

**Interpretive Educational Scheme (iED)
Clinical Scenario 1/2023 – Renal Transplantation**

Dispatched on 30th May 2023

Summary of Results

Samples from a patient requiring a kidney transplant were received in the laboratory. Details of the patient are shown in Table 1. The patient has not been tolerating dialysis well and has issues with venous access.

Table 1: Patient Information

Patient ID	JB
Primary Disease	Pyelonephritis/Interstitial Nephritis
Donor Age	39
Donor Gender	Male
Patient HLA Type	A*01, A*02; B*08, B*39; C*07, C*-; DRB1*01, DRB1*03:01; DQB1*02, DQB1*05; DQA1*01, DQA1*05; DPB1*01:01, DPB1*10:01; DPA1*02, DPA1*-
ABO Group	A+
Sensitising Events	<i>Previous Transplant from Donor X:</i> Transplanted on 13/02/2009 Donor HLA type: A*01, A*02; B*08, B*35 ; C*07, C*12 ; DRB1*01, DRB1*03:01; DQB1*02, DQB1*05; DPB1*04:01, DPB1*04:02; DPA1*01:03, - <i>Blood Transfusion:</i> 10 units received in 2019

The patient was tested using One Lambda LABScreen Single Antigen Bead (SAB) kits. Results are shown in Table 2a and 2b. All results are technically valid.

Table 2a: Results from LABScreen SAB Class I Testing Across Multiple Sample Dates

One Lambda SAB Class I Kit - MFI			Sample Date		
Bead ID	Allele Specificity	Specificity	03/12/2021	20/08/2021	03/03/2021
3	A*01:01	A1	0	0	215
5	A*02:03	A2	2102	545	1193
6	A*02:06	A2	468	41	309
4	A*02:01	A2	0	21	56
7	A*03:01	A3	0	0	0
9	A*11:02	A11	1731	378	1659
8	A*11:01	A11	1282	290	1571
10	A*23:01	A23	0	10	145
11	A*24:02	A24	315	46	406
12	A*24:03	A24	0	103	670
13	A*25:01	A25	192	127	913

14	A*26:01	A26	346	127	1234
17	A*29:02	A29	1256	292	1301
15	A*29:01	A29	1183	252	1092
19	A*30:02	A30	1159	56	423
18	A*30:01	A30	394	54	396
20	A*31:01	A31	0	12	212
21	A*32:01	A32	0	109	858
100	A*33:03	A33	2705	766	4854
22	A*33:01	A33	831	284	1712
23	A*34:01	A34	3076	816	3388
24	A*34:02	A34	2353	569	4154
25	A*36:01	A36	0	67	446
26	A*43:01	A43	2941	428	1526
28	A*66:02	A66	15596	5337	15227
27	A*66:01	A66	848	310	1449
30	A*68:02	A68	12138	414	2868
29	A*68:01	A68	3716	1040	5552
31	A*69:01	A69	1608	245	2474
32	A*74:01	A74	0	89	488
33	A*80:01	A80	13148	5673	15132
97	B*13:01	B13	6276	1197	4948
36	B*13:02	B13	6174	1655	5345
47	B*18:01	B18	17203	6585	17669
48	B*27:08	B27	5391	761	3076
16	B*27:05	B27	3825	528	3515
49	B*35:01	B35	27597	14421	24224
50	B*37:01	B37	6483	2307	7595
51	B*38:01	B38	897	265	1359
52	B*39:01	B39	308	128	839
55	B*41:01	B41	3123	478	1912
56	B*42:01	B42	1168	262	962
58	B*44:03	B44	5444	1215	3222
57	B*44:02	B44	5250	667	1948
59	B*45:01	B45	5233	1174	5327
63	B*46:01	B46	27553	15839	23994
61	B*47:01	B47	2910	348	2135
62	B*48:01	B48	1427	326	1915
60	B*49:01	B49	24090	12403	21418
64	B*50:01	B50	22885	11102	19389
66	B*51:02	B51	27696	15572	23833
65	B*51:01	B51	26541	14732	24217
67	B*52:01	B52	25960	8450	16974
68	B*53:01	B53	27355	15176	24713
69	B*54:01	B54	14828	4148	10413

70	B*55:01	B55	7491	1109	4757
71	B*56:01	B56	24980	11102	1950
73	B*57:03	B57	16751	5174	9077
72	B*57:01	B57	18834	5150	9682
74	B*58:01	B58	20168	5778	10968
75	B*59:01	B59	4385	754	3824
53	B*40:01	B60	3106	613	2651
99	B*40:06	B61	7931	1476	4611
54	B*40:02	B61	3876	1037	3482
40	B*15:01	B62	25079	9498	17040
46	B*15:16	B63	23661	9166	15435
37	B*14:01	B64	4290	1277	4519
38	B*14:02	B65	3662	759	3341
76	B*67:01	B67	697	311	1171
34	B*07:02	B7	10220	3687	7065
43	B*15:10	B71	25316	11043	19336
42	B*15:03	B72	22457	9470	15974
77	B*73:01	B73	19828	4375	12684
98	B*15:11	B75	26462	12661	20271
41	B*15:02	B75	26833	11405	19516
44	B*15:12	B76	6930	1189	3238
45	B*15:13	B77	27314	10092	17466
78	B*78:01	B78	29223	14375	24192
35	B*08:01	B8	474	91	751
79	B*81:01	B81	2208	424	1753
80	B*82:01	B82	2056	348	1880
81	C*01:02	Cw1	27135	15206	23505
83	C*03:02	Cw10	27962	15413	24421
85	C*03:04	Cw10	26353	16014	23826
91	C*12:03	Cw12	27703	17263	24379
92	C*14:02	Cw14	33080	15027	25061
93	C*15:02	Cw15	26874	15574	22884
94	C*16:01	Cw16	33452	17344	27108
95	C*17:01	Cw17	25486	8460	16084
96	C*18:02	Cw18	30038	15723	26483
82	C*02:02	Cw2	31494	17204	25283
86	C*04:01	Cw4	35287	15740	26924
87	C*05:01	Cw5	28356	16422	24019
88	C*06:02	Cw6	31248	17579	25169
89	C*07:02	Cw7	6108	1565	4913
90	C*08:01	Cw8	29108	16649	25399
84	C*03:03	Cw9	27289	15507	23750

Table 2b: Results from LABScreen SAB Class II Test Results Across Multiple Sample Dates

