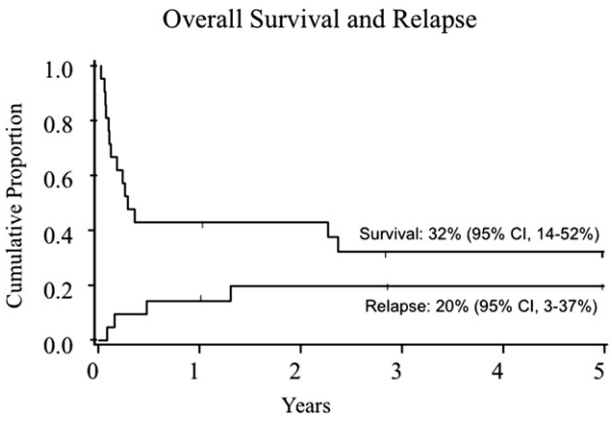
conditioning regimen consisted of Cyclophosphamide with either total body irradiation or Busulfan, with the addition of Fludarabine in 13 patients (62%). In vivo T cell depletion with Anti-Thymocyte Globulin was performed in 18 patients (85%), and 11 donor grafts underwent ex vivo T cell depletion (52%). Donor source included HLA-matched sibling (n=3), mismatched related donor (n=1), unrelated marrow (n=12) and unrelated cord blood (n=5). 58% of unrelated donors had at least 1 HLA mismatch. Neutrophil engraftment for the entire cohort was 90%, and 100% for those patients that received Fludarabine. The incidence of acute GVHD was 19% for the entire cohort. 5 year Overall Survival (OS) was 32%, with a relapse rate of 20% (Figure). Of the patients that received Fludarabine, 5 year OS was 38% with a relapse rate of 30%. For the patients with biallelic BRCA2 mutation, 5 year OS was 33% with a relapse rate of 50%



Our study provides evidence for use of HCT with a Fludarabine containing regimen for FA patients with acute leukemia or advanced MDS, who would otherwise have a dismal prognosis. The role of pre-HCT chemotherapy remains unclear, and requires further investigation. BRCA2 patients are a unique subset of FA patients and require tailored therapy to optimize HCT outcomes.

99

Treosulfan for Conditioning in Children and Adolescents Before Hematopoietic Stem Cell Transplantation (HSCT)

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To identify possible dose related toxicities of treosulfan containing regimen and determine the incidence of engraftment, treatment related mortality (TRM), overall survival (OS) and event free survival (EFS) we explored 616 patients (pts) below 18 years who underwent HSCT between January 2005 and July 2010 for malignant (n= 270, 43%) or non malignant disease (n = 356, 57%). To investigate a potential non-linear association between dose and outcome, fractional polynomials were used.533 pts underwent allogeneic, 93 autologous HSCT. 513 (83%) pts received a treosulfan-based conditioning regimen during their first HSCT. 124 (20%) had a matched sibling donor (MSD). The stem cell source was bone marrow (BM) in 274 pts (44%) and peripheral blood in 264 pts (42%).In the group of pts with allogeneic HSCT, 41 were below the age of 6 months and 65 between 6-months and 1 year. 314 were between 1 and 12 years and 101 above 12 years. For allogeneic HSCT, the median treosulfan dose was 42 g/msq (12-46). 24 pts (5%) received less then 33 g/msq. 153 pts (29%) received between 33 and 39 g/msq. The majority of pts received a treosulfan dose between 39 and 45 g/msq.

Results: There is no significant correlation of the time to ANC $>$ 0.5x10e9/L with age and treosulfan-dose. Primary graft failure occurred in 2% of cases with no significant correlation with age, treosulfan dose and underlying disease in uni- and multivariate analysis. Acute graft-versus-host disease (GvHD) of grade III-IV occurred in 10% of the patients and the rate of limited and extended chronic GvHD was 13% and 6%, respectively. The most common grade 3 or 4 toxicities were diarrhoea (24%), stomatitis (22%), and SGOT elevation (25%). Veno-occlusive disease was described in 5% of all pts. There was a significant association between age and VOD-incidence, with higher VOD-rates in children below the age of 0.5 years (12%), that are exclusively children with non-malignant diseases. Treosulfan-dose has no significant impact on VOD and GVHD in both univariate and multivariate analysis. There is a border-line significant impact of age on overall survival. The 3-years pOS in children below 6 months, between 6 months and 1 year between 1-12 years and $>$ 12 years is 75%, 84%, 70% and 60%, respectively. This difference is mainly caused by a difference in disease related mortality (DRM). TRM is not significantly different in the different age groups. With respect to dose, we did not find a significant impact on overall survival, neither in univariate nor in adjusted analysis. However, there was a better OS after first HSCT (0,74%) compared to second or third HSCT (0,51%), $P < .001$.

Conclusion: These results emphasise the low toxicity profile of treosulfan, even in heavily pre-treated children and adolescents and in patients undergoing a second HSCT. It was shown that treosulfan is highly efficient to enable engraftment without increasing the risk for severe acute or chronic GVHD.

100

Reduced Toxicity Conditioning with Busulfan, Fludarabine, Alemtuzumab and Allogeneic Stem Cell Transplantation From HLA-Matched Sibling Donors in Children with High Risk Sickle Cell Disease Results in Long Term Donor Chimerism and Low Incidence of aGVHD

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Background: Myeloablative conditioning with busulfan and cyclophosphamide (200 mg/kg) (Bu/CY) followed by HLA-