the incident newsletters in HTDU and Ambulatory Care/WW from January to August 2025, which was organised and interpreter to elicit themes present in the Newsletter.

Results: A qualitative thematic analysis identified four overarching themes, each with its own set of subthemes, consistently present across Incident Newsletter in HTDU and Ambulatory Care/ WW: (1) incidents and learning, captured the incidents investigated monthly and the sharing learning from them; (2) good practice, highlighted situations where incidents were either unavoidable but managed appropriately through adherence to protocols and SOPs (e.g., transfusion reactions), or potentially avoidable but mitigated by exemplary nursing practice (e.g., ensuring patient safety despite missing consent documentation prior to SACT administration); (3) implementation of new clinical practices reflected proactive measures introduced to reduce recurrence of incidents and enhance patient safety, such as transfusion observation checklist in HTDU or Ambi SACT checklist in Ambulatory Care/WW; and (4) sharing general information, presented in the form of "Did you know?" segments to broaden staff awareness on diverse incident-related topics including duty of candour, cross-match guidelines or extravasation management. Within Ambulatory Care/WW, a recurring feature across all newsletters was the inclusion of inpatient Mini-CODE feedback,

encompassing patient perspectives, staff experiences, and sustainable action plan to maintain gold.

Conclusions: These findings demonstrate how Incident Newsletter *Learning Share to Improve Care* can serve as vehicle for share the learning from incidents, dissemination of best practices, and reinforcement of safety culture. By integrating incident-based learning with staff, the newsletters not only foster transparency but also contribute to embedding sustainable learning culture for improvements.
While this research provides valuable insights of the incident newsletters, future initiatives should incorporate structured staff feedback to ensure a more comprehensive understanding of their impact and to further enhance the effectiveness of the learning share process.

Disclosure: Nothing to declare.

NP79

PATIENT INFORMATION VIDEOS: ENHANCING EXPERIENCE IN AUTOLOGOUS STEM CELL TRANSPLANTATION

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Background: Effective patient information is essential to empower individuals to make informed decisions, improve health care outcomes, and strengthens communication between patients and healthcare providers (Coulter and Ellins 2007). The Sheffield Teaching hospital Stem Cell Transplant CNS team (STH CNST) conducted a service evaluation audit to offer patients the option to view a series of short videos covering the pathway from Peripheral blood stem cell harvest (PBSCH) to Autologous stem cell transplantation (ASCT). The aim was to improve patient and family satisfaction and experience, and enable a more time effective and efficient patient preparation for someone undergoing ASCT.

Methods: Project funding was successfully sought from the hospital innovation ideas team, this enabled collaboration with the media company with expertise re: how to deliver the content incorporating the recommended optimal length of the videos to support attention span and information retention and engagement (O'Connor A et al 2014). five different videos were created to cover the pathway were created.
The project was evaluated 10 months after the introduction of the videos using a qualitive approach. Patients that had undergone an ASCT were offered the option to complete a questionnaire for video feedback. A QR code was forwarded onto the patients who gave consent to take part. Data was also obtained from the media company to give the results of how many time each individual section had been viewed.

Results: The Videos were watched a total of 800 times, this dose not account for patient and family watching the videos multiple times. Of this introduction the stem cell transplants had the most views.
32 people was contacted received ACST in the last 10 months. 2 people had not watched the

videos, one declined as this was their 2nd ASCT and the remaining 29 had questionnaires sent out to complete. 14 have responded with the highest number of responses coming from the over 55 and male categories.
100% of the patients agreed that the content and the way the information was delivered had a positive impact in their understanding the process of harvest and ASCT, with a 9.6/10 rating for patients understanding of the process of a stem cell harvest and ASCT.
100% of patients found this resource aided them in delivering the information to friends and family effectively.

Conclusions: The implementation of patient information videos for individuals undergoing Autologous Stem Cell Transplantation has demonstrated clear benefits in enhancing patient understanding and engagement. Feedback indicates that the videos support improved health literacy, greater confidence in decision-making, and a more positive overall patient experience. This digital approach has also contributed to improved communication between patients, families, and the multidisciplinary team, promoting shared decision-making and patient empowerment.
By providing accessible and consistent information, the videos have the potential to improve safety, reduce errors, and streamline the patient journey ,delivering both patient-centred and economic benefits for the Bone Marrow Transplant team. Future plans include ongoing evaluation and expansion of the video series to other transplant pathways to further embed digital education within routine care.

Clinical Trial Registry: N/A

Disclosure: N/A

NP84

CONFIDENCE IN A BOX: NURSE-SUPPORTED MEDICATION SELF-MANAGEMENT FOR PATIENTS AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Patients discharged after allogeneic stem cell transplantation face substantial, complex and frequently changing medication regimens. These medications are critical for this patient group to prevent complications such as infections and graft-versus-host disease (Amonoo et al, 2025). In the outpatient clinic, concerns were raised about the accuracy of patients' self-reported medication adherence. Incomplete medication summaries and limited patient education at discharge increase the risk of medication errors, unplanned readmissions, and preventable adverse effects (Becker et al, 2021).

Methods: Medication adherence was primarily supported by clinician involvement, patients' prior experience with medication management, and the use of organizational aids such as pill boxes and phone timers to help structure doses and ensure consistent timing across the day

(Amonoo et al., 2023). A pilot at the hematology ward was designed and implemented whereby allogeneic stem cell transplantation patients take responsibility for managing their own medication administration during the final phase of their inpatient admission.
A multidisciplinary approach was essential, with nurses, a pharmacist and a physician ensuring clinical accuracy and safe implementation. To ensure consistency, nurses follow a protocol with clear instructions for supporting medication self-management. In the last days of admission, patients receive a pill organizer that can be filled with three days of medication. From that point forward, they take the lead in preparing and administering their own medication while still in the hospital. Nurses play a key role by providing tailored support: they supervise medication rounds, guide patients through the steps, and intervene when uncertainties arise. This supervised practice helps patients gradually develop confidence, understand their treatment better, and recognize potential risks (Dalari et al, 2019).

Results: A patient survey was conducted to evaluate their experience with the intervention. Early results also showed that they felt more confident in managing their medication regimen and appreciated being given greater autonomy prior to discharge. Furthermore, patients described gaining a better understanding of their medication regimen and the correct administration of each drug, consistent with findings by Polito et al. (2021).
Although the intervention requires additional nursing time during hospitalization, it is expected to contribute to improved long-term outcomes, higher patient satisfaction, and potentially reduced medication-related complications or hospital readmissions following patient discharge.

Conclusions: The intervention demonstrates a feasible and scalable approach to promoting medication self-management within inpatient hematology and transplant care. The requirements are low-cost and minimally resource-intensive, enabling straightforward implementation in similar clinical settings. Other units can use this quality improvement project to help patients become more involved and increase medication safety after discharge.

Disclosure: No disclosures.

NP99

WHEN INFECTION DELAYS TRANSPLANTATION – A CASE REPORT OF A PATIENT WITH NECK WOUND INFECTION AND SEPSIS

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Background: Patients undergoing chemotherapy and preparation for allogeneic hematopoietic stem cell transplantation (HSCT) are at high risk of severe infectious complications due to deep immunosuppression. Local infections, such as dental sources, can rapidly progress and jeopardize patient safety, delay treatment, and compromise transplant eligibility. Early recognition of infection and adherence to high standards of nursing care—

particularly through continuous assessment, timely intervention, and vigilant monitoring by specialized nurses—are essential to prevent life-threatening outcomes. This case highlights how infection progression can significantly affect clinical decision-making and the success of hematologic therapy.

Methods: This case report is based on a retrospective review of medical and nursing documentation, clinical observations, and multidisciplinary management during hospitalization, surgical treatment, and follow-up in a patient preparing for HSCT. Particular focus was placed on infection progression, surgical complications, and the scope of nursing interventions required.

Results: A patient with acute lymphoblastic leukemia (ALL) developed progressive infectious complications following an initial dental infection, which worsened during post-chemotherapy aplasia and resulted in gram-negative sepsis caused by Pseudomonas aeruginosa. The infection spread to the soft tissues of the face, requiring surgical incision, removal of necrotic tissue, and later reconstruction with a pectoral flap. Intensive nursing monitoring was required due to swelling, pain, fever, and hemodynamic instability. Postoperatively, continuous pain management, twice-daily wound care, monitoring for secretion and infection, and supervision of Penrose drains were essential. Fifteen days after the initial surgical debridement and removal of necrotic tissue, purulent discharge, necrosis, and a fistulous opening with passage of food developed. The patient refused nasogastric feeding, making enhanced oral hygiene, assisted feeding, and patient-family education crucial components of nursing care. Due to progressive local and systemic deterioration, a second reconstructive surgery was performed. Postoperatively, the patient required intensive monitoring of vital signs, laboratory values, drain output, and hemodynamic stability, including treatment in the intensive care unit during sepsis and aplasia. Nursing care played a central role throughout all phases of treatment: detailed wound assessment, documentation of changes, pain monitoring, administration of analgesics, mobilization support, nutritional assistance, and extensive education on hygiene and home care. After discharge, the patient was followed through home care and community nursing services. Two weeks later, deterioration of general condition, wound worsening, and relapse of the underlying disease resulted in a fatal outcome.

Conclusions: This case highlights how a localized dental infection can rapidly progress into life-threatening complications in immunocompromised patients and delay HSCT eligibility. It underscores the essential role of continuous, highly specialized nursing care in recognizing deterioration, managing complex wounds, preventing complications, and ensuring patient safety. Severe infections, despite preventive measures, remain a major threat to survival and may significantly impact the success of hematologic treatment.

Disclosure: Nothing to declare.

Psycho-social Issues

NG07-01

JOURNEY MAPPING AS A METHOD TO EXPLORE THE ADOPTIVE CELL THERAPY EXPERIENCE OF PATIENTS, INFORMAL CAREGIVERS, AND HEALTHCARE PROFESSIONALS

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Background: Adoptive Cell Therapy (ACT) is a personalized immuno-oncology approach for hematologic and solid malignancies, increasingly delivered in clinical trial and standard-of-care settings. Current modalities include tumor-infiltrating lymphocyte (TIL) therapy and chimeric antigen receptor T-cell (CAR-T) therapy. The ACT pathway is lengthy and complex, posing unique challenges for patients, informal caregivers (ICs), and healthcare professionals (HCPs). Understanding their psychosocial experiences is essential for providing timely, tailored support. Journey mapping, originally developed in marketing research, is increasingly applied in healthcare to capture how individuals navigate and experience care. As part of a broader service improvement co-design study involving patients, ICs, and HCPs, this project used journey maps to examine shared and distinct psychosocial experiences across ACT care settings, including HCPs' perceptions of patient experiences.

Methods: A qualitative exploratory design with purposive, pragmatic sampling was employed. Participants included patients receiving standard-of-care CAR-T (n=10) or TIL through clinical trial (n=11), their ICs (CAR-T n=7, TIL n=6), and HCPs (n=10; nurses, oncologists, a psycho-oncologist, and research coordinators/associates). Journey mapping was conducted at the end of interviews. Participants received a visual timeline and an optional list of emotions, feelings, and perceptions. They validated key steps, indicated predominant psychological processes at each stage, and reflected on their meaning, co-creating a depiction of the ACT pathway. HCPs completed two maps: one reflecting professional experience and one representing their perceptions of patient experiences. All interviews were audio-recorded and transcribed. Maps were analyzed using a content approach, organizing emotions, perceived social support and control, and coping strategies across care phases (therapy presentation, pre-treatment, treatment, post-treatment). Contextual information was extracted from interviews and findings were triangulated across participant groups and settings to identify convergent and divergent experiences.

Results: Fifty-three maps were analyzed, revealing the ACT pathway as emotionally intense and ambivalent, with actor and setting-specific psychosocial challenges. In general, for patients and ICs, during therapy presentation, hope for a potentially life-extending option

coexisted with fear of complexity, severe toxicities and possible non-efficacy. Pre-treatment stress increased due to diagnostic procedures, logistics, and anticipated hospitalization, while clear communication and preparation enhanced trust. During treatment, relief and hope upon receiving therapy coexisted with fear and surprise at toxicity intensity. Post-treatment trajectories diverged: positive outcomes brought joy, gratitude, and cautious optimism, whereas poor outcomes elicited sadness or anger. Across phases, participants reported periods of high social support, episodes of loneliness, and fluctuating perceived control, ranging from manageability to feeling overwhelmed. Coping strategies spanned emotion-, problem-, and meaning-focused approaches. Notably, HCPs underestimated the emotional impact of care coordination during pre-treatment and physical debilitation during post-treatment, highlighting these two phases as periods with the greatest unmet psychosocial needs and highest priority for targeted interventions.

Conclusions: This study identifies critical psychosocial pressure points across the ACT pathway. Discrepancies between HCP perceptions and lived experiences highlight the importance of proactive, structured psychosocial assessment and the need for targeted support interventions at key moments. Journey mapping proved valuable in capturing emotional shifts and revealing unmet needs that are less evident in traditional interviews, offering actionable insights to strengthen person-centered care across ACT services.

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NG07-04

GENDER MATTERS: UNDERSTANDING RETURN-TO-WORK EXPERIENCES AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Hematopoietic cell transplantation (HCT) is a common treatment for individuals diagnosed with hematologic cancers. However, HCT can lead to side effects that significantly impact work participation. Recent reviews highlight that gender may influence the return-to-work (RTW) experience. As hematologic cancers affect both men and women, it is important to contrast their RTW experiences to better understand how to support them. The aim of this study was to explore and describe similarities and differences between men and women affected by hematologic cancer regarding factors influencing RTW after allogeneic hematopoietic stem cell transplantation (allo-HCT) in Canada.

Methods: This study is part of a larger mixed-method project exploring RTW after allo-HCT. We used a convergent mixed-method design combining quantitative and qualitative approaches to examine gender-based similarities and differences in RTW factors. Quantitative data included a retrospective review of medical records and an electronic vocational survey completed by eligible patients aged 18–60 who underwent allo-HCT between 2016 and 2022 in Montreal (Canada). Qualitative data were collected through semi-structured Zoom™ interviews with purposively sampled survey participants reporting RTW challenges. The categories of determinants for RTW identified by the REWORK framework (Porro et al., 2021) informed the design of the survey and interview guide. Data integration provided a comprehensive understanding of medical, psychosocial, and work-related influences on RTW.

Results: Among 89 participants, a total of 61 patients were included in the survey analysis. Of these, 22 participants took part in a qualitative interview: 9 identified as women and 13 identified as men. Both men and women shared common challenges such as financial insecurity, fear of losing disability benefits, and decreased importance of work post-transplant, alongside medical complications like chronic GVHD and fatigue. However, women reported greater income loss (41% vs. 27%), a slightly lower perception of the importance of work post-transplant, and were more likely to remain in the same job (72% vs. 47%), whereas men experienced more job changes. Men reported greater support for RTW (p=0.011), while women more frequently requested task adjustments (p=0.005) and described struggles to regain previous responsibilities. Fatigue intensity differed (p=0.012), with men reporting high-intensity fatigue and women moderate-intensity fatigue, compounded by increased mental workload for women. Additional contrasts included men's positive perception of family support versus women's negative perception, and women's tendency to seek complementary medical support.

Conclusions: Overall, men and women experienced similar RTW challenges, but notable gender differences emerged. Greater attention is needed to address women's financial losses after allo-HCT and workplace reintegration issues. Assessing social support remains essential, as women may experience less support than men. These findings underscore the need for gender-sensitive RTW interventions tailored to financial, psychosocial, and workplace challenges. Future studies should explore long-term RTW trajectories and evaluate interventions addressing gender-specific barriers.

Disclosure: Nothing to declare

NG12-05

PERCEIVED BURDEN IN PRIMARY CAREGIVERS FOR AT-HOME HOSPITALIZATION AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION: A SINGLE CENTER EXPERIENCE

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Background: At-Home hospitalization (AHH) offers multiple benefits for participating patients, such as greater comfort and a potential reduction in the risk of nosocomial infections. However, its implementation requires intensive participation from the primary caregiver, whose physical, emotional, and social involvement is still poorly known. The aim of this study is to evaluate the perceived burden of primary caregivers of patients undergoing autologous HSCT in an AHH program, by using a structured questionnaire.

Methods: From May 2024 to November 2025, 15 patients underwent autologous HSCT in AHH. All caregivers completed the Modified Caregiver Strain Index (MCSI), a tool that assesses the pressure associated with caregiving for adults of any age. The questionnaire consists of 13 items evaluating the perceived burden of caregiving, with five main domains assessed by at least one item: Financial, Physical, Psychological, Social, and Personal. Each item is scored with 2 points ("yes, on a regular basis"), 1 point ("yes sometimes"), or 0 points ("no"), generating a total score between 0 and 26, where higher values indicate a greater level of burden. The questionnaire was completed once the patients were medically discharged and completed the AHH process.

Results: The primary caregiver were: 9 spouses (60%), 3 siblings (20%), 2 daughters (13%) or 1 parent (7%). They were women in 13 (87%) and men in 2 cases (13%). The Caregiving was provided full-time in 9 cases (60%) and combined with another caregiver in the remaining 6 (40%). The mean overall MSCI score was 9.06/26, being 1/26 the lowest score and 24/26 the highest.
The most frequent low scoring items were "Caregiving is a physical strain" (73% "no"), "Some behaviour is upsetting" (67% no), "There have been other demands on my time" (67% no) and "Caregiving is a financial strain" (67% no) suggesting a very limited physical and financial burden, although a small subgroup reported significant economic strain (27% "yes, on a regular basis"). The subjective feeling of being overwhelmed showed a moderate impact (13% "yes, on a regular basis" and 47% "yes, sometimes"). Among the highest score ("yes on a regular basis") we observed a punctuation for "Caregiving is confining", "There have been changes in personal plans." and "There have been family adjustments," each reported by four caregivers (27%), reflecting a predominantly emotional and organizational burden. Sleep disturbance was frequent (73% reporting "yes, on a regular basis" or "yes, sometimes"), while work-related impact was intermediate (20% and 40% respectively). Overall, the results suggest a moderate caregiver burden with substantial variability across domains.

	YES on a regular basis *2 points*	**YES sometimes** *1 point*	**NO** *0 points*

My sleep is disturbed	2	9	4
Caregiving is inconvenient	2	5	8
Caregiving is a physical strain	1	3	11
Caregiving is confining	4	7	4
There have been family adjustments	4	5	6
There have been changes in personal plans	4	7	4
There have been other demands on my time	2	3	10
There have been emotional adjustments	3	7	5
Some behaviour is upsetting	0	5	10
It is upsetting to find the person I care for has changed so much from his / her former self	1	7	7

There have been work adjustments	3	6	6
Caregiving is a financial strain	4	1	10
I feel completely overwhelmed	2	7	6

Conclusions: Personal limitations, changes in family life, and sleep disturbances were the most significant aspects. In contrast, the physical and financial burden was lower, although a significant impact on employment was identified for some caregivers. These findings underscore the need to incorporate psychological and emotional support interventions, assistance with family reorganization, and resources aimed at reducing caregiver burden in ASCT programs in hematology.

Disclosure: Nothing to declare.

NP56

NURSE LED HOLISTIC NEEDS REVIEW CLINIC 100 DAYS POST ALLOGENEIC STEM CELL TRANSPLANT: A SERVICE EVALUATION

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Background: Patients are at risk of significant complications in the early phase of recovery post allogeneic haematopoietic stem cell transplantation (AHSCT). These include infections, acute graft versus host disease (GVHD), and graft failure. Intensive follow-up post discharge focuses on:

- maintaining therapeutic immunosuppression levels
- screening for, treatment and monitoring of acute GVHD
- screening and treatment of infection
- observation of chimerism and disease response

Clinically focussed care is imperative to reduce mortality and morbidity post AHSCT. However, this intensive treatment may have psychosocial and/or spiritual consequences that are not discussed or addressed in standard post-transplant follow up reviews.
A nurse-led holistic needs review clinic at 100 days post AHSCT (HNR100) was established to offer patients the opportunity to share and discuss their concerns, psychological impact and to signpost to places for relevant support.

A 12-month review of the clinic looked at themes of outcomes to establish the relevance and shape future clinic development to best serve patient need.

Methods: Patients were offered an appointment with the post AHSCT clinical nurse specialist at around 100 days post-transplant. This was optional by telephone or in person. Patients were invited to bring a person of significant support to the clinic review.
A clinic proforma was used to standardise and document conversations and outcomes. The proforma was uploaded onto the patient's clinical record with patient consent.
The discussion centred around:

- patient and family expectations in early phase post ASCT recovery
- post ASCT vaccinations
- diet and exercise
- psychological impact
- sex function/contraception
- potential premature ovarian insufficiency (POI)
- work and employment/financial issues
- managing fatigue

The service evaluation gathered 12-month data on the patient population, type of AHSCT, outcomes of holistic review by themes.

Results: 36 (male 58% ,female 42%) patients in 12 month period attended the HNR100 clinic. Median age 53 yrs (range 18-74 years). Telephone was preference for 14%, in person preference for majority (86%).
14% myeloablative, 86% reduced intensity conditioning.
Questions re financial impact (14%) and psychological impact (14%) was joint lead for patients' concerns resulting in referral to benefits advisor or clinical psychology support.
Sex function (8%) and discussions and potential POI (8%) was identified as an outcome of the clinic. This resulted in referrals to finance advisor, clinical psychology, gynaecology, erectile dysfunction clinic as appropriate. All patients given contact details re post-transplant nurse specialist, and signposting information re how to access support and advice post-transplant from relevant charity organisations.
All patients evaluated the clinic as helpful, and welcomed the opportunity to discuss worries and concerns that regular medically led reviews did not always offer.

Conclusions: The HNA100 has been a well-evaluated clinic for both patients and family support members. There is evidence that concerns re financial impact and sex function/POI has been identified at an earlier timepoint by direct questioning in a holistic review, with prompt referral to access help and support. There is an opportunity to formally evaluate psychological impact using an evaluated tool, this is the next phase of the clinic development.

Disclosure: Nothing to declare.

NP89

POST-TRAUMATIC STRESS DISORDER SCREENING FOR PRE-HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Background: Global Hematopoietic Stem Cell Transplant (HSCT) are increasing in frequency. Research has shown that ~40% of HSCT patients develop a clinically significant psychiatric disorder during and after treatment. Anxiety and depression are common during HSCT, affecting 15-40% of patients. In addition, 6.6-26% of HSCT patients meet the criteria for Post-Traumatic Stress Disorder (PTSD), which peaks at 6 months post-transplant, affecting 28% of transplant recipients. No recommended psychosocial screening currently exists. Known risk factors for PTSD among HSCT patients include limited social support, pre-existing psychological distress, and poor coping skills. These factors are crucial to recognize prior to HSCT to minimize psychological sequelae and improve post-transplant outcome. The PTSD Checklist for DSM-5 (PCL-5) is a validated, reliable tool useful for assessing PTSD symptom severity. This project assessed how PCL-5 screening affected coping support referrals for pre-HSCT patients with PTSD symptoms.

Methods: **Setting:** Conducted at the outpatient Multiple Myeloma (MM) and Bone Marrow Transplant (BMT) clinics at an academic center in an urban city.
Participants: Adult participants with a diagnosis of hematological malignancies. Scheduled for Auto or Allo- HSCT hospitalization (N=18).
Objectives:
To implement a standardized PTSD screening process using the PCL-5, a validated 20-item questionnaire, during pre-transplant evaluations to identify patients at risk for PTSD. At an early stage to identify patients at risk for PTSD via implementing PTSD screening (PCL-5, a validated 20-item self-administered questionnaire) during pre-HSCT evaluations.
To facilitate timely psychosocial intervention by ensuring that all screening results are communicated to the Social Worker (SW), who then addresses positive scores by providing individualized coping support, including psychotherapy or referral to psycho-onc.
PCL-5 score calculation method:
The PCL-5 could determine a provisional diagnosis of PTSD in two ways:
Sum Score Method**:** Total score > 31-33 (range: 0-80) (See Figure 1) or
Symptom-Based Method: Endorse at least:
Re-experiencing: 1 from B (Q1-5)
Avoidance: 1 from C (Q6-7)
Negative cognition/mood: 2 from D (Q8-14)
Hyper-arousal: 2 from E (Q15-20) (See Figure 2)

Demographic and medical characteristics

Sociodemographic Characteristics of Participants (n=18)

Characteristic	Description	
	n	%
Gender		
Female	6	33.3%
Male	12	66.7%
Relationship status		
Married/ Partnered	14	78.2%
Single/separated/divorced/widowed	4	22.2%
Race		
Black or African American	2	11.1%
White	14	77.8%
More than one race	2	11.1%
Diagnosis		
AML/MDS/MPL/MF	6	33.3%
ALL	1	5.6%
Multiple Myeloma	10	55.6%
Lymphoma (Non-Hodgkin)	1	5.6%
Transplant Type		
Autologous	11	61.1%
Allogenic-RIC (Reduced Intensity Conditioning)	5	27.8%
Allogenic-MAC (Myeloablative Conditioning)	2	11.1%
Psychiatric Disorder		
None	14	77.8%
Anxiety	2	11.1%
Depression	1	5.6%
Anxiety/Depression	1	5.6%
Psychosocial support pre HSCT		
Took a prescription drug for anxiety or depression	1	5.6%
Seen Psychologist or Psychiatrist	1	5.6%
Seen by SWs	13	72.2%
None	3	16.7%

*AML (Acute Myeloid Leukemia)
MDS (Myelodysplastic Syndrome)
MPL (Myeloproliferative neoplasms)
MF (Myelofibrosis)
ALL (Acute Lymphoid Leukemia)

Results:

2 patients were positive for PCL-5

A:

Score 35

DSM-5 4 symptoms +

SW made aware to patient's A's Psychiatrist since already seen by Psychiatrist for Dx. Depression & Anxiety

B:

Score 28

DSM-5 4 Symptoms +

No Psychiatric History. SW did not refer to Psych-Onc. SW followed closely during hospitalization

Q. Can positive PCL-5 affect coping support referral?

A total of 18 out of 2 patients were positive for PCL-5 +

1) PCL-5 score positive = 2/18 x 100 = 11.1% →2 patients **(11.1%)** were positive for PTSD

2) The rate of positive screened referrals = 1/2 x 100 = 50% → 1 patient **(50%)** was referred to Psychiatry.

Fisher's exact test (p = 0.111)

The relationship between screening PCL-5 and referral for coping support was not statistically significant (p = 0.111)

Conclusions: Pre-Allo and Auto HSCT patients, both females and males, are equally experiencing provisional PTSD
There was no statistical significance between the frequency of PTSD and psychosocial referrals **(p= 0.111).**
Pre-HSCT patients reported experiencing insomnia, feeling distant, and recurring repeated disturbing memories, highlighting the need for psycho-oncologist evaluation.

Disclosure: Nothing to declare.

Vaccination, Infection Control and Prevention

NP97

NURSE-DRIVEN INTERVENTIONS LEAD TO NEAR-ZERO CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION RATES IN ADULT STEM CELL TRANSPLANT PATIENTS: A RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Central line–associated bloodstream infections (CLABSIs) remain a major cause of morbidity and mortality in hematopoietic stem cell transplant (HSCT) patients, who are uniquely vulnerable due to prolonged neutropenia and intensive central venous catheter (CVC) use. Evidence from prior research consistently demonstrates that nurse-driven central line maintenance bundles significantly reduce CLABSI rates in high-risk populations. Studies by Pronovost et al. and subsequent bundle-based interventions have shown reductions of 60–70% or more in CLABSI incidence when consistent nursing practices, chlorhexidine (CHG) dressings, and access port disinfection devices (e.g., Curos caps) are implemented. Similarly, multiple HSCT-specific studies have reported substantial decreases in CLABSI when standardized nursing-driven protocols are adopted, with some centers achieving near-zero rates.

Methods: A retrospective observational study was conducted involving 22 adult HSCT patients (autologous and allogeneic). Data extracted included line insertion and removal dates, duration of CVC use, type of line dressing (CHG vs non-CHG), and use of Curos port protection. The primary outcome was CLABSI occurrence during stem cell infusion and the subsequent inpatient transplant period. All patients received nurse-driven standardized line care, including CHG Tegaderm dressings and mandatory Curos cap use.

Results: Across 22 patients with central line durations ranging from 19 to 50 days, zero CLABSI events were documented (0 CLABSI per 1,000 CVC-days). All patients received CHG

dressings and Curos caps, with 100% adherence to the nurse-driven bundle elements. These findings are consistent with previous literature demonstrating that rigorous nursing-led maintenance practices can achieve near-zero CLABSI incidence in high-risk cohorts.

Conclusions: Implementation of standardized nurse-driven interventions, including CHG dressings, Curos disinfecting port protectors, and consistent daily maintenance practices, was associated with near-zero CLABSI rates in adult HSCT patients. The results reinforce existing evidence that nurse-led care bundles are among the most effective strategies for CLABSI prevention. Sustained adherence and nursing empowerment appear critical for maintaining low infection rates in stem cell transplant populations.

Disclosure: Nothing to declare

Quality of Life, Late Effects, Survivorship Care and Health Promotion

NG07-03

ENHANCING PREPAREDNESS AND WELL-BEING IN ALLOGENEIC STEM CELL TRANSPLANTATION: A MIXED-METHODS EVALUATION AND OPTIMISATION OF THE NURSE-LED ANIMO SUPPORT NETWORK

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Background: Patients undergoing allogeneic stem cell transplantation (allo-SCT) and their caregivers face profound physical and psychological challenges across the pre-, peri- and post-transplantation trajectory. Despite advances in clinical standardisation, many still experience fragmented, insufficient or non-individualised information, which increases uncertainty, fear and difficulty navigating the transplant process. To address these gaps, the nurse-led ANIMO Network, a monthly, hybrid, support programme, was established at TUM Klinikum Rechts der Isar with the aim of strengthening preparedness, safety and well-being through the allo-SCT continuum. This study systematically evaluated informational needs and perceived informational quality to guide a structured optimisation of the programme using Step 4 of the PEPPA Framework.

Methods: A mixed-methods design integrated quantitative and qualitative approaches. In the quantitative component, twenty-one adult allo-SCT patients completed the EORTC QLQ-INFO25 questionnaire (response rate 95%). Data were analysed descriptively following EORTC guidelines, using linear transformation of raw scores (0–100) and calculation of a Global Score representing overall informational quality. The qualitative component consisted of twelve semi-structured interviews with patients and caregivers (5h 02min total duration),

analysed using Mayring's summarising content analysis. Deductive were expanded inductively. Triangulated findings informed targeted optimisation strategies within the ANIMO Network.

Results: Quantitative analysis revealed substantial variation across the four official INFO25 scales. Information about the medical tests received the highest ratings (mean 3.49), with all participants selecting "quite a bit" or "very much". Information about the disease was also rated positively (mean 3.11), though items concerning causes and mechanisms showed substantial variability.
Information about the treatment indicated moderately high satisfaction (mean 3.09), yet important gaps emerged in sensitive areas. The lowest-rated item concerned the impact of treatment on sexual activity, with 76.2% reporting "not at all" or "a little" information. The lowest overall ratings appeared in Information about other services (mean 2.84). Items related to self-help groups (mean 2.48) and rehabilitation services (mean 2.76) showed limited awareness of supportive resources.
The transformed Global Score ranged from 50.67 to 76.00 (mean 59.33), reflecting moderate overall informational quality. Despite strengths in several areas, 61.9% of respondents expressed a wish for more information, signalling the need for programme optimisation.
Qualitative findings mirrored the quantitative results. Early, personalised and clearly structured information was described as reducing anxiety and enhancing preparedness. Recurrent unmet needs concerned long-term effects of transplantation, daily self-management, psychosocial support and navigation of supportive services. Peer-to-peer exchange emerged as uniquely validating and an essential complement to professional education. Following optimisation measures, interviewees described improved clarity, emotional stability and a stronger sense of safety.

Conclusions: This mixed-methods evaluation identified significant informational gaps among allo-SCT patients, particularly regarding supportive services, long-term implications and sexual health. Using the PEPPA Framework, the ANIMO Network was systematically optimised, leading to qualitative improvements in perceived preparedness, confidence and emotional well-being. These findings offer a scalable model for supportive care in allo-SCT and underline the strategic value of advanced nursing practice in high-complexity haematology settings.

Disclosure: Nothing to declare.

NG07-05

IMPACT OF A STRUCTURED PRE-TRANSPLANT NUTRITION PROGRAM WITHIN A FRAILTY-PREHABILITATION STRATEGY IN ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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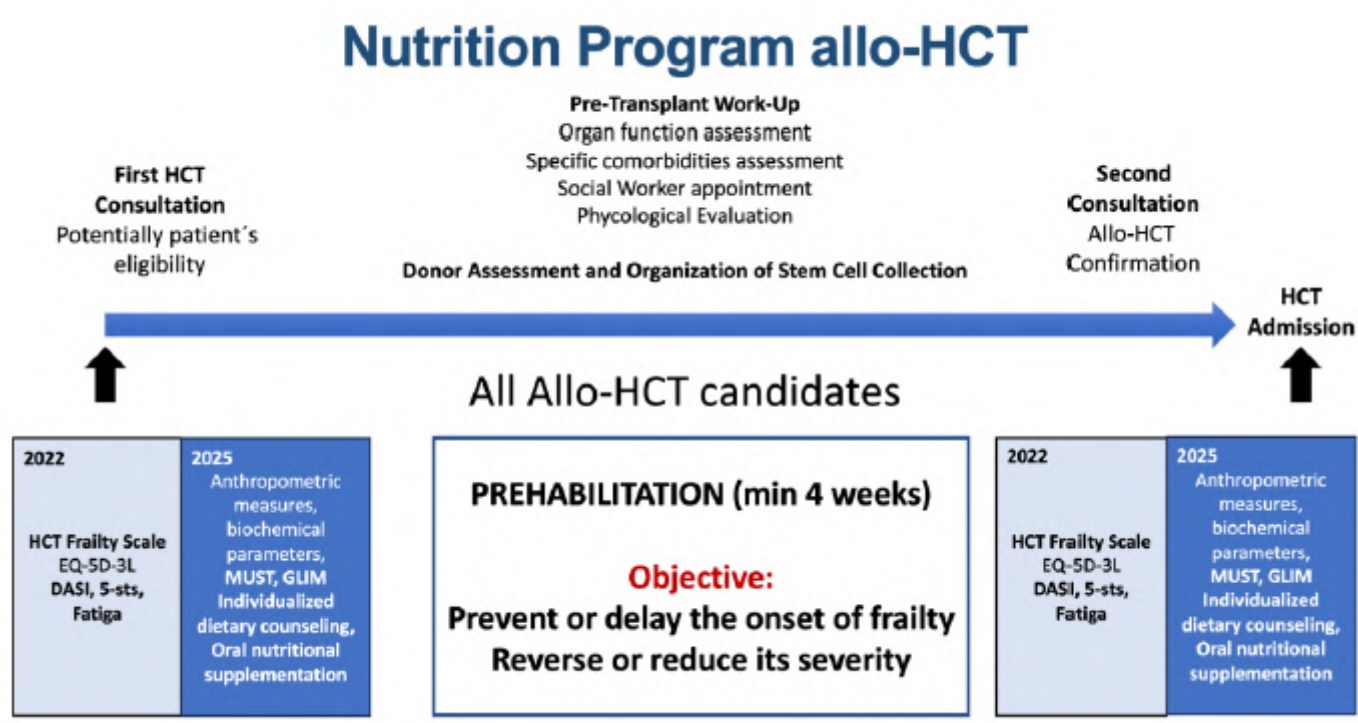
Background: Nutritional status is a critical determinant of transplant tolerance and outcomes in allogeneic hematopoietic cell transplantation (allo-HCT). Malnutrition and inadequate intake are frequent among candidates and contribute to frailty, functional decline, and impaired transplant readiness.
Since 2022, our institution has implemented a Frailty Program for all adult allo-HCT candidates, combining frailty assessments with physical prehabilitation. In 2025, a structured Nutrition Program was integrated to optimize nutritional status prior to allo-HCT, enhance prehabilitation effectiveness, and reduce nutritional-related complications. This study reports preliminary results on the feasibility and impact of this intervention during the pre-transplant period.