One Lambda SAB Class II Kit - MFI			Sample Date		
Bead ID	Allele Specificity	Specificity	03/12/2021	20/08/2021	03/03/2021
68	DPA1*02:01, DPB1*01:01	DP1	0	0	0
67	DPA1*01:03, DPB1*01:01	DP1	7847	6141	8338
80	DPA1*02:02, DPB1*10:01	DP10	337	169	319
81	DPA1*01:03, DPB1*11:01	DP11	7659	7192	8434
97	DPA1*02:02, DPB1*11:01	DP11	1652	572	599
85	DPA1*03:01, DPB1*13:01	DP13	26009	19985	23740
83	DPA1*02:01, DPB1*13:01	DP13	290	165	270
84	DPA1*02:02, DPB1*13:01	DP13	261	240	277
86	DPA1*02:01, DPB1*14:01	DP14	198	258	207
87	DPA1*02:01, DPB1*15:01	DP15	26943	20124	23716
88	DPA1*02:01, DPB1*17:01	DP17	16704	12963	15466
89	DPA1*02:01, DPB1*18:01	DP18	28548	23560	24690
91	DPA1*01:04, DPB1*18:01	DP18	27548	22610	24684
90	DPA1*01:05, DPB1*18:01	DP18	27441	22879	24642
92	DPA1*01:03, DPB1*19:01	DP19	9541	7492	8501
93	DPA1*03:01, DPB1*20:01	DP20	27732	21712	24113
94	DPA1*01:03, DPB1*23:01	DP23	7840	7838	8690
82	DPA1*01:03, DPB1*28:01	DP28	8647	7438	8831
95	DPA1*01:05, DPB1*28:01	DP28	28629	23244	24756
69	DPA1*01:03, DPB1*02:01	DP28	8553	7582	9497
96	DPA1*04:01, DPB1*28:01	DP28	27503	22799	24554
72	DPA1*01:05, DPB1*03:01	DP3	8907	6837	8450
71	DPA1*01:03, DPB1*03:01	DP3	8599	5570	8517
73	DPA1*02:01, DPB1*03:01	DP3	129	62	170
74	DPA1*01:03, DPB1*04:01	DP4	8919	6215	8754
75	DPA1*01:03, DPB1*04:02	DP4	8258	6348	8691
76	DPA1*02:01, DPB1*05:01	DP5	1816	477	770
70	DPA1*02:02, DPB1*05:01	DP5	0	0	0
78	DPA1*01:03, DPB1*06:01	DP6	6779	7550	9747
77	DPA1*02:01, DPB1*06:01	DP6	831	677	1075
79	DPA1*02:01, DPB1*09:01	DP9	65	98	134
42	DQA1*05:01, DQB1*02:01	DQ2	528	686	848
43	DQA1*02:01, DQB1*02:02	DQ2	0	38	58
41	DQA1*04:01, DQB1*02:01	DQ2	0	19	54
40	DQA1*03:01, DQB1*02:01	DQ2	0	24	27
39	DQA1*02:01, DQB1*02:01	DQ2	0	0	0
47	DQA1*04:01, DQB1*04:02	DQ4	195	133	109
44	DQA1*02:01, DQB1*04:01	DQ4	14	104	199
46	DQA1*02:01, DQB1*04:02	DQ4	0	79	80

45	DQA1*03:03, DQB1*04:01	DQ4	0	0	0
49	DQA1*01:02, DQB1*05:02	DQ5	0	0	0
48	DQA1*01:01, DQB1*05:01	DQ5	0	0	31
50	DQA1*01:03, DQB1*06:01	DQ6	264	314	337
53	DQA1*01:03, DQB1*06:03	DQ6	115	90	114
55	DQA1*01:02, DQB1*06:09	DQ6	0	0	0
54	DQA1*01:02, DQB1*06:04	DQ6	0	57	39
52	DQA1*01:01, DQB1*06:02	DQ6	0	32	0
51	DQA1*01:02, DQB1*06:02,	DQ6	0	12	31
59	DQA1*05:05, DQB1*03:19	DQ7	1481	938	1291
56	DQA1*03:01, DQB1*03:01	DQ7	998	207	315
58	DQA1*05:03, DQB1*03:01	DQ7	420	344	404
60	DQA1*06:01, DQB1*03:01	DQ7	304	447	482
57	DQA1*02:01, DQB1*03:01	DQ7	50	89	71
61	DQA1*02:01, DQB1*03:02	DQ8	449	190	292
63	DQA1*03:02, DQB1*03:02	DQ8	295	186	285
62	DQA1*03:01, DQB1*03:02	DQ8	250	97	273
65	DQA1*03:01, DQB1*03:03	DQ9	740	142	219
66	DQA1*03:02, DQB1*03:03	DQ9	124	138	204
64	DQA1*02:01, DQB1*03:03	DQ9	51	70	62
4	DRB1*01:02	DR1	0	0	0
3	DRB1*01:01	DR1	0	0	0
17	DRB1*10:01	DR10	0	0	0
5	DRB1*01:03	DR103	0	0	13
19	DRB1*11:04	DR11	12	36	86
18	DRB1*11:01	DR11	0	0	27
21	DRB1*12:02	DR12	0	0	0
20	DRB1*12:01	DR12	0	0	0
23	DRB1*13:03	DR13	0	0	0
22	DRB1*13:01	DR13	0	0	0
24	DRB1*14:01	DR14	90	135	171
26	DRB1*14:54	DR14	0	0	0
25	DRB1*14:02	DR14	0	0	0
27	DRB1*15:01	DR15	115	152	253
29	DRB1*15:03	DR15	0	0	0
28	DRB1*15:02	DR15	0	49	50
31	DRB1*16:02	DR16	0	155	225
30	DRB1*16:01	DR16	0	0	0
6	DRB1*03:01	DR17	0	0	0
7	DRB1*03:02	DR18	0	0	0
13	DRB1*04:03	DR4	307	201	249
11	DRB1*04:05	DR4	0	0	3
10	DRB1*04:04	DR4	0	0	0
9	DRB1*04:02	DR4	0	0	0

8	DRB1*04:01	DR4	0	0	0
38	DRB5*02:02	DR51	0	0	0
37	DRB5*01:01	DR51	0	0	0
32	DRB3*01:01	DR52	108	137	94
34	DRB3*03:01	DR52	0	155	227
33	DRB3*02:02	DR52	0	18	103
36	DRB4*01:03	DR53	0	0	0
35	DRB4*01:01	DR53	0	0	0
12	DRB1*07:01	DR7	0	0	13
14	DRB1*08:01	DR8	0	94	70
15	DRB1*09:01	DR9	10	203	134
16	DRB1*09:02	DR9	0	0	10

The patient was listed on the deceased donor transplant register for a kidney transplant in December 2021.

Q1.1) What, if any, antibodies would you class as unacceptable to transplant against (unacceptable antigens)?

Specificity	Summary		
	UK&I %	RoW %	Total %
A1	0	0	0
A2	14	14	14
A3	0	0	0
A11	7	14	11
A23	0	0	0
A24	0	0	0
A25	0	0	0
A26	0	5	3
A29	7	5	6
A30	0	10	6
A31	0	0	0
A32	0	0	0
A33	57	62	60
A34	93	62	74
A36	0	0	0
A43	36	38	37
A66	86	67	74
A68	100	71	83
A69	43	38	40
A74	0	0	0
A80	100	76	86
B13	93	67	77
B18	100	76	86
B27	93	57	71
B35	100	100	100
B37	93	62	74
B38	0	10	6
B39	0	0	0
B41	57	43	49
B42	0	10	6
B44	86	57	69
B45	93	67	77
B46	100	81	89
B47	71	48	57
B48	14	14	14
B49	100	76	86
B50	100	81	89
B51	93	81	86
B52	93	76	83
B53	93	81	86

Specificity	Summary		
	UK&I %	RoW %	Total %
B54	93	76	83
B55	93	57	71
B56	93	76	83
B57	93	76	83
B58	93	81	86
B59	86	62	71
B60	86	48	63
B61	100	57	74
B62	100	76	86
B63	100	76	86
B64	93	52	69
B65	93	48	66
B67	0	14	9
B7	100	57	74
B71	100	76	86
B72	100	76	86
B73	100	71	83
B75	100	76	86
B76	100	48	69
B77	93	81	86
B78	100	76	86
B8	0	0	0
B81	50	38	43
B82	50	38	43
Cw1	100	71	83
Cw10	100	71	83
Cw12	100	90	94
Cw14	100	71	83
Cw15	100	71	83
Cw16	100	71	83
Cw17	100	67	80
Cw18	100	71	83
Cw2	100	71	83
Cw4	100	71	83
Cw5	100	71	83
Cw6	100	71	83
Cw7	14	33	26
Cw8	100	71	83
Cw9	100	71	83

