was 11%. Incidence of chronic GVHD was 20%, severe chronic GVHD was 4%. 5 children died due to transplant related mortality (TRM), all of them were class 3 Thalassemia; 2 patients transplanted from unrelated donor and unrelated cord and 2 died after second HSCT. Causes of deaths were severe infections secondary to engraftment failure; severe hemorrhagic cystitis and multiorgan failure; pulmonary and intracranial bleeding during engraftment and TTP. 1 child died 3.5 years after HSCT from severe multisystemic GVHD and complications of immunosuppressive therapy.

Conclusion: Our results showed that children with hemoglobinopathy who received HSCT had excellent results with survival above 80% despite of majority of patients with class 3 Thalassemia and number of children who underwent second HSCT. Factors affecting prognosis were: advanced class of Thalassemia type of donor and second HSCT with myeloablative regimen. Engraftment failure continues to be a problem for Thalassemia patients. There is a need for controlled trials to evaluate the effectiveness of different treatment regimens for specific group of patients.

325

Unrelated Donor Hematopoietic Stem Cell Transplantation for Treatment of Non-Malignant Genetic Diseases Using a Myeloablative Reduced Toxicity Conditioning Regimen

Hisham Abdel-Azim [1], *Quan Zhao* [1], *Kris Michael Mahadeo* [1], *Sajad Khazal* [1], *Donald B. Kohn* [2], *Gay M. Crooks* [2], *Ami J. Shah* [2], *Neena Kapoor* [1]. [1] *Division of Hematology, Oncology and Blood & Marrow Transplantation, Children's Hospital Los Angeles, Los Angeles, CA;* [2] *Division of Hematology/Oncology, Mattel Children's Hospital, University of California, Los Angeles, Los Angeles, CA*

Background: Hematopoietic stem cell transplant is a curative option for a variety of non-malignant, sub-lethal genetic diseases in children. However, the probability of finding a suitable histocompatible sibling donor is less than 30%, especially for patients with genetic diseases, whose siblings may also carry the affected gene. The use of matched unrelated donors (MUD) for patients with genetic diseases is limited by regimen related toxicity (RRT), high rates of graft failure/rejection and graft-versus-host-disease (GVHD).

Objective: To determine if the reduced toxicity conditioning regimen: Alemtuzmab with Busulfan, Fludarabine and reduced dose of cyclophosphamide, would maintain adequate immune-suppression and allow for acceptable rates of sustained donor engraftment, low rates of RRT and GVHD.

Methods: 15 eligible patients were consented at Children's Hospital Los Angeles between 2007 and 2013. The conditioning regimen consisted of Busulfan 16mg/kg, Alemtuzmab 52mg/m^2, Fludarabine 140mg/m^{2}and Cyclophosphamide 105mg/kg. GVHD prophylaxis consisted of Tacrolimus and Methylprednisolone.

Results: The study population was 73.3% male with median age 7 (0.8–17.6) years old at transplant. Patients diagnoses included HLH (n=2), CD-40 ligand deficiency (n=2), congenital dyserythropoietic anemia (n=2), adrenoleukodystrophy (n=1), Sickle Cell Disease (n=7), Thalassemia (n=1). The mean total nucleated cell count (TNC) and CD34 dose was 5.6x10^8 (± 2.2x10^8) cells/kg and 6.4x10^6 (± 3.4x10^6) cells/kg respectively. The mean Busulfan CSS and AUC were 888 (± 242) µg/L and 1297 (± 363) µmol/L-min, respectively. The median time to clearance of Alemtuzmab was 14 (4 to 21) days. Median time to neutrophil engraftment and platelet engraftment were 15 (12–28) and 25 (17–30) days respectively. One patient had primary graft loss. Two patients had secondary graft loss. For 11 patients who reached and sustained engraftment, 9 patient's donor chimerism were more than 97% and 2 patient's donor chimerism was 78.1% and 82% respectively, in the most recent follow up. There were no cases of Grade III/IV, mucositis or acute GVHD (aGVHD). Two patients developed mild sinusoidal obstruction syndrome (SOS). Nine patients had detectable viral reactivation. Only 1 patient developed extensive cGVHD. One patient expired due to progressive encephalopathy and multi-organ failure. The median length of follow-up was 2 (0.2-5.4) years. The overall survival (OS) and disease free survival (DFS) at 5 years were 93.3% and 73.3% respectively.

Conclusion: This Alemtuzmab-based reduced toxicity regimen appears promising with durable unrelated donor engraftment, effective cure of clinical disease, and low rates of RRT and GVHD. The major adverse effect was activation of viral infections.