

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

<b>Location:</b>	Marseille, France	<b>Date:</b>	27/03/2017
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<b>Participants:</b>	<b>EBMT:</b>	Baron Frédéric, Beohou Eric, Brunet Mauri Salut, Bug Gesine , Czerw Tomasz, Czyz Anna, Diez Martin Jose Luis, Djabali Azedine, Eapen Mary, Esquirol Sanfeliu Albert, Esteve Jordi, Gedde-Dahl Tobias, Giannotti Federica, Giebel Sebastian, Gluckman Eliane, Gulbas Zafer, Halaburda Kazimierz, Hirschbuehl Klaus, Houhou Mohamed, Kimouche Mohamed, Labopin Myriam, Laroulandie Martine, Le Bourgeois Amandine, Mailhol Audrey, Mohty Mohamad, Nagler Arnon, Pavlu Jiri, Piemontese Simona, Polge Emmanuelle, Ringden Olle, Ruggeri Annalisa, Savani Bipin, Schmid Christoph, Shimoni Avichai, Shouval Roni, Gilleece Maria, Kanda Junka, Astsuta Yoshiko, Takahashi Satoshi, Hayashi Hiromi, Okamoto Shinichiro, Cappeli Barbara, Medinger Michael, Takagi Shinsuke, Paviglianiti Annalisa, Sica Simona, Ivetta Danylesko, Ligen Liu, Ilhan Osman, Frankiewicz Andrzej, Tsilimidos Gerasimos
	<b>Other:</b>	
<b>Apologies</b>		

<b>Distribution:</b>	EBMT members
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## 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 alloHCT and the number of transplants is continuously growing. In 2015 patients with AML and ALL accounted for 39% and 16% of all alloHCT recipients, respectively. 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 and 2017); (ii) designing and support to prospective clinical trials in the field of acute leukemia across member centers (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 25 scientific papers published in Journal of Clinical Oncology, Leukemia, Haematologica, The Oncologist, Oncotarget, Cancer, Journal of Hematology and Oncology, British Journal of Haematology, American Journal of Hematology, Experimental Hematology and Bone Marrow Transplantation. Results of the studies were presented at major congresses such as the ASH meeting 2016 (including 8 oral and 10 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 ALWP business meeting and educational symposium is planned in Paris on 24-25.11.2017.

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

#### Ongoing studies discussed during the meeting

- Comparison of the outcomes of reduced intensity versus myeloablative conditioning in the setting of allogeneic hematopoietic cell transplantation in patients with acute myeloid leukemia with or without pre-transplant minimal residual disease (M. Gilleece). It is hypothesized that MRD-negative patients may benefit from RIC transplants while for MRD-positive patients myeloablative conditioning may be superior. A preliminary analysis has been performed including 2292 AML CR1 patients. For MRD-positive patients <50 y.o. results of MAC were significantly better than RIC. Among older MRD-positive as well as among MRD-negative patients results of MAC and RIC transplants were equivalent.
- Comparison of FLAMSA-RIC with Fludarabine/Busulfan in AML patients in first or second complete remission (T. Heinicke). The goal is to compare FLAMSA-TBI4Gy, FLAMSA-BU and Bu2Flu for patients with AML treated in CR1 or CR2 with alloHSCT. The study is feasible. So far 386, 184 and 1775 patients have been identified in respective three groups.
- Impact of donor age on haploidentical hematopoietic cell transplantation outcome after RIC or MAC regimen for AML (J. Canaani) – According to preliminary analysis, for patients older than 40 years treated with haploHSCT, better results are observed when the donor is younger than 40 years (reduced NRM, increased LFS, OS). For patients younger than 40 years the donor no significant impact of the donor age can be demonstrated.

#### Other ongoing studies & proposals

- IV Busulfan vs Treosulfan based conditioning for AML (A. Shimoni). Poster at ASH 2016 meeting. Oral at EBMT 2017 meeting.
- Impact of conditioning regimen intensity on transplant outcome for secondary acute myeloid leukemia (B Savani). Oral at ASH 2015 meeting. Data collection is ongoing
- 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). Oral at Tandem 2017 meeting.
- Impact of HLA high resolution typing on outcome of RIC-URD-HSCT for AML (C. Craddock). Abstract submitted to EHA 2017 meeting.
- What is the outcome of patients with acute leukemia who survive severe acute graft-versus-host disease (O. Ringden). Poster at Tandem 2017 meeting.
- TBF vs Bu-Flu in Sibling versus MUD (F. Saraceni). 3122 patients have been identified. Oral 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). Abstract submitted to EHA 2017 meeting.

