SUCCESSFUL TRANSPLANTATION OF HIGHLY SENSITIZED PATIENTS USING VIRTUAL CROSSMATCHING

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BACKGROUND

The Hartford Hospital Kidney Transplant (Tx) program has been performing virtual crossmatches (VXM) as the final approval to proceed with Tx surgery for almost ten years. The majority of these VXMs are for unsensitized patients with low calculated panel reactive antibody (CPRA). The aim of this study was to determine how effective and accurate our VXM testing is in highly sensitized patients, resulting in a successful Tx outcome.

METHODS

We reviewed highly sensitized patients with CPRA ≥95% (n=22), who received a deceased donor kidney Tx in the past five years. The parameters selected to evaluate and compare in these patients were the following: CPRA, pre-Tx Donor Specific Antibody (DSA), VXM result (Risk assessment), flow XM result and whether a pre-Tx (P-Prospective) or post-Tx (R-Retrospective) flow XM was performed, post-Tx DSA, post-Tx creatinine (Cr) levels, rejection episodes.

RESULTS and CONCLUSIONS

See Table below. Most recipients in this cohort (19/22) currently have a functioning kidney graft with stable or acceptable Cr levels. Six recipients had pre-Tx DSA (five of whom retained the same DSA post-Tx but showed no evidence of antibody mediated rejection), while two others (without pre-Tx DSA) developed de novo DSA post-Tx. Thirteen recipients were considered VXM low risk, five moderate risk and four did not have a VXM performed at the time of kidney offer (assigned retrospectively). All recipients had negative flow T cell XMs, and 19/22 recipients had negative flow B cell XMs. All thirteen patients with low risk VXM had negative flow T and B cell XMs. Three recipients had weak positive flow B cell XMs, which correlated with multiple low-level DSA in each patient. Fifteen recipients had prospective flow XMs done while the remaining seven recipients had flow XMs performed retrospectively, i.e. post-Tx. Regarding the three failed kidney grafts (Recipients **RL,AL,CM**), two were lost to infection (one having pre-Tx DSA) and the third was reported to have biopsy proven chronic antibody mediated rejection despite testing negative for both HLA DSA and non-HLA antibodies.

An additional five highly sensitized patients (CPRA 96.89-99.81%) each received a living donor kidney Tx during this period, and all have functioning kidneys with acceptable Cr levels and no rejection episodes.

Highly sensitized kidney patients, even with CPRA values up to 100%, can be effectively and safely transplanted following accurate, vigilant and frequent pre-Tx antibody screening. However, despite low-moderate VXM risk, prospective flow XMs were still requested and performed in most of this cohort of patients. This study will help improve our Tx process moving forward and enable our program to confidently rely on retrospective flow XMs in higher risk kidney patients.

Recipient	CPRA (%)	Tx Date	Pre Tx DSA	VXM Result (Risk assessment)	Flow XM Result (P/R)	Post-Tx DSA	Post Tx Cr (current/nadir)	Rejection Episodes
AW1	99.98	8/31/24	DRB3*01 (H)	Moderate	Neg (P)	DRB3*01 (H)	1.77 / 0.90	None
VW	99.89	11/8/23	A2(L), A30(L)	Moderate	Neg/Pos (P)	A2 (L)	2.28 / 1.50	biopsy-chronic TCR and AMR
AW2	99.87	6/1/24	A25,DP23(L) DPB1*04:01(M)	Moderate	Neg (P)	*A32(M),Cw12,Cw5(H)*	1.85 / 1.57	None
SS	99.75	2/3/24	None	Low	Neg (R)	*A74(H) - de novo*	1.03 / 0.70	None
RL	99.65	10/26/20	Cw5,Cw16 (M)	Moderate	Neg (P)	?Cw5,Cw16 (L)	**8.80** / 1.58	acute TCR ?ACR 2A; Natera low
RN	99.60	11/17/23	B63,DR13,DPB1*02:01 (L)	Moderate	Neg/Pos (P)	B63,DR13,DPB1*02:01 (L)	1.41 / 1.13	None
LV	99.56	12/30/20	None	Low	Neg (P)	None	1.39 / 1.30	None
ED	99.53	12/28/23	None	Low	Neg (R)	None	0.97 / 0.89	None
MB	99.32	2/21/22	None	Low	Neg (R)	**Not tested**	1.40 / 1.40	None
EO	98.96	11/7/21	None	*Low*	Neg (P)	**Not tested**	0.68 / 0.57	None
TD	98.59	3/28/21	B38 (L)	Low	Neg (P)	None	0.78 / 0.70	None
TK	98.35	2/17/24	None	Low	Neg (R)	**Not Tested**	1.34 / 1.10	None
JC	98.32	4/6/25	None	*Low*	Neg (P)	None	1.99 / 0.98	None
CS	97.93	2/25/21	None	*Low*	Neg (P)	*DQ7(H) - de novo*	1.60 / 1.60	acute, few wks post-Tx (diffuse cortical necrosis)
MS	97.81	10/3/24	None	Low	Neg (R)	**Not Tested**	1.01 / 0.80	None
CG	97.18	12/14/22	None	Low	Neg (R)	None	1.11 / 0.90	None
JW	97.10	1/22/22	None	Low	Neg (P)	None	1.20 / 0.80	None
TH	97.03	2/6/22	DQ4,DQ9 (L)	*Low/Moderate*	Neg/Pos (P)	DQ4,DQ9 (L)	1.18 / 0.82	biopsy suspicious for acute TCR
JP	95.95	7/3/24	None	Low	Neg (P)	None	2.95 / 1.90	early ACR; later borderline acute cellular rejection
AL	95.86	7/25/21	None	Low	Neg (P)	None	**3.90** / 0.77	biopsy-AMR, (possible ACR?); Natera high
NH	95.07	7/25/25	None	Low	Neg (R)	None	1.01 / 0.89	None
CM	94.95	8/25/20	None	Low	Neg (P)	None	**9.80** / 1.44	None