Columbia University; [5]Immunogenetics and Transplantation Laboratory, UCSF.

There is a significant amount of morbidity and mortality following myeloablative UCBT, in part secondary to a log less TNC/CD34+ cells/kg infused compared to matched BM or PBSC (Cairo et al, Blood, 1997). RI conditioning followed by BM or matched PBSC may potentially reduce the incidence of TRM and the late effects associated with myeloablative regimens without increasing the risk of graft failure or relapse (Satwani/Cairo, BBMT, 2005). Since UCB has a log less cells, it remains to be determined whether RI conditioning will be as successful when combined with UCBT. We currently report the results of RI-UCBT in 21 pediatric pts, median age 7.5 years (0.33-20 yrs). HLA match: 4/6 -13, 5/6-5, 6/6-3. Malignant diseases n=14, Hodgkin's disease n=5 (CR2-2, SD -1 and PD-2), NHL n=2 (ALCL-PR1 and DLBCL-SD), CML (CP-1), AML n=3 (CR1-2and CR2-1), MDS n=3 and non-malignant diseases n=7, HLH-2, WAS-1, B-Thal-1, SAA -1, SCID's-2. RI conditioning consisted of fludarabine (150-180mg/m^2)with either busulfan (8mg/kg)+ATG (n=16) or cyclophosphamide+ATG±etoposide (n=5). GHVD prophylaxis consisted of FK-506 and MMF (Osunkwo/Cairo, BBMT, 2004). The median TNC/ kg was 3.58×10^7(0.92-22.61) and the median CD34$^+$ cell dose/kg was 2.54×10^5(0.34- 9.57). The median time for neutrophil and platelet engraftment was 17.5 days (1-47) and 52 days (6-170), respectively. There were 6 primary graft failures (1 CML, 1 b-Thal, 2 HLH, 1 MDS, and 1 AML), 4/6 who were regrafted with myeloablative conditioning followed by a UCBT achieved100% engraftment. In the remainder 14 evaluable patients the donor chimerism at 30 and 180 days was 74± 20% and 90± 10%, respectively. The probability of developing grade II-IV aGVHD and cGVHD was 28.6% and 16.7%, respectively. Incidence of TRM was 14%. The 2yr OS in all patients was 59.8% (CL_{95}: 37.9-81.6). The 2yr OS for patients with average risk malignancy was 77.8% (CL_{95}: 50.6-100) and poor risk malignancy was 20.2% (CL_{95}: 0-55.1). These preliminary results indicate that despite a log less TNC/CD34+ cells/kg infused compared to matched BM or PBSC, RI-UCBT may result in rapid hematopoietic reconstitution while decreasing TRM compared to myeloablative UCBT and be associated with high donor chimerism. Patients with some diseases such as CML, b-Thal, and HLH may require increased intensity of conditioning. Further follow-up is required to evaluate long-term effects in pediatric patients following RI-UCBT.

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GVHD PROPHYLAXIS WITH TACROLIMUS OFFERS LOW EARLY MORTALITY AND BETTER SURVIVAL AFTER REDUCED-INTENSITY CORD BLOOD TRANSPLANTATION IN ELDERLY PATIENTS (≥55 YEARS)

Uchida, N.[1], Wake, A.[1], Takagi, S.[1], Yamamoto, H.[1], Kato, D.[1], Matsubashi, Y.[1], Seo, S.[1], Matsuno, N.[1], Masuoka, K.[1], Yoneyama, A.[1], Miyakoshi, S.[2], Taniguchi, S.[1] [1]Toranomon Hospital, Minato-ku, Tokyo, Japan; [2]Tokyo Metropolitan Geriatric Hospital, Itabashi-ku, Tokyo, Japan.

