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GVHD prophylaxis consisted of the continuous infusion of tacrolimus, 1 mg/kg/day of methylprednisolone, and 15 mg/kg/day of MMF. PBSC containing 1.78-8.46 * 10e6/kg of CD34+ cells were transplanted in all cases.
Findings & Interpretation: Granulocyte engraftment was achieved on days 9-11 in all cases. Complete spousal chimerism in PB was confirmed on days 3-13 by STR-PCR. Acute GVHD was controllable except in the rejection case, who died of grade IV GVHD on day 39. All five relapse cases achieved complete remission once, and three could be discharged. One patient died of VOD/SOS on day 62, and one patient was transferred to her local hospital. The remaining four patients excluding GVHD and VOD/SOS cases finally developed disease relapse (in BM 2, CNS 2) on days 106-334, and died as a direct result on days 152-548. Discussion & Implications: Since these cases are refractory and they received their third SCT, we cannot refer to the GVL effect, and GVHD would be acceptable in spousal SCT. The immune recovery remains to be elucidated over a long-term follow-up.

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Pretransplant Sirolimus Improves Outcome of Haploidentical Peripheral Blood Stem Cell Transplantation with Post-Transplant Cyclophosphamide for Patients with Severe Aplastic Anemia

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In a pilot study, we carried out Haploidentical transplantation for 10 patients with severe aplastic anemia (SAA) using peripheral blood stem cell (PBSC) graft and post-transplantation cyclophosphamide (PTCY). The conditioning comprised of Fludarabine 150 mg/m^2, CY 30 mg/kg, horse ATG 45 mg/kg and Melphalan 120 mg/m^2, followed by PTCY 50 mg /kg on D+3, +4 and cyclosporine and mycophenolate from D + 5. Prompt engraftment was followed by early alloreactivity, resulting in transplant-related mortality in 4 of the first 5 patients, all with NK Ligand mismatched donors. In the subsequent 5 patients, Sirolimus was introduced from Day -7 to maintain a trough level of 8-14 ng/ml on the day of transplant and was continued for 12 months post-transplant, with a reduced trough level for cyclosporine. All 5 patients had prompt engraftment with 78-100% donor chimerism and mild chronic GVHD in one patient only. The only significant toxicity observed in these patients was Sirolimus associated acneform lesions. Analysis of Regulatory T cells at 45 days posttransplant was 0.09 $\pm$ 0.13% in the first 3/5 patients compared to 2.6 $\pm$ 0.77% in those receiving Sirolimus (p=0.001). Our study demonstrates that NK cell ligand mismatched donors are associated with early alloreactivity following Haploidentical PBSC transplantation for SAA but addition of Sirolimus to PTCY improves tolerance and outcome.

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The Impact of HLA Mismatch Only in the Host-Versus-Graft Direction on the Outcome of Related Hematopoietic Stem Cell Transplantation for Patients with HLA-Homozygous Haplotypes: A Retrospective Analysis of the JSHCT HLA Working Group Study

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Background: Almost 1% of the Japanese population has HLA-homozygous haplotypes (the same HLA haplotypes). An HLA mismatch between patients with HLA-homozygous haplotypes and their children or parents is absent in the graft-versus-host (GVH) direction. Hematopoietic stem cell transplantation (SCT) from a haploidentical donor with HLA mismatch only in the host-versus-graft (HVG) direction was feasible using standard GVHD prophylaxis (Ikegame K, et al. IJH 2012). However, this should be validated in a larger cohort.
Methods: We analyzed 229 patients with hematologic malignancies who had homozygous HLA-A, -B, and -DR antigens and received their first allogeneic SCT from a related donor without an HLA mismatch in the GVH direction between 1998 and 2012 in Japan. In total, 155 patients received SCT from an HLA-matched related donor (homo-to-homo SCT) and 74 received SCT from a haploidentical donor with HLA mismatch only in the HVG direction (hetero-to-homo SCT). High-risk disease and the use of tacrolimus were more frequently observed in the hetero-to-homo SCT group. The number of HLA mismatches in the HVG direction was 1 in 16 patients, 2 in 27 patients, and 3 in 31 patients. The impact of hetero-to-homo versus homo-to-homo SCT was analyzed after adjusting for transplant year, age, and other significant variables.
Results: There was no significant difference in the cumulative incidence of neutrophil engraftment and severe acute GVHD between the hetero-to-homo and homo-to-homo SCT groups (neutrophil engraftment at 50 days, 91% vs. 95%; adjusted hazard ratio (aHR) 1.05, P = 0.768; severe acute GVHD at 100 days, 10% vs. 5%; aHR 1.68, P = 0.320). Non-relapse mortality was significantly higher in the hetero-to-homo SCT group than in the homo-to-homo SCT group (26% vs. 10% at 5 years; aHR 2.42, P = 0.013), whereas there was no significant difference in the relapse rate. This resulted in non-significant lower overall survival in the hetero-to-homo SCT group (35% vs. 57% at 5 years; aHR 1.41, P = 0.083).
Conclusions: Hetero-to-homo SCT is usually considered only when transplantation should be performed immediately for high-risk disease. Therefore, differences in patient background between the homo-to-homo and hetero-to-homo SCT groups may have biased the comparison. However, it should be noted that there was no significant difference in neutrophil engraftment as well as severe acute GVHD. Although non-relapse mortality and overall mortality rates were higher in the hetero-to-homo SCT group than