amphotericin B therapy (p = 0.08) were not statistically significant. There was a slight trend towards a higher rate of chronic GVHD in patients with ES (p = 0.11). However, after a median follow up of 9.5 years overall survival (48% with ES vs. 50% without ES; p = 0.53) and transplant related mortality (21% vs. 17%; p = 0.65) did not differ between the two groups. Prednisolone (2 mg/kg/d) was administered in 62% of children with ES. **Conclusion:** ES presenting with fever, rash, weight gain and pulmonary symptoms should be recognized as a frequent complication of allogeneic HSCT after myeloablative conditioning in children. Treatment with G-CSF and a high nucleated cell count of the graft predisposed for the development of ES in this study. Overall survival and transplant related mortality in this cohort were not affected by the occurrence of ES, possibly due to therapeutic intervention with prednisolone in a high proportion of patients.

66

EXCELLENT ENGRAFTMENT AND RAPID IMMUNE RECOVERY IN HAPLOIDENTICAL STEM CELL TRANSPLANTATION USING CD3/CD19 DEPLETED PERIPHERAL STEM CELL GRAFTS AFTER REDUCED INTENSITY CONDITIONING

Bader, P.[1], Soerensen, J.[1], Koehl, U.[1], Kreyenberg, H.[1], Jarisch, A.[1], Weber, G.[1], Sach, G.[1], Willasch, A.[1], Kuci, S.[1], Tonn, T.[2], Esser, R.[1], Klingebiel, T.[1]. [1]JW Goethe University Children's Hospital, Frankfurt, Germany; [2]Institut für Transfusionsmedizin, Frankfurt, Germany.

Transplantation of haploidentical stem cells has become a well established treatment procedure in many children with malignant and non malignant diseases. Positive enrichment of stem cells by anti-CD34 magnetic micro beads provides a graft profoundly depleted of T and B cells facilitating engraftment without inducing severe GVHD. However, despite transplanting "mega doses" ($>10^7$/kgBW) of stem cells, primary graft rejection and delayed immune recovery associated with increased transplant related mortality remained major obstacles. Grafts after depletion of CD3/CD19 cells consist of remarkable amounts of effector cells which might help to improve engraftment and immune reconstitution.

We report the results of our pilot study including 29 children and adolescents (ALL, n = 10; AML, n = 3; RMA, n = 10; aplastic anaemia, n = 1, MDS, n = 2 and NBL/HB n = 2). All patients received CD3/CD19 depleted peripheral stem cell grafts containing a median number of 7.4^6/kgBW CD34+ cells. Grafts also contained NK-cells (median number: 14.3^6/kgBW), dendritic cells, precursor T-cells and mono-/granulocytes (median number: 423.4^6/kgBW). All patients but two received a reduced conditioning regimen with FLU-MEL-THIO and short course of OKT-3. All twenty-nine patients achieved rapid engraftment at day 14 and 156 days, respectively. Immune recovery was excellent with a median time to achieve more than 100 CD3+ and CD4+ cells/µl was 61.0 and 63.5 days, respectively. Five/29 patients developed acute GvHD grade II and grade III (n = 2). Fourteen out of 29 patients (48%) are alive and in CR with a median follow-up of 282 days (range: 42–968 days). Two heavily pre-treated patients died due to TRM. Ten patients died due to relapse of their underlying disease. Two patients died of Adeno virus infection. In conclusion, haploidentical transplantation using CD3/CD19 depleted grafts seems to be a feasible strategy to overcome the high risk of graft rejection and to improve immune reconstitution.

67

CLINICAL OUTCOMES OF ADOLESCENT PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT

Midura, B.[2], Lehmann, L.[1], Duncan, C.[1]. [1]Dana-Farber Cancer Institue, Boston, MA; [2]Children's Hospital, Boston, Boston, MA.

