Minutes of Acute Leukemia Working Party (ALWP) Business Meeting

EBMT Meeting, Paris
Sunday April 3rd, 2011
8:00 – 10:00

Welcome, achievements & future plans (M. Mohty):

Prof. Mohamad Mohty presented major objectives/missions of the ALWP, which 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. He also summarized main achievements of the ALWP in 2010: a) high quality publications with the mean IF=10.881, b) organization of ALWP symposium "Therapeutic options in early AML at high risk: ALWP meets EU trail groups", which took part in Milan on 13.11.2010, c) conducting prospective study on the role of RIC transplant for elderly AML, which now includes investigators from HOVON, OSHO, SAKK, ALPHA, GOELAMS.
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) or secretary (S. Giebel) of the ALWP. 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.

Main publications of the group in 2010 are:

- Results and factors influencing outcome after fully haploidentical hematopoietic stem cell transplantation in children with very high-risk acute lymphoblastic leukemia: impact of center size: an analysis on behalf of the Acute Leukemia and Pediatric Disease Working Parties of the European Blood and Marrow Transplant group. Klingebiel T, Cornish J, Labopin M, Locatelli F, Darbyshire P, Handgretinger R, Balduzzi A, Owoc-Lempach J, Fagioli F, Or R, Peters C, Aversa F, Polge E, Dini G, Rocha V; Pediatric Diseases and Acute Leukemia Working Parties of the European Group for Blood and Marrow Transplantation (EBMT). Blood. 2010; 115(17):3437-46. IF=10.555
- Effect of graft source on unrelated donor haemopoietic stem-cell transplantation in adults with acute leukaemia: a retrospective analysis. Eapen M, Rocha V, Sanz G, Scaradavou A, Zhang MJ, Arcese W, Sirvent A, Champlin RE, Chao N, Gee AP, Isola L, Laughlin MJ, Marks DI, Nabhan S, Ruggeri A, Soiffer R, Horowitz MM, Gluckman E, Wagner JE; Center for International Blood and Marrow Transplant Research; Acute Leukemia Working Party Eurocord (the European Group for Blood Marrow Transplantation); National Cord Blood Program of the New York Blood Center. Lancet Oncol. 2010; 11(7):653-60. IF=14.47
- Association of Human Development Index with rates and outcomes of hematopoietic stem cell transplantation for patients with acute leukemia. Giebel S, Labopin M, Ehninger G, Beelen D, Blaise D, Ganser A, Bacigalupo A, Czerw T, Holowiecki J, Fagundes EM, Nowara E, Frassoni F, Rocha V; Acute Leukemia Working Party of the European Group for Blood and Marrow Transplantation. Blood. 2010; 116(1):122-8. IF=10.555
- Higher incidence of relapse for acute myelocytic leukemia patients infused with higher doses of CD34+ cells from leukapheresis products autografted during the first remission. Gorin NC, Labopin M, Reiffers J, Milpied N, Blaise D, Witz F, de Witte T, Meloni G, Attal M, Bernal T, Rocha V. Blood. 2010; 116(17):3157-62. IF=10.555

- Reduced-intensity versus conventional myeloablative conditioning allogeneic stem cell transplantation for patients with acute lymphoblastic leukemia: a retrospective study from the European Group for Blood and Marrow Transplantation. Mohty M, Labopin M, Volin L, Gratwohl A, Socié G, Esteve J, Tabrizi R, Nagler A, Rocha V. Blood. 2010; 116(22):4439-4443. IF=10.555
- Factors Predicting Outcome after Unrelated Donor Stem Cell Transplantation in Primary Refractory Acute Myeloid Leukaemia. C Craddock, M Labopin, S Pillai, J Finke, D Bunjes, H Greinix, G Ehninger, NK Steckel, AR Zander, R Schwerdtfeger, S Buchholz, HJ Kolb, L Volin, A Fauser, E Polge, C Schmid, M Mohty, and V Rocha. Leukemia 2010 IF=8.6

Activity of the subcommittees:

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

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. More ditailed analysis is planned

New proposal:

- Results of allogeneic HSCT for patients with acute myeloid leukemia (AML): comparison of EM-BMT and EBMT participating centers (A. Bazarbachi). Study is feasible, will be preformed in 2011r.

