significant morbidity and mortality. Factors likely include pathogenesis of the disease as well as prolonged prior exposure to cytotoxic chemotherapy and immune suppression. Clinical approaches to improve outcomes should optimize disease control while minimizing toxicity before and after transplant.

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IMPROVED SURVIVAL FOLLOWING HLA-MATCHED RELATED MARROW TRANSPLANTATION IN PEDIATRIC PATIENTS WITH SEVERE APLASTIC ANEMIA: (A 39-YEAR RETROSPECTIVE ANALYSIS)

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Allogeneic marrow transplantation offers curative therapy for pediatric patients with severe aplastic anemia. Over the past 4 decades, significant improvements in the long term outcome of patients treated with allogeneic marrow grafts have resulted from progress in the prevention and treatment of graft rejection and graft-versus-host disease (GVHD). Here we report the outcome of 149 pediatric patients, ages 2-19 years who received HLA-matched related marrow grafts for treatment of severe aplastic anemia between 1971 and 2009. Patients were divided into 3 groups, reflecting changes in conditioning and GVHD prophylaxis regimens that occurred over time. Group 1 consisted of 100 patients who were conditioned with Cyclophosphamide (CY; 200 mg/kg) followed by "long" (102 days) Methotrexate (MTX) for GVHD prevention. Group 2 consisted of 19 patients who received CY followed by "short" (days 1, 3, 6, and 11) MTX and cyclosporine (CSP; through day 180). Group 3 consisted of 30 patients who were conditioned with CY and horse antithymocyte globulin (ATG) followed by MTX and CSP for GVHD prevention. The risk of mortality was significantly different between the 3 groups ($p < 0.0001$). With a median follow up of 25.2 (range, 0.3-37) years, the 5-year survival estimates were 66% for group 1, 95% for group 2, and 100% for group 3. There was a suggestion that the risk of rejection was different between the 3 groups ($p = 0.06$) and the 3-year estimates of graft rejection were 22%, 32%, and 12%, respectively. The estimated probabilities of grades III-IV acute GVHD were 15% for group 1, 0% for group 2, and 3% for group 3. The 2-year estimates of chronic GVHD were 21%, 21%, and 7%, respectively. In summary, advances in conditioning and GVHD prophylaxis regimens as well as supportive care during the past 39 years have led to improved outcomes for pediatric patients with severe aplastic anemia. These results strongly support the use of allogeneic marrow transplantation for newly diagnosed pediatric patients with severe aplastic anemia who have an HLA-matched related donor.

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HIGH DOSE ORAL BUSULFAN AND INTRAVENOUS MELPHALAN AS CONDITIONING THERAPY FOR AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) FOR THE TREATMENT OF PEDIATRIC SOLID TUMORS

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Disseminated or relapsed pediatric solid tumors usually have dismal prognosis and HSCT has been used as a treatment option for children with chemo-sensitive tumors. With modern intensive protocols, patients usually have been treated with many different drugs and may have some degree of renal or cardiac compromise. One interesting alternative would be to use two alkylating agents, busulfan and melphalan: these drugs are not used in pediatric chemotherapy protocols, their most important dose-limiting toxicity is marrow suppression, and they are not toxic to the heart or kidneys. Our objective is to describe the institutional experience with autologous HSCT with busulfan-melphalan for the treatment of relapsed or disseminated pediatric solid tumors.

Results: Nineteen patients with a median age of 11 years (2-33), 10 male, were transplanted, 12/19 with measurable disease. Diagnoses were alveolar sarcoma (1), desmoplastic small round cell tumor (DSRCT, 1), Wilms tumor (1), primitive neuroectodermal tumor (PNET, 2), synovial sarcoma (2), Ewing sarcoma (6, all but 1 with advanced disease), and stage-4 neuroblastoma (6, only 1 in 1st remission). All patients had normal marrow aspirate and biopsy prior to transplant, including immunocytochemistry. Conditioning therapy was busulfan 1 mg/kg/dose q 6 hours PO for 4 days on D-5 to D-2 and melphalan 140 mg/m^2 IV on D-1. Local irradiation, when planned, was postponed for the post transplant period. Three received bone marrow grafts and 16 peripheral blood stem cells with target cell dose of $5x10^6$ CD34 cells/kg. All patients engrafted promptly and none of them had severe toxicities. One had late sinusoidal obstruction syndrome and one Ewing sarcoma patient had Guillain Barre Syndrome at the time of post HSCT irradiation to his leg. One patient with PNET, the patient with DSRCT, Wilms tumor and 3/6 with Ewing sarcoma died of their primary disease after a median of 320 days post HSCT. The patient with alveolar sarcoma, both with synovial sarcoma, 3 with Ewing sarcoma and all neuroblastoma patients remain in remission and well after a median of 10.5 months post transplant (2-119). In conclusion, busulfan-melphalan was very well tolerated and 13/19 patients with advanced tumors remain well and in remission. Longer follow up and a larger number of patients are needed to define the – promising – role of this preparative regime for high dose chemotherapy and HSCT in the treatment of relapsed or disseminated solid tumors.

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INCIDENCE OF SECOND MALIGNANCIES (SMN) IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) RECIPIENTS: A REPORT COMPARING THOSE WITH AND WITHOUT EXOSTOSES

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Among 650 patients transplanted in our institution between 1992 and 2008, 19 (3%) are known to have developed a SMN post-HSCT. We have studied HSCT survivors who developed exostoses. We identified 27 patients with clinical and/or radiologic exostoses transplanted between 3/1992 and 12/2003. One patient with exostosis had co-existent malignancies and was treated elsewhere so was excluded from all analyses due to incomplete data and the possibility of a genetic cancer susceptibility. This group was compared to controls that were matched for gender, age within 3 years and on same side of puberty, malignancy/not and HSCT type. Our aim is to describe whether the exostosis patients have a higher risk for developing SMNs post-HSCT. There were 6/26 (23%) with SMNs in the exostosis group, 4/26 (15%) in the control group (McNemar p-value

	+ TBI	Focal radiation n (%)	Age at first HSCT	Time HSCT to SMN	A/C GvHD
	n (%)	SMN in field n (% with focal)	Mean (range)	Mean (range)	%
Cases with SMN (n=6)	5 (83%)	5 (83%) 2/5 (40%)	5.5y (0.5-9.1)	11.3y (6.6-16.1)	AGvHD 17% CGvHD 50%
Controls with SMN (n=4)	3 (75%)	2 (50%) 1/2 (50%)	4.9y (1.4-9.1)	9.0y (4.3-13.3)	AGvHD 75% CGvHD 25%