Interpretive Educational Scheme (iED)
Clinical Scenario 1/2025 – Solid Organ Transplantation

Dispatched on 6th May 2025

We received 42 responses in total. 16 responses from UK and Ireland (UK&I) based laboratories and 26 responses from laboratories based in the Rest of the World (RoW).

Summary of Results

Samples from a patient, FA, assessed as suitable for kidney transplant, were received in your laboratory in October 2024. Details of the patient and initial test results are shown in Table 1.

The patient had previously received a liver transplant for alcohol related liver disease.

Table 1: Patient Information

Patient ID	FA
Primary Disease	Chronic renal disease
Current Age	44
Patient Sex	Female
Ethnicity	White British
Dialysis	Haemodialysis
Patient HLA Type	HLA-A*01, A*03; B*08, B*18, Bw6; C*07, -; DRB1*07, DRB1*15; DRB4*01:03:01:02N; DRB5*01; DQA1*01, DQA1*02; DQB1*03:03+, DQB1*06; DPB1*04:01, -
ABO Group	A Rh(D)+
Sensitising Events	*Previous Transplants*: Liver transplant in November 2021 HLA-A*02:01, A*24:02; B*07:02, B*52:01; C*07:02, C*12:02; DRB1*01:01, -; DQA1*01, -; DQB1*05:01, -; DPB1*02:01, DPB1*04:02
	Blood Transfusions: Multiple – dates unknown
	Pregnancies: 3 live births 2000, 2010, 2013

HLA antibody detection was performed using One Lambda LABScreen Single Antigen Bead (SAB) kits on two serum dates taken prior to the liver transplant and two serum dates after the liver transplantation. A summary of the results are shown in Table 2.

Table 2: LABScreen SAB Kit Testing Across Multiple Sample Dates

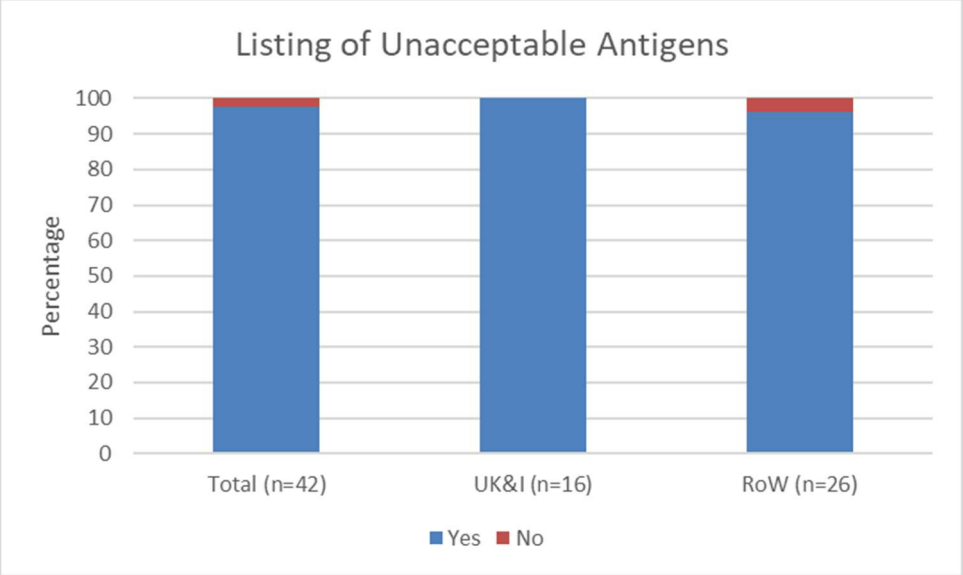
Specificity*	Pre-Liver Transplant		Post-Liver Transplant	
	19/08/2021	23/11/2021	04/10/2024	06/01/2025
A2**	18,114	13,757	Neg	Neg
A68**	16,271	8,281	Neg	Neg
A69	16,860	12,588	Neg	Neg
B57**	22,061	21,029	Neg	Neg
Cw5	11,987	7,226	2,111	1,232
Cw6	2,373	2,692	Neg	Neg

Cw15	10,106	6,307	2,635	2,126
Cw17	Neg	3,900	1,163	1,564
Cw18	9,906	6,238	2,956	1,452
DR13**	4,759	5,254	1,597	1,145
DR17	2,548	2,684	Neg	Neg
DR18	3,597	2,921	Neg	Neg
DQ2**	1,450	1,682	1,248	1,352
DQ4**	9,268	8,924	6,396	5,555

** Only specificities with MFI >1,000 are displayed, where multiple beads are present for a specificity only the highest MFI level is shown.*
*** All beads positive for specificity listed.*

Q1.1 Would you list unacceptable antigens for this patient when registering them on the deceased donor register for kidney transplantation?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	41	**98**	16	**100**	25	**96**
No	1	**2**	0	**0**	1	**4**

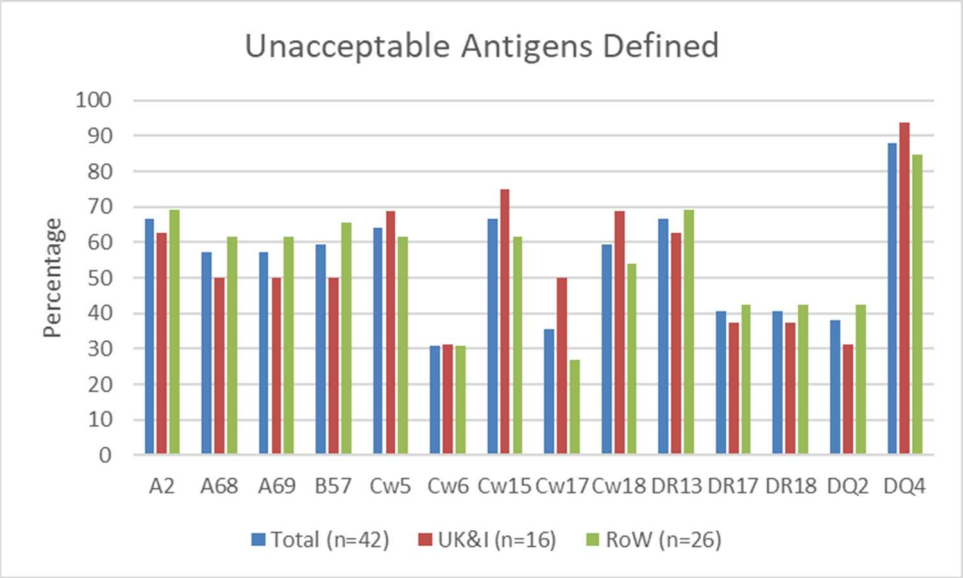


Q1.2 If you answered yes, what unacceptable antigens would you list for this patient?