We have reported the feasibility of reduced-intensity cord blood transplantation (RICBT) for elderly patients with hematological malignancies at the last Tandem meeting (Abstract#18). Despite of its efficacy, treatment-related mortality (TRM) at day 100 post-transplant was considerably high (50%). Our preliminary data suggested that tacrolimus (TAC) as GVHD prophylaxis reduced TRM. Therefore, we conducted a retrospective analysis of 35 consecutive patients ≥55 years who underwent RICBT with single CB unit at our institute using TAC as GVHD prophylaxis from Jan. 2004 to Apr. 2006. Diagnoses were AML/MDS (21), CML (4), ALL (6), and ML (4), 11 of them were categorized as standard risk (those who were in CR, CP, and untreated MDS) and 24 of them were as high risk diseases (other than standard). Median total nucleated cell and CD34$^+$ cell numbers were 2.25 ×10E7 /kg (range, 1.82-3.6) and 0.78 ×10E7 /kg (range, 0.11-1.9), respectively. Thirty-two patients (91%) were conditioned with 125 mg/sqm of fludarabine, 80 mg/sqm of melphalan, and 4 Gy of TBI, and the other 3 were with slight modification. TAC was started at day -1 of transplant at 0.03 mg/kg for 24 hr. Thirty-three of them were treated with TAC alone, and 2 were with TAC and mycophenolate mofetile. Eight patients died before day 28. Among the remaining 27 patients, 24 (88.9%) of them achieved neutrophil engraftment at a median 19 days (range, 12-33). Fifteen out of 25 (60%) and 9 out of 17 (53%) evaluable patients experienced acute GVHD (grade II-IV: 12, III-IV: 8) and chronic GVHD (limited: 5, extensive: 4), respectively. Twelve patients (37%) died before day 100 post-transplant. At the median 420 days post-transplant (range, 54-773), 18 survived, with 16 being disease-free. Overall (OS) and progression-free survival at 1 year post-transplant were 54.6% and 41.3%, respectively. Remarkably, OS at 1 year post-transplant for those with standard risk diseases was 91%, whereas it was 38% for those with high risk. Among 17 deaths observed, 6 were from disease progression and the other 11 were from non-relapse causes. Multivariate analyses revealed that age older than 60, poor ECOG performance status (≥2) before transplant, higher disease risk were associated with an increased risk for mortality. To conclude, RICBT with TAC is a feasible approach for elderly patient, especially for those with standard risk diseases. Longer follow-up is necessary to further evaluate the curability of this approach.

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OUTCOMES OF UNRELATED DONOR HEMATOPOIETIC STEM CELL TRANSPLANTATIONS FOR PEDIATRIC PATIENTS IN THAILAND

Vanichsetakul, P.[1], Wattanapaiboon, P.[2], Seksarn, P.[1], O-Charoen, R.[3], Kupatawintu, P.[3] [1]Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Pathumwan, Bangkok, Thailand; [2]Synphaet Hospital, Kannayao, Bangkok, Thailand; [3]National Stem Cell Donor Registry, National Blood Centre, Thai Red Cross Society, Pathumwan, Bangkok, Thailand.

Clinical trials using unrelated donors are accepted choices worldwide for patients in need of transplant but lacking HLA-matched related donors. To study the outcome we reviewed our experience with 28 Thai pediatric patients (22 male; 6 female) given hematopoietic stem cell transplantations from unrelated donors (UD-HSCT) selected using DNA high-resolution typing of both HLA class I and II loci, from May 2001 to September 2006. Median age and weight were 7 years 7 months (1 y 3 m-16 y 9 m), and 24.5 kg (7.8-68.8), respectively. Twenty patient/donor pairs (71.43%) were fully matched; eight (28.57%) were 5/6 matched. Patients had either non-malignant (n=23) or malignant (n=5) diseases. Among non-malignant group there were beta-thalassemia major (n=16), adrenoleukodystrophy (n=3), severe aplastic anemia (n=2), Wiskott-Aldrich syndrome (n=1), and Griscelli syndrome (n=1); while there were acute lymphoblastic leukemia (n=2), chronic myeloid leukemia (n=1), juvenile chronic myelomonocytic leukemia (n=1), and relapsed Hodgkin disease (n=1) in malignant group. Besides umbilical cord blood transplant (CBT) recipients (n=3) for whom graft-versus-host disease (GvHD) prophylaxis with mainstay cyclosporine was used, GvHD prophylaxis for bone marrow (BMT) and peripheral blood stem cell transplant (PBSCT) composed of cyclosporine plus short-term methotrexate in first 12 recipients; tacrolimus plus short-term methotrexate in last 13. Median numbers of infused CD34+ cells were 5.15×10^6/kg (1.24-33.6) in BMT (n=17), 6.8×10^6/kg (3.91-17.17) in PBSCT (n=8), and 3×10^5/kg (2.26-25) in CBT (n=3). The probability of hematopoietic recovery at day 30 was 85.71%. Of the engrafted patients (n=25) the cumulative probability of acute and chronic GvHD were 32 and 16%, respectively. Ten patients died of transplant-related complications. The probability of transplant-related mortality (TRM) at 30 days, 100 days, 1 year, and 2 years were 10.71, 28.57, 28.57, and 35.71%, respectively. Median follow-up time for surviving patients was 1 year 6 months (2 m-5 y 4 m). Overall (OS) and disease-free survival (DFS) rates were 64.29 and 57.14%, respectively. Of the beta-thalassemia patients group (n=16) the OS and DFS rates were superior; 81.25 and 75%, respectively. UD-HSCT with donor selection based on high-resolution HLA typing is associated with low incidence of graft failure and GvHD. This observed outcome is favorable and comparable to that of children transplanted from HLA-identical siblings.