Symposium Abstracts

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ANALYSIS OF RISK FACTORS IN ADULTS TRANSPLANTED WITH UCB FOR TREATMENT OF HEMATOLOGIC MALIGNANCY

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Risk factors analyses are urgently required for determining which variables should guide the selection of the best UCB unit for transplantation in adults. This study evaluated prognostic factors of outcome in 92 adults with hematologic malignancy undergoing single-unit UCBT in a single institution. Conditioning consisted of thiotepa, busulfan, cyclophosphamide or fludarabine, and antithymocyte globulin (ATG). Median age and weight were 31 yr and 71 kg. Degree of HLA was 6/6 in 5, 5/6 in 33, and 4/6 in 54 cases. The median number of nucleated and CD34+ cells infused was 2.1 × 10E7/kg and 1 × 10E5/kg respectively. The cumulative incidence of myeloid engraftment, grade III-IV acute GVHD, and non-relapse mortality (NRM) at 100 days was 90%, 18%, and 25% respectively. The cumulative incidence of relapse and the probability of disease-free survival (DFS) at 3 years were 21% and 39% (median follow-up, 26 months). Multivariate analyses showed that the absolute number of CD34+ cells in the UCB unit was the most important predictor of myeloid and platelet engraftment. The use of rabbit ATG was related to faster platelet engraftment and lower incidence of acute GVHD. The development of grade II-IV acute GVHD was associated with slower platelet engraftment and greater NRM. Older patients had a greater NRM whereas conditioning with thiotepa, fludarabine, intravenous busulfan as a single daily dose, and rabbit ATG and higher numbers of CD3+ cells infused were associated with a lower NRM. Relapse risk was lower for patients with chronic myelogenous leukemia and those transplanted in early stage. The only variable independently associated with DFS was the stage of the disease at transplant. The number of nucleated cells and HLA mismatches did not impact any outcome. These results show that the current criteria for selecting the best unit for UCBT in adults need to be modified.

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DONOR-RECIPIENT HOST-VERSUS-GRAFT HUMAN LEUKOCYTE ANTIGEN MISMATCHES AND OUTCOME OF CORD BLOOD TRANSPLANTS

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The influence of HLA mismatches on outcomes of cord blood transplants (CBT) is yet to be fully understood. We hypothesized that donor-recipient mismatches in the host-versus-graft (HVG) and graft-versus-host (GVH) direction impact engraftment, non-relapse mortality (NRM) and survival after CBT, and addressed the question studying CBT performed in our institution. We also analyzed the possible contribution of HVG and GVH mismatches, and graft-versus-graft mismatches in predicting which CB unit would prevail after double CB transplants. We studied 91 patients. Diagnoses were high-risk hematologic malignancies (n=85; 93%) or non-malignant disorders (n=6; 7%). Conditioning was myeloablative (n=86; 95%), while patients not eligible for high-dose therapy received reduced-intensity (n=5; 5%) regimens. ATG was part of the preparative regimen in 45 cases (49%). Graft-versus-host disease (GVHD) prophylaxis was tacrolimus with (n=83; 91%) or without methotrexate (n=6; 6%), and cyclosporine and MMF (n=2; 2%). Grafts were single (n=70; 77%) or double (n=21; 23%) CB units. Nine patients received ex-vivo expanded grafts. For patients receiving a double CBT, the engrafted unit was used as the reference for this analysis. HLA-A, B (intermediate resolution) and DRB1 typing (high-resolution) was available for all donor-recipient pairs. Median age was 18 years (range, 1-57); 46 (51%) were younger than 18 years old and 50 patients (55%) were males. The patients were heavily pre-treated with 18 (20%) having received prior autologous transplants. Disease status at CBT was complete remission (CR; n=43; 47%) and active disease (n=48; 53%). Median number of infused total nucleated cells (TNC) was 3.45x10E7/kg (0.81-23.6). Numbers of mismatches in the HVG direction were as follows: zero (n=11), 1 (n=37), 2 (n=36), 3 (n=6), and 4 (n=1). Numbers of mismatches in the GVH direction were as follows: zero (n=8), 1 (n=35), 2 (n=41), and 3 (n=7). 78 patients engrafted neutrophils (86%) at a median of 22 days (4-60). 65 patients engrafted platelets (71%) at a median of 42 days (0-133). 13 patients (14%) failed to engraft. Grade II–IV and III–IV acute GVHD rates were 49% and 8%, respectively, and chronic GVHD incidence was 33%. 35 patients are alive with a median follow-up of 25 months. 2-year actuarial survival is 21%. 100-day and 1-year NRM is 22% (14-32) and 37% (28-49). One-year NRM was 21% (CI: 6-74) for patients that received grafts without HVG HLA mismatches, while it was 33% (CI: 20-54) for those with one mismatch, 47% (CI: 33-67) for those with two mismatches, and 33% (CI: 11-100) for those with three mismatches (P=NS). The proportion of patients that engrafted was 100% for the group without HVG mismatches, while it was 89%, 85% and 83%, respectively for patients with one, two or three mismatches. The decreasing 2-year survival and worse NRM associated with increasing number of HVG mismatches was limited to the group of patients younger than 18 years. There was no difference in the proportion of patients in CR, or in the distribution of infused TNC/Kg across the HVG mismatch subgroups. There was no correlation between mismatches in the GVH direction and NRM or 2-year survival. In addition, the number and direction of HLA mismatches among CB units and recipient did not predict which unit would prevail after double CB transplants. We conclude that HVG mismatches may influence outcomes of CBT.

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UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT) IN CHILDREN WITH ACUTE LEUKEMIA: RISKS AND BENEFITS OF UMBILICAL CORD BLOOD (UCB) VERSUS ALLELE-MATCHED BONE MARROW (BM)

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Though UCB has proven to be an acceptable alternative to BM for transplantation, it is unknown how UCB mismatched at HLA 0-2 loci compares to HLA matched BM. Therefore, we compared transplant results observed in 503 recipients of UCB with those in 116 recipients of allele-matched (at HLA A, B, C, DRB1) BM. Of UCB recipients, 35 were matched at HLA A, B (antigen-level) and DRB1 (allele-level), 201 were mismatched at 1-locus and 267 were mismatched at 2-loci. Compared to recipients of allele matched BM, UCB recipients were younger, non-Caucasian, more likely to have advanced disease at HSCT, less likely to receive radiation and somewhat more likely to receive cyclosporine. As previously observed, probability of neutrophil recovery (≥500/ul) at day 42 depended on graft type, HLA disparity and cell dose: 97% with BM; 85% with HLA matched UCB; 79% with 1-2 locus mismatched UCB/high cell dose ($>0.3 \times 10^8$/kg) and 64% 1-2 locus mismatched UCB/low cell dose ($\leq 0.3 \times 10^8$/kg). Compared to allele-matched BM, risks of grade 2-4 graft-versus-host disease (GVHD) was lower with HLA matched CB (RR 0.45, p=0.04) and similar after 1 or 2 loci HLA mismatched UCB. Risks of chronic