Unacceptable Antigen	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
A2	28	**67**	10	**63**	18	**69**
A68	24	**57**	8	**50**	16	**62**
A69	24	**57**	8	**50**	16	**62**
B57	25	**60**	8	**50**	17	**65**

Cw5	27	**64**	11	**69**	16	**62**
Cw6	13	**31**	5	**31**	8	**31**
Cw15	28	**67**	12	**75**	16	**62**
Cw17	15	**36**	8	**50**	7	**27**
Cw18	25	**60**	11	**69**	14	**54**
DR13	28	**67**	10	**63**	18	**69**
DR17	17	**40**	6	**38**	11	**42**
DR18	17	**40**	6	**38**	11	**42**
DQ2	16	**38**	5	**31**	11	**42**
DQ4	37	**88**	15	**94**	22	**85**

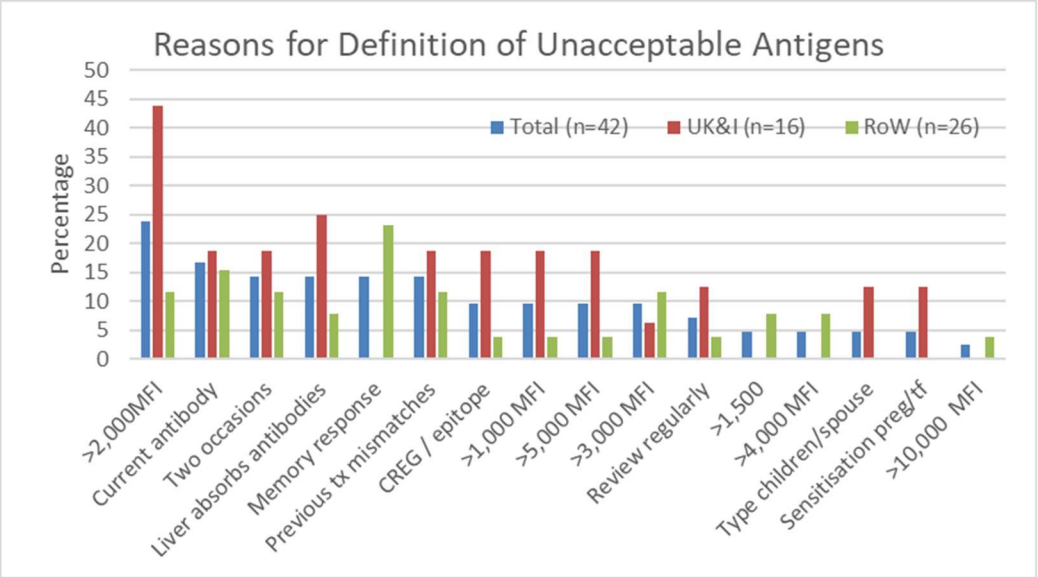
Additional comments:
2 RoW laboratories would list A*24:02, B*07:02, B*52:01 and DRB1*01:01 as previous transplant mismatches are also listed as unacceptable antigens even if there are no antibodies.



Q1.3 Please give a reason for your answer.

Reasons	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
>2,000 MFI	10	**24**	7	**44**	3	**12**
Current antibody	7	**17**	3	**19**	4	**15**
Two occasions	6	**14**	3	**19**	3	**12**
Liver absorbs antibodies	6	**14**	4	**25**	2	**8**
Memory response/ risk of AMR	6	**14**	0	**0**	6	**23**
Previous transplant mismatches	6	**14**	3	**19**	3	**12**
CREG / epitope	4	**10**	3	**19**	1	**4**
>1,000 MFI	4	**10**	3	**19**	1	**4**
>5,000 MFI	4	**10**	3	**19**	1	**4**

>3,000 MFI	4	**10**	1	**6**	3	**12**
Review regularly	3	**7**	2	**13**	1	**4**
>1,500	2	**5**	0	**0**	2	**8**
>4,000 MFI	2	**5**	0	**0**	2	**8**
HLA type children/spouse	2	**5**	2	**13**	0	**0**
Sensitisation from pregnancies / transfusions	2	**5**	2	**13**	0	**0**
>10,000 MFI	1	**2**	0	**0**	1	**4**



