MINUTES OF MEETING

Meeting title:	Acute Leukemia Working Party Business Meeting
WP/Others:	ALWP

Location:	Marseille, France	**Date:**	25/11/2016

Author:	Sebastian Giebel, Arnon Nagler

Participants:	EBMT:	Aljurf Mahmoud ; Baron Frédéric ; Battipaglia Giorgia ; Bazarbachi Ali ; Beohou Eric ; Boumendil Ariane ; Brunet Mauri Salut ; Ciceri Fabio ; Civril Bozdag Sinem ; El Fakih Riad ; Esquirol Sanfeliu Albert ; Esteve Jordi ; Floisand Yngvar ; Giebel Sebastian ; Gorin Norbert Claude ; Guimaraes Jose Eduardo ; Halaburda Kazimierz ; Heinicke Thomas ; Houhou Mohamed ; Kimouche Mohamed ; Labopin Myriam ; Laroulandie Martine ; Lorentino Francesca ; Mailhol Audrey ; Mannone Lionel ; Nagler Arnon ; Piemontese Simona ; Poiré Xavier ; Polge Emmanuelle ; Remes Kari ; Ringden Olle ; Ruggeri Annalisa ; Salamero Garcia Olga ; Salomaki Soile ; Saraceni Francesco ; Schmid Christoph ; Sevillano Belen ; Vey Norbert ; Wittnabel Sebastian ; Finn Petersen ; Piauger Bénédicte; Mear Jean Baptiste ; Levast Benoît
	Other:	
Apologies		

Distribution:	EBMT members

MINUTES & record of decisions

Introduction (ALWP Chair: A. Nagler; ALWP secretary: S. Giebel; ALWP statistician: M. Labopin)

Prof. Arnon Nagler pointed out that acute leukemias remain the most frequent indication for alloHSCT and the number of transplants is continuously growing reaching 6871 procedures reported to the EBMT in 2014. He presented major achievements of ALWP, which include (i) organization of high level accredited educational activities pertinent to acute leukemia (latest symposiums: Nantes in 2008, Barcelona in 2009, Milan in 2010, Warsaw in 2011, Milan in 2012, Marseille in 2013, Paris in 2014 and 2015, Marseille in 2016); (ii) designing and support to prospective clinical trials in the field of acute leukemia across member centres (the elderly AML randomized trial is currently recruiting patients: ClinicalTrials.gov Identifier: NCT00766779); (iii) generation of high quality retrospective studies addressing different issues related to acute leukemia management and therapy; (iv) Increase within the registry the quality of data pertinent to SCT for acute leukemia; (v) generation of guidelines pertinent to management of acute leukemia.
In 2016, the activity of ALWP was reflected by over 33 scientific papers published in Journal of Clinical Oncology, Leukemia, Haematologica, The Oncologist, Oncotarget, Cancer, Journal of Hematology and Oncology, Bone Marrow Transplantation and other high quality journals. Results of the studies were presented at major congresses such as the ASH meeting 2016 (including 8 oral and 11 poster presentations).

So far structure of ALWP includes 7 subcommittees: Autologous SCT (NC. Gorin), Immunotherapy (C. Schmid), Alternative donors (F. Ciceri), Conditioning regimens (B. Savani), Molecular markers (J. Esteve), Acute lymphoblastic leukemia (S. Giebel), and Cord blood (F. Baron).
The next business meeting is planned during the EBMT meeting in Marseille on 27.03.2017, between 7 am – 9 am.
New study proposals are kindly invited. They should be addressed either to the ALWP chairman or subcommittee appropriate leader (see: email addresses at the end of the minutes).

Activity of the subcommittees:

Subcommittee: Cord Blood (Leader: Dr F. Baron)

Ongoing Studies

- Umbilical Cord Blood Transplantation Outcomes in FLT3 Mutation Positive Patients with Acute Myelogenous Leukemia, Proposal from University of Minnesota- Eurocord- EBMT (C. Ustun). UBCT yields similar outcomes compared with matched related and unrelated donors for FLT3-positive AML. The paper has been accepted to Leukemia.
- A data mining approach to predict 1-year mortality in cord blood transplantation for AML: Identifying Overall Survival Predictors and Related Interactions in Umbilical Cord Blood Transplantation Using Random Survival Forests: A Eurocord - Acute Leukemia Working Party - Paediatric Diseases Working Party – EBMT Study (R Shouval). Disease status, diagnosis, cell dose, age, center experience, cytomegalovirus sero-status, degree of HLA mismatch, previous autograft, and anti-thymocyte globulin administration were found to affect outcome. Abstract has been selected for oral presentation at ASH 2016. The paper has been submitted to Blood.
- Single vs. double UCBT in patients given RIC for AL. A study by the Eurocord and the ALWP of the EBMT (F. Baron). Oral presentation at EHA 2016. The manuscript has been submitted to Leukemia.
- Impact of donor type (MSD, MUD, MMUD, Haplo, UCB) on transplantation outcomes in patients with sAML (F. Baron). The study is ongoing. Further data collection is needed.
- Revisiting graft-versus-leukemia effects after UCBT for AML: an analysis from the ALWP of the EBMT and from Eurocord (F. Baron). Both acute and chronic GVHD are associated with increased risk of mortality without significant effect on relapse rate. Abstract has been selected for poster presentation at ASH 2016. The paper is in preparation.
- Impact of ATG in high-risk AML patients given allo-HCT in CR1 (I. Ofran, A Nagler). Abstract has been selected for poster presentation at ASH 2016. The paper is in preparation.
- TBI vs Chemotherapy-based Myeloablative Conditioning in Adults with Acute Lymohoblastic Leukemia Undergoing Umbilical Cord Blood Transplantation (J. Sanz). EUROCORD study in collaboration with ALWP. Feasibility of the study needs further evaluation.

Proposals

- CBT with TBF vs Haplo non T deplete with TBF (F. Gianotti, A. Ruggeri). 149 SUCBT and 130 NTD Haplo-SCT conditioned with a TBF-based MAC have been identified. Abstract has been submitted to EBMT 2017 meeting.
- Comparison of outcomes in AML patients given BMT without ATG versus PBSC with ATG following myeloablative conditioning (F. Baron). The study appears feasible. Abstract has been submitted to EBMT 2017 meeting.

- Unrelated donor versus umbilical cord blood transplantation in adults with relapsed or refractory AML (F. Baron, A. Ruggeri). 285 CBT and 2678 URD-SCT have been identified. Abstract has been submitted to EBMT 2017 meeting.
- Collaborative study of adult unrelated cord blood transplantation by the European Group for Blood and Marrow Transplantation and Japan Society for Hematopoietic Stem Cell Transplantation (J. Kanda; ALWP; Eurocord). The collaboration with JSHSCT in the field of CBT is highly desired.
- Review: Indication for CBT in AML (F. Baron; A. Ruggeri). A position statement will be prepared.
- Second HSCT after CB failure (A. Ruggeri, A. Nagler). Feasibility of the study needs further evaluation.
- CB versus Haplo in elderly patients (>=60y old). (A. Ruggeri, F. Gianotti). Abstract has been submitted to EBMT 2017 meeting.

Subcommittee: Molecular Markers (Leader: Dr Jordi Esteve)

Ongoing Studies

- Comparative analyses of different post-remission strategies (alloHSCT vs. other) for patients with intermediate-risk AML and triple negative genotype: a CETLAM, AMLSG and EBMT joint study (R. Schlenk, J. Esteve). The study has been concluded. AlloHSCT in first CR is associated with a marked relapse reduction and survival benefit compared to CHT or autoHSCT in the two cooperative group cohorts with prospective treatment data as well as in the whole cohort including the EBMT registry data. Manuscript is in preparation.
- AlloHSCT in AML with 3q26 (EVI1) rearrangement (K. Halaburda). The analysis including 106 patients indicate poor outcome with relapse being the major cause of treatment failure. Oral presentation at ASBMT Tandem meeting 2016. The manuscript has been submitted to Haematologica.
- Comparison of MSD- vs. URD-alloHSCT for primary refractory AML (E. Brissot). 1/3 of patients may be rescued. No difference between two types of donors. The study has been concluded. Manuscript is in preparation.
- Allogeneic stem cell transplantation in adult patients with acute myeloid leukemia and 17p abnormalities in first complete remission: a study from the Acute Leukemia Working Party (ALWP) of the European society of Blood and Marrow Transplantation (EBMT) (X. Poiré). Oral presentation at EBMT 2016. The manuscript has been accepted by J Hematol Oncol.
- Allogeneic stem cell transplantation for patients over 60 years or older with acute myeloid leukemia with normal karyotype and internal tandem duplication of FLT3 (X. Poiré). Poor outcome due to high incidence of relapse. Poster presentation at EBMT 2016.
- AlloHSCT for Ph-positive AML (V. Lazarevic). 65 patients including 57 allo-SCT and 8 auto-SCT recipients have been analyzed. Age and disease status were found to affect outcome. Abstract has been submitted to the EBMT 2017 meeting.
- Efficacy of Sorafenib before or after allogeneic transplant for FLT3-ITD acute myeloid leukemia. A retrospective study of the EBMT Acute Leukemia Working Party (A. Bazarbachi, M. Mothy). 1557 potentailly evaluable patients have been identified. Data collection is ongoing.
- Outcome of stem cell transplantation in adult patients with Core Binding Factor AML transplanted in second complete remission (K. Halaburda). 678 allo-SCT and 59 auto-SCT recipients have been identified. Data collection is ongoing.

- Role of alloHCT for patients with AML and MLL partial duplication (M. Pratcorona). Preliminary analysis indicates MLL-PTD to be associated with increased risk of relapse and reduced survival after allo-SCT.
- Significance/association of FAB classification with transplant outcomes in AML (J. Canaani). Adverse impact of FAB M6/M7 subtypes has been identified. Abstract has been selected for poster presentation at ASH 2016. The manuscript has been accepted by Am J Hematol .
- Autologous versus allogeneic stem cell transplantation in patients with acute myeloid leukemia in first remission harbouring an intermediate-risk karyotype with a mutated NPM1 without FLT3 mutations. (X. Poiré). In a mutivariate model MSD-SCT is associated with reduced risk of relapse and improved LFS compared with auto-SCT. Abstract has been selected for poster presentation at ASH 2016.

Proposals

- Allo for AML with Monosomy 5 (X. Poiré). The study appears feasible. Data collection will be started.
- Allogeneic hematopoietic stem-cell transplantation in early phase might overcome the adverse prognosis of acute myeloid leukemia with translocation t(6;9)(p23;q34)/DEK-NP214(CAN) rearrangement. (M. Diaz Beya, J. Esteve). The study appears feasible. Data collection will be started.

Subcommittee: Alternative Donors (Leader: Dr F. Ciceri)

Ongoing Studies

- A comparison between allogeneic stem cell transplantation from unmanipulated haploidentical and unrelated donors in acute leukemia (S. Piemontese). Better OS and LFS due to lower NRM for 10/10 MUD compared to haplo-SCT. No differences between 9/10 MUD and haplo-SCT. The manuscript has been accepted by J Hematol Oncol.
- HLA mismatches in T-cell replete haplo-HSCT (F. Lorentino). HLA matching on the unshared haplotype has a limited impact, with only antigenic HLA-DRB1 mismatches significantly associated with the single endpoint aGvHD 2-4 in transplants performed under PTCy regimen.
- Allogeneic hematopoietic stem cell transplantation with alternative donors in patients with poor risk AML in CR1 (J. Versluis, J. Cornelissen). For patients with HR AML in CR1 results of MSD-HSCT, 10/10 URD-HSCT and haplo_HSCT are comparable. The outcome after 9/10 URD-HSCT and UCBT is worse. Paper is under revision in Blood Advances.
- Impact of NIMA in MUD alloHSCT for AML. Proposal initiated by the DKMS and CIBMTR (A. Schmidt, J. Pingel). Data collection is ongoing.
- Match pair analysis Haplo versus MUD in poor-risk cytogenetic AML in CR (F. Lorentino). Poster EBMT 2016. Survival after haploidentical donor transplantation is comparable to that after HLA matched and mismatched unrelated donor transplantation for poor risk cytogenetics AML in CR1. Poster presentation at EBMT meeting 2016.
- Risk factor analysis of non-T-cell depleted haplo-HSCT for adults with ALL (N. Santoro). Analysis is ongoing.
- GRFS after TCD and non-TCD haplo-HSCT (S. Sestilli). Oral presentation at EBMT meeting 2016.
- Haplo-HSCT vs. URD-HSCT in PIF and CR1 AML (E. Brissot). Oral presentation at EBMT meeting 2016.
- Haplo TK HSV (M. Mohty, F. Ciceri). Abstract has been selected for oral presentation at ASH 2016.

- Haplo BM vs PB (A. Ruggeri). For acute leukemia patients treated with haplo-SCT followed by post-transplant cyclophosphamide the use of PB is associated with increased risk of grade II-IV aGVHD. No impact on NRM, RI, OS, LFS. Abstract has been selected for oral presentation at ASH 2016.
- The role of KIR- ligand incompatibility in the outcome of T-cell replete haplo-identical transplantation with post-transplant cyclophosphamide (A. Shimoni). 531 patients have been identified including 165 with KIR ligand mismatch. According to preliminary analysis – KIR ligand mismatch is associated with increased overall mortality. Abstract has been submitted to the EBMT 2017 meeting.
- Role of donor CMV serological status on outcome after non T depleted haploidentical HSCT. Proposal initiated by the IDWP (R. Crocchiolo & S. Cesaro). Feasibility of the study will be assessed.

Proposals

- Donor selection for allogeneic stem cell transplantation: HLA-haploidentical children, siblings, or parents versus HLA-matched siblings. Proposal initiated by the CIBMTR (E. Fuchs). Feasibility of the study will be assessed.

Subcommittee: Immunotherapy (Leader: Dr C. Schmid)

Ongoing Studies

- Pre-emptive or prophylactic use of DLI (C. Schmid). According to results of a matched-pair analysis prophylactic DLI is associated with improved OS. Abstract has been selected for Oral presentation at ASBMT Tandem meeting 2017. A survey for strategies to use one or another option is planned.
- Second allograft versus DLI in relapsed AML (M. Kharfan-Dabaja). Data collection and entry is ongoing.
- Relapse after Haploidentical allogeneic stem cell transplantation for AML (S. Piemontese). 191 relapsed patients have been identified. The study is ongoing.
- Kinetic of relapse (C. Craddock/Hovon). Risk factors for relapse vary according to post-transplant period. Abstract has been selected for poster presentation at ASH 2016. Paper is being revised pre resubmission.
- Acute biphenotypic leukemias (R. Munker). 519 patients have been included in the analysis. The outcome is affected by age, year of SCT and type of conditioning (better LFS for MAC TBI). Abstract has been selected for Oral presentation at ASBMT Tandem meeting 2017.

Proposals

- Efficacy and toxicity of prophylactic DLI given as maintenance after allogeneic stem cell transplantation in high-risk AML – a prospective observational audit by the ALWP (C. Schmid) Centers currently performing this strategy may be identified via survey- monkey. Those willing to participate should prospectively register their patients.

- Efficacy and toxicity of prophylactic DLI given as maintenance after allogeneic stem cell transplantation in high-risk AML – a prospective observational audit by the ALWP (C. Schmid)

Acute Lymphoblastic Leukemia (Leader: Pr. S. Giebel):

Ongoing Studies

- AloHSCT for patients older than 60 years (G. Roth). Enhancing results for selected patients. Outcome similar for Ph-pos and Ph-neg ALL. The manuscript is being circulated.
- The role of ATG in alloPBCST for ALL in CR1 (W. Mendrek, S. Giebel). The use of ATG is associated with improved GRFS. Abstract has been selected for oral presentation at ASH 2016.
- Auto vs Al lo in Ph+ ALL (S. Giebel). Comparable LFS and OS after auto-SCT, matched sibling donor –SCT and unrelated donor-SCT for patients with Ph-positive ALL being in complete molecular remission. Abstract has been selected for oral presentation at ASH 2016.
- Thiotepa vs TBI as part of the conditioning regimen in ALL (S. Eder). Thiotepa-based conditioning may provide similar results TBI-based conditioning. Oral presentation at EBMT 2016. Manuscript is being prepared.
- Survey on the use HSCT for adults in ALL (S. Giebel). Increasing use of allo-SCT for patients with ALL despite development of novel agents. Oral presentation at EHA 2016.
- RIC-alloHSCT vs autoHSCT in elderly patients with ALL (S. Giebel). Data collection is ongoing. So far the numbers are too small for reliable analysis.
- Allogeneic hematopoietic stem cell transplantation for primary refractory acute lymphoblastic leukaemia. (J. Pavlu). Enhancing results for TBI-based conditioning and female to male gender combination. Abstract has been selected for poster presentation at ASH 2016. Manuscript has been accepted for publication in Cancer.
- Impact of dose fractionation on the efficacy and safety of TBI for acute leukemia (Y. Belkacemi). Myeloablative doses of TBI may be safely delivered in 3 instead of 6 fractions. Abstract has been selected for oral presentation at ASH 2016.
- Alternative donor in ALL CR2 (E. Brissot). Allo-SCT may rescue more than one third of patients with ALL in CR2. the donor type did not have any impact on patients' LFS, RI, NRM and GRFS. However an HD compare to a MUD 10/10 was associated with lower OS and higher aGVHD II-IV. Abstract has been selected for poster presentation at ASH 2016.

Proposals

- Ponatinib after alloHSCT for adults with Ph(+) ALL (K. Hirschbuehl). Scarce data on the use of ponatinib after SCT available so far. Centers will be approached to collect data.
- Impact of cytogenetic abnormalities on results of alloHSCT for Ph(-) ALL (T. Czerw). Few patients with abnormalities other than t(9;22) reported to the registry. At the moment insufficient statistical power.
- Optimal conditioning for patients with ALL (S. Giebel). The impact of conditioning has not been prospectively evaluatyed although retrospective studies indicate superiority of TBI. The combination of TBI with cyclophosphamide vs. etoposide will be compared. The abstract will be prepared for EHA 2017 meeting.
- Pediatric-inspired therapy compared to allografting for Philadelphia chromosome-negative adult ALL in first complete remission (M.D.S. Aljurf). To run the study, cooperation with collaborative ALL groups is needed. Attempts to incorporate PETHEMA are suggested.

Subcommittee: Autologous HSCT (Leader: Pr. N.C. Gorin)

Ongoing Studies

- Updating the follow-up of AutoHSCT for AML (N.C. Gorin). Data on 3833 auto-SCT collected so far (84% of expected).
- Quality of live (Karnofsky) in AML patients transplanted in first remission and still in complete remission two years after either autologous stem cell transplantation or unrelated transplants 10/10 and 9/10 matched (F. Saraceni).
- Data mining approach for predicting LFS post Auto in AML and ALL patients transplanted in CR (R. Shouval, A Nagler). The aim is to establish a data driven decision support system, based on ML algorithms, for the prediction of Leukemia Free Surival (LFS) in AML patients who are candidates for ASCT, as post-remission therapy.
- Second transplant Allo after AML relapse post Auto for AML (M. Christopeit). 537 patients identified with 40% OS rate. The use of TBI is associated with increased mortality. Abstract has been submitted to the EBMT 2017 meeting.
- Autologous versus matched unrelated transplantation in adult patients with acute myelocytic leukemia in first molecular remission (NC. Gorin). 708 patients have been identified. According to preliminary analysis no difference in terms of LFS but higher OS after auto-SCT, especially in standard risk karyotype subgroup. Abstract has been submitted to the EBMT 2017 meeting.

New proposals

- Reduced intensity chemotherapy with ponatinib followed by autologous stem cell transplant in patients with Philadelphia (Ph) positive ALL. (R. El Fakih, M. Aljurf, M. Mohty).

Subcommittee: Conditioning (RIC) (Leader: Dr B. Savani)

Ongoing Studies

- Survey on the use of Treosulfan as part of the conditioning regimen in ALL and AML (A. Nagler, B. Savani). Paper is under consideration in J Hematol Oncol.
- IV Busulfan vs Treosulfan based conditioning for AML (A. Shimoni). Abstract has been selected for poster presentation at ASH 2016. Abstract has been submitted to the EBMT 2017 meeting.
- ABO compatibility in Haplo-SCT (B. Savani; J Canaani; A Nagler). Abstract has been selected for oral presentation at ASBMT Tandem meeting 2017. Paper with major revision in Haematologica.
- ABO in Unrelated donor - SCT (B. Savani; J Canaani;A Nagler). Abstract has been selected for Oral presentation at ASBMT Tandem meeting 2017.
- Impact of conditioning regimen intensity on transplant outcome for secondary acute myeloid leukemia (B Savani). Oral at ASBMT Tandem meeting 2016.
- FB4 in sibling HSCT, ATG vs. no ATG (M.T. Rubio). According to the preliminary analysis the use of ATG is associated with increased OS, LFS and GRFS, while reduced risk of cGVHD. The manuscript has been accepted by J Hematol Oncol.

- Comparison of outcomes between reduced intensity and myeloablative conditioning for AML patients with complex cytogenetics in collaboration with MDACC. (S. Ciurea, B. Savani, A. Nagler). Abstract has been selected for poster presentation at ASH 2016.

- Impact of HLA high resolution typing on outcome of RIC-URD-HSCT for AML (C. Craddock).
- What is the outcome of patients with acute leukemia who survive severe acute graft-versus-host disease (O. Ringden). Poster at EHA 2016.

Proposals

- TBF vs Bu-Flu in Sibling versus MUD (F. Saraceni). 3122 patients have been identified. In a propensity score matched pair analysis the use of TBF was associated with reduced risk of relapse while increased NRM. Abstract has been submitted to the EBMT 2017 meeting.
- Outcome of allogeneic hematopoietic stem cell transplantation from sibling an unrelated donor for patients with acute leukemia above 70 years of age (O. Ringden). The aim is to comparison of outcome in patients with acute leukemia above 70 years of age with patients between 50-69 years of age. 810 patients >70 y.o. treated with SCT have been identified. Data analysis was done.
- GVL vs. GVHD in MAC vs RIC Allo for AML in various decade of Age i.e 20-30y…60-70y; >70y (F. Baron, A. Nagler).
- Long-term survival and late events after allo-SCT from HLA- matched unrelated donors for acute myeloid leukemia with myeloablative compared to reduced-intensity conditioning. (A. Shimoni)

Various proposals/studies

Ongoing Studies

- Impact of ATG dose and timing on allo-SCT outcome (R. Devillier). Higher doses of ATG are associated with increased risk of relapse in AML CR1 after MSD-HSCT. Paper is under consideration in Cancer.
- Transplantation outcome based on EBMT Mega file (R. Shouval, A Nagler). Abstract has been selected for oral presentation at ASH 2016.
- Non-interventional study on stem cell transplantation in Blastic Plasmocytoid Dendritic Cell Neoplasia (BPDC): An LWP/ALWP proposal (S. Dietrich).
- Center Effect (L. Biard/M. Labopin). Abstract has been selected for poster presentation at ASH 2016.
- GRFS in AML patients receiving allogeneic HSCT from HLA-identical and unrelated donors (G. Battipaglia). UD transplant is associated with lower GRFS, probably due to higher incidence of GVHD and NRM. In-vivo TCD might improve outcomes of UD recipients, leading to a GRFS comparable to MSD recipients. Abstract has been selected for poster presentation at ASH 2016.

Proposals

- Ex-vivo T cell depletion versus in vivo T cell depletion using ATG for GvHD prophylaxis after HLA-identical related or unrelated peripheral blood myeloablative HSCT in adults with AML: a collaborative study of the MSKCC and the ALWP of the EBMT (M. Perales & F. Malard).
- Long term impact of hyperleukocytosis in newly diagnosed AML patients undergoing allogeneic stem cell transplantation (S. Canaani). The manuscript has been submitted to Haematologica.

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