Haploidentical Stem Cell Transplantation (HAPLO-HSCT) with Post-Transplant Cyclophosphamide (PT-CY) As Gvhd Prophylaxis in High Risk Hematologic Malignancies: Bone Marrow or Peripheral Blood Progenitors Render Same Results

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Introduction: Allogeneic transplantation is the only curative option for patients with high risk hematologic malignancies. Only one third of them have an HLA identical sibling donor and around 60-70% will find an unrelated donor, that’s why HAPLO-HSCT offers a therapeutic option to most of these patients. Donor availability is becoming much easier and is the main advantage of using peripheral blood stem cells (PBSC) instead of bone marrow (BM). The use of PT-CY in the prophylaxis of acute GvHD increases the overall survival and relapse-free survival.

Patients and Methods: We retrospectively evaluated the results of HAPLO-HSCT with reduced conditioning regimens and GvHD prophylaxis based on PT-CY (50 mg/kg on days -3 and -4) and a calciumin inhibitor plus mycophenolate from day +5 performed in GETH centers, with focus on the graft source.

Results: From Dec-2007, 118 HAPLO-HSCT have been done in 17 centers. Median age was 36 years (16-67); 64% were males and all were in advanced phases of their disease or presented high risk features (Hodgkin’s 43%, AML/ALL/MDS 36%, NHL/myeloma/others 21%). Previous HSCT had been performed in 64% (autologous 66, allogeneic 19), and in 36% the HAPLO-HSCT was their first transplant. Disease status at HAPLO-HSCT was CR in 44%, with persistent disease in 55%. BM was the graft source in 48 patients (41%) and PBSC in 70 (59%), non T-cell depleted in all cases. The haploidentical donor was the patient’s mother (28%), father (10%), siblings (44%) or offspring (18%). Baltimore’s reduced conditioning (RIC) including 200cGy was employed in 15% and RIC based on IV busulfan in 85% (44% with 3.2 mg/kg on day -2 (BUX1), and days -3 and -2 (BUX2) in 41%). Median neutrophils engraftment was reached at day +18 (13-45) and platelets >20K at day +26 (11-150), without significant differences (NS) between BM and PBSC.

Main toxic complications were grade II-III mucositis in 36%, febrile neutropenia in 75% and CMV reactivations in 62%. Transplant related mortality rate (TRM) at 1 year was 19% with BM vs 23% with PBSC (NS). Day +100 grade II-IV acute GvHD cumulative incidence (CI) was 46% vs 48%, and grade III-IV was 15% and 10% with BM and PBSC respectively. Chronic GvHD CI at 1 year was 40% vs 24% (NS), being extensive in 16% and 9% (NS) respectively. No differences in acute or chronic GvHD CI were seen when comparing BM against PBSC. After a median follow-up of 10 months (3-61), estimated event-free survival (EFS) and overall survival (OS) at 18 months were 41% and 59% respectively. CI of relapse or progression was 29%. No significant differences in TRM, EFS, OS and relapse incidence were detected between BM and PBSC.

Conclusions: HAPLO-HSCT with PT-CY in the treatment of high risk hematologic malignancies, offers long-lasting remissions with manageable toxicity and GvHD, employing either BM or PBSC that render similar results as graft source.
was done in all patients and 5 patients had 1-3 courses of DLI. On follow up of the 43 patients with MC, 24 achieved complete chimerism, 10 had stable mixed chimerism and 9 had rejection (mostly level 3 MC). Two patients developed mild graft versus host disease after DLI.

**Conclusion:** Occurrence of mixed chimerism is common after allogeneic HSCT for thalassemia after Fludarabine/Treosulfan/Tiostepa conditioning. Rapid tapering of immnosuppression and judicious use of DLI helps in reducing the risk of secondary graft rejection. Closer monitoring of chimerism after HSCT needs to be done when such conditioning regimens are used.

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**Enlarged Spleen Prior to Allogeneic Transplantation for Myelofibrosis Is Associated with Poor Engraftment and Increased Non-Relapse Mortality**

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**Introduction:** Allogeneic stem cell transplantation (SCT) is potentially curative for patients with Myelofibrosis (MF). However, treatment failure is common and often associated with slow engraftment or graft failure, risk factors for which are poorly defined.

**Patients:** From 2000 to 2014, 30 adult patients (median age, 49 (range 18-68) underwent SCT for primary or secondary MF at WCMC/NYP. All patients received PBSC from matched related (MRD-14) or matched unrelated donors (MUD-16). Most patients received fludarabine and melphalan (n=22) conditioning. ATG or alemtuzumab were used for patients who underwent MUD SCT. Only a minority of patients had low risk disease by DIPPS (26.7%) or Lille (20%) risk scores. Twenty patients had splenomegaly, 6 by physical exam and 14 by imaging studies (median 24.5 Cm, range 16.2-34).

**Results:** After a median follow-up of 49.5 months (range 3 to 154 months), the 4-year OS and RFS are 44% (95%CI: 29%-67) and 37% (95%CI: 23%-61) respectively. Neutrophil engraftment by day 18 occurred in 63% of patients. Platelets were engrafted by day 25 in 41% of patients. We used a Fine and Gray's proportional subdistribution hazard model. Splenomegaly was associated with delayed neutrophil engraftment (SHR=0.42, 95% CI=0.21, 0.83, p=0.01), delayed platelet engraftment (SHR=0.18, 95%CI=0.07, 0.48, p=0.001) and non-relapse mortality (NRM) (SHR=3.24, 95%CI=0.94, 11.2, p=0.06). Elevated LDH was associated with delayed platelet engraftment (SHR=0.39, 95% CI=0.16, 0.94, p=0.04) and NRM (SHR=2.82, 95%CI= 1.08, 7.35, p=0.03), MUD grafts were marginally associated with delayed neutrophil engraftment (SHR=0.55, 95% CI= 0.27, 1.12, p=0.10) but not platelet engraftment or NRM.

**Conclusion:** Splenomegaly contributed to delayed neutrophil and platelet engraftment and NRM. Splenectomy should be considered for patients with splenomegaly in need of transplantation. Elevated LDH was associated with delayed platelets engraftment and NRM and might indicate more aggressive disease.

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**Assessment of Additional Consolidation Chemotherapy Effects in Patients with Acute Myeloid Leukemia before Allogeneic Stem Cell Transplantation**

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**Objectives:** To assess the effects of additional consolidation therapy in acute myeloid leukemia (AML) patients before allogeneic hematopoietic stem cell transplantation (HSCT).

**Methods:** Seventy-two AML patients (range: 18-55 years) who transplanted in CR1 after being treated with a standard chemotherapy (7+3) regimen were randomly divided into two groups. Thirty-six patients in group A directly underwent transplantation and 36 in group B received chemotherapy regimen (5+2) prior to allogeneic HSCT. All patients received fully HLA-matched transplants.

**Results:** The median age at transplantation was 38.3 in group A and 37.2 in group B. The male to female ratio was 21:15 and 23:13 in groups A and B, respectively. The median time to neutrophil and platelet recovery was 8 and 27 days in group A, while it was 9 and 19 days in group B, respectively (P: 0.77, 0.01). Acute graft-versus-host disease (GvHD) was more frequent in group A (26 vs. 23) patients(P:0.44). Chronic