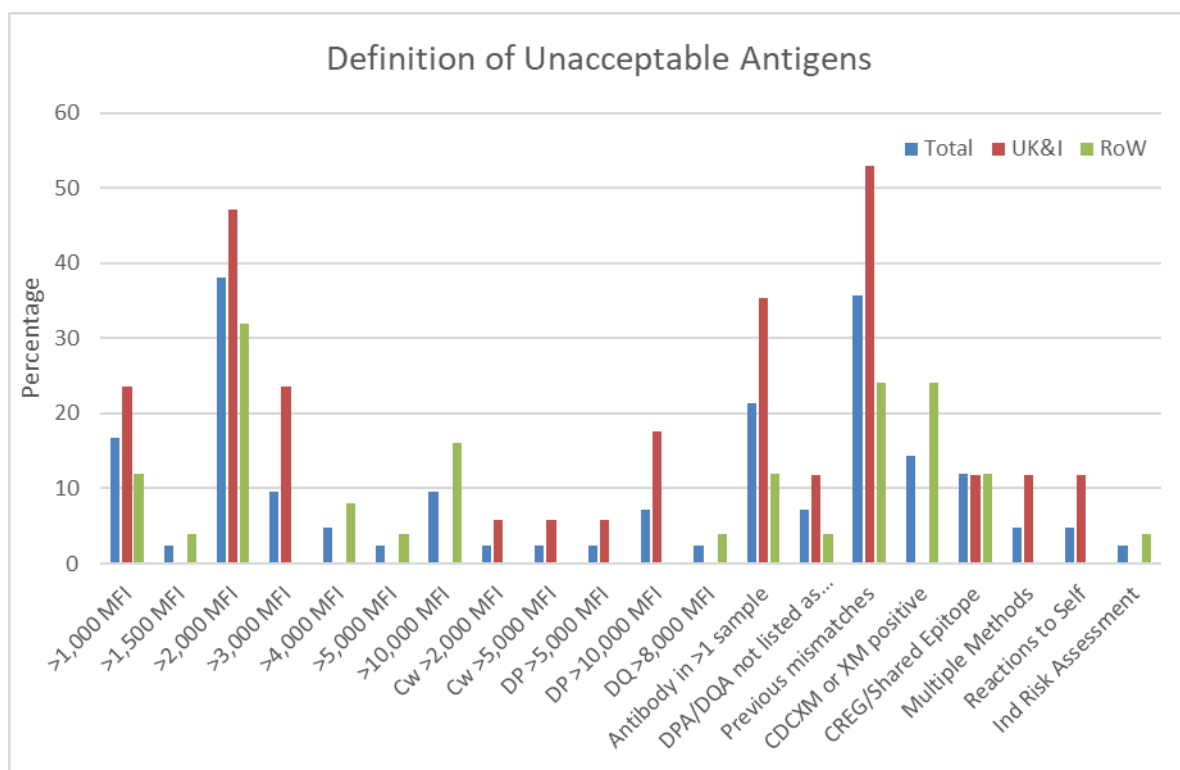
Specificity	Summary		
	UK&I %	RoW %	Total %
DP1	0	4	3
DP2	29	13	19
DP10	0	9	5
DP11	7	17	14
DP13	21	13	16
DP14	0	0	0
DP15	100	65	78
DP17	100	65	78
DP18	100	65	78
DP19	50	30	38
DP20	71	39	51
DP23	64	35	46
DP28	93	65	76
DP3	14	13	14
DP4:01	79	65	70
DP4:02	79	70	73
DP5	0	4	3
DP6	21	22	22
DP9	0	0	0
DQ2	0	0	0
DQ4	0	0	0
DQ5	0	0	0
DQ6	0	0	0
DQ7	0	0	0
DQ8	0	0	0
DQ9	0	0	0
DR1	0	0	0
DR10	0	0	0
DR103	0	0	0
DR11	0	0	0
DR12	0	0	0
DR13	0	0	0
DR14	0	0	0
DR15	0	0	0
DR16	0	0	0
DR17	0	0	0
DR18	0	0	0
DR4	0	0	0
DR51	0	0	0
DR52	0	0	0
DR53	0	0	0
DR7	0	0	0
DR8	0	0	0
DR9	0	0	0
DPA1*01:03	36	70	57
DPA1*01:04	14	26	22
DPA1*01:05	29	39	35
DPA1*03:01	21	39	32
DPA1*04:01	7	4	5
DPA1*02:01	0	9	5
DQA1*05:05	0	9	5
DQB1*03:19	0	4	3

Other responses:

UK&I	<ul style="list-style-type: none"> List everything above potential Cw self (C*07:02). From associations patient likely type C*07:01 (not on OL kit) so this may not be self. There are two epitope differences between C*07:01 and C*07:02 (including 65QKR). Interestingly the 65QKR epitope is present on the previous MM likely C*12 allele. List DPB specificities with strong association with reacting DPA specificities. A note to the patients file indicating the risk of a positive crossmatch would be made. We would class any antibody with an MFI over 3,000 which is seen on two occasions and list all as unacceptable antigens. For DPB1 list with MFI over 10,000. Broadly, we would list specificities >2000 MFI as Unacceptable Antigens, based on most-recent serum sample. We note, however, the high MFI of the Cw7 bead, which is a self antigen that cannot be listed. This calls into question the reliability of this assay for making these decisions without other evidence of whether these antibody specificities are genuine.
RoW	<ul style="list-style-type: none"> All with MFI over 2000. All Antibodies against HLA-A, -B, DRB1 > 1000 MFI and anti-HLA-DQ >8000 MFI. All HLA-antibodies directed against repeated HLA-mismatches (independent of MFI). Generally renal transplantation against DSAs > 3000 MFI is not performed. We do not generally define unacceptable mismatches for our common waitlist. Any antigen to which the patient has DSA antibodies to with an MFI over 1500.

Q1.2) How do you define unacceptable antigens?

Definition	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
>1,000 MFI	7	17	4	24	3	12
>1,500 MFI	1	2	0	0	1	4
>2,000 MFI	16	38	8	47	8	32
>3,000 MFI	4	10	4	24	0	0
>4,000 MFI	2	5	0	0	2	8
>5,000 MFI	1	2	0	0	1	4
>10,000 MFI	4	10	0	0	4	16
Cw >2,000 MFI	1	2	1	6	0	0
Cw >5,000 MFI	1	2	1	6	0	0
DP >5,000 MFI	1	2	1	6	0	0
DP >10,000 MFI	3	7	3	18	0	0
DQ >8,000 MFI	1	2	0	0	1	4
Antibody in >1 sample	9	21	6	35	3	12
DPA/DQA not listed as UA	3	7	2	12	1	4
Previous mismatches	15	36	9	53	6	24
CDCXM or XM positive	6	14	0	0	6	24
CREG/Shared Epitope	5	12	2	12	3	12
Detected by Multiple Methods	2	5	2	12	0	0
Adjust Against Reactions to Self	2	5	2	12	0	0
Individual Risk Assessment	1	2	0	0	1	4



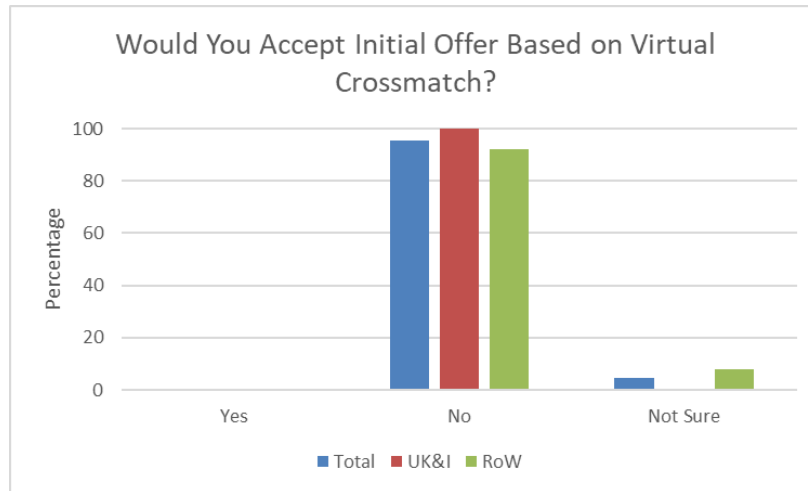
The patient receives a deceased donor offer in January 2022. Details of the donor are provided in Table 3.

