Abstract: P1261

Title: NEGATIVE IMPACT OF HLA-B LEADER MISMATCH ON OUTCOMES OF HCT WITH PTCY FOR LYMPHOID MALIGNANCIES: A RETROSPECTIVE ANALYSIS FROM THE JAPANESE SOCIETY FOR TRANSPLANTATION AND CELLULAR THERAPY

Abstract Type: Poster Presentation

Session Title: Stem cell transplantation - Clinical

Background:

HLA-B leader encodes methionine (M) or threonine (T) at position 2 and gives rise to TT, MT, or MM genotype. The HLA-B leader mismatch is a risk factor for worse outcomes in HLA 1 allele mismatched unrelated hematopoietic stem cell transplantation (HCT) (Petersdorf EW et al. Lancet Haematol. 2020 and Blood. 2020), cord blood transplantation (Petersdorf EW et al. Haematologica 2020), and haploidentical HCT (Fuchs EJ et al. Blood. 2022).

Aims:

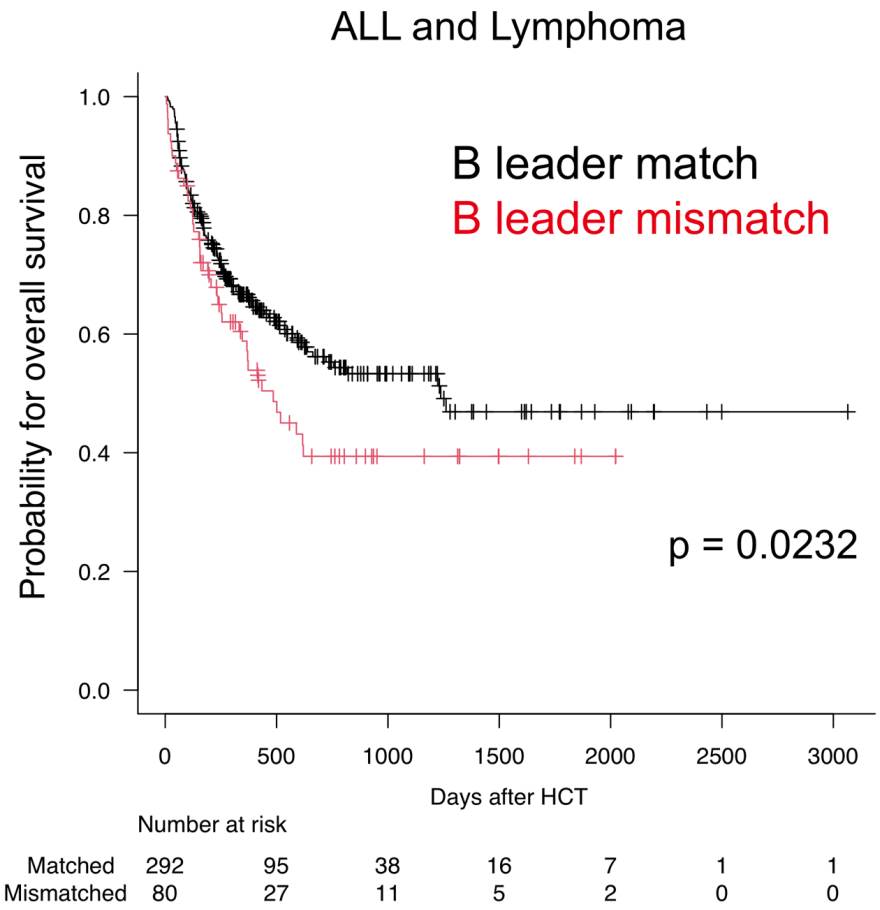
We performed a retrospective analysis of large-scale Japanese cohort data to elucidate the clinical significance of HLA-B leader in related HCT with post-transplant cyclophosphamide (PTCy).

Methods:

We assessed outcomes in 1,004 patients who underwent HCT from related donors with PTCy between 2010 and 2020 using registry data from the Japanese society of transplantation and cell therapy (JSTCT). HLA-A, -B, -C, and –DRB1 were tested at allele level by genotyping. The leader genotype was determined based on HLA-B allotype in each individual. Study outcomes were overall survival (OS), relapse, non-relapse mortality (NRM), grade II-IV acute GVHD, and any-grade chronic GVHD. Multivariable models using Cox regression analysis assessed transplant outcomes associated with patient age, patient sex, donor sex, donor age, diagnosis, disease risk index (DRI), donor source (bone marrow or peripheral blood), conditioning intensity, patient/donor CMV serostatus and, HLA B-leader mismatch. All statistical analyses were performed using EZR.

Results:

The study included 446 AML, 157 MDS (603 myeloid malignancies), 169 ALL, and 232 lymphoma patients (401 lymphoid malignancies). 955 (95%) donors were haploidentical donors, which is more than 2 allele GVH or HVG direction mismatch. In DRI, low risk was 32 (3%), the intermediate risk was 498 (50%), high risk was 400 (40%), and very high risk was 74 (7%). The median patients age was 53 (range 0-77) years. Peripheral blood was the graft source in 951 recipients (95%). Myeloablative conditioning (MAC) was used in 469 (47%) patients. PTCy 100mg/kg (50+50) was used in 602 (60%) cases, and PTCy 80mg/kg (40+40) was in 294 (29%) cases. Tacrolimus + Mycophenolate mofetil (MMF) GVHD prophylaxis was used in combination with PTCy in 879 (84%) patients. The number of HLA-B leader matched HCT was 769 (77%), and mismatched donor/recipient combination was 235 (23%). In myeloid malignancies, HLA-B leader mismatch was not a risk factor for all transplantation outcomes, such as OS, NRM, relapse, and GVHD. On the other hand, HLA-B leader mismatch was associated with worse OS and higher incidence of relapse compared to B-leader matched HCT in patients with lymphoid malignancies in univariate analysis ($p = 0.023$ for OS, and $p = 0.055$ for relapse) (Figure). In multivariate analysis, HLA-B leader mismatched HCT for lymphoid malignancy was independent risk for significantly poor OS (HR 1.450, [95% CI, 1.009 – 2.085]; $p = 0.045$), likely due to higher incidence of relapse (HR 1.470, [95% CI, 0.994 – 2.187]; $p = 0.054$).



Summary/Conclusion:

We for the first time demonstrated that HLA-B leader mismatch was associated with significantly worse OS and trend toward higher incidence of relapse after HCT with PTCy for patients with ALL and lymphoma. Interestingly, HCT outcomes in AML and MDS patients were not affected by HLA-B leader mismatch. The mechanism of this phenomenon has not been elucidated yet, but it should be highly recommended to consider the HLA-B leader mismatch status for donor selection in PTCy-HCT for ALL and lymphoma patients.

Keywords: Acute lymphoblastic leukemia, HLA, Cyclophosphamide, Haploidentical stem cell transplantation