Methods: All adult allo-HCT candidates were prospectively enrolled in the Frailty Program and subsequently included in the Nutrition Program. The intervention comprised **(Figure 1)**:

- Comprehensive in-person nutritional assessment by a specialized team.
- Individualized dietary counseling.
- Oral nutritional supplementation when indicated.
- Close follow-up until HCT admission (in-person or telemedicine).

Effectiveness was evaluated by longitudinal changes in nutritional risk (Malnutrition Universal Screening Tool [MUST] and Global Leadership Initiative on Malnutrition [GLIM] criteria), anthropometric and biochemical parameters, and frailty status between first consultation and

HCT admission.



Results: Twenty-five patients were analyzed (median age 52 years, range 18–73; 28% ≥65 years). At baseline, frailty status was: fit 28%, pre-frail 68%, frail 4% according to the HCT Frailty Scale. Nutritional risk (MUST) was identified in 28% of patients; 71.4% met GLIM criteria for malnutrition, mainly due to >5% weight loss in <6 months and insufficient intake **(Table 1)**. Patients at nutritional risk were more often ≥65 years (57.1% vs. 16.7%) and showed higher rates of underweight (Body Mass Index [BMI] <18.5 kg/m²; 14.3% vs. 0%) and clinically relevant weight loss (71.4% vs. 0%).
Insufficient oral intake was universal (100%), prompting individualized dietary counseling and supplementation. Adherence was 100% with no gastrointestinal intolerance or aversion reported.
At HCT admission: fit 40%, pre-frail 56%, frail 4%. BMI remained stable, with an increase in patients within healthy range (from 32% to 40%). Nutritional risk decreased (from 28% to 24%), and only one patient (4%) lost weight during follow-up. Severe hypoalbuminemia remained rare (4%), suggesting overall nutritional stabilization.

Baseline Characteristics	**All patients N = 25 (100%)**	**Normal MUST N = 18 (72%)**	**Anormal MUST N = 7 (28%)**

Median Age **≥65 years**	52 (18-73) 7 (28.0)	52 (18-73) 3 (16.7)	53 (26-71) 4 (57.1)
Sex Male Female	 15 (60.0) 10 (40.0)	 10 (55.6) 8 (44.4)	 5 (71.4) 2 (28.6)
Baseline Diagnosis Acute Myeloid Leukemia Myelodisplastic Syndrome Myeloproliferative Neoplasia Acute Lymphoblastic Leukemia Lymphoproliferative Disease Others	 9 (36.0) 2 (8.0) 4 (16.0) 4 (16.0) 1 (4.0) 5 (20.0)	 6 (33.3) 2 (11.1) 3 (16.7) 3 (16.7) 1 (5.6) 3 (16.7)	 3 (42.9) 0 1 (14.3) 1 (14.3) 0 2 (28.5)
HCT-CI>3	1 (4.0)	0	1 (14.3)
KPS<90%	6 (24.0)	3 (16.7)	3 (42.9)
First Consultation			
Frailty Assessment Fit Pre-frail Frail	 7 (28.0) 17 (68.0) 1 (4.0)	 5 (27.8) 12 (66.7) 1 (5.6)	 2 (28.6) 5 (71.4) 0
BMI Underweight <18.5 kg/m2 Healthy 18.5-24.9 kg/m2 Overweight >25 kg/m2	 1 (4.0) 8 (32.0) 16 (64.0)	 0 4 (22.2) 14 (77.8)	 1 (14.3) 4 (57.1) 2 (28.6)
Laboratory Markers Proteins < 63 g/L	3 (12.0)	2 (11.1)	1 (14.3)

Albumin < 34 g/L Pre-albumin < 0.200 g/L	0 7 (28.0)	0 5 (27.8)	0 2 (28.6)
GLIM: malnutrition diagnosis (moderate and severe)	5 (20.0)	0	5 (71.4)
Significant Weight Loss (>5% in <6 months)	5 (20.0)	0	5 (71.4)
Insufficient oral intake	25 (100.0)	18 (100.0)	7 (100.0)
HCT Admission (Post Intervention)			
BMI Underweight <18.5 kg/m2 Healthy 18.5-24.9 kg/m2 Overweight >25 kg/m2	 1 (4.0) 10 (40.0) 14 (56.0)	 0 6 (33.3) 12 (66.7)	 1 (14.3) 4 (57.1) 2 (28.6)
Laboratory Markers Proteins < 63 g/L Albumin < 34 g/L Pre-albumin < 0.200 g/L	 11 (44.0) 1 (4.0) 4 (16.0)	 8 (44.4) 0 3 (16.7)	 3 (42.9) 1 (14.3) 1 (14.3)
MUST: risk of malnutrition (medium and high)	6 (24.0)	1 (5.6)	5 (71.4)
Significant Weight Loss (>5% during the pre-transplant period)	1 (4.0)	1 (5.6)	0

Conclusions: Nutritional vulnerability was common and associated with adverse baseline profiles. Preliminary data indicate that individualized pre-transplant nutritional intervention is feasible, well-tolerated, and contributes to stabilizing nutritional status before allo-HCT, supporting its integration into pre-transplant care pathways.

Disclosure: This study has no funding.
Authors have no conflicts of interest.

NG12-02

HIGH LEVELS OF SYMPTOMS ARE LINKED TO STRONGER SELF-CARE MANAGEMENT IN ALLO-HCT SURVIVORS

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Background: Long-term survivors after allogeneic hematopoietic stem cell transplantation (allo-HCT) often live with persistent symptoms that require ongoing self-care. Empirical knowledge about self-care management post-transplant is limited. This study examined self-care management, levels of symptoms and associated factors among allo-HCT survivors.

Methods: This retrospective cross-sectional survey study included allo-HCT survivors 1-4 years post-transplant (n=126). Data were collected using the Self-Care Management Scale (0-100) from the SC-CII questionnaire, based on the middle-range theory of self-care of chronic illness, as well as the global health item and the nine symptom scales from the EORTC QLQ-C30, which assess the occurrence and levels of common cancer-related symptoms. Scores were dichotomized into a "high-symptom group" and a "low-symptom group". A high-symptom score was defined as ≥66 on any EORTC QLQ-C30 symptom scale (0-100). Differences at the group level were analyzed with t-tests, and predictors of self-care management were examined using multivariable linear regression. The significance level was set to $p \leq 0.05$.

Results: The sum score for the self-care management scale showed a mean value of 57.8 (SD 20.1), indicating that self-care management varied among participants. A distributional plot showed marked heterogeneity within the high-symptom group, with a median self-care management score of 60 (range 25-100) (Figure 1). 10% reported no symptoms, while 72% reported at least three different symptoms of any level on the EORTC QLQ-C30 symptom scales.Survivors with high levels of fatigue, pain or dyspnea reported statistically significantly higher levels of self-care management compared with those with no or low levels of symptoms. When summarizing symptom levels across the nine sub-scales, the high-symptom group reported higher self-care management than the low-symptom group (mean 63.6 versus 54.2, p=0.012).

Younger survivors reported higher self-care management. In multivariable linear regression, younger age (β ≈ −0.37 per year, p=0.011) and high symptom levels (β ≈ 8.65, p=0.020) were independently associated with higher self-care management, while global health showed no association. The model explained 13% of the variance in self-care management.

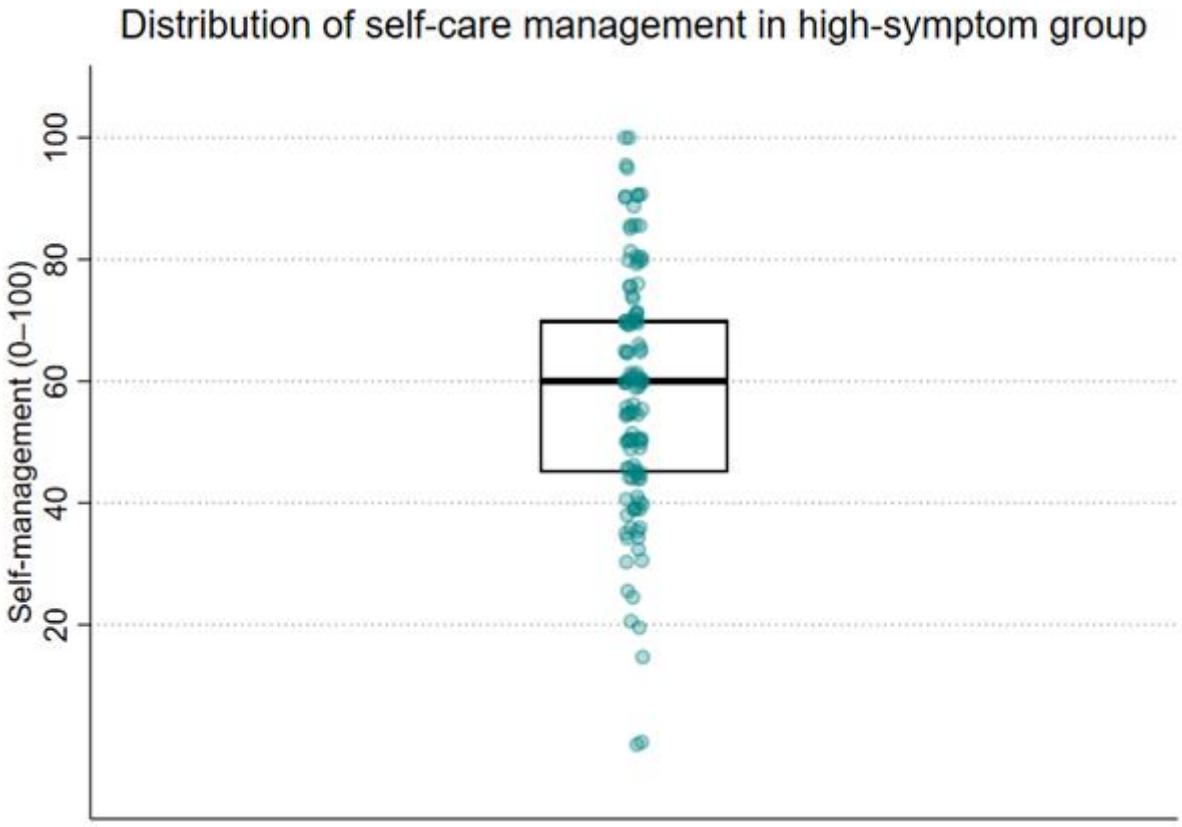

Figure 1. Distribution of self-care management scores among allo-HCT survivors classified in the high-symptom group (n=57).

Conclusions: Self-care management among allo-HCT survivors varied, with survivors with high levels of symptoms reporting higher self-care management. The associations suggest that higher levels of symptoms may prompt self-care management efforts but do not fully explain the variation observed between individuals. These findings add to current knowledge of long-term survivorship after allo-HCT and indicate that considering both symptom levels and self-care management patterns in structured follow-up may better reflect survivors' ongoing needs.

Disclosure: Nothing to declare.

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NG12-03

LONGITUDINAL ASSESSMENT OF STRENGTH, FITNESS, NUTRITION AND QUALITY OF LIFE IN ADULTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION: CALL FOR MULTIMODAL AHP CLINICS ACROSS TRANSPLANT CONTINUUM

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Background: Allogeneic haematopoietic stem cell transplantation (allo-HSCT) is a potentially curative for haematological cancers but is accompanied by treatment-related toxicities and prolonged inactivity that drive deconditioning, fatigue and reduced quality of life (QoL). Evidence for routine prehabilitation in allo-HSCT remains limited in real-world practice, and longitudinal datasets capturing objective function alongside patient-reported outcomes across admission, discharge and early survivorship are scarce. Objective pre-transplant function and nutritional impairment are clinically relevant, yet serial multimodal assessment is inconsistently embedded across the transplant continuum, limiting benchmarking and timely allied health professional (AHP) input. We embedded a pragmatic minimum dataset to characterise trajectories from pre-transplant to early survivorship and identify delivery barriers to inform multimodal AHP clinic development.

Methods: Following Royal Marsden Quality Improvement Committee approval, outcome measures were embedded using Plan-Do-Study-Act (PDSA) methodology and ASCT candidates were recruited (April 2024-September 2025). Assessments occurred pre-transplant (T1), on admission (T2), pre-discharge during (T3), and 12 weeks post-discharge (T4). Outcomes measured were BMI as pragmatic nutritional indicator, 30-second sit-to-stand (30-STS), grip strength, peak power output (PPO) and estimated VO_2peak (T1/T4 only, for safety and logistical reasons), Functional Status Score-ICU (FSS-ICU), FACIT-Fatigue, and EQ5D-5L. Data was summarized descriptively and contextualised to age-related norms. Reasons for missed assessments were prospectively recorded; usual-care AHP input occurred but was not standardised for evaluation.

Results: Eighteen patients were recruited (mean age 59.8 years; 77.8% male) over 16 months versus a forecast of 20 completing within 6 months. Completeness decreased across time points (T1 n=18; T2 n=16; T3 n=15; T4 n=13–15) due to intercurrent illness, competing appointments, travel burden and variable transplant timelines. BMI declined from 26.7 to 23.9 kg/m². 30-STS remained sub-normative from baseline median 11.5 (IQR 9.8–14.3) to 11.0 (IQR 7.8–15) at T4, with 69–80% below an age-expected threshold across time points. Handgrip strength fell from 33.8 kg to 25kg (left) and 33.1 kg to 26.3 (right). Aerobic capacity was low and worsened: PPO 1.37±0.38 to 1.20±0.51 W/kg and estimated VO2peak 17.7±4.1 to 15.2±5.2 mL·kg−1·min−1, remaining below conservative age-expected values in nearly all participants indicating reduced physical capacity and endurance. Mean FACIT-Fatigue dropped from 39.9 to 29.1 before partial recovery to 36.5 with scores <43 occurring in 50% at T1 and 93.3% at T3. EQ-5D-5L VAS declined from 74.4 to 52.0 with

partial recovery to 66.8 and drop of index score from 0.88 (T1) to 0.78 (T4). FSS-ICU declined from 35.0±0.0 (T1) to 32.0±5.3 (T4), with 35.7% <35 at T4 despite inpatient rehabilitation.

Outcome Measure	Baseline (4-8 weeks) (n=17-18)	Admission (n=16)	Pre-DC (n=15)	12-weeks Post-DC (n=13-15)	Normative Values (Age 60)
BMI	26.7 (SD 5.2)	26.5 (SD 4.6)	25.3 (SD 4.8)	24.0 (SD 4.5)	18.5–24.9 (healthy)
30-STS (reps)	11.5 (IQR 9.8–14.3)	12.5 (IQR 9.3–17.3)	13.0 (IQR 9–14)	11.0 (IQR 7.8–15.0)	Male: >14 Female: >12
Left Grip Strength	33.8 (SD 8.0)	31.6 (SD 7.5)	28.7 (SD 8.4)	25.0 (SD 8.1)	Male: 37.25kg Female: 23.47kg
Right Grip Strength	33.1 (SD 9.0)	33.0 (SD 8.9)	30.2 (SD 9.4)	26.3 (SD 7.2)	Male: 37.25kg Female: 23.47kg
Peak Power Output (W/kg)	1.37 (SD 0.38)	N/A	N/A	1.20 (SD 0.51)	1.5
Estimated VO_2peak (ml/kg/min)	17.7 (SD 4.1)	N/A	N/A	15.2 (SD 5.2)	Male: 26 Female: 18
FACIT-Fatigue	39.9 (SD 9.9)	37.8 (SD 10.9)	29.1 (SD 12.3)	36.5 (SD 13.4)	43-50
EQ-5D-5L VAS	74.4 (SD 16.4)	66.9 (SD 17.9)	52.0 (SD 22.3)	66.8 (SD 15.4)	N/A 100 (perfect state)
EQ-5D-5L Health Index State	0.88 (SD 0.14)	0.89 (SD 0.12)	0.75 (SD 0.26)	0.78 (SD 0.24)	N/A 1.0 (perfect state)
FSS-ICU	35 (SD 0)	34 (SD 2.2)	34 (SD 1.82)	32.0 (SD 5.3)	35 (ceiling)

Conclusions: Allo-HSCT recipients demonstrated prevalent baseline impairment, predictable inpatient deterioration and incomplete recovery by 12 weeks post-discharge across strength, fitness, fatigue, QoL and independence. A PDSA-embedded multimodal dataset can standardise longitudinal assessment, but access constraints and measurement limitations require further iterative refinement. These data provide a strong rationale to design and prospectively evaluate structured multimodal AHP-led clinics spanning prehabilitation, early survivorship and late effects. Limitations include generalizability of findings due to small sample size and data sets changes due to scheduling constraints, geography and agile transplant timelines.

Disclosure: Nothing to declare.

NG16-01

LATE EFFECTS AND SYMPTOM BURDEN AMONG LONG-TERM SURVIVORS AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A NATIONWIDE CROSS-SECTIONAL STUDY

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Background: Survival after allogeneic hematopoietic stem cell transplantation (allo-HSCT) has improved substantially, resulting in an expanding population of long-term survivors who might be expected to have quality-of-life levels comparable to the general population. However, many remain at risk of late effects, prolonged immunosuppression, and chronic graft-versus-host disease (cGvHD), which may impair functioning and overall well-being. Despite this, long-term outcomes from the survivor perspective are insufficiently described, and large multicenter studies using patient-reported outcomes (PROs) are limited. This study aimed to assess symptom burden, functional outcomes, and survivorship-related quality of life among Danish allo-HSCT survivors, including comparisons with population norms.

Methods: We conducted a nationwide, multicenter cross-sectional study including all adults (≥18 years) who received a first allo-HSCT at Copenhagen University Hospital, Rigshospitalet (since 1973) or Aarhus University Hospital (since 2009). Eligible participants resided in Denmark or Greenland at survey initiation (May 2024).
PROs were assessed using the validated European Organization for Research and Treatment of Cancer Quality of Life Cancer Survivorship Core Questionnaire (EORTC QLQ-SURV100), which captures survivorship-specific domains and allows calculation of EORTC QLQ-C30 scores, and the Modified 7-Day Lee cGvHD Symptom Scale (MLSS). Clinical data included diagnosis, comorbidity, treatment characteristics, and cGvHD status. The study was approved by the Danish Data Protection Agency (P-2022-391) and the ethics committee.

Results: Of 2.701 patients who underwent allo-HSCT, 1.341 were eligible, and 895 responded (66.7%). The median age at survey was 55 years, with a median time since transplantation of 6.2 years; 34.6% of participants were ≥10 years post-HSCT.
The most frequently reported symptoms were joint pain (31%), fatigue (27%), muscle weakness (25%), and sexual problems (25%). Psychosocial strain was common, with 37% reporting moderate-to-severe problems related to loss of income. Survivors reported a significantly higher symptom burden compared with Danish population norms, including fatigue (mean diff 14.7, $p < 0.0001$), pain (mean diff 5.1, $p < 0.0001$) and financial

difficulties (mean diff 10.6, p < 0.0001). Across functional domains, survivors consistently scored lower than the general population, including physical functioning (mean diff −15.7, p < 0.0001), role functioning (mean diff −16.0, p < 0.0001), emotional functioning (mean diff 4.8, p < 0.0001), cognitive functioning (mean diff −11.7, p < 0.0001), and social functioning (diff −18.4, p < 0.0001). Overall, survivors reported significantly reduced global health scores compared to population norms (mean diff −5.1, p < 0.001).
Employment status indicated that 36% were employed, while 14% received disability pensions despite a median age of 55 years. Fertility concerns were reported by a subset of participants (n=187), with 52% indicating a severe impact. Approximately 60% had documented cGvHD, which was associated with higher MLSS symptom scores.

Conclusions: This nationwide study highlights the substantial symptom burden, functional impairments, and psychosocial challenges experienced by allo-HSCT survivors. The findings underscore the need for structured survivorship care, including routine PRO monitoring and targeted interventions to address fatigue, pain, sexual health, psychosocial concerns, and socioeconomic vulnerability. These insights can inform the development of nurse-led, individualized survivorship programs aimed at optimizing long-term quality of life in this population.

Clinical Trial Registry: Clinicaltrial.gov NCT06277479

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Conflict of interest
The authors declare that they have no conflict of interest.

NG16-02

EMOTIONAL BURDEN PREDICTS MORTALITY 5 YEARS AFTER ADULT HEMATOPOIETIC CELL TRANSPLANTATION: THE PROSPECTIVE SWISS TRANSPLANT COHORT STUDY

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Background: Emotional burden (EB)—including depressive symptomatology, anxiety, and stress—can occur independently of a clinical diagnosis and is assessed via Patient-Reported Outcomes (PROs). EB affects a substantial proportion of hematopoietic cell transplantation (HCT) recipients and may influence survival. However, prior studies often lacked longitudinal assessments and adjustment for critical clinical predictors such as relapse or graft-versus-host disease (GvHD). This study aimed to
(1) describe EB trajectories from pre- to 5-years post-HCT and
(2) to evaluate the impact of EB on 5-year overall survival (OS).

Methods: We conducted a secondary data analysis of the Swiss Transplant Cohort Study (STCS), a multicentre prospective open cohort study. We analyzed adult HCT recipients (≥18 years) from Zurich, Geneva and Basel enrolled in the STCS from 2013–2018, linked to the EBMT-Registry for clinical data (demographic and clinical outcome data). Datasets were deterministically linked using core identifiers. In the STCS, EB (depressive symptomatology, anxiety, stress) is assessed using HADS-D, one EQ-5D-5L anxiety item, and a single-item stress scale at ~3 months pre-HCT, 6 and 12 months post-transplant, and annually thereafter. Primary outcome was OS at 5 years. Aim 1 used descriptive statistics and alluvial (Sankey-style) diagrams to characterize trajectories. Aim 2 employed Cox proportional hazards models with time-dependent EB measures. Models were adjusted for baseline sociodemographic and clinical covariates (age, sex, education, diagnosis, conditioning regimen, graft source, donor type, remission status, and GvHD) to estimate hazard ratios (HRs). Synergistic effects were tested by averaging our three standardized outcomes into one single score. Analyses were conducted in SAS 9.4 (two-sided α=0.05).

Results: The cohort included 1,028 HCT recipients (mean age 51.7 years; 61.6% male, Table 1)

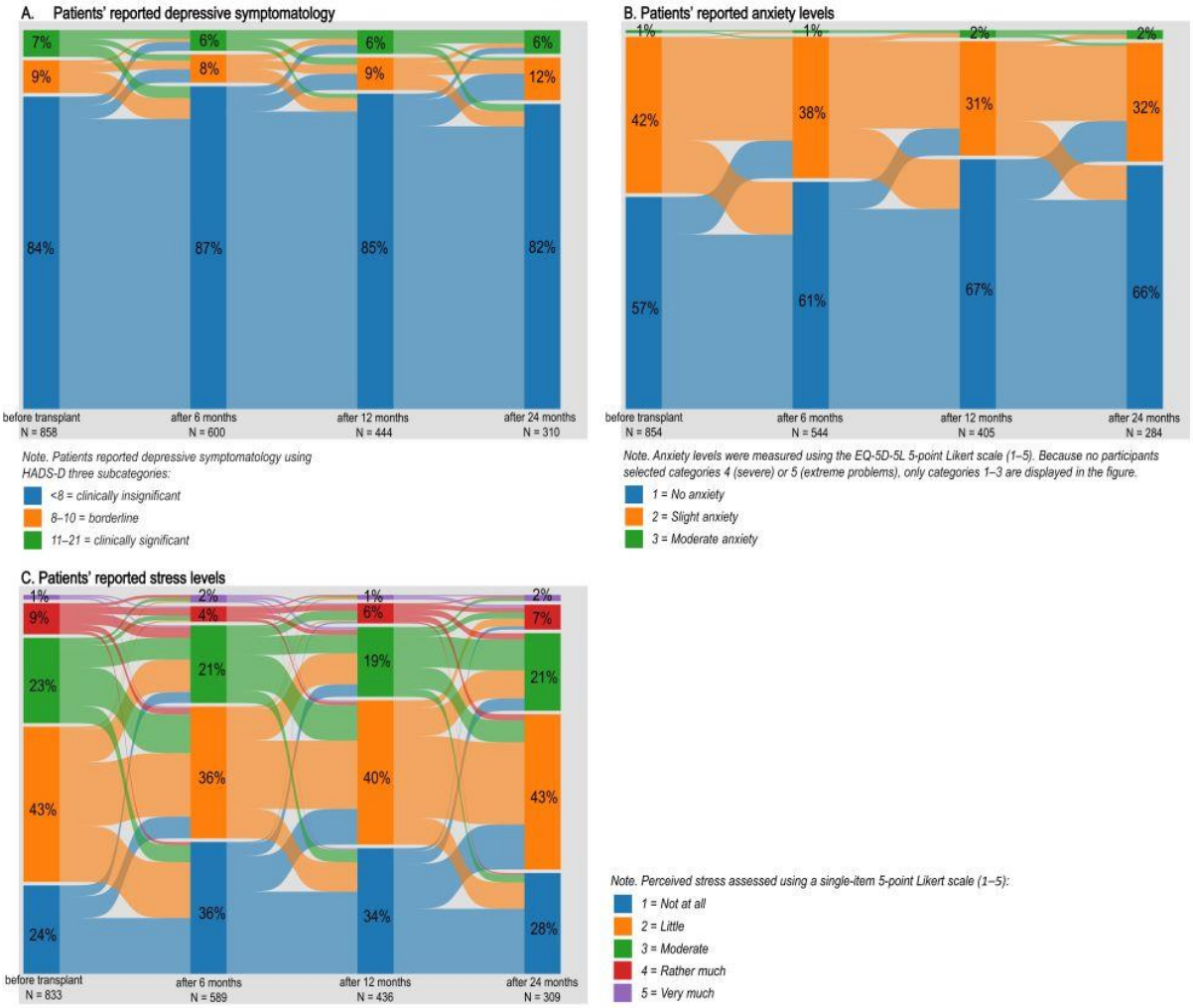
Table 1. Sociodemographic and clinical characteristics of the study population (N = 1028)

Characteristic	**Value**
Sex, male	633 (61.6%)
Age (years)	Mean = 51.7 (SD 13)
Living alone	264 (29%)
Underlying diagnosis	
– Acute leukemia	530 (53%)
– Myelodysplastic syndrome	231 (23%)
– Lymphoma	108 (11%)
Time from diagnosis	Median = 7 months (IQR 17)
Donor type	
– Sibling	346 (34%)
– Unrelated	499 (50%)
Remission at transplant	577 (59%)
Acute GvHD (Grade I–II)	322 (32%)
Chronic GvHD	202 (21%)

Note. Values are presented as n (%), mean (SD), or median (IQR).

As shown in the alluvial diagram (Fig. 1A–C), depicting the first two years post-HCT, EB remained relatively stable over time. However, across all measurement timepoints, 6–7% reported clinically relevant depressive symptomatology, about one-third anxiety, and up to 9% very high stress levels.

Figure 1A-C. Emotional burden (depressive symptomatology, anxiety & stress) from pre- to 2 years post HCT



EB significantly predicted 5year-OS: Each one-point increase in depressive symptoms was associated with a 7% higher mortality risk (HR 1.07, 95% CI 1.04–1.10, $p < 0.0001$). Higher anxiety levels conferred a 35% increased risk (HR 1.35, 95% CI 1.09–1.68, $p = 0.0069$). Elevated stress predicted an 18% higher risk (HR 1.18, 95% CI 1.05–1.33, $p = 0.0071$). Importantly, all EB associations remained significant after adjusting for the clinical and demographic variables, i.e. they did not attenuate the effect of depressive symptomatology, anxiety, or stress on OS, suggesting an independent prognostic role of EB. The combined EB

score showed a 29% higher mortality risk than any single dimension, suggesting synergistic effects.

Conclusions: EB independently and robustly predicted poorer 5-year OS in HCT recipients, even when accounting for key clinical risk factors such as relapse and GvHD. These findings highlight the clinical relevance of systematically assessing EB and integrating timely psychosocial support into post-HCT care to potentially improve long-term outcomes.

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NG16-04

A MULTIMODAL APPROACH TO SEXUAL FUNCTION FOLLOWING ALLOGENEIC STEM CELL TRANSPLANTATION: A RANDOMIZED CONTROLLED STUDY

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Background: Improved survival after allogeneic HSCT has led to a growing population of long-term survivors who frequently experience sexual dysfunction. Genital chronic GVHD (cGVHD) is a key contributor, with reported prevalence of 19–66% in women and 5–20% in men, yet it remains underdiagnosed due to nonspecific symptoms and limited routine screening. Sexual function may be further affected by GVHD in other organs, medication effects, body image concerns, and psychological distress. Although guidelines recommend systematic assessment, sexual health is often insufficiently addressed in clinical practice. This study investigated the feasibility and effect of a multimodal randomized intervention targeting sexual function in HSCT recipients.

Methods: This multicenter, prospective randomized controlled trial was conducted at two Danish transplant centers from 2022–2025. Adults scheduled for allogeneic HSCT were enrolled before transplantation and randomized 1:1 to a multimodal intervention or usual care. The intervention comprised six assessments over 18 months, including sexual health questionnaires (EORTC QLQ-SH22), specialist genital evaluations, and nurse-led consultations guided by a standardized protocol. Usual care involved symptom-driven evaluation only. Sexual function was measured using the Female Sexual Function Index (FSFI) for women and the International Index of Erectile Function (IIEF-15) for men.

Secondary outcomes included broader sexual health indicators, levels of sexual distress, and feasibility measures related to intervention implementation and participant adherence.

Results: Of 135 eligible patients, 117 (86.7%) were enrolled and randomized; 41 discontinued by 18 months due to relapse, death, or withdrawal. Overall sexual function did not differ significantly between groups for women (difference 3.3, P=0.391) or men (difference 0.9, P=0 .761). Significant improvements favoring the intervention group were observed in women's sexual pain (diff -2.1, P=0.019) and, for both genders, in sexual pain (diff -13.6, P=0.030), communication with professionals (diff -15.5, P=0.017), and partnership quality (diff -22.8, P=0.040). Genital cGVHD occurred in 17.1%, with earlier detection in the intervention group. In the control group, only three cases were identified outside protocolized assessments. Median onset occurred earlier in the intervention group (365 vs. 547 days). Most cases were mild. Adherence to questionnaires, genital assessments, and nurse-led consultations was high. Across 205 counseling sessions, common concerns among women included vaginal dryness, low desire, and internal pain; men most frequently reported erectile difficulties and reduced desire.

Conclusions: We conclude that the multimodal intervention was feasible with improved sexual health, and facilitated earlier recognition of genital cGVHD, supporting the integration of interdisciplinary sexual health assessments into routine post-HSCT care.

Clinical Trial Registry: **Clinical trial registration number:** NCT05222282

Disclosure: None

NG27-03

QUALITY OF LIFE AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION IN ADOLESCENTS AND YOUNG ADULTS: INSIGHTS FROM A DANISH CROSS-SECTIONAL STUDY USING THE EORTC QLQ AYA QUESTIONNAIRE

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Background: In Denmark, approximately 1,400 adolescents and young adults (AYAs) are diagnosed with cancer each year, with hematological malignancies accounting for around 30% of cases. Hematopoietic stem cell transplantation (HSCT) is a well-established curative treatment for a subgroup of these patients. Advances in transplantation procedures, supportive care, and post-transplant monitoring have significantly improved survival outcomes for AYA's. Nevertheless, survivors remain at increased risk of late complications and premature mortality, highlighting the need to better understand their long-term quality

of life (QoL) and supportive care needs in this population. Notably, the recently developed and validated EORTC QLQ-AYA questionnaire provides a comprehensive, AYA specific assessment of quality QoL, complementing existing generic instruments. The aim of this study is to investigate QoL, symptom burden and sexual health in Danish AYAs following HSCT, using the newly validated EORTC QLQ-AYA, to inform strategies for optimizing long-term outcomes.

Methods: This nationwide cross-sectional study includes AYA's aged 18–29 years at transplantation who underwent a HSCT for a hematologic malignancy in Denmark, and who were ≤39 years at study participation. Participants completed four electronically administered validated questionnaires; The European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Adolescents and Young Adults (EORTC QLQ AYA27), EORTC QLQ-C30, EORTC Sexual Health Questionnaire 22 (EORTC QLQ-SHQ22), and the Lee Symptom Scale.

Results: A total of 48 participants completed the survey (45,3 %), with a mean age of 31.1 years and an equal gender distribution. Overall QoL was generally high, however women reported lower QoL than men with significantly lower scores on global health ($p = 0.04$), emotional functioning ($p < 0.001$), and cognitive functioning ($p < 0.001$). Participants reported positive personal changes (mean: 53.1 ± 27.5) but also notable concerns regarding future worry (mean: 32.2 ± 24.6) self-esteem (mean: 31.0 ± 31.9), and sexual life (mean: 32.5 ± 35.9). Compared with existing reference data, participants scored lower on emotional functioning, cognitive functioning, and financial difficulties than other hematological patient groups and Danish population norms.
Sexual health assessment revealed that 44.7% of participants had never been asked about their sexual wellbeing. Gender-specific symptom patterns were evident as women reported high levels of vaginal dryness, whereas men expressed notable concerns regarding confidence in erection. Importantly, women also reported substantially poorer body image, scoring approximately twice as poorly as men, underscoring a marked gender disparity in body-related wellbeing.

Conclusions: This study, employing the newly validated EORTC QLQ-AYA, provides a detailed assessment of QoL, symptom burden, and sexual health in AYA HSCT survivors. Findings highlight significant gender disparities and unmet supportive care needs, emphasizing the importance of tailored interventions and follow-up strategies to optimize long-term QoL in this population.

Disclosure: Nothing to delare.

NP04

QUALITY OF LIFE, ANXIETY AND DEPRESSION IN HSCT RECIPIENTS. A 12-MONTH LONGITUDINAL STUDY

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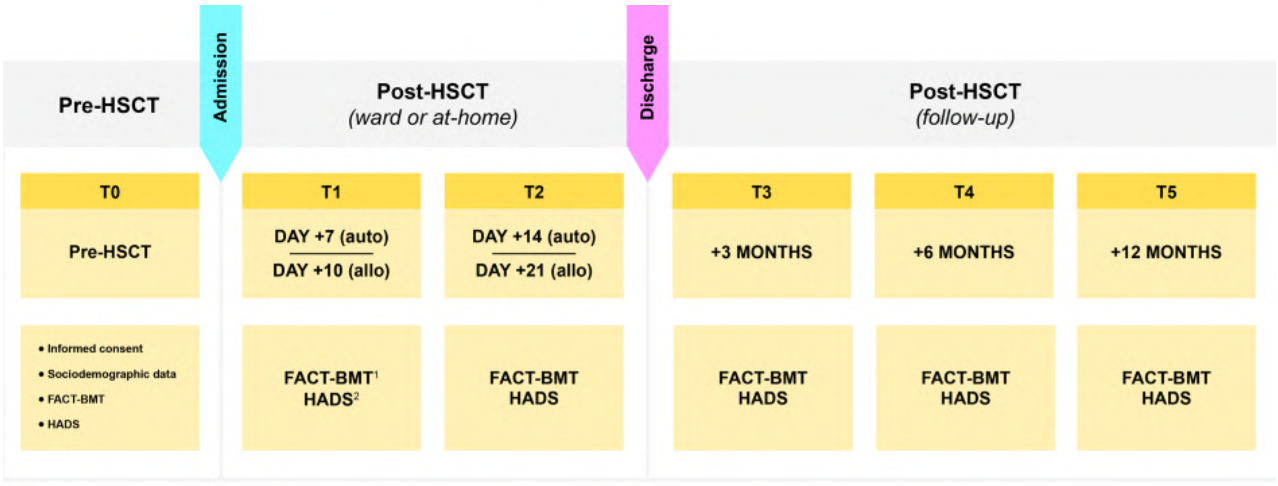
Background: Receiving an HSCT has been associated with impaired quality of life (QoL) and mental health. Our aim is to describe the evolution of QoL, anxiety and depression, in HSCT recipients from pre-HSCT to 1-year post-HSCT.