Table 3: Details of Deceased Donor Offer 1

Donor Type	DBD
Donor HLA Type	A*01, A*24:02 ; B*08, B*39; C*07, C*-; DRB1*08 , DRB1*03:01; DQB1*02, DQB1*04 ; DQA1*04 , DQA1*05; DPB1*01:01, DPB1*03:01 ; DPA1*01:03 , DPA1*02
Mismatch Grade	101
Donor Age	49
Donor Gender	Male

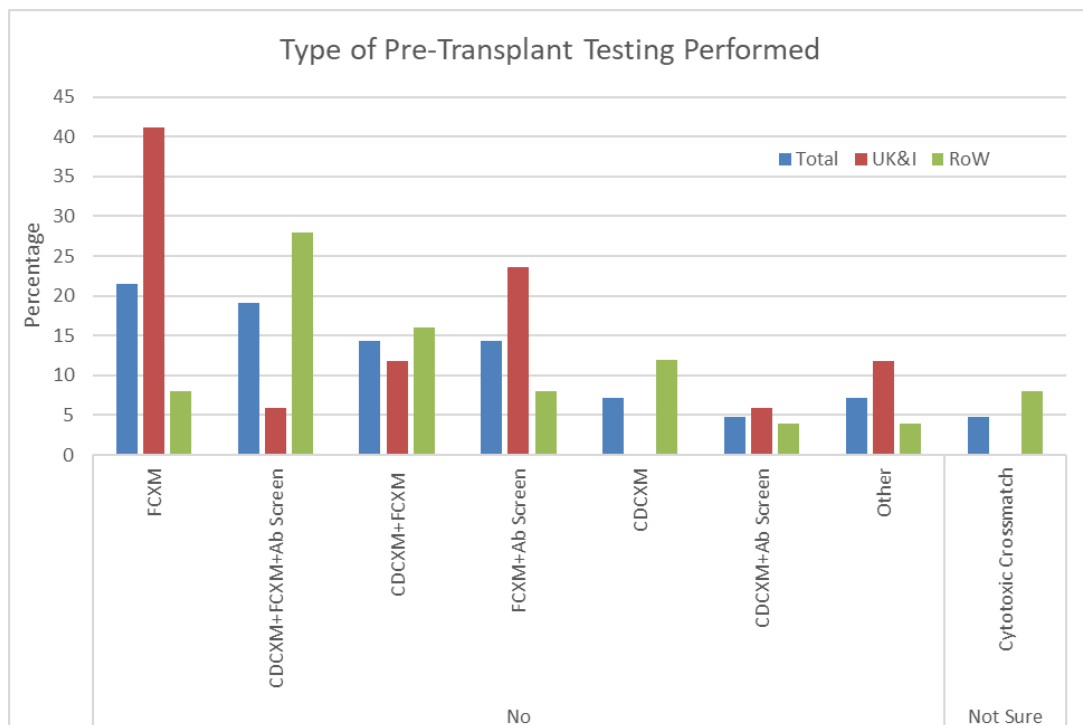
Q2.1) Would you accept this offer based on a virtual crossmatch (the omission of any pre-transplant testing)?

Response	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
Yes	0	0	0	0	0	0
No	40	95	17	100	23	92
Not Sure	2	5	0	0	2	8



Q2.2) If you would not accept this offer based on a virtual crossmatch what pre-transplant testing would you perform?

Response	Reason	Total (n=42)		UK&I (n=17)		RoW (n=25)	
		Count	%	Count	%	Count	%
No	FCXM	9	21	7	41	2	8
	CDCXM+FCXM+Ab Screen	8	19	1	6	7	28
	CDCXM+FCXM	6	14	2	12	4	16
	FCXM+Ab Screen	6	14	4	24	2	8
	CDCXM	3	7	0	0	3	12
	CDCXM+Ab Screen	2	5	1	6	1	4
	Other	3	7	2	12	1	4
Not Sure	Cytotoxic Crossmatch	2	5	0	0	2	8

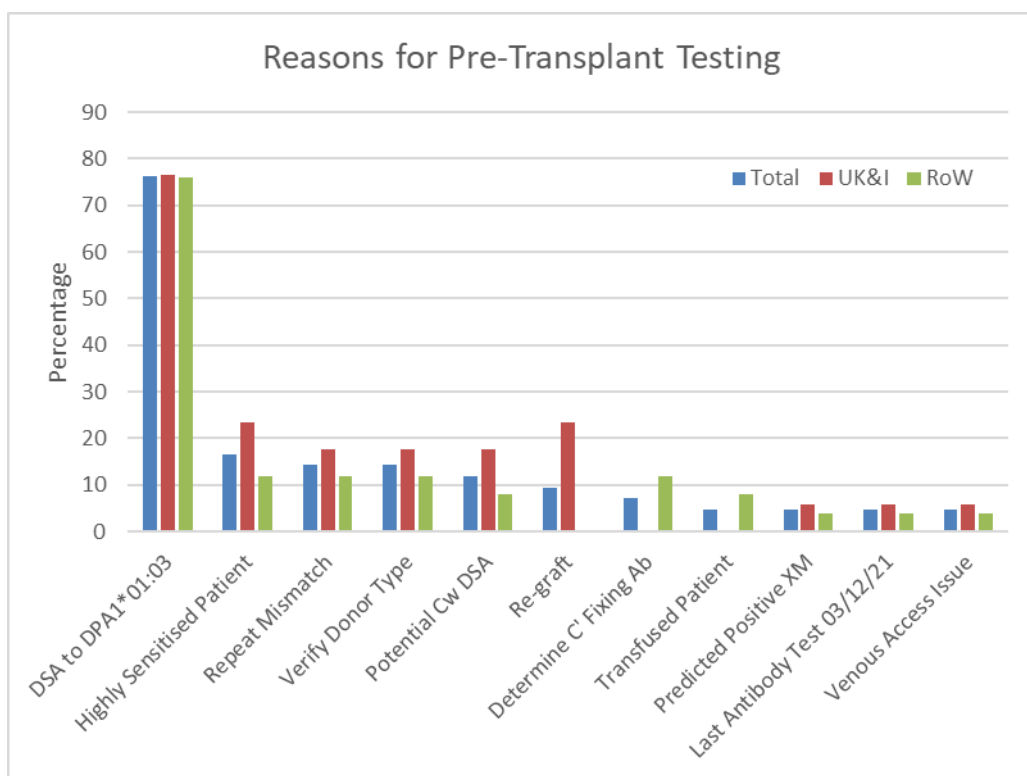


Other responses:

UK&I	<ul style="list-style-type: none"> • A discussion would be had with the clinical team to discuss the high likelihood of a positive flow crossmatch due to the presence of high level of DPA1*01:03 DSA which is also a repeat mismatch. The discussion would also include the option of doing further testing including CDC and flow cytometry crossmatching to confirm the level of risk. • In addition to allogeneic flow cytometric crossmatch, we would also perform autologous flow cytometric crossmatch. • HLA typing using LinkSeq SABR kit if time allowed and samples available, to ascertain Cw7 alleles present in donor and recipient. • None. A compatibility check at time of offer would highlight unacceptable DPA1*01:03 antigen and the offer would be rejected. • Verification of donor HLA type.
RoW	<ul style="list-style-type: none"> • Two fields donor HLA-C*typing. • B cell Cytotoxic Crossmatching. • We would not omit from pre-transplant testing as it is an immunological challenging patient (highly immunized due previous TX and transfusions). • C1q, NGS typing on donor. • High resolution HLA typing on both donor and patient. • Check LABScreen results on seraclean treated serum and on Immucor Lifescreen and LSA kits (notably to confirm locus C immunisation)

Q2.3) Why have you made this decision?