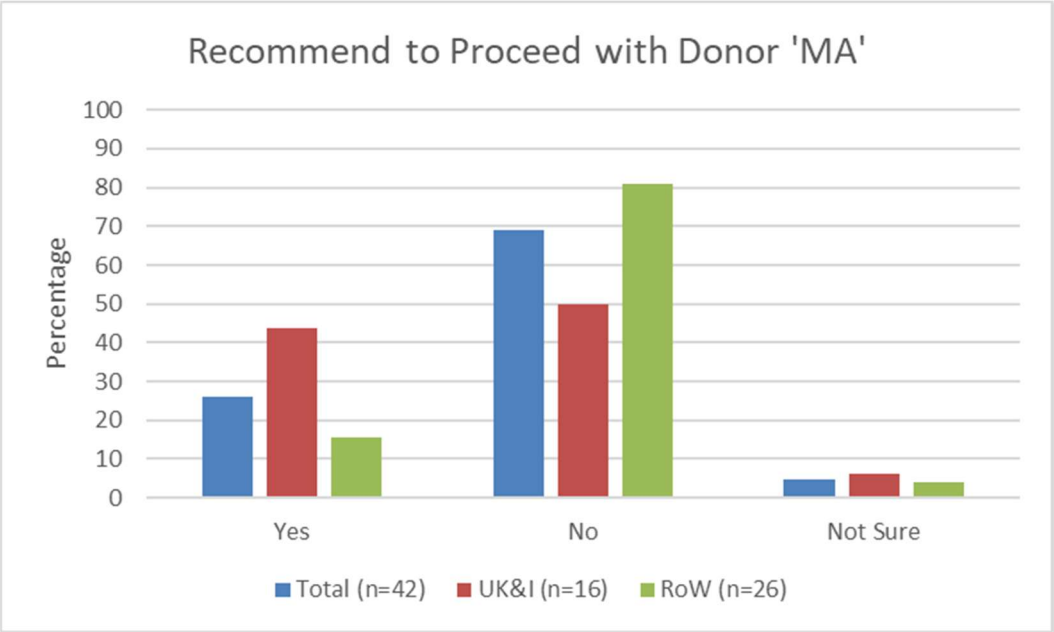
The patient's husband, MA, expressed an interest in becoming a live kidney donor and preliminary investigations for suitability were started, see Table 3.

Table 3: Husband Information

Husband ID	MA
Current Age	46
Husband HLA Type	A*01, -; B*08, B*57; C*07, C*06; DRB1*03:01, -; DQB1*02:01, -; DQA1*05, -
ABO Group	A Rh(D)+

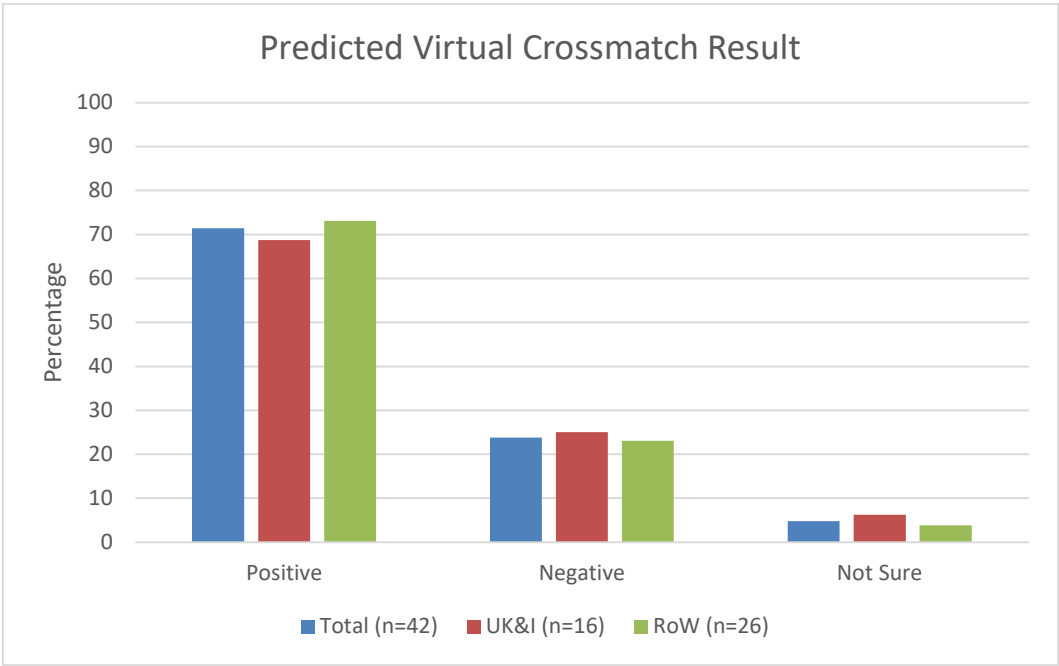
Q2.1 Would you recommendation the patient's husband continue further investigation as a kidney donor?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	11	**26**	7	**44**	4	**15**
No	29	**69**	8	**50**	21	**81**
Not Sure	2	**5**	1	**6**	1	**4**



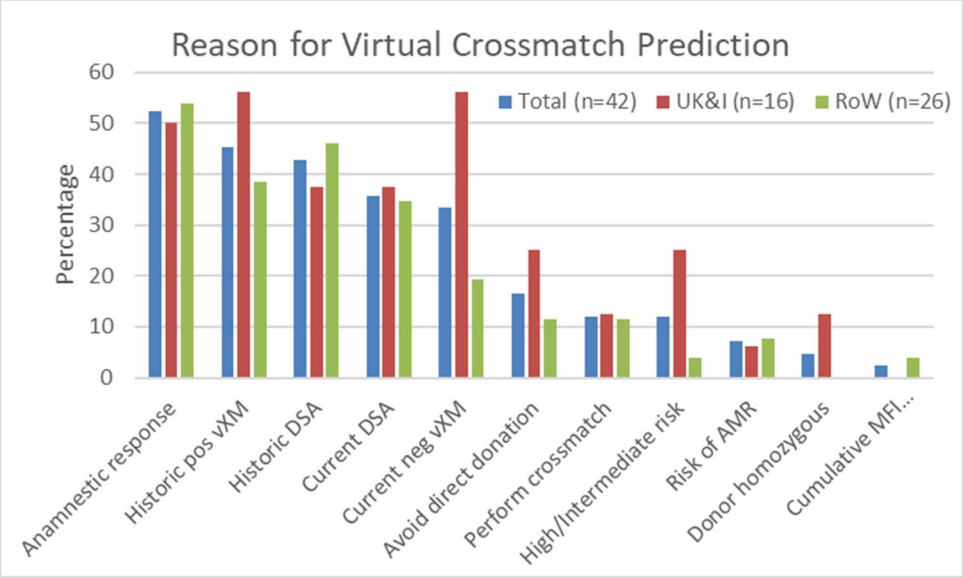
Q2.2 What do you predict the virtual crossmatch result will be for this patient and donor combination?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Positive	30	**71**	11	**69**	19	**73**
Negative	10	**24**	4	**25**	6	**23**
Not Sure	2	**5**	1	**6**	1	**4**



Q2.3 Give reasons for your answers.