There is concern that the outcome for adolescent oncology patients is worse than that of younger patients with the same disease. The effect of patient age on outcome following pediatric allogeneic hematopoietic stem cell transplant (HSCT) has not been well described. We retrospectively reviewed the medical records of all pediatric allogeneic HSCT patients at our institution between January 1, 2001 and December 31, 2006. We investigated survival, cause of death, and occurrence of graft-versus-host disease (GVHD) in patients 15–21 years old at time of HSCT compared with patients 10–14.9 years old at transplant. 127 patients greater than 10 years old (10–14.9 years = 73 patients; greater than 15 years = 54 patients) were transplanted during the study period. Indications for HSCT were similar in both groups (see table). 53.4% of patients in the younger group received unrelated donor (URD) transplants compared with 48.1% in the older group. A greater percentage of patients in the younger group received cells from a donor matched at less than 6 HLA loci (20.5% versus 9.3%). There was no statistically significant difference in the incidence of chronic GVHD (younger 42.5%, older 46.2%). Patients greater than 15 years old had a higher risk of mortality compared to younger patients (odds ratio = 1.85). Relapse was the cause of death (COD) in 13.7% of patients in the younger group and 16.7% of patients in the older group. Transplant related mortality (TRM) was greater in the older group (younger 16.4%, older 27.8%). Older adolescents had increased toxicity resulting in increased mortality following HSCT compared to younger adolescents with similar underlying disease and transplant characteristics. Further study is needed to better understand these findings and their potential impact on the care of adolescent stem cell transplant patients.

Younger Adolescents Compared with Older Adolescents

	Age 10–14.9 years (n = 73)	Age >15 years (n = 54)
Death	22 (30.1%)	24 (44.4%)
Cause of death: Relapse	10	9
Cause of death: TRM	12	15
Chronic GVHD	31 (42.5%)	25 (46.2%)
Related donor	34 (46.6%)	28 (51.9%)
Source: bone marrow	65 (89%)	51 (94.6%)
Acute lymphoblastic	24 (32.9%)	14 (25.9%)
Acute myelogenous leukemia/ myelodysplasia	26 (35.6%)	20 (37%)
Chronic myelogenous leukemia	8 (11%)	8 (14.8%)
Nonmalignant hematologic disease	9 (12.3%)	10 (18.5%)
Other	6 (8.2%)	2 (3.7%)

68

GENE THERAPY FOR ADENOSINE DEAMINASE (ADA)-DEFICIENT SEVERE COMBINED IMMUNE DEFICIENCY (SCID): COMPARATIVE RESULTS WITH OR WITHOUT PEG-ADA WITHDRAWAL AND MYELOSUPPRESSIVE CHEMOTHERAPY

Podsakoff, G.[1], Engel, B.C.[1], Sokolic, R.[2], Carbonaro, D.A.[1], Muul, L.[2], Garabedian, E.[2], Ireland, J.[1], Hershfield, M.[3], Wayne, A.[4], Dunbar, C.[5], Candotti, F.[2], Kohn, D.B.[1]. [1]Childrens Hospital Los Angeles, Los Angeles, CA; [2]National Institutes of Health, Bethesda, MD; [3]Duke University Medical Center, Durham, NC; [4]National Institutes of Health, Bethesda, MD; [5]National Institutes of Health, Bethesda, MD.

In 2001–2002, we treated 4 ADA-SCID patients in a gene therapy (GTx) clinical trial evaluating the efficacy of 2 different retroviral vectors while continuing enzyme replacement with pegylated bovine ADA (PEG-ADA). No cytoreductive conditioning was used. All patients have been monitored for 6 years. No treatment-related SAE occurred. A mild transient elevation in absolute lymphocyte count (ALC) was seen in 2 patients early post-treatment, however, no durable immunologic changes were observed. Low levels (0.1–0.7%) of vector-marked PBMC persist for at least five years in 2 patients treated at the age of 4–5 years. All patients remain on PEG-ADA, prophylactic antibiotics and IVIg. In 2004, we revised the protocol to facilitate engraftment and selective advantage of gene-corrected cells by withdrawing PEG-ADA and giving busulfan (75 mg/m^2) before GTx. In November 2005, a 1st patient was treated who developed unexpected prolonged bone marrow (BM)