Definition	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
DSA to DPA1*01:03	32	76	13	76	19	76
Highly Sensitised Patient	7	17	4	24	3	12
Repeat Mismatch	6	14	3	18	3	12
Verify Donor Type	6	14	3	18	3	12
Potential Cw Allele Specific DSA	5	12	3	18	2	8
Re-graft	4	10	4	24	0	0
Determine Complement Fixing Antibodies	3	7	0	0	3	12
Transfused Patient	2	5	0	0	2	8
Predicted Positive Crossmatch	2	5	1	6	1	4
Last Antibody Test 03/12/21	2	5	1	6	1	4
Venous Access Issue	2	5	1	6	1	4



A flow cytometry crossmatch was performed, the results are shown in Table 4.

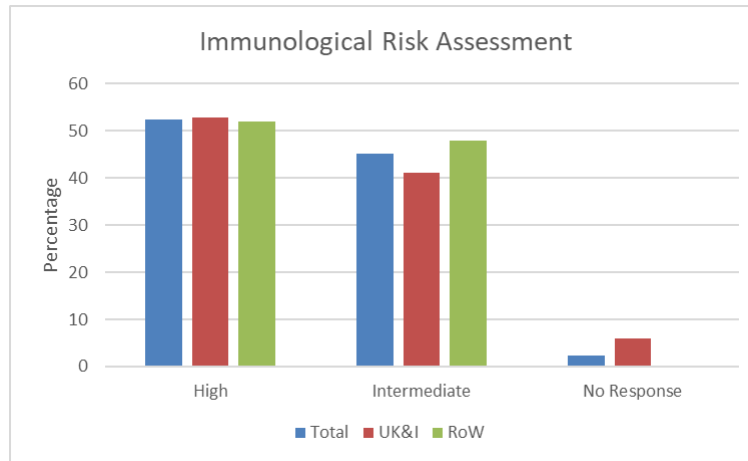
Table 4: Details of Flow Cytometry Crossmatch Results for Deceased Donor Offer 1

FCXM Results	Allogeneic Results			
	T-Cell	LCS*	B-Cell	LCS*
03/03/2021	NEG	11	POS	106
03/12/2021	NEG	2	POS	96

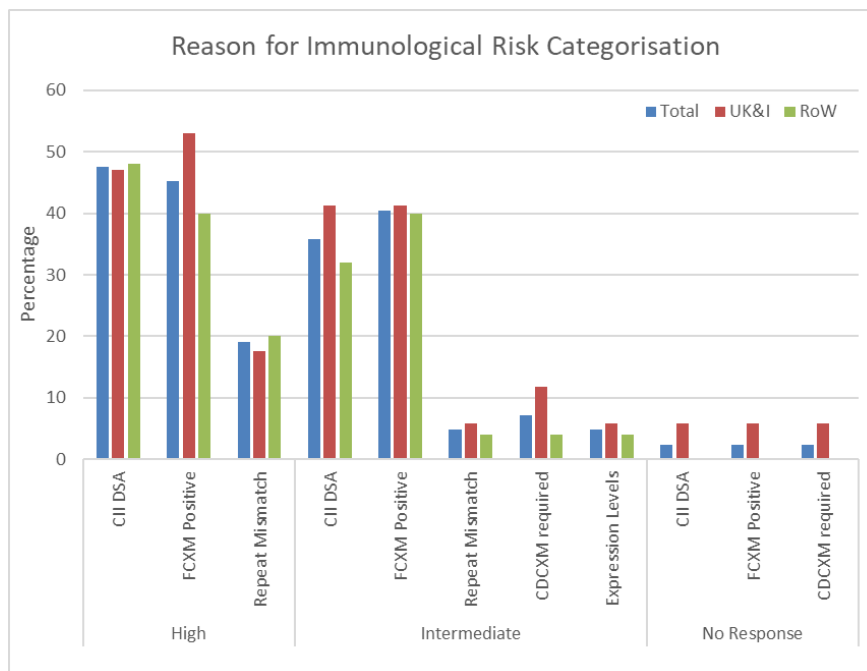
*A Linear Channel Shift (LCS) of ≥ 40 is considered positive

Q2.4) – What immunological risk would you now assign to this transplant and why?

Response	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
High	22	52	9	53	13	52
Intermediate	19	45	7	41	12	48
No Response	1	2	1	6	0	0

