Using the Mexican approach to conduct non ablative stem cell transplantation (NST), we have prospectively done 58 allografts in individuals with various malignant and non-malignant hematological diseases using sibling donors, either HLA identical (6/6) or compatible, with one mismatch (5/6). When comparing allografts done from HLA identical (n = 40) or compatible (n = 18) siblings, respectively, the overall median survival was found to be 33 *versus* 8 months ($p < .01$), the 52-month survival was 47 *versus* 38% ($p > .2$), the prevalence of acute graft versus host-disease (GVHD) 57 *versus* 38%, that of chronic GVHD 25 *versus* 11% and the relapse rate 45 *versus* 55%. The two patients who failed to engraft were both 5/6 matches. Probably stemming from the low number of patients, and despite a trend toward worse results in patients allografted from HLA compatible (5/6) siblings, most differences in outcome were not significant. It seems that NST can be offered to individuals with either an HLA identical or a compatible sibling donor.

152

SUCCESSFUL UNRELATED UMBILICAL CORD BLOOD TRANSPLANTATION FOR SHWACHMAN-DIAMOND SYNDROME

Vibhakar, R.; Rumelhart, S.; Tatman, D.; Radhi, M.; Goldman, F. University of Iowa Hospitals & Clinics, Iowa City, IA.

Shwachman-Diamond Syndrome (SDS) is an autosomal recessive disorder characterized by pancreatic insufficiency and variable degrees of neutropenia. Additional clinical features include short stature, skeletal abnormalities and bone marrow dysfunction. SDS patients are at increased risk of developing myelodysplasia, aplastic anemia and leukemic transformation. The role and timing of allogeneic hematopoietic stem cell transplantation (HSCT) in SDS remains controversial due to a poorly defined predisposition toward peri-transplant complications and overall poor survival. Here we report three SDS patients (age 13 mo, 16 mo and 8 yr) with severe aplasia successfully transplanted using 5/6 HLA matched unrelated umbilical cord blood. All patients received a previously described "cardiac sparing" conditioning regimen consisting of Melphalan (180 mg/m^2), Etoposide (1200 mg/m^2), anti-thymocyte globulin (90 mg/kg), and low dose total lymphoid irradiation (500 cGy) with graft versus host disease (GVHD) prophylaxis consisting of cyclosporine and prednisone. Patients received grafts containing 6.7–9.1 $\times$ 10^5 CD34$^+$ cells/kg. Myeloid engraftment occurred promptly with the ANC >500 cells/mm^3 on day 15 $\pm$ 5. Platelet recovery (>20k without transfusion) occurred on day 20, 30 and 140 days post transplant. All patients displayed 100% donor chimerism by 2 months post transplant. Patients were discharged between 25–60 days post transplant without severe complications, though all patients displayed grade II or III acute GVHD, and one developed chronic GVHD. The patients are alive 85, 390 and 850 days post transplant. Factors that may be important in HSCT outcome for SDS include transplantation at a relatively young age prior to malignant transformation, avoidance of cyclophosphamide in the preparative regimen, and adequate GVHD prophylaxis. Importantly, these cases also suggest that unrelated umbilical cord blood, in the absence of a matched family member, should be considered as the preferred source of donor stem cells in SDS patients undergoing HSCT.

153

DONOR AGE AND DEGREE OF HLA MATCHING HAVE A MAJOR IMPACT ON RESULTS OF THE UNRELATED HAEMATOPOIETIC CELL TRANSPLANTATION (UD-HCT) FOR CHRONIC MYELOID LEUKAEMIA (CML)

Carreras, E.[1]; Jimenez, M.[1]; Gomez-Garcia, V.[2]; de la Camara, R.[2]; Martin, C.[3]; Martinez, F.[3]; Iriondo, A.[4]; Sanz, G.[5]; Canizo, C.[6]; Cabrera, R.[7]; Sierra, J.[8]; Vallejo, C.[9]; Lopez, J.[10] 1. Hospital Clinic, Barcelona, Spain; 2. Hospital de la Princesa, Madrid, Spain; 3. Hospital Reina Sofia, Cordoba, Spain; 4. Hospital Marques de Valdecilla, Santander, Spain; 5. Hospital La Fe, Valencia, Spain; 6. Hospital Universitario, Salamanca, Spain; 7. Hospital Puerta de Hierro, Madrid, Spain; 8. Hospital de Sant Pau, Barcelona, Spain; 9. Hospital Universitario, Murcia, Spain; 10. Hospital Ramon y Cajal, Madrid, Spain.

