

Variation in Unacceptable HLA Antigen Mismatch Policies for Deceased Donor Kidney Transplantation

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Introduction

Educational clinical scenarios are distributed annually to UK Histocompatibility and immunogenetics (H&I) laboratories as part of the UK NEQAS for H&I external quality assessment service. These patient scenarios provide relevant test results and require result interpretation and clinical decisions/advice reflective of agreed policies between laboratories and transplant centres.

Two clinical scenarios since 2013 have required labs to define unacceptable antigens for patients requiring kidney transplantation. Responses to these scenarios were used to investigate the consistency of unacceptable HLA antigen mismatch listing between H&I laboratories.

Scenario 1 Results

This case from 2014 was based on a multiparous female patient requiring registration on the deceased donor kidney transplant waiting list. H&I laboratories were asked to detail the HLA specificities they would list as unacceptable antigens, based on results from two Luminex Single Antigen Bead tests.

All 19 laboratories that responded listed some specificities as unacceptable antigens. There was good agreement on HLA-A and -B specificities with an MFI over 2,500, however lower MFI and HLA-C antibodies were more varied (Table 1). Listing of unacceptable antigens was generally based on MFI values above a locally defined threshold.

Specificity	Luminex MFI	Number of Labs (n=19)	Specificity	Luminex MFI	Number of Labs (n=19)
A2	5497-7879	19	B18	1627-1859	13
B57	2595-6341	19	Cw2	1454-1643	13
B58	2987-4621	19	DQ2	423-1187	10
A69	2710-2676	19	DR9	342-1255	6
B35	2872-3006	19	DR7	881-921	1
Cw4	3489-3768	17	A68	0-475	1

MFI range is the lowest and highest MFI values recorded over several samples

The number of unacceptable antigens listed by each laboratory varied from 5-10 (median 8), resulting in 10 different unacceptable antigen profiles for this scenario (Table 2). The variation in unacceptable antigen listing would result in the patient being listed with a calculated reaction frequency (cRF) of between 62-88% depending on the centre.

Unacceptable Antigen Profile	No. of labs	cRF
A2 A69 B35 B18 B57 B58 Cw2 Cw4	4	71%
A2 A69 B35 B57 B58 Cw4	3	65%
A2 A69 B35 B18 B57 B58 Cw2 Cw4 DQ2	3	87%
A2 A69 B35 B18 B57 B58 Cw2 Cw4 DR9 DQ2	3	87%
A2 A69 B35 B57 B58	1	62%
A2 A69 B35 B18 B57 B58 Cw4	1	69%
A2 A69 B35 B57 B58 Cw4 DQ2	1	84%
A2 A69 B35 B18 B57 B58 Cw4 DR9 DQ2	1	86%
A2 A69 B35 B18 B57 B58 Cw2 Cw4 DR9	1	71%
A2 A68 A69 B35 B18 B57 B58 DR7 DR9 DQ2	1	88%

Scenario 2 Results

This case from 2019 was based on a multi transfused male, with a functioning heart transplant (mismatch grade 112) and failed live donor kidney graft (mismatch grade 010), requiring registration on the kidney transplant waiting list. H&I laboratories were given results of four Luminex Single Antigen bead tests, which consisted of a complex Class II profile with self-reacting beads i.e. beads displaying self alleles were positive in the test. There were responses from 22 H&I laboratories.

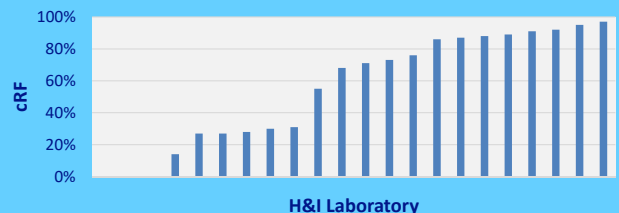
Specificity	Luminex MFI	Number of Labs (n=22)	Specificity	Luminex MFI	Number of Labs (n=22)
None	-	3	B8 ^{a,b}	-	6
DR7	1238-3520	18	A30 ^b	-	6
DR9	1557-4242	17	DR52	3154	4
DR103	1125-3669	13	DR14	1001-2575	4
DR10	704-2229	12	DQ2 ^a	-	4
DR17 ^a	930-2527	12	Cw3 ^b	-	4
DR15 ^a	1102-1749	11	DQ9 ^b	-	4
DR8	1053-3234	8	A1 ^a	-	3
DR51	912-2991	8	DQ6 ^a	-	3
DR13	1069-2716	7	DR1	838-2597	1
DR12	601-2481	6			

^a Functioning heart transplant mismatch, ^b Failed live kidney transplant mismatch
MFI range is the lowest and highest MFI values recorded over several samples

The number of unacceptable antigens listed by each laboratory varied from 0-21 (median 5). Three laboratories listed no unacceptable antigens due to the self reactivity in the Luminex test. The remaining laboratories had limited agreement on the unacceptable antigen profile for this challenging scenario (Table 3), with 18 different unacceptable antigen profiles.

In addition to MFI value, reasons for unacceptable antigen listing included MFI consistency, historic/current detection and differences in how laboratories handled self-reactivity in the Luminex test. Differences in management of previous graft mismatches were also apparent; some did not list any, others listed if antibody present, while others considered all previous graft mismatches as unacceptable antigens regardless of antibody detection. This contributed to the large variation in cRF for this scenario 0-97% (Figure 1).

Figure 1: Scenario 2 calculated reaction frequency variation



Comment

Unacceptable antigen definition can be extremely complex. These educational scenarios highlight important differences in unacceptable antigen listing practices, especially for low MFI antibodies and previous graft mismatches. This variation is likely to be due to different centre policies, risk appetite and experience. The differences could have equity of access implications for patients awaiting transplantation.