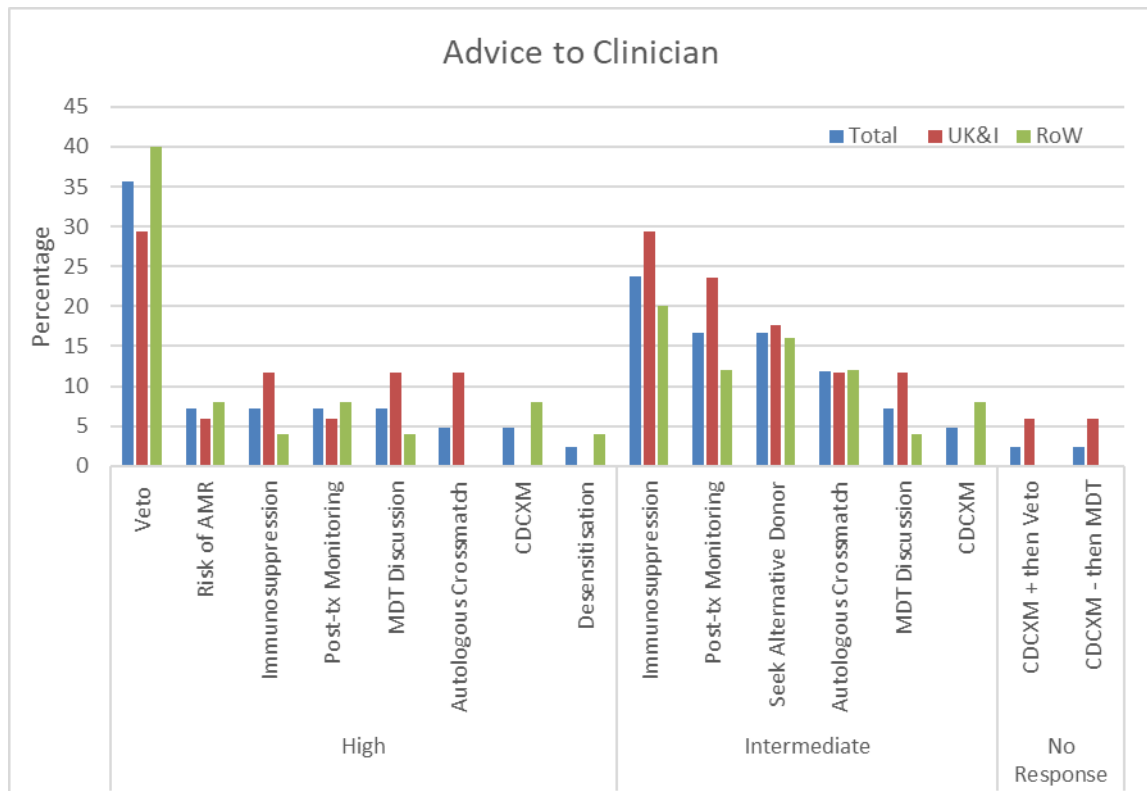


Risk Categorisation	Reason	Total (n=42)		UK&I (n=17)		RoW (n=25)	
		Count	%	Count	%	Count	%
High	CII DSA (High MFI, Current Date)	20	48	8	47	12	48
	FCXM Positive	19	45	9	53	10	40
	Repeat Mismatch	8	19	3	18	5	20
Intermediate	CII DSA (High MFI, Current Date)	15	36	7	41	8	32
	FCXM Positive	17	40	7	41	10	40
	Repeat Mismatch	2	5	1	6	1	4
	CDCXM required	3	7	2	12	1	4
	Expression Levels of Cw and DP	2	5	1	6	1	4
No Response	CII DSA (High MFI, Current Date)	1	2	1	6	0	0
	FCXM Positive	1	2	1	6	0	0
	CDCXM required	1	2	1	6	0	0



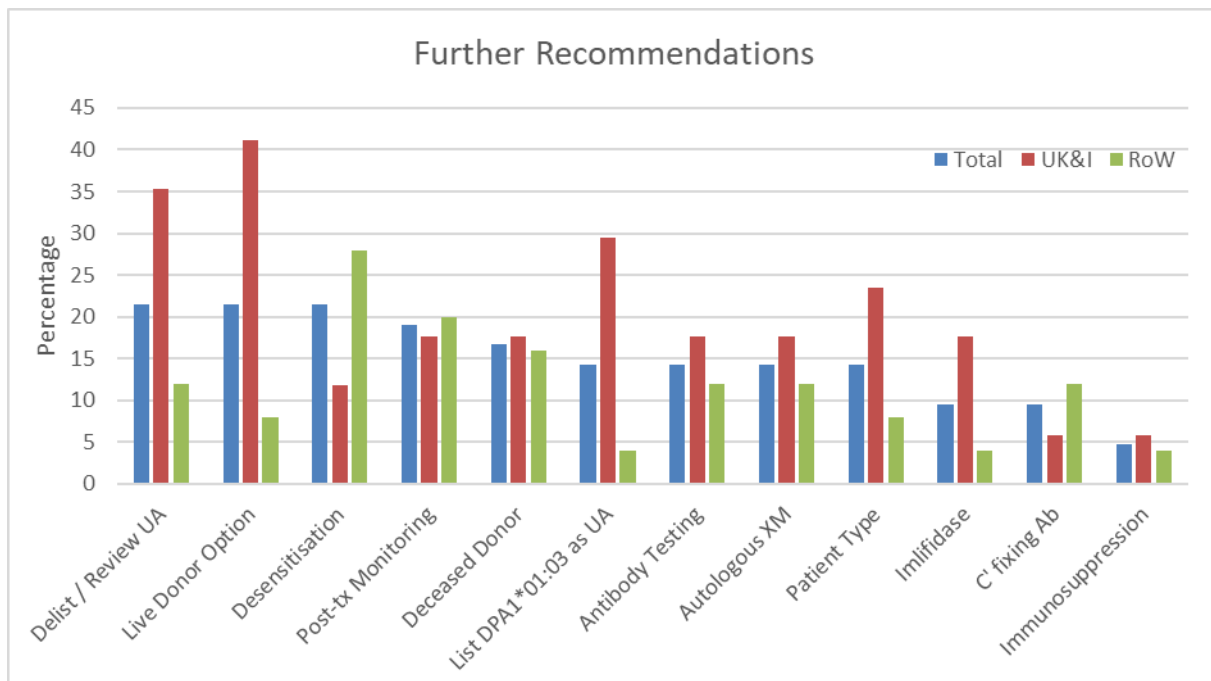
Q2.5) – What advice would you provide to a Clinician?

Risk	Clinical Advice	Total (n=42)		UK&I (n=17)		RoW (n=25)	
		Count	%	Count	%	Count	%
High	Veto / Seek Alternative Donor	15	36	5	29	10	40
	Risk of Antibody Mediated Rejection	3	7	1	6	2	8
	Augmented Immunosuppression	3	7	2	12	1	4
	Post-transplant Monitoring	3	7	1	6	2	8
	MDT Discussion	3	7	2	12	1	4
	Autologous Crossmatch	2	5	2	12	0	0
	CDCXM	2	5	0	0	2	8
	Desensitisation	1	2	0	0	1	4
Intermediate	Augmented Immunosuppression	10	24	5	29	5	20
	Post-transplant Monitoring	7	17	4	24	3	12
	Seek Alternative Donor	7	17	3	18	4	16
	Autologous Crossmatch	5	12	2	12	3	12
	MDT Discussion	3	7	2	12	1	4
	CDCXM	2	5	0	0	2	8
No Response	If CDCXM + then Veto	1	2	1	6	0	0
	If CDCXM - then MDT Discussion	1	2	1	6	0	0



Q2.6) – Would you make any further recommendations?

Recommendation	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
Delist / Review UA	9	21	6	35	3	12
Live Donor Option	9	21	7	41	2	8
Desensitisation	9	21	2	12	7	28
Increased Post-transplant Monitoring	8	19	3	18	5	20
Wait for Alternative Deceased Donor	7	17	3	18	4	16
List DPA1*01:03 as UA	6	14	5	29	1	4
Further Antibody Testing	6	14	3	18	3	12
Autologous XM	6	14	3	18	3	12
High Resolution Patient Type	6	14	4	24	2	8
Treat with Imlifidase	4	10	3	18	1	4
Determine C' fixing Antibodies	4	10	1	6	3	12
Offer Enhanced Immunosuppression	2	5	1	6	1	4



The patient received a second deceased donor offer in March 2023. Details of the donor are shown in Table 5.

Table 5: Details of Deceased Donor Offer 2

Donor Type	DCD
Donor HLA Type	A*24:02, A*30; B*08, B*40:02; C*07, C*-; DRB1*16, DRB1*03:01; DQB1*02, DQB1*05; DQA1*01, DQA1*05; DPB1*01:01, DPB1*03:01; DPA1*01:03, DPA1*02
Mismatch Grade	211
Donor Age	05/12/1983
Donor Gender	Female

A summary of potential donor directed antibodies are provided in Table 6 and results from a flow cytometry crossmatch between the patient and Donor 2 are provided in Table 7.

