-7 through -2, before 200 cGy TBI. Unmodified G-CSF-mobilized peripheral blood stem cells (PBSC) from DLA-haploidentical donors were infused followed by immunosuppression with MMF (5-10 mg/kg BID SQ for 28-101 days) and CSP (3-15mg/kg BID PO for 102 days). Two dogs received additional weekly methotrexate (0.4 mg/kg IV from days 42 through 105) and 2 dogs received escalating dose of donor lymphocyte infusions (DLI) from their donors. **Results:** All dogs achieved prompt initial engraftment with donor chimerism of PBMC ranging from 5-90% (median; 60%) 3 weeks after transplant. However, of 21 dogs evaluable for engraftment, 15 (71%) rejected their donor grafts after discontinuation or dose-reduction of MMF/CSP (5-16 weeks after transplant). Graft rejections occurred later in dogs given prolonged immunosuppression when compared to those treated with short courses (median time to rejection; 13.5 weeks vs. 7 weeks). Sustained allografts for more than 20 weeks were observed in 6 dogs (29% of evaluable dogs). One of the 2 dogs given DLI achieved conversion to full donor chimerism after the third DLI dose (CD3+ cells infused; $1x10^7$/kg) with subsequent graft-versus-host disease requiring therapy. **Conclusion:** Initial engraftment of DLA-haploidentical PBSC can be achieved by anti-CD44 therapy and 200 cGy TBI with MMF/CSP. In some cases, sustained allografts were achieved, however, half the dogs rejected their donor grafts after discontinuation or dose-reduction of MMF/CSP. Modification to current protocols will be needed to consistently achieve long-lasting engraftment.

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UNRELATED CORD BLOOD TRANSPLANTATION (UCBT) FROM HLA DISPARATE DONORS RESULTS IN A VERY LOW RISK OF ≥GRADE II ACUTE & CHRONIC GVHD: CD34 DOSE AND NON-TBI CONDITIONING PREDICT FOR SIGNIFICANTLY IMPROVED SURVIVAL

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We and others have demonstrated that UCB has been successfully used as an alternative source of hematopoietic stem cells for both malignant and non-malignant diseases (Cairo et al, Blood 90:4665, 1997). We analyzed the results of 31 UCBT in 29 pts between 1997-2002. Age: median 9 (0.7-20) yrs; 17M:12F; and med wt 21 kg (range 8-95). Dx: 23 malignant (9 ALL, 4 AML, 1 CML, 3 HD, 3 NHL, 2 NBL, 1 HLH), and 6 non-malignant (1 B-Thal, 1 WAS, 1 FEL, 1 SAA, 1 FA, 1 Krabbe dis). HLA typing was done by serology class I (A & B) and high resolution DNA typing class II (DRB1). Donor sources: 3 (6/6), 7 (5/6), 21 (4/6). Conditioning: TBI-based (15), chemotherapy-based (6) and reduced intensity chemotherapy (10). 28 received ATG/MoAb. GVHD prophylaxis: MMF/FK506 (20), CsA+steroids±MMF (7) or CsA+Mtx (4). UCB median TNC $4.9x10^7$/kg (1.1-16.9), median CD34+ $2.8x10^5$/kg (0.2-9.9). 84% survived more than 30 days. Of those surviving 30 d: med time to ANC $\geq 0.5x10^9$/L 24 d (1-79); med time to PLT $\geq 20x10^9$/L 31 d (1-206); 81% had ANC $\geq 0.5x10^9$/L by day +60; 67% had PLT $\geq 20x10^9$/L by day +180. There was a 10% primary graft failure. 23 were evaluable for A/CGVHD. 35% developed ≥grade II AGVHD, med 29d (7-53), 22% developed ≥grade III AGVHD; 5.9% developed extensive CGVHD. The estimated 1-yr OS is 42%. 14 remain alive and dis free 1-62 mo. Factors predicting positive outcome by univariate analysis: number of CD34+ cells/kg (p=0.045), number of TNC/kg (p=0.072), non-TBI conditioning (p=0.027), standard risk vs poor risk (p=0.036), and sex (F) (p=0.015). By multivariate analysis: number of CD34+ cells/kg (p=0.035), non-TBI conditioning (p=0.026) and sex (F) (p=0.031). Patients who survived received more CD34+ cells/kg (3.1 vs $2x10^5$, p=0.045) and more TNC/kg (5.1 vs $3x10^7$, p=0.11). HLA disparity did not predict for OS. In summary, this experience with HLA disparate UCBT continues to demonstrate a very low incidence of ≥grade II AGVHD and extensive CGVHD, and more importantly, in a multivariate analysis, non-TBI conditioning and higher CD34/kg dose are the most important predictors for significantly improved survival.

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OPTIMAL SELECTIVE TYPING STRATEGIES FOR DONOR REGISTRIES

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A reasonable measure for the quality of the composition of a registry is the fraction of patients finding at least one matching donor on the first search of the registry. This indicates to which extent the phenotype spectrum of population is covered by the registry. For a population Hardy-Weinberg-Equilibrium, this "population coverage" can be estimated using the size of the registry and the HLA haplotype frequencies. Due to limited funds, many registries contain a majority of donors which are only typed for HLA-A and -B. We have designed an algorithm to select such donors for HLA-DRB1-typing by their HLA-A, B-phenotype so that after a defined number of typings performed the expected population coverage is maximized. This algorithm uses HLA haplotype frequencies to estimate absolute HLA-A, B, DR-phenotype frequencies as well as conditional distributions of HLA-DRB1 subtypes for each HLA-A, B-phenotype. Then, taking into account the current registry composition, a sequence of donors to be typed for HLA-DRB1 can be established optimizing the chance of a patient to have an HLA-A, B, DRB1-matching donor instantly. A computer simulation of this process revealed that our strategy can save initially up to 60% of typing costs over a random selection of HLA types and that the gain in efficiency will then remain between 15% and 25% until over 80% of the donors are fully typed. Since HLA typing costs are the largest burden on the budget of most registries this strategy can have a substantial economic impact.

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OUTCOME OF UNRELATED UMBILICAL CORD-BLOOD TRANSPLANTS (UCBT) IN PEDIATRIC PATIENTS: EXPERIENCE OF ONE CENTER

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Unrelated UCBT have been used as an alternative source of stem cells in the treatment of non-malignant and malignant disorders. From 7/6/95 to 7/11/02 seventy-one children underwent UCBT at Childrens Memorial Hospital. Fifty-three had malignant disorders and 18 non-malignant. Thirty-eight were male and 33 females with a mean age at transplant of 6.5 years (range 0.6-20.5 years). The ablation regimen consisted of fTBI 1200cGy in 150cGy fractions (days -8, -7, -6, -5), cyclophosphamide 60 mg/kg/day (days -4, -3, -2); and for patients with malignant disorders VP-16 was given at a 1000mg/m2/day as a CI (day -4). The GVHD prophylaxis consisted of CSA 5 mg/kg/day as a 24 hr CI, MTX 15/m2 on day 1 and 10mg/m2 on day +3 and +6 plus ATG 40 mg/kg/day on days +1, +3, +5, and +7. Selection of UCB was made based on the HLA typing and total cell dose. HLA typing was originally performed by serological methods for class I and by DNA-based methods for DRB1. Since March 2000, HLA typing has been performed using DNA-based typing methods only. Eighteen patients were HLA-A, B, and DR typed serologically only, and the degree of matching was 6/6 (n= 1), 5/6 (n= 6), 4/6 (n= 10) and 3/6 (n= 1). Fifty-three patients were DNA-typed, HLA-A and B at the group level and DRB1 at the allele level. In these patients the degree of matching was: 6/6 (n=4), 5/6 (n=14), 4/6 (n=33), and 3/6 (n=2). The total cell dose infused was a mean 0.63 x108/kg, (range 0.11- 1.92 x108/kg). The time to achieve ANC> 500/Ul were 27.4 (range 14-58 days) was achieved in 58 pts. And for sustained platelets >20/Ul 47days, (range 10-128 days). And were achieved in 47pts. From the 71 patients, 35 died from infection (n= 11), relapse (n= 8), transplant related toxicity (n= 3), PTLD (n= 1), chronic GVHD (n= 1), and others (n= 9) from these 7 did not engraft. Forty-seven patients developed AGVHD (grade I/II n= 32 or grade III/IV n= 15), in 40 of them, AGVHD resolved with immune-suppressive therapy. CGVHD in 10 patients (resolved in 7, persisted in 3). The actuarial 3-year