between those transplanted at <30 days (n = 12) and >30 days of life (n = 7).
Results: Sixteen patients were diagnosed due to family history, and 3 patients were identified by newborn screening (NBS). Five were prematurely delivered, 35-37 weeks gestational age. Median age at transplant was 27 days (range 19-61). Overall survival (OS) for the cohort at 5 and 10 years post-transplant was 84.2% (95% CI: 58.7-94.6%) and 78.6% (95% CI: 52.5-91.4%), respectively. Only 1 death was due to disease progression and occurred 15 years post-HSCT. Outcomes for the 16 patients who survived to 5 years post-HSCT are reported below. Median time from transplant was 11.3 years (range 0.01–18.2). Nine patients (56%) were able to communicate normally; 4 (25%) had difficulty with speech articulation, 2 (12%) required assistive devices, and 1 was noncommunicative. Eleven patients (69%) attended school at the appropriate grade level. Twelve patients (75%) fed themselves independently. Ten patients (63%) were ambulatory, 5 with and 5 without assistive devices; 6 patients (37%) were wheelchair bound. Three patients (16%) have seizures. In domains of communication (P=0.01), feeding (P=0.01), and mobility (P=0.004), poorer outcomes occurred more frequently in those who were transplanted at >30 days.
Conclusions: In this study, a critical period for early intervention with HSCT for infantile KD was confirmed in a cohort of patients followed for over a decade post-HSCT. Improved functional outcomes were observed when HSCT was performed in the first month of life. These results highlight the need for an accelerated timeline for evaluation and decision-making regarding HSCT. Our findings will inform guidelines for long-term follow-up care and influence public policy regarding NBS for KD.

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HSCT for DOCK8 Deficiency - an International Study on 74 Patients

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Background: In 2009, mutations in the *DOCK8* gene were identified as the cause of autosomal recessive Hyper-IgE syndrome, a combined immunodeficiency characterized by elevated IgE, respiratory infections, viral infections, eczema, severe food allergies and a high cancer risk. Cohort studies have shown that this disease has a dismal natural disease outcome with most patients dying prematurely, suggesting that early allogeneic HSCT should be the standard of care. A number of case reports have suggested that HSCT can cure all disease manifestations with the exception of food allergies, which can persist for years.
Rationale: We sought to investigate the results of HSCT for DOCK8 deficiency in a large international study and to analyze how variables such as donor, age at HSCT, year of HSCT or conditioning affected the outcome.
Methods: Data were collected by retrospective chart review from centers participating in the cohort study by Aydin et al. Additional patients were identified via the PIDTC and EBMT-IEWP mailing lists.
Results: A total of 74 patients from 18 centers transplanted at a median age of 10 years (range: 2-27) between 1995 and 2015 could be included. Stem cell source was BM in 57, PBSC in 16 and one cord blood. After a median follow-up of 25 months (0-133), 61 of 74 patients are alive (82%). Acute GVHD grades 2-4 and grades 3-4 was observed in 25% and 11%; chronic GVHD of NIH scores 1, 2 and 3 in 4%, 3% and 3%, respectively. Causes of death were sepsis (n=4), GVHD (4), multi-organ failure (4) and undefined infection (1). Survival after HSCT from MSD/MFD (n=40) or MUD (27) or MMFD (6) was 88%, 84% and 67%, respectively. One UCB recipient died. There was a trend towards better survival in patients receiving treosulfan-based (n=15) versus myeloablative busulfan-based conditioning (n=27) or any other reduced intensity (n=32) regimen (100% vs 83% vs 76%, p=0.07 for treosulfan vs myeloablative busulfan), as well as for patients <8 (n=26) compared to those ≥8 years (n=48) at time of

HSCT (96% vs 77%, p=0.06), and for HSCTs since 2010 (n=62) compared to those before (n=12; 88% vs 64%, p=0.06). Of 67 patients with chimerism data available at last follow-up, 64 (96%) had >80% donor T-cell chimerism. Two patients rejected their graft, both died during or after 2nd HSCT. Eczema improved in 74% (55/74), infections in 55% (41/74), mollusca in 45% (29/64), allergies improved in 50% (37/74) and pulmonary function tests improved in 36% (25/70) and remained unchanged in the remaining patients, albeit with a relatively short follow-up in some.