Methods: An observational prospective longitudinal study was conducted between October 2019 and February 2022. Participants were recruited through consecutive sampling. FACT-BMT and the Hospital Anxiety Depression Scale were administered in 6 time points (Figure 1) to evaluate QoL and anxiety and depression, respectively. Instrument score changes over time were analyzed using an adjusted linear mixed model.



Results: 72 patients were included, 63.9% of whom were men, with mean age 52 (SD 12.6). 52.8% HSCTs were allogeneic and 50% were conducted in an at-home programme. The main reasons for HSCT were a diagnosis of leukaemia (36.1%), multiple myeloma (31.9%) and lymphoma (20.8%).
A significant decrease in QoL was observed, with a drop of 8.93 points on the FACT-BMT scale (p.0.01) during admission (T1). Results gradually recovered and improved baseline outcomes at 6 and 12 months post-HSCT. The most affected QoL domains during the acute period (T1) were physical (loss of 4.68 points, p <0.001) and functional (loss of 4.16 points, p <0.001). In contrast, the social domain remained stable through all the trajectory, while the emotional domain presented a slight, gradual improvement in values up to six months post-HSCT (p. 0.01).
Regarding anxiety, 32.4% of participants met anxiety criteria at pre-HSCT. Results didn't change during admission (T1) but decreased to 18.7% as discharge approached (T2). Results worsened when achieving 3 months post-HSCT, with 31.1% of participants meeting anxiety criteria, and results dropped to 24.1% at 12 months. For depression, we observed

12.5% incidence prior to HSCT. Patients with depression increased to 36.5% during the acute period (T1 and T2) but then progressively fell to 16.7% at 12 months.
Allogeneic recipients scored 2.51 points lower in physical well-being (p = 0.001) but 1.91 points higher in social well-being (p = 0.011) than autologous recipients. Patients receiving homecare HSCT scored 1.91 points lower in social well-being (p = 0.011) than hospitalised patients, with no other differences observed.

Conclusions: Patients' QoL declined during the acute phase but improved in the medium term. Heightened psychological distress at all time-points was observed, but values improve during follow-up. Admission proved critical for early detection and treatment of depression, while anxiety was lowest at T2 (+14 days post-autoHSCT, +21 days post-alloHSCT). Except for social well-being, QoL outcomes were similar between hospitalised and homecare patients, supporting at-home HSCT programmes as a safe and feasible option.
Understanding QoL and mental health trajectories is key to refining interventions that enhance physical, functional, and psychological wellbeing, specifically during the acute HSCT period.

Clinical Trial Registry: Not applicable.

Disclosure: Nothing to declare.

NP13

COULD PROPHYLACTIC NASOGASTRIC TUBE FEEDING REDUCE WEIGHT LOSS FOR PATIENTS UNDERGOING HIGH-TOXICITY CONDITIONING REGIMENS DURING AUTOLOGOUS STEM CELL TRANSPLANT?

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Background: Autologous stem cell transplant (auto-SCT) patients are vulnerable to malnutrition due to reduced oral intake from conditioning-related gastrointestinal toxicities. Identifying which conditioning regimens place patients at highest risk may help determine who could benefit most from prophylactic nasogastric tube feeding.

Methods: A retrospective, quantitative, single-centre study of adult haematological cancer patients who received auto-SCT at University College London Hospital from April 2023 to March 2025 was undertaken. Data including weight change, mode of nutritional support and length of stay were collected from the centre's electronic patient records and compared between different conditioning regimens using appropriate parametric and nonparametric statistics.

Results: Three hundred and eighty four patient were included, 60% male, median age 58 years, 69% had multiple myeloma, 21% Non-Hodgkin lymphoma, 51% were conditioned

with melphalan 200, 20% with L(B)EAM (lomustine or carmustine with cytarabine, etoposide and melphalan), 19% with melphalan 140, 10% with TT-BNCU (thiotepa and carmustine). From day 0 to day 11-13 there was a significantly greater percentage weight loss in those who received conditioning with TT-BNCU compared to those who received melphalan 200 (mean ±SD, -4.22% ±4.20 v -1.46% ±4.04, p=0.0008) and melphalan 140 (0.55% ±3.88, p=0.0001). Patients who had L(B)EAM had a significantly longer length of hospital stay (24.76 days ±20.67) than those who had melphalan 200 (18.65 days ±6.10, p<0.001) and melphalan 140 (20.52 days ±9.63, p=0.0016), as did those who had TT-BNCU (45.10 days ±52.21) compared to melphalan 200 (p<0.001) and melphalan 140 (p<0.001). Those who did not receive nasogastric tube feeding (92%, 352/384) lost significantly more weight than those who did (8%, 32/384), -2.06% ±3.91 v -0.93% ±4.98, p=0.000064. There was a significantly greater frequency of early neutrophil engraftment (<13 days) in those who received nasogastric tube feeding than those who did not (100% vs 85.5%, p=0.021).

Conclusions: Haematological cancer patients undergoing auto-SCT with TT-BNCU or L(B)EAM conditioning regimens are at significantly higher risk of early weight loss and longer hospital stay compared to those receiving melphalan 200 and 140. These results highlight a potential role for prophylactic nasogastric tube feeding in patients receiving high-toxicity regimens to minimise unintentional weight loss and support nutritional recovery throughout auto-SCT to reduce length of stay. Further prospective research is warranted to evaluate the feasibility, safety and long-term impact of prophylactic nasogastric tube feeding in patients receiving high-toxicity regimens.

Disclosure: Nothing to declare.

NP15

LATE TOXICITIES AND QUALITY OF LIFE AFTER VARNIMCABTAGENE AUTOLEUCEL (VAR-CEL): THE ROLE OF ADVANCED PRACTICE NURSING

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Background: As long-term survival after CAR-T therapy increases, late toxicities and health-related quality of life (QoL) have become a priority. Current evidence highlights immune dysfunctions, recurrent infections, and neurocognitive, emotional, and social challenges. However, findings remain limited, and structured frameworks for the care of long-term survivors are lacking. This study aims to evaluate late toxicities and QoL among Varnimcabtagene Autoleucel® (var-cel) survivors and to examine the contribution of advanced practice nursing (APNCART) in longitudinal follow-up.

Methods: We conducted a cross-sectional observational study between October and December 2025. Eligible participants were adults treated with var-cel (an autologous CD19-directed CAR-T) between 2017 and 2022. Sociodemographic, clinical, and occupational data were extracted from electronic medical records. QoL was assessed using the EORTC QLQ C100 instrument. Descriptive statistics were used to summarise functional and symptom scales, and exploratory analyses identified areas for potential supportive care intervention.

Results: Forty-four survivors treated with var-cel were included. The median age was 52 years (range 27 to 80). Acute lymphoblastic leukaemia was the most common indication (64%), and 57% had prior haematopoietic stem cell transplantation (HSCT). Following var-cel, 72%Seventy-two percent developed cytokine release syndrome, 36% suffered any-grade infections, and no cases of ICANS were reported.
Regarding QoL, most survivors reported preserved functioning: Eighty-six percent maintained physical functioning (86%), and preserved functional status (91%), with stable emotional functioning (80%), and cognitive performance (82%).Social relationships were satisfactory in 82%, and 64% reported improved interactions. Half of the individuals noted a positive body image, and 50% a greater sense of purpose following treatment Healthier habits were adopted by 75%, 73% expressed a positive outlook, and 57% reported enhanced social relationships. Additionally, 41% reported strengthened romantic partnerships. Sexual satisfaction was maintained in 50%, while 34% experienced sexual difficulties, and 70% reported fertility problems. The most frequent symptoms were fatigue (75%), sleep disturbances (73%) and general discomfort (66%). Severe pain was reported by fewer than 9%. Financial stress was mild to moderate in most cases (83%).
In terms of late toxicities, recurrent infections were experienced in 75%, with 59% requiring immunoglobulin supplementation, and 11% developed chronic graft-versus-host disease (all related to prior HSCT). Almost all survivors (98%) adhered to vaccination and preventive screening programs. In employment status, 39% were working; the remainder were retired or pensioners.

Conclusions: Adult long-term survivors treated with var-cel generally maintain functional status and psychosocial resilience. However, fatigue, sleep disturbances, sexual/fertility issues, and immune vulnerability remain prevalent, alongside moderate financial stress. These findings underscore the importance of APNCART in designing and implementing structured survivorship programs. Through long-term follow-up, APNCART coordinates comprehensive care by monitoring symptom, ensures adherence to vaccination and preventive measures, and supports symptom management. Direct involvement in fatigue control, sexual health counselling, and psychosocial support reinforces continuity of care and promotes active self-management.
In summary, the results describe clinical stability and social adaptation, with manageable late toxicities. Developing integrative nurse-led models is essential to optimise long-term outcomes and enhance QoL beyond survival.

Disclosure: Not conflict interest.

NP18

THE EXPERIENCE OF PATIENTS UNDERGOING CAR T CELL THERAPY: A PHENOMENOLOGICAL-INTERPRETATIVE STUDY

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Background: In recent years, immune therapy, particularly that based on chimeric antigen receptor T cells (CAR-T), has represented one of the most promising treatments in the oncology and haematological field(1-3). Despite clinical efficacy, CAR T-cell therapy is associated with adverse events, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS)(4–6). CAR-T cell therapy and its associated toxicities can have a significant impact on patients' quality of life(7). A qualitative study found that a significant portion of patients undergoing CAR T therapy experienced difficulties in maintaining social relationships, during and after therapy; while 72% experienced fears regarding the efficacy of the treatment(8) The scientific literature still shows a lack of qualitative studies that explore the experience lived by patients during this therapeutic path. The aim of this study was to investigate the experiences of people undergoing CAR T therapy, exploring their fears, difficulties encountered, and the strategies adopted to address them.

Methods: A qualitative phenomenological-interpretative approach inspired by Patricia Benner's theoretical framework was adopted(9). This perspective allowed us to grasp the participants' experience in their embodied dimension, valorising the meaning attributed to illness and treatment(10)
Five semi-structured interviews were conducted with patients treated with CAR T cells at the National Cancer Institute in Milan, between 1° February 2025 – 1° October 2025. The interviews were analyzed through a circular hermeneutic process that allowed the emergence of profound meanings and recurring themes.

Results: The sample has a homogeneous distribution by gender, composed of 3 women and 2 men, with a mean age of 54.6 years (range between 35 and 63 years, median 58 years). The analysis revealed four main themes that describe the participants' experiential trajectory: "A leap into the dark"," Relation as an act of care", "From fear to rebirth," and "The Return to Non-Normal". The first theme recounts the entry into the CAR T path, experienced as "A leap into the dark" in which the fear of unknowns and the awareness of refractory disease intertwine. The second theme concerns the relationship with the healthcare team, experienced as an" Act of care." Transparent communication, along with autentic listening generates trust. The third theme, "From fear to rebirth", concerns strategies that help patients nurture hope. The final theme is "The return to new normality", which highlights the need to redefine everyday life, listening to one's own fragilities after therapy**.**

Conclusions: Participants describe a transformative process in which illness, therapy, and convalescence redefine body, relationships, and time, producing a new, more fragile, and consecrated-vole "non-normality".

The findings offer a deeper understanding of the experience of patients undergoing CAR T therapy, orienting nursing practice toward a care model that is more attentive to the needs of patients and their caregivers, placing greater importance on communication and education.

Disclosure: I have no conflicts of interest.

NP40

FINANCIAL TOXICITY AND ITS INFLUENCING FACTORS IN PATIENTS WITH ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CHINA: A CROSS-SECTIONAL STUDY

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a potentially curative treatment for various hematologic malignancies. However, the substantial and prolonged costs associated with the procedure, lifelong immunosuppression, and management of complications such as graft-versus-host disease impose a severe economic strain on patients and their families, a phenomenon termed financial toxicity (FT). While FT is increasingly recognized globally, data specific to Chinese allo-HSCT patients remain scarce. Given China's unique healthcare system and socio-cultural context, understanding the prevalence and determinants of FT in this population is crucial for developing tailored supportive interventions.

Methods: A cross-sectional study was conducted at a major tertiary hospital in Shanghai between March 2024 and June 2025. A sample of 114 adult patients who had undergone allo-HSCT was recruited via convenience sampling. FT was measured using the validated Chinese version of the Comprehensive Score for Financial Toxicity (COST), where lower scores indicate higher toxicity. Perceived social support was assessed with the Perceived Social Support Scale (PSSS), and psychological resilience was evaluated using the Connor-Davidson Resilience Scale (CD-RISC). Demographic, clinical, and socioeconomic data were collected via a structured questionnaire. Statistical analyses included descriptive statistics, univariate tests (t-tests, ANOVA), Pearson/Spearman correlations, and hierarchical multiple linear regression to identify independent predictors of FT.

Results: The mean COST score was 18.73 ± 7.25, indicating severe financial toxicity (established threshold: COST<22). Univariate analyses identified several significant correlates of FT ($p<0.05$), including lower educational attainment, rural residence, lower monthly household income per capita (<3000 RMB), unemployment or sick leave due to illness, and type of health insurance. Correlation analyses revealed that both higher perceived social support ($r=0.303$, $p=0.001$) and greater psychological resilience ($r=0.365$, $p<0.001$) were significantly associated with lower FT (higher COST scores). Hierarchical regression, controlling for significant demographic and clinical variables, demonstrated that social support independently explained 8.7% of the variance in FT ($\Delta R^2=0.087$, $p<0.001$), and resilience contributed an additional 2.1% ($\Delta R^2=0.021$, $p=0.023$). A monthly household

income >5000 RMB was a strong protective factor. A notable and counterintuitive finding was that patients with a junior high school education reported significantly higher FT than those with only an elementary school education.

Table Hierarchical regression analysis of FT in patients with allogeneic hematopoietic sten

Variable		Model 1 β (95%CI)	*P*	Model 2 β (95%CI)	*P*
Employment status	Employed/Retired	/	/	/	/
	unemployed	-3.372 (-6.502, -0.243)	0.035	-3.313 (-6.172,-0.454)	0.024
	Sick leave	-4.103 (-7.892, -0.313)	0.034	-4.753 (-8.228, -1.279)	0.008
Residence	Countryside				
	City	-0.401 (-3.454, 2.652)	0.795	0.164 (-2.637, 2.964)	0.908
Family per capita income (monthly) RMB	<3000	/	/	/	/
	3000~	0.95 (-2.634, 4.535)	0.6	1.186 (-2.091, 4.463)	0.474
	> 5000	6.819 (3.391, 10.246)	< 0.001	6.791 (3.659, 9.923)	0
Primary insurance status	New rural cooperative medical insurance	/	/	/	/
	Urban residents' medical insurance	-1.069 (-4.888, 2.75)	0.58	-0.732 (-4.225, 2.761)	0.678
	Urban employees' medical insurance	-3.316 (-7.276, 0.644)	0.1	-3.434 (-7.052, 0.185)	0.063
	Commercial insurance	0.181 (-4.8, 5.161)	0.943	-0.549 (-5.111, 4.013)	0.812
be with other diseases	Yes	/	/	/	/
	No	-2.034 (-5.129, 1.06)	0.195	-1.204(-4.055, 1.646)	0.404
Education level	Primary school and below	/	/	/	/
	Junior high school	-2.235 (-6.962, 2.492)	0.35	-3.609(-7.969, 0.751)	0.104
	Senior high schoo	2.065 (-2.308, 6.437)	0.351	0.474(-3.581, 4.528)	0.817
	College and above	-0.368 (-4.744, 4.009)	0.868	-1.874(-5.925, 2.178)	0.361
Social support				0.166(0.094, 0.238)	<0.001
Resiliency					
adjustR2		0.439		0.531	
ΔR2		0.033		0.087	
ΔF		2.198		20.996	

Conclusions: This study reveals a high burden of financial toxicity among Chinese allo-HSCT survivors, driven by intersecting socioeconomic vulnerabilities such as low income and

unemployment. Importantly, it identifies modifiable psychosocial factors—specifically, robust social support and psychological resilience—as significant independent buffers against FT. The paradoxical finding regarding education level suggests a non-linear relationship and highlights a potentially vulnerable "awareness-penalty" subgroup that may be overlooked. These results underscore the necessity of integrating systematic FT screening into post-transplant care. They also support the development of multi-faceted, evidence-based interventions that combine financial navigation services with strategies to strengthen patients' psychosocial resources, ultimately aiming to improve treatment adherence, quality of life, and long-term outcomes for this high-risk population globally.

Clinical Trial Registry: NA

Disclosure: "Nothing to declare"

NP43

AN APPLIED STUDY OF STEPWISE EXERCISE NURSING PROGRAM FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION PATIENTS

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Background: In recent years, various rehabilitation nursing interventions for HSCT patients have been reported.However, studies focusing on exercise interventions for HSCT patients have mostly been small-sample feasibility studies, lacking high-quality randomized controlled trials, and there is still no unified standard for intervention formats and safety criteria.Moreover, during HSCT, patients often experience significant fluctuations in hematological parameters and are prone to infection or bleeding risks. Therefore, how to conduct effective exercise interventions while ensuring safety remains unclear and lacks evidence-based support.

Methods: A single-center, parallel-group, single-blind randomized controlled trial was conducted. A total of 66 adult HSCT patients were enrolled and randomly assigned to the experimental group (n=33) or the control group (n=33). Based on literature review and data analysis, a stepwise exercise program was developed for patients during HSCT. The experimental group received the stepwise exercise intervention, while the control group received routine exercise education. After the intervention, cardiopulmonary function, joint muscle strength, and self-care ability were compared between the two groups.

Results: After the intervention, patients in the experimental group showed significantly better lower limb muscle strength and longer six-minute walking distances than those in the control group ($P<0.001$), with marked improvement in daily living ability ($P<0.001$). The experimental group also demonstrated better nutritional status and a lower incidence of grade II or higher oral mucositis ($P=0.006$). In terms of psychological status, anxiety and depression were significantly alleviated ($P<0.05$). Regarding transplantation outcomes, the experimental group exhibited faster hematopoietic recovery, reduced transfusion

requirements, shorter febrile duration, and shorter hospital stays (P<0.05). No serious exercise-related adverse events occurred during the intervention.

Conclusions: Stepwise exercise intervention during HSCT in adults is safe and feasible, and it can improve cardiopulmonary function, exercise endurance, psychological status, and nutritional condition. This provides a new model and evidence-based approach for exercise rehabilitation management during HSCT.

Clinical Trial Registry: ChiCTR2200057599 https://www.chictr.org.cn/

Disclosure: Nothing to declare.

NP45

INVESTIGATION OF THE ACCEPTANCE AND APPLICABILITY OF ACCELEROMETRIC MEASUREMENT OF PHYSICAL ACTIVITY BEFORE, DURING, AND AFTER ALLOGENEIC STEM CELL TRANSPLANTATION

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Background: Allogeneic stem cell transplantation (allo SCT) is a complex and demanding form of therapy that can lead to long-term limitations in muscle strength, function and activity levels in affected individuals. Continuous and objective recording of physical activity makes it possible to detect these changes at an early stage and initiate targeted therapeutic measures during treatment and after care.
The aim of the study was to investigate the applicability and acceptance of accelerometric measurement of physical activity before, during and after allo SCT, as well as to analyze subjective and objective activity patterns and changes in strength and body composition.

Methods: The pilot study used a mixed method design with three measurement points. Physical activity was measured using accelerometry and using the Movement and Sports Activity Questionnaire. In addition, handgrip strength, body composition and acceptance were recorded. Qualitative data was evaluated according to Mayring, while quantitative data were analyzed descriptively and by using ANOVA or the Friedman test.

Results: Twelve of the fifteen recruited individuals completed all surveys and measurements. A high level of acceptance and good applicability of the accelerometric measurement were determined. Objectively recorded activity data showed a distinct decline during hospitalization and only partially recovered after discharge. In contrast the duration of bed rest increased continuously over all three measurement points. The subjective assessment reflected this downward trend, but underestimated the level of activity. In addition, handgrip strength, muscle mass and phase angle decreased. At the same time, extracellular mass and its ratio to body cell mass increased, indicating a reduced nutritional and hydration status. Due to the small and heterogeneous sample size the results should be interpreted with caution and confirmed in larger studies with longer observation periods.

Conclusions: The pilot study highlights the relevance of objective activity assessment and shows clinically relevant deterioration in activity, strength, and body composition. At the same time, the high acceptance and applicability of accelerometric measurement prove that this method can be used in the context of allo SZT. The results underline the need for further studies, early identification of at-risk patients, and intensified after care programs. Overall, the study makes a valuable contribution to a field that has otherwise been hardly researched in Germany and contributes to sustainably improve the care structures for this vulnerable patient group.

Disclosure: Nothing to declare.

NP46

LIVED EXPERIENCES AND PERCEIVED QUALITY OF CARE IN ALLO-HSCT: A QUALITATIVE SUBSTUDY OF THE PHARALLO PROGRAMME

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Background: Allogeneic haematopoietic stem cell transplantation (allo-HSCT) profoundly influences patients' emotional, physical and social experiences. The PHARALLO study (PHARmaceutical care program in patients undergoing ALLOgeneic hematopoietic stem cell transplantation), a historically controlled intervention programme conducted at our hospital between 2023 and 2024, evaluated whether a comprehensive pharmaceutical care model improves health and patient-reported outcomes. The programme included structured follow-up through day +100 post-transplant, covering the critical early recovery period. Within this framework, this qualitative substudy explored participants' lived experiences and examined how patients and families perceive care, information and support throughout the transplant process.

Methods: A descriptive qualitative design was used. Patients included in PHARALLO were invited to participate voluntarily in an in-person semi-structured group interview. All participants had already completed the PHARALLO follow-up period (Day +100), ensuring that interviews captured their full early post-transplant recovery experience. Purposeful sampling yielded three patients and one accompanying family member, limited by feasibility constraints related to distance, recent complications or admissions. The interview, facilitated by an expert in qualitative research, was audio-recorded, transcribed verbatim and analysed through thematic analysis. The analytic process included: (1) literal transcription; (2) open coding to identify units of meaning; and (3) axial coding to integrate codes into broader conceptual categories. This inductive–deductive approach enabled a reconstruction of the experiential trajectory of allo-HSCT. All participants provided written informed consent. The

study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (Code: 245/23).

Results: Multiple descriptive codes were grouped into families representing emotional responses, physical symptoms, coping strategies, social challenges and interactions with healthcare teams. Through axial coding, three overarching categories were identified:

1. **Diagnosis of the disease: biographical rupture and fear**
   Patients described the diagnosis as a "vital blow", characterised by fear of death, shock, perceived injustice and sudden disruption of daily life. Immediate hospitalisation intensified anxiety and loss of control. Emotional containment by relatives and clear explanations from professionals mitigated early distress.
2. **Hospital admission: vulnerability and multidimensional support**
   Patients experienced profound physical fragility—weakness, mucositis, pain, fatigue, dysphagia and functional decline. Nurses, haematologists and pharmacists were perceived as a stabilising anchor, providing safety, trustworthy information and therapeutic education. Family caregivers served as key emotional and practical support.
3. **Post-discharge uncertainty: living on a tightrope**
   The post-discharge period was dominated by persistent fear of relapse, hypervigilance towards bodily changes and heightened anxiety around follow-up analyses. Patients used active coping strategies (e.g. walking, yoga, guided exercises), promoting a sense of agency. Recovery was described as a fluctuating "roller coaster", with ongoing physical limitations and emotional instability. Social and financial vulnerability emerged as major stressors. Despite this, participants reported personal growth, redefined priorities and renewed hope.

Conclusions: This qualitative substudy highlights allo-HSCT as a transformative experience marked by emotional rupture, bodily fragility, caregiver dependence and persistent uncertainty after discharge. The multidisciplinary support offered in PHARALLO was perceived as essential for safety, education and emotional containment. Qualitative research provides valuable insights that deepen understanding of patient needs and inform refinement of person-centred care strategies in allo-HSCT.

Disclosure: Nothing to declare

NP47

EVALUATION OF THE EFFICACY OF ULTRASOUND-GUIDED MEDIUM-LENGTH CATHETERS IN THE COLLECTION OF PERIPHERAL BLOOD HEMATOPOIETIC STEM CELLS FROM HEALTHY DONORS

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Background: The efficacy of peripheral blood hematopoietic stem cell collection is influenced by catheter placement. Clinically, 16G cannula needles are commonly used for the puncture of the median cubital vein at the elbow. However, approximately 5% of healthy

donors have inadequate peripheral venous access. When peripheral venous puncture fails or insufficient blood flow for collection is obtained, central venous catheterization or arterial catheterization is often selected. How to efficiently and safely collect peripheral blood hematopoietic stem cells while minimizing donor discomfort remains a key focus in current hematopoietic stem cell transplantation research.

Methods: A retrospective study was conducted on 95 healthy donors who underwent peripheral blood hematopoietic stem cell collection at our center between January and June 2025. The control group (n=47) from January to March utilized 16G arteriovenous fistula puncture needles. The observation group (48 cases) used ultrasound-guided placement of medium-to-long-length catheters as the collection access route from April to June. The study compared the following parameters between groups: first-puncture success rate, puncture pain intensity, anxiety level, collection comfort, incidence of catheter-related complications, attainment rate of blood flow rate, and number of low-pressure alarms during collection.

Results: Compared with the control group, the observation group demonstrated significantly higher first-attempt puncture success rates ([100% vs 87.23%], P<0.05). Puncture pain scores (NRS) among donors in the observation group were significantly lower than those in the control group (P<0.05). Donors in the observation group reported significantly higher comfort scores during the collection process than those in the control group (P<0.01). Regarding complications, the overall complication rate was significantly lower in the observation group than in the control group ([6.25% vs 23.40%], P<0.05). No significant differences were observed between the two groups in anxiety scores (GAD-7), blood flow rate attainment rates, or the number of low-pressure alarms in the collection pathway (P>0.05).

Conclusions: In the collection of peripheral blood hematopoietic stem cells from healthy donors, the use of ultrasound-guided placement of medium-to-long-length catheters offers advantages such as high puncture success rates, ease of operation, stable blood flow velocity, high donor comfort, and fewer complications. This technique represents a safe, effective, and ideal method for establishing vascular access and warrants widespread adoption in clinical practice.

Disclosure: Nothing to declare.

NP118

APPLICATION OF FAMILY CONSTRUCTION MODEL IN HEMATOPOIETIC STEM CELL TRANSPLANTATION COMBINED WITH CAR-T CELL THERAPY IN PATIENTS WITH LYMPHOMA

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Background: Objective To evaluate the Family-Centered Care Model (FCCM) in improving psychosocial support and treatment outcomes for relapsed/refractory lymphoma patients undergoing hematopoietic stem cell transplantation (HSCT) combined with chimeric antigen receptor T-cell (CAR-T) therapy.

Methods: A prospective cohort study was conducted from 2023 to 2024, enrolling 30 leukemia patients receiving HSCT followed by CAR-T therapy. Participants were divided into an FCCM intervention group and a conventional care group. The intervention group received the following FCCM interventions: 1. Family collaboration plan: Multidisciplinary teams worked with families to establish treatment goals, nursing responsibilities, and emergency protocols. 2. Family empowerment education: Online/offline training to enhance families' ability to recognize and manage complications (e.g., chronic fatigue syndrome [CRS], infections). 3. Psychological support: Weekly family group counseling and emotional management sessions. Outcome measures included HADS anxiety/depression scores, treatment adherence, complication rates, and Family Assessment of Disease (FAD) scores.

Results: The intervention group showed significantly lower anxiety (HADS-A: 6.2±1.8 vs. 10.5±2.3) and depression (HADS-D: 5.8±1.6 vs. 9.1±2.1) scores compared to the control group (*P*<0.01). Treatment adherence improved to 94.3% (control group: 74.3%, *P*=0.021). The Family Activity Domain (FAD) score showed significant improvement (1.9±0.4 vs. 2.7±0.5, *P*<0.001), with a marked reduction in severe chronic fatigue syndrome (CRS, grade 3 or higher) incidence (14.3% vs. 34.3%, *P*=0.047).

Conclusions: By enhancing family involvement and collaborative management, the family support model effectively alleviates psychological stress in lymphoma patients and reduces treatment-related complications, providing a robust nursing support strategy for the complex treatment regimen of hematopoietic stem cell transplantation (HSCT) combined with chimeric antigen receptor T-cell therapy (CAR-T).

Disclosure: Nothing to declare.

NP53

SECONDARY CANCERS AFTER STEM CELL/BONE MARROW TRANSPLANT: INCIDENCE, SCREENING, AND EDUCATION IN A SINGLE-CENTRE REVIEW

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Background: Stem cell/bone marrow transplant (BMT) is a curative treatment for haematological malignancies but carries long-term risks, including secondary cancers reported to be seen in 5-10% of patients (Martelin et al, 2019) . In our centre once patients are medically stable and in remission, they transition to the late effects of transplant clinic for lifelong monitoring. This clinic is led by a haematology consultant and supported by

Advanced Nurse Practitioners (ANPs) who together play a pivotal role in delivering education, health promotion, and implementing health screening strategies. Early detection of secondary cancers is essential so treatment can be initiated to improve outcomes and reduce morbidity and mortality (EBMT, 2024).
Objective: Review the incidence of secondary cancers among BMT patients attending a late effects clinic over 12 month and evaluate the impact of screening and education strategies.

Methods: A prospective and retrospective review was conducted of all BMT patients attending the late effects clinic during a 12-month period. Data collection included:

- Original haematology diagnosis
- Transplant type, conditioning regimen, and donor type
- Type of cancer developed and time post-transplant
- Method of cancer detection
- Prior cancer history

Screening strategies included annual prostate-specific antigen (PSA) testing and adherence to national cancer screening programs. Patients were educated on lifestyle risk reduction (e.g., weight loss, exercise, smoking cessation, sun protection and skin monitoring).

Results: The results indicate that 10% of patients seen over the 12-month period developed a secondary cancer post-transplant. In addition, the data highlighted that 14% of our total patient group had been diagnosed with a cancer before or after BMT. Of these:

- 70% developed cancer post-transplant
- 30% had a different cancer prior to transplant
- 6 patients had cancers both pre- and post-transplant
- 5 patients had more than two cancers

The most common pre-transplant cancers were:

- Breast (18%)
- Bladder (18%)
- Prostate cancer (12%)
- Haematology cancers (15%) (Hodgins disease, myeloma, lymphoma- not the transplant indication)

Other cancers included lung, rectal, cervical, bowel, liver and oesophageal
The most common post-transplant cancers were:

- Skin (49%)
- Prostate (25%)
- Breast (6%)
- Lung (6%)
- Brain (3%)

Other cancers included oral, ovarian, genitourinary, gastric, and additional haematological malignancies.

Additionally, MGUS was detected in 6 patients.
Notably, 18 prostate cancers were diagnosed through early PSA screening (non-symptomatic patients), enabling timely intervention and treatment.

Conclusions: Secondary cancers remain a significant late effect following BMT, with an incidence of approximately **10%** in our patient group, similar to the reported incidence (Martelin et al, 2019), risk factors in our patient population will be further analysed. Along with medical colleagues ANPs are integral to implementing education, surveillance, and screening strategies. Early detection, such as targeted PSA testing can demonstrate benefit in reducing delays to diagnosis and improving patient outcomes. Continued emphasis on patient education, lifestyle modification, and proactive screening is essential to reduce cancer-related morbidity and mortality in this patient group.
Reference: EBMT, (2024). The EBMT handbook. open-access
Martelin et al, (2019). Incidence and risk factors of secondary cancers after allogeneic stem cell transplantation: analysis of a single centre cohort with a long follow-up, *Bone Marrow Transplantation* volume 54, pages334–337.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare.

NP72

SETTING UP A PRE AND POST ALLOGENIC BONE MARROW TRANSPLANT (BMT) OUTPATIENT PHYSIOTHERAPY SERVICE IN A UK TERTIARY HOSPITAL SETTING - INITIAL RESULTS AND REFLECTIONS

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Background: A Physiotherapist was recruited for the first time in to our BMT service to develop and provide a new, highly specialist, evidence-based Physiotherapy service to patients treated within the BMT Team within the Haematology Department at the Churchill Hospital, Oxford University Hospitals NHS Trust (OUHFT). A new pathway was implemented for Stem Cell Transplant patients offering Physiotherapy input both pre and post transplant to optimise quality of life and functioning and to monitor standards of practice and the impact on patient care and outcomes.

Methods: A Physiotherapist was embedded in to our Bone Marrow Transplant clinics and services to see people pre and post Allograft.
All pre Allogeneic Transplant patients receive either an in person consultation or telephone call with Prehabilitation (Prehab) guidance and advice prior to transplant, including targeted exercise prescription.
Post Allograft patients are referred on a need by need basis via the nursing and medical team. Referral criteria include join and skin Graft versus Host Disease, mobility issues,

fatigue and deconditioning/sarcopenia. Onward referrals are completed for those needing to access local exercise interventions or Community Physiotherapy/OT/Dietetics support. Outcome measures collated include the FACIT fatigue scale, 1 minute sit to stand, OUH GVHD range of movement score and SARC-F sarcopenia score.

Results: To date 66 patients have received prehab. 76 patients have been treated post Allograft.
Incomplete data sets exist currently for the outcome measures outlined above and collation of these are ongoing. Despite this, sarcopenia has been identified in our patients pre transplant across age groups, with some scoring higher than expected, indicating the potential for complications during and after transplant.
14/19 patients showed signs of sarcopenia on discharge post transplant, with 6/19 of these with sarcopenia at levels indicative for poor outcomes.12/19 patients were still showing signs of sarcopenia 100 days post transplant but only 4 at a level considered indicative for poor outcome.

Conclusions: The Physiotherapy service has been well received by staff and patients with positive feedback received.
The levels of sarcopenia identified in patients pre and post transplant demonstrates a need for timely access to clinicians trained in prehab, rehab and exercise prescription for this patient cohort.
Challenges have been recognised with regards to delivering an equitable Physiotherapy service within a tertiary centre setting. During the first year of service, Prehab was an opt in for patients, with most receiving a telephone call rather than in person prehab consultations due to the distance required to travel to hospital. As of January 2026, we plan to integrate the Physiotherapy Prehab service as an opt out component to patient's work up investigations pre transplant and include MUST score screening to identify those at risk of malnutrition. We plan to complete additional outcome measures during this appointment, including hand grip dynamometry, timed up and go and EORTC QLQ 30, to further demonstrate the impact of prehab screening and intervention for our patients.

Disclosure: Physiotherapy role has been funded on a trial basis for 3 years by Anthony Nolan.

NP90

NUTRITION IMPACT SYMPTOMS AND NUTRITIONAL STATUS IN ADULT ALLO-HSCT RECIPIENTS DURING 1-YEAR FOLLOW-UP

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Background: Nutrition impact symptoms (NIS) are contributors to impaired nutritional status in allo-HSCT patients. However, the impact of patients' reported NIS on nutritional

status are poorly described. This study investigated changes in NIS and nutritional status, and associations between NIS and nutritional status during a 1-year follow-up of allo-HSCT patients.

Methods: We used data from 117 patients (57 intervention, 60 control) who participated in a randomized controlled nutritional intervention trial. Linear mixed models were used to analyse changes in NIS over time. Ordinal logistic regressions were used to analyse associations between NIS and nutritional status.

Results: Nausea and vomiting and constipation were significantly lower in the intervention group than the control group during 1-year follow-up ($p = 0.015$ and $p < 0.001$, respectively). Initially, nutritional status declined in both study groups post-allo-HSCT but improved over time. Significantly fewer patients in the intervention group were malnourished at 3 weeks ($p = 0.020$) and 6 weeks post-transplantation ($p = 0.028$). Associations between NIS and nutritional status varied over time and differed between the study groups at 6 weeks post-transplantation (OR 3.702, 95% CI: (1.355, 10.100), $p = 0.011$).

Conclusions: In conclusion, our findings emphasize the need for long term monitoring of symptoms and nutritional status in allo-HSCT patients, supporting individualized nutritional assessments as part of long-term care strategies.

