Conclusions: GvHD prophylaxis with Pt-Cy/Ben/csa decreased by 3-times 1y-NRM, proved superior to Pt-Cy/sirolimus in engraftment and NK cell 30-day recovery. Although the historical cohort comparison is not absent of various biases, the association was robust after adjusting for many potential confounders. We consider that this novel strategy deserves further research in larger and better-designed studies.

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Outcome of Children Developing Grade III-IV Acute Graft-Versus-Host Disease after Allogeneic Hematopoietic Stem Cell Transplantation

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Acute graft versus host disease (aGvHD) remains one of the major causes of procedure-related morbidity and mortality after allogeneic hematopoietic stem cell transplantation (HSCT). Information on the outcome of pediatric patients experiencing this complication is limited. We conducted a retrospective registry-based analysis on children who developed grade III-IV acute GVHD and were reported to the European Blood and Marrow Transplantation (EBMT) registry. Included in the study were children below age of 18 years who were transplanted between 2004 and 2016 (n=28109). Of these children, 1968 experienced grade III-IV acute GvHD: 1370 were had malignancies, while 598 were affected by a non-malignant disorder (NMD). Median year at HSCT was 2009 for patients with malignancies and 2010 for patients with NMD. In this latter group, as expected, the median age at HSCT was lower (5.8 years), in comparison with those affected by malignancies (9 years). The donor was an HLA-identical sibling in 576 cases and an unrelated donor in 895 cases. Umbilical cord blood (UCB) was employed in 282 cases, while a relative other than a compatible sibling in 215 cases. Overall, 1075 patients were given bone marrow (BM), while 598 received peripheral blood stem cells (PBSC). A fully myeloablative conditioning regimen has been employed in 94% of patients with malignancies in comparison with 75% of children with NMD. As a post-transplant pharmacological GvHD prophylaxis, a different strategy of immune suppressive treatment have been used: it consisted in the association of Cyclosporine-A (CSA) and Methotrexate in 40%, CSA alone in 30% and CSA plus Mycophenolate mofetil in 10% of patients. Grade III aGvHD occurred in 1383 patients (70%), while grade IV aGvHD was diagnosed in 585 (30%). Chronic GvHD occurred in 48.2% and 49.3% of patients with malignant and NMD, respectively. It was extensive in 262 (26.8%) patients with malignancies and in 111 (28%) children affected by NMD. Within patients with malignancies, the 2-year Kaplan-Meyer probability of overall survival (OS) was 65.7% (confidence interval 95, 63 - 68.4). In this group, the cumulative incidence of non-relapse mortality (NRM) was 23.1%. Notably, the occurrence of GvHD was responsible of death in 228 patients (CI 14.5%). In the NMD cohort, the 2-year Kaplan-Meyer probability of overall survival (OS) was 67.8% (confidence interval 95, 63.8 - 71.9). Sixty-one patients died to GvHD, being the 2-year cumulative incidence of GvHD-related mortality 19%. These data indicate that the occurrence of grade III-IV aGVHD is associated with a dismal outcome also in pediatric patients. The main cause of fatality is represented by NRM, while leukemia recurrence affected outcome of a lower number of children. Thus, strategies aimed at preventing this immune-mediated complication and at optimizing its treatment are desirable.

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Outcomes of Infliximab in Management of Steroid-Refractory Acute Graft Versus Host Disease

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Corticosteroids are considered the standard first-line treatment for moderate/severe acute graft versus host disease (aGVHD), yet there is no consensus on the optimal management of patients that are steroid-refractory (SR). Infliximab is a chimeric monoclonal antibody with anti-TNF-α activity that has previously demonstrated efficacy in SR-aGVHD.

We performed a retrospective review of 59 patients at Indiana University who underwent allogeneic stem cell transplantation and developed SR grade III-IV aGVHD from January 2007 to August 2018. Infliximab was administered 10 mg/kg weekly intravenously. Response criteria was in accordance with Martin et al (*BBMT* 2009; 12:777-784).

Median age of treated patients was 49.5 years (range, 34.5-60) and median time from transplant to diagnosis of aGVHD was 106 days (range, 42-185) Patients received a median of 12 days (range, 8-20) of systemic steroids prior to infliximab. At the start of infliximab, 52 (88%) patients were on non-steroidal immunosupressants and 39 (66%) on non-absorbable steroids concurrently with systemic steroids. Patients received a median of 3 doses of infliximab with 37 (62.7%) patients receiving <4 doses. At 28 days after first infliximab dose, overall response was seen in 16 (27.1%) patients, with 8 patients achieving a complete response and 8 with a very good partial response. From the start of infliximab, the median overall survival was 104 days with 76.3% (n=45) non-relapse mortality and 5% (n=3) relapse mortality. Bacterial infections were seen