A RETROSPECTIVE STUDY ON DESENSITISATION TREATMENT FOR HLA-DONOR SPECIFIC ANTIBODIES IN EX-VIVO T CELL DEPLETED HAPLOIDENTICAL ALLOGENEIC HAEMATOPOIETIC STEM CELL TRANSPLANTATION IN SINGAPORE

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Aims: Haploidentical haematopoietic stem cell transplantation (haplo-HCT) involves human leukocyte antigen (HLA) mismatch between donor and recipient. Donor specific HLA antibodies (DSA) in recipients can negatively impact engraftment. Data on the efficacy of DSA desensitisation prior to HCT is limited. We evaluate desensitisation treatment in ex-vivo T cell depleted haplo-HCT and assesses the impact of DSA on engraftment.
Methods: Adult patients undergoing ex-vivo T-cell (TCRαβ and CD45RA+)-depleted haplo-HCT (haplo-TCD) in Singapore from 2017 to 2023 were analysed. Recipient blood samples pre-HCT were screened for HLA antibodies by flow cytometry, followed by solid phase single antigen testing (Luminex) to characterise HLA antibodies and quantify antibody mean fluorescence intensity (MFI). Antibody MFI was assessed at baseline and after desensitisation.
Results: Out of 65 haplo-TCD patients, 11 patients with at least 1 DSA were identified. All received desensitisation with 3 sessions of plasma exchange (PE; 1.5-times total plasma volume), 1 dose of intravenous immunoglobulin (IVIg) (1g/kg) and 1 dose of intravenous rituximab (375mg/m2). One patient received an additional session.
A median of 24 (interquartile range; IQR13-37.5) HLA class I, and 8 (IQR2-18) class II allele-specific antibodies were found. Median MFI at baseline was 6483 (IQR2930-13880) compared to 2308 (IQR0-6991) post-desensitisation ($p<0.0001$). MFI analysis was stratified by >5000 (clinically significant) versus <5000. A significantly greater proportion of reduction was observed in those with baseline MFI <5000; median change was 100% (IQR59.3-100) to an undetectable MFI, compared to median change of 53.1% (IQR35.7-66.1) in those with baseline MFI >5000. Donor-specific HLA-antibody MFI at baseline was 5387 (IQR2348-14656) compared to 1559 (IQR0-9478) post-desensitisation ($p<0.0001$). MFI remained above 5000 post-desensitisation in 5 out of 11 patients.
Time to engraftment in this cohort was compared to that of haplo-TCD patients without DSA (n=49). No significant difference was observed in the median time to neutrophil engraftment (11 vs. 13 days) and platelet engraftment (12 vs. 11 days).
Conclusion: Our data suggests that desensitisation with PE, IVIg and rituximab is effective in reducing DSA MFI, resulting in robust engraftment kinetics, similar to those without DSA.