SUPPLEMENTARY APPENDIX

Comparable composite endpoints after HLA-matched and HLA-haploidentical transplantation with post-transplantation cyclophosphamide

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Supplementary Materials

Multivariable Analyses and Post-Relapse Survival

Multivariable analyses were conducted separately by GRFS and CRFS outcomes via Cox proportional hazard models stratified by BMT year in order to examine the association of transplant platforms with outcomes after adjusting for potential confounders. Not only was there a higher proportion of patients undergoing haplo BMT than MA HLA-matched BMT from 2009-2012, but the hazards for GRFS and CRFS were significantly different between these year categories. Thus we stratified by BMT year to account for the impact of experience with PTCy-based transplantation platforms. Further, we considered all characteristics shown in Table 1 as candidate risk factors except patient gender and disease diagnosis. These were excluded because female into male allografting, which has been shown to be prognostic of GVHD and is determined by patient gender, and the disease risk index (DRI), which includes disease diagnosis and is associated with relapse and survival after BMT,[1] were both included. Final multivariable models were selected via backward procedures with p-values <0.05 as inclusion criteria with patient age and transplant platforms always included in the model.

Due to the high correlation between the time from BMT to relapse and relapse to death a cut point to categorize the groups was set at 6 months, based on numbers of patients at risk and events in our data. Kaplan-Meier curves for post-relapse survival were presented and stratified by time to relapse at 6 months. Similar to prior publications of post-relapse survival, time zero for post-relapse survival was relapse date and relapse time was not time-dependent after observing the relapse event.[2-5] Furthermore, a multivariable analysis for post-relapse survival to evaluate the difference among transplant platforms was conducted via the same model selection procedures as used for GRFS and CRFS, but with the additional inclusion of time of relapse as a candidate risk factor.

All analyses were carried out using the statistical software R version 3.2.0 (R Foundation for Statistical Computing, Vienna, Austria). All reported p-values were two sided. In order to adjust for multiple testing, p-values less than .01 were interpreted as statistically significant.

Donor Selection and Treatment Plan

Donors were molecularly typed at HLA-A, -B, -Cw,- DRB1, and -DQB1 and were either 10/10 MRD or MUD, or, if haploidentical were 1st degree or half sibling related donors who had one to five mismatches at the antigen or allele level in either the GVH or host-versus-graft direction. All patients undergoing MRD or MUD BMT received MA conditioning. MA conditioned patients received either busulfan 1mg/kg PO or 0.8mg/kg IV (days -6 to -3) every six hours with adjustments based on pharmacokinetic measurements to achieve an area under the concentration curve of 800 to 1400 micromol*min/L and Cy 50mg/kg IV (days-2 and -1) (n=270)[6] or busulfan IV daily based on a test dose to achieve a targeted daily systemic exposure of 4600 µMol-min (acceptable range 3600-5600 µMol-min) and fludarabine 40mg/m^2

IV (both days -5 to -2) (n=42) as previously published.[7, 8] Patients receiving haplo grafts received NMA conditioning, which consisted of fludarabine (30 mg/m^2 IV days -6 to -2), Cy (14.5 mg/kg IV days -6 and -5), and total body irradiation (TBI, 200 cGy day -1).[9] All patients received a T-cell-replete bone marrow graft (day 0) collected with a targeted total nucleated cell (TNC) count of 4.0 x 10^8 TNC/kg of recipient ideal body weight followed by PTCy (50 mg/kg IV on days +3 and +4) with mesna. Haplo transplant recipients received MMF and tacrolimus starting on day +5 and standardly stopped without taper in the absence of GVHD at day +35 (MMF) and either day +90 (n=45) or +180 (n=327) (tacrolimus). NMA haplo patients received filgrastim from day +5 until neutrophil recovery, while MA MRD or MUD patients did not receive growth factor support. Patients receiving second or subsequent allogeneic transplants or regimens other than the three defined above were excluded from the study. Patients receiving posttransplant maintenance therapy with hypomethylating agents, tyrosine kinase inhibitors, or rituximab were included in this analysis.

Supplementary References

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