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DESENSITIZATION OF HLA DONOR-SPECIFIC ANTIBODIES RESULTS IN HIGH ENGRAFTMENT RATES IN PATIENT UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Allogeneic hematopoietic stem cell recipients may have preformed antibodies directed against foreign HLA antigens. The use of partially HLA-mismatched allogeneic hematopoietic stem cell donors allows for the possibility of the presence of circulating HLA donor-specific antibodies (DSAs) in the recipient. The presence of DSAs at the time of stem cell infusion increases the risk of primary graft failure. Recently developed technology using solid phase immunoassays (SPIs) with fluorochrome-conjugated beads has greatly improved the ability to detect and classify DSAs. When used in combination with the classic lymphocytotoxic complement-dependent and flow cytometric cross match tests, SPIs help provide DSA strength assessment. Both CD34+ cells and T-cells are required for donor engraftment; however, the expression of HLA antibodies varies between these cells: all HLA loci are expressed on CD34+ cells (HLA-A highest, HLA-DQ lowest); HLA-A and B expression is higher on CD34+ cells than on T cells; HLA-C expression is lower on CD34+ than on T cells. Parous females frequently harbor DSAs. DSAs tend to be of higher intensity when directed against haploidentical first-degree relatives. DSA assessment requires frequent monitoring as their relative strength can change over time. Importantly, patients who harbor flow cytometric cross match detectable DSA who are treated with a combination of plasma exchange with intravenous immune immunoglobulin, tacrolimus and mycophenolate mofetil can often lower DSA levels to well below flow cross match detection. Although the criteria that constitutes a prohibitive DSA is unknown, desensitization can result in engraftment rates as experienced in fully HLA-matched allogeneic blood or marrow transplantation recipients.

DSA/XM Strength	Number of TPE/IVIg		
	Pre-Conditioning	Day -1	Day +1/Day +2
Low level DSA: + FC-XM: -	0	0-1	
FC-XM: + CDC-XM: -	3-4	1	Based on Day -1 DSA Level
FC-XM: ++ High Risk Factors: + CDC-XM: -	5-6	1	Based on Day -1 DSA Level
CDC-XM: +	DESENSITIZATION RECOMMENDED		NOT

Figure 1: Desensitization recommendations

Recent Publications

- Gladstone D E and Bettinotti M P (2017) HLA donor-specific antibodies in allogeneic hematopoietic stem cell transplantation: challenges and opportunities. Hematology American Society of Hematology Education Program 17:645-650.
- Leffell M S, Jones R J and Gladstone D E (2015) Donor HLA-specific Abs: to BMT or not to BMT? Bone Marrow Transplant 50(6):751-8.

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3. Gladstone D E et al. (2013) Partially mismatched transplantation and human leukocyte antigen donor-specific antibodies. *Biology of Blood and Marrow Transplantation* 19(4):647-52.
4. Ciurea S O et al. (2015) Complement-binding donor-specific anti-HLA antibodies and risk of primary graft failure in hematopoietic stem cell transplantation. *Biology of Blood and Marrow Transplantation* 21(8):1392-1398.

Biography

Douglas E Gladstone is an Associate Professor in the Department of Oncology at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins. He is a Clinical Director of the Outpatient Bone Marrow Transplant Unit. In 2017, he led an educational program discussing how to lower donor specific antibodies to permissible levels for allogeneic bone marrow transplantation at the Annual American Society of Hematology conference

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