

## HLA Selected Platelet Units for a Difficult Case

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Introduction: Platelet refractoriness can be caused by sensitization events (exposure and antibody formation) to foreign HLA (Human Leukocyte Antigen) Class I antigens<sup>1</sup>. Recipient HLA antibodies bind specific targets on HLA antigens called epitopes<sup>2</sup>. Epitopes can be private (present on one HLA antigen) or public (one epitope shared by multiple HLA antigens)<sup>3</sup>. Amino acid residues 77-83 of the alpha helix of HLA-B antigens contain either public epitope Bw4 or Bw6<sup>4</sup>. The case presented here is from the Red Cross HLA Laboratory (Charlotte, NC) and will walk the reader through a refractory patient workup, demonstrating the challenges posed when a patient is homozygous at one position and generates antibodies directed against the alternate public epitope. The goal of testing is to identify compatible platelet products for the patient.

Methods: Patient workup included HLA-A and HLA-B typing to determine HLA-A and HLA-B alleles and allele groups; HLA class I antibody analysis to identify antibodies the patient has made; and solid phase platelet crossmatch with eleven potential donors to determine the best products. A positive crossmatch indicates incompatibility whereas a negative crossmatch suggests compatibility.

Results: The patient HLA type was determined to be HLA-A3, A31; B60(w6), B65(w6). **Antibody specificities were Bw4, B82(Bw6), B45(Bw6) and B76(Bw6)**. The average mean fluorescence intensity (MFI) for Bw6 expressing single antigen beads was 5500. HLA typing of donor units and platelet crossmatch results are presented in Table I. Crossmatches with all four homozygous Bw4 donors were positive. One of two crossmatches with Bw4/Bw6 donors was positive. Crossmatches with all five homozygous Bw6 donors were negative.

	ABO	Type	Crossmatch Result
<b>Patient</b>	<b>O+</b>	<b>B60 (w6), B65 (w6)</b>	<b>n/a</b>
Donor 1	A+	B53 (Bw4), B57 (Bw4)	Positive
Donor 2	A+	B44 (Bw4), B51 (Bw4)	Positive
Donor 3	O+	B44 (Bw4), B49 (Bw4)	Positive
Donor 4	A+	B27 (Bw4), B57 (Bw4)	Positive
Donor 5	A+	B55 (Bw6), B57 (Bw4)	Positive
Donor 6	O+	B7 (Bw6), B57 (Bw4)	Negative
Donor 7	O+	B7 (Bw6), B72 (Bw6)	Negative
Donor 8	A+	B18 (Bw6), B62 (Bw6)	Negative
Donor 9	O-	B8 (Bw6), B60 (Bw6)	Negative
Donor 10	O+	B35(Bw6), B62 (Bw6)	Negative
Donor 11	A+	B7 (Bw6), B8 (Bw6)	Negative

Fig. 1. Results of solid phase platelet crossmatch and associated Bw public epitope.

Conclusions: The patient was found to have significant reactivity to **Bw4**, strongly correlating with the positive platelet crossmatches (as seen in Figure 1). This greatly reduces the pool of compatible platelet donors for this patient, as approximately 60% of donors will be at least heterozygous for Bw4 based on the data provided by the OPTN CPRA calculator as of July 30, 2021. HLA selected platelets that avoid Bw4 antigens will increase the likelihood of producing a satisfactory response in the patient.

1. Murphy, M. F., & Waters, A. H. (1990). Platelet transfusions: the problem of refractoriness. *Blood reviews*, 4(1), 16–24. [https://doi.org/10.1016/0268-960x\(90\)90013-i](https://doi.org/10.1016/0268-960x(90)90013-i)
2. Duquesnoy R. J. (2016). Reflections on HLA Epitope-Based Matching for Transplantation. *Frontiers in immunology*, 7, 469. <https://doi.org/10.3389/fimmu.2016.00469>
3. Amy E Schmidt, MD PhD, Majed A Refaai, MD, Myra Coppage, PhD. (2019). HLA-Mediated Platelet Refractoriness: An ACLPS Critical Review. *American Journal of Clinical Pathology*, 151(4), 353-363. <https://doi.org/10.1093/ajcp/aqy121>
4. Lutz C. T. (2014). Human leukocyte antigen Bw4 and Bw6 epitopes recognized by antibodies and natural killer cells. *Current opinion in organ transplantation*, 19(4), 436–441. <https://doi.org/10.1097/MOT.000000000000103>

Links:

<https://www.redcrossblood.org/biomedical-services/blood-diagnostic-testing/hla-testing.html>

<https://insights.unos.org/content/6/>

[CPRA Calculator - OPTN \(hrsa.gov\)](https://www.hrsa.gov/opa/cpra-calculator)