Table 6: Details of Donor Directed Antibodies from the LABScreen SAB Class I and Class II Kits Across Multiple Sample Dates

One Lambda SAB			Sample Date							
Bead ID	Allele Spec	Spec	08/03/23	21/12/22	15/07/22	01/04/22	13/01/22	03/12/21	20/08/21	03/03/21
11	A*24:02	A24	195	0	197	0	73	315	46	406
12	A*24:03	A24	315	0	424	0	109	0	103	670
19	A*30:02	A30	180	69	418	0	170	1159	56	423
18	A*30:01	A30	236	10	388	0	179	394	54	396
99	B*40:06	B61	3155	1910	6871	4014	2897	7931	1476	4611
54	B*40:02	B61	2079	1155	4705	2221	1751	3876	1037	3482
31	DRB1*16:02	DR16	0	0	0	0	0	0	155	225
30	DRB1*16:01	DR16	0	0	0	0	0	0	0	0
38	DRB5*02:02	DR51	0	0	0	0	0	0	0	0
37	DRB5*01:01	DR51	0	0	0	0	0	0	0	0
72	DPA1*01:05, DPB1*03:01	DP3	7530	7868	8070	6192	7347	8907	6837	2480
71	DPA1*01:03, DPB1*03:01	DP3	8602	8537	7101	7292	7203	8599	5570	8517
73	DPA1*02:01, DPB1*03:01	DP3	0	0	0	18	150	129	62	170
74	DPA1*01:03, DPB1*04:01	DP4	8866	7530	8171	7069	7070	8919	6215	8754
75	DPA1*01:03, DPB1*04:02	DP4	8556	7502	8446	8500	7444	8258	6348	8691
67	DPA1*01:03, DPB1*01:01	DP1	8592	9104	8299	7027	7201	7847	6141	8338
81	DPA1*01:03, DPB1*11:01	DP11	9405	8840	9152	8493	8415	7659	7192	8434
92	DPA1*01:03, DPB1*19:01	DP19	9807	8147	8704	7777	6825	9541	7492	8501
94	DPA1*01:03, DPB1*23:01	DP23	8597	9102	8898	9551	8991	7840	7838	8690
82	DPA1*01:03, DPB1*28:01	DP28	8784	7575	7771	7499	7991	8647	7438	8831
69	DPA1*01:03, DPB1*02:01	DP28	9892	8149	9943	8602	7409	8553	7582	9497
78	DPA1*01:03, DPB1*06:01	DP6	9250	7856	8438	9159	8492	6779	7550	9747

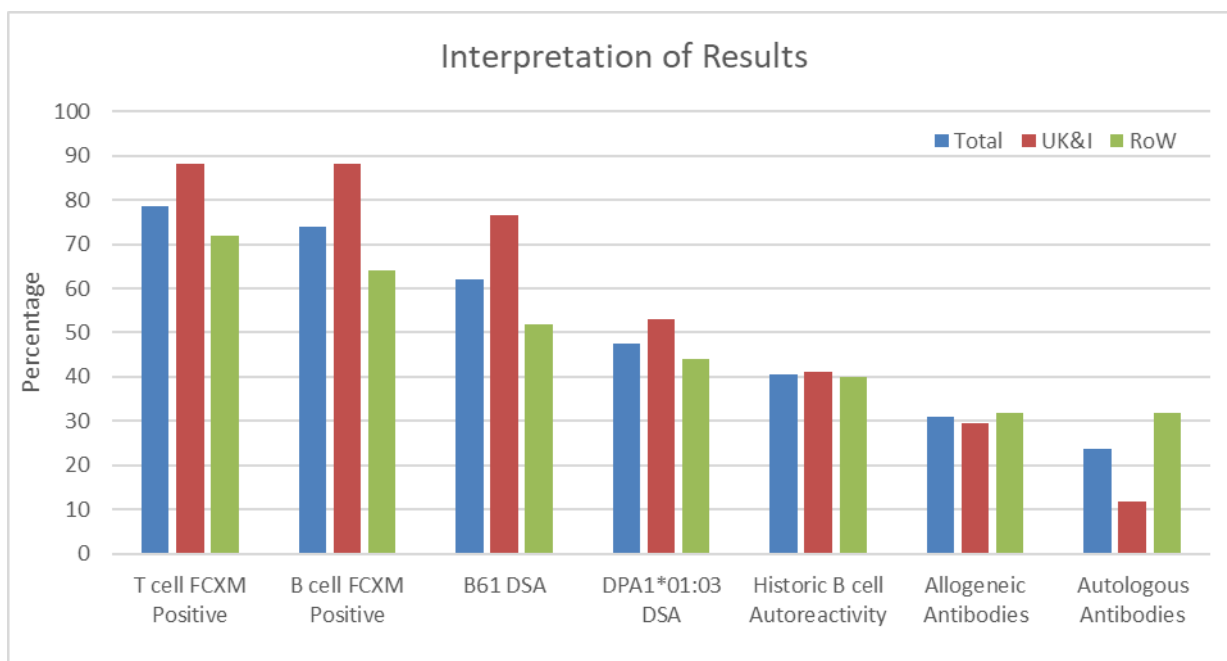
Table 7: Results of Flow Cytometry Crossmatch for Deceased Donor Offer 2

FCXM Results	Allogeneic Results				Autologous Results			
	T-Cell	LCS*	B-Cell	LCS*	T-Cell	LCS*	B-Cell	LCS*
03/12/2021	POS	65	POS	99	NEG	6	POS	75
15/07/2022	POS	53	POS	89	NEG	1	POS	80
08/03/2023	POS	54	POS	62	NEG	4	NEG	39

*A Linear Channel Shift (LCS) of ≥ 40 is considered positive

Q3.1) – How would you interpret these results?

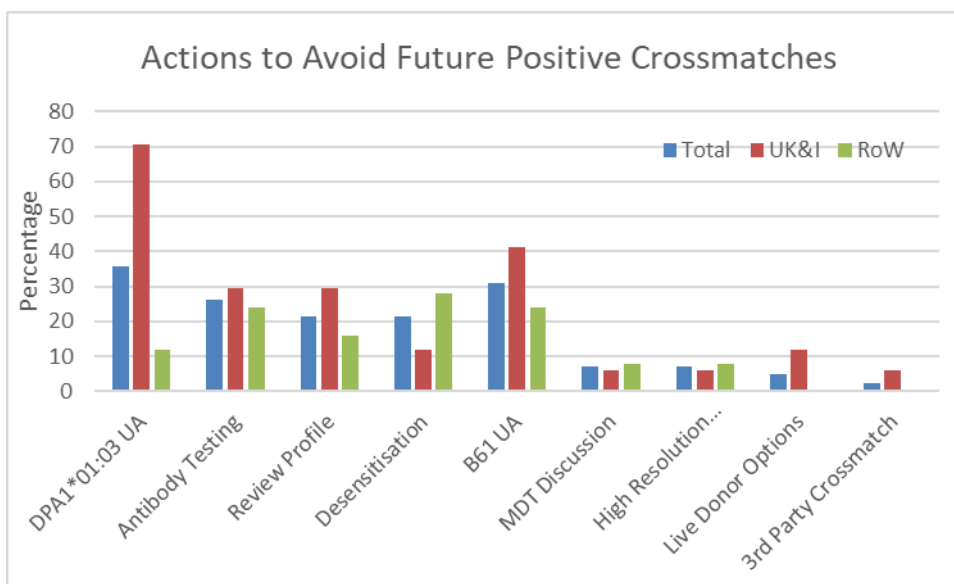
Interpretation	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
T cell FCXM Positive	33	79	15	88	18	72
B cell FCXM Positive	31	74	15	88	16	64
B61 DSA	26	62	13	76	13	52
DPA1*01:03 DSA	20	48	9	53	11	44
Historic B cell Autoreactivity	17	40	7	41	10	40
Allogeneic Antibodies	13	31	5	29	8	32
Autologous Antibodies	10	24	2	12	8	32



This offer was also declined by the clinical team.