Conclusion: HSCT is curative in a high proportion of DOCK8 deficient patients, confirming this approach as the treatment of choice. In this study HSCT at an early age from a matched donor using a treosulfan-based regimen resulted in the best survival rates. Longer-term observation will be needed to assess the response rate of all disease manifestations to HSCT.

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Results of the Blood and Marrow Transplant Clinical Trials Network Study BMT CTN 0601: Scurt - a Multicenter Phase II Trial of Unrelated Donor Reduced Intensity Bone Marrow Transplantation (BMT) for Children with Severe Sickle Cell Disease

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Patients with severe sickle cell disease (SCD) experience organ damage, poor quality of life and premature mortality. BMT halts disease progression if donor erythropoiesis is established. BMT from matched sibling donors is effective, but most patients lack such donors. Myeloablative conditioning (MAC) can result in long term side effects such as infertility – a barrier to patient acceptance of BMT. The SCURT trial was a prospective, multicenter trial evaluating matched unrelated donor (MUD) BMT in children following reduced intensity conditioning (RIC). The hypothesis was that an immunosuppressive regimen could support donor engraftment without myeloablation. The primary endpoint was one year event free survival (EFS) ≥75%. Eligibility (severe SCD) was defined based on CNS manifestations (overt stroke or persistently high transcranial doppler velocity), recurrent acute chest syndrome, and/or severe pain crises. Symptoms were adjudicated for eligibility by an external review committee.

The preparative regimen consisted of alemtuzumab (48 mg) (-22 to -19), fludarabine (150 mg/m^2)(day -8 to -4), and melphalan (140 mg/m^2) (day -3). Donors and recipients were matched at the HLA allele-level at A, B, C and DRB1 loci. GVHD prophylaxis consisted of calcineurin inhibitor, methotrexate (3 doses- days 1, 3 and 6) and methylprednisolone (from day +7; tapered after day +28).

Twenty-nine patients 5.9-19.3 years old (median 14.0 years) enrolled at 19 centers were evaluable with median follow up of 25.2 months (range, 12-61.5 months). All patients recovered neutrophils (median 12 days) and platelets >50x10^9/L (median 24 days). Graft rejection (GR) in 3 patients (10%) occurred before day 100, followed by autologous hematopoietic recovery. No late GR occurred. The primary endpoint was met with1-year EFS of 76% and OS of 86%. The cumulative incidence of grade II-IV and III-IV acute GVHD at day 180 were 31% and 17% respectively; chronic GVHD at 1 year was 62% with 38% extensive cGVHD. Six deaths (all in patients >14 years) occurred between 143 and 960 days, from GVHD. Another patient died after a second transplant for graft rejection. Posterior reversible encephalopathy syndrome (PRES) occurred in 35%, all in the first 6 months post-BMT; all recovered without obvious sequelae. No patient developed VOD, IPS or cerebral hemorrhage. Infections occurred in 76% (CMV and EBV reactivation each in 23%). Surviving patients report performance scores of 100% (n=14), 90% (n=5), and 80% (n=3) at 2 years or last assessment, and 13 had successfully discontinued immunosuppression.

In summary, this RIC regimen resulted in low rates of regimen-related organ toxicity except PRES (associated in each case with hypertension), had a 1-year EFS of 76% with regression of SCD symptoms, and a GR rate of 10%. Chronic GVHD was the leading cause of toxicity and mortality. Future trials should focus on effective GVHD prophylaxis after URD BMT.

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National Institutes of Health (NIH) Consensus Criteria Describe the Clinical Features of Chronic Graft-Versus-Host Disease (cGVHD) in Children and Improve the Accuracy of cGVHD Diagnosis in a Multi-Institution Trial (ABLE / PBMTC 1202)

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cGVHD in children is an understudied area of HSCT. The Applied Biomarkers of Late Effects (ABLE) / Pediatric Blood and Marrow Transplant Consortium 1202 study is a multi-institution study at 24 North American pediatric HSCT centers that prospectively enrolled (before the start of conditioning) patients <18 years undergoing myeloablative HSCT for malignant and non-malignant indications. The main objective was to validate prognostic biomarkers of pediatric cGVHD. A secondary aim was to collect clinical data on pediatric cGVHD using NIH consensus criteria (NIH-CC). Onset