Reasons	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	**%**	**Count**	**%**	**Count**	**%**
Anamnestic response	22	**52**	8	**50**	14	**54**
Historic positive virtual XM	19	**45**	9	**56**	10	**38**
Historic donor specific antibodies	18	**43**	6	**38**	12	**46**
Current donor specific antibodies	15	**36**	6	**38**	9	**35**
Current negative virtual XM	14	**33**	9	**56**	5	**19**
Avoid direct donation	7	**17**	4	**25**	3	**12**
Perform laboratory crossmatch	5	**12**	2	**13**	3	**12**
High/Intermediate risk	5	**12**	4	**25**	1	**4**
Risk of antibody mediated rejection	3	**7**	1	**6**	2	**8**
Donor homozygous	2	**5**	2	**13**	0	**0**
Cumulative MFI <5,000	1	**2**	0	**0**	1	**4**



A cousin of the patient, LA, also expresses an interest in becoming a live kidney donor, see Table 4a and 4b.

Table 4a: Live donor Information

Live Donor ID	LA
Current Age	36
Live Donor HLA Type	A*02:01, A*68:02; B*44:02, B*53:01; C*06:02, C*04:01; DRB1*13:02, DRB1*11:01; DQA1*01, -; DQB1*06:04, DQB1*03:01; DPB1*04:01, DPB1*04:02
ABO Group	O Rh(D)+

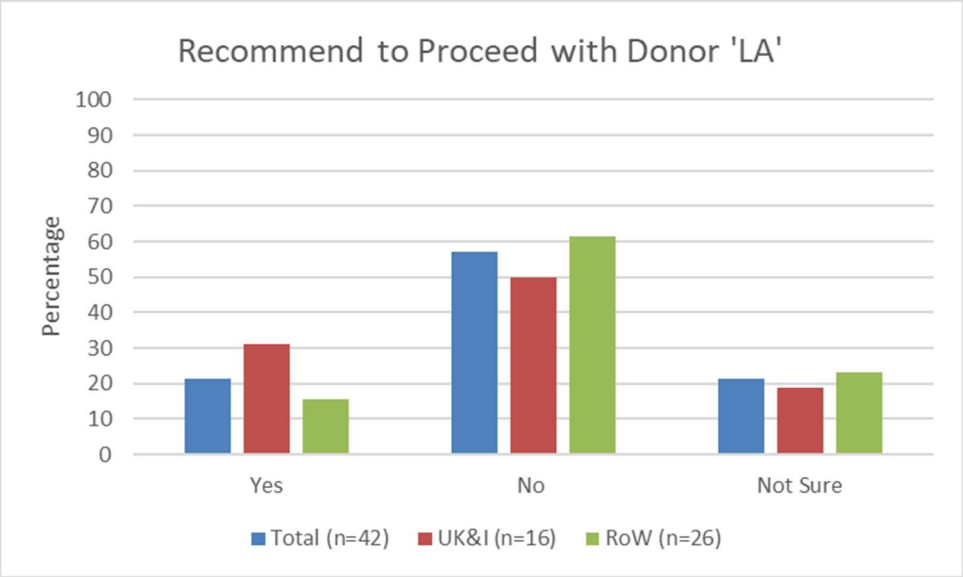
Table 4b: Details of Flow Cytometry Crossmatch Results for Live Donor

XM Results	Allogeneic Results			
	T-Cell	LCS*	B-Cell	LCS*
04/10/2024	**NEG**	19	**NEG**	25
06/01/2025	**NEG**	16	**NEG**	30

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

Q3.1 Would you recommend proceeding to transplant with live donor, LA?

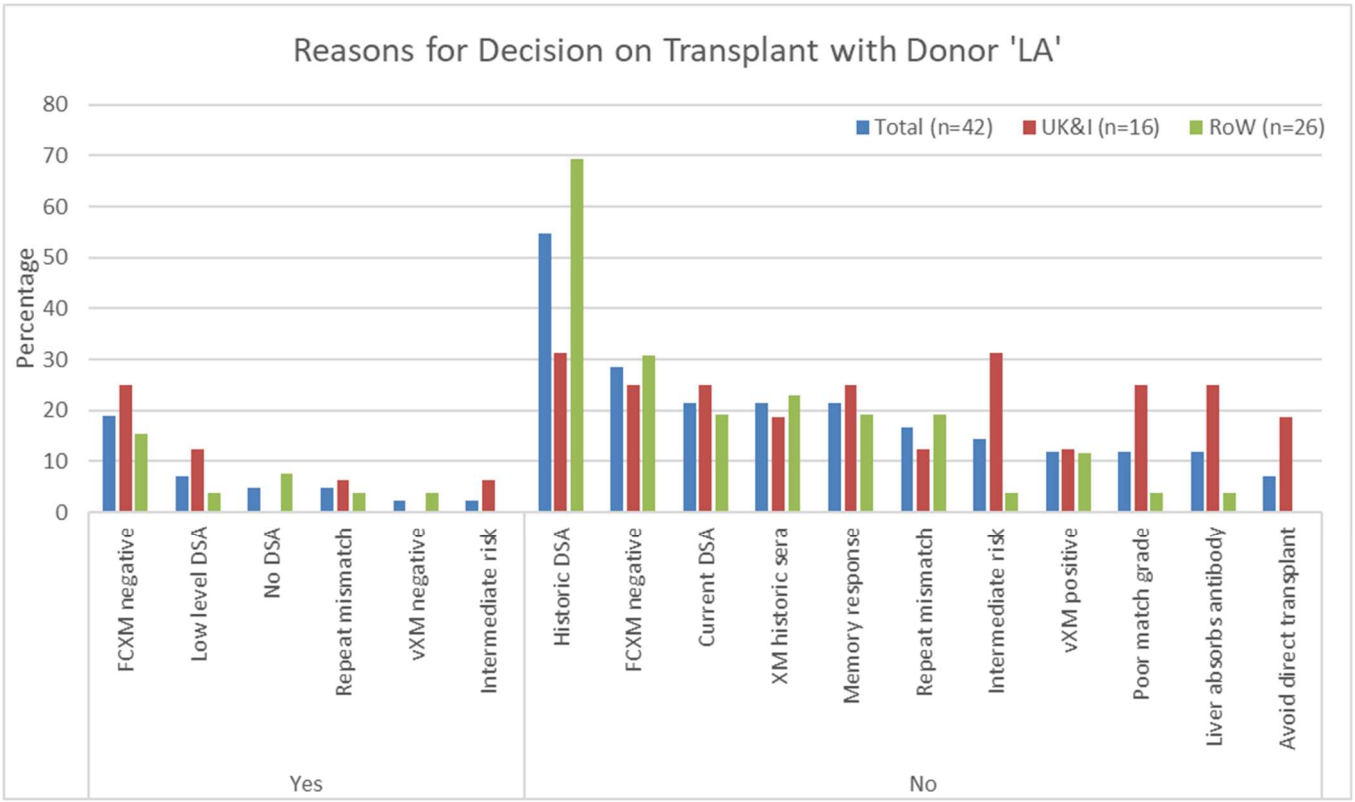
Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	9	**21**	5	**31**	4	**15**
No	24	**57**	8	**50**	16	**62**
Not Sure	9	**21**	3	**19**	6	**23**



