

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

<b>Location:</b>	Paris, France	<b>Date:</b>	28/11/2014
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	<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 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); (ii) designing and support to prospective clinical trials in the field of acute leukemia across member centres; (iii) generation of high quality retrospective studies addressing different issues related to acute leukemia management and therapy.

In 2014, the activity of ALWP was reflected by over 15 scientific papers published in Leukemia, Haematologica, Cancer and other high quality journals. Results of the studies were presented at major congresses such as the EBMT and ASH meetings.

So far structure of ALWP includes 7 subcommittees: Autologous SCT (NC. Gorin), Immunotherapy (C. Schmid), Alternative donors (F. Ciceri), RIC allo-SCT (B. Savani), Molecular markers (J. Esteve), Acute lymphoblastic leukemia (S. Giebel), and Cord blood (F. Baron).

The ALWP general session program planned for March 23rd 2015, 11:30-13:00 during the next EBMT meeting in Istanbul was detailed as well as the next ALWP business meeting that was moved from traditionally Sunday to Monday March 23rd 2015, 07:00-09:00.

The next educational event organized by the EBMT including ALWP: "Master Classes in Transplantation and Hematology (MATH): A focus on conditioning", which will take place in Paris 30th Jan 2015 was announced.

### Activity of the subcommittees:

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

##### Ongoing Studies

- Outcome of alloHSCT for T-ALL (X. Cahu). The paper indicating the advantage of TBI over chemotherapy in advanced disease and comparable results for sibling vs. MUD transplants has been submitted for publication.
- Impact of socio-economic factors on non-relapse mortality after alloHSCT for acute lymphoblastic leukemia (S. Giebel). The study demonstrated that early NRM is related to the current health care expenditure of a country while the overall NRM is associated with the Human Development Index. The manuscript is in circulation prior to submission.
- Allogeneic stem cell transplantation for patients older than 60 years with acute lymphoblastic leukemia (G. Roth). Data collection is ongoing.
- RIC vs auto in elderly patients with ALL (S. Giebel). The preliminary results indicate that both RIC-allo and autoHSCT are valuable treatment options. AutoHSCT may have advantage in Ph-neg. ALL, which should be verified after collection of additional data on MRD status and karyotype. The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- Non-relapse mortality after alloHSCT for ALL according to donor type and age groups (S. Giebel). A survey analysis including 4859 patients indicates survival improvement over time for all age groups after sibling and MUD-HSCT related mainly to the reduction of NRM. Additional data collection on karyotype is needed.
- Impact of dose intensity in RIC allo-SCT for ALL: a joint EBMT and CIBMTR study (R. Ashley, M. De Lima). Data have been sent to CIBMTR.

##### Proposals

- Allogeneic hematopoietic stem cell transplantation for primary refractory acute lymphoblastic leukaemia. (J. Pavlu). In the era of new drugs the role of alloHSCT in PIF should be re-evaluated. It was suggested to restrict the population to those transplanted within 4 months from diagnosis. More detailed study plan should be prepared.

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

##### Ongoing Studies

- Comparison of outcomes after cord blood and haploidentical stem cell transplantation for adult patients with acute leukemia in remission, on behalf of Eurocord-EBMT (A. Ruggeri, M Mohty). The manuscript has been submitted for publication.

- Umbilical Cord Blood Transplantation Outcomes in FLT3 Mutation Positive Patients with Acute Myelogenous Leukemia, Proposal from University of Minnesota- Eurocord- EBMT. (C. Ustun). The study in collaboration with CIBMTR. 117 patients in the EBMT-Eurocord database have been identified. CIBMTR data are being collected. It was suggested to collect and analyze data on FLT3 ratio, which, however, may be difficult.
- Analysis of risk factors for unrelated double unit cord blood transplantation in adult patients with acute leukemia, on behalf of Eurocord-EBMT (F. Giannotti). 669 eligible patients have been identified. Data collection is ongoing.

### Proposals

- Comparison of UCBT and unmanipulated haplo-HSCT after TBF conditioning regimen, for adults with AML, on behalf of Eurocord-EBMT (F. Giannotti). Preliminary analysis was performed suggesting advantage of haploHSCT in terms of survival. It was suggested to consider the issue of TBF intensity (RIC vs. MAC).
- Impact of transplanting female cord blood to male recipients in transplanted acute leukemia patients, on behalf of Eurocord-EBMT (F. Baron). Preliminary analysis including 815 patients was performed indicating increased risk of GVHD and decreased OS for female to male gender combination.
- Impact of conditioning intensity on cord blood transplantation outcomes in acute leukemia patients, on behalf of Eurocord-EBMT (F. Baron). The study is feasible. Preliminary analysis and further data collection will be performed.

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

#### Ongoing Studies

- Long term results after second transplant for relapsed AML (G. Andreoli) . The manuscript is in circulation prior to submission.
- Impact of CD3+ cell dose on outcome after RIC-alloHSCT for AML (T. Czerw). According to the preliminary analysis both CD3 and CD34 dose influence the risk of GVHD. The abstract has been accepted for oral presentation during the ASH 2015 meeting. The manuscript will be prepared.
- Use of azacitidine after alloHCT for AML (C. Craddock). Final analysis regarding patients treated with AZA for relapse after alloHSCT has been performed. The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- Determinants of the kinetics of disease relapse after an allograft for AML (C. Craddock) . The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- The GVL effect in HLA-identical siblings and haplo transplants (O. Ringden). Results of final analysis indicate similar risk of relapse after MSD and haploidentical transplants suggesting comparable GVL effect. The manuscript has been submitted for publication.
- Pre-emptive or prophylactic use of DLI (C. Schmid). Data collection is ongoing.
- Sequential Chemotherapy Followed by RIC allo-SCT in Adult Patients with Relapsed or Refractory AML (O. Ringden). Data collection is ongoing.
- Second allograft versus DLI in relapsed AML (M. Kharfan-Dabaja). Data collection is ongoing.

#### Proposals

- Revisiting the impact of ex-vivo T-cell depletion of PBSC on allo-SCT outcome in patients given myeloablative allo-SCT for AML in CR (F. Baron).

- Relapse after HaploHSCT (C. Schmid; S Piemontese). Preliminary analysis was performed indicating prolonged survival for late vs. early relapse. Further data collection is needed regarding prevention and treatment of relapse as well as the incidence of GVHD.
- The GVL effect in HLA-identical siblings, MUD and haploidentical transplants using RIC as opposed to MAC (O. Ringden).

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

#### Ongoing Studies

- Autologous versus haplo transplant in AML (N.C. Gorin). A matched-pair analysis has been performed suggesting that results of haploHSCT and autoHSCT may be comparable. In particular, no advantage of haploHSCT over autoHSCT with regard to LFS could be demonstrated in AML CR1 with IR karyotype. The manuscript is under revision in Haematologica.
- Long-Term Follow-up of Autologous Hematopoietic Stem Cell Transplantation (AHSCT) for Acute Myeloid Leukemia (AML): A Survey of 3567 Patients From the ALWP (T. Czerw). The manuscript is in preparation.
- Updating the follow-up of ASCT (N.C. Gorin).

#### Proposals

- Autologous versus Unrelated Stem Cell Transplantation in Acute Leukemia (N.C. Gorin). Preliminary analysis has been performed suggesting LFS advantage for URD-HSCT compared to autoHSCT for AML with IR karyotype, without significant effect on OS. Update of the follow-up is needed. Additional analyses including the impact of HLA-compatibility and intensity of the conditioning are planned.
- Conditioning in Autologous Stem Cell (N.C. Gorin). The impact of various conditioning regimens on outcome will be analyzed in a setting of autoHSCT for AML in CR1 and CR2. The study is feasible. Detailed plan of the analysis will be prepared.

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

#### Ongoing Studies

- Impact of the intensity of prophylactic immunosuppressive therapy in genotypical allo-SCT for AML conditioned with a Flu-Bu2 regimen (M.T. Rubio). The manuscript is under revision in Haematologica.
- Equivalent Outcome between Older Siblings and Unrelated Donors After RIC Allo HSCT for Patients Older Than 50 Years with AML in CR1 (R. Peffault de Latour). Final analysis has been performed. The manuscript is in circulation prior to submission.
- iv Bu-Cy vs Cy-TBi in advanced phase/relapsed AML (B. Savani, A. Nagler). Final analysis has been performed indicating no difference between iv Bu-Cy and Cy-TBi in terms of survival while reduced risk of GVHD for iv Bu-CY. The manuscript has been submitted for publication.
- Effect of conditioning intensity on outcome of AML with monosomal karyotype transplanted in CR1 in patients over 50 year-old (X. Poiré). The data on monosomal karyotype are being double checked before final publication.
- RIC versus MAC in AML CR1 adjusted for comorbidities, cytogenetics and age (J. Passweg). The study indicating no significant difference between RIC and MAC alloHSCT for AML patients between 40-60 years old has been submitted for publication.

- Comparison of two RIC regimens (Bu-Flu versus Flu-Mel) for allo-HSCT as treatment for acute myeloid leukemia (F. Baron). Results of the final analysis indicate reduced risk of relapse for Flu-Mel compared to Bu-Flu while no impact on survival. The manuscript has been accepted for publication in Cancer. The abstract has been accepted for oral presentation during the ASH 2015 meeting.
- Data mining study (R. Shouval). The manuscript has been submitted for publication.
- Survival advantage for patients with AML and MDS given allo-SCT using MAC versus RIC may become apparent 5-10 years after transplantation: RIC studies may need to be revisited after long-term follow-up (A. Shimoni). An abstract for the EBMT 2015 meeting will be prepared.
- Influence of stem cell source (bone marrow versus peripheral blood) on outcome after reduced-intensity conditioning regimens for acute leukemia (B. Savani). The analysis demonstrated that PB grafts were associated with higher LFS for AML, but not for ALL while no significant differences with regard to OS were found. The results will be presented during the ASBMT 2015 meeting.
- RIC vs MAC in MMUD (B. Savani). No significant outcome difference between RIC and MAC regimens after MM-URD allo-SCT in patients younger than 50 years could be demonstrated. The results will be presented during the ASBMT 2015 meeting.
- Survey on the use of Treosulfan as part of the conditioning regimen in ALL and AML (A. Nagler). Data collection is ongoing.
- Allogeneic transplantation to treat secondary AML diagnosed after autologous transplant (L. Metheny). Study in collaboration with CIBMTR. Data has been sent.

### Proposals

- Haploidentical stem cell transplantation in acute leukemia outcome after ablative vs. non-ablative conditioning regimens (B. Savani). According to the preliminary analysis the two groups do not differ in terms of LFS. More details on the conditioning regimens and potential sequential therapies as well as reasons for the use of RIC in young patients are needed for full interpretation of the results.
- URD- MM vs Match (8/10 and 9/10 vs. 10/10) RIC vs. MAC (all patients and separate analysis for aged >50 year and < 50 year) (B. Savani, A Nagler).
- Role of ATG in HLA identical sibling allogeneic HSCT for AML in CR1 conditioned with Fludarabine and 4 days Busulfan (M. T. Rubio). 435 patients have been identified. Additional data collection is needed with regard to: ATG dosage, immunosuppressive regimens, follow-up.
- Role of ATG in HLA identical sibling allogeneic HSCT for AML in CR1 conditioned with Fludarabine and Melphalan (M. T. Rubio). Over 400 patients have been identified treated with either ATG, Campath or no T-cell depletion.
- Role of the dose of ATG +/- post-transplant GVHD prophylaxis in HLA matched unrelated allogeneic HSCT for AML in CR1 (M. T. Rubio). Data on ATG timing in addition to brand and dose would be required.
- GVHD data mining proposal (R. Shouval).

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

#### Ongoing Studies

- Outcome of transplantation for AML with 11q23 (MLL) rearrangement (MLL-r AML) (A. Pigneux). The manuscript has been accepted for publication in Leukemia.

- Impact of NPM1 & FLT3-ITD mutational status on the outcome of alloHSCT for normal cytogenetics AML (C. Schmid). Results of NPM1wt/FLT3-ITD(-) are good and comparable to NPM1(+)/FLT3-ITD(-). Final analysis has been performed. The manuscript is in preparation.
- Outcome of alloHSCT for Ph (+)-ALL in CR1 in the era of TKIs (E. Brissot). In a large analysis including 473 alloHSCT recipients the use of pre-transplant TKI was associated with reduced risk of relapse and increased LFS. The manuscript has been accepted for publication in Leukemia.
- AlloHSCT in CR1 for patients with AML associated to a monosomal karyotype (AVM Brands-Nijenhuis). The manuscript is being circulated prior to submission.
- 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). The analysis including 630 patients showed superiority of alloHSCT vs. autoHSCT or chemotherapy in terms of LFS and OS. The abstract has been accepted for oral presentation during the ASH 2015 meeting.
- Predictive determinants of outcome following allogeneic hematopoietic cell transplantation for AML with normal karyotype and isolated NPM1 mutation (A. Bazarbachi, M. Kharfan-Dabaja). The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- AlloHSCT in AML with 3q26 (EVI1) rearrangement (K. Halaburda). Data collection is ongoing.
- Outcome of allogeneic stem cell transplantation for acute myeloid leukemia in first complete remission carrying (17p) abnormalities (X. Poiré). Cytogenetic data are being verified for appropriate coding.
- HSCT for APL in the ATO era. An analysis of 89 patients treated with HSCT in CR2 indicates relatively good results, comparable for auto and allo-transplantations. (J. Sanz) & Auto vs. ATO (C. Ganzel). CIBMTR joint study. Data has been sent to CIBMTR. According to preliminary analysis no significant difference could be demonstrated between allo and autoHSCT.

### Proposals

- Acute biphenotypic leukemias (R. Munker). A joint study with CIBMTR.

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

#### Ongoing Studies

- Survey on unmanipulated graft haploidentical transplantation (S. Piemontese). Results of the analysis including 129 patients has been prepared for publication and accepted by Leukemia.
- Allogeneic hematopoietic stem cell transplantation with alternative donors in patients with poor risk AML in CR1 (J. Verluis, J. Cornelissen). The abstract including final results has been accepted for oral presentation during the ASH 2015 meeting.
- Comparison of CBT vs HaploSCT in acute leukemia (A. Ruggeri). The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- Matched and Mismatched Unrelated Donor versus Unmanipulated Haploidentical graft from family donors for hematopoietic stem cell transplantation in acute leukemia: a comparative analysis on the behalf of EBMT-ALWP (S. Piemontese). Results of the analysis indicate equivalent outcome of T-cell replete haplo-HSCT and 9/10 mismatched URD-HSCT while improved survival for 10/10 matched URD-HSCT. The abstract has been accepted for oral presentation during the ASH 2015 meeting.
- Gender mismatch in unmanipulated Haplo (S. Piemontese, A. Ruggeri).
- Impact of the different GVHD prophylaxis on outcomes of unmanipulated Haplo (A. Ruggeri.)

- Impact of NIMA in MUD alloHSCT for AML (A. Schmidt; J. Pingel). Data have been sent to DKMS & CIBMRT. The analysis is ongoing.

### Proposals

- Comparative study of HLA id sibling versus MUD for adults with relapsed acute leukemia. (A. Ruggeri).

### Various proposal/studies

#### Ongoing Studies

- 2nd allogeneic transplant as rescue strategy for acute leukemia patients who relapse after an initial RIC allogeneic transplant (R. Vrhovac). Final analysis has been performed. The manuscript is being circulated prior to submission.
- Impact of ATG dose and timing on allo-SCT outcome (R. Devillier). The study demonstrated that higher doses of ATG are associated with increased risk of relapse in AML CR1 after MSD-HSCT. The abstract has been accepted for oral presentation during the ASH 2015 meeting.
- Impact of pre-existing invasive mould infections on transplant-related complications and survival after allo-SCT (O. Penack). The study in cooperation with infectious diseases WP demonstrated a tendency towards decreased survival for patients with pre-existing Aspergillosis. The abstract has been accepted for oral presentation during the ASH 2015 meeting.
- Survey on the use of Thiotepa as part of the conditioning regimen in ALL and AML (S. Eder). The manuscript is under revision. The abstract has been accepted for poster presentation during the ASH 2015 meeting.
- Center effect impact on outcomes after HLA matched HSCT for AML in France (J. Rossignol; S. Katsahian).
- Impact of previous gemtuzumab administration in AML patients after allo-SCT (G. Battipaglia). Data collection is ongoing.

#### Proposals

- Secondary Acute Leukemia (secondary to therapy or MDS transformed to AML) in AML & ALL (A. Nagler).
- MDS > 55y female to male donor matching and donor age interaction (A. Nagler).

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