CIBMTR Best Abstract Awards for Clinical Research

Each year the Center for International Blood and Marrow Transplant Research presents Best Abstract Awards to recognize outstanding clinical research. The abstracts receiving the award are those that were scored highest by the Abstract Review Committees. Each award is accompanied by a prize of $1,000. The awards are supported by an unrestricted educational grant from Pfizer Inc.

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ALLOGENEIC STEM CELL TRANSPLANTATION (ALLO SCT) IN ADULT ALL: DOES PROPHYLACTIC DONOR LYMPHOCYTE INFUSION (DLI) IMPROVE SURVIVAL?

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Patients with high-risk (HR) ALL (Ph+, B-lineage high WBC and/or CR > 4 weeks, mature T-ALL) are candidates for allo SCT in CR-1. Despite SCT in CR-1, relapse rates are high and increase in advanced stages. Prognosis of relapsed ALL after SCT is poor and could not be improved by therapeutic DLI. We therefore studied the effect of prophylactic DLI on the incidence of relapse after allo SCT. Between 1995 and 2004, 105 adult HR-ALL patients (median, 28 years [17–54]) (CR-1, n = 45; >CR-1, n = 60) underwent allo SCT (related, n = 51; unrelated, n = 54) after standard (n = 100) or reduced-intensity conditioning (n = 5). Median follow-up of all ALL patients was 10 months (range, 0.7–112 months). Since 1998, prophylactic DLI was given to 24 of 105 patients without active GvHD. One DLI was given on d+111 (29–324). In median, the patients received 2 DLIs (1–4) with a total of 2.37 (0.1–20.6) $\times$ 10^7 CD3+ cells/kg; 18/24 patients (75%) are alive in CR and 6/24 (25%) are dead. A total of 81 of 105 patients received no prophylactic DLI; 27 of these 81 are alive in CR (33%) and 54 are dead (67%). The probability of survival at 3 years was 0.41 for all 105 patients. Overall survival is 0.77 for the patients with DLI and 0.29 for those without DLI (P <.001). Stage of disease at SCT (CR-1 vs > CR-1) was a significant factor for survival at 3 years: 0.55 versus 0.31 (P = .008). Prophylactic DLI versus no DLI improved survival after allo SCT either in CR-1 (0.60 vs 0.38; P = .089) or > CR-1 (0.49 vs 0.20; P = .004). Better survival for the DLI group was caused by decreased relapse probability in patients with DLI compared to those without DLI: 0.56 versus 0.74 (P = .002). Our data support a GvL effect induced by DLI in HR-ALL patients, leading to a decreased relapse rate and improved survival after allo SCT.

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ADULT TRANSPLANT OUTCOMES, SINGLE VERSUS POOLED CORD BLOOD TRANSPLANTS

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Adequate cell dose can be a limiting factor in using umbilical cord blood (UCB) for adult transplantation; therefore, clinical protocols to combine 2 UCB products have been developed. Adult data using UCB products from the SLCBB was evaluated to determine if augmentation of cell dose increases the safety of adult transplant. We evaluated 106 cord blood unit transplants performed at 27 transplant centers for adult patients (>18 years of age) in which minimum 0–3 month outcomes and postthaw total nucleated cell count (TNC) were reported, for pooled UCB transplants where both units infused were from the SLCBB. Population characteristics include an even distribution in gender, primarily treated for malignant diseases (95.1%), median age of 43.8 years (range, 18.6–64.8), median weight of 72.0 kg (range, 41.0–120.4). For single-cord blood transplants, units providing a median postprocessing dose of 2.6 $\times 10^7$ cells/kg (range, 1.1–8.5) were selected, but postthaw data indicates that only a median cell dose of 2.0 $\times$ 10^7 cells/kg (range, 0.62–6.9) were infused. In the dual-cord protocol, 2 units chosen to supply a median postprocessing dose of 4.7 $\times$ 10^7 cells/kg (range, 2.8–6.7) yielded a median infused dose of 3.6 $\times$ 10^7 cells/kg (range, 2.3–5.7) once thawed. TNC recoveries after cryopreservation average 80%, but the impact is more profound in the single transplant setting, where cell dose is diminished to < 2.0 $\times$ 10^7 cells/kg in 51.8% of all cases, a dose proven to be associated with less successful outcomes. When combining 2 units, a cell dose of > 2.0 $\times$ 10^7 cells/kg was maintained in all cases. This finding led the bank to evaluate potential differences in overall survival and neutrophil engraftment between the 2 transplant populations. Probabilities were estimated by the Kaplan-Meier method. Median time to ANC > 500/mm^3 was similar in both groups (pooled 18 days, n = 21; single 21 days, n = 73; P = .3027), but the difference in overall survival between the 2 groups approached significance (P = .0555). Overall patient survival was 13.26 months in the pooled setting (n = 23) and 3.32 months in the single-cord setting (n = 83). Because TNC recovery is unaffected by product size, selection of a single UCB unit for transplant in adults based on the postprocessing cell dose may result in a less than adequate dose. Preliminary data indicate that pooling 2 units uniformly allows the maintenance of a cell dose of > 2 $\times$ 10^7 cells/kg, resulting in improved patient outcome.

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RESULTS OF THE CORD BLOOD TRANSPLANTATION STUDY (COBLT): CLINICAL OUTCOMES OF 193 UNRELATED DONOR UMBILICAL CORD BLOOD TRANSPLANTATION IN PEDIATRIC PATIENTS WITH MALIGNANT CONDITIONS

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The Cord Blood Transplantation Study (COBLT), supported by the National Heart, Lung, and Blood Institute, created 2 unrelated donor cord blood banks with an inventory of approximately 8,000 units (CBUs). Six core and 22 collaborating transplant centers enrolled patients on a phase II clinical trial employing a common preparative regimen (TBI/cyclophosphamide/ATG) and prophylaxis against GvHD (cyclosporine/steroids). Children (n = 193; 61% males, 57% Caucasian, 52% CMV+) with ALL, ANLL, MDS or CML not in relapse or blast crisis, median age 7.8 years were transplanted with ≥ 5/6, 4/6, or 3/6 HLA-matched CBUs as defined by intermediate-resolution HLA typing at Class IA and IB and high-resolution typing at DRB1. The primary study end point was 180-day survival. CBUs delivering a median precryopreservation cell dose of 5.5 $\times$ 10^7 total nucleated cells (TNC)/kg and 1.5 $\times$ 10^5 CD34 cells/kg were selected from COBLT or other banks. The cumulative incidence of neutrophil and platelet engraftment with > 90% donor cells was 73% at a median of 28 days and 52% by 180 days, respectively. The cumulative incidence of grade III and IV acute GvHD was 20%, and that of chronic GvHD was 22%. HLA mismatching at the 5/6, 4/6, or 3/6 level by original lower resolution or retrospective high-resolution DNA typing performed on donor/recipient pairs did not correlate with engraftment, GvHD, or survival. In multivariate analysis, seronegativity for CMV was the only factor that correlated with improved survival. TNC and CD34 dose correlated with engraftment of neutrophils and platelets. The COBLT study represents the first multi-institutional, prospective clinical trial in children with malignancies undergoing UCBT. Survival in patients transplanted with low-resolution 4/6 and 5/6 matched grafts is favorable. Partially HLA-matched unrelated cord blood donors provide access to transplantation therapy for pediatric patients with malignancies lacking a matched living donor.