- 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). Abstract submitted to EHA 2017 meeting.
- The impact of ABO mismatch in MMUD (J Canaani). Oral at Tandem 2017 meeting. Paper has been circulated.
- Proposal: FLAMSA vs TBF – synopsis needed, feasibility to be assessed, may be merged.
- Proposal: FLAMSA vs Flu/Treo – synopsis needed, feasibility to be assessed, may be merged.
- Proposal: FTBP vs Flu/Treo – synopsis needed, feasibility to be assessed, may be merged.

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

#### Ongoing studies discussed during the meeting

- Auto vs Allo in Ph+ ALL in molecular remission (S. Giebel). Oral at ASH 2016 meeting. AutoHSCT is associated with reduced risk of NRM and increased risk of relapse as compared to MSD- or MUD-HSCT. LFS and OS rates are equivalent. Considering the risk of cGVHD after alloHSCT, it appears that patients Ph-positive ALL being in molecular remission do not necessarily benefit from allogeneic transplantation.
- Second and third generation TKIs after alloHSCT for adults with Ph+ ALL (K. Hirschbuehl). Efficacy and toxicity of 2nd and 3rd generation TKI in the treatment of persisting MRD and molecular/hematological relapse after allo- or auto-HSCT. 2414 alloHSCT recipients and 190 autoHSCT recipients with Ph-positive or Ph-unknown status have been identified. Centers will be approached to search for those treated with 2<sup>nd</sup> or 3<sup>rd</sup> generation TKIs.

#### Other ongoing studies & proposals

- The role of ATG in alloPBCST for ALL in CR1 (W. Mendrek, S. Giebel). Oral at ASH 2016 meeting.
- Survey on the use HSCT for adults in ALL (S. Giebel). Manuscript in preparation.
- RIC-alloHSCT vs autoHSCT in elderly patients with ALL (S. Giebel). Oral at ASH 2016 meeting.
- Alternative donor in ALL CR2 (E. Brissot). Poster at ASH 2016 meeting.
- Etoposide vs. cyclophosphamide in combination with TBI as conditioning for alloHCT in ALL (S. Giebel). Oral at EHA 2017 meeting.
- Proposal: Pediatric-inspired therapy compared to allografting for Philadelphia chromosome-negative adult ALL in first complete remission (M.D.S. Aljurf).

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

#### Ongoing studies discussed during the meeting

- 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.
- Proposal: 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. The primary objective is to identify prognostic factors for overall survival after adult sUCBT among Eurocord/ALWP of EBMT and JSHCT/JDCHCT registries. 1085 and 3501 acute leukemia patients have been identified in respective registries.

### Other ongoing studies & proposals

- 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). The paper has been submitted to Clin Cancer Res.
- Single vs. double UCBT in patients given RIC for AL. A study by the Eurocord and the ALWP of the EBMT (F. Baron). Oral at EHA 2016 meeting. The manuscript is being revised and will be resubmitted.
- Revisiting graft-versus-leukemia effects after UCBT for AML: an analysis from the ALWP of the EBMT and from Eurocord (F. Baron). Poster presentation at ASH 2016. Paper is about to be circulated
- Impact of ATG in high-risk AML patients given allo-HCT in CR1 (I. Ofran, A Nagler). Poster presentation at ASH 2016. The paper is in preparation.
- TBI vs Chemotherapy-based Myeloablative Conditioning in Adults with Acute Lymphoblastic Leukemia Undergoing Umbilical Cord Blood Transplantation (J. Sanz). EUROCORD study in collaboration with ALWP. Feasibility of the study needs further evaluation.
- CBT with TBF vs Haplo non T deplete with TBF (F. Gianotti, A. Ruggeri). Oral EBMT 2017.
- Comparison of outcomes in AML patients given BMT without ATG versus PBSC with ATG following myeloablative conditioning (F. Baron). Oral EBMT 2017.
- Unrelated donor versus umbilical cord blood transplantation in adults with relapsed or refractory AML (F. Baron, A. Ruggeri). Oral EBMT 2017.
- CB versus Haplo in elderly patients ( $\geq 60$ y old). (A. Ruggeri, F. Gianotti). Oral EBMT 2017.
- Proposal: Review: Indication for CBT in AML (F. Baron; A. Ruggeri). A position statement will be prepared.
- Proposal: Second HSCT after CB failure (A. Ruggeri, A. Nagler). Feasibility of the study needs further evaluation.

### Subcommittee: Immunotherapy (Leader: Dr C. Schmid)

#### Other ongoing studies

- Pre-emptive or prophylactic use of DLI (C. Schmid). Oral presentation at ASBMT Tandem meeting 2017. Manuscript in preparation.
- Second allograft versus DLI in relapsed AML (M. Kharfan-Dabaja). Data base in preparation.
- Relapse after Haploidentical allogeneic stem cell transplantation for AML (S. Piemontese). 191 relapsed patients have been identified. Oral at EBMT 2017 meeting.
- Prospective evaluation of prophylactic DLI in HR-AML (C. Schmid).
- Proposal: Evaluating the development of treatment and outcome of post-transplant relapse in AL over time (C. Schmid).
- Proposal: Third allogeneic SCT in acute leukaemia (A. Rank, Augsburg, Germany) .
- Kinetic of relapse (C. Craddock/Hovon). Poster presentation at ASH 2016. Paper submitted.
- Acute biphenotypic leukemias (R. Munker). Oral presentation at ASBMT Tandem meeting 2017, manuscript circulating.

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

#### Ongoing studies discussed during the meeting

- Matched-pair analysis: Haplo- versus MUD-HSCT in poor-risk cytogenetic AML in CR (F. Lorentino). Poster at EBMT 2016 meeting.
- Risk factor analysis of non-T-cell depleted haplo-HSCT for adults with ALL (N. Santoro). Paper submitted to Haematologica.
- Improvement over time after T-Cell depleted haploidentical stem cell transplantation in adults with acute leukemia (S. Sestili). Poster at EBMT 2017 meeting.
- Haplo- vs. MSD-HSCT (G. Battipaglia).

#### Other ongoing studies & proposals

- HLA mismatches in T-cell replete haplo-HSCT (F. Lorentino). Submitted to Blood.
- Impact of NIMA in MUD alloHSCT for AML. Proposal initiated by the DKMS and CIBMTR (A. Schmidt, J. Pingel). Data collection is ongoing.
- GRFS after TCD and non-TCD haplo-HSCT (S. Sestili). Oral at EBMT meeting 2016.
- Haplo-HSCT vs. URD-HSCT in PIF and CR1 AML (E. Brissot). Oral at EBMT meeting 2016.
- Haplo TK HSV (M. Mohty, F. Ciceri). Oral at ASH 2016 meeting.
- Haplo-BMT vs. -PBSCT (A. Ruggeri). Oral at ASH 2016 meeting.
- The role of KIR-ligand incompatibility in the outcome of T-cell replete haplo-identical transplantation with post-transplant cyclophosphamide (A. Shimoni). Oral at EBMT 2017 meeting.
- Post transplantation cyclophosphamide (PT-Cy) as GVHD prophylaxis in sibling and unrelated allogeneic stem cell transplantation (HSCT) for patients with acute leukemia (A Ruggeri). Oral at 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.
- Non T cell-depleted haploidentical HSCT versus HSCT from matched sibling donors in patients with Acute Myeloid Leukemia in first complete remission (D. Salvatore). Abstract submitted to EHA 2017 meeting.
- Impact of **conditioning RIC vs MAC** on outcomes of T cell repleted haploidentical transplantation for patients over 45 years-old with AML. (D. Nasso). Abstract submitted to EHA 2017 meeting.
- Proposal: Donor selection for allogeneic stem cell transplantation: HLA-haploidentical children, siblings, or parents versus HLA-matched siblings. Proposal initiated by the CIBMTR (E. Fuchs). Data were send to CIBMTR.
- Proposal: Comparison of PTCy regimens i.e days of administration and additional IS post non T depleted Haplo ,PTCy d 3,4 in conjunction with FK506/MMF d+5 vs PTCY d 3,5 in conjunction with CSA d0 +MMF d1 (P. Chiusolo). Feasibility assessment is needed.

