Minutes of Acute Leukemia Working Party (ALWP) Business Meeting

London
April 7th, 2013
08:00 – 10:00

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

Prof. Mohamad Mohty presented scientific activity report indicating that in the ALWP registry more than 85000 transplant procedures for AML and ALL (auto and allo-HSCT) were registered thus far.
The ALWP objectives are: (i) to organize high level accredited educational activities pertinent to acute leukemia (latest symposiums: Nantes in 2008, Barcelona in 2009, Milan in 2010, Warsaw in 2011, and Milan in 2012); (ii) to design and support prospective clinical trials in the field of acute leukemia across member centres (the pan-european elderly AML randomized trial is currently recruiting patients: ClinicalTrials.gov Identifier: NCT00766779); (iii) to generate high quality retrospective studies addressing different issues related to acute leukemia management and therapy; (iv) to increase within the EBMT registry the quality of data pertinent to HSCT for acute leukemia; and (v) to generate guidelines pertinent to the management of acute leukemia.
Over the last 12 months, the studies portfolio of the ALWP has grown quickly, and generated an amazing number of published manuscripts and communications at major meetings such as the EBMT and ASH meetings.
Structure of ALWP includes 6 subcommittees: Autologous SCT (NC. Gorin), Immunotherapy (C. Schmid), Alternative donors (F. Ciceri), RIC allo-SCT (A. Nagler), Molecular markers (J. Esteve), and Developing centers (S. Giebel).
Everyone is welcome to participate in the activity of ALWP and to submit the study proposals as synopsis sent to either chairman (M. Mohty), secretary (S. Giebel) or subcommittee leader. The proposals will further be evaluated in terms of the scientific merit, financial aspects, and the feasibility from the point of view of statistical analysis and data management.

E.mail addresses:
Mohamad Mohty: mohamad.mohty@univ-nantes.fr
Sebastian Giebel: sgiebel@io.gliwice.pl
Myriam Labopin: myriam.labopin@upmc.fr
Fabio Ciceri: ciceri.fabio@hsr.it
Jordi Esteve : jesteve@clinic.ub.es
Norbert Claude Gorin: norbert-claude.gorin@sat.aphp.fr
Arnon Nagler : arnon.nagler@sheba.health.gov.il
Christoph Schmid: christoph.schmid@klinikum-augsburg.de

Ongoing surveys

- TBI in current clinical practice (S. Giebel): The aim of the survey is to explore the diversity of TBI techniques across Europe. Results may be helpful in interpretation of clinical results. This may be the first step in a way to optimize and standardize the method.

- Chemotherapy dosing (A. Nagler): There is a lot of controversy regarding optimal dose calculation of drugs used in conditioning with regard to adjustment for body mass and body surface. The aim of the survey is to determine current practice in Europe.

Activity of the subcommittees:

Auto-HSCT (Leader: Pr. NC Gorin):

Completed studies

- Granulocyte colony-stimulating factor after autologous hematopietic stem cell transplantation for acute myelocytic leukemia – association with outcome (T. Czerw). Results indicate that post-transpplant use of G-CSF has no impact on long-term results. G-CSF may be used in tis setting without increasing the risk of relapse.
- AutoHSCT for ALL (S. Giebel). In Ph-positive ALL dramatic improvement over time has been found suggesting that introduction of TKIs in recent years decresed relapse rate. AutoHSCT in teh TKI era appears a potentially curative option.
- 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). Results of a survey indicate that even after more than 2 years after autoHSCT there is still considerable risk of relapse (16% at 10y).

New Proposal

- Autologous versus haplo transplant in AML (NC. Gorin). Retrospective data suggest that results of haploHSCT and autoHSCT may be comparable. Appropriate adjustment for risk factors is necessary.

Developing centers (Leader: Dr. S. Giebel):

Completed study

- Results of allogeneic HSCT for patients with acute myeloid leukemia (AML): comparison of EMBMT and EBMT participating centers (A. Bazarbachi). Results of siblingHSCT for AML in CR1 are comparable for EBMT and AMBMT.

