Minutes of Acute Leukemia Working Party (ALWP) Business Meeting

Warsaw
Saturday, November 18th, 2011
10:00 – 18:00

Introduction – ALWP organization, proposals' submission process, achievements and perspectives (ALWP Chair: M. Mohty; ALWP secretary: S. Giebel; ALWP statistician: M. Labopin)

Prof. Mohamad Mohty presented data indicating that acute leukemias are the most frequent indication for HSCT in Europe. Major objectives/missions of the ALWP are: a) organization of educational activities pertinent to acute leukemia, b) design and activation of prospective trials in the field of acute leukemias across member centers, c) generation of high quality retrospective studies addressing different issues related to acute leukemia therapy, d) increase within the registry the quality of data pertinent to SCT for acute leukemia, e) generation of guidelines pertinent to management of acute leukemia. Among major achievements are: a) high quality publications with the mean IF=10.881 in 2010, b) organization of 4 international educational symposia: Nantes 2008, Barcelona 2009, Milan 2010, and currently in Warsaw 2011; the 2011 ALWP symposium "HSCT for Adult Acute Lymphoblastic Leukemia. Current Practice and Future Perspectives" is aimed to integrate transplant specialists with investigators designing and leading European ALL treatment protocols, c) conducting prospective study on the role of RIC transplant for elderly AML, for which 68 patients have been registered so far.
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.

Activity of the subcommittees:

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

Completed study:

- The impact of center experience on results of reduced intensity allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia (S. Giebel, V. Rocha). Final version of the manuscript have been submitted to Leukemia.

On-going study:

- Association of Health Care Expenditure (HCE) with results of alloHSCT (S. Giebel). Results of the first statistical analysis has been presented showing that alloHSCT performed in countries with the highest HCE is associated with increased LFS and reduced risk of relapse. Final analysis is planned including more European countries and adjustment for HDI.
- Results of allogeneic HSCT for patients with acute myeloid leukemia (AML): comparison of EM-BMT and EBMT participating centers (A. Bazarbachi). Initial comparison revealed major differences between patients treated in EM-BMT and BMT. An EM-BMT survey should first be done followed probably by case-match comparison.

New proposal:

- Can JACIE accreditation overcome the impact of socio-economic status and center experience on results of alloHSCT (S. Giebel, T. Czerw). Study integrating various socio-economic and center-dependent variables has been proposed. Details to be elaborated.

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

Completed study:

- The impact of Flt3ITD and NPM1 mutation in adult patients with acute myelocytic leukemia autografted in first remission (C. Gorin). Results have been presented indictaing encouraging results for all subgroups of normal karyotype patients excluding FLT3-ITDpos/NPM-neg AML. In particular the message is that patients with FLT3ITD mutation (poor prognosis) can still go to autologous stem cell transplantation if they also have a NPM1 mutation. The data will be presented as a poster at ASH. The paper has been submitted to JCO and refused by the editorial office (no review). It has been then submitted to Blood (submitted)

On-going study:

- Pretransplant regimen with IV busulfan prior to autologous stem cell transplantation in AML (A. Nagler). 209 patients treated with i.v. Busulfan have been identified with encouraging results after autoHSCT. Retrospective comparison of iv Bu vs. TBI has been suggested (S. Giebel).

New proposal:

- A retrospective comparison of haplo mismatch transplant versus ASCT in AML CR1 (C. Gorin). Feasibility has been discussed with suggestion for case matched control. In addition, follow-up comparison of RIC-alloHSCT vs. autoHSCT was proposed.
- The role of maintenance after autoHSCT for adult ALL in CR1 (S. Giebel). A survey of autoHSCT between 2000-2010 has been proposed focusing on the use of post-transplant maintenance together with type of conditioning, source of stem cells, and MRD status. A piviotal prospective study by the PALG will be performed. Prospective non-interventional EBMT study for autoHSCT followed by Mtx/MP maintenance will be discussed.
- Non-interventional study of maintenance therapy following ASCT for AML. In low/intermiediate risk AML there is rationale for autoHSCT followed by maintenance using demethylating agents. Details will be discussed including the choice of agent.

