

Minutes of Acute Leukemia Working Party (ALWP) Business Meeting

Geneve

Sydney, April 1st, 2012

08:00 – 10:00

Introduction (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 amounting for almost 50% of allogeneic transplants. The registry includes data of over 62 000 procedures in adults. Among EBMT members, ALWP is indicated as the most popular working party. 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, b) oral and poster presentations during most important international congresses, c) organization of 4 international educational symposia: Nantes 2008, Barcelona 2009, Milan 2010, and Warsaw 2011; the 2010 and 2011 ALWP symposia integrated transplant specialists with investigators designing and leading European AML and ALL treatment protocols, d) conducting prospective study on the role of RIC transplant for elderly AML, for which 80 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.

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Activity of the subcommittees:

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 dosage. 913 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 is planned.

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

Proposals:

- “Granulocyte colony-stimulating factor after autologous hematopoietic stem cell transplantation for acute myelocytic leukemia – association with outcome” (T. Czerw). Initial analysis indicates that post-transplant use of G-CSF may impair DFS. The analysis will be done based on available data.
- Maintenance therapy following AutoHSCT for AML (N.C. Gorin). The proposal is to use azacitidine maintenance after autoHSCT performed in MRD-negative AML patients in order to reduce the risk of relapse. The idea has been approved. Details of the protocol remain to be discussed.
- AutoHSCT for ALL. The role of post-transplant maintenance (S. Giebel). A survey analysis of results of autoHSCT in ALL has been performed including 535 patients. In Ph-positive ALL marked improvement over time has been found suggesting that introduction of TKIs in recent years decreased relapse rate. Final analysis will be focused on this subgroup.

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). 80 patients have been registered so far among whom 39 were randomized to RIC-alloHSCT or observation arm.

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 consolidation 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 (M. Kharfan-Dabaja). Preliminary results based on the analysis of 379 patients suggest comparable results for FB2 and FB4 in AML CR1 patients, advantage of FB4 in CR>1 setting and no difference in advanced disease.

Proposal:

- 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.

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

Ongoing studies

- 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.

- 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 123 patients have been received. Further 41 patient files are pending.
- 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 T-ALL (X. Cahu). 932 patients have been identified in the registry. Questionnaire has been prepared to be distributed in April/May 2012.

Proposals

- Outcome of alloHSCT for AML with abn(17p) (JM Middeke/J Schetelig). 59 patients with AML in CR1 were identified to have abn(17p). So far no impact on LFS could be demonstrated
- Outcome of alloHSCT for AML associated to 7p abnormalities (M Brands-Nijenhuis). The goal is to compare results for monosomy 7, del(7p), and other chromosome 7 abnormalities. The analysis has been done. Needs to be updated.

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

Ongoing studies discussed during the meeting

- 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.

Proposals

- Survey on unmanipulated graft haploidentical transplantation (F Ciceri). The study is feasible and important. 430 patients have been identified (300 AML and 130 ALL)
- Auto vs. Haplo in AML (A Nagler, F. Ciceri). The comparison could be done independently for CR1 and CR2 patients.

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

Completed study:

- Impact of economical factors on results of alloHSCT (S. Giebel) (S. Giebel, V. Rocha). Final version of the manuscript have been submitted to Leukemia.

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 factors 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.
- Results of allogeneic HSCT for patients with acute myeloid leukemia (AML): comparison of EMBT and EBMT participating centers (A. Bazarbachi). In a

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.

Other proposals:

- Proposal for a survey on the use of Thiotepea as part of the conditioning regimen in ALL and AML (M. Mohty). Thiotepea is used in various conditioning regimens for various indications. The goal of the study is to identify patient population that benefits from this drug.
- Proposal “The therapy and outcome of allogeneic transplantation in adults with ALL who have CNS involvement at diagnosis or relapse” (D. Marks). Various strategies are used for the treatment of CNS involvement in ALL. To compare the approaches detailed questionnaire is needed and the data collection may be difficult.

List of participants:

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