FALSE POSITIVE HLA ANTIBODY REACTIVITY POST-TRANSFUSION: THE CRITICAL ROLE OF PHYSICAL CROSSMATCH IN EVALUATING ORGAN OFFERS

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Introduction

A 42-year-old female was evaluated for simultaneous liver-kidney transplant, due to primary biliary cirrhosis, nonalcoholic steatohepatitis, and diabetes mellitus. At the time of evaluation, she had end-stage liver disease.

November 2023: HDPRA class I and II reactivity, calculated panel reactive antibody (CPRA) = 73%

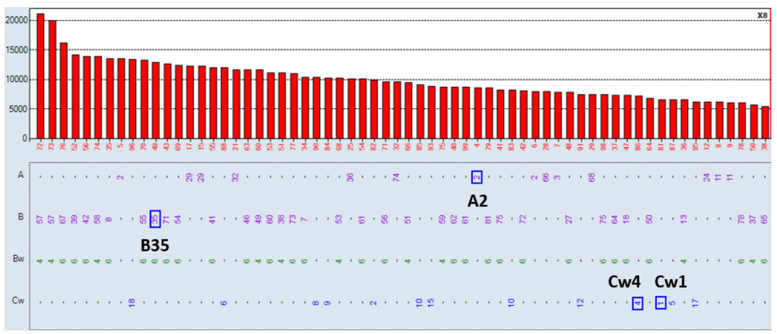
June 2024: HDPRA class I reactivity, class II negative, CPRA = 6%

September 2024: Patient receives two blood transfusions

December 2024: HDPRA class I and II reactivity, CPRA = 98%, patient is UNOS listed at this time

January 2025: Prior to listing unacceptable antigens in UNet, laboratory receives crossmatch request with UNOS deceased donor AMAD341

Virtual Crossmatch with Donor AMAD341



Virtual crossmatch was performed, based on patient HDPRA from serum sample collected in December 2024.

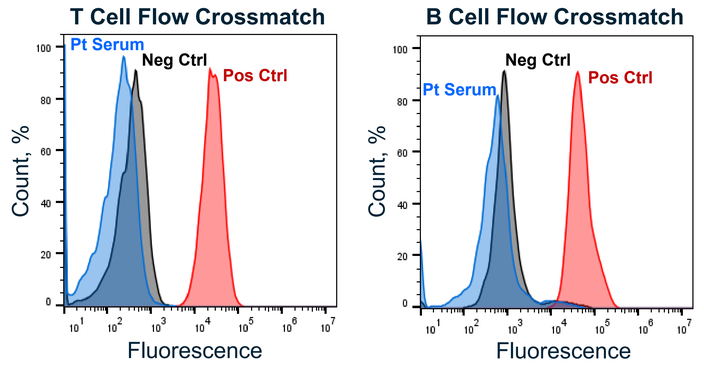
Donor specific antibody (DSA) detected:

A2 (Self, MFI = 8548)
B35 (MFI = 12953)
Cw1 (MFI = 6609)
Cw4 (MFI = 7142)

Virtual crossmatch interpretation:

T cell positive, B cell positive

Physical Crossmatch with Donor AMAD341

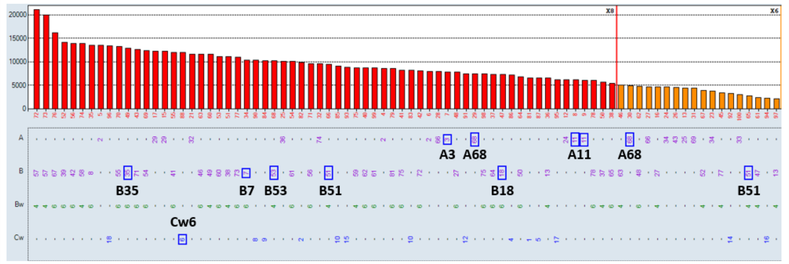


Flow crossmatch was performed using patient serum sample collected in December 2024.

Physical crossmatch interpretation:

T cell negative, B cell negative

Surrogate Donor Crossmatches



Surrogate donor crossmatches were performed using patient serum sample collected in December 2024 and cells expressing the following antigens:

A3 (MFI = 7795)
A11 (MFIs = 6040, 6129)
A68 (MFIs = 4948, 7404)
B7 (MFI = 10386)
B18 (MFI = 7349)
B51 (MFIs = 2718, 9414)
B53 (MFI = 10255)
Cw6 (MFI = 11987)

Surrogate crossmatch interpretation in all cases:

T cell negative, B cell negative

Alternate Vendor SAB Assay

The patient's December 2024 serum was tested using an alternate vendor's (Vendor 2) single antigen bead (SAB) assay platform.

HDPRA class I reactivity reported by Vendor 2's platform was similar to that reported by the original vendor's (Vendor 1) assay platform, CPRA = 98%.

Many false positive reactivities observed in Vendor 1's platform were observed in Vendor 2's platform.

MFI values of false positive reactivities reported using Vendor 1's platform were consistent with those reported using Vendor 2's platform.

Proven False Positive Reactivities

Vendor 1	A2	A3	A11	A68	B7	B18	B35	B51	B53	Cw1	Cw4	Cw6
(SAB MFI)	8548	7795	6040, 6129	4948, 7404	10386	7349	12953	2718, 9414	10255	6609	7142	11987
Vendor 2	--	A3	--	A68	B7	B18	B35	--	B53	--	--	--
(SAB MFI)	--	3500-7999	--	3500-7999	8000-11999	3500-7999	12000-16000	--	12000-16000	--	--	--

Conclusions

Both SAB assay platforms yielded misleadingly high CPRA and apparent DSA, ultimately disproven by surrogate crossmatches.

Reliance on virtual crossmatch alone can lead to erroneous exclusion of viable organs due to false positive antibody results in the SAB assay.

Physical flow crossmatch remains the gold standard, particularly for patients with recent immunologic events such as transfusion.

This patient successfully underwent simultaneous liver-kidney transplant in January 2025.

One month post-transplant, the patient's HDPRA showed overall reduced reactivity, CPRA = 54%. Only one false positive reactivity of MFI > 2000 remained, A11.

Patient is doing well with no evidence of graft rejection.