Q3.2 Give reasons for your answers.

Proceed to Transplant	Reasons	Total (n=42)		UK&I (n=16)		RoW (n=26)	
		Count	%	Count	%	Count	%
Yes	FCXM negative	8	**19**	4	**25**	4	**15**
	Low level DSA	3	**7**	2	**13**	1	**4**
	No DSA	2	**5**	0	**0**	2	**8**
	Repeat mismatch	2	**5**	1	**6**	1	**4**
	vXM negative	1	**2**	0	**0**	1	**4**
	Intermediate risk	1	**2**	1	**6**	0	**0**
No	Historic DSA	23	**55**	5	**31**	18	**69**
	FCXM negative	12	**29**	4	**25**	8	**31**

	Current DSA	9	**21**	4	**25**	5	**19**
	XM historic sera	9	**21**	3	**19**	6	**23**
	Memory response	9	**21**	4	**25**	5	**19**
	Repeat mismatch	7	**17**	2	**13**	5	**19**
	Intermediate risk	6	**14**	5	**31**	1	**4**
	vXM positive	5	**12**	2	**13**	3	**12**
	Poor match grade	5	**12**	4	**25**	1	**4**
	Liver absorbs antibody	5	**12**	4	**25**	1	**4**
	Avoid direct transplant	3	**7**	3	**19**	0	**0**



The live donors are yet to have a medical assessment for fitness. At the same time that the live donors are being investigated for suitability the patient receives a deceased donor offer, see Table 5a and 5b. HLA antibody testing was performed at the same time on a new sample, see Table 5c.

Table 5a: Potential Deceased Donor Information

Donor ID	DD
Donor Type	Donation after brain death
Donor Age	46
Donor Sex	Female
Donor HLA Type	A*01, -; B*08, -, Bw6; C*07, -; DRB1*03:01, -; DRB3*01, -; DQA1*05, -; DQB1*02, -; DPB1*04:01, DPB1*-; DPA1*01, DPA1*-
ABO	A Rh(D)+

Table 5b: Details of Flow Cytometry Crossmatch Results for Deceased Donor

XM Results	Allogeneic Results			
	T-Cell	LCS*	B-Cell	LCS*
06/01/2025	**NEG**	19	**NEG**	39
10/04/2025	**NEG**	16	**POS**	132

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

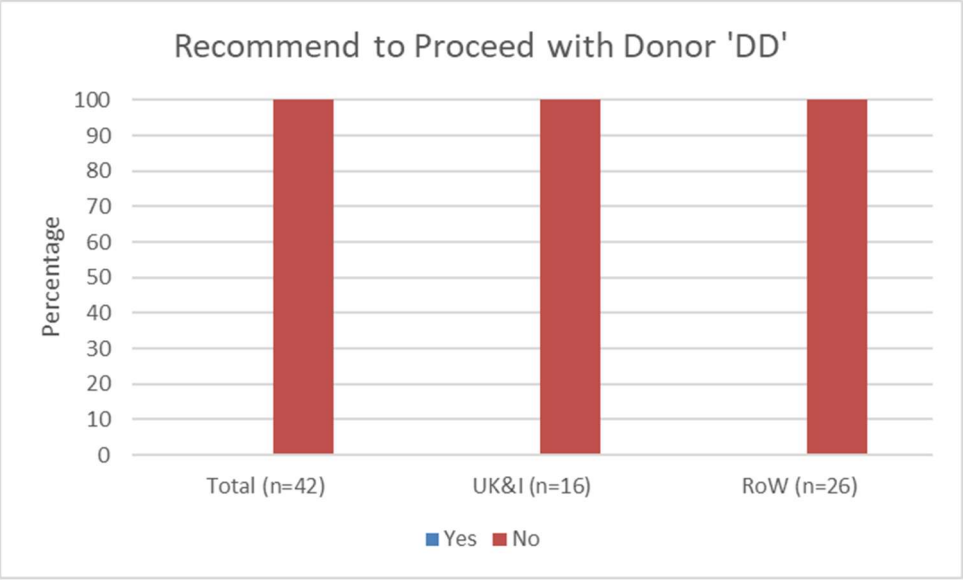
Table 5c: LABScreen SAB Kit Testing Summary

Specificity	10/04/2025
DR13**	6,145
DR17	5,857
DR18	3,742
DQ2**	6,352
DQ4**	10,555