### Subcommittee: Molecular Markers (Leader: Dr Jordi Esteve)

#### Ongoing studies discussed during the 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. Mohty). The contribution of 51 centers with 365 eligible patients has been declared. Data collection is ongoing.

- Allo for AML with monosomy 5 (X. Poiré). Submitted to EHA 2017 meeting. Monosomy 5 or 5q deletion has an independent negative prognostic impact on results of alloHSCT. On the other hand, a single monosomy is associated with better outcome compared with multiple monosomies.
- Allogeneic hematopoietic stem-cell transplantation for patients with translocation t(6;9)(p23;q34)/DEK-NP214(CAN) rearrangement. (M. Díaz Beyá, J. Esteve). 182 patients with t(6;9) have been identified including 130 patients treated with alloHSCT in CR1. According to preliminary analysis t(6;9) is associated with reduced risk of relapse compared to other high-risk AML subtypes.

### Other ongoing studies & proposals

- Role of alloHCT for patients with AML and MLL partial duplication (M. Pratcorona).
- 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). Manuscript is in preparation.
- AlloHSCT in AML with 3q26 (EVI1) rearrangement (K. Halaburda). Oral presentation at ASBMT Tandem meeting 2016. Submitted to J Hematol Oncol .
- Comparison of MSD- vs. URD-alloHSCT for primary refractory AML (E. Brissot). Manuscript is in preparation.
- 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). Poster at EBMT 2016 meeting.
- AlloHSCT for Ph-positive AML (V. Lazarevic). Poster at EBMT 2017 meeting.
- Outcome of stem cell transplantation in adult patients with Core Binding Factor AML transplanted in second complete remission (K. Halaburda). Data collection is ongoing.
- 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). Poster at Tandem 2017 meeting.
- Outcomes of Allogeneic Hematopoietic Cell Transplantation for AML with Complex Karyotypes: A Retrospective Study from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation and MD Anderson Cancer Center (S. Ciurea). Oral tandem 2017 meeting.
- Cytogenetics in Ph negative ALL (J. Esteve). Number of patients with known karyotype is too low to run the study at the moment.

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

#### Ongoing studies discussed during the meeting

- Second Allo-HSCT after AML relapse post Auto-HSCT for AML (M. Christopeit). Poster at EBMT 2017 meeting. Based on analysis of 537 patients it has been found that approximately one third of patients relapsing after autoHSCT may still be rescued with alloHSCT. Long CR duration after autoHSCT, no previous use of TBI, transplantation in CR2 from MSD are associated with improved outcome.
- Revisiting BU/MEL over BU/CY for autografting high-risk adult patients with AML in CR1 (N.C. Gorin, M. Labopin, M. Mohty and A. Nagler). Previous analysis by the ALWP showed superior results of BU/MEL vs. BU/CY. According to the current one with doubled population, patients with high-risk disease benefit from BU/MEL while for all remaining individuals results of BU/MEL and BU/CY are comparable.

### Other ongoing studies & proposals

- Updating the follow-up of AutoHSCT for AML (N.C. Gorin, M. Houhou). Data on 3833 auto-SCT collected so far (84% of expected).
- Data mining approach for predicting LFS post Auto in AML and ALL patients transplanted in CR (R. Shouval, A. Nagler).
- Autologous versus matched unrelated transplantation in adult patients with acute myelocytic leukemia in first molecular remission (N.C. Gorin). Oral at EBMT 2017 meeting. Paper is being circulated.

### Various proposals/studies

#### Ongoing studies discussed during the meeting

- Transplantation outcome based on EBMT Mega file (R. Shouval, A Nagler). Oral presentation at ASH 2016 meeting.
- GRFS in AML patients receiving allogeneic HSCT from HLA-identical and unrelated donors (G. Battipaglia). Poster at ASH 2016 meeting. Oral at EBMT 2017 meeting. 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.

#### Other ongoing studies & proposals

- Impact of ATG dose and timing on allo-SCT outcome (R. Devillier). Paper is under consideration in Cancer.
- Center Effect (L. Biard/M. Labopin). Poster at EBMT 2017 meeting.
- 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).
- Non-interventional study on stem cell transplantation in Blastic Plasmocytoid Dendritic Cell Neoplasia (BPDC): An LWP/ALWP proposal (S. Dietrich).

Arnon Nagler  
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