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Objective: We have previously reported that an HLA 8 of 8 allele-matched unrelated donor (8/8 MUD) is superior to a related donor with HLA-1 antigen mismatch in the graft-versus-host (GVH) direction (RD/1AG-MM-GVH) in transplantation for leukemia (Kanda J, et al. Blood 2012). However, the risk of relapse during the unrelated donor coordination period biases this comparison. Therefore, we performed decision analysis of donor selection in allogeneic stem cell transplantation for acute myeloid leukemia (AML) and acute lymphoblastic leukemia (ALL) in first remission (CR1); this method can consider various factors including risk of relapse during the donor coordination period and the decrease in quality of life (QOL) as a result of chronic graft-versus-host disease (GVHD).

Methods: The incidences of relapse during the coordination period of 8/8MUD or RD/1AG-MM-GVH were estimated using the data from published studies on chemotherapeutic treatment for AML and ALL. Transition probabilities after transplantation were estimated using the database of the Transplant Registry Unified Management Program for the Japan Society for Hematopoietic Cell Transplantation. The expected 5-year survival probabilities with or without QOL adjustments were estimated using TreeAgePro software. One-way sensitivity analysis was performed by varying each transition-probability value within its plausible range.

Results: In transplantation for AML-CR1, the expected 5-year survival probability was higher on selection of 8/8MUD than RD/1AG-MM-GVH (59% vs. 47%), and this superiority remained unchanged by sensitivity analysis of various factors, including the interval between achievement of CR1 and actually receiving transplantation. In transplantation for ALL-CR1, the 5-year survival probability was higher on selection of 8/8 MUD (48% vs. 43%). In one-way sensitivity analysis, the 5-year survival probability was higher on selection of RD/1AG-MM-GVH when the interval between CR1 and 8/8 MUD transplantation was $\geq$7 months. However, 8/8 MUD was superior after QOL adjustments. If the 5-year survival rate was increased by 3% (7% after QOL adjustment) in transplantation using RD/1AG-MM-GVH, the merit of selecting RD/1AG-MM-GVH outweighs that of 8/8 MUD.

Conclusions: 8/8 MUD should be prioritized in transplantation for AML-CR1. In transplantation for ALL-CR1, RD/1AG-MM-GVH should be prioritized only when the interval between CR1 and 8/8 MUD transplantation is expected to be long. However, MUD should be prioritized if QOL is considered.

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Missing KIR-Ligands in Single Mismatched Unrelated Hematopoietic Stem Cell Transplantation

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Occurrences of relapse and transplantation related mortality (TRM) are major complications after allogeneic hematopoietic stem cell transplantation (HSCT). In haploidentical transplantation, mismatches for inhibitory killer cell immunoglobulin-like receptor (KIR)-ligand in GvHD direction have been shown to be associated with lower rates of relapse.

To investigate a potential effect of NK alloreactivity as predicted by the missing ligand model in the setting of unrelated transplantation, we investigated 496 patients transplanted for malignant disorders with single HLA-B or HLA-C mismatched donors and T-cell-replete grafts. "Missing ligand" was defined as absence of a donor KIR ligand HLA-C group 1,2 or HLA-Bw4 allele in the patient in GvH-direction only or in combined HvG/GvH direction. Overall survival (OS), disease free survival (DFS), relapse, and treatment related mortality (TRM) were assessed using Kaplan-Meier analysis, competing risks regression and extended Cox regression models.

Out of the 496 transplantation pairs, 109 (22.0%) were identified as belonging to the "missing ligand"-group, the remaining 387 (78.0%) were used as a control group. Univariate and multivariate analysis did not show any differences regarding OS or DFS between the two groups. Univariate analysis showed no significant difference regarding TRM (31.6% vs. 21.1%, $P = .13$) and a significant higher risk for relapse (29.0% vs. 38.7%, $P = .048$) in the "missing ligand" group. Multivariate competing risks regression showed no significant difference for TRM (HR 0.76, CI 0.49-1.23, $P = .28$) and a trend towards increased rates of relapse (HR 1.49, CI $1.00 - 2.20$, $P = .05$) for the patients within the "missing ligand" group.

The results of this study do not confirm previous results seen in haploidentical HSCT. T-cell alloreactivity dominates over NK cell alloreactivity and leads to a diminished reconstitution of KIR expression in T-cell-replete grafts and potentially impaired "licensing" compared to T-cell depleted transplantations. This effect could explain differences between the haploidentical related and single mismatched unrelated transplantation.

POSTER SESSION 2: SOLID TUMORS

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Bi-Specific T Cell Therapy for Pancreatic Cancer

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Adoptive transfer of T cells directed to tumor-associated antigens (TAAs) by transgenic expression of chimeric antigen receptors (CARs) can produce tumor responses, even in patients with resistant malignancies. However targeting a single TAA may lead to selection of the nontargeted TAA population, leading to tumor immune escape. To overcome this limitation, we have targeted two distinct TAAs, MUC1 and PSCA, both commonly express in pancreatic cancer. We first constructed a CAR targeting MUC1, which coexpressed a truncated form of CD19 (ΔCD19) as a selectable marker. After retroviral transduction, primary T cells stably expressed both transgenes (83±4% and 66±8%, CAR-MUC1 and ΔCD19, respectively). CAR-MUC1 T cells were able to specifically kill MUC1+ target cell lines, CAPAN1 and DU145, with no recognition of MUC1- targets, 293T (35±5%, 23±4% and 3±2% specific lysis, respectively, 10:1 E:T). To further evaluate the longer term killing effects, we cultured these MUC1+