clinical communities, for up-to-date data on matching and transplant outcome. Only data with the explicit consent of the participating center have been entered into this database. All data have been stripped of personal identifiers and links to submitting centers in order to protect patient anonymity. All centers contributing to this resource are listed on the main page of this project. Currently updates of the data contained at this site are submitted via the IHWG database. The HCT database currently contains data on 1551 unrelated donor transplants from 24 centers in 15 countries. Data cover high resolution HLA typing for patient and donor of HLA-A, B, C, DRB, DQB, DPB, diagnosis and stage at transplant, patient and donor age and gender, survival and relapse. Transplant pairs can be analyzed as defined by the user. Data can be sorted, viewed and downloaded by HLA allele or allele groups (i.e., HLA-A*02), level of mismatch, and diagnosis. A special tool allows users to interactively calculate, display, and download Kaplan Meier Survival estimates for each user-defined group of transplant pairs. Download options of the data are available as individual data sets of donor recipient pairs, as calculated data representing the outcome of the Kaplan Meier estimate, or as images of Kaplan Meier Curves. The database has been designed to include additional genotyping data, e.g. KIR typing, SNPs, or microsatellites for each donor-recipient pair. As data on additional genes becomes available, the database will be expanded to allow queries for combinations of different genetic loci.

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THE IMPACT OF AGE AND OBESITY ON PLASMA BUSULFAN LEVELS

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IV busulfan is an alternative to oral busulfan in myeloablative regimens prior to hematopoietic stem cell transplantation (HSCT). Compared to oral busulfan which has variable bioavailability, IV busulfan assures consistent drug delivery and may be associated with a lower incidence of regimen-related toxicity. We were interested in the effect of the type of body weight calculation used for dosing busulfan on plasma busulfan levels. We investigated the pharmacokinetic data from 58 sequential patients (age 7 m to 67 y) who received IV busulfan. In addition, the pharmacokinetic data for 11 patients who were obese or under weight who received oral busulfan during the study period were also reviewed. Patients received IV busulfan (0.8 mg/kg), or oral busulfan (1 mg/kg). Patients whose actual weight exceeded 140% of their ideal body weight were dosed according to ideal [n=12] or adjusted [n=29] body weight. The target Css range for all patients was 600–900 ng/ml. Plasma busulfan Css was measured at a single reference laboratory by gas chromatography and mass spectrometry. Based on the pharmacokinetic result, remaining busulfan doses were adjusted to achieve the desired Css target when averaged over the 4-day dosing period. There was a significant difference in mean Css values between the IV and oral busulfan groups (727 ng/ml vs 986 ng/ml respectively) ($p<0.001$); furthermore there was less variability in the Css for the IV group compared to the oral group ($p=0.01$). When IV busulfan patients were analyzed, a significant difference was observed among mean Css values of the actual, ideal, and adjusted ideal body weight groups (658 ng/ml, 707 ng/ml, and 797 ng/ml) ($p=0.01$). Consistent with other studies, we found an inverse association between the age and busulfan clearance in IV busulfan group ($p=0.004$). In addition, 6/9 patients between the age of 1 to 10 years had Css below the minimum target. In this study, patients from 1 to 10 were all dosed by actual body weight. In conclusion, use of IV busulfan produces a narrower range of Css values. Both age and the choice of body weight calculation for dosing impacts plasma busulfan levels. Consideration should be given to increase dosing for children <10 years old. Both adjusted and ideal body weight calculations led to Css values in the target range. The use of ideal rather than adjusted ideal body weight for dosing obese patients yielded Css values similar to that achieved when using actual body weight for non-obese patients.

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BONE MARROW TRANSPLANTATION FOR DYSKERATOSIS CONGENITA: ANALYSIS OF COMPLICATIONS AND LONG TERM FOLLOW-UP

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Introduction: DC is a rare bone marrow failure syndrome associated with aplastic anemia in approximately 50% of the cases. It's usually inherited in a X-linked manner and the diagnostic triad includes reticulate hyper pigmentation, nail dystrophy and mucous leukoplasia. Bone marrow transplantation (BMT) remains the only potential curative treatment for these pts. **Material and Methods**: Between 07/1993 and 07/2001, 5 pts with DC received an HLA identical sibling BMT in our service. Sex M/F: 4/1. Median age at BMT: 17 y (8–21).Median previous blood transfusions: 25 UI (6–50 UI). All but one presented with nail dystrophy, abnormal skin pigmentation and oral leukoplasia and had severe pancytopenia. Preparative regimen: Cyclophosphamide 200 mg/kg. GVHD prophylaxis: Cyclosporine (csa) + methotrexate. Stem cell source: bone marrow. TNC infused ranged from $2.2–5.13 \times 10^8$/kg (M: 2.27). Prophylactic antibiotics were given according to common practice. **Results:** All pts are alive with a median follow up of 6 years (range: 3.2–11.2 y) and have full donor engraftment. Median time to reach neutrophils >500/μl was 27 days and platelets >20,000/μl was +26 days after transplant. Two pts have a lower platelet count (80,000/μl) without any symptoms. Mucositis grade II occurred in most pts. No pt developed acute or chronic GVHD, VOD or autoimmune complications. Four pts developed eye complications and two of them had to be submitted to eye surgery (posterior uveitis and cornea transplantation for bilateral keratoconus). Only one pt complained of dry cough and progressive dyspnea 10 years after transplant. He was evaluated at our BMT Unit in 07/2004 when he presented with severe dyspnea and hypoxemia (pO2: 61 mmHg). The chest CT showed diffuse interstitial lesions and spirometry revealed a severe restrictive defect. Echocardiogram was normal without pulmonary hypertension. Pulmonary biopsy showed interstitial pulmonary fibrosis with focal areas of lymphocyte infiltrates. He was treated with steroids in 08/2004 and despite the very short follow up there is evidence of clinical improvement (less fatigue and dyspnea and pO2: 89 mmHg). **Conclusions:** This preparatory regimen is safe and effective for the correction of the hematopoietic failure in pts with DC, followed by a low complication rate. The mucocutaneous abnormalities remain unchanged. Late pulmonary complications occurred despite the absence of TBI in the preparative regimen.

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NK CELL ALLOREACTIVITY IS AN IMPORTANT MEDIATOR OF COSTIMULATION-BLOCKADE-RESISTANT REJECTION DURING ALLOGENEIC TRANSPLANTATION

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Introduction: Immunologic tolerance remains an elusive goal of clinical transplantation. Work in murine systems has demonstrated that T-cell tolerance can be accomplished by providing T cells with "signal 1" (alloantigen) while blocking "signal 2" through costimulation blockade. We have used the costimulation blockade reagents CTLA4-Ig and anti-CD40L in conjunction with nonmyeloablative bone marrow transplant to produce transplantation tolerance in a fully MHC-mismatched murine system. However, relatively large bone marrow doses ($>10 \times 10^9$/kg) must be used. Costimulation-blockade-resistant rejection occurs when smaller cell doses are transplanted. In this study, we investigated the contribution of NK cell alloreactivity to this costimulation-blockade-resistant rejection response. **Methods:** We transplanted increasing doses of Balb/C ($NK1.1^-$) bone marrow (0.5-, 2-, 5-, 10-, and 20×10^6 cells) into C57BL/6 ($NK1.1^+$) mice after treatment with 20 mg/kg busulfan. Costimulation-blockade with CTLA4-Ig and anti-CD40L was given in the peritransplant period. Three

groups were investigated: (1) The effect of NK depletion (with the depleting antibody, PK136) on engraftment and tolerance was determined. (2) The effect of NK depletion on engraftment efficiency was tested by transplanting in the presence or absence of busulfan. (3) We determined if blocking NK signalling with the anti-adhesion antibody anti-LFA1 could produce effects on engraftment similar to those observed with whole-scale NK depletion. **Results:** (1) Animals with unmanipulated NK cells exhibited costimulation-blockade resistant rejection when transplanted with $\leq 5 \times 10^6$ donor cells. However, NK depletion promoted stable chimerism even when very low doses of donor marrow (0.5×10^6) were infused. The chimeric animals in both the NK replete and NK-depleted groups were tolerant to their allografts: they exhibited deletion of donor-reactive $v\beta5^+$ and $v\beta8^+$ CD4 cells and accepted Balb/C skin grafts. (2) NK depletion had a powerful effect on engraftment efficiency: NK depletion promoted engraftment even in the absence of busulfan. (3) Blocking NK function with the anti-LFA1 antibody had the same effect as whole-scale NK depletion with PK136: treated animals became stably chimeric and tolerant even when very low doses of donor marrow were infused. **Implications:** These data highlight the central role that NK cells play in rejection of allogeneic bone marrow and underscores the need to control NK alloreactivity during clinical transplantation.

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A MULTI-INSTITUTIONAL STUDY OF EXTRACORPOREAL PHOTOIMMUNE THERAPY (ECP) WITH UVADEX® FOR THE PREVENTION OF ACUTE GVHD IN PATIENTS (PTS) UNDERGOING STANDARD MYELOABLATIVE CONDITIONING AND ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHCT)

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ECP with UVADEX® has shown benefit in pts with acute and chronic GVHD. ECP has shown to reduce the incidence of GVHD in a reduced intensity conditioning regiment (Foss. BMT. 2004 May). We report preliminary results of the first multi-institutional phase 2 study examining ECP with a standard myeloablative preparative regimen prior to AHCT. ECP was given on 2 consecutive days between D-10 and D-6, followed by cyclophosphamide 60 mg/kg/day for 2 days and TBI 1200 cGy over 3 days. GVHD prophylaxis was Cyclosporine 3–5 mg/kg IV daily beginning D-1, and later switched to PO, adjusted to keep levels 200–600 ng/ml, and methotrexate 10 mg/m^2 on D1, 3, 6, and 11 for pts who had matched unrelated donors (MUD) or HLA class 1 one-antigen mismatched related donors (MMRD), or 10 mg/m^2 on D1 and 5 mg/m^2 on D3, 6, and 11 for pts who had matched related donors (MRD). Enrollment has been completed and data are available on 61 of 65 pts. The median age was 39 (20–60) years and 40 (66%) pts were male. Diagnoses included AML/MDS (n=20), ALL (n=14), CML (n=16), lymphoma (n=5), CLL (n=3), and other (n=3). 29 pts had MRD, 31 MUD, and 1 MMRD. 28 pts received bone marrows and 33 patients had PBPC for their transplant. All patients engrafted. Acute GVHD grade 2–4 occurred in 11 (37.9%) pts and grade 3–4 occurred in 2 (7%) pts, who received MRD transplants (n=29); and grade 2–4 in 16 (51.6%) pts and grade 3–4 in 10 (32.3%) pts, who received MUD transplants (n=31). No aGVHD occurred in 1 pt who received a MMRD transplant. Mild reversible hypotension related to ECP occurred in 1 pt who was able to continue on study. Chronic GVHD occurred in 23 of 61 evaluable pts; limited in 15, extensive in 6, and unknown in 2 pts. There are 43 (70.5%) pts alive at a median follow up of 303 (168–560) days. Actuarial estimates of survival at one year are 83% for pts who received MRD transplants and 63% for pts who received MUD or MMRD transplants. Causes of death include relapse (n=5), aGVHD (n=3), multi-organ-system-failure (n=3), pneumonitis (n=4, interstitial/CMV/aspergillus), and 1 each of infection, neurologic toxicity, and arterial thrombosis. Preliminary results of this study reveal no adverse affects of ECP on regimen related toxicity or engraftment after a standard myeloablative AHCT. The overall survival of pts in this trial is encouraging and warrants further study.

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HUMAN HERPESVIRUS 6 MANIFESTING AS ENCEPHALITIS IN HEMATOPOIETIC PROGENITOR CELL RECIPIENT AFTER REDUCED INTENSITY ALLOGENEIC TRANSPLANTATION

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Diagnosis of active Human Herpesvirus 6 (HHV-6) infection in Hematopoietic Progenitor Cell (HPC) recipients can be difficult because the virus is ubiquitous and persistent in the human body. HHV-6 infection usually occurs within 2 to 4 weeks following transplantation. Infection with HHV-6 can be primary infection or reactivation. Viral infection can result in clinical symptoms including fever, rash, pneumonia, bone marrow suppression, encephalitis and rejection. There is also a possible correlation between graft versus host disease and HHV-6. We report a case of a 50 year old male with a history of refractory Acute Myelogenous Leukemia (AML). The patient was induced with Etoposide, Ara-C and Daunorubicin. He relapsed despite consolidation chemotherapy with HiDAC and Etoposide. He underwent other inductions without lasting response. Bone marrow biopsy after Myelotarg and HiDAC was hypocellular and he was taken directly to transplantation. The patient underwent a 5/6 HLA mismatched sibling donor transplant. The preparative regimen included Fludarabine 25 mg/m^2/d $\times$ 5, Melphalan 70 mg/m^2/d $\times$ 2 and ATG. His GVHD prophylaxis included Cyclosporine and Methotrexate. The patient engrafted on day 23. Donor chimerism was 100% on day 30. Approximately 3 weeks after transplant, the patient developed fever, severe myoclonus, mental status changes and amnesia. A brain MRI showed temporal lobe enhancement. Lumbar puncture revealed total protein of 58 mg/dL, glucose 80 mg/dL, WBC 1/μL, and RBC 1940/μL. HHV-6 IgG was 1:320 and IgM was negative prior to transplantation. The patient required intubation and blood pressure support. He was treated with IVIG weekly and Acyclovir initially. Multiplex RT-PCR analysis (Argene, Inc.) of the CSF was positive for HHV-6. The patient was started on ganciclovir when the data was obtained; however his status had improved prior to the change in medications. Follow-up HHV-6 titers 4 weeks after decompensation revealed HHV-6 IgG 1:1280. The patient developed grade 2–3 GVHD of the gut approximately day 55. Based on the MRI findings, the PCR positivity of the spinal fluid and the amnesia, we suspect that this is active HHV-6 infection. There have been several cases of encephalitis due to HHV-6 in HPC transplant patients who have presented with amnesia and who have temporal enhancement on MRI. HHV-6 can be a serious pathogen in HPC recipients receiving reduced-intensity preparative regimens.

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PERI-TRANSPLANT IMATINIB ADMINISTRATION RESULTS IN SIGNIFICANT MORTALITY OF RECIPIENTS OF ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTS DUE TO IMPAIRED BONE MARROW RECOVERY

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Allogeneic hematopoietic stem cell transplantation (HSCT) is the only known cure for chronic myeloid leukemia (CML). Imatinib mesylate is able to induce a complete hematologic response in