Audit of the Application of the Virtual Crossmatch Policy for Deceased Donors in the Welsh Transplantation and Immunogenetics Laboratory Over 45 Months

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Introduction

A virtual crossmatch (vXM) is the prediction of a pre-transplant crossmatch (XM) result based on a patient's antibody profile and a donor's HLA type.

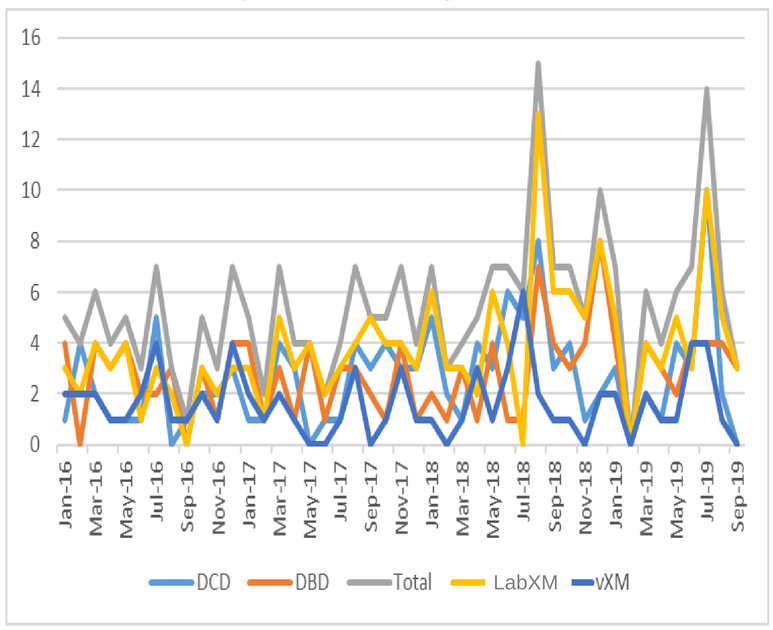
WTAIL has successfully operated a vXM policy since 2011. This policy was originally introduced for patients who have no clinically relevant HLA-antibodies defined by Luminex and complement dependent cytotoxicity screening (unsensitised patients), but has now been extended to include patients who have HLA antibodies (sensitised patients) but who do not have clinically relevant donor-specific HLA antibodies (DSA). This is possible due to the introduction of solid phase assays, most notably Luminex One Lambda Single Antigen (LSA) kits which has greatly improved the ability to detect and define HLA antibodies and thus accurately predict XM outcome.

Omission of the prospective pre-transplant laboratory XM test reduces cold ischaemia time which has a significant benefit on transplant survival.

Data Analysis

In this audit 348 deceased donor XM, where a result had been reported between 01/01/16 to 30/09/19, were analysed. 70% (245/348) of these XM proceeded to transplant, 74% (258/348) were prospective laboratory XM, 26% (90/348) were vXM. The average time to perform patient selection for a vXM was 112 minutes. For prospective XM patient selection (94 mins) and testing/reporting results (209 mins) time taken was 303 minutes, a 171% increase.

Graph 1: The Type of Donor and XM Performed in Cases that Proceeded to Transplantation During the Audit Period



Of those suitable for vXM 74% (67/90) were sensitised vXM and 26% (23/90) were unsensitised vXM.

The reasons patients were deemed unsuitable for vXM are shown in Table 1.

Table 1: Breakdown of Reason Patients Deemed Not Suitable for vXM

% Patients	Reason Patients Not Suitable for vXM
81%	Presence of unlisted DSAs
12%	Presence of HLA-DP antibodies
6%	Presence of HLA-DQA antibodies
5%	Requirement for fresh serum sample
5%	Ambiguous antibody screening results
2%	Unverified antibody screening results

There were 81% (200/248) cases where patients were deemed unsuitable for vXM due to the presence of suspected DSAs, see Table 2. Note that some patients had multiple reasons necessitating a prospective XM.

Table 2: Breakdown of Patients with Suspected DSA

Class of DSA	Number of Cases	Median cMFI
Class I	52/200	1670
Class II	102/200	3237
Class I and II	35/200	2720
Suspected DSA later proved not to be DSA once full donor HLA type known	11/200	N/A

Of the 52 XM performed with Class I DSA present, 39/52 proceeded to transplant. In 15/52 cases where a positive flow cytometry crossmatch (FCXM) was observed 11/15 proceeded to transplant, see Table 3.

Cases where positivity was likely due to non-HLA antibodies (n=5/11) were excluded from further analysis (5/5 had no apparent rejection episodes evidenced by requests for DSA testing within 6 months post-transplant).

Table 3: Results and Outcomes in Cases Where Class I DSA Only was Present

Flow Cytometry XM Result	Number	Autologous FCXM Results	Number Proceeding to Tx	Number Tx Excluding Non-HLA cases	Average FCXM Linear Channel Shift (>40 LCS +)	Median cMFI	DSA Monitoring (first 3 months post-tx)
T Cell +	1/52	2/3 Neg 1/3 Void	1	1	T - 54	1667	1/1 Neg
B Cell +	12/52	6/12 Pos 5/12 Neg 1/12 Void	8	4	B – range 51-80 LCS	4712	2/4 NT 1/4 Neg 1/4 Pos*
T&B Cell +	2/52	1/2 Neg 1/2 Void	2	1	T - 94 B - 61	4020	1/1 Pos*

NT = Not Tested

Of the 102 XM performed with Class II DSA present, 68/102 proceeded to transplant. In the 36/102 cases where a positive FCXM was observed 22/36 proceeded to transplant, See Table 4. Cases where positivity was likely due to non-HLA antibodies (17/22) were excluded (15/17 had no rejection episodes and 2/17 were DSA negative).

Table 4: Results and Outcomes in Cases Where Class II DSA Only was Present

Flow Cytometry XM Result	Number	Autologous FCXM Results	Number Proceeding to Tx	Number Tx Excluding Non-HLA cases	Average FCXM Linear Channel Shift (LCS)	Median cMFI	DSA Monitoring (first 3 months post-tx)
T Cell +	2/102	2/2 Neg	2	2	T – range 58-86 LCS	3964	2/2 NT
B Cell +	33/102	25/33 Pos 6/33 Neg 2/33 Void	19	2	B – range 48-53 LCS	2724	2/2 NT
T&B Cell +	1/102	1/1 Neg	1	1	T - 194 B - 54	5322	1/1 NT

NT = Not Tested

Of the 35 XM performed with Class I and II DSA present, 18/35 proceeded to transplant. 1/35 XM had T and B cell positive XM (LCS T-56, B-226; autologous negative, did not proceed to tx) and 12/35 had a B-cell positive result (avLCS B-109; autologous XM 1 negative, 9 positive and 2 void). There was 13 cases where a positive FCXM was observed 3/13 proceeded to transplant, in 2/3 of these cases positivity was likely due to non-HLA antibodies and no rejection monitoring was performed. In 1/3 DSA were present with a cMFI 30374, rejection monitoring was positive for DSA*.

**In all cases where rejection monitoring was positive the result correlated to pre-transplant DSA levels and no clinical rejection episodes were noted for these patients.*

Discussion

No cases of antibody mediated rejection due to DSA were noted in the transplanted patients. This audit validates the current unacceptable antigen listing strategy and provides scope to modify and extend the sensitised vXM policy.