post-transplant was 69% (95% CI 64%, 74%). For pts with malignant disease, disease-free survival at 1 year was 50% (95% CI 43%, 56%). Based on Cox proportional hazards models, the success of transplantation was predominantly dependent on pt characteristics: pts with non-malign disease, CMV seronegativity, and males had improved outcomes. CD34+ dose was associated with improved neutrophil and platelet engraftment. In multivariate analyses, TNC (95% pts had $\geq 2.5 \times 10^7$/kg), HLA match (4/6 vs 5 or 6/6 types at transplant) or HR HLA match (<8/10 vs ≥8/10) were not significantly associated with any of the end points. In conclusion, HLA 4-6 of 6 matched CBUs with $\geq 2.5 \times 10^7$/kg TNC provide excellent transplant results for pediatric patients with malign (OS 57% [95% CI 50%, 63%] at 1 year) and non-malign (OS 71% [95% CI 61%, 80%] at 1 year) diseases.

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UNRELATED CORD BLOOD TRANSPLANTATION AFTER MYELOABLATIVE CONDITIONING IN ADULT PATIENTS WITH ACUTE LEUKEMIA

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Although allogeneic stem cell transplantation from a human leukocyte antigen (HLA)-identical related donor offers a potential cure for patients with acute leukemia, a suitably matched related donor is unavailable for approximately two-thirds of patients. Recently, umbilical cord blood from unrelated donors has been used as an alternative stem cell source for adult patients with hematological malignancies. Here, we updated the results of unrelated cord blood transplantation (CBT) after myeloablative conditioning for 69 adult patients with acute leukemia. Between August 1998 and April 2005, 69 adult patients with acute leukemia were treated with unrelated CBT at The Institute of Medical Science, University of Tokyo. Diagnoses at transplantation included de novo AML (n = 38), ALL (n = 16), and MDS-related secondary AML (n = 15). All patients received four fractionated 12 Gy total body irradiation and chemotherapy as myeloablative conditioning. 66 patients received standard cyclosporine (CyA) and methotrexate, and 3 patients received CyA only as a graft-versus-host disease (GVHD) prophylaxis. Among the patients the median age was 41 years (range, 18-55 years), the median weight was 55 kg (range, 36-76 kg) and the median number of cryopreserved nucleated cells was 2.50×10^7/kg (range, $1.16\text{-}5.29 \times 10^7$/kg). 65 patients had myeloid reconstitution and the median time to more than 0.5×10^9/L absolute neutrophil count was 21 days. A self-sustained platelet count more than 50×10^9/L was achieved in 59 patients at a median time of 39 days. Acute GVHD above grade II occurred in 39 of 65 evaluable patients and chronic GVHD occurred in 37 of 47 evaluable patients. Among 37 chronic GVHD patients, 12 patients were extensive type. 46 patients are alive and free of disease at between 126 and 2562 days after transplantation. With a median follow-up of 1259 days, the probability of disease-free survival at 3 years was 69.0%. These results suggest that adult acute leukemia patients without suitable related or unrelated bone marrow donors should be considered as candidates for CBT.

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IMPACT OF DONOR KIR GENOTYPE AND RECIPIENT HLA LIGAND INCOMPATIBILITY ON RELAPSE RELATED MORTALITY AND ACUTE GRAFT VERSUS HOST DISEASE IN HIGH-RISK PATIENTS UNDERGOING HAPLOIDENTICAL NON-MYELOABLATIVE PERIPHERAL BLOOD STEM CELL TRANSPLANTS: DIFFERENCES BETWEEN LYMPHOID AND MYELOID MALIGNANCIES

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Failure to recognize the appropriate HLA class I ligands on the target cell triggers the inhibitory killer Ig-like receptors (KIR) to initiate cytotoxicity and may contribute to graft-vs.-leukemia (GVL) effect. Past studies have shown GVL advantage of the absence (incompatibility) of recipient HLA ligands to donor KIR genes in select patients (pts) undergoing myeloablative transplantation. Here we examine if similar advantage is seen in non-myeloablative transplant (NMT). The KIR-HLA ligand combinations studied were: KIR2DL1-Cw4 (Asn77Lys80); KIR2DL2/3-Cw3 (Ser77Asn80); KIR3DL1-Bw4; and KIR3DL2-A3/A11. The KIR typing was performed by rSSOP and HLA-C allele typing by SBT. Twenty-two lymphoid malignancy (LM) pts with ALL, HD, or NHL and 20 myeloid malignancy (MM) pts with AML or MDS were studied. The median age of LM and MM were both 45 years. All had relapsed/refractory disease, and/or co-morbidities precluding ablative transplantation. Peripheral blood hematopoietic stem cell graft from haploidentical family donors with alemtuzumab (20 mg × 5), fludarabine (30 mg/m^2 × 4), and cyclophosphamide (500 mg/m^2 × 4) regimen and mycophenolate ± cyclosporine ± in vitro alemtuzumab prophylaxis was used. Most donors were 3-4/6 HLA matched (75% in MM and 82% in LM). Each pair was evaluated for the donor KIR genotype and lack of corresponding class I ligands. Kaplan-Meier curves were compared using log-rank test. The impact of NK cell cytotoxicity was assessed by relapse related mortality (RRM). RRM in MM group was appreciably lower if there was KIR/HLA-C ligand incompatibility ($P = .059$). One year probability of RRM is 14% (95% confidence: 0-37%) in the incompatible group compared to 71% (95% confidence: 28-89%) in the compatible group ($P = .059$). In addition, RRM is lower though not reaching statistical significance ($P = .070$) if the incompatibility existed for 2 or 3 KIR/HLA ligand combinations (17%; 95% confidence: 0-42%) in comparison to no or 1 combination (66%; 95% confidence: 25-85%). There were no differences in RRM in LM group ($P = .784$ for HLA-C; $P = .16$ for Bw4; 0.752 for A3/11) with regard to KIR/HLA ligand matching. KIR-HLA ligand incompatibility did not increase the probability of grade 2-4 AGVHD in the MM group ($P = .247$ for HLA-C; $P = .467$ for Bw4; 0.357 for A3/11). These results suggest that KIR/HLA ligand incompatibility contributes to GVL effect without an increase in GVHD in high-risk pts with myeloid malignancy undergoing haploidentical NMT.

IMMUNE RECONSTITUTION

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ADOPTIVE IMMUNOTHERAPY WITH ALLODEPLETED DONOR T-CELLS IMPROVES IMMUNE RECONSTITUTION AFTER HAPLOIDENTICAL STEM CELL TRANSPLANT

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One of the major barriers to the broader use of haploidentical stem cell transplantation (SCT) is the high mortality from viral infections due to poor immune reconstitution. One approach to safely overcome this problem is to infuse donor T-cells from which alloreactive lymphocytes have been selectively depleted, but the immunological benefit of this approach is unknown. We have previously demonstrated that an anti-CD25 immunotoxin effectively depletes alloreactive donor lymphocytes from co-cultures of donor mononuclear cells and host lymphoblastoid cell lines with preservation of in vitro anti-viral responses. In the current study we have compared immune reconstitution after allodepleted donor T-cells were infused at 2 dose levels into recipients of haploidentical SCT. Patients were scheduled to receive 3 doses of allode-