We analyzed consecutive adult patients with CML in first chronic phase that had received a blood or marrow UD-HCT in Spain during last decade. Only donor-recipient pairs typed, at least, at antigen level for HLA-A and B loci and at allele level for DRB1 locus were included. Between November 1994 and January 2003, 92 patients fulfilling these criteria underwent UD-HCT in the ten centers participating in the study. These centers performed 89% of the UD-HCT for CML in Spain during this period. The median age of the patients was 32 years (range, 15 to 49). Seventy three pairs (79%) matched for DRB1 $\pm$ DQB1 loci at allele level and for A, B $\pm$ C loci at antigen or allele level and 19 pairs had one or more mismatch. The actuarial probability of survival and disease free survival at 4 years for the whole group was 50% (95% CI: 39%-61%) and 46% (95% CI: 35%-57%), respectively. Univariate analysis showed that factors associated with a better survival were donor age less than 36 years ($p = 0.012$), matching for 8/8, 9/10 or 10/10 loci by high resolution techniques ($p=0.003$), and use of CsA since day -7 as GvHD prophylaxis ($p=0.001$). In multivariate analysis, only donor age ($p=0.003$; RR=2.9 [95% CI: 1.4 - 6]) and donor-patient HLA-matching 8/8, 9/10 or 10/10 ($p=0.009$; RR: 4.9 [95% CI: 1.5 - 16]) maintained their significance. The two-year probability of survival in the subgroup of patients receiving a UD-HCT from a donor younger than 36 years that matched for 8/8, 9/10 or 10/10 loci, was 91% (95% CI: 74%-100%). Our results indicate that the outcome of UD-HCT has notably improved and that this therapeutic approach should be considered in CML patients with young donors matching at allele level for A, B, C, DRB1 and DQB1 or with a single allelic mismatch.

154

DONOR FACTORS INFLUENCING UNRELATED VOLUNTEER DONOR SELECTION FOR HAEMATOPOIETIC STEM CELL TRANSPLANTATION

Little, A.-M.; Cleaver, S.; Maldonado Torres, H.; Marsh, S.G.E.; Bronwen, S.; Madrigal, A. The Anthony Nolan Trust, London, United Kingdom.

An important question that is faced by all unrelated donor registries is how to improve the provision of matching donors. In order to address this question it is necessary to understand the genetic diversity of the donor pool. Within the Anthony Nolan Trust (ANT) donor database, 268,321 individuals have defined HLA-A, -B, -DRB1 phenotypes, of which 44% are distinct, and 71% of distinct phenotypes are unique. Analysis of the ANT database has shown that new phenotypes continue to be added to the register from North European donors. Thus recruitment from all ethnicities will continue to add diversity to the register. In 2003 of the 314 donors provided for transplant by the ANT Register, 76% were male, with 60% of recipients being male. In 2003 46% of donors added to the ANT register were male. Therefore there is disparity between recruitment and usage of donors based on gender. The use of mobilised peripheral blood (PB) stem cells as an alternative form of donation has increased for unrelated donor donations. In 2003 the majority of requests (65%) from transplant centres were for PB. For these requests 58% of donors agreed to give PB donations. Within the ANT patient/donor cohort an increase in time to engraftment was observed for patients receiving BM transplants ($p=0.002$) and an increase in the time to onset of cGVHD was also observed for BM recipients compared with PB ($p=0.023$). It is important for Registries to follow the use of PB donations as this may influence donor recruitment in the future with different medical criteria being necessary to assess the two routes of donation. CMV status and donor age are linked factors within the ANT donor population, with 77% of potential donors aged 18–35 and 53% of potential donors aged 46–60 being CMV negative. In 2003, 72% of the donating donors were CMV negative (61% of patients were CMV negative). Studies of the ANT cohort have shown significant differences in survival of patients for the following factors with the first factor associated with increased survival: patients under 40 versus over 40 ($p=0.029$); donor under 30 versus over 30 ($p=0.024$) and patients CMV negative versus CMV positive ($p=0.014$). In summary, to increase the efficiency of unrelated donor registries it is necessary to have a clear understanding of the various factors that influence donor selection.