Poster Session I

ALLOGENEIC

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ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION WITH NON-MYELOABLATIVE CONDITIONING IN PATIENTS WITH ACUTE MYELOGENOUS LEUKEMIA ELIGIBLE FOR CONVENTIONAL ALLOGRAFTING: RESULTS OF A PROSPECTIVE, MULTICENTER STUDY

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Using a lymphoablative, non-myeloablative stem cell trasplantation (NST) program, 25 allografts were prospectively given to 24 patients with acute myelogenous leukemia (AML) eligible for conventional allografting; two individuals had secondary forms of AML. The median age of the patients was 35 years, with a range of 12 to 56. All patients engrafted; median time to achieve an absolute neutrophil count $>0.5 \times 10^9$/L was 12 days (range 0-26), whereas the median time to a platelet count $>20 \times 10^9$/L was 13 days (range 0-26). Patients developed chimerism 15 to 100 (median 30) days after the allograft. The follow-up periods range between 33 and 2664 days (median 450). The median post-transplant overall survival has not been reached and is above 89 months, whereas the 89-month both, overall and progression-free survival is 56%, the 683-day survival being 66%. In 14 grafts (56%) acute GVHD ensued; in 12 cases grades I-II and in 2 cases grade IV which was fatal in both. In 9/20 grafts (45%) limited chronic GVHD developed. In 22 cases (88%), the procedure could be completed fully on an outpatient basis. The 100-day and the transplant-related mortality were both 8%. The median cost of the allografts until day 100 was 20 000 USD. NST appears to be an effective additional therapeutic option for patients with AML in remission and a matched donor available.

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A SINGLE CENTRE, RANDOMISED TRIAL ON HARVEST CELL YIELD AND MARROW ENGRAFTMENT USING HAEMOPOIETIC GROWTH-FACTOR PRIMED BONE MARROW

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The use of haemopoietic growth factors (HGFs) in the BMT setting is most often administered to recipients during the post-BMT period to enhance neutrophil recovery. However, there is little or no effect on platelet recovery when HGFs are administered in this fashion. The aim of this study is to compare HGFs primed and unprimed marrow in terms of: the haemopoietic stem and progenitor cell yields; the neutrophil and platelet engraftment in allogeneic BMT; and the incidence and severity of GVHD as well as other complications in allogeneic BMT. **Methods:** Thirteen patient-donor pairs were randomized to the G-CSF group, eleven pairs to the GM-CSF group and thirteen pairs to the control group. The donors randomized to group I received 10μg/kg per day G-CSF subcutaneously for four days before the bone marrow was harvested. The donors randomized to group II received 10μg/kg per day GM-CSF subcutaneous injection for four days before the bone marrow was harvested. The donors randomized to the control arm did not receive any growth factors before the bone marrow was harvested. **Results:** The median total nucleated cell count was slightly higher in primed BM graft. For the G-CSF primed BM , 5.77×10^8/kg, and for the GM-CSF primed BM 3.18×10^8/kg compared to 2.23×10^8/kg for the unprimed BM graft (Kruskal Wallis test, $P < 0.001$). The central tendency was significantly different (Kruskal Wallis Test, $P < 0.003$) between the three groups for the CFU-GM/kg measure. The median was 17.44×10^4/kg in the G-CSF group, 6.14×10^4/kg in the GM-CSF group and 10.12×10^4/kg in the control group. The mean time to obtain an ANC value above 1.0×10^9/L was statistically significant among the three groups (ANOVA, $P < 0.046$); the mean duration for group I, II and III was 23 days, 30 days and 29 days, respectively. We found that G-CSF primed BM had significantly faster engraftment of ANC $> 1.0 \times 10^9$/L, compared to GM-CSF primed BM and unprimed BM. Besides, the units of RBC used post BMT were significantly less than the other two groups. G-CSF priming increased total nucleated cells and proliferation of CFU-GM in the marrow graft.

In summary, we found that BM priming with both G-CSF and GM-CSF increases the number of total nucleated cells in marrow. BM priming with G-CSF also increased the number of CFU-GM and promoted early engraftment post BMT. Post BMT complications and death rate were relatively lower.

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OPTIMIZING RESULTS OF NON-MYELOABLATIVE ALLOGENEIC TRANSPLANTATION (NMAT): IDENTIFICATION OF PATIENTS AT HIGH RISK OF TREATMENT FAILURE BASED UPON PRE-TRANSPLANT VARIABLES

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47 consecutive patients (27-68 y; median 51) with hematologic malignancies were studied to develop a scoring system to identify those at high (HR) and low (LR) risk of transplant-related mortality (TRM) and relapse (REL) based on pretransplant factors. The conditioning regimen was 100 mg/m^2 melphalan on day-1 (+50 mg/kg cyclophosphamide on day-2 if no prior autograft), cyclosporine (HLA-matched sibling; n = 32) or tacrolimus (1-locus mismatched sibling; n = 3, or unrelated; n = 12), and mycophenolate mofetil. The 2-y cumulative incidences of TRM and REL were 20% and 50%, with 2-y actuarial disease-free (DFS) and overall (OS) survival probabilties of 30% and 40% respectively. TRM was higher with creatinine >1.5 mg/dL (2 points), HLA mismatch (2 points), poor performance status (0-3 points), and age 60 (1 point). The 11 patients with a total score of >2 points (HR-TRM) had significantly higher TRM than the 36 with a score of 0-2 (LR-TRM) (64% vs 7%; P = 0.0005). REL was higher with non-chemosensitive disease (2 points), platelets $<100 \times 10^9$/L (1 point), and prior autograft (1 point). The 15 patients with a total score of >2 points (HR-REL) had significantly higher REL than the 21 with a score of 0-2 (LR-REL) (83% vs 21%; P = 0.003) after eliminating HR-TRM patients from the analysis. Overall, the outcome of the 21 LR patients was significantly better than the 26 HR patients (11 HR-TRM, 15 HR-REL) in terms of OS (92% vs 19% at 1.5 y; $P < 0.0001$) and DFS (70% vs 6% at 1.5 y; $P < 0.0001$). The model will be tested in the next 50 patients treated similarly. If it is validated, the regimen intensity will be lowered for HR-TRM patients to reduce TRM. From the remaining patients, HR-REL patients will be identified and their regimen intensified to decrease REL. For both the groups with modified conditioning, GVHD prophylaxis will be changed (e.g. omission of mycophenolate) to augment graft-vs-tumor. Patients who are LR for both TRM and REL will continue to receive the current therapy in view of their excellent outcome. We conclude that the outcome of LR patients undergoing NMAT is excellent. In such patients, this mode of transplantation should be considered standard therapy rather than investigational. Confirmation of our observations may justify using NMAT as a safer alternative procedure for patients who fulfill the LR criteria specified here but who would normally undergo conventional allogeneic transplantation. Modified treatment may improve the outcome of HR patients.