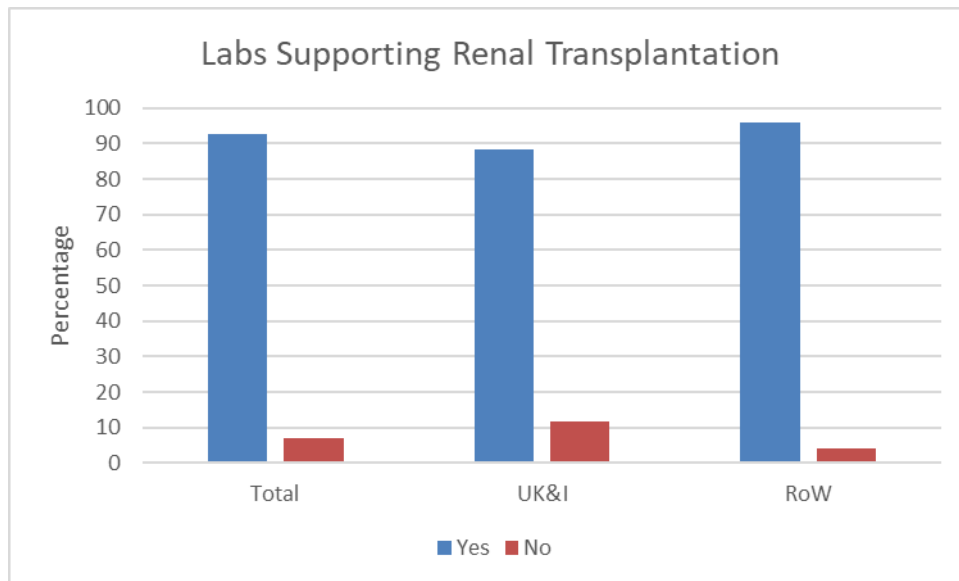
Q3.2) – What action, if any, would you take to avoid further positive crossmatches?

Action	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
List DPA1*01:03 as UA (Surrogate listing of DPB1)	15	36	12	71	3	12
Further Antibody Testing/Epitope Analysis	11	26	5	29	6	24
Review Antibody Profile / Delist	9	21	5	29	4	16
Desensitisation	9	21	2	12	7	28
List B61 as UA	13	31	7	41	6	24
MDT Discussion	3	7	1	6	2	8
Patient High Resolution Typing	3	7	1	6	2	8
Consider Live Donor Options	2	5	2	12	0	0
3rd Party Crossmatch	1	2	1	6	0	0



Q4) – Does your laboratory support testing for kidney transplantation?

Response	Total (n=42)		UK&I (n=17)		RoW (n=25)	
	Count	%	Count	%	Count	%
Yes	39	93	15	88	24	96
No	3	7	2	12	1	4



Q5) – Do you have any further comments on this case?

- This patient could potentially be a suitable candidate for Imlifidase treatment to increase their chances of being transplanted.
- Results provided on only 3 samples and 20/08/21 sample was inconsistent – would have repeated this sample and confirm UAGs with further sample. Cw7 self reactivity? - Perform SABs with a second SABs kit to confirm UAGs.
- It would be helpful to see the CDC XM result. Matchability score/ patient tier is not provided.
- Organ type of previous transplant. Need to know when first transplant was deemed to have failed and whether transplant nephrectomy was performed and/or date of cessation of immunosuppression, if applicable.
- It would be helpful to have more information on the patient such as medication (whether the patient is currently on any immunosuppressants or any other medication that would impact on the antibody level or FCXM results).
- More data required around high resolution typing for recipient to aid antibody analysis.
- We would have performed an autologous crossmatch result for the first kidney transplant to aid interpretation.
- The middle antibody result dated 20/08/21 seems lower than the other two results and would question the results obtained and would repeat to confirm.
- Use of further testing kits, extended panels and surrogate crossmatching maybe informative and help avoid positive crossmatches.
- Based on the results of table 1, HLA-B61 would have been listed as unacceptable and the offer from donor 2 would never have been received.
- Review the results of sample dated 20/08/21; results are significantly reduced compared to the other two samples (particularly for the Class I).
- At this moment our laboratory does not offer yet for HLA-DP typing. This case study had helped us regarding the importance of performing HLA-DP and check the DSA against the HLA-DP locus.
- We are a little bit surprise of the FCXM result because in our experience DSA DPA* never give positive XM.

- Desensitisation treatment can help to reduce Antibody level. Recommend follow up Luminex test and regularly review antibody assignment (or surrogate flow XM for Unacceptable Antigen assignment from time to time). Donors' ABO results need to be provided.
- Patient may get to paired kidney program.
- In view of presence of multiple antibodies, we would recommend to do a physical crossmatch prior to transplant instead of depending solely on virtual crossmatch. Finding alternative donor for this highly sensitised patient for example registering into paired kidney exchange scheme.
- We have just started doing kidney transplantation. The scenario is quite challenging for us at present since we are novice. But it is very helpful and brainteasing.

Comments and suggested responses from the UK H&I experts providing this scenario*

Question 1

UK NEQAS for H&I cannot comment on the validity of unacceptable antigen definition strategies but we note some variability between individual responses. Laboratories should have robust processes to align testing to expected crossmatch results or clinical outcome. We would encourage all laboratories to complete regular clinical audits to determine if their definition of unacceptable antigens remains relevant.

Question 2

We would not consider it appropriate for the offer from Donor 1 to be assessed by virtual crossmatch (complete omission of laboratory testing pre-transplant). This is due to the presence of potential donor directed antibodies to DPA1*01:03 and DPB1*03:01 at an MFI level that could be clinically relevant. DPA1*01:03 is also a previous mismatch from the patient's previous graft.

UK NEQAS for H&I would state this transplant is an Intermediate level risk (https://bts.org.uk/wp-content/uploads/2016/09/06_BTS_BSHI_Antibodies-1.pdf). We have made this decision because the patient has a current and historic B cell flow cytometry crossmatch positive result in the presence of Class II donor specific antibodies.

We could advise performing an autologous crossmatch to determine if the reaction seen in the allogeneic crossmatch is due to allogeneic or autologous antibodies. High resolution typing of the patient would also assist in antibody definition as the patient has a potential allele specific Cw7 antibody. It would also be beneficial to test for antibodies using other methods such as Immucor Single Antigen Bead kits.

Question 3

The flow cytometry crossmatch against Donor 2 is T cell positive probably due to B61 donor directed antibody. The B cell flow cytometry crossmatch is positive probably due to DPA1*01:03 donor directed antibody. An autologous B cell crossmatch is historically positive but current negative which suggests the patient has autoantibodies in addition to donor directed antibodies.

In terms of further actions to avoid future positive crossmatches we would consider performing 3rd party crossmatching to inform the significance of the DPA antibody detected. We would consider listing of DPA1*01:03 via surrogate listing of the most common associated DPB antigens e.g. all DPB types that are in linkage with DPA1*01:03 such as DPB1*04:02 and DPB1*03:01 would be listed as unacceptable antigens to prevent future DPA incompatible offers.

We would also recommend liaising with the clinical team to discuss any live donor options, acceptable risk for the patient and whether the patient could tolerate desensitisation treatment. As the patient is highly sensitised it would be prudent to regularly review the patient's antibody profile and consider delisting antibodies to increase the likelihood of a transplant offer, especially if the patient is suffering venous access issues.

***Please note:**

These comments have been compiled by subject matter experts from the NEQAS Steering Committee in accordance with current guidelines. We accept that guidelines are not always explicit for every situation and therefore the responses may be aligned with the clinical practices of an individual transplant centre and may not be directly applicable across all settings. NEQAS are not necessarily endorsing these responses as the only correct action, just one possible view which, we acknowledge, may be biased towards UK practice.