Disclosure: Geir Erland Tjønnfjord has received research grants from Mundipharma and Alexion Pharmaceuticals, advisory board honoraria from Alexion Pharmaceuticals and Johnson & Johnson, and lecture honoraria from Novartis, Johnson & Johnson, Alexion Pharmaceuticals, and Mundipharma. The other authors declare no competing interest.

Symptom Management and Supportive Care

NG10-01

PAIN MANAGEMENT PRACTICES DURING PAEDIATRIC ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

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Background: Pain during paediatric haematopoietic stem cell transplantation (HSCT) is severe, prolonged, and frequently refractory to multimodal treatment. Existing literature focuses largely on acute mucositis, providing limited insight into pain and pain-related

distress across the broader early post-transplant period. Understanding real-world analgesic practices and supportive care use is essential to optimising care for this vulnerable population.
The objective of this study was to characterise pharmacological and supportive care practices used to manage pain and pain-related distress in children undergoing allogeneic HSCT from conditioning to day +100 post-transplant.

Methods: We conducted a single-centre retrospective cohort study of paediatric patients (0–18 years) undergoing first allogeneic HSCT at a tertiary paediatric cancer centre in Australia between 2016 and 2022. Data were extracted from the electronic medical record using automated retrieval. Descriptive analyses summarised patient characteristics and pain management practices across the HSCT trajectory. Continuous variables were reported as medians with interquartile ranges (IQR), and categorical variables as frequencies and percentages. Analyses were conducted using R software in accordance with a pre-specified analysis plan.

Results: Of 203 children undergoing first allogeneic HSCT, 190 (93.6%) had complete pain management data and were included. Among these, 110 (57.9%) had malignant indications, most commonly acute myeloid leukaemia (35/110, 31.8%). Median age at transplant was 6.8 years (IQR 3.0–13.1), and matched unrelated donors were most frequent (77/190, 40.5%).
All children (190/190) received analgesic medication post-HSCT. Morphine and oxycodone were used in >90% of patients, and fentanyl in 87 (45.8%). During days 1–30, median duration of opioid use was 18 days (IQR 9–25) for morphine, 11 days (IQR 4–19) for fentanyl, and 2 days (IQR 1–4) for oxycodone. Paracetamol was used universally (median 11 days, IQR 7–17). Common adjuvant agents included ketamine (112/190, 59.0%; median 10 days, IQR 4–15.5) and gabapentin (35/190, 18.4%; median 12 days, IQR 0–22).
Although most pain assessments indicated no or mild pain (88%), 137 children (72%) experienced at least one episode of severe pain. Severe pain episodes occurred predominantly during days 1–30 (104, 55%), with persistence through days 31–60 (44, 23%) and days 61–100 (29, 15%). Acute pain services were accessed via inpatient referral orders in 72 children (35%, median day +12), whereas palliative care consultation occurred in 51 children (27%) and was initiated later (median day +59).

Conclusions: Children undergoing HSCT experience a substantial and enduring pain burden requiring complex multimodal analgesia, with severe pain episodes remaining common despite widespread pharmacological and supportive care use. Specialist pain and palliative care services were accessed in a subset of patients and were often initiated later in the transplant course. These findings provide important real-world evidence of current pain management practices during paediatric HSCT and identify opportunities to optimise the timing, coordination, and standardisation of multimodal pain care.

Disclosure: No conflicts of interest to disclose.

NP17

ASSESSMENT AND MONITORING OF NUTRITIONAL STATUS IN ONCO-HEMATOLOGICAL PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): TOOLS, SCALES AND MULTIDISCIPLINARY APPROACH

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Background: Allogeneic Hematopoietic Stem Cell Transplantation (Allo-HSCT) is a therapeutic approach for numerous onco-hematological diseases. Conditioning chemotherapy and the transplant itself expose patients to a high risk of malnutrition due to multiple adverse effects. Despite the importance of nutritional monitoring, the current assessment tools adopted for patients undergoing allo-HSCT are poorly specific and obsolete in the Italian setting. The primary aim of this review is to identify specific methods and tools for the assessment and monitoring of the nutritional status of patients undergoing allo-HSCT. Considering the Lombardy Regional Resolution No. 1812 of January 3, 2024, which mandates the use of the *Malnutrition Universal Screening Tool* (MUST) or the *Nutritional Risk Screening 2002* (NRS-2002), the secondary aim is to determine which of the two tools is more effective to evaluate the target population.

Methods: A scoping review was conducted searching in the following databases: MEDLINE (PubMed), CINAHL (EBSCO), and Scopus (Elsevier). Articles published between 2000 and 2025 in English or Italian language were included. Other inclusion criteria were: population of onco-hematological patients aged >18 years undergoing Allo-HSCT; nutritional assessment and screening tools in patients undergoing allo-HSCT; and bio-psycho-physical outcomes resulting from the systematic use of targeted nutritional scales and multidisciplinary approaches.

Results: From the 23 articles included in the review, five nutritional scales used in patients undergoing HSCT emerged. The tools identified in the literature as particularly relevant and effective in the onco-hematological and transplant setting were the *Patient-Generated Subjective Global Assessment* (PG-SGA) and the NRS-2002, both validated in Italian. The former allows the early identification of malnutrition and detailed information collection. The latter, NRS-2002, allows a quick stratification of the nutritional risk distinguishing the onco-hematological and the transplanted patients. The MUST appeared to be poorly sensitive and specific for the screening and monitoring of malnutrition risk in the target population.

Conclusions: The identified scales are effective in detecting the risk of malnutrition and improving clinical outcomes in the population of interest. Among the tools evaluated, only the *Malnutrition Screening Tool* (MST) has not yet been validated in Italian. Between MUST and NRS-2002, the NRS-2002 proved to be more sensitive and specific. The integration of PG-SGA or NRS-2002 appears to be the most appropriate approach for nutritional screening and monitoring in oncohematological and transplant in the Italian settings.

The findings of this work represent a solid starting point for the progressive implementation of NRS-2002 in the Bone Marrow Transplant Unit in IRCCS San Raffaele Scientific Institute in Milan. It is advisable to develop a specific pathway combining assessment tools with biochemical and anthropometric parameters. In a preliminary phase, NRS-2002 could be integrated to the MUST which is currently mandatory according to the Standard Operating Procedures in all the Units. Its systematic introduction could promote the adherence to the most recent clinical-nutritional recommendations.

Disclosure: Nothing to declare.

NP25

EARLY NURSING ASSESSMENT AND MANAGEMENT OF OCULAR GRAFT-VERSUS-HOST DISEASE IN TAIWANESE LONG-TERM ALLO-HSCT SURVIVORS: A TWO-YEAR RETROSPECTIVE STUDY

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Background: Ocular graft-versus-host disease (oGVHD) is a frequent complication among long-term survivors after allogeneic hematopoietic stem cell transplantation (Allo-HSCT) and significantly impairs quality of life. Data on its timing, severity, and the role of nursing interventions in Taiwanese populations are limited. This study aimed to characterize the clinical features of oGVHD and to evaluate the impact of early nursing assessment and intervention.

Methods: A total of 30 adult Allo-HSCT recipients at National Taiwan University Hospital who were continuously followed by a designated case manager were retrospectively enrolled in 2023. Patients who died post-transplant, underwent a second transplant, or had pre-existing ocular disease were excluded. Eighteen long-term survivors (>2 years post-HSCT) were analyzed. Standard assessments were conducted at 3, 6, 12, 18, and 24 months post-transplant. oGVHD was graded using the NIH Chronic GVHD Eye Scoring System. Patients with eye score ≥1 received standardized nursing education (humidification, warm compresses, artificial tear use), counseling for ocular red-flag symptoms, and referral to ophthalmology. Demographics, GVHD organ involvement, and oGVHD onset, severity, and course were collected.

Results: The cohort included 12 males and 6 females with a mean age of 45 years (range 22–69). Related donors accounted for 77.8% of transplants; 44.4% were fully HLA-matched, 44.4% haploidentical, and 11.1% partially mismatched. The most common GVHD manifestations were skin (66.7%) and oral involvement (61.1%), with oGVHD as the third most frequent (44.4%). Other affected organs included liver (16.7%), lung (11.1%), and gastrointestinal tract (11.1%).
Most oGVHD cases developed within 3–6 months post-transplant (75%), with one case each at 12 months and 25 months. All patients initially presented with eye score 1 and received nursing intervention and ophthalmology referral. Two patients progressed to score 2: one

due to poor adherence to artificial tears while working overseas, which improved back to score 1 after treatment; the other following three donor lymphocyte infusions for early relapse associated with worsening skin GVHD, remaining stable at score 2 without functional impairment. Of the remaining six patients, five maintained stable score 1 disease, and one achieved complete resolution (score 0) by 22 months post-transplant.

Conclusions: Despite the limited sample size, oGVHD was the third most common manifestation of chronic GVHD in this cohort and most frequently developed within 3–6 months after transplantation. Persistent ocular symptoms were associated with functional limitations, including difficulty with work and driving. Our findings suggest that early nursing assessment, prompt self-care education, and timely ophthalmologic referral may effectively prevent disease progression from eye score 1 to score 2.
Larger prospective studies with longer follow-up are warranted to further evaluate nursing intervention outcomes and to explore associations between oGVHD severity and quality of life. Early identification and early intervention remain essential strategies for optimizing long-term survivorship outcomes following Allo-HSCT.

Disclosure: Nothing to declare.

NP33

ASSESSING THE TOLERANCE OF FIBRE BASED FEEDS FOR PAEDIATRIC PATIENTS DURING AN ALLOGENEIC STEM CELL TRANSPLANT

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Background: Enteral nutrition is an inevitable part of treatment for a Haematopoietic Stem Cell Transplant (HSCT), due to the side effects of chemotherapy. The prescription of fibre-devoid hydrolysed (HF) and amino acid formulas (AAF) is standard practice for the management of gastrointestinal mucositis. However, within this complex cohort, there is limited evidence to support these formulas over whole protein fibre-based formulas. Conversely, there is growing evidence to support the beneficial role of fibre in promoting a healthy gut microbiome, which may mitigate the gastrointestinal side effects of HSCT as well as improve transplant-related outcomes. Therefore, from June 2024, whole protein fibre-based formulas were prescribed for patients undergoing an HSCT,
Aim: To compare the gastrointestinal tolerance and incidence of parenteral nutrition (PN) between whole protein fibre-based formulas with fibre-devoid HF and AAF during HSCT.

Methods: Data were collected retrospectively from EPIC on demographics, diagnoses, conditioning regimens, enteral formula type, and PN from June 2023 to June 2025.

Results: 99 patients were included in the data collection. 33 (33%) children received a fibre formula, 44 (44%) received a HF, 21 (21%) received an AAF and 4 (4%) received a whole

protein non fibre feed (4%). PN was required by 52 patients (53%). Fibre and AAF **reduced** the likelihood of PN in children who had **Myeloablative Conditioning Reduced-Toxicity (MAC RT): p=0.01.**
The type of feed formula (fibre vs non fibre) did not impact the likelihood of PN in children who had Minimal/Reduced Intensity Conditioning (MIC/RIC) conditioning: p=0.73
Fibre
Of the 33 patients; 16 patients (48%) required PN. 10 patients (63%) received MAC, 5 (31%) patients received MAC RT and 1 patient (6%) received MIC/RIC.
HF
Of the 41 patients; 28 patients (68%) required PN. 12 patients (42%) received MAC, 13 (46%) patients received MAC RT and 3 patient (12%) received MIC/RIC
AAF
Of the 21 patients; 7 patients (33%) required PN. 1 patient (14%) received MAC, 5 (72%) patients received MAC RT and 1 patient (14%) received MIC/RIC
Whole protein
Of the 4 patients; 1 patient (25%) required PN. This patient received MAC,

Conclusions: Fibre- based feeds are well tolerated during conditioning as well as during mucositis and does not increase the use of PN. Children receiving MAC may tolerate fibre feeds during transplant and not require escalation to PN. Longer term data is needed to assess the clinical outcomes between fibre and non-fibre-based enteral formula including graft vs host disease.

Disclosure: nil

NP105

NURSING MANAGEMENT OF A COMPLEX PEDIATRIC ALLO-HSCT CASE FOR BETA-THALASSEMIA MAJOR WITH MULTIPLE SEVERE POST-TRANSPLANT COMPLICATIONS

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is one of the curative treatment options for beta-thalassemia major. However, pediatric patients undergoing allo-HSCT—especially from partially matched donors—are vulnerable to early life-threatening complications that require vigilant, highly skilled nursing care. This report describes a complex case in a 4-year-old girl who developed multiple severe post-transplant complications. The case highlights the essential role of transplant nursing in early recognition, timely intervention, and coordinated management during critical phases of clinical deterioration.

Methods: Case Presentation: A 4-year-old girl with transfusion-dependent beta-thalassemia major underwent allo-HSCT from an HLA 9/10 sibling donor. On Day +4, she developed persistent high-grade fevers occurring every 4 hours, ranging from 38°C to 42°C,

accompanied by marked fatigue, poor oral intake, irritability, and limited cooperation due to her young age. Blood culture on Day +4 grew Enterobacter cloacae. Despite antimicrobial adjustment, she continued to spike high fevers, and by Day +6, blood cultures were positive for multidrug-resistant Klebsiella pneumoniae. On Day +11, the patient developed severe veno-occlusive disease with hepatomegaly, painful abdominal distension, respiratory distress, and hemodynamic instability requiring ICU transfer. Additional complications included acute kidney injury from Cyclosporin A inhibitors, BK virus–related hemorrhagic cystitis presenting as painful red urine, severe mucositis, diarrhea, and prolonged febrile episodes.
Nursing Management:
(1) Early detection of sepsis through continuous monitoring of recurrent high fevers, rapid clinical changes, and escalation for antimicrobial adjustment.
(2) Central-line management, including strict aseptic technique, wound assessment, removal of the infected catheter, and preparation for the placement of a new line.
(3) VOD monitoring, assessing weight gain, abdominal girth, hepatomegaly, worsening dyspnea, and coordinating timely initiation of Defibrotide.
(4) Respiratory and hemodynamic support, including monitoring work of breathing, oxygen saturation, fluid overload, and assisting with ICU-level interventions.
(5) Renal care, optimizing hydration and adjusting immunosuppressive therapy.
(6) Management of BK cystitis, documenting hematuria, ensuring bladder comfort, hydration, and pain relief.
(7) Symptom relief for mucositis, anorexia, fatigue, and distress, while providing age-appropriate emotional support for a poorly cooperative young child.
(8) Family education, helping parents understand evolving complications and treatment expectations.

Results: Result: Neutrophil and platelet engraftment occurred on Days +22 and +40. Donor chimerism reached 90% by Day +30. All major complications—including VOD, MDR sepsis, respiratory distress, renal toxicity, and BK virus cystitis—gradually resolved with intensive supportive care. At long-term follow-up on Day +552, the patient remains clinically stable, transfusion-independent, and demonstrates 93% donor chimerism with normal organ function and appropriate growth for age.

Conclusions: Conclusion: This complex case illustrates how comprehensive nursing surveillance and rapid multidisciplinary coordination are critical to managing multiple life-threatening complications after pediatric allo-HSCT. Early detection of sepsis, meticulous catheter care, close monitoring of VOD and organ dysfunction, and age-appropriate supportive strategies contributed significantly to the successful recovery of this high-risk patient.

Disclosure: Nothing to declare

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NP112

"LIGHTING THE WAY" -ENABLERS OF IMPLEMENTING PHOTOBIOMODULATION THERAPY FOR MUCOSITIS IN PAEDIATRIC HSCT

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Background: Oral mucositis (OM) is a common, painful, and debilitating complication of haematopoietic stem cell transplant (HSCT). Guidelines recommend photobiomodulation (PBM) therapy to prevent and treat OM in children and adolescents undergoing HSCT. However, healthcare professionals caring for this cohort have resisted adopting this intervention. This review aims to synthesise knowledge supporting the implementation of guidelines to inform clinical practice, improve patient care, enhance quality of life, and reduce healthcare costs.

Methods: A comprehensive search strategy was developed to identify pre-existing evidence addressing the implementation research question: What factors facilitate the implementation of photobiomodulation therapy for managing mucositis in children and adolescents undergoing haematopoietic stem cell transplants? Yielding relevant studies across the evidence hierarchy advanced the understanding of the implementation challenges. The iPARIHS (Promoting Action on Research Implementation in Health Services) framework was employed to frame the synthesis (Huang et al., 2024)

Results: Results after synthesising and analysing 17 studies that met the inclusion criteria, four themes emerged as significant components in translating PBM into clinical practice:
• Standardisation and protocol development
• Stakeholder support - education and training
• Organisational leadership and collaboration
• Innovation integration - resource allocation
Although translating evidence into practice is considered complex and challenging, the author proposes a series of strategic actions guided by implementation science and systems thinking to facilitate a coordinated, multidimensional approach that engages interdisciplinary stakeholders in implementing PBM therapy to prevent and treat OM in children and adolescents undergoing HSCT.

Conclusions: This study identifies barriers and facilitators that influence the implementation of PBM therapy to prevent and treat OM in children and adolescents undergoing HSCT. Successful implementation has the potential to improve patient care practices in the management of mucositis. Future studies exploring patients' and clinicians' preferences and values would gain a more holistic understanding of their diverse insights and perspectives. As the evidence for PBM therapy evolves, the role of ANP as a facilitator is crucial in championing and leading change, bridging the gap between current evidence and clinical practice, harnessing the potential to alleviate suffering and improve the quality of life for paediatric HSCT patients

Disclosure: No Conflict of interest

NP113

PHOTOBIOMODULATION IN THE TREATMENT OF ORAL MUCOSITIS IN THE TRANSPLANT SETTING FOR CHILDREN AND YOUNG PEOPLE

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Background: Oral mucositis is a frequent complication affecting children and young people (CYP) receiving high dose treatment for cancer and undergoing bone marrow transplantation. Mucositis causes loss of mucosal lining leading to pain, ulceration and consequently poses an increased risk of systemic infection. Current treatment modalities include both preventative and symptomatic control which include difficulties with administration, cooperation and unwanted side effects/toxicities.
Effective treatment and prevention are paramount to patients, families and oncology services to reduce the impact on CYP with cancer, to reduce the disruption to their cancer treatment and to prevent the subsequent rise in the expense and burden of cancer care.
Photobiomodulation is a national and international supported treatment option of mucositis for CYP with research shown to improved quality of life, reduced pain levels leading to a reduction in treatment pain modalities, improved nutrition, reduced prolonged hospitalisation and reduced risk of infection.

Methods: **Intervention:** Photobiomodulation is a form of light therapy involving LED in the visible and infrared spectrum. It is a simple, quick, non-invasive and non-thermal treatment which alters cellular metabolism through absorbing light energy by photoreceptors situated in the mitochondrial membrane. This encourages mucosal repair, promotes tissue damage and prevents cellular breakdown.
The aim is to commence the first photobiomodulation treatment within 24-hours of chemotherapy and continue daily for the duration of treatment. For treatment of established oral mucositis, treatment should be delivered a minimum of three times per week until completion of treatment or resolution of symptoms. Treatment is delivered across five areas with one minute per treatment area – extra oral over right cheek, extra oral over left cheek, extra oral over lips and closed mouth, intra oral above tongue/below tongue. Where intra-oral treatment is not possible extra oral treatment can be delivered alone.
Photobiomodulation cannot be used over known malignant or infected lesions.

Results: **Improvement:** The photobiomodulation service was introduced in November 2025 administered to CYP within the inpatient setting.
Seven patients have been/are being treated with photobiomodulation - five allografts and two autografts. So far, four patients did not require a PCA/NCA with no/minimal oral mucositis suggestive of a potential reduction in mucositis/improvement in pain management.
* Retrospective data collection and analysis will commence at six months since implementation to explore the impact on patient and family experience, pain levels including use of analgesic medications and impact on nutrition.

Conclusions: **Applicability:** Improving pain from mucositis and improving CYP quality of life is a primary objective in implementation. Improvements seen thus far and discussions with other NHS Trusts offering this service suggests this is a valuable service. However, research is required to evidence this effectively and is the next phase in this new service. Currently, photobiomodulation is only available for inpatients. Research findings will inform a business case to expand this service offering it in the outpatient setting.
*Data on numbers of patients will be updated at the time of poster presentation .

Disclosure: Nothing to declare.

NP114

COMPREHENSIVE SYMPTOM MANAGEMENT AND SUPPORTIVE NURSING CARE IN A PRETERM TODDLER UNDERGOING HSCT FOR PYRUVATE KINASE DEFICIENCY

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Background: Preterm toddlers undergoing hematopoietic stem cell transplantation (HSCT) are highly susceptible to treatment-related toxicities, infections, and poor medication tolerance. Pyruvate kinase deficiency (PKD) further increases transfusion dependence and infection risk. Nursing-led interventions are essential for early detection of complications, prevention of adverse events, and facilitation of safe home care, yet detailed reports of pediatric nursing strategies in this context are limited.

Methods: A descriptive case study was conducted on a 2.5-year-old preterm boy (36 weeks, 1.9 kg) with transfusion-dependent PKD undergoing allogeneic HSCT from a fully HLA-matched sibling after Busulfan-Cyclophosphamide-Thiotepa-Fludarabine conditioning. Nursing interventions were central to care delivery:
(1) **Proactive symptom monitoring and rapid intervention**: hourly temperature checks, immediate blood cultures, and nursing-initiated IV antibiotic escalation for neutropenic fever.
(2) **Nursing-led mucositis and pain management**: frequent oral hygiene, multimodal analgesia, and hydration optimization.
(3) **Medication and nutritional support**: tailored administration strategies to overcome poor oral tolerance and maintain adherence.
(4) **Central line management**: strict nursing protocols to prevent catheter-related bloodstream infections during prolonged Hickman use.
(5) **Family-centered education**: caregiver training in line care, infection monitoring, medication administration, oral hygiene, and safe home follow-up.

Results: Despite severe mucositis, difficulty swallowing medications, and neutropenic fever, no major infections or organ toxicities occurred. Platelet and neutrophil engraftment were achieved on Days +14 and +15; full donor chimerism (100%) was established by Day +28 and remained stable at one year. Nursing-led interventions directly prevented complications, optimized treatment adherence, and enabled safe transition to home care.

Conclusions: This case highlights the pivotal role of specialized nursing in high-risk pediatric HSCT. Proactive symptom surveillance, rigorous infection prevention, medication and nutritional management, and structured caregiver education are key nursing contributions to safe and successful transplant outcomes.

Disclosure: Nothing to declare

NP132

NURSING CARE OF A PATIENT WITH REFRACTORY HEMOPHAGOCYTIC SYNDROME UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: This report summarizes the nursing experience of a patient with refractory hemophagocytic syndrome who underwent salvage haploidentical hematopoietic stem cell transplantation.Prior to transplantation, the patient's hemophagocytic syndrome was uncontrolled, presenting with recurrent fever, persistently elevated serum ferritin, cytokines, and liver function, accompanied by EBV infection and pulmonary infection. During the early treatment phase, complications included atrial fibrillation, internal environment disturbances, bloodstream infection, hypoalbuminemia, and limb mobility impairment. The transplantation process carried a high risk of life-threatening complications such as arrhythmia and multiple organ failure, posing significant challenges for both medical treatment and nursing care.

Methods: Key nursing interventions included:
Pre-transplant Multidisciplinary Assessment: A multidisciplinary team evaluated the patient’s organ functions to formulate a chemotherapy regimen and implement anticipatory nursing measures.Close Monitoring During Transplantation: Vital signs, laboratory parameters, and clinical changes were strictly monitored. Medications were administered as prescribed to control body temperature and prevent complications like arrhythmia.
Enhanced Caregiver Management: Strict protocols were enforced to minimize the risk of cross-infection.
Focus on Psychological Support: Psychological nursing was emphasized to alleviate negative emotions.
Comprehensive Rehabilitation Support: A tailored nutritional plan was developed by the dietetics department, and functional exercises were guided by the rehabilitation team to promote recovery.
Personalized Education and Follow-up: Individualized health education and follow-up management were conducted to ensure continuity of care and condition monitoring.

Results: No severe complications occurred during the transplantation period. By day 30 post-transplant, the patient achieved hematopoietic engraftment (WBC 6.66×10^9/L, Hb

69g/L, PLT 72×10⁹/L), with infections controlled and liver function normalized. The patient was discharged as ordered and remains in good condition during outpatient follow-up.

Conclusions: Hematopoietic stem cell transplantation (HSCT) is a lifesaving treatment for patients with refractory hemophagocytic lymphohistiocytosis (HLH), whose nursing care is highly specialized and challenging. Effective nursing centers on comprehensive management with infection prevention and control as the cornerstone and proactive complication management as the priority. Alongside disease treatment, equal emphasis must be placed on providing psychological, nutritional, and social support. The entire process requires close multidisciplinary collaboration among the medical team, pharmacists, and nutritionists to implement evidence-based, individualized nursing care plans.

Disclosure: Nothing to declare.

NP58

ASSESSMENT OF EXERCISE TOLERANCE IN PATIENTS UNDERGOING ALLOGENEIC STEM CELL TRANSPLANTATION DURING HOSPITALIZATION: AN OBSERVATIONAL STUDY

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Background: Allogeneic hematopoietic stem cell transplantation (HSCT) is associated with physical and psychological side effects, and the related period of protective isolation is known to contribute to functional decline and decreased exercise tolerance. Physical performance is commonly assessed using the Six-Minute Walking Test; however, this test is often not feasible within isolation settings. Conversely, the 1-Minute Sit-to-Stand Test (1MSTS) may represent a valid alternative, as it is reliable, reproducible, and easy to administer even in environments with limitations.
The aim of this study was to assess and quantify exercise tolerance impairment in adult patients undergoing allogeneic HSCT during hospitalization using the 1MSTS.

Methods: This ongoing monocentric observational study enrolls patients aged 18-70 years with hematologic malignancies admitted to the Transplant Unit. Exclusion criteria include inability to maintain an upright position, clinical instability at the time of assessment, or severe psychiatric disorders. Functional evaluations are performed on the first day of hospitalization (T0) and on day 28 (T1). The 1MSTS is administered to assess functional exercise tolerance, while perceived exertion is measured using the Borg Scale. Descriptive statistics are reported as means and standard deviations or as absolute and relative frequencies. Paired Student's t-tests are used for inferential analysis.

Results: To date, 18 patients have been enrolled (partial data), including 9 females. The mean age was 58.8 years (SD = 7.58). The 1MSTS showed a significant decrease from T0 (mean repetitions: 23.1) to T1 (mean repetitions: 18.7; $p < 0.00025$), indicating a 19.05%

reduction. Beyond statistical significance, these findings also exceed the minimally clinically important difference reported in the literature (3 repetitions). Linear regression analysis indicated that sex and baseline (T0) performance influence performance at T1. The Borg Scale also showed significant differences between T0 and T1 ($p < 0.021$).

Conclusions: Preliminary results indicate a significant and clinically relevant decline in functional performance on the 1MSTS, accompanied by increased perceived exertion assessed with the Borg Scale. The 1MSTS also appears feasible in other clinical settings requiring functional assessment of immunocompromised or hospitalized patients.

Disclosure: Nothing to declare

NP69

BEYOND THE PCR: CMV PNEUMONIA DESPITE NEGATIVE SERUM AND BRONCHIAL LAVAGE CMV VIRAL LOAD – CHALLENGE FOR ADVANCED NURSE PRACTITIONER

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Background: Cytomegalovirus (CMV) pneumonia is a life-threatening complication in hematopoietic stem cell transplantation (HSCT) recipients. Standard preemptive therapy relies on monitoring CMV PCR viral load in serum or bronchoalveolar lavage (BAL). However, due to intracellular localization of CMV, tissue-invasive disease may exist despite low or negative viral loads from extracellular specimen, e.g. blood or bronchial lavage. This diagnostic discordance poses a significant challenge for Advanced Nurse Practitioners in decision-making or interpretation of clinical situation with physicians, leading to delayed treatment.

Methods: We shared a series of 7 adult hematological patients (post-HSCT or chemotherapy) presenting CMV pneumonia with diagnostic discordance in CMV pneumonia and serum or bronchial lavage. We compared clinical severity against CMV PCR levels in serum and BAL. We evaluated the outcomes based on the timing of interventions, specifically the combination of CMV treatment of Ganciclovir and CMV hyperimmune globulin (Cytotect).

Results: **Case 1 (DLBCL)** and **Case 2 (NHL)** presented with severe interstitial pneumonia and respiratory failure but had low serum and **undetectable** BAL viral loads while pneumonia was severe. Due to the lack of virological evidence, CMV directed treatment was delayed, and both patients died of the pneumonia. CMV pneumonia were diagnosed via postmortem autopsy/biopsy.
Case 3 (T-LBL) and **Case 4 (AML)** presented with interstitial pneumonia and respiratory failure after chemotherapy but without transplantation,
BAL viral load was undetectable and antibiotics were ineffective in intensive unit for more than one month. But therapeutic trial of Cytotect and Ganciclovir resulted in full resolution of pneumonia and discharge of the patients. Case 5 had pneumonia but undectable BAL viral

load, but survived due to early initiation of CMV treatment because of detectable serum CMV viral load. Case 6 survived the CMV pneumonia due to early administration of CMV medication despite undetectable CMV viral load from serum and BAL specimen, but died of lung GVHD related infection. Case 7 had CMV pneumonia proven by lung biopsy but had undetectable CMV viral load from BAL specimen. He died of CMV pneumonia despite initiation of CMV medications. Retrospectively, all patients had predisposing factors contributing to the CMV pneumonia (listed in table).

Case	Age / Sex	Diagnosis	Transplant / Status	CMV PCR (Serum)	CMV viral load (Bronchial wash)	Risk factor	Clinical Severity (Organ Involvement)	Key Treatment	Duration of Therapy	Outcome
1	58 /M	DLBCL	10/10 Sibling PBSCT	Undetectable	Undetectable	Post CAR-T, immediate after Bendamustine	Severe Pneumonia	GCV + foscarnet + Cytotect (delayed)	4 weeks	Expired (Autopsy confirmed CMV inclusions)
2	74 /F	AML	MUD PBSCT	Low (<1000 IU/ml)	Undetectable	Extensive chronic GVHD prolonged steroid use	Pneumonitis	Valcyte+ GCV + Cytotect + DLI Foscarnet	9 months	ARDS, Expired
3	70 /F	T-LBL	Pre-HSCT (Post-Chemo)	Low (296 IU/ml)	Undetectable	Lymphoid malignancy, after steroid	Pneumonia, Severe GGO	GCV + Cytotect	~14 weeks	Recovered (GGO disappeared) connect to HSCT
4	56 /M	AML	Post-Chemo (Relapsed)	High (15.5k IU/ml)	Undetectable	Steroid use for lung inflammation	Pneumonia	GCV + Cytotect	~6 weeks	Success / Recovered

5	31/F	Ph ALL	MUD PBSCT	Undetectable	Undetectable	Delayed immune reconstitution after HSCT	CNS/Retinitis/ Pneumonitis	GCV + Cytotect	N/A	Survived (Chronic complications)
6	64/F	AML	Haplo-PBSCT	Low (<1000 IU/ml)	Undetectable	Prolonged steroid use and immediate after pulse steroid for lung GVHD	Pneumonia	Valcyte+ GCV + Foscarnet Cytotect	Intermittent (~1 month)	Died of GVHD related infection
7	48/M	ATLL	MUD PBSCT	Undetectable	Undetectable VATS biopsy: CMV pneumonitis	Prolonged steroid use for grade III acute GVHD	Fatal Pneumonitis	Late GCV +Cytotect	N/A	Expired (CMV pneumonitis)

Conclusions: This case series illustrates that relying solely on viral loads extracellular specimen could be misleading. A negative CMV PCR in serum—or even in bronchial lavage—does not definitively preclude tissue-invasive CMV pneumonia. For Advanced Nurse Practitioners, interpretation of these data with physicians and explanations to the patients and their families should be cautious. Experienced Advanced Nurse Practitioners could identify risk factor of CMV disease, e.g. after chemotherapy, especially bendamustine, prolonged or high dose corticosteroid for intractable GVHD, after allogeneic transplantation, or lymphoid malignancy using steroid in the treatment. Early reminding the physician about the possibility of CMV pneumonia in patients with interstitial pneumonia refractory to all the current medication based on the risk factor and clinical judgment could be important. Multidisciplinary team work may also be pivotal for these difficult hematological patients.

Clinical Trial Registry: **N/A**

Disclosure: Nothing to declare.

Cell and Gene Therapy (CART, IEC)

NG27-04

EVERY MINUTE COUNTS: DO THAW-TO-INFUSION INTERVALS AND INFUSION TIME OF DAY INFLUENCE CRS ONSET AND HOSPITAL STAY IN CAR-T THERAPY? A NURSE-LED RETROSPECTIVE REAL-WORLD ANALYSIS

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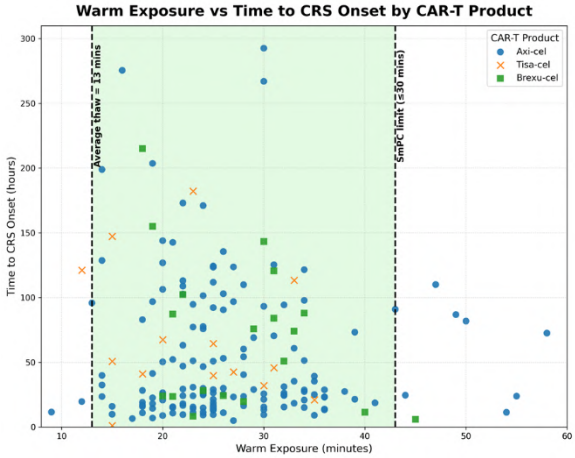
Background: Safe delivery of CAR-T therapy depends on precise, nurse-controlled procedures during product thawing and infusion, time-critical steps rarely reported in clinical trials but essential in real-world care. Nurses are the final custodians of this process, ensuring that thawed CAR-T cells are handled within manufacturer limits to preserve viability and safety. While manufacturing and transport are tightly regulated, the bedside phase introduces subtle, human-controlled variability. Strict procedural adherence is vital to preserve cell integrity and consistency. Once thawed, CAR-T cells lose viability rapidly, and manufacturer guidance specifies infusion within 30 minutes. Prolonged warm exposure may impair cell viability and cytokine kinetics. This nurse-led study examined whether thaw-to-infusion interval and infusion time of day influence cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity (ICANS), or hospital length of stay (LOS), using timing precision as a marker of nursing quality.

Methods: A retrospective, single-centre review included 243 CAR-T infusions (2019–2025). Products with alternative thawing workflows were excluded. After timestamp validation, 198 infusions were analysed (axi-cel n=154; brexu-cel n=24; tisa-cel n=20). Data included thaw start and end times, infusion start and end times, and time of first fever >38°C as a proxy for CRS onset. CRS and ICANS were graded per ASTCT criteria. Analyses used Spearman correlation, Kruskal–Wallis tests, and partial correlations controlling for product type ($p<0.05$).

Results: Median age was 63 years with 62% male. Diagnoses included large B-cell lymphoma (84%), mantle cell lymphoma (9%), B-cell acute lymphoblastic leukaemia (6%), and follicular lymphoma (2%) under clinical-trial indication. Median warm exposure was 25 minutes (range 9–58) and infusion duration 11 minutes (range 1–37). Most infusions (77%) occurred between 12:00–15:59, and 85% met the 30-minute specification. Median time to CRS onset was 29.6 hours, varying by product: axi-cel 29.8 h, brexu-cel 74 h, tisa-cel 50.7 h ($p<0.01$). No correlation was seen between warm exposure and CRS onset ($\rho=-0.03$, $p=0.68$). CRS grade ≥2 occurred in 50% and ICANS grade ≥2 in 34%. A weak, non-significant trend suggested higher ICANS grades with longer exposure ($\rho=0.14$, $p=0.054$).