Hot Topic

"EBMT implicated in the exclusion of autologous stem cell transplantion for ALL in Germany". ALWP will prepare statement regarding the current role of autoHSCT in ALL for German authorities explaining that this is a 'developmental' procedure, which means that it may be of value for selected patients and should not be denied.

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). 68 patients have been registered so far among whom 32 were randomized to RIC-alloHSCT or observation arm.

Completed studies

- Impact of AML cytogenetics on the outcome of RIC allo-HSCT (P. Chevallier, submitted)
- Comorbidity index (CI) in RIC transplant for AML (M Mohty; manuscript in preparation)
- PB vs BM in RIC AlloSCT from MUD (A. Nagler, submitted)
- Chronic GvHD and GVL after reduced-intensity allogeneic transplantation for acute myeloid leukemia (F. Baron; submitted, Oral presentation at ASH2011).
- Clofarabine-based conditioning prior to allo-SCT (P. Chevallier, submitted, Poster presentation at ASH2011).
- PB vs. BM in RIC allotransplant from HLA-identical sibling for AML (A. Nagler, manuscript in preparation)
- Risk factors for VOD in patients with AML receiving IV Busulfan (A. Nagler, manuscript in preparation)
- Comparison of CY+TBI versus IV BU+CY in alloHSCT from HLA-identical related & unrelated donor for AML in remission (A. Nagler, manuscript in preparation)
- RIC vs. MAC in AML/MDS (R. Martino, manuscript in preparation)

Ongoing studies

- TBI Cy vs. IV Bu Cy for RIC MUD AlloSCT in resistant AML (A. Nagler, Oral presentation at ASH2011). According to initial analysis the outcome after ivBuCY appears better compared with TBI/Cy, however more data on the characteristics of relapse should be collected.
- RIC MUD for ALL (P. Medd).
- Correlation of number of consolidation courses and outcome after RIC allo-SCT for AML (M. Yeshurun). 64 centers declared their participation so far. Deadline for participation is 15th of Dec 2011.
- Comparison of FB2 versus FB4 in alloHSCT for AML (M. Kharfan-Dabaja)
- Second RIC for relapse after first RIC (M. Mohty)

New proposals

- PB vs. BM grafts for resistant AML from MUD and Sib (A. Nagler)
- Impact of conditioning intensity on outcome of AML patients with AlloSCT in CR1 age 40-60 (J. Passweg). According to initial analysis results of RIC and MAC URD-HSCT appear comparable.
- Impact of ATG on outcome after alloHSCT for AML (F. Baron). All ATG formulations, dosage and timing should be analyzed. Similar analysis may be of value in ALL (S. Giebel)
- Treosulfan based-conditioning for AlloSCT-re-visit (A. Nagler). Treosulfan-based conditioning is increasingly used in Europe. Comparison with other MAC is warranted.
- Secondary malignancies after RIC alloSCT in AML (A. Nagler, M. Mohty in collaboration with the LEWP of the EBMT)
- Is there an optimal reduced-intensity protocol for HSCT? (O. Rindgen). Definition of RIC should be re-evaluated. For the initial analysis data already abvailable in the database could be used.

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

Prospective studies

- Updated results of the GMALL randomized study of imatinib post allo-SCT for Ph+ALL (O. Ottmann). Results have been presented indicating high LFS rates in the TKI era. However, the use of IM post-transplant is associated with high rate of discontinuations.

Completed studies

- Impact of FLT3-ITD on the outcome of related and unrelated alloHSCT (S Brunet; accepted JCO)
- AlloHSCT for AML with t(6;9)/DEK-CAN rearrangement (J Esteve; manuscript in preparation)
- Outcome of alloHSCT for AML with 11q23 rearrangement (A Pigneux, oral communication ASH2011; manuscript in preparation). The outcome strongly depend on the MLL-partner gene, suggesting different GVL effects.