Immunotherapy (Leader: Dr. C. Schmid)

Completed studies:

- Management of relapse after RIC alloHSCT for AML (C. Schmid). Results has been presented including overall outcome; prognostic score for survival has been elaborated including time to relapse, limited bone marrow infiltration and no GVBHD after HSCT being associated with better outcome; potential therapeutic interventions ahve been discussed.
- Outcome of relapsed ALL after allogeneic transplant (A. Spyridonidis). Overall outcome is poor. Prognostic fators asscoiated with poor outcome are: blasts in PB >10%, CR2 at HSCT and short interval form HSCT to relapse.
- Matched pair analysis comparing T-cell depleted haploidentical transplantation with or without transfer of donor NK cells (B. Friedrichs). Adoptive transfer of NK cells has positive impact on OS.

Ongoing studies

- Treatment of relapse (DLI, second transplant) after transplantation from a haploidentical donor (M. Stadler, F. Ciceri, C. Schmid). “True haplo-HSCT” have been defined and identified in the registry. The study will be intensified within next few months.
- Pre-emptive or prophylactic use of DLI (A. Rank, C. Schmid). Reasons for pre-emptive and prophylactic DLI hgave been identified. The stduy will be started soon as a retrospective one and as prospective observational audit.
- Second transplant for the treatment of relapse in acute leukaemia (G. Andreola, D. Laszlo). Study will be continued.
- Use of azacitidine after alloHCT for AML (C. Craddock, V. Rocha). Feasibility has been discussed. There is need for financial supprot.
- Impact of unrelated donor-host HLA disparity in the outcome after RIC transplant for AML (C. Craddock, V. Rocha). More data on HLA genotyping is required.

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). Preliminary results have been presented indicating that administration of growth factors given to patients with acute leukemia is associated with decreased LFS, increased NRM after sibling-HSCT. The effect was observed in the overall popultaion, as well as separately for those receiving TBI or chemotherapy only.

New proposals

- Graft-versus-leukemia effect using haploidentical transplants, compared to HLA-identical sibling transplants in acute leukemia (O. Ringden). Synopsis has been presented. The dtsuy is feasible and will be performed.
- Alternative donor options for AML-HR in CR1: a prospective joint study ALWP-trialists (F. Ciceri). Requires cooperation of national study groups. The collaboration already initiated during the ALWP symposium in Milano 2010.
- Impact of donor age after unrelated donor allogeneic hematopoietic stem cell transplantation (HSCT) for AML (F. Baron).

New proposals of joint studies Immunobiology-ALWP

- Identification of immunological biomarkers predictive of clinical outcome after haploidentical stem cell transplantation (C. Bonini, A. Bondanza, A. Velardi IBWP)
- Analysis of the NIMA effect on the outcome of unrelated adult PBSC/BM transplantation (A. Schmidt, J.J. Van Rood)

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

Prospective studies

- Randomized comparison of RIC vs. chemotherapy as post-remission therapy in elderly patients with AML (D. Niederwieser). The first study to prospectively evaluate the role of RIC-HSCT has been approved by regulatory boards of HOVON, OSHO, SAKK, ALPHA, GOELAMS that is in the process of registration in other countries. The recruitment started.

Completed studies

- Impact of AML cytogenetics on the outcome of RIC allo-HSCT (P. Chevallier, M. Mohty). The manuscript is in preparation.
- Comorbidity index (CI) in RIC transplant for AML (M. Mohty). Results of the final analysis of this study, performed in 345 patients who received a RIC alloHSCT for an AML in 1st CR, confirmed the clinical value of this index for predicting NRM in this particular setting. The manuscript is in preparation.
- PB vs. BM in RIC allotransplant from MUD and HLA-identical sibling for AML (A. Nagler). The manuscript is in circulation.
- IV Busulfan in autologous HSCT (A. Nagler). About 50 autoHSCT with iv. Busulfan-based conditioning have been identified and analysed. The manuscript is in circulation.
- Risk factors for VOD in patients with AML receiving IV Busulfan (R. Berger, A. Nagler). The manuscript is in circulation.
- Comparison of CY+TBI versus IV BU+CY in alloHSCT from HLA-identical related & unrelated donor for AML in remission (A. Nagler). The manuscript is in circulation.

Ongoing studies

- RIC vs. MAC in AML/MDS (R. Martino). This is a collaborative proposed between ALWP and CLWP is in the phase of gathering complete data on conditioning regimens.

- Chronic GvHD and GVL after reduced-intensity allogeneic transplantation for acute myeloid leukemia (F Baron). Final analysis is ongoing.
- Clofarabine-based conditioning prior to allo-SCT (P. Chevallier). The oral presentation of the EBMT survey during the EBMT Meeting 2011 has been announced.
- TBI Cy vs. IV Bu Cy in resistant AML (A. Nagler). Based on the analysis of 783 patients, results after CY+TBI and iv. BU+CY are comparable. The manuscript is in circulation.
- RIC MUD for ALL (P. Medd). The poster presentation during the EBMT Meeting 2011 has been announced.