Conclusions:

Nurse-controlled thaw-to-infusion timing was measurable, auditable, and aligned with manufacturer standards, underscoring nursing precision in advanced cell therapy. Over 85% of infusions met the manufacturer-specified ≤30-minute interval, confirming this standard is achievable and safe in practice. Thaw-to-infusion warm exposure and infusion time of day showed no association with CRS, ICANS, or LOS, reflecting high procedural fidelity. Product-specific biology, rather than procedural timing, remains the principal determinant of outcomes. The absence of timing effects on toxicity or hospitalisation indicates consistent, safe nursing delivery. Findings informed updates to nursing education and competency frameworks and support inclusion of thaw-to-infusion monitoring as a nursing quality indicator. A UK multicentre, nurse-led CAR-T registry is in development to benchmark these variables and strengthen national auditing and JACIE alignment. Emerging fresh, non-cryopreserved CAR-T products may remove freeze–thaw timing variability, making this cryopreserved cohort an important benchmark for comparison. By quantifying the impact of bedside precision on safety and efficacy, this study reaffirms that in CAR-T therapy, every minute — and every nurse — counts.

Disclosure: Nothing to declare

NP03

OPTIMISATION OF CAR-T LEUKAPHERESIS USING A MONONUCLEAR CELL–BASED PREDICTIVE COLLECTION TOOL: A SINGLE-CENTRE EXPERIENCE

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Background: Chimeric Antigen Receptor T-cell (CAR-T) therapy has transformed the management of hematologic malignancies. Treatment depends on the efficient collection of mononuclear cells (MNCs) through leukapheresis. Accurate prediction of MNC yield is critical for optimising collection efficiency (CE), minimising patient toxicities by reducing leukapheresis time and ensuring adequate starting material for CAR-T cell manufacturing. This study aimed to validate a predictive calculation tool for MNC yield to optimise the leukapheresis procedure for CAR-T therapy recipients.

Methods: We retrospectively analysed all consecutive leukapheresis procedures for axicabtagene ciloleucel (axi-cel, n=43) and ciltacabtagene autoleucel (cilta-cel, n=6) at our centre (Oct 2022-May 2025). Apheresis was performed on the Spectra Optia, using the Continuous Mononuclear Cell Collection (CMNC) protocol. Peripheral collection was utilised if patients had adequate venous access, otherwise central venous access was used. Peripheral blood flow cytometry was performed prior to apheresis. The MNC calculation tool, adapted from our locally validated stem cell collection model, used the pre-apheresis peripheral blood monocyte plus lymphocyte counts multiplied by a collection efficiency of 60% to determine the total blood volume to process to achieve the MNC Target.
Figure 1.0 FSH MNC Calculation

$$\frac{\text{Target MNC (absolute count)} ____ \times 10^9}{0.6 \times (\text{Lymphocytes} ____ 10^9/\text{L} + \text{Monocytes} ____ 10^9/\text{L})} = _____ \text{L} + \text{IEV*} _____ \text{L} = \textbf{Volume to process in Litres} _____ \text{L}$$

*IEV - Interface Establishment Volume – Volume of blood processed to establish interface
*CE- Collection Efficiency – Previously validated collection efficiency

Results: Forty-nine CAR-T leukapheresis procedures were analysed, (axi-cel n=43; cilta-cel n=6), All collections (100%) achieved or exceeded the prescribed MNC target, resulting in a 100% manufacturing success rate. 67% (n=36) of axi-cel collections and 100% (n=6) of cilta-cel Leukapheresis collections processed <12L whole blood to achieve the MNC target. The median collection efficiency was 71% for axi-cel and 74% for cilta-cel. For axi-cel, the median whole blood volume processed was 11 L, with a median reduction in collection time of 30 minutes compared with historical practice. For cilta-cel, 100% of collections processed ≤10.5 L of whole blood, with a median reduction in collection duration of 77 minutes compared with the historic cohort (median 270 vs 192.5 minutes).

Conclusions: The validated MNC calculation tool reliably ensured 100% collection success for CAR-T manufacturing while reducing leukapheresis time and processed blood volume at our centre. These findings support the incorporation of the MNC calculation tool into routine clinical practice for local CAR-T leukapheresis. Prospective multicentre studies are needed to validate our results.

Disclosure: Nothing to declare.

NP05

OPTIMIZING CRS AND ICANS MANAGEMENT IN CAR-T CELL THERAPY: IMPACT OF A NURSE-LED STRUCTURED WORKFLOW ON EARLY RECOGNITION AND MANAGEMENT OF CRS AND ICANS

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Background: Despite the therapeutic success of chimeric antigen receptor T-cell (CAR-T) therapy for the treatment of hematologic malignancies, this therapy is commonly complicated by cytokine release syndrome (CRS) and Immune Effector Cell-Associated Neurotoxicity Syndrome (ICANS), both of which may progress rapidly and result in significant morbidity. Early detection, accurate grading, and timely intervention are therefore essential. Given their continuous patient contact and central coordination role, nurses are uniquely positioned to identify early clinical deterioration. However, standardized nurse-driven processes for CRS and ICANS assessment and escalation remain limited. This study aimed to evaluate the effectiveness of a novel, nurse-centric workflow designed to enhance early recognition and management of CAR-T-related toxicities.

Methods: A prospective, single-centre study was conducted over 12 months following the development and implementation of an interdisciplinary workflow focused on structured nursing assessment and escalation. The intervention comprised three key components: (1) development of a standardized assessment tool aligned with the American Society for Transplantation and Cellular Therapy (ASTCT) consensus grading criteria for CRS and ICANS; (2) establishment of a nurse-led escalation protocol enabling direct activation of physicians upon identification of early toxicities; and (3) an intensive training program delivered to 39 nursing staff, covering symptom recognition, grading, and initiation of early supportive interventions. The primary outcomes reviewed included review of the confidence level of nurses as well as assessment of time to symptom escalation and time to treatment initiation. Secondary outcomes included duration of CRS/ICANS episodes and incidence of grade 3 and above toxicities. Pre-implementation data served as the historic control.

Results: Primary outcomes: Post implementation, nurses' confidence increased substantially, rising from 58.5% to 96.8%. The median time to symptom escalation decreased from 60 minutes to 15 minutes, while the median time to treatment initiation reduced from 60 minutes to 15 minutes.
Secondary outcomes: Consequently, CRS and ICANS resolution time decreased by 1-2 days. In the post-implementation cohort, the incidence of grade 3 CRS or ICANS was 0%. Notably, the incidence of cerebral oedema, a severe manifestation of ICANS, was reduced from two cases in the pre-implementation group to zero cases post-implementation. All patients in the post-implementation group achieved complete resolution of symptoms without progression to severe CRS or ICANS, and no case of long-term neurotoxicity was reported.

Conclusions: The structured workflow significantly enhanced nurse-physician collaboration and supported timely, coordinated management of CAR-T therapy complications. Nursing vigilance and proactive collaboration proved vital in early recognition and management of CRS and ICANS. This study demonstrates the crucial impact of early recognition and escalation of symptoms in reducing complication severity and resolution time, underscoring the indispensable role of specialized nursing care in CAR-T therapy.

Disclosure: Nothing to declare

NP10

MONITORING TOXICITY-RELATED COMPLICATIONS IN PATIENTS UNDERGOING CAR-T: OBSERVATIONAL, PROSPECTIVE STUDY

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Background: CAR-T cell therapy represents an advanced treatment option for refractory hematologic malignancies but is associated with relevant toxicities, including Cytokine Release Syndrome (CRS), Immune effector Cell–Associated Neurotoxicity Syndrome (ICANS), cytopenias, and infectious complications. These events may affect patients' functional status and Quality of Life (QoL), emphasizing the critical role of nursing care in early detection, symptom management, and implementation of supportive interventions. Regular follow-up with validated scales should be used to facilitate early detection and suitable management.

Methods: This observational, prospective, monocentric, non-interventional study aimed to monitor toxicities in patients undergoing CAR-T therapy in our Italian center. Consecutive patients were enrolled from April 2022 to April 2025. Secondary objectives included the evaluation of Patient-Reported Outcomes (PROs), grading of toxicity severity, and duration of hospitalization. Data collection was performed at predefined time points using validated instruments: the Immune Effector Cell-associated Encephalopathy (ICE) Score for neurotoxicity, EuroQol-5D (EQ-5D) for QoL, Hospital Anxiety and Depression Scale (HAD) for psychological status, Patient-Generated Subjective Global Assessment (PG-SGA) for nutritional condition, and Cancer Linear Analogue Scale (CLAS) for symptom burden and daily functioning.

Results: Fifty-seven patients were included, 59.6% were men, with a median age of 59.4 years (range 24-75). Diagnoses mainly included Diffuse Large B-Cell Lymphoma (75.4%) and Multiple Myeloma (15.8%). The median hospital stay was 20.65 days (range 12-41), and 7% needed Intensive Care Unit (ICU) admission. ICANS did not occur in 77% of patients, while grades 3 to 4 were reported in 3.6%. CRS onset happened at a median of 2.69 days (range 0-11), with 5.3% experiencing grades 3 to 4. Anxiety scores, measured by HAD, significantly decreased over time (global p=0.038; T0 to T2 p=0.020), while depression scores remained stable. CLAS scores for movement, energy, and daily activities did not show

significant changes. However, overall QoL improved significantly between T1 and T2 (p=0.025). PG-SGA indicated a significant worsening from T0 to T1 (p<0.001), followed by improvement from T1 to T2 (p<0.001), with no difference between T0 and T2 (p=0.94). At baseline, 66.7% of patients were PG-SGA A (well nourished) and 33.3% PG-SGA B (moderate or suspected malnutrition). At T2, 67.6% were PG-SGA A, and only one patient (2.9%) was PG-SGA C (severe malnutrition). EQ-5D Index values showed good perceived health at baseline (0.830), a slight drop at T1 (0.795), and recovery at T2 (0.850), with a statistically significant improvement from T1 to T2 (p=0.0419). CAR-HEMATOTOX stratification classified 33.3% of patients as high-risk and 66.7% as low-risk.

Conclusions: CAR-T–related toxicities were generally manageable, with low rates of severe ICANS and rapid CRS resolution. QoL was mostly stable, with a notable improvement observed during the second week after CAR-T infusion. Hematotoxicity risk stratification was feasible. These findings emphasize the vital role of nursing care in monitoring, early recognition of complications, and integration of PROs during the acute post-CAR-T hospitalization phase.

Disclosure: The authors have no conflicts of interest to disclose

NP104

NURSING PRACTICE AND SAFETY IN ANTI-CD19 CAR-T CELL THERAPY FOR PEDIATRIC REFRACTORY SLE: A CASE SERIES OF 10 PATIENTS

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Background: Anti-CD19 chimeric antigen receptor (CAR) T-cell therapy provides a novel treatment option for refractory systemic lupus erythematosus (SLE). However, specific practical experience data, particularly regarding the clinical application of nursing-led toxicity monitoring and management, remain limited. This study aimed to investigate the nursing implementation points and safety management measures for this therapy in pediatric patients with refractory SLE, to provide an evidence-based reference for improving clinical nursing quality and reducing adverse events.

Methods: We conducted a retrospective analysis of the first 10 pediatric patients with refractory active SLE who received anti-CD19 CAR-T cell therapy at our center. The nursing team implemented a structured and standardized whole-process monitoring protocol. The nursing protocol comprised the following core measures: First, a reinforced post-infusion monitoring plan was implemented, which included systematic vital signs and oxygen saturation checks every 4 hours, alongside dynamic neurological assessments using the Immune Effector Cell-Associated Encephalopathy (ICE) score sheet. Second, cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) were strictly graded according to the American Society for Transplantation and Cellular Therapy (ASTCT) consensus criteria, with corresponding alert and management protocols activated upon identification. Third, for patients with grade 1–2 CRS, standardized non-

pharmacological interventions—such as physical cooling and ensuring adequate fluid intake—were prioritized. Finally, medication orders (e.g., for tocilizumab or corticosteroids) for patients requiring pharmacological treatment were executed accurately and promptly.The entire nursing process emphasized systematic monitoring, standardized grading, stepwise intervention, and team collaboration to ensure treatment safety.

Results: Among the ten treated patients, four (40%) developed cytokine release syndrome (CRS), with all cases categorized as grade 1 (according to ASTCT criteria). The median time to CRS onset was four days post-infusion. No instances of immune effector cell-associated neurotoxicity syndrome (ICANS), macrophage activation syndrome, or treatment-related mortality were observed. Neurological monitoring was performed systematically, with an average of 20 assessments completed per patient. Fever associated with CRS was effectively managed in all cases through initial nursing-led non-pharmacological interventions. At the last follow-up (median 3 months), all patients exhibited B-cell clearance and showed a reduction in SLEDAI scores.

Conclusions: This preliminary experience indicates that during anti-CD19 CAR-T therapy for SLE, CRS is common but mostly mild and manageable. A systematic and proactive nursing monitoring and management pathway is crucial for early toxicity identification, ensuring timely intervention and patient safety. These early findings provide a foundation for optimizing nursing protocols in larger-scale studies.

Disclosure: Nothing to declare.

NP124

COMMON ORGAN DYSFUNCTIONS AMONGST POST CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY PATIENTS: A SINGLE CENTRE SURVEY

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Background: Chimeric antigen receptor (CAR) T-cell therapy, a novel immune effector cell therapy that uses genetically engineered T-cells to target cancer cells has revealed significant efficacy in the management of haematological malignancies, autoimmune diseases and solid tumours. While capable of producing protracted durable remissions in several malignancies, there are associated treatment toxicities with the two most common being Cytokine release syndrome (CRS) and Immune effector cell-associated neurotoxicity syndrome (ICANS). However, as CAR T-cell procedures increase and the therapeutic applications expand, the increased risk of off-target effects is emerging, where healthy cells expressing tumour-associated antigens (TAA) or similar markers are inadvertently targeted. This can lead to a range of other unpredicted treatment-related toxicities and significant tissue/organ damage. Expanding clinical knowledge and expertise to enable early detection and rapid intervention is essential for which nursing assessment plays a critical role in strategies to reduce adverse outcomes.

Methods: A retrospective analysis of the case notes from the electronic health records (EHR) of all 33 post CAR-T cell patients of Hammersmith Hospital was done for this abstract. This review focused on identifying the common organs affected by the off-target toxicity ability of CAR T-cells observed in the clinical area.

Results: The review revealed that the most common organ affected by CAR-T cell therapy is the liver, with 48.5% of the 33 patients had mild to moderate transaminitis few days post CAR-T infusion. The lungs ranked second as 13 out of 33 patients developed tachypnoea and hypoxemia requiring oxygen support using nasal cannulas ranging from 1 to 5 litres/min and some up to the use of non-invasive ventilation. Tachycardia and hypotension requiring inotropic support were also seen in 27% of this cohort of patients, leading to admission to intensive care unit. While most patients come back to the ward about 3 to 5 days after ITU transfer, 2 patients remained longer averaging up to 1 week due to overlapping conditions such as prolonged inotropic support and difficult oxygen weaning. Gastric affectation manifested by non-infectious diarrhoea were also noted in one fifth of these patients or 21%. While only three patients developed rashes of more than 10% of their body surface area, and two patients had significant rise in ferritin levels after infusion of CAR-T cells, signalling significant inflammation.

Conclusions: The use of CAR T-cell therapy is becoming more widespread globally and as the efficacy of this immunotherapy treatment is proven in certain types of haematological malignancies and research continues the therapeutic application of this treatment modality is rapidly expanding. Side by side with this is the rise in complex and rare side-effects. Hence, a systematic and comprehensive approach to tracking the occurrence of these adverse events is crucial for aiding better understanding of the aetiology and underlying mechanisms that trigger these treatment-related toxicities, to improve prevention and management strategies, or at least to mitigate severity, to improve patient safety and outcomes.

Disclosure: Nothing to declare.

NP55

EMERGENCY: IEC-COLITIS POST CAR-T CELL THERAPY IN MULTIPLE MYELOMA

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Background: A 69-year-old man with IgM kappa multiple myeloma presented in 2021 with pancytopenia, hypercalcemia, extensive lytic lesions and bone marrow biopsy with 90% kappa-restricted plasma cells. Received five lines of therapy including cilta-cel (Carvykti) CAR-T in February 2023. In October 2025 was diagnosed with immune effector cell–associated colitis (EIC-colitis), raising concern for a late, T cell–mediated gastrointestinal toxicity in the context of prior CAR-T exposure.
This case is unusual for the very late onset of severe colitis more than two years post–CAR-T, its overlap with recurrent enteric infections (C. difficile, Salmonella and norovirus), and the

prolonged, relapsing course required combined anti-infective, immunosuppressive and supportive nursing strategies.

Methods: admitted for endorsing up to 20 watery and later bloody bowel movements per day, associated with abdominal pain, lightheadedness and impaired oral intake. Evaluation showed positive C. difficile and Salmonella PCR positivity; he received sequential oral vancomycin, fidaxomicin, and intravenous ceftriaxone with only transient improvement, and was repeatedly discharged still symptomatic. On readmission in September 2025, stool PCR again confirmed Salmonella without C. difficile toxin- GI, ID and cellular therapy teams differential of persistent infectious colitis, CAR-T–associated enteritis and immunodeficiency-associated colitis. Management included repeat stool cultures, serial fecal calprotectin, escalation to rifaximin plus high-dose oral prednisone with a taper. Ongoing elevation in fecal calprotectin and relapsing diarrhea prompted introduction of vedolizumab (Entyvio) every four weeks, careful monitoring for hepatotoxicity and infection, adjustment of antimicrobial therapy (oral vancomycin then Vantin) and initiation of IVIG every two weeks to address probable post–CAR-T hypogammaglobulinemia.

Results: With combined antimicrobial therapy, corticosteroids and gut-selective biologic therapy - stool frequency gradually decreased and abdominal pain improved, allowing maintenance of oral intake and functional status in the outpatient setting. The patient continued to experience intermittent loose stools, and fluctuating fecal calprotectin.
Close nursing surveillance of fluid balance, weight, infection signs and treatment toxicity supported safe steroid tapering, timely vedolizumab dosing and coordination of frequent laboratory and stool testing. The patient reported feeling more secure and engaged in self-management through nurse-led education on infection prevention, symptom monitoring and when to seek urgent care

Conclusions: This case underscores that severe colitis in CAR-T recipients may emerge long after infusion, with overlapping infectious and immune-mediated mechanisms that can be easily misattributed to isolated infection or irritable bowel disease. For HCT and cellular therapy nurses, key lessons include maintaining a high index of suspicion for serious late gastrointestinal toxicity, advocating for repeated microbiologic testing and biomarker assessment when diarrhea persists despite standard therapy, and coordinating early GI and ID involvement.
Nursing practice should prioritize meticulous assessment of stool pattern, hydration, nutrition and functional status; patient and caregiver education about promptly reporting diarrhea; and vigilant monitoring for complications of combined antibiotics, steroids, biologics and IVIG. Application of these principles may facilitate earlier recognition, multidisciplinary management and improved outcomes for other CAR-T and HCT survivors presenting with complex, recurrent colitis.

Clinical Trial Registry: None

Disclosure: Daniel Verina:
Speaker Board - GSK, J&J, Sanofi, Amgen, Karyopharm
Ad Board: Sanofi

Transplant and CAR-T Coordination, and Early Follow-up

NP27

THE IMPACT OF DOSE REDUCTION OF POST-TRANSPLANT CYCLOPHOSPHAMIDE TO 70 MG/KG ON EARLY TOXICITY: A SINGLE-CENTRE EXPERIENCE

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Background: Post-transplant cyclophosphamide (PtCy) is associated with significant adverse effects that negatively impact quality of life during hematopoietic cell transplantation. Based on previous reports and preliminary data, we reduced the PtCy dose from 2×50 mg/kg to 2×35 mg/kg with the aim of decreasing toxicity while maintaining efficacy. Here, we report a retrospective single center analysis of the incidence of the most common early complications, including mucositis, hemorrhagic cystitis, and cardiotoxicity.

Methods: All patients who underwent allogeneic HCT at the Institute of Hematology and Blood Transfusion in Prague using PtCy based GvHD prophylaxis between 2018 and 6/2025 were included in the analysis. The data were retreived from our institute‘s transplant database and by chart review.

Results: A total of 367 patients were analyzed and divided into two cohorts: the pre–dose-reduction PtCy cohort (n = 307) and the post–dose-reduction PtCy cohort (n = 60). Patient and transplant characteristics are summarized in Table 1. The cohorts receiving PtCy 70 mg/kg and 100 mg/kg differed in age, comorbidities (HCT-CI), and distribution of donor types (MRD/MUD/MMUD/haplo).
In the pre-reduction cohort, hemorrhagic cystitis occurred in 46 patients (15 %), predominantly Grade 1 (11,4 %, n = 35) and Grade 2 (2,6 %, n = 8), with a single case of Grade 3 (1 %). In the post-reduction cohort, the incidence was 10 patients (16,7 %), again with predominance of Grade 1 (15 %, n = 9). No Grade 2 cases were observed, and one patient experienced Grade 3 (1,7 %).
The incidence of mucositis was high in both cohorts. Before dose reduction, most patients experienced Grade 2 (36,2 %, n = 111) or Grade 3 (28 %, n = 86) mucositis; Grade 4 occurred in six patients (2 %). Following the dose adjustment, severity shifted toward lower grades: Grade 2 (30 %, n = 18) and Grade 3 (30 %, n = 18) predominated, and Grade 4 occurred in only one patient (1,7 %).
Early cardiac events were reported in 24 patients (7.8%) before dose reduction and in five patients (8.3%) after dose reduction.
Mechanical ventilation was needed in 13 patients (4,25 %) in the pre-reduction group and 3 (5 %) in the post-reduction group, dialysis incidence was similar at 10 patients (3,3 %) before dose reduction and 2 (3,3 %) after.

		PtCy 70 mg/kg N = 60
Age	years (median, range)	53 (22, 68)
Donor type	Haplo	11 (18%)
	MMUD	13 (22%)
	MRD	7 (12%)
	MUD	29 (48%)
HCT-CI	>2	23 (38%)
	0	21 (35%)
	1-2	16 (27%)
Karnofsky	<90	15 (25%)
	>=90	45 (75%)
Diagnosis Group	ALL a LBL	4 (6.7%)
	AML	37 (62%)
	MDS	11 (18%)
	MPN	4 (6.7%)

	NHL	2 (3.3%)
	other	2 (3.3%)
Conditioning	myeloablative	39 (65%)
CMV D/R = neg/neg	neg/neg = TRUE	4 (6.8%)
F donor / M recipient	F > M = TRUE	7 (12%)

Conclusions: Overall, the comparison of early toxicity between 70 mg/kg and 100 mg/kg PtCy did not show significant differences. The incidence and severity of mucositis, hemorrhagic cystitis, cardiac events, and the need for organ support (mechanical ventilation or dialysis) were similar between groups.

Disclosure: Nothing to declare

NP108

EVALUATION OF NURSE CASE MANAGER FOLLOW-UP IN PEDIATRIC POST-HSCT PATIENTS

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Background: Hematopoietic stem cell transplantation (HSCT) is the treatment of choice for several hematologic, oncologic, and congenital disorders in children. The specialized HSCT nurse case manager is associated with improved quality of life, treatment adherence, and reduced readmissions. This study evaluates the follow-up activities performed by the nurse case manager in the outpatient setting after HSCT.

Methods: A descriptive observational study was conducted in the HSCT Outpatient Clinic (2023–2025). Activities were categorized into clinical, educational, and administrative domains. Variables analyzed included: follow-up visits (SEGIN), scheduled telephone consultations (ATELEF), and urgent telematic consultations (ATTEL). Data were obtained from internal clinical records. Frequencies, percentages, measures of central tendency, and Pearson correlations were calculated using Microsoft Excel 365. Retrospective analysis with anonymized data; ethics and data protection principles were observed.

Results: A total of 3,894 follow-up visits, 764 urgent telematic consultations, and 493 scheduled telephone consultations were recorded. SEGIN was the predominant activity

(80.94% in 2023; 73.74% in 2024; 71.45% in 2025), showing a slight relative decrease. ATTEL increased steadily (12.32% to 17.11%), while ATELEF rose from 6.74% to 11.44%. Correlation analysis revealed a strong positive relationship between SEGIN and ATTEL (up to r=1.00), suggesting that higher in-person follow-up is associated with increased urgent telematic demand. ATELEF showed low correlations, indicating independence from other activities.

Conclusions: The nurse case manager plays a key role in post-HSCT care, providing clinical monitoring, pharmacological management, education (self-care, school reintegration), psycho-emotional support, and multidisciplinary coordination. In-person follow-up remains predominant, but the rise in urgent telematic care highlights the need for flexible resources tailored to the complexity of pediatric transplant patients. Joint planning of in-person and remote follow-up, continuous training, and updated protocols are recommended to ensure quality and safety.

Disclosure: "Nothing to declare"

NP68

IMPLEMENTING A NURSE-LED CAR-T PATIENT CARE PATHWAY IN A DISTRICT GENERAL HOSPITAL: ENHANCING PRE- AND POST-TREATMENT SUPPORT THROUGH ADVANCED CLINICAL PRACTICE

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Background: Chimeric antigen receptor T-cell (CAR-T) therapy has emerged as one of the most significant advances in the treatment of haematological malignancies in recent decades. Its demonstrated clinical effectiveness has led to rapidly expanding eligibility, enabling increasing numbers of patients to access this innovative treatment (Porter et al., 2011). While CAR-T infusion and acute management must take place within specialised centres, referring district general hospitals (DGHs) are responsible for preparing patients prior to treatment and providing safe and effective follow-up after discharge. These responsibilities demand streamlined collaboration, clear communication and a skilled workforce capable of recognising and managing CAR-T complications. Without effective structure and continuity, patient outcomes may be compromised through delayed referral, unmanaged toxicities or inadequate holistic care. In response to this challenge, a nurse-led CAR-T pre- and post-treatment pathway was developed and implemented in a DGH setting.

Methods: The pathway was designed and led by an Advanced Clinical Practitioner (ACP) specialising in transplantation and cellular therapies. The objective was to create a structured, nurse-led service that ensured timely pre-assessment, coordination of bridging therapy, delivery of comprehensive patient education, and consistent post-CAR-T follow-up. To ensure clinical governance and alignment with best practice, a standard operating procedure (SOP) was developed in accordance with the specialised centre recommendations and reviewed by relevant stakeholders through the DGH governance framework. A formal

nurse-led initial assessment was introduced to accompany referral documentation, capturing holistic needs and clinical stability indicators to streamline communication with the treating centre's multidisciplinary team (MDT).
Targeted nurse education covering treatment principles and complication recognition, including cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), was incorporated into annual competency programmes. Education resources were recorded and made available across the MDT. A nurse-led review clinic was also established to provide consistent follow-up during bridging therapy and after patient discharge.

Results: Early referral to specialist centres continued, supporting timely eligibility assessment and optimal treatment planning. The initial assessment tool enabled proactive identification of supportive needs, such as psychological support, dietetic input and physiotherapy, facilitating early interventions that supported patients' wellbeing and preparedness for treatment. Clear communication strengthened patient trust and improved collaboration with specialist centres.
The ACP-led clinic provided a single point of continuity, allowing regular monitoring and early complication management. Pre-treatment complications, including pleural effusion and PICC-line infections, were identified promptly, preventing delays to CAR-T admission.
Post-treatment complications—such as neutropenia, infection and early relapse—were managed swiftly due to consistent monitoring and patient access to the ACP outside of scheduled appointments. Patients received follow-up appointments before discharge from specialist care, demonstrating improved coordination between centres.

Conclusions: Implementation of a nurse-led CAR-T care pathway within a DGH demonstrates that advanced nursing leadership can improve treatment coordination, safety and patient experience. The ACP role delivers expert knowledge, clinical decision-making and collaboration that strengthens the wider MDT and improves continuity of care. Structured local pathways support timely referrals, early intervention and effective complication management, ultimately contributing to optimised outcomes for patients undergoing CAR-T therapy.

Clinical Trial Registry: NA

Disclosure: nothing to declare

NP91

COLLABORATION BETWEEN TRUSTS TO MAINTAIN CONTINUITY OF AUTOLOGOUS STEM CELL TRANSPLANTATION DURING SERVICE DISRUPTION

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Background: In early 2025, a regional hospital experienced an unexpected interruption in chemotherapy compounding services, following the closure of part of its sterile preparation unit after a regulatory inspection. This disruption rendered the site unable to supply chemotherapy essential for autologous stem cell transplantation (ASCT). This created an immediate risk of treatment delays for patients.
Our centre, which already has an established collaborative working relationship with the regional hospital for allogeneic transplant patients were approached to provide urgent support. Given the clinical urgency and potential impact on patient outcomes, we rapidly integrated their patients into our service, using are protocols and guidelines.
Aim: To describe how inter-trust collaboration enabled uninterrupted delivery of ASCT, during an unplanned service disruption, and to outline the operational and pathway adaptations implemented.

Methods:

- **Rapid Integration:** Immediate incorporation of patients from the regional hospital into our ASCT programme, following our standard operating procedures and existing clinical governance structures.
- **Initial Informal Coordination:** Leveraging pre-existing allogeneic transplant pathways and resources to facilitate urgent communication and scheduling.
- **Enhanced Communication:** Establishment of dedicated communication channels between teams, to ensure seamless care.
- **Formalisation:** Transition from informal collaboration to a formal service-level agreement, when it became evident that the disruption would persist beyond initial expectations.
- **Operational Adaptations:** Adjustments to resource allocation and documentation processes to accommodate increased patient volume without compromising safety or quality.

Results:

- All patients requiring ASCT were treated equally, maintaining compliance with national standards and institutional protocols.
- Adaptations included flexible scheduling, intensified multidisciplinary communication to support continuity of care.
- No adverse events reported, and patient safety was preserved throughout the process.
- Minimal disruption to patient care was achieved, despite the sudden increase in workload.

Conclusions: This case highlights the critical role of established inter-trust relationships, rapid operational response, structured communication in safeguarding and essential transplant services during unforeseen disruptions.
Future work should incorporate patient-reported outcomes to evaluate experience and satisfaction. This should provide a more comprehensive assessment of the impact of such collaborative interventions.
The poster will illustrate the adapted ASCT pathway, operational modifications and communication strategies that facilitated seamless patient transition and continuity of care.

Disclosure: Sheila Fox - Nothing to declare
Jo Mayo - Nothing to declare

NP93

ASSESSMENT OF NUTRITIONAL STATUS IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The nutritional status of patients undergoing allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a factor that must be taken into account because of its involvement in the impact of early and late complications, particularly mucositis, graft-versus-host disease (GVHD), and infectious complications.

Methods: Analysis of data from pre-transplant nutritional assessments conducted by the Nutrition Department of our center during the period from April 2025 to November 2025. Descriptive statistics were performed using SPSS v25.

Results: During the study period, 41 patients scheduled to undergo allogeneic hematopoietic stem cell transplantation (allo-HSCT) within the following 4–6 weeks were evaluated. Of these 41 patients, one was excluded from the subsequent analysis because allo-HSCT was ultimately not performed, although previous evaluation had been assessed. Demographic data are presented in Table 1. All patients were advised to perform physical exercise prior to allo-HSCT, as well as to follow dietary recommendations. The 10 patients who presented disease-related malnutrition (DRM) had received chemotherapy prior the nutritional assessment was performed.

Sex	Men: 23 (56.1%) Women: 18 (43.9%)
Age (mean)	51.79 years (range: 20–72)
Hematological diagnosis	Acute Myeloid Leukemia: 11 (26.8%) Myelofibrosis: 7 (17.1%) Non-Hodgkin Lymphoma: 6 (14.6%) Acute Lymphoblastic Leukemia: 5 (12.2%) Myelodysplastic Syndrome: 7 (17.1%) Plasma Cell Leukemia: 2 (4.9%) Hodgkin Lymphoma: 1 (2.4%) Others: 1 (2.4%) Chronic Myelomonocytic Leukemia: 1 (2.4%)

Chemotherapy prior to the nutritional assessment	No: 14 (34.1%) Yes: 27 (65.9%)
Previous HSCT prior the nutritional assessment	No: 33 (80.5%) Yes: 8 (19.5%)
Type of allo-HSCT planned	Related donor allo-HSCT: 12 (29.3%) Unrelated donor allo-HSCT: 25 (61.0%) Haploidentical allo-HSCT: 4 (9.8%)
Disease-related malnutrition (DRM) prior to allo-HSCT	No: 31 (75.6%) Yes: 10 (24.4%) - Moderate: 5 (50%) - Severe: 5 (50%)
Nutritional supplementation prior to allo-HSCT	No: 29 (70.7%) Yes: 12 (29.3%)

Table 1. Demographic characteristics

Conclusions:

Pre-transplant nutritional status is important for assessing potential post-transplant complications. The prevalence of malnutrition prior to allo-HSCT is higher among patients who have received standard chemotherapy before allo-HSCT. Receiving novel agents prior to allo-HSCT, instead of standard chemotherapy, does not appear to affect nutritional status. Further follow-up of this study is important to evaluate post-transplant complications in relation to nutritional status.

Disclosure: No disclosure.

Advanced Nursing Practise

NG27-01

DEFINING NATIONAL RESEARCH PRIORITIES IN HSCT NURSING USING THE DONABEDIAN MODEL, DELPHI METHODOLOGY, AND CONSENSUS RATIFICATION

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Background:

The rapid progression of Haematopoietic Stem Cell Transplantation and Cell Therapies necessitates the identification of standardized, evidence-based nursing research areas. National research priorities in Haematopoietic Stem Cell Transplantation (HSCT) nursing are crucial due to variations in local infrastructure, resource constraints, and clinical practice across countries. To establish a national, evidence-based roadmap, this study aimed to define and prioritize HSCT nursing research areas in Turkey, guided by the Donabedian Quality Model (Structure, Process, Outcome).

Methods: A rigorous three-round modified Delphi study was conducted nationwide. Our expert panel was highly selected, consisting of academic and clinical HSCT nurses with a minimum of 10 years of intensive clinical experience (n=17).
Round 1 (Qualitative Data): 456 raw research suggestions were initially gathered from practicing nurses (n=51) across the country. These suggestions were subjected to thematic analysis and refined into 23 distinct research categories, mapped to Donabedian's Structure, Process, Outcome, and Special Themes dimensions.
Rounds 2 & 3 (Quantitative Rating): The expert panel rated the 23 categories using a 5-point Likert scale. In Round 3, individual scores and the group's statistical feedback (Median and Interquartile Range - IQR) were provided to promote convergence.
Consensus Criteria: Consensus for a priority item was strictly defined by a Median ≥4.0 and an IQR ≤1.0.To enhance methodological robustness and promote national implementation, all consensus items will be ratified at a National Consensus Meeting scheduled for January 2026. Representatives from all Turkish national HSCT centers will be invited to this session to facilitate immediate integration of the findings into clinical practice.

Results: 14 HSCT nursing experts participated in all rounds of this study. Following the third round, consensus was achieved for 19 out of 23 categories (82.6%), demonstrating a high degree of agreement among national experts.
The highest-ranking thematic areas (Median=5.00) were predominantly concentrated in the Process and Outcome dimensions. Specific high-priority areas identified in the Structure dimension included Y1: Nursing Workload and Personnel Optimization. High-priority Outcome areas included O4: Nurse Burnout and Mental Health (although it did not reach the IQR consensus threshold, the Median score of 5.00 indicated very high perceived importance).

The three highest-ranked research priorities that achieved full consensus based on Round 3 Median scores are:

1. S-5 (Process): Medication Management and Toxicity Monitoring (Median: 5.00, IQR: 1.00)
2. S-2 (Process): Central Venous Catheter (CVC) Care (Median: 5.00, IQR: 1.00)
3. O-6 (Outcome): Patient Safety and Satisfaction (Median: 5.00, IQR: 1.00)

The four research categories that did not reach consensus (IQR > 1.0) were S3 (Mucositis Management), S4 (GVHD Nursing Management), O4 (Nurse Burnout), and ÖZ3 (Biological/Genetic Factors).

Conclusions: This study defines HSCT and CT nursing research priorities specific to the national healthcare system realities, providing a rigorous, evidence-based foundation for future research. The high consensus on items related to Process and Patient/Staff Outcomes underscores the need to focus resources on clinical practice standardization and personnel well-being. The prioritized findings, following ratification by the National Consensus Meeting, will provide a concrete, nationally relevant roadmap for advancing evidence-based practice across all Turkish HSCT centers.

Clinical Trial Registry: Not applicable.

Disclosure: None.

NG27-05

ECP 2.0: TECHNICAL, ORGANIZATIONAL AND PATIENT-CENTERED EVALUATION OF HIGH-FLOW VENOUS PORTS AS SYSTEMATIC ACCESS FOR POST-TRANSPLANT EXTRACORPOREAL PHOTOPHERESIS

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Background: Extracorporeal photopheresis (ECP) is a well-established therapy for acute and chronic graft-versus-host disease (GVHD). At the Cellular Therapies Program (CTP) of the Oncology Institute of Southern Switzerland, high-flow venous ports were systematically introduced to improve continuity, safety, and patient comfort in post-transplant ECP pathways. Despite the increasing use of this device, evidence supporting its routine adoption remains limited. The primary aim of this study was to assess technical safety and procedural efficiency of ECP performed through high-flow ports compared with peripheral or central venous access. Secondary aims included evaluating organizational impact, access stability,

acceptability, emphasizing the importance of patient experience in ECP, and preliminary biological results within a multicenter European analysis.

Methods: A retrospective observational descriptive-analytic study was conducted on ECP procedures performed between May 2022 and November 2023. 13 patients (9 chronic GVHD, 4 acute GVHD) underwent more than 200 ECP procedures. Machine-recorded data (alarms, duration, treated volumes) were integrated with anonymized clinical variables (age, sex, GVHD type and site, venous access) and organizational indicators from 2022–2024. Statistical analysis included descriptive measures, ANOVA comparisons across access types, Pearson correlations, and selected graphical representations. Cell viability and apoptosis profiles from the associated European multicenter study were also analyzed.

Results: **Use of access devices:** The high-flow port was the most frequently used access (9 patients, 69%), demonstrating sustained stability over time.
Technical safety:

- Mean alarm frequency showed no significant differences between access types (ANOVA $p > 0.05$).
- Alarms related to Vascular Access Devices were rare and not specifically associated with port use.
- Technical issues did not lead to procedures interruption.

Operational efficiency:

- Procedure duration was longer with ports (mean 140 min) compared with peripheral (103 min) and CICC access (88 min) ($p < 0.001$), consistent with single-needle modality, without compromising procedural quality.
- Maximum treated volumes were comparable across access types, with no clinically meaningful differences.

Correlations:

- No significant correlation between alarm frequency and procedure duration (Figure 1).
- No association between access type and alarms related to Vascular Access Devices.

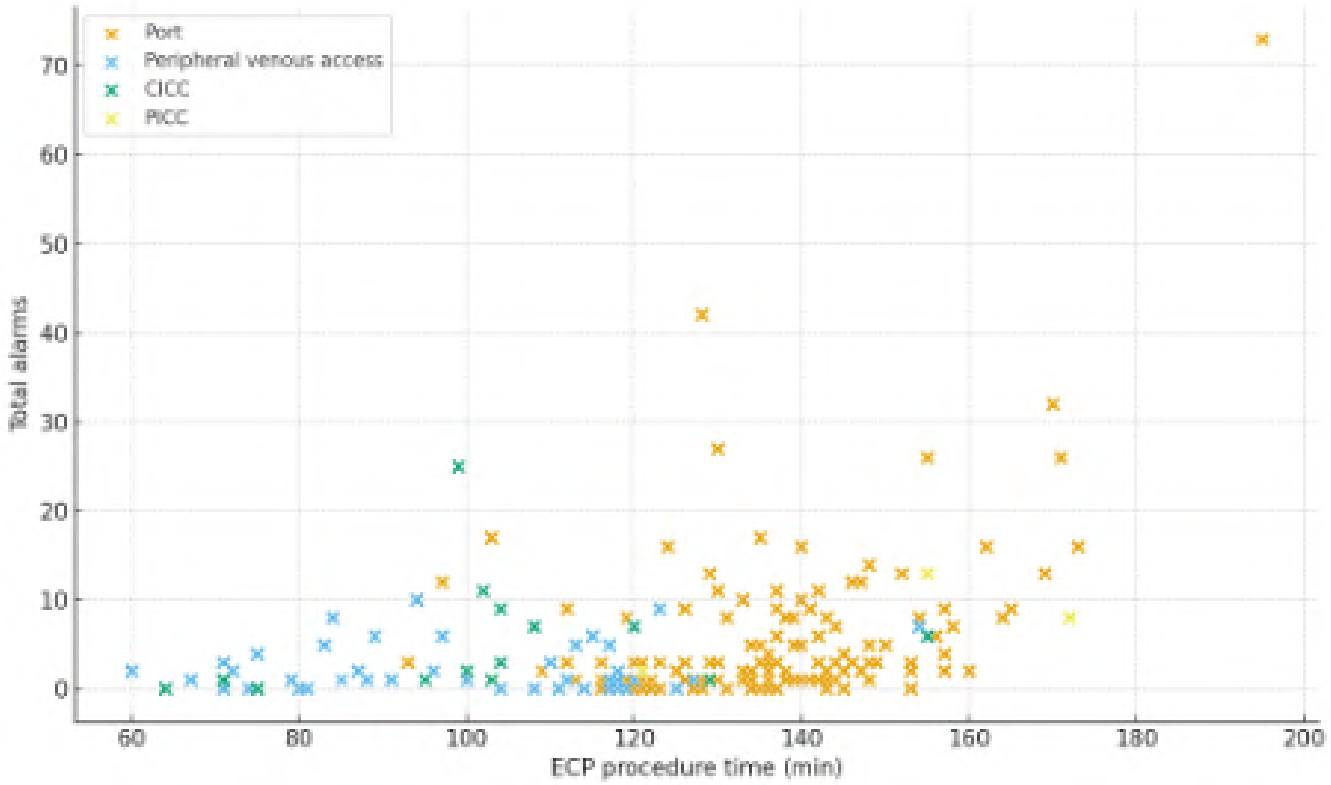

Figure 1 Correlation between procedure time and total alarms by vascular access

Organizational impact: ECP activity increased markedly, from 71 procedures in 2022 to 221 in 2023 and 317 in 2024, confirming sustainability of the model and absence of port-related operational limitations.
Preliminary biological findings: Cell viability and apoptosis profiles before and after photoactivation were comparable across access types, supporting biological equivalence.

Conclusions: Systematic use of the high-flow venous port for ECP procedures is safe, technically stable, and comparable to other venous access options. The longer duration associated with single-needle modality does not compromise overall efficiency. Beyond technical performance, adopting the port represents an ethical, patient-centered choice: it prevents repeated peripheral punctures and enables patients to rely on a single, well-tolerated access throughout their therapeutic journey, including outpatient visits and supportive treatments. Its reproducibility across organizational models and the equivalence of biological outcomes further support its use. A validation phase assessing patient-reported quality is planned to integrate the patient perspective into the global evaluation of the procedure.

Disclosure: Nothing to declare.

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NP20

PATIENT SATISFACTION OF A NURSE-LED BONE MARROW ASPIRATION (BMA) SERVICE

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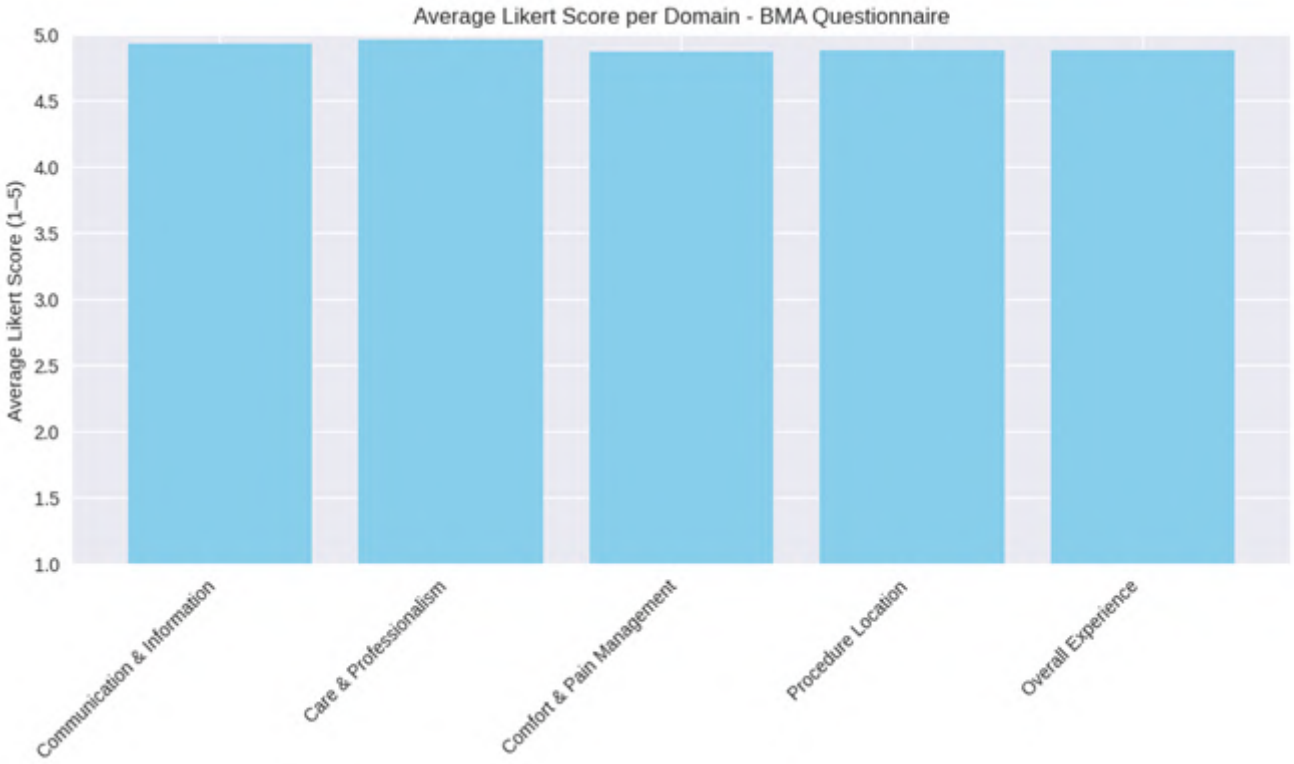
Background: Bone marrow aspirations (BMAs) are essential after haematopoietic stem cell transplant (HSCT) to assess disease status and donor chimerism (Qin et al., 2014). With the rising number of allogeneic transplants, the burden of BMAs on medical staff became overwhelming, resulting in delays, procedures performed at incorrect time points, and long patient waits. To address this, the SWBMT Programme introduced nurse-led BMA lists in 2017 to improve patient experience, ensure timely procedures, and provide holistic care. Patient feedback is vital for service improvement and recognition of clinical excellence (Kumah et al., 2017). A satisfaction questionnaire was therefore developed to evaluate the nurse-led BMA service.

Methods: Between July and November 2025, satisfaction questionnaires were prospectively collected from 80 patients using a 5-point Likert scale (Batterton and Hale, 2017). The cohort included 49 males and 31 females, median age 61 years (range 20–77). Feedback was obtained immediately post-procedure by the nurse performing the aspiration.

Results: The questionnaire covered five domains: communication, care and professionalism, comfort and pain management, procedure location, and overall experience, with space for comments.

- **Communication and information**: 93% strongly agreed they received clear explanations before, during, and after the procedure, with opportunities to ask questions.
- **Care and professionalism**: 97% strongly agreed nurses were professional, respectful, and competent.
- **Comfort and pain management**: 89% strongly agreed pain was managed effectively and appropriate aftercare advice was given; 10% agreed, while 1% were neutral or dissatisfied.
- **Procedure location**: 90% strongly agreed the environment was clean, safe, private, and well-equipped; 8% agreed, 2% were neutral or dissatisfied.
- **Overall experience**: 93% strongly agreed they were satisfied, would undergo nurse-led BMAs again, and would recommend the service.

Overall, ratings across domains were overwhelmingly positive, with most responses at "strongly agree." Notably, 86% had prior experience of nurse-led BMAs.
Qualitative feedback Comments frequently described the service as "professional," "pain-free," "compassionate," "gentle," and praised "excellent communication." A small number highlighted areas for improvement, including waiting times, bed size, and space constraints.



Conclusions: This evaluation demonstrates that nurse-led BMAs are safe, effective, and highly valued by patients. Across all domains—communication, professionalism, comfort, environment, and overall experience—feedback was overwhelmingly positive, with most participants rating their care as excellent. Qualitative comments reinforced these findings, particularly nurses' compassion and skill in pain management. Minor concerns regarding space and waiting times were noted but did not detract from overall satisfaction.
Implications The results support continued development and expansion of nurse-led services in haematology. This model offers patient-centred, professional, and efficient care, enhancing both patient experience and clinical outcomes.

Disclosure: Nothing to declare.

NP110

NURSE LEADERSHIP IN MANAGING ATG REACTIONS IN PEDIATRIC ONCOLOGY: "KOV IN THE LEAD"

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Background: Antithymocyte globulin (ATG) administration in pediatric hematology and oncology is frequently associated with infusion-related reactions, ranging from mild fever and rash to severe anaphylaxis. Traditionally, physicians were primarily responsible for intervention during such reactions. To enhance nurse autonomy and ensure timely, high-quality care, a nurse-led protocol, *"Kinderoncologieverpleegkundige (Pediatric Oncology Nurse) in the lead" (KOV in the lead)*, was developed at the Princess Máxima Center for Pediatric Oncology *.

At the Princess Máxima Center, nurses work every day with dedication and passion to push boundaries in pediatric oncology care. The center's vision emphasizes professional leadership, collaboration, and continuous improvement, ensuring that every child receives the best possible care.

Methods: A structured protocol was implemented on the pediatric oncology ward, defining clear actions for mild (Pediatric Early Warning Score [PEWS] 0–4), moderate (PEWS 5–8), and severe (PEWS ≥8) ATG reactions **. Nurses were educated to recognize symptoms such as fever, urticaria, dyspnea, and hypotension, and to administer appropriate medication (paracetamol, clemastine, and prednisolone) as part of their pediatric oncology education. The protocol specifies when to act autonomously and when to consult a physician. Team education, simulation sessions, and debriefings were used to enhance clinical confidence and decision making.

Results: Following implementation, nurses demonstrated greater leadership and confidence in managing ATG reactions. The initial responses from the pediatric oncology nurses are positive. This emerged during the daily team time-out in the day shift. They feel more confident and believe that this leads to faster collaboration with the physicians on the ward. The initiative reinforced a culture of shared responsibility, where nurses take an active, leading role in patient safety and acute care. Evaluation and team feedback supported continuous learning and refinement of the protocol.

Conclusions: The "KOV in the lead" initiative shows how passionate and forward thinking nurse leadership can drive improvements in safety, autonomy, and quality of care. By giving nurses the confidence and clear guidelines to make important decisions, this approach helps different healthcare professionals work better together and improves pediatric cancer care, leading to the best possible outcomes for children now and in the future. This aligns with our mission: to cure every child with cancer, while ensuring the best possible quality of life.

Disclosure: Nothing to declare

NP54

ESTABLISHING A NURSE-LED BONE MARROW ASPIRATION (BMA) SERVICE POST-HAEMATOPOIETIC STEM CELL TRANSPLANT (HSCT): SHARING EXPERTISE TO IMPROVE PATIENT EXPERIENCE AND SERVICE DELIVERY

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Background: Bone marrow aspirations (BMAs) are a critical element of post-haematopoietic stem cell transplant (HSCT) care, providing essential information on disease status and donor chimerism. However, the rising number of allogeneic transplants has placed considerable pressure on clinical teams, leading to delays, procedures being undertaken at inappropriate timepoints, and negative patient experiences due to prolonged waiting times and inadequate facilities. To address these challenges, the South Wales Bone Marrow Transplant (SWBMT) Programme introduced a nurse-led BMA service in 2017. This initiative was designed to improve patient care and experience, ensure procedures are performed in a timely manner, and streamline processes to enhance service sustainability. At present, only a limited number of health boards in Wales offer such a service, highlighting an important opportunity to share learning and extend provision across the region.

Methods: A robust governance and competency framework was established to support the development of the nurse-led BMA service. Training was delivered through a structured pathway in which an Advanced Nurse Practitioner (ANP), initially trained by a Specialist Registrar (SpR), subsequently trained Clinical Nurse Specialists (CNSs). This pathway progressed from observation to supervised practice and finally independent sign-off, typically completed within three to four months. Competence was maintained through re-assessment every two years, with a requirement to perform a minimum of twelve BMAs annually. Clinical governance measures included the introduction of a lidocaine Patient Group Direction (PGD), standard operating procedures (SOPs), a competency booklet, and a clear escalation plan for medical support. Service delivery was organised through dedicated nurse-led BMA lists held twice weekly, supported by a referral system, administrative infrastructure, and routine audit to ensure quality and sustainability.

Results: The introduction of the nurse-led BMA service has delivered clear benefits for both patients and staff. Patient outcomes have improved through reduced waiting times, procedures being carried out at the correct timepoints, and enhanced continuity of care, all contributing to a more positive overall experience. For staff and service delivery, the initiative has released medical time for other priorities, expanded the nursing scope to include advanced practice, and generated high levels of staff satisfaction alongside improved efficiency. In the past twelve months alone, 384 BMAs were performed by the nurse-led team, and since the service was established, medical staff have rarely needed to undertake BMAs. Feedback from patients and staff has been overwhelmingly positive. The work has been shared more widely through a presentation to the Wales Haematology Cancer Site

Group, and a survey has been distributed to other health boards to gauge interest in adopting similar models.

Conclusions: The nurse-led BMA service has delivered substantial benefits, including improved patient experience, timely and efficient service delivery, enhanced nursing competencies, and optimal use of resources. This model demonstrates scalability across Wales, the wider UK, and internationally, offering significant potential for shared learning and broader adoption. By promoting best practice in post-transplant care, it provides a framework for sustainable service development and improved outcomes for patients and healthcare systems alike.

Disclosure: Nothing to declare

NP70

PATIENT REPORTED EXPERIENCE OF BONE MARROW ASPIRATE AND TREPHINE BIOPSY. A NURSE LED SERVICE ESTABLISHMENT AND IMPROVEMENT PROJECT

Sara Main[1], *Mariam Amer*[1], *Annie Major*[1], *Kelly Lanaghan*[1], *Deborah Richardson*[1], *Christopher Dalley*[1], *Jing Hiew*[1], *Amy Creighton*[1], *Alice Jenkins*[1], *Kim Orchard*[1], *Madeleine Norbury*[1]
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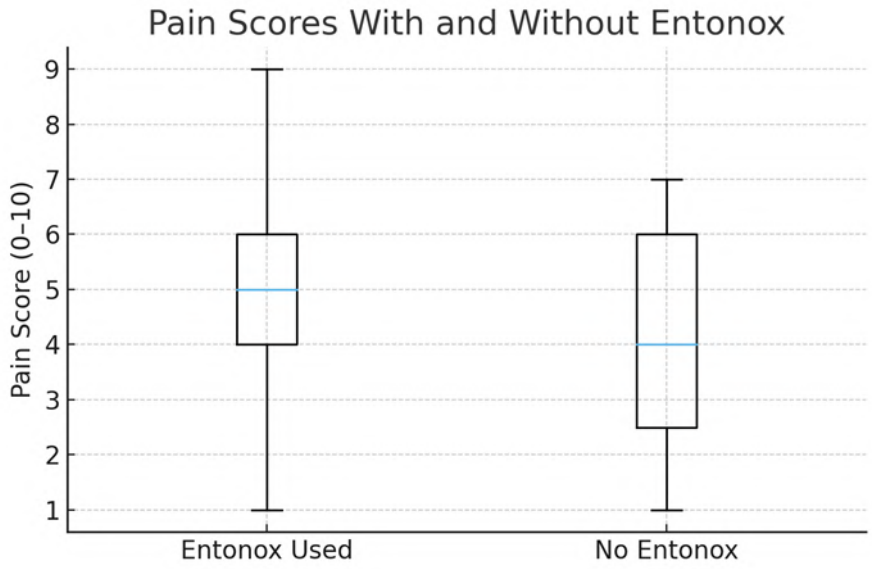
Background: Bone marrow aspirate and trephine (BMAT) biopsy is an essential diagnostic procedure but is often associated with anxiety and procedural pain. As part of a programme to strengthen nurse-led practice within a regional transplant programme, a new Standard Operating Procedure (SOP) and competency framework were developed to support consistent, safe delivery of BMAT by advanced and specialist nurses. Understanding patient-reported experience was essential both to evaluate the newly formalised nurse-led service and to identify opportunities for improvement, including enhanced analgesic options. This baseline audit aimed to describe current patient experience of BMAT and use these findings to inform a prospective evaluation of inhaled methoxyflurane (Penthrox) as an alternative to Entonox.

Methods: A prospective baseline audit was undertaken between September and December 2025. Adults undergoing BMAT on the haematology day unit were invited to complete an anonymous questionnaire assessing: pre-procedure anxiety (0–10), procedural pain (0–10), satisfaction with pain management (1–5), use and perceived benefit of Entonox, recall of consent and aftercare advice, and free-text feedback. Findings were analysed descriptively and used to refine the SOP, education materials, and local guidance. Concurrent preparatory work included submission of an updated SOP incorporating Penthrox, approval through the Drugs and Therapeutics Committee, creation of an ARIA protocol for methoxyflurane prescribing, and development of staff education and a revised audit tool for prospective evaluation beginning January 2026.

Results: A MS Forms link to the questionnaire was sent out to 72 sequential patients via email. Forty patients participated (20 male, 20 female). Median pre-procedure anxiety was 5/10 (IQR 3–7), with 30% reporting anxiety ≥7. Median procedural pain was 5/10 (IQR 3–6); 55% reported pain ≥5 and 40% reported pain ≥6. Entonox was used by 21/40 (52.5%); of these, two-thirds found it helpful, though several reported dislike of the device or a preference to avoid it. Satisfaction with pain management was high (82.5% rated 4–5 stars; 60% rated 5 stars). Consent was recalled in 93% of cases, and aftercare advice in 100%. Free-text feedback emphasised the value of skilled, confident operators; clear explanations; reassurance; and continuity—strengths consistently associated with the nurse-led model. A minority expressed desire for improved analgesia or anxiolysis.



Conclusions: This audit demonstrates that while overall satisfaction with BMAT is high, many patients continue to experience moderate–severe pain or significant anxiety. The findings support targeted refinements to nurse-led BMAT practice, including enhanced pre-procedure information, improved psychological support, and access to alternative analgesia for suitable patients. The SOP, competency framework, and preparatory governance work have established the foundations for a prospective evaluation of methoxyflurane for procedural pain management commencing January 2026. Penthrox is reported to be both quicker and superior as a short acting, reversible inhaled analgesic. It is also more sustainable that using bottled Entonox. Based on our baseline audit, around 50% of BMAT patients use Entonox. Substituting Penthrox (0.84 kg CO_2e) for Entonox (98.89 kg CO_2e) in this group would save ~4.9 tonnes CO_2e for every 100 BMAT procedures, supporting a low-carbon analgesia strategy.

Disclosure: educational sponsorship from Sanofi

NP98

GRAFT VS. HOST DISEASE - ADVANCED PRACTICE NURSE. A POTENTIAL KEY ROLE IN THE INTERPROFESSIONAL CARE OF PATIENTS WITH GVHD

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Background: Graft-versus-host disease (GVHD) is a serious complication associated with allogeneic stem cell transplantation that severely affects patients physically, psychologically, and psychosocially. The complex care required necessitates cross-sector, interprofessional support. An advanced practice nurse (APN) can play a central role in this. A systematic literature review (March 2025) reveals a research gap regarding the specific care needs of this patient group and therefore also the relevance of an APN in this field in Germany.

Methods: The aim is to highlight the specific care needs of patients with GvHD and how these can be addressed by the care provided by an APN within an interprofessional team. The qualitative research will be conducted in two phases using guided expert interviews evaluated according to Kuckartz. In phase 1 (April 2025), APNs who already work with GvHD patients will be interviewed. In phase 2 (June 2025), an interprofessional team without APN structures will be interviewed. This will be followed by a comparison of the perspectives.

Results: In phase 1, a total of four APNs from three German clinics will be interviewed online. The requirements for the structural implementation of an APN and the psychosocial and long-term care needs of patients will be recorded. In phase 2, a total of five professional groups from a multidisciplinary team at a German clinic will be interviewed in six focus group interviews. A diverse range of care needs is identified, with a focus on a standardized care system and the resulting areas of activity for an APN. The need for a continuous, cross-sectoral contact person with bundled expertise is emphasized.
The results highlight a specific need for care. Depending on the perspective, the focus varies: the multi-professional team reflects a standardized and acute need to restore functionality. The APNs surveyed focus on the long-term consequences and psychosocial aspects. The study situation reinforces both perspectives. The results are embedded in the needs pyramid according to the needs hierarchy. The APNs surveyed focus on the long-term consequences and psychosocial aspects. The study situation reinforces both perspectives. The embedding of the results in Maslow's hierarchy of needs serves as an organizational model and is intended to support the prioritization of care needs. The dynamic progression of needs must be taken into account here. With the help of the trajectory model according to Corbin and Strauss, chronic care management can be carried out in a structured manner.

Conclusions: A generally transferable care requirement for patients with GvHD exists in the areas of safety and information transfer, physical, psychological, and psychosocial stability, as well as comprehensive GvHD expertise with adequate networking. Providing optimal care for GvHD patients is a balancing act between standardization and individualization, from acute to long-term care with internal and supraregional networks. An APN can address these needs as a continuous care coordinator within an interprofessional collaboration.

Disclosure: Nothing to declare.

Nursing Research in Transplant, Cell and Gene Therapy

NG27-06

DIFFERENCES BETWEEN PHYSICIANS' AND NURSES' PERSPECTIVES IN DEFINING CORE NURSING-SENSITIVE OUTCOMES IN ADULT HSCT AND CAR-T THERAPY: AN INTERDISCIPLINARY ITALIAN DELPHI CONSENSUS

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Background: Haematopoietic stem cell transplantation (HSCT) and chimeric antigen receptor T-cell (CAR-T) therapy are gold-standard treatments for refractory haematologic malignancies but remain burdened by significant toxicity affecting prognosis and quality of life. Complications include treatment-specific syndromes—such as GvHD, CRS, and ICANS—and shared side effects like fatigue, mucositis, and fever. Nursing care is crucial in preventing, recognizing, and managing these complications, directly influencing patient outcomes. Nursing-sensitive outcomes (NSOs) reflect conditions or perceptions directly affected by nursing interventions and allow objective evaluation of care quality. However, NSOs may differ between HSCT and CAR-T contexts, and no standardized framework currently defines them in adult populations. This study aimed to identify relevant NSOs for adult HSCT and CAR-T therapy.

Methods: A two-round Delphi consensus was conducted to identify nursing-sensitive outcomes (NSOs) relevant to HSCT and CAR-T-cell therapy. The process, carried out anonymously via Microsoft Forms, involved two groups: a Research Team (RT, Table 1), responsible for developing and validating the preliminary list of NSOs, and an Expert Panel (EP) of nurses and physicians from Italian GITMO-accredited centres. The initial NSO pool, derived from Oncology Nursing Society outcomes (Given, 2005) BAand literature review, was refined through RT input and evaluated by the EP for clarity and relevance on a 4-point Likert scale. Consensus was defined as the minimum agreement required for inclusion in the final set. Descriptive and inferential statistics were applied to compare responses by round, profession, and clinical activity, with significance set at $p<0.05$.

Results:

Table 1: *The Expert Panel (EP)* Characteristics*

		ROUND			PROFESSION		
		1	**2**		**Nurse**	**Hematology Physician**	
		N (%)	**N (%)**	**p-value**	**N (%)**	**N (%)**	**p-value**
Gender	*Male* *Female*	22 (26,8) 60 (73,2)	12 (32,4) 25 (67,6)	0,531	6 (50,0) 20 (80,0)	6 (50,0) 5 (20,0)	0.062
Age group (years)	*<25* *26-30* *31-35* *36-40* *41-45* *46-50* *51-55* *56-60* *≥61*	2 (2,4) 6 (7,3) 10 (12,2) 6 (7,3) 7 (8,5) 7 (8,5) 20 (24,4) 18 (22,0) 6 (7,3)	- 1 (2,7) 3 (8,1) 2 (5,4) 6 (16,2) 6 (16,2) 8 (21,6) 8 (21,6) 3 (8,1))	0,735	- 1(100) 3 (100) 2 (100) 6 (100) 5 (83,3) 5 (62,5) 4 (50,0) -	- - - - - 1 (16,7) 3 (37,5) 4 (50,0) 3 (100)	**0,044**
Territorial unit	*North-West* *North-East* *Central* *South* *Islands*	28 (34,2) 21 (25,6) 14 (17,1) 18 (22,0) 1 (1,2	14 (37,8) 7 (18,9) 10 (27,0) 6 (16,2) -	0,609	11 (78,6) 5 (71,4) 7 (70,0) 3 (50,0) -	3 (21,4) 2 (28,6) 3 (30,0) 3 (50,0) -	0,649
Profession	*Nurse* *Hematology*	65 (79,3) 17 (20,7)	26 (70,3) 11 (29,7)	0,284	-	-	-
Work experience at the	*< 2* *3 - 5*	9 (11,0) 14 (17,1)	- 7 (18,9)	0,219	- 7 (100)	- -	0,158

centre (years)	*6 - 10* *> 11*	9 (11,0) 50 (61,0)	5 (13,5) 25 (67,6)		3 (60,0) 16 (64,0)	2 (40,0) 9 (36,0)	
Previous knowledge of NSOs	*Yes* *no*	48 (58,5) 34 (41,5)	31 (83,8) 6 (16,2)	**0,007**	24 (77,4) 2 (33,3)	7 (22,6) 4 (66,7)	**0,031**

Research Team (RT), which participated in the preliminary development and validation of NSOs. RT members were eight nurses with at least three years of professional experience in transplant care and held or were pursuing a PhD, Master's Degree in Nursing, or postgraduate training in research methodology.
Expert Panel (EP): comprised nurses and physicians from centres accredited by the Italian Group for Bone Marrow Transplantation (GITMO). In these centres, haematology physicians serve as program directors for transplant activities, while nurses are designated by the directors as official representatives. Participation in the panel was voluntary and based on professional experience in HSCT or CAR-T-cell therapy.
North-West: Piedmont, Aosta Valley, Lombardy, and Liguria; **North-East**: Emilia-Romagna, Friuli Venezia Giulia, Veneto, and Trentino-Alto Adige; **Center**: Tuscany, Marche, Lazio, and Umbria; **South**: Abruzzo, Molise, Campania, Apulia, Basilicata, and Calabria; **Islands**: Sicily and Sardinia. **HSCT**: Hematopoietic stem-cell transplantation; **CAR-T**: Chimeric Antigen Receptor T-cell; **NSO**: Nursing Sensitive Outcome.

Figure 1: The Delphi consensus results, conducted by an Expert Panel (EP)*

NSO	1° ROUND															2° ROUND										
	Overall - All respondents (N=82)					Nurse (N=65)					Hematology physician (N=17)					Overall - All respondents (N=37)					Nurse (N=26)					Hematology physician (N=11)				
	Med	IQR	M	SD	%3-4	Med	IQR	M	SD	%3-4	Med	IQR	M	SD	%3-4	Med	IQR	M	SD	%3-4	Med	IQR	M	SD	%3-4	Med	IQR	M	SD	%3-4
Activities of daily living (ADLs)	3	1	3,4	0,6	**93,9**	3	1,0	3,4	0,6	**95,4**	3	1,0	3,2	0,7	**88,2**	4	1,0	3,6	0,5	**100**	4	1	3,6	0,5	**100**	3	1	3,5	0,5	**100**
Anorexia	3	2	3,0	0,7	73,2	3	1,0	3,0	0,7	**75,4**	3	2,0	3,0	0,8	64,7	3	1,0	2,9	0,8	73,0	3	0	2,9	0,7	**80,8**	3	2	2,8	1,1	54,5
Anxiety	3	1	3,4	0,6	**92,7**	3	1,0	3,4	0,6	**95,4**	3	1,0	3,3	0,8	**82,4**	3	1,0	3,5	0,5	**100**	3	1	3,4	0,5	**100**	4	1	3,6	0,5	**100**
CAUTIs	4	1	3,4	0,7	**87,8**	4	1,0	3,5	0,7	**89,2**	3	1,0	3,3	0,8	**82,4**	4	1,0	3,5	0,7	**89,2**	4	0	3,7	0,5	**96,2**	3	1	3,0	0,8	72,7
CLABSIs	4	1	3,7	0,6	**92,7**	4	0,0	3,7	0,5	**95,4**	4	1,0	3,4	0,8	**82,4**	4	0,0	3,8	0,5	**94,6**	4	0	3,9	0,4	**96,2**	4	1	3,5	0,7	**90,9**
Constipation	3	1	3,1	0,7	**80,5**	3	1,0	3,3	0,6	**90,8**	2	1,0	2,6	0,9	41,2	3	1,0	3,0	0,8	**78,4**	3	0	3,0	0,7	**80,8**	3	1,5	3,1	0,8	72,7
Depression	3	1	3,2	0,7	**84,1**	3	1,0	3,1	0,7	**83,1**	3	1,0	3,3	0,7	**88,2**	3	1,0	3,1	0,7	**81,1**	3	0	3,0	0,5	**88,5**	4	2	3,1	1,1	63,6
Diarrhoea	3	2	3,0	0,8	67,1	3	2,0	3,0	0,8	69,2	3	2,0	2,9	0,9	58,8	3	0,0	3,1	0,7	**86,5**	3	0	3,1	0,6	**92,3**	3	1,5	3,1	0,8	72,7
Drug extravasation	4	1	3,5	0,8	**84,1**	4	1,0	3,4	0,8	**83,1**	4	1,0	3,6	0,7	**88,2**	4	1,0	3,6	0,5	**100**	4	1	3,7	0,5	**100**	4	1	3,6	0,5	**100**
Dyspnoea	3	2	3,0	0,8	67,1	3	2,0	3,0	0,8	70,8	3	2,0	2,9	0,9	52,9	3	2,0	2,9	1,0	73,0	3	1	2,9	1,0	**80,8**	3	2	2,9	1,1	54,5
Emotional distress	3	1	3,2	0,7	**85,4**	3	1,0	3,2	0,7	**84,6**	4	1,0	3,4	0,7	**88,2**	3	1,0	3,4	0,7	**86,5**	3	1	3,3	0,7	**88,5**	4	1	3,5	0,8	**81,8**
Falls	4	1	3,4	0,7	**85,4**	4	1,0	3,4	0,7	**86,2**	4	1,0	3,5	0,8	**82,4**	4	0,0	3,7	0,6	**94,6**	4	0	3,7	0,6	**92,3**	4	1	3,6	0,5	**100**
Fatigue	3	1	3,3	0,7	**85,4**	3	1,0	3,2	0,7	**84,6**	3	1,0	3,4	0,7	**88,2**	3	1,0	3,2	0,6	**86,5**	3	1	3,3	0,6	**92,3**	3	0,5	2,8	0,6	72,7
Mucosal alterations (mucositis)	3,5	1	3,4	0,7	**87,8**	4	1,0	3,4	0,6	**92,3**	3	2,0	3,2	0,9	70,6	4	1,0	3,4	0,8	**86,5**	4	1	3,5	0,8	**92,3**	4	1,5	3,3	0,9	72,7
Nausea	3	1	3,2	0,7	**82,9**	3	1,0	3,2	0,6	**87,7**	3	2,0	3,1	0,9	64,7	3	1,0	3,2	0,8	**86,5**	3	1	3,3	0,8	**88,5**	3	1	3,2	0,8	**81,8**
Nutritional status	3	1	3,3	0,7	**89,0**	3	1,0	3,3	0,6	**92,3**	3	1,0	3,2	0,8	**76,5**	3	1,0	3,3	0,7	**86,5**	3	1	3,4	0,6	**96,2**	3	2	3,0	0,9	63,6
Pain	4	1	3,5	0,7	**91,5**	4	1,0	3,5	0,6	**92,3**	4	1,0	3,4	0,7	**88,2**	4	1,0	3,6	0,6	**91,9**	4	1	3,7	0,5	**100**	4	1,5	3,4	0,9	72,7
Patient satisfaction with nursing care	4	1	3,7	0,5	**96,3**	4	1,0	3,7	0,5	**96,9**	4	0,0	3,8	0,6	**94,1**	4	0,0	3,9	0,3	**100**	4	0	3,9	0,3	**100**	4	0	4,0	0,0	**100**
Quality of life	3	1	3,4	0,7	**90,2**	3	1,0	3,4	0,6	**92,3**	3	1,0	3,2	0,9	**82,4**	3	1,0	3,4	0,7	**89,2**	3,5	1	3,5	0,6	**96,2**	3	1,5	3,1	0,8	72,7
Recognition of clinical instability	4	1	3,5	0,6	**95,1**	4	1,0	3,6	0,6	**96,9**	4	1,0	3,4	0,9	**88,2**	4	1,0	3,7	0,5	**97,3**	4	1	3,7	0,5	**100**	4	0,5	3,6	0,7	**90,9**
Self-efficacy	3,5	1	3,4	0,6	**93,9**	4	1,0	3,4	0,6	**93,8**	3	1,0	3,4	0,6	**94,1**	4	1,0	3,5	0,6	**97,3**	4	1	3,5	0,5	**100**	3	1	3,4	0,7	**90,9**
Skin ulcers	4	1	3,4	0,7	**86,6**	4	1,0	3,4	0,7	**86,2**	3	1,0	3,4	0,7	**88,2**	4	1,0	3,5	0,6	**91,9**	4	1	3,5	0,7	**88,5**	4	1	3,5	0,5	**100**
Sleep disturbances	3	1	3,1	0,7	**82,9**	3	1,0	3,1	0,6	**87,7**	3	2,0	3,1	0,9	64,7	3	0,0	3,1	0,6	**86,5**	3	0	3,1	0,6	**88,5**	3	0,5	3,1	0,7	**81,8**
Therapy-related knowledge	4	1	3,6	0,6	**92,7**	4	1,0	3,6	0,6	**93,8**	4	1,0	3,4	0,7	**88,2**	4	0,0	3,7	0,6	**94,6**	4	0	3,8	0,5	**96,2**	4	0,5	3,6	0,7	**90,9**
Vomiting	3	2	3,1	0,8	73,2	3	1,0	3,1	0,8	**75,4**	3	2,0	3,1	0,9	64,7	3	1,0	3,1	0,8	**78,4**	3	1	3,0	0,8	**76,9**	3	1	3,2	0,8	**81,8**

Definition of Consensus: Consensus was defined as the level of agreement required for an NSO to be considered validated and retained in the final set. Specifically, an item was considered to have reached consensus if the following occurred: *At least 75% of all respondents rated it as 3 or 4 on the 4-point Likert scale (where 1 = not relevant and 4 = highly relevant) and at least 75% agreement was observed within each professional subgroup, namely, nurses and haematology physicians.* This dual-level threshold was applied to ensure that the consensus reflected a balanced and shared perception across different professional perspectives, enhancing the validity and acceptability of the selected NSOs in interdisciplinary transplant and CAR-T-cell care settings. ***The Expert Panel (EP)**: Comprised nurses and physicians from centres accredited by the Italian Group for Bone Marrow Transplantation (GITMO). In these centres, haematology physicians serve as program directors for transplant activities, while nurses are designated by the directors as official representatives. Participation in the panel was voluntary and based on professional experience in HSCT or CAR-T-cell therapy. **NSO**: Nursing Sensitive Outcome; **Med**: Median; **M**: Mean; **IQR**: Interquartile Range; **SD**: Standard Deviation; **%3-4**: % of responses rated 3 or 4; **CAUTIs**: Catheter-Associated Urinary Tract Infections; **CLABSIs**: Central Line-Associated Bloodstream Infections; **Bold**: NSOs with ≥75% responses of 3 or 4 on the Likert scale.