Ongoing studies

- Impact of monosomal karyotype on alloHSCT for AML (M Brands-Nijenhuis; oral communication ASH2011). Outcome of AML with MK is associated with poor outcome in contrast to other poor-risk cytogenetic features.
- 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). Data from 91 patients have been collected. 2nd reminder is planned for Nov 2011.
- Outcome of alloHSCT for Ph(+)-ALL in CR1 in the era of TKIs (E Brissot, Poster ASH2011). AlloHSCT performed in the imatinib era (2007 or later) is associated with significantly improved outcome. More clinical data are needed to discriminate patients actually receiving IM pre- and post-transplant.
- Outcome of alloHSCT for AML with MLL Partial Tandem Duplication (MLL-PTD) (U. Bacher)
- Outcome of cytogenetics for B-ALL (A Gerbitz, C Schmid). In a preliminary analysis OS differ according to karyotype. More detailed analysis is planned for t(4;11).
- Outcome of alloHSCT for AML with 3q26/EVI1 rearrangement (J Esteve)

New proposals

- Outcome of alloHSCT for AML with abn(17p) (JM Middeke)
- Outcome of alloHSCT for T-ALL (X. Cahu). Detailed data from transplant centers will be needed inclding immune phenotype and MRD status.

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

Ongoing studies

- Analysis of G-CSF induced acute and chronic GVHD and the role of total body irradiation (O Ringden). Additional analyses are asked by the reviewers prior to publication.
- Impact of NIMA in MUD alloHSCT for AML (A. Schmidt, J. Pingel). 518 donors and mothers have been contacted so far allowing identification of 14 NIMA matches. To increase the study population next steps are required: identification of appropriate recipient and donor pairs from the EBMT and DKMS databases, contact with donors and asking mothers for participation.

New proposals

- Graft-versus-leukemia effect using haploidentical transplants, compared to HLA-identical sibling transplants in acute leukemia (O Ringden). The study is feasible.
- Unrelated donor transplantation for AML-HR in CR1: is time from diagnosis to transplant (as indicator of National Registry performance) relevant for outcome? (F Ciceri). The study requires cooperation with natiolnal registries which may be difficult.
- Survey on unmanipulated graft haploidentical transplantation (F Ciceri). The study is feasible and important. On this occasion the center effect should be analysed.

Prospective study proposal

- Patterns of chronic GvHD in unrelated, cord blood and haploidentical transplantation according to NIH criteria: a prospective study (M. Lupo Stanghellini). NIH criteria are used by very few centers. Their introduction would require substantial changes in PROMISE. Altogether at the moment the study is difficult to run.

Immunotherapy (Leader: Dr. C. Schmid)

Completed studies

- Outcomes and Prognostic Factors of Adults with Acute Lymphoblastic Leukemia who Relapse after Allogeneic Hematopoietic Cell Transplantation (A. Spyridonidis, Accepted Leukemia)
- Treatment, Risk Factors and Outcome of Adults with relapsed AML after Reduced Intensity Conditioning for Allogeneic SCT (C. Schmid, accepted Blood)

Ongoing studies

- Pre-emptive or prophylactic use of DLI (A. Rank, C. Schmid). 811 patients have been identified. Missing data should be completed. Centers will be invited for the observational non-interventional study.
- Use of azacitidine after alloHCT for AML (C. Craddock, V. Rocha). Retrospective analysis has been proposed and accepted.
- Impact of unrelated donor-host HLA disparity in the outcome after RIC transplant for AML (C Craddock, V Rocha).
- Second transplant for the treatment of relapse in acute leukaemia: 10 years update of the original study and second transplant in the MUD setting (G Andreola, D. Laszlo).
- Treatment of relapse (DLI, second transplant) after transplantation from a haploidentical donor (F. Ciceri, M. Lupo Stanghellini).

List of participants:

Arnold Renate, Baron Frédéric, Basak Grzegorz, Bassan Renato, Becht Rafael, Bodzenta Ewa, Bouveur Betty, Brissot Eolia, Brunet Salut, Budziszewska Bozena Katarzyna, Bug Gesine, Butrym Aleksandra, Cahu Xavier, Całbecha Malgorzata, Ciceri Fabio, Cioch Maria, Czerw Tomasz, Dawidowska Dorota, Deptala Andrzej, Dombret Hervé, Dwilewicz-trajaczek Jadwiga,

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