Ongoing studies

- Correlation of number od consolidation courses and outcome after RIC allo-SCT for AML (M. Yeshurun, A. Nagler). Rationale: Due to high risk of ralapse after RIC allo-SCT the intensity of preceding chemotherapy may be critical.
- PB vs. BM grafts for resistant AML from MUD and Sib (A. Nagler). Rationale: PB transplants are associated with increased risk of cGVHD, which may confer GVL effect resulting in redeuced risk of relapse.

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

Completed studies

- Allo-HSCT for normal cytogenetics AML according to FLT3-ITD status (S. Brunet). The manuscript is in circulation.
- Allo-HSCT for AML with t(6;9)/DEK-CAN rearrangement (J. Esteve). The manuscript is being prepared.

Ongoing studies

- Outcome of transplantation for AML with 11q23 (MLL) rearrangement (A. Pigneaux). Analysis of 172 patients has been presented. OS at 2 years was 56%. LFS varied according to rearrangement subtype with best results for t(9;11) and t(11;19). Oral presentation during the EBMT Meeting 2011 has been announced.
- Impact of monosomal karyotype on alloHSCT for AML (M. Brands-Nijenhuis). Preliminary results has been presented showing worse outcome of patients with monosomal karyotype compared to complex karyotype. Potential improvement with alloHSCT has been suggested.
- Impact of NPM & FLT3-ITD mutational status on the outcome of alloHSCT for normal cytogenetics AML (C. Schmid). 183 patients treated with FLAMSA-RIC has been presented. NPM1mit/FTL3wt is associated with the best OS.
- Outcome of HSCT for APL in the ATO era (J. Sanz). 379 patients have been analyzed treated with auto(49%) and allo(51%)-HSCT. In a univariate analysis a tendency to better LFS has been observed in favor of autoHSCT.
- Outcome of cytogenetics for B-ALL (A. Gerbitz, C. Schmid). Results of preliminary analysis has been presented. Outcome appears to vary according to karyotype abnormalities. Efforts should be made to increase the study population. Multivariate analyses are planned.
- Outcome of alloHSCT for AML with MLL Partial Tandem Duplication (MLL-PTD) (U. Bacher).
- Outcome of alloHSCT for AML with 3q26/EVI1 rearrangement (J. Esteve). Outcome of 112 patients has been presented. New cases are planned to be included. Additional information on cytogenetic abnormalities is needed.

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

EBMT 2011 Special Workshop: “Update on ASCT in AML: is there a future?” has been announcedwith the follfowing list of lectures:

- ASCT for AML in Spain and proposals for clinical trails (J. Sierra)
- ASCT for AML in Italy and proposals for clinical trials (F. Ferrara)
- ASCT for AML in Eastern Europe and proposals for clinical trials (B. Labar)
- ASCT for AML in Poland (J. Holowiecki)
- ASCT for AML in the US and proposals for clinical trials (C. Linker)
- Selective monitoring and targeting of MRD (A. Olivieri)
- The “marvellous 2” marrow miner (G. Ehninger)

List of participants:

ALJURF Mahmoud, ANDREOLA Giovanna, BAROIS Alain, BARON Frédéric, BAZARBACHI Ali, BOUVEUR Betty, BRANDS-NIJENHUIS Monique, BRINCH Lorentz, BRUNET Salut, BUG Gesine, CICERI Fabio, CIOCH Maria, CORNELISSEN Jan J,, CRADDOCK Charles, ESPIGADO Ildefonso, ESTEVE Jordi, GIEBEL Sebastian, GORIN Norbert Claude, HOLOWIECKI Jerzy, HEMMERTI Philipp, KLYUCHNITOV E, LABOPIN Myriam, LAROULANDIE Martine, LENHOFF Stig, MEDD Patrick, MOHTY Mohamad, MOHTY Bilal, NAGLER Arnon, PAGLIUCA Antonio, PASSWEG Jakob, PENIKET Andy, PEREZ Isabel, PIGNEUX Arnaud, POLGE Emmanuelle, RINGDEN Olle, SAMEY Bénédicte, SANZ Miguel A., SANZ CABALLER Jaime, SCHMID Christoph, SPYRIDONIDIS Alexandro, SVAHN Britt Marie, ZUCKERMAN Tsila

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