Eighty-two professionals participated in Round 1 (79% nurses, 21% physicians), and 37 completed Round 2 (70% nurses). Most respondents were female, aged 51–55 years, with over 11 years' experience in HSCT or CAR-T settings (Table 1).In Round 1, 25 NSOs were assessed, and 17 (68%) reached the consensus threshold. Highest agreement concerned pain, fatigue, ADLs, nutritional status, anxiety, depression, emotional distress, and major safety indicators (falls, CLABSIs, CAUTIs, drug extravasation).
In Round 2, 14 NSOs (56%) achieved consensus, showing partial consolidation of opinions. ADLs, anxiety, drug extravasation, and patient satisfaction reached 100% agreement; recognition of clinical instability, self-efficacy, and therapy-related knowledge remained ≥95%. Conversely, pain, fatigue, and nutritional status fell below the threshold, while sleep disturbances, nausea, and vomiting reached consensus only in Round 2.
Full results are available in Figure 1.

Conclusions: This study identified 14 nursing-sensitive outcomes (NSOs) relevant to adult HSCT and CAR-T therapy, covering symptom management, functional ability, psychological well-being, and patient safety. Differences between nurses and physicians were limited and progressively narrowed through the Delphi process, highlighting its value in fostering interdisciplinary alignment. Nurses consistently attributed greater importance to patient-centred domains such as comfort, empowerment, and emotional health.The main limitation

was the modest Round 2 response rate, which may have favoured participants more aware of NSO concepts; moreover, results reflect expert perceptions rather than objective measurements.
This study provides a validated 14-item NSO framework for adult HSCT and CAR-T care and supports integrating nursing perspectives to promote holistic, patient-centred, and truly multidisciplinary practice, fostering the development of more consistent and shared models of care.

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NP21

COMMUNICATION COMPETENCE, SELF-EFFICACY, AND SPIRITUAL INTELLIGENCE: EVIDENCE FROM NURSES WORKING IN BMT UNIT

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Background: Nurses working in Bone Marrow Transplant (BMT) units manage complex clinical care alongside significant emotional and psychosocial demands. Effective communication, strong self-efficacy, and spiritual intelligence are essential for ensuring patient safety, supporting patients and families, facilitating teamwork, and maintaining professional resilience. Despite their importance, limited evidence is available regarding these psychosocial competencies among BMT nurses in the Indian healthcare context.

Methods: A descriptive cross-sectional study was conducted among 50 nurses working in the BMT unit of a tertiary cancer center. Data were collected using a structured, anonymous, self-administered questionnaire comprising three validated instruments: the Nurses' Communication Competence Scale (NCCS-18) developed by Hur, Kwak, and Jang (2011), the Communication Self-Efficacy Scale developed by McCroskey and McCroskey (1988), and the Spiritual Intelligence Scale (22 items) developed by King (2008). Demographic and professional variables included age, gender, educational qualification, total clinical experience, BMT experience, and prior training exposure.

Data were entered in Microsoft Excel and analyzed using SPSS version 26. Categorical variables were summarized using frequencies and percentages, while continuous variables were summarized using mean ± standard deviation. Associations between demographic

variables and categorized competency levels were analyzed using the Chi-square test or Fisher's exact test. Differences in mean scores between two groups (e.g., prior training: yes vs no) were assessed using the independent t-test, while comparisons across more than two groups (e.g., qualification and experience categories) were performed using one-way ANOVA with post-hoc Tukey analysis. A p-value <0.05 was considered statistically significant.

Results: All 50 nurses (100%) completed the survey. Most participants were female (36, 72%), with the highest representation in the 20–25 years (15, 30%) and 31–35 years (15, 30%) age groups. The majority held a BSc Nursing qualification (35, 70%), followed by GNM (11, 22%). Prior training related to communication skills, confidence-building, or spiritual well-being was reported by 28 nurses (56%), while 22 (44%) had not received such training.

Overall communication competence and self-efficacy scores were moderate to high, reflecting satisfactory interpersonal effectiveness and professional confidence among BMT nurses. Spiritual intelligence scores were consistently high across all domains, with the strongest performance observed in compassion and moral values, highlighting a strong ethical and empathetic foundation. Nurses who had received prior training demonstrated significantly higher communication competence and self-efficacy scores compared with those without training ($p < 0.05$). Additionally, increasing total clinical experience and longer BMT exposure were associated with progressively higher scores across communication competence, self-efficacy, and spiritual intelligence.

Conclusions: BMT nurses demonstrated satisfactory communication competence, self-efficacy, and strong spiritual intelligence. Higher competency levels were associated with greater experience and prior training exposure. These findings support the need for structured educational interventions focusing on communication skills, confidence-building, and spiritual well-being to further enhance nursing performance and quality of care in high-intensity BMT settings.

Clinical Trial Registry: Not applicable. This observational questionnaire-based study did not require clinical trial registration. The study received approval from the Institutional Ethics Committee of ACTREC, Tata Memorial Centre, Kharghar, India.

Disclosure: All authors declare no conflicts of interest and no external funding.

NP36

EXPLORING DETERMINANTS OF STAFF RETENTION IN PAEDIATRIC BONE MARROW TRANSPLANT NURSING

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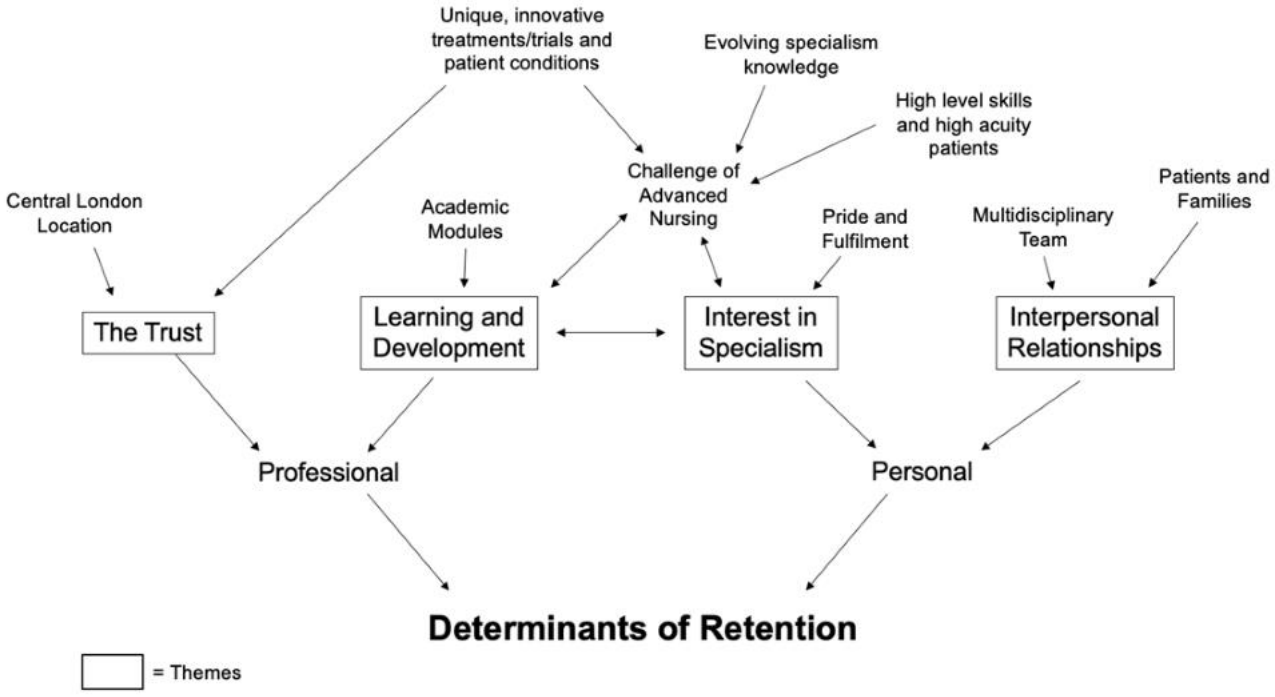
Background: Retention of nursing staff is a constant battle across the NHS, and directly impacts patient safety. With a growing number of paediatric Bone Marrow Transplants (BMTs) being undertaken in the UK and the expansion of the service – coupled with the niche,

specialist skills required to care for these patients and families, the retention of Paediatric BMT nurses is critical. A review of the literature has found there is little UK based research in this area.

Methods: Nurses (n=68) working in inpatient BMT care at a single London Tertiary Centre were recruited via purposive sampling. Participants completed an open-ended questionnaire, created for this study based on existing literature and Appreciative Inquiry perspective. Thematic and documentary analysis was conducted by the study lead using the Ritchie and Spencer Framework and READ approach, respectively.

Results:



Themes identified as professional and personal motivating factors for paediatric nurses to remain working in this area included 'The Trust', 'Learning and Development', 'Interest in Specialism' and 'Interpersonal Relationships'. Through in-depth critical analysis, it became apparent that these factors could not be solely categorised as either professional or personal motivators. Rather, the workplace environment and the individual's personal beliefs intersected, thus contributing to multiple overlapping themes.

Conclusions: **Discussion:** While these findings align with existing literature on advanced nursing practice, and peer and family relationships in the long-term haemato-oncology patient group, it highlights a gap in personal interest in BMT as a retentive factor, and the impact of specific diagnoses and treatment regimes, suggesting a need for further research. Research should focus on the wider specialist paediatric nursing population at this Trust, as well as BMT inpatient nursing across the UK.

Disclosure: **Ethical Considerations:** Ethical approval was granted by the School of Health and Social Care Ethics Committee at London South Bank University, London (Reference - 24/A/16) on 20th January 2025. NHS Trust Approval was granted by [Local Trust Name] Hospital NHS Foundation Trust Research and Development Team (Reference - 4011) on 24th November 2024.
Author Contributions:
Charlotte Rigby (CR) is the lead researcher in this study and has been working in Paediatric Haematology/Oncology and BMT Nursing at two world-leading centres. She was responsible for all aspects of this study – background research, methodology, data collection, data analysis, discussion, manuscript write up and dissemination.
Dr Tamzin Dawson (TD) is a Senior Lecturer and the Deputy Head of School for Children's and Community Nursing, and Mental Health and Learning Disability Nursing at London South Bank University. She is an accomplished academic, and has published many qualitative studies, with a keen interest in PICU and Nursing Education. She acted as Academic Supervisor for this Dissertation service evaluation study.
Milli Lipshaw (ML) is a Lecturer of Children's Nursing at London South Bank University with clinical experience working in Paediatric Oncology and Orthopaedics in the NHS. She is a member of the Children & Young People's Cancer Association (CCLG) and acted as co-supervisor for this Dissertation service evaluation study.
Declaration of Conflicting Interest: CR declared potential conflict of interest, as they were employed by [Local Trust Name] Hospital NHS Foundation Trust throughout the research process and at time of publication.
TD and ML declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.
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A DESCRIPTIVE NURSING STUDY ON GUT MICROBIOTA AND GRAFT-VERSUS-HOST DISEASE IN PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: The gut microbiota maintains immune homeostasis, intestinal barrier integrity, and inflammation control, profoundly influencing outcomes after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Dysbiosis strongly correlates with acute gastrointestinal graft-versus-host disease (GVHD), infections, delayed immune reconstitution, graft failure, and elevated transplant-related mortality. Different factors like conditioning regimens, prolonged neutropenia, immunosuppressants, and broad-spectrum

antibiotics devastate microbial diversity. Nurses drive impact through vigilant surveillance, targeted nutrition, patient education, and early intervention, aligning with EBMT Handbook recommendations for infection prevention and supportive care in HSCT.

Methods: Narrative review of peer-reviewed literature (2015-2025) on microbiota, allo-HSCT outcomes, and nursing, per EBMT evidence standards. Structured via NANDA diagnoses, NIC interventions, and NOC outcomes. Key protocols: systematic nutrition assessments (EBMT nutritional guidelines), neutropenic/protective diet education, gastrointestinal monitoring (stool frequency/consistency/pain scales), infection control (hand hygiene, isolation), and adherence promotion across transplant phases.
The aim is primarily to describe gut microbiota profiles in adult allo-HSCT patients and their link to intestinal GVHD onset/severity, leveraging nursing outcomes (NOC) to gauge care efficacy. Secondarily, delineate nurses' roles in sample collection, monitoring, and education; propose recognized recommendations for microbiota-preserving strategies, emphasizing high-impact nursing interventions like diet optimization and adherence support.

Results: NOC outcomes track nutrition (stable weight/BMI, normal albumin), gut function (reduced stool frequency, firmer consistency, less pain), fluid balance (adequate diuresis, stable electrolytes), and tolerance (no nausea/vomiting/distension)—directly impacting GVHD prophylaxis. Additional metrics: infection rates <5%, >90% adherence, improved quality-of-life scores (gut symptoms/psychosocial distress). Early dysbiosis detection via nursing surveillance enables 20-30% faster interventions, per cohort studies. EBMT-supported strategies like pre/probiotic use, fecal microbiota transplantation (FMT), and high-fiber/low-residue diets restore diversity, slashing GVHD risk by up to 40% and boosting survival. Nurses enforce tolerance monitoring, reinforce prescriptions, and educate on risks/benefits, curbing pathogenic dominance linked to grade 3-4 GVHD.

Conclusions: Microbiota modulation elevates nursing to a high-impact frontier in EBMT programs, slashing GVHD incidence, accelerating recovery, and enhancing graft survival—potentially improving 1-year OS by 15-25%. Integrate standardized protocols: daily microbiota risk screens, personalized diets (e.g., Mediterranean-style pre-HSCT), FMT coordination post-engraftment, and multidisciplinary audits. EBMT should champion nurse-led trials on these interventions for scalable, cost-effective GVHD mitigation, transforming transplant care. Further research is needed to define standardized nursing interventions aimed at microbiota preservation in transplant settings.

Disclosure: "Niente da dichiarare"

NP75

KNOWLEDGE AND SKILLS OF NURSES IN RECOGNIZING EARLY SIGNS OF VENO-OCCLUSIVE DISEASE (VOD) AMONG HSCT PATIENTS: A CROSS-SECTIONAL STUDY AT ACTREC

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Background: Hepatic Veno-Occlusive Disease (VOD), also known as Sinusoidal Obstruction Syndrome, is a potentially life-threatening early complication following hematopoietic stem cell transplantation (HSCT). Early recognition is essential to prevent rapid progression to severe VOD, which carries high morbidity and mortality. Nurses play a critical role in detecting early indicators such as sudden weight gain, hepatomegaly, rising bilirubin, fluid retention, and abdominal girth changes. Limited Indian data exist regarding nurses' preparedness in identifying early VOD signs in HSCT settings.

Methods: A descriptive cross-sectional study was conducted among **60 nurses** working in HSCT/BMT units at ACTREC. A validated 29-item questionnaire assessed demographics, VOD knowledge, skills, case-scenario interpretation, and training needs. Knowledge items (Q7–12) and scenario items (Q22–25) were scored, generating:

- Knowledge score (0–6)
- Scenario score (0–4)
- Total competency score (0–10) categorized as:
  Adequate (8–10), *Average* (5–7), *Inadequate* (0–4).

Descriptive and inferential statistics (chi-square, t-test, ANOVA) were applied; significance set at **$p < 0.05$**.

Results: A total of 60 nurses participated. Most were **female (71.7%)**, aged 31–35 years (31.7%) and >35 years (28.3%). The majority held **BSc Nursing qualifications (70%)**, and more than half had ≥1 year HSCT experience. Only **19 nurses (31.7%)** reported prior VOD-related training.
Knowledge performance was moderate, with a mean score of **4.63 ± 1.50** (range: 0–6). Knowledge gaps were notable in diagnostic criteria understanding, although early signs such as unexplained weight gain and bilirubin elevation were recognized by most.
Scenario-based interpretation skills were comparatively strong, with a mean score of **3.50 ± 1.03** (range: 0–4). Nurses demonstrated high accuracy in identifying early red-flag patterns such as rapid weight gain, increases in abdominal girth/ascites, and bilirubin-associated abdominal pain.
The overall **total competency score** was **8.13 ± 2.32**. Categorization demonstrated:

- **Adequate:** 46 nurses (76.7%)
- **Average:** 8 nurses (13.3%)
- **Inadequate:** 6 nurses (10%)

Inferential analysis found no significant association between prior training and competency level ($\chi^2 = 3.54$, $p = 0.17$). Although trained nurses had higher mean scores (8.79 vs 7.85), the difference was not statistically significant ($t = 1.89$, $p = 0.063$). Educational qualification also showed no significant association with knowledge scores (ANOVA $F = 0.30$, $p = 0.82$). Overall, findings highlight a workforce with **strong clinical judgment** but **uneven foundational VOD knowledge**, particularly among nurses without formal training.

Conclusions: HSCT nurses at ACTREC demonstrated strong ability to recognize early VOD indicators in clinical scenarios, but theoretical understanding remains variable. Strengthening structured education, simulation-based learning, and VOD-specific competency training may

bridge existing knowledge gaps and further enhance early detection. Improved nurse preparedness has the potential to optimize patient monitoring, reduce delays in escalation, and improve outcomes in HSCT patients at risk for VOD.

Clinical Trial Registry: Not applicable.
This observational questionnaire-based study did not require clinical trial registration. The study received approval from the Institutional Ethics Committee of ACTREC, Tata Memorial Centre, Kharghar, India.

Disclosure:

All authors declare **no conflicts of interest** and no external funding.

NP78

A STUDY TO ASSESS NURSES' KNOWLEDGE ON CYTOKINE RELEASE SYNDROME IN HAPLOIDENTICAL HSCT: A CROSS-SECTIONAL STUDY AT TERITARY CARE CENTRE, INDIA

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Background: Cytokine release syndrome (CRS) is a potentially life-threatening toxicity after haploidentical hematopoietic stem cell transplantation (HSCT). Bedside nurses play a critical role in early recognition and escalation of care. Evidence on CRS-related nursing knowledge in transplant settings, especially in India, is limited.

Methods: A descriptive cross-sectional study was conducted among registered nurses working in the bone marrow transplant (BMT) services at Tertiary care Centre, India. A validated 40-item multiple-choice questionnaire assessed knowledge of CRS definition, symptoms, grading, monitoring, laboratory investigations, and management. Each correct response scored 1 point (maximum 40). Knowledge levels were categorized as good (≥30), moderate (20–29), and poor (<20). Descriptive statistical methods were used.

Results: Forty-seven nurses completed the survey. The majority were female (74.5%), aged 31–35 years (34%), and held BSc Nursing qualifications (70.2%). Nearly half (48.9%) had more than five years of clinical experience, and 87.2% reported previous HSCT exposure. The mean knowledge score was **36.2 ± 3.4** (range 20–40). Most participants demonstrated **good knowledge** of CRS (46/47; 97.9%), while 1 (2.1%) had moderate knowledge and none had poor knowledge. Knowledge gaps were identified in accurately recognizing **non-primary CRS treatments** (44.7% correct) and understanding the **time of CRS onset** (51.1% correct). Because almost all participants scored within the "good" category, analysis of associations with demographic variables was not statistically meaningful.

Conclusions: Nurses working in the BMT units of this tertiary cancer Centre demonstrated strong overall knowledge of Cytokine Release Syndrome (CRS), reflecting good preparedness

for early recognition and prompt escalation in haploidentical HSCT care. Although most participants achieved high scores, specific knowledge gaps were observed in recognising the timing of CRS onset and differentiating non-primary treatment options. Addressing these gaps through focused educational sessions and structured CRS competency modules may further enhance nursing readiness, ensure timely interventions, and strengthen patient safety within transplant services.

Clinical Trial Registry: NO

Disclosure: The author declares no conflicts of interest and has received no financial support, sponsorship, or institutional funding for this study. The work was conducted independently as part of nursing research and quality improvement at ACTREC. Nothing to declare.

NP81

NURSING ASPECTS AND OUTCOMES OF PATIENTS WITH MYELODYSPLASTIC SYNDROMES UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: A FIVE-YEAR RETROSPECTIVE STUDY (2020-2024)

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Background: Myelodysplastic syndromes (MDS) are a heterogeneous group of clonal hematopoietic disorders characterized by ineffective hematopoiesis, peripheral cytopenias, and a variable risk of progression to acute myeloid leukemia. Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative treatment option for eligible patients. The role of nurses is crucial throughout the transplant process, particularly in patient preparation, complication management, and post-transplant care. This study presents a retrospective overview of MDS patients who underwent HSCT over a five-year period at the University Hospital Centre Zagreb, Department of Hematology.

Methods: This retrospective study included all patients diagnosed with MDS who underwent allogeneic HSCT between 2018 and 2023 at the University Hospital Centre Zagreb. Data were collected from the hospital information system (BIS), physicians' records, and nursing documentation (nursing decursus). The analyzed variables included demographic data (age, sex), disease characteristics, type of donor, conditioning regimen, complications, and patient outcomes. The data were analyzed descriptively and presented in numerical and percentage form.

Results: During the five-year study period, a total of 52 patients with MDS underwent allogeneic HSCT. The median age at transplantation was 59.3 years (48,1% male, 51,9% female). Most transplants were performed using unrelated donors 71%, with reduced intensity conditioning regiments (46%).The average length of hospital stay was 39.8 days, while the mean time to neutrophil recovery was 17.6 days. .The most common early post-

transplant complications included ferbrile neutropenia (94,2%) mucositis (63.5%). During hospitalization, participants most frequently reported hypertension (57.7%), diarrhea (57.7%), headache (53.8%), and skin rash and redness (50%). Nursing documentation emphasized key nursing interventions related to infection prevention, nutritional support, pain control, and psychological support. A total of 86.5% of patients developed sepsis. Overall, 42.3% of patients had or currently have GVHD. Among the affected organ systems, cutaneous GVHD was the most common (29.7%), followed by gastrointestinal involvement (27%), hepatic GVHD (16.2%), ocular and oral involvement (10.8%), and pulmonary GVHD (5.8%). A survival rate analysis showed that 48.1% of patients were alive, while 51.9% had died. The cause of death was relapse or transformation into leukemia in 52.4% of cases, whereas sepsis accounted for 28.6% of deaths.

Conclusions:

Patients with myelodysplastic syndromes undergoing allogeneic hematopoietic stem cell transplantation face significant clinical challenges, including high rates of sepsis, graft-versus-host disease, and transplant-related complications. Nursing care plays a critical role in monitoring, early detection, and management of these complications to improve patient outcomes. Our five-year retrospective analysis highlights the importance of comprehensive nursing interventions in supporting survival, reducing morbidity, and enhancing quality of care in this high-risk population.

Clinical Trial Registry:

Disclosure: nothing to declare

Artificial Intelligence and Digital Solutions in HSCT Nursing

NG16-03

IMPROVING CHRONIC GVHD CARE: DEVELOPMENT OF A CHRONIC GVHD-MODULE WITHIN AN EHEALTH FACILITATED INTEGRATED CARE MODEL: *SMILE*

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Background: Re-engineering follow-up care after allogeneic stem cell transplantation (alloSCT) is essential given the increasing numbers of long-term survivors with complex needs related to complications such as chronic Graft-versus-Host Disease (cGvHD). cGVHD affects up to 50-70% of alloSCT recipients and significantly reduces quality of life and physical functioning while imposing severe psychological, emotional, and socio-economic burdens. Early detection and timely treatment are crucial to prevent severe and irreversible organ damage, especially in lung-cGvHD, where treatment options are limited. However, current health care structures insufficiently address the complex, long-term needs of cGvHD-patients.
An *Integrated Care Model (ICM) for allogeneic SteM cell transplantatIon faciLitated by eHealth* (SMILe-ICM) has been developed, evaluated and established as a routine follow-up post-alloSCT at the University Hospital Freiburg (Germany). The SMILe-ICM comprises two main components: (1) An advanced practice nurse (APN) team to support patient self-management and to enable early detection of acute health deteriorations by structured nursing interventions, (2) the SMILeApp connecting patients with the APN team by remotely monitoring medical, symptom, and behavioral parameters during the first post-transplant year. To address the specific and long-term needs of cGvHD-patients, we aimed to extend the SMILe-ICM based on patients' needs, provider insights and existing evidence.

Methods: Following the SMILe-ICM development methodology, we performed a contextual analysis steering the development process, running from 9/2024-10/2025. We applied the following steps:
1. Conducting 7 semi-structured interviews with cGvHD-patients and one focus group with clinicians (n=8), analyzed by deductive-inductive qualitative content analysis based on the Chronic-Care-Model;
2. Performing an unsystematic literature review;
3. Developing intervention content, timing, dosing and frequency using the Behavior Change Wheel (BCW);
4. Applying iterative user-tests (n=5 patients) of the eHealth components;
5. Starting a feasibility study with 15 patients.

Results: Interviews and literature revealed that cGvHD affects all aspects of patients' lives and presents substantial physical, psychological, and emotional challenges. Patients require self-management support addressing cGvHD prevention, symptom recognition, cGvHD management and resources enhancing their coping strategies. Clinicians highlighted the potential of remote monitoring of cGvHD-specific symptoms for early detection and monitoring to improve therapeutic and supportive measures. Both patients and healthcare professionals emphasized the importance of a multidisciplinary team including cGvHD-specialists and consistent, trusted care providers as first points of contact and identified APNs as suitable primary contacts and care-coordinators.
Consequently, we developed a cGvHD-specific SMILe-module comprising:
1. At least five APN-led, face-to-face interventions ensuring continuity of care and promoting prevention, early detection and self-management after alloSCT by using up to 28 BCW behaviour-change-techniques.;
2. cGvHD-specific symptom detection and monitoring via the cGvHD-module, including an adaption of the Lee Symptom Scale and home spirometry (3x/week) for early detection of lung-cGvHD;

3.Implementation of a well-connected multidisciplinary care team including cGvHD-experts and APNs as first points of contact.

Conclusions: cGvHD-patients often face unmet and specific care needs. The cGvHD-SMILe-module aims to address these needs, strengthen patient self-management, improve patient care quality and enhance treatment monitoring. The ongoing feasibility testing will evaluate the module's acceptance, appropriateness, and patient adherence, providing insights for refinement and scalable integration into routine patient care.

Clinical Trial Registry: DRKS00035022
https://drks.de/search/de

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NP42

THE POTENTIAL OF AI CHATBOTS AS CLINICAL DECISION-SUPPORT TOOLS IN NURSING: AN EVALUATION OF SYMPTOM MANAGEMENT RECOMMENDATIONS DURING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is a complex and high-risk procedure frequently associated with severe complications such as acute graft-versus-host disease (aGVHD), infections, and multi-organ toxicities. Effective symptom management and accurate nursing decision-making are essential to improving patient outcomes during this demanding treatment process. In recent years, large language models (LLMs) have emerged as potential tools to support clinical reasoning, interpret patient data, and assist in the development of nursing care plans. However, their reliability, guideline adherence, and clinical applicability within allo-HSCT settings remain insufficiently explored, highlighting the need for further investigation in this area.

Methods: This study aimed to evaluate the effectiveness of three large language models (ChatGPT-4o, DeepSeek-V3, Gemini 2.5 Flash) in generating nursing care recommendations for symptom management during the allogeneic hematopoietic stem cell transplantation (allo-HSCT) process using a hypothetical case study.To this end, five researchers with expertise in hematology and nursing evaluated the models' performance based on the European Society for Blood and Marrow Transplantation (EBMT) guidelines, focusing on the accuracy and relevance of nursing care recommendations, appropriateness of symptom management strategies, clarity and organization of responses, use of professional terminology, and overall effectiveness.

Results: The results indicated that while all language models were able to generate relevant nursing care recommendations for major symptoms during the allo-HSCT process, their overall performance varied across evaluation criteria. In the present study, the three major language models were examined. While these models were able to accurately diagnose aGVHD in the study's cases, it is noteworthy that they employed different sets of criteria for diagnosis. ChatGPT and Gemini EBMT satisfied only two of the three criteria, while DeepSeek satisfied one. This further highlights the discrepancy between the models in terms of guidance. In terms of overall performance, ChatGPT has been found to demonstrate a more reliable approach to clinical decision-making through its use of evidence-based methods. However, it has been observed that the system has been prone to certain inaccuracies in certain data details. In comparison, DeepSeek has been found to produce more comprehensive and detailed nursing care plans, while Gemini has been identified as the most effective system in terms of risk analysis. However, Gemini has been found to demonstrate the least success in accurately identifying nursing diagnoses.

Conclusions: The findings indicate that the AI model has considerable potential in the domains of allo-HSCT process diagnosis, symptom management and nursing decision support. However, further advanced model development is necessary for critical aspects such as compatibility, data accuracy, standardisation of nursing diagnoses and generation of evidence-based recommendations. Further research is warranted to advance model optimization through the integration of domain-specific datasets, adherence to clinical guidelines, and expert-informed algorithmic refinement. The reliability, safety, and translational applicability of these technologies in evidence-based nursing practice must be established through controlled evaluations within real-world clinical environments.

Clinical Trial Registry: N/A

Disclosure: Nothing to declare

NP57

NURSES' AWARENESS AND READINESS TOWARD FUTURE USE OF ARTIFICIAL INTELLIGENCE (AI) TOOLS IN PREDICTING GVHD AND INFECTION IN HSCT PATIENTS: A CROSS-SECTIONAL STUDY AT ACTREC

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Background: Artificial intelligence (AI)-enabled prediction tools for graft-versus-host disease (GVHD) and infections are increasingly explored in hematopoietic stem cell transplantation (HSCT). As frontline caregivers, nurses play a pivotal role in early recognition, monitoring, and integration of emerging digital technologies. Their awareness and readiness to adopt AI tools will be critical for future implementation in HSCT settings. However, evidence describing AI preparedness among HSCT nurses in India remains scarce.

Methods: A descriptive cross-sectional survey was conducted among **91 consenting nurses** in HSCT/BMT units at ACTREC using a structured, validated questionnaire incorporating Technology Acceptance Model (TAM) and Unified Theory of Acceptance and Use of Technology (UTAUT) constructs (Likert scale 1–5). Descriptive statistics summarized demographic and domain data. Associations were examined using chi-square, t-tests, and one-way ANOVA. A multivariable linear regression model identified predictors of readiness. Significance was set at $p < 0.05$.

Results: A total of 91 nurses participated. More than half (59.3%) had heard of AI in healthcare, while only 9.9% reported receiving formal AI training. Mean readiness to use AI tools was high (4.03 ± 0.57). Perceived usefulness (4.05 ± 0.49) and performance expectancy (4.09 ± 0.55) were the highest scoring domains, whereas trust/anxiety was moderate (3.10 ± 0.77). Internal consistency across domains was acceptable to excellent (Cronbach's α = 0.69–0.88).

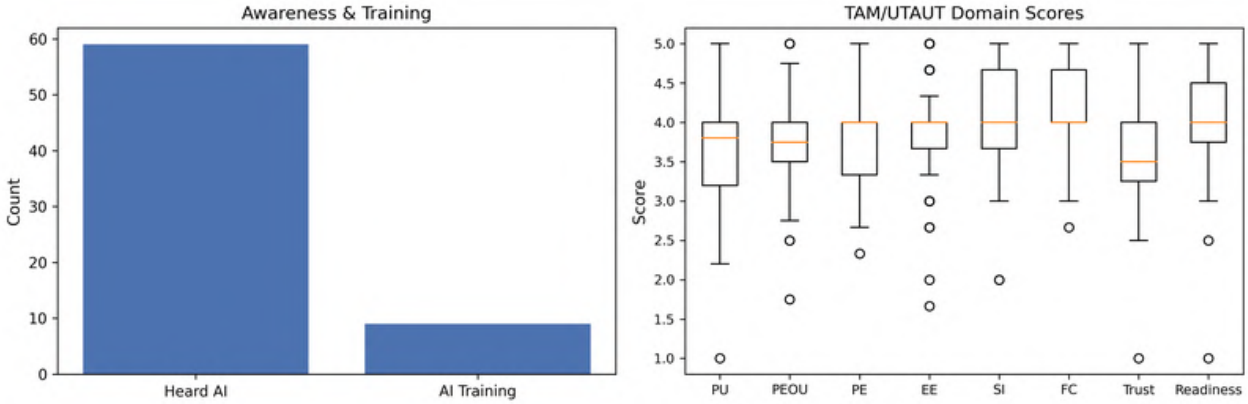

Figure 1 summarizes AI awareness, training status, and the distribution of TAM/UTAUT domain scores.