** Only specificities with MFI >1,000 are displayed, where multiple beads are present for a specificity only the highest MFI level is shown.*
*** All beads positive for specificity listed.*

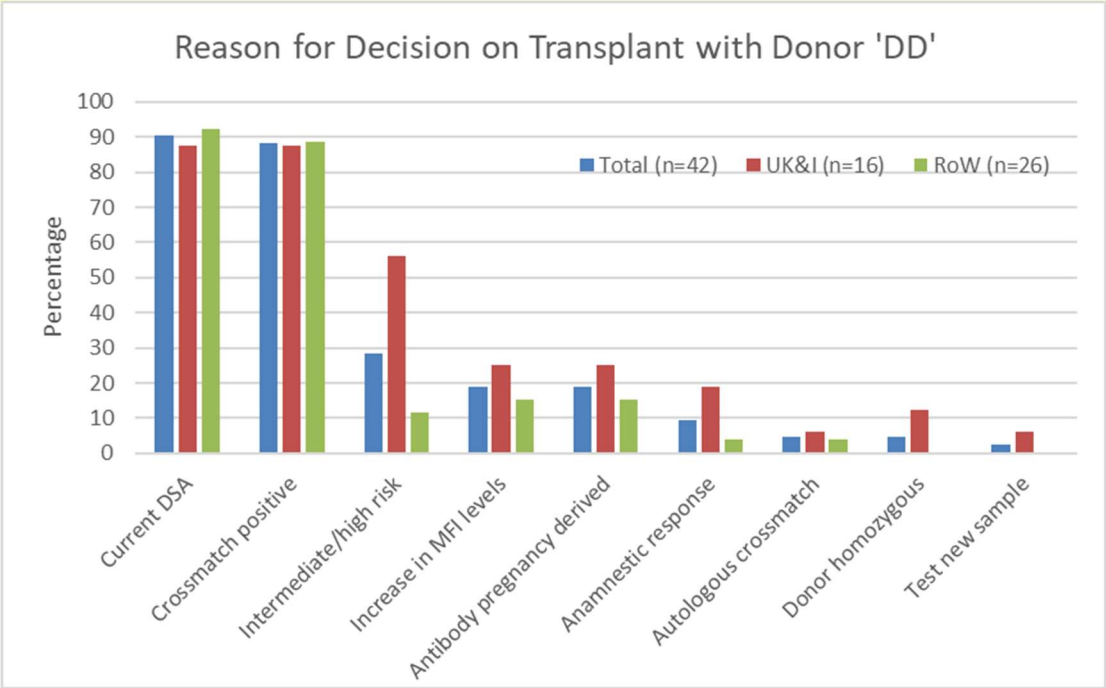
Q4.1 Would you recommend proceeding to transplant with the deceased donor?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	0	**0**	0	**0**	0	**0**
No	42	**100**	16	**100**	26	**100**



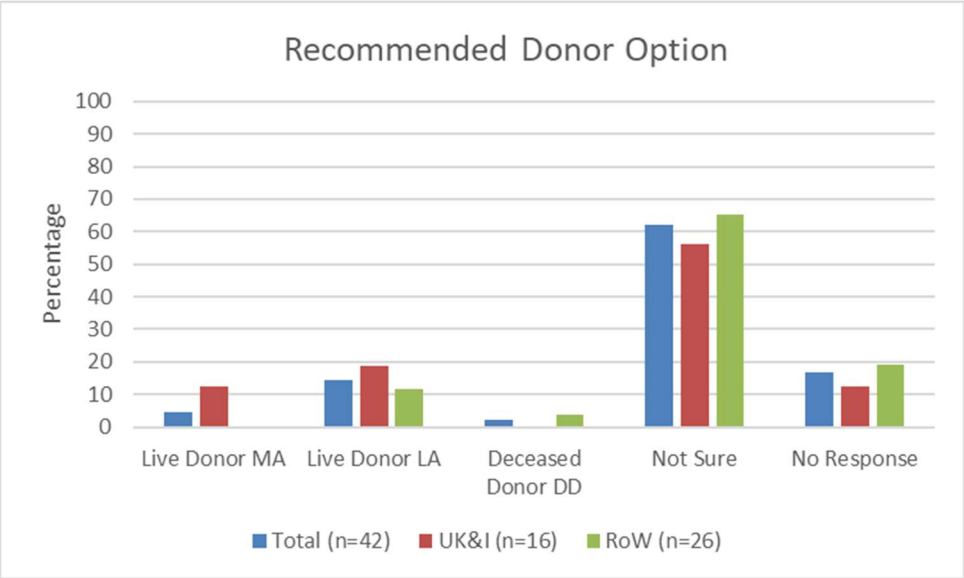
Q4.2 Give reasons for your answers.

Reasons	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	**%**	**Count**	**%**	**Count**	**%**
Current donor specific antibodies	38	**90**	14	**88**	24	**92**
Crossmatch B cell positive	37	**88**	14	**88**	23	**88**
Intermediate/high risk	12	**29**	9	**56**	3	**12**
Increase in MFI levels	8	**19**	4	**25**	4	**15**
Antibody pregnancy derived	8	**19**	4	**25**	4	**15**
Anamnestic response	4	**10**	3	**19**	1	**4**
Autologous crossmatch	2	**5**	1	**6**	1	**4**
Donor homozygous	2	**5**	2	**13**	0	**0**
Test new sample	1	**2**	1	**6**	0	**0**



Q5.1 What donor option, if any, would you recommend proceeding to transplant for this patient?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	**%**	**Count**	**%**	**Count**	**%**
Live Donor MA	2	**5**	2	**13**	0	**0**
Live Donor LA	6	**14**	3	**19**	3	**12**
Deceased Donor DD	1	**2**	0	**0**	1	**4**
Not Sure	26	**62**	9	**56**	17	**65**
No Response	7	**17**	2	**13**	5	**19**