Ongoing studies discussed during the meeting

- Impact of economical factors on results of alloHSCT (S. Giebel). Impact of Health Care Expenditure, Human development Index and distribution of centers among countries and other dactors has been analyzed in a setting of adult ALL CR1 treated with alloHSCT. Lack of data on Ph-status is a limitation for interpretation of the data. Fro final analysis the study will focus on early and late NRM.
- Center effect impact on outcomes after HLA matched HSCT for AML in France (S. Katsahian).

Immunotherapy (Leader: Dr. C. Schmid)

Ongoing studies discussed during the meeting

- Pre-emptive or prophylactic use of DLI (A. Rank, C. Schmid). The aim is to analyze feasibility, safety and efficacy of the procedure taking into account timing and cell doseage. 913 patients have been identified. Missing data should

- Use of azacitidine after alloHCT for AML (C. Craddock). Retrospective analysis is planned.
- Sequential Chemotherapy Followed by RIC allo-SCT in Adult Patients with Relapsed or Refractory AML (O. Ringden).
- Long term results after second transplant fore relapsed AML (G. Andreoli).

Proposals:

- The GVL effect in HLA-identical siblings and MUD using RIC as opposed to MAC (O. Ringden). It is hypothesized that GVL is stronger after RIC than MAC. Association of LFS and RI with aGVHD and cGVHD will be analyzed and compared for the two treatment modalities.
- Second allograft versus DLI in relapsed AML (M. Kharfan-Dabaja). Such comparison has not been published so far. This is an important issue. Feasibility will be considered.

Reduced Intensity Conditioning (RIC) (Leader: Pr. A. Nagler):

Ongoing prospective studies

- Randomized comparison of RIC vs. chemotherapy as post-remission therapy in elderly patients with AML (D. Niederwieser, M. Mohty). Recriutment to this first study prospectively evaluating the role of RIC-HSCT is active.

Ongoing studies discussed during the meeting

- Correlation of number of consolidation courses and outcome after RIC allo-SCT for AML (M. Yeshurun). The main goal is to compare any consolidation vs. No consiolidation prior to RIC/NMA alloHSCT. Preliminary analysis including 325 patients (40 without consolidation) suggests that administration of consolidation results in higher LFS rate.
- Comparison of FB2 versus FB4 in alloHSCT for AML in CR1 (M. Kharfan-Dabaja, M. Mohty). Results of FB4 vs. FB2 for AML CR1 patients were presented with no apparent differences between the treatment schedules.
- Significance of Busulfan Dose Intensity On Outcomes of Hematopoietic Cell Allografting for AML in Second Complete Remission or Beyond (A. Bazarbachi, M. Kharfan-Dabaja, M. Mohty). According to preliminary analysis FB4 is a reasonable preferred conditioning in patients with AML in ≥CR2 (better LFS) Collection of missing cytogenetic data is important.
- Effect of conditioning intensity on outcome of AML with monosomal karyotype transplanted in CR1 in patients over 50 year-old (X. Poiré)
- iv Bu-Cy vs Cy-TBi in advanced phase/relapsed AML (A. Nagler). For patients with AML in CR iv Bu-Cy appears not inferior to Cy-TBI. In advanced disease there may be advantage of TBI-based conditioning.
- Comorbidities score (J. Verluis, J. Cornelissen).
- Data mining study (R. Shoval). Encouraging preliminary results have been presented. The model predicts better overall mortality than NRM at day 100.

Proposal:

- Impact of dose intensity in RIC allo-SCT for ALL: a joint EBMT and CIBMTR study (M. De Lima; R. Ashley; M. Mohty)

- Survey on the use of Treosulfan as part of the conditioning regimen in ALL and AML (A. Nagler, F. Ciceri, M. Mohty). 795 AML patients treated with treosulfan in various combinations were identified. Results of initial statistical analysis was presented.
- RIC versus MAC in AML CR1 adjusted for comorbidities; cytogenetics and age (J. Passweg). There are data indicating that among patients with AML in CR1 aged 40-60 years results of RIC-alloHSCT may be not inferior or superior to MAC-alloHSCT. Results of preliminary ALWP anaysis apears to confirm this hypothesis, however, more data is needed with regard to cytogenetics and co-morbidities.