Awareness of AI was associated with higher readiness ($\chi^2 = 3.84$, $p = 0.050$). Nurses with prior AI training demonstrated higher readiness, although this was not statistically significant ($p = 0.096$). Readiness did not differ significantly by qualification ($p = 0.566$).

In multivariable regression ($R^2 = 0.164$), **having heard about AI was the only independent predictor** of readiness ($\beta = 0.31$, $p = 0.034$). Trust demonstrated a positive, non-significant trend ($p = 0.092$). Age, total nursing experience, BMT experience, and AI training were not significant predictors.

Conclusions: Nurses demonstrated high readiness to use AI tools despite limited formal exposure. AI awareness emerged as the strongest independent determinant of readiness, underscoring the importance of early digital literacy and foundational AI education. These findings highlight the need for structured AI training programs and capacity-building

initiatives within HSCT nursing to support safe, effective integration of predictive technologies in future clinical practice.

Clinical Trial Registry: Not applicable.
This study is an observational, non-interventional survey and does not require clinical trial registration.
The study received approval from the **Institutional Ethics Committee** of ACTREC, Tata Memorial Centre, Kharghar, India.

Disclosure: All authors declare no conflicts of interest and no external funding

Patient and Donor Information and Education

NG16-05

DIGITAL HEALTH STRATEGIES FOR PATIENT EDUCATION IN HAEMATOPOIETIC STEM CELL TRANSPLANTATION: A SCOPING REVIEW

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Background: Haematopoietic Stem Cell Transplantation (HSCT) is a life-saving but highly intensive treatment associated with a heavy symptom burden, complex self-care requirements, and significant psychosocial distress. Effective patient education is paramount for promoting adherence, early symptom recognition, and improved quality of life (QoL).Where traditional education methods often fall short, technology-based Interventions (TTMs)—such as mobile applications, e-learning platforms, and virtual reality—are rapidly emerging as critical tools to deliver education, monitor symptoms, and offer psychosocial support remotely. A synthesis of the current evidence is needed to guide the development and implementation of high-quality digital health strategies within HSCT nursing practice.

Methods: This comprehensive scoping review was carried out in line with the PRISMA-ScR guidelines. A broad and systematic search was conducted across six major databases (PubMed, Cochrane Library, Scopus, Web of Science, CINAHL, and Medline) using a combination of keywords related to: "stem cell transplantation," "patient education," "digital health," "mobile application," "e-learning," and "telehealth." Two independent reviewers screened the titles, abstracts, and full texts of the retrieved articles. Eighteen studies met the inclusion criteria, focusing on TTMs designed for HSCT patient education across the pre-transplant, peri-transplant, and post-transplant phases. Information regarding the study design (e.g., RCT, Qualitative), intervention type, specific technology functionalities, target outcomes (clinical and patient-reported), and evidence level was collected using a standardized extraction tool and analyzed thematically.

Results: The analysis of the 18 studies revealed a high concentration of research originating from North America and Europe, with study designs increasingly including high-quality randomized controlled trials. The most prevalent TTMs identified were Mobile Applications and Web-based Patient Portals. These technologies were leveraged primarily to support three core nursing roles: information delivery and adherence, remote symptom monitoring and management, and psychosocial support. The first theme includes providing accessible, tailored, and interactive educational content on infection control, medication schedules, and self-care tips. The second primarily focuses on enabling patients to digitally track symptoms (e.g., fatigue, mucositis, graft-versus-host diseas signs) and receive instant, algorithm-driven feedback or alerts for nurse review. The last one is about incorporating virtual reality for distraction during procedures, providing guided mindfulness exercises, and facilitating peer support access. As a result, TTMs consistently demonstrated effectiveness in improving outcomes. The findings highlighted significant increases in patient knowledge and self-efficacy, alongside reductions in anxiety, depression, and symptom distress. While the evidence for direct clinical outcomes, like readmissions, is still developing, the strong impact on preparatory, psychological, and self-management capabilities underscores their value.

Conclusions:

Technology-based interventions represent a powerful paradigm shift in HSCT patient education, moving care towards personalized, continuous, and accessible models. Nurses are uniquely positioned to lead the integration of these tools to optimize patient self-management, symptom burden, and ensure continuity of care. Nursing practice must evolve to incorporate the use of digital data for timely intervention, focus on training patients in digital literacy, and advocate for the development of TTMs specifically targeting critical post-transplant issues like chronic-GVHD management and long-term survivorship. The review strongly supports the continued adoption and rigorous evaluation of digital solutions to elevate the quality of care for patients.

Disclosure: None.

Paediatric and AYA/TYA Care

NG10-02

SAFETY PROFILES OF TWO ANTI-THYMOCYTE GLOBULIN FORMULATIONS IN PEDIATRIC HEMATOPOIETIC CELL TRANSPLANTATION: IMPLICATIONS FOR NURSING CARE

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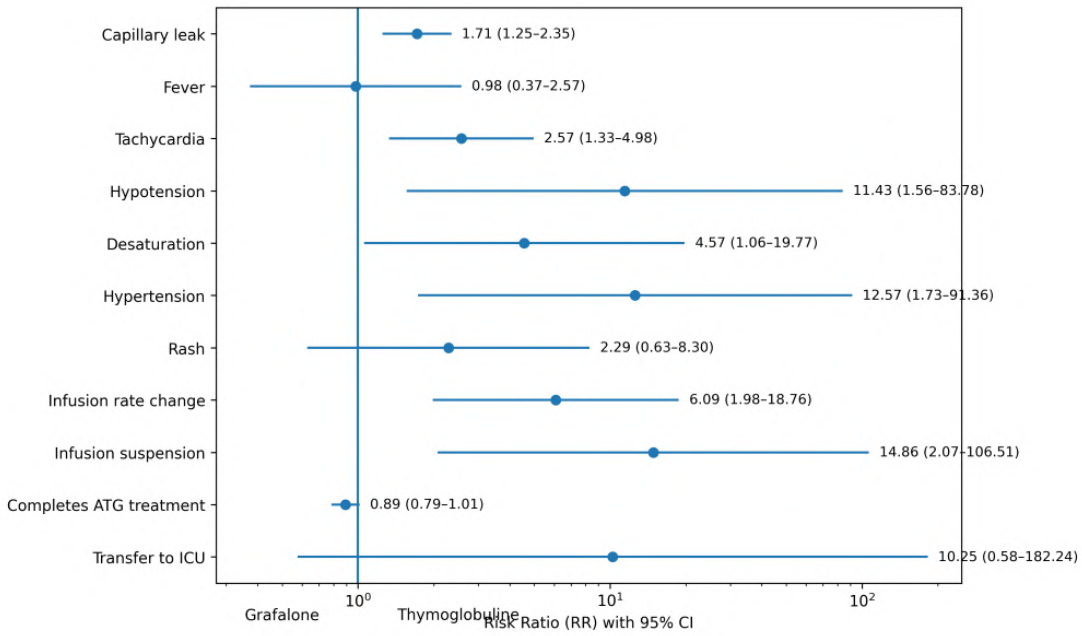
Background: **Introduction:** The use of immunosuppressive agents such as anti-thymocyte globulin (ATG) for hematopoietic cell transplantation (HCT) has become essential due to the increasing use of alternative donors. Currently, two main ATG formulations are used in clinical practice: Thymoglobulin® (rabbit-derived anti-human thymocyte immunoglobulin) and Grafalon® (anti-human T lymphocyte immunoglobulin). While some studies have compared their efficacy, evidence regarding threir safety profiles, particularly in the pediatric population, remains limited.
The occurrence of ATG-related AE has a direct impact on nursing workload, nurse-to-patient ratios, and the need for highly trained nursing staff capable of early detection and management of infusion-related events and potentially serious complications, such as capillary leak syndrome. Although the reported AE of both formulations are generally similar, clinical nursing observations have identified a reduction in immediate infusion-related AE following Grafalon over Thymoglobuline, which requires further investigation.
The aim of the study is to evaluate the incidence of AE associated with the administration of Grafalon® and Thymoglobulin® in pediatric patients undergoing HCT.

Methods: We conducted a multicenter, retrospective cohort study based on electronic health records. Inclusion criteria: pediatric patients (0–18 years) undergoing HCT between 2018 and July 2025 who received either Thymoglobuline® or Grafalon® as part of conditioning. Exclusion criteria: use of both drugs in the same regimen or ATG for GVHD treatment.
The units of analysis were HCT procedures. Baseline variables included sociodemographic and HCT-related characteristics. Outcomes included adverse events (capillary leak syndrome, fever, rash, hypotension, hypertension, tachycardia, desaturation), infusion modifications/suspension and ICU transfer, all within 72 hours of ATG initiation. Relative risks (RR) with 95% confidence intervals and Fisher's exact test were used for comparisons. The study was approved by the Research Ethics Committee.

Results: Preliminary data from a single centre are shown. More data will be available for the annual meeting.A total of 60 HCT procedures performed in 56 patients between February-2020 and July-2025 were analyzed (4 excluded for receiving ATG as treatment); 58.3% were male; the median age was 6 years (range 0–19). Among HCTs using ATG (n=60), 46.7% (n=28) used Thymoglobuline and 53.3% (n=32) Grafalon. Statistically significant differences were observed before ATG in stem cell source (81.2% peripheral blood in Grafalon vs 53.6% in Thymoglobuline; p=0.0354) and graft manipulation (62.5% in Grafalon vs 33.3% in Thymoglobuline; p=0.0384) (Table 1). HCTs performed with Thymoglobuline showed significantly higher risk of AE (hypotension, hypertension, tachycardia, desaturation), infusion rate changes/suspension, capillary leak syndrome (RR: 1.714; IC 1.253-2.346), and ICU transfer. None of Grafalon patients required ICU transfer within 72 hours, whereas 14.3% (n=4) of Thymoglobuline patients did (p=0,042) (Figure 1).

Table 1. Pre-transplant characteristics of study population according to ATG Type

	Baseline	Thymoglobuline (n=28)	Grafalon (n=32)	p-value
Age at HCT	Years: Median (IQR)	4.5 (8.5)	6.5 (9.5)	0.372
Sex	Male Female	18 (64.3%) 10 (35.7%)	17 (53.1%) 15 (46.9%)	0.278
Disease	Malignant Non malignant	8 (28.6%) 20 (71.4%)	11 (34.4%) 21 (65.6%)	0.5057
HCT source	Peripheral blood Bone marrow Umbilical cord blood	15 (53.6%) 7 (25%) 6 (21.4%)	26 (81.2%) 5 (15.6%) 1 (3.1%)	0.0354
Graft manipulation	Yes No	9 (33.3%) 18 (66.7%)	20 (62.5%) 12 (37.5%)	0.0384
Type of donor	Haploidentical Identical related Identical non related Non identical-non related	8 (32%) 5 (20%) 10 (40%) 2 (8%)	18 (58.1%) 7 (22.6%) 4 (12.9%) 2 (6.4%)	0.1027
Conditioning regimen	Myeloablative Non myeloablative	21 (75%) 7 (25%)	20 (62.5%) 12 (37.5%)	0.379
Functional status (Lansky)	100 90 80 70	19 (70.4%) 6 (22.2%) 2 (7.4%) 0	12 (37.5%) 15 (46.9%) 4 (12.5%) 1 (3.1%)	0.128
*HCT: Hematopoietic Cell Transplantation				



Conclusions: Grafalone demonstrated a more favorable safety profile during the first 72 hours of ATG infusion compared to Thymoglobuline. Its higher incidence of capillary leak and ICU transfer underscores the need for adequate nursing staffing and training to ensure patient safety. These findings should be interpreted with caution as they are based on preliminary data from a single center; results will be complemented by data from additional centers and multivariate analyses to control for confounding factors.

Clinical Trial Registry: N/A

Disclosure: None.

NG10-03

LISTENING TO THE YOUNG: EMPOWERING CHILDREN AND ADOLESCENTS IN SHAPING HEALTHCARE PLANNING

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Background: Humanization strategies within the healthcare system aim to incorporate the patient's experience to enhance the quality of care. Traditionally, in pediatric and adolescent care, the voices of children have often been represented by adults: parents, guardians, or healthcare professionals. However, listening to the voices of children and adolescents in the

hospital setting is their right.
At the Niño Jesús University Children's Hospital, as part of its humanization program, strategies have been developed to capture the perspectives of children and adolescents (the patient's voice). This approach ensures that their views inform the design of care planning that is truly centered around their physical, psychological, and social needs.

Methods: We launched the first oncology and hematopoietic stem cell transplantation course, taught by patients themselves, for healthcare professionals.
The course covered key topics affecting pediatric oncohematology and transplanted patients. A total of 6 topics were delivered by 3 children and 3 adolescents: What is cancer and an hematopoietic stem cell transplant?; What is a porth-a-cath and how to take care of it?; What is chemotherapy and its side effects?; What is neutropenia and how to manage it?; Daily life in hospitalization and day hospital care; Long-term effects, focused on fertility. The final session, about how information is delivered to patients and families and decision-making, was held as a roundtable discussion.
Each session was co-prepared by the child or adolescent alongside a healthcare professional (nurse, physician, or healthcare assistant), blending scientific evidence with real-life experiences to offer actionable insights, concluding with suggestions for improvement.

Results: Children and adolescents who participated completed a satisfaction survey using a Likert scale (1 to 5, from very dissatisfied to very satisfied). 100% (6 participants) expressed being very satisfied with the experience. They were asked to write down the improvements that they had proposed during the course. The primary feedback, especially from adolescents, was focused on the need for clearer, more transparent information about their treatment process and having a private space for consultations with healthcare professionals. Other suggestions included making the porth-a-cath less visible by using different type of dressings and providing more detailed information about the side effects of certain medications, such as corticosteroids.

Conclusions: These strategies have allowed us to capture the perspectives of children and adolescents going through an onco-hematological disease journey. As a result, the hospital is implementing continuous improvements in care planning that is child and adolescent centered. Collaborative educational materials were developed, and a focus group is being established to further refine and implement the proposed improvements.

Disclosure: Nothing to declare.

NG10-04

LEXI'S LEGACY - A LETTER TO HEALTHCARE PROFESSIONALS

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Background: Teenagers undergoing a haematopoietic stem cell transplant (HSCT) for an inborn error of immunity (IEI) have often undergone multiple hospital admissions, referrals to different specialities and multiple investigations and treatments prior to their referral to the specialist HSCT team. Their journey through HSCT can be a long and difficult road, with prolonged admissions, involvement of specialists' teams and complex medical language. While most teenagers are enjoying spending time with their peers, developing their independence, testing boundaries and learning who they are as a person. Those undergoing HSCT are often isolated for long periods, with only their parent or caregiver for company. This can be especially difficult for those with IEI, who may have already spend much of their childhood in hospital away from their peers.

Methods: Lexi was 12 years old when she was referred to her specialist HSCT centre and the decision was made to proceed with a HSCT for her IEI. She admitted to the HSCT unit just after her 13th Birthday. Lexi's transplant course wasn't smooth, and she endured a prolonged stay in hospital, requiring TPN and then ECP treatment for GVHD. Lexi met many different specialist teams and healthcare professionals having spent time long periods in both her local hospital and her transplant centre. Lexi experienced varied levels of care during her treatment, often feeling left out of conversations, unsure of what was being discussed and a lack of understanding by some professionals. With a desire to address these issues Lexi wrote a letter to healthcare professionals after her transplant in the hope of highlighting her observations and improving care for other young people.

Results: Lexi together with her family and Touch Design Ltd. developed Lexi's letter to HCP's, producing an animation of the original letter. Sadly, Lexi was unable to complete the project herself, so her sister Ella completed the narration of the animation, on her behalf. Lexi's wish was for the letter and animation to be used as a learning tool for HCP's to improve patient care for young people spending long periods in hospital. She hoped it would be shared on her behalf and her words used to improve patient care.
Lexi's Letter

Conclusions: Teenagers often report experiences of being 'treated like a child' not being included in decisions or involved in their care by health professionals and being misunderstood during hospital admissions, impacting on their wellbeing and development. This can be compounded during complex admissions for treatments such as HSCT, where they are faced with complicated procedures and conversations. Lexi wrote her letter and developed her animation with the hope of sharing her experiences of this with HCP's to help them understand how it feels for teenagers and young people. Lexi's wish was to improve the experiences in the future for other teenagers and young people. We hope by sharing Lexi's story, letter and animation we can help make Lexi's wish a reality and improve the patient experience for other teenagers and young people.

Disclosure: None

NG10-05

SERVICE EVALUATION OF 'READY STEADY GO' TRANSITION QUESTIONNAIRE IN POST-CD34⁺ EX-VIVO GENE THERAPY PAEDIATRIC PATIENTS

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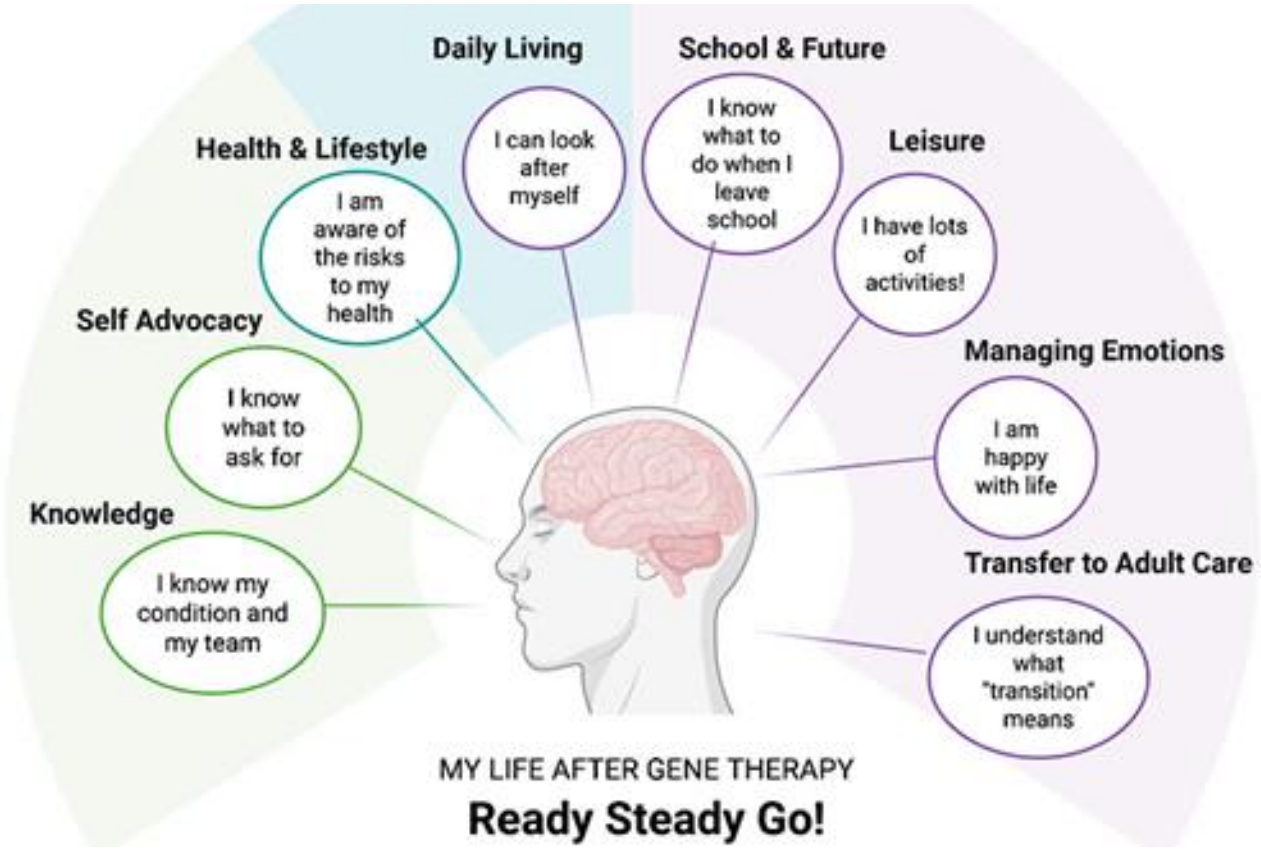
Background: CD34⁺ ex-vivo gene therapy has transformed outcomes for children with genetic primary immune deficiencies through using their own modified stem cells. The U.S. Food and Drug Administration recommend 15 years of follow-up, often extending into adulthood, making transition planning essential. These therapies are mainly delivered in paediatric centres, with few adult services having established gene therapy pathways. Transition readiness research in this population is limited and may not capture their unique long-term implications. The 'Ready, Steady Go' (RSG) questionnaire is a validated tool assessing healthcare independence, but gene therapy patients face extra challenges like complex regimens and psychosocial issues.

Methods: This cross-sectional evaluation included nine post-CD34⁺ gene therapy patients (aged 12–18) with chronic granulomatous disease, severe combined immunodeficiency, and adrenoleukodystrophy, attending routine follow-up. They completed the RSG questionnaire covering eight areas: Knowledge, Self, Health & Life, Daily Living, School, Leisure, Emotions, and Transition, answering "Yes," "No," or "Comment." Correlations between readiness, age, and time since therapy were analysed.



Results: Nine patients (aged 12–18), 1–12 years post-ex vivo CD34⁺ gene therapy, completed the RSG questionnaire. The overall readiness rate was 86.1%, with 33.3% "Ready," 55.6% "Mostly Ready," and 11.1% needing additional support. Readiness was highest in Daily living, School, and Leisure domains (100%), while Self-advocacy was lowest at 56%, indicating a key area for intervention. Older age correlated positively with readiness ($r = +0.583$), whereas longer time since gene therapy correlated negatively ($r = 0.552$), suggesting that readiness may decline over time without structured, ongoing support.

Conclusions: The Ready Steady Go questionnaire effectively assessed transition readiness in post-CD34⁺ gene therapy patients. Despite good overall readiness (86.1%), variation across domains highlighted the need for improved self-advocacy, age-appropriate transition planning, and sustained long-term follow-up. Embedding structured transition support may enhance continuity of care and long-term independence for this growing patient population.

Disclosure: Nothing to declare

NP34

PREVENTION AND MANAGEMENT OF ORAL MUCOSITIS IN PEDIATRIC ONCO-IMMUNO-HEMATOLOGICAL PATIENTS: A SCOPING REVIEW

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Background: Oral mucositis is one of the most common and debilitating complications in patients undergoing myeloablative chemotherapy, hematopoietic stem cell transplantation, and gene therapies, with a significant impact on quality of life and the therapeutic pathway. Despite the existence of consolidated guidelines for the management of mucositis in the adult population, evidence in the pediatric setting remains heterogeneous. Prevention and management of mucositis in pediatric onco-immuno-hematological patients therefore represent a clinical and care priority. The aim of this scoping review is to identify multidisciplinary therapeutic and preventive strategies for mucositis in pediatric onco-immuno-hematological patients.

Methods: A scoping review was conducted in accordance with the Joanna Briggs Institute Manual criteria. The following databases were searched: MEDLINE via PubMed, EBSCO Cumulative Index of Nursing and Allied Health Literature (CINAHL), and Elsevier Scopus. Inclusion criteria encompassed articles addressing the management and/or prevention of mucositis in pediatric oncologic and immuno-hematological patients, with particular attention to non-pharmacological interventions promoted by nurses and other healthcare professionals. Articles regarding combined pharmacological and non-pharmacological interventions managed by a multidisciplinary team were also included.

Results: A total of 46 articles were included in the review. Promising results emerged regarding photobiomodulation. Favorable evidence was also found for the use of honey, olive oil, and Aloe vera, owing to their anti-inflammatory and wound-healing properties. Education on oral hygiene promotes prevention and early recognition of signs and symptoms. Other emerging treatments, including glutamine and palifermin, have demonstrated efficacy in reducing the incidence of mucositis. Among treatments of questionable effectiveness in prevention, mouthwashes containing chlorhexidine at concentrations equal to or below 0.2% were identified; although widely used, they appear excessively irritating and not statistically significant in terms of outcomes for the management of pediatric mucositis.

Conclusions: In conclusion, for the prevention and management of pediatric mucositis in the onco-immuno-hematological setting, there is a need to combine pharmacological and non-pharmacological treatments within a multidisciplinary care approach. Prevention consists of promoting oral hygiene educational interventions for young patients and caregivers through demonstrations and simulations. Education should be accompanied by targeted clinical oral examinations and the use of tailored products selected by dental hygienists, nurses, and physicians. Several authors suggest the introduction of natural substitutes, such as honey, olive oil, and Aloe vera, combined with photobiomodulation in the management of pediatric oral mucositis, which may be proposed as alternatives to chlorhexidine, whose

effectiveness remains uncertain. In daily practice, a multidisciplinary approach is recommended, with early involvement of the dental hygienist and primary nurse for the prevention and early identification of the first signs of mucositis. Recommended non-pharmacological and pharmacological interventions include daily observation of oral cavity assessment forms, oral hygiene education, and the routine introduction of products based on alcohol-free formulations combined with photobiomodulation. Interventions should be adapted to the characteristics of the individual patient.

Disclosure: Nothing to declare

NP37

PERCEIVED BARRIERS AND FACILITATORS OF FAMILY-CENTERED ROUNDS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION, A HEALTH CARE PROFESSIONALS SURVEY

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Background: Family-centered care is an important core principle in pediatric care. Family-centered rounds are an important approach to engage patients and their family caregivers in daily care and treatment decision-making. Research shows that family-centered rounds lead to improved care, reduced stress and pain in children, and increased satisfaction among both family caregivers and children. Besides, it can also save time for healthcare professionals, improve communication, satisfaction, understanding and relationship. Our aim is to investigate which barriers and facilitators healthcare professionals perceive and what is needed for successful implementation of family-centered rounds in the pediatric HSCT and CT unit.

Methods: A survey based on a literature search, consisting of 13 questions, including eight closed-ended multiple-choice and five open-ended questions. Closed questions were analyzed using descriptive statistics, and open responses were categorized. The online survey was distributed by email to the medical team in October 2025.

Results: A total of 30 healthcare professionals completed the survey. Of these, 50% were specialized pediatric nurses, 23% medical residents, 10% pediatric immunologists/hematologists, 3% team lead, and 13% nursing trainees. The current rounds received an average satisfaction score of 7 (0=not satisfied and 10=totally satisfied), with a range of five to nine.
The most frequently reported facilitating factor for family-centered rounds was that family caregivers and children are better informed about current care (22/30), and receive care more aligned with their needs, which increases the satisfaction score (22/30). For additional facilitating factors see Table 1.
The most frequently mentioned barrier was the presence of language barriers and/or cultural

differences (23/30), and that nurses and physicians may feel less free to speak openly (23/30). Frequently repeated open responses included concerns that family-centered rounds may take more time and that family caregivers might misinterpret physicians' explanations. Respondents also mentioned that having rounds inside the patient's room could involve too many people to maintain isolation guidelines. For additional barriers see Table 1.
Respondents were also asked how often they would prefer family-centered rounds to take place; most preferred once per week (53%), followed by 3 times a week (23%), and on a daily basis (21%). They also indicated a preference for as few staff members as possible in the room to avoid overwhelming the child and family caregivers.
The majority of the respondents indicated that information about family-centered rounds should be provided by the nurse (21/30). The nurse would introduce the topic and provide information to family caregivers and children. Many respondents also indicated it would be a good idea to create an informational leaflet about family-centered rounds, which could be distributed during the admission interview. (20/30). And 7/13 of the respondents answered 'other'.

Conclusions: Most healthcare professionals in our survey believe that family-centered care is highly important during stem cell transplantation. Our findings support the literature that family-centered rounds can improve recovery and satisfaction among both family caregivers and children. Based on the barriers and facilitators, we currently are working with a multi-disciplinary team on a strategy to implement and evaluate family-centered rounds within our unit.

Perceived barriers	Total
1. The presence of language barriers and/or cultural differences	23 (77%)
2. Nurses and physicians may feel less free to speak openly	23 (77%)
3. There is less time for education of residents	6 (20%)
4. Other	21 (70%)
Perceived facilitators	
1. Family caregivers participation in ward rounds ensures that they are more thoroughly informed about prescribed medications and discharge-related matters	22 (73%)
2. Clarity for family caregivers when to ask their questions and to whom	12 (40%)
3. Child and family caregivers participation leads to care that better meets the needs of both the child and the parent, resulting in higher satisfaction with the care for both parties.	22 (73%)
4. Children understand why they need to take a certain medication or why they are not yet allowed to get out of bed. As a result, children and family	5 (17%)

caregivers adhere more closely to the treatment recommendations, because they support them themselves. All of this has a positive effect on recovery	
5. It leads to less pain and distress (negative emotions such as fear, sadness, and panic) in children	1 (3%)
6. It saves time for nurses and physicians. By conducting an immediate clinical assessment of the patient, a comprehensive overview is obtained, enabling the formulation of an appropriate treatment strategy	18 (60%)
7. Other	3 (10%)
Disciplines needed	
1. Pediatric Nurse	29 (97%)
2. Medical resident	25 (83%)
3. Pediatric immunologist/hematologist	28 (93%)
4. Physiscian assistant	14 (47%)
5. Other	5 (17%)
Tabel 1: Outcome online survey	

Disclosure: No conflicts of interest

Outreach Programmes for HCT, Cell and Gene Therapy in Low Resource Settings

NP35

ROLE OF TANZANIAN NURSES IN OPENING A PEDIATRIC BONE MARROW TRANSPLANT UNIT AND NURSING CARE IN SICKLE CELL PATIENTS AT BENJAMIN MKAPA HOSPITAL IN DODOMA

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Background: Sickle cell disease (SCD) is a hereditary blood disorder that causes severe anemia, pain, and organ damage. In Tanzania, an estimated 11,000 children are born with SCD annually, with 15–20% of the population carrying the sickle cell trait. Newborn screening shows 0.8–1.2% of infants are affected by SCD. The disease accounts for 7% of childhood deaths under five years old. Pediatric Bone Marrow Transplantation (BMT) is a life-saving therapy for children with malignant and non-malignant hematological disorders. However, delivering safe and effective pediatric BMT care in low- and middle-income countries (LMICs) is challenged by limited infrastructure, shortage of trained personnel, constrained finances, and high patients' burden. Nurses play a central role in bridging these gaps, as they are continuously involved in direct patient care, family education, infection prevention, and psychosocial support. This abstract describes the nursing experience in establishing a pediatric BMT program within a limited-resource setting, highlighting challenges, adaptive strategies, and lessons learned with the support of an Italian no-profit association HELP3-ODV.

Methods: This narrative experience is based on nursing practice in a newly established pediatric BMT unit in a resource-constrained hospital: Benjamin Mkapa Hospital in Dodoma, Tanzania. The project was promoted in different phases starting in 2018 with the first Italian mission. The first step consisted in setting and resources assessment to manage BMT in pediatric sickle cell patients. The main nursing competences were identified and promoted through the support of voluntary HELP3-ODV nurses through in presence teaching, simulation and remote training. Observations were gathered from daily clinical practice, multidisciplinary meetings, and interactions with patients and caregivers. Evaluations of nurses' competences and educational needs are collected through personalized questionnaires.

Results: Nurses faced multiple challenges, including limited availability of isolation rooms, shortages of personal protective equipment, restricted access to essential medications, and inadequate laboratory and diagnostic support. High nurse-to-patient ratios increased workload and risk of error. Despite these constraints, nurses adopted innovative and cost-effective strategies to maintain quality care. These included strict hygiene enforcement, rational use of available resources, development of simplified nursing protocols, task sharing, and close collaboration with physicians, pharmacists, and laboratory staff. Continuous bedside education for caregivers improved adherence to infection prevention measures and early reporting of complications. Nurses also played a critical role in monitoring graft-versus-host disease, managing chemotherapy side effects, and providing emotional support to children and families facing prolonged hospitalization. Standard Operating Procedures were elaborated. All the implementation phases were supported by the Nurses Italian team of HELP3-ODV.

Conclusions: The Benjamin Mkapa Hospital experience demonstrates that pediatric BMT nursing care is feasible in limited-resource settings when nurses are empowered with appropriate training, strong teamwork, and context-adapted protocols. Nurses serve as advocates, educators, and frontline defenders against complications, significantly influencing transplant outcomes. Investment in nursing education, supportive supervision, and basic

infrastructure is essential to strengthen pediatric BMT services in LMICs. Sharing nursing experiences from resource-limited units is crucial to inform best practices, promote capacity building, and improve survival and quality of life for children undergoing BMT.

Disclosure: Nothing to declare.

NP111

NURSING TRAINING IN A PEDIATRIC HSCT UNIT: IMPLEMENTATION, SATISFACTION OUTCOMES AND EVALUATION FRAMEWORK IN RABAT (MOROCCO)

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Background: Morocco, a lower-middle-income country, has a population of 38 million, with 31% <15 years, and <9% of the population lives in poverty. The Pediatric Haematology and Oncology Service (SHOP) in Rabat, part of the Francophone Africa Pediatric Oncology Group (GFAOP) network, operates a 6-bed transplant unit and has performed 144 hematopoietic stem cell transplants (HSCT) since 2014, including 36 allogeneic transplants. A national and hospital nursing shortage means only 2 nurses are assigned each shift. Initial BMT nursing training has been done. However, the increasing complexity of pediatric HSCT and rising activity highlighted the need for structured and standardised nursing training to ensure safe, high-quality care.

Methods: A visiting (JACIE-inspector) pediatric bone marrow transplant (BMT) nurse expert from Spain attended the unit for two weeks in September 2025. An initial introduction to the team included a presentation of transplantation of a child with Fanconi anaemia, a discussion of nursing training in general, and planning with 4 local nurse experts for a full-day structured pediatric BMT training. For the training, 40 participants (27 nurses) attended. The curriculum covered: 1) an overview of HSCT activity in Rabat, 2) HSCT fundamentals, 3) patient preparation, 4) stem cell collection, 5) nursing management on transplant day (Day 0), 6) early complications, 7) acute and chronic GVHD care, 8) long-term follow-up organisation, and 9) JACIE accreditation requirements.
Evaluation included:

- a satisfaction questionnaire using a 5-point Likert scale,
- a pre- and post-test to objectively measure knowledge acquisition; results will be reported once analysis is completed.

Results: Feedback from the training satisfaction questionnaire showed consistently high ratings across all domains, with ratings of 4–5/5 indicating that participants found the item

satisfactory to very satisfactory. Twenty-one participants rated the clarity of objectives and relevance of the material 5/5, while 17–21 participants rated the applicability and knowledge enrichment between 4 and 5/5. Trainers were also highly rated: 20 participants gave a score of 5 for communication clarity, 22 for adherence to objectives, and 20 for enthusiasm. Practical examples were rated 4–5/5 by 22 participants. Logistic aspects, including organisation and audiovisual conditions, mostly received scores of 4–5/5, with 16–18 participants rating them 5. Overall satisfaction was similarly high, with 17 participants giving 5/5 and 6 participants 4/5. Qualitative feedback highlighted the richness and relevance of the content, the quality of discussions, and strong team engagement. The pre- and post-test was administered and are currently under analysis.

Conclusions: This structured training day was highly valued by participants and effectively addressed core competencies required in pediatric HSCT nursing. While satisfaction indicators were strong across all domains, the forthcoming pre- and post-test analysis will provide an objective measure of knowledge acquisition. Implementing recurring, standardised training sessions with continuous evaluation will strengthen nursing capacity and support high-quality HSCT care within the GFAOP network.

Disclosure: Nothing to declare.