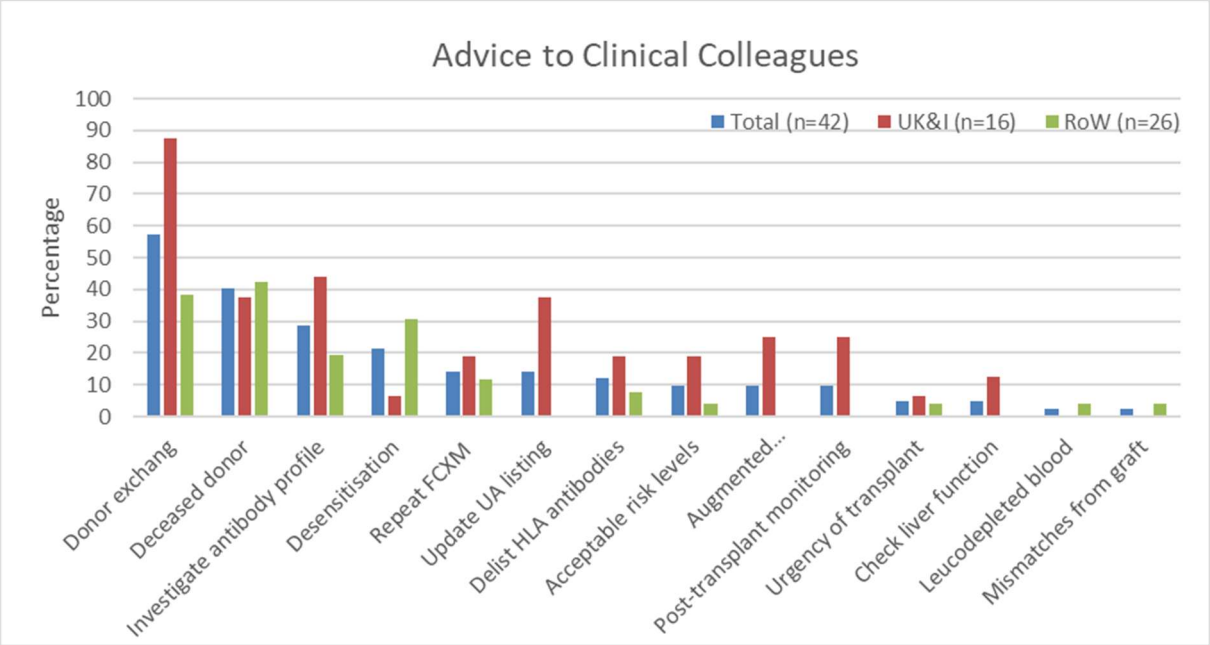
Q5.2 Give reasons for your answers.

Donor option	Reasons
MA	Preferred over LA
LA	Negative virtual crossmatch Negative flow cytometry crossmatch ABO Compatible Historic DSA Liver cleared DSA Repeat crossmatch
DD	Continue to wait for deceased donor options
Not sure / no response	No donor option suitable Intermediate / high risk DSA to all donors Use paired donor exchange scheme Re-test patient – changing antibody profile Liver absorbed class I antibodies

Q5.3 What advice would you provide to clinical colleagues regarding the management of this patient?

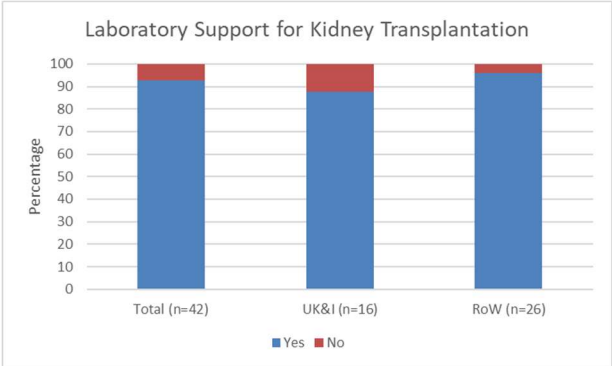
Check liver function	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Live donor exchange programme	24	**57**	14	**88**	10	**38**
Wait for deceased donor	17	**40**	6	**38**	11	**42**
Investigate rising antibody profile	12	**29**	7	**44**	5	**19**
Desensitisation	9	**21**	1	**6**	8	**31**
Repeat FCXM against live donors	6	**14**	3	**19**	3	**12**
Update unacceptable antigen listing	6	**14**	6	**38**	0	**0**

Delist HLA antibodies	5	**12**	3	**19**	2	**8**
Discuss acceptable risk levels	4	**10**	3	**19**	1	**4**
Augmented immunosuppression	4	**10**	4	**25**	0	**0**
Regular post-transplant monitoring	4	**10**	4	**25**	0	**0**
Discuss urgency of transplant	2	**5**	1	**6**	1	**4**
Check liver function	2	**5**	2	**13**	0	**0**
Use leuco-depleted blood products	1	**2**	0	**0**	1	**4**
Select donor with mismatches from functioning graft	1	**2**	0	**0**	1	**4**



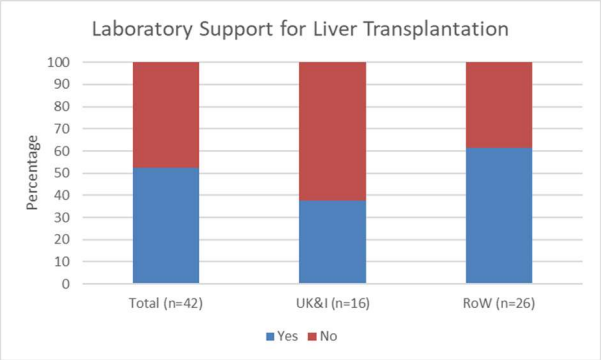
Q6.1 Does your laboratory support testing for kidney transplantation?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	39	**93**	14	**88**	25	**96**
No	3	**7**	2	**13**	1	**4**



Q6.2 Does your laboratory support testing for liver transplantation?