Molecular Markers (Leader: Dr. J. Esteve):

Ongoing studies

- Impact of NPM1 & FLT3-ITD mutational status on the outcome of alloHSCT for normal cytogenetics AML (C. Schmid). According to initial analysis results of NPMmut/FLT3wt is better compared to other combinations and does not depend on the disease status. Further analysis on CR1 vs. >CR1 and in PIF are planned.
- Outcome of HSCT for APL in the ATO era (J. Sanz, J. Esteve). An analysis of 89 patients terated with HSCT in CR2 indicate relatively good results, comparable for auto and allo-transplantations.
- Outcome of alloHSCT for AML with monosomal karyotype (M. Brands-Nijenhuis). Outcome of AML with MK is associated with poor outcome in contrast to other poor-risk cytogenetic features.
- 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. Post-transplant TKIs were associated with reduced risk of chronic GVHD.
- Outcome of alloHSCT for T-ALL (X. Cahu). Preliminary analysis indicates favrabe outcome after TBI-based compared to CHT-based conditioning. Data collection is ongoing.

Proposals

- Survey on treatment with FLT3 inhibitors for relapsed FLT3-ITD AML after alloHSCT (J. Esteve). The aim is to assess the efficacy and predictors of response. Data from previous EBMT studies could be used for the analysis in addition to approaching national study groups.

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

Completed study

- 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)

Ongoing studies discussed during the meeting

- Impact of NIMA in MUD alloHSCT for AML (A. Schmidt, J. Pingel). So far 369 donors contacted, 173 maternal samples received form CIBMTR, 9 NIMA matches identified (9/10 cases); 832 donor contacted, 373 maternal samples received from EBMT, 12 NIMA match cases (9/10 Match), 17 pot.

- Survey on unmanipulated graft haploidentical transplantation (S. Piemontese, F. Ciceri). Initial analysis including 173 patients suggests encouraging results, in particular for AML CR1.

Proposals

- HLA-DP functional matching in unrelated donor SCT: proposal of a prospective study (K. Fleischhauer). The aim is to determine prognostic value of 'permissive' and 'non-permissive' mismatches. Italian and German donor registries have been approached.
- Allogeneic transplantation using alternative donors (CB and haplo) for refractory acute leukemia (M. Mohty).
- Immune determinants of outcome in haploidentical SCT (A. Bondanza). The study requires collaboration with IBWP.

Other proposals/studies:

- CMV serostatus impact (M. Schmidt-Hieber). Completed study, manuscript circulated.
- For male patients with ALL and AML, who is the best donor? (O. Ringden). Completed study, manuscript circulated.
- Survey on the use of Thiotepa as part of the conditioning regimen in ALL and AML (S. Eder).
- Impact of ATG dose and timing on allo-SCT outcome (D. Blaise).
- Impact of previous gemtuzumab administration in AML patients after allo-SCT (P. Chevallier).

List of participants:

Mahmoud Aljurf, Frédéric Baron, Ali Bazarbachi, Didier Blaise, Lorentz Brinch, Eolia Brissot, Salut Brunet, Xavier Cahu, Jia Chen, Fabio Ciceri, Tomasz Czerw, Jordi Esteve, Hervé Finel, Yngvar Floisand, Tobias Gedde-Dahl, Sebastian Giebel, Aurélie Gómez, Norbert Claude Gorin, Raffaella Greco, Yosr Hichri, Jerzy Holowiecki , Maija Itälä-Remes, Mohamed Kharfan-Dabaja, Myriam Labopin, Martine Laroulandie, Yin Lu, Florent Malard, Mohamad Mohty, Leila Moukhtari, Arnon Nagler, Dietger Niederwiser, Oliver Ottmann, Jakob Passweg, Jiri Pavlu, Isabel Pérez Requejo, Arnaud Pigneux, Emmanuelle Polge, Kari Remes, Josep Maria Ribera Santasusana, Olle Ringden, Annalisa Ruggeri , Roni Shouval, Christine Ta Thanh Minh, Luca Vago, Iman Zakaria

Sebastian Giebel
Secretary of the ALWP
sgiebel@io.gliwice.pl

Mohamad Mohty
Chair of the ALWP
mohamad.mohty@univ-nantes.fr