Response	Total (n=42)		UK&I (n=16)		RoW (n=26)	
	Count	%	Count	%	Count	%
Yes	22	**52**	6	**38**	16	**62**
No	20	**48**	10	**63**	10	**38**



Q7. Do you have any comments on scientific content of this scenario?

- An interesting case that generated much discussion in the lab. Difficult to find clear guidance on how to manage a clinical scenario such as this.
- We haven't experienced this scenario in our centre. We commented that there is a gap in the guidelines for this scenario.
- Would have been helpful to understand the patient's clinical urgency to transplant/risk appetite.
- Q5.1 We wouldn't recommend any of the donor options.
- We would not recommend any of the donors (MA, LA, DD).
- There is no suitable donor available who meets the requirements of our department's transplant protocol. If the waiting time becomes too long, it depends on the clinicians whether certain unacceptable HLA antigens should be deleted (liver transplantation is a favourable factor for the delisting of specific HLA antigens).
- None of the donor options are optimal. The husband is a sensitizer and there are strong HLA DSA antibodies in the patient in the past sera. The liver may present some protection, but there is still increased risk. The cousin perhaps presents the best from an immunological perspective but there is still risk of amnestic response and DR13 would be listed as UA in our protocol. There is a positive crossmatch with the deceased donor and strong DSA in the current serum.
- If we have this case of this patient, we would accept none of these donors. Maybe a kidney exchange program can be proposed to the patient or a desensitization protocol.
- Missing information on whether the husband is the father of the children.
- A good learning opportunity for centres that do renal transplant but not liver transplants.
- This case would require discussion with renal team, so we could discuss the impact of hepatic antibody clearance on antibodies. With rising MFI in current sample, they would likely not want to proceed with transplant if the current sample is crossmatch positive.
- A challenging but interesting scenario, but felt we had little guidance to go off. Would be helpful if BSHI guidelines could contain advice regarding this topic.

- This case highlights the importance of regular antibody monitoring post-transplant and careful donor selection to avoid sensitization-related complications.
- Is there any sensitizing event to explain the increasing MFI of anti-DR17, DR13 and DQ2 in the last serum (10/04/2025) compared to the serum of 06/01/2025?
- We would recommend doing a crossmatch between donor and patient sera from year 2021 prior to transplant to determine the risk level for the patient. Finding alternative donor for this highly sensitized patient for example, deceased donor or registering into paired kidney exchange program.
- The patient had liver transplant (LT) in 2021, DSAs tend to disappear after LT with special preference to Class I DSAs (mostly absent at 12 months) while Class II DSAs persist. In this scenario, after 3 years+ Class I DSA (especially previous donor MM) still negative; for Class II the profile changed; Do we still need to consider all previous donor MM when selecting new donor or only those to which patient develop DSA.
- We might have different criteria for matching compared to other laboratories in the world.
- Interesting case.
- It is for me a learning experience too. With significant pre-transplant DSA, the possibility of liver being unable to neutralise a repeat challenge from her cousin who has A2 and A68.
- The importance of serial antibody monitoring post-transplant and comprehensive donor evaluation using both virtual and flow crossmatch to mitigate the risk of AMR
- We do not have experience with Kidney Tx following Liver Tx, are there any specific guidelines to follow on selecting Kidney donor.

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

The patient's husband, MA, has mismatches at HLA-B*57, C*06, DRB1*03:01, DQB1*02:01 and DQA1*05. The HLA antibody testing performed indicated potential pregnancy derived antibodies to B57, Cw6, DR17 (historic positive, current negative) and DQ2 (current positive). It is likely a flow cytometry crossmatch would be T and B cell historic positive and current negative.

Question 3

The patient's cousin, LA, has mismatches at HLA-A*02:01, A*68:02, B*44:02, B*53:01, C*06:02, C*04:01, DRB1*13:02, DRB1*11:01 and DQB1*03:01. LA shares a mismatch with the previous liver transplant at HLA-A*02:01.

HLA antibody testing has indicated potential antibodies to A2 and A68 (historic positive, current negative), Cw6 (potentially pregnancy derived; historic positive, current negative) and DR13 (current positive). The flow cytometry crossmatch performed using sera only taken post-liver transplant is negative.

Question 4

A deceased donor offer DD, has mismatches at HLA-DRB1*03:01, DRB3*01, DQA1*05 and DQB1*02. HLA antibody testing performed at the time of the offer has indicated current potential donor specific antibodies to DR17 and DQ2 (both potentially pregnancy derived). The testing also suggests the patient's HLA antibody profile is evolving. The flow cytometry crossmatch performed using sera only taken post-liver transplant is current B cell positive, T cell negative.

Question 5

It is unlikely that any of these donor options are suitable for direct donation depending on the risk acceptance level for this patient and the clinical urgency of transplantation. UK NEQAS would suggest entering the patient and live donors in a donor exchange programme. It would also be prudent to investigate the increase in MFI levels in the patient's recent serum sample and review potential unacceptable antigen listed for the patient.

Suggested reading:

Battle R, Pritchard D, Peacock S, Hastie C, Worthington J, Jordan S, McCaughlan JA, Barnardo M, Cope R, Collins C, Diaz-Burlinson N, Rosser C, Foster L, Kallon D, Shaw O, Briggs D, Turner D, Anand A, Akbarzad-Yousefi A, Sage D. BSHI and BTS UK guideline on the detection of alloantibodies in solid organ (and islet) transplantation. Int J Immunogenet. 2023 Nov;50 Suppl 2:3-63. doi: 10.1111/iji.12641. Epub 2023 Nov 2. PMID: 37919251.

Norman DJ, Enestvedt CK, Naugler WE, Erhan R, Shaut CA. The fate of anti-HLA antibodies following liver transplantation. Front Nephrol. 2024 Jun 12;4:1403096. doi: 10.3389/fneph.2024.1403096. PMID: 38933742; PMCID: PMC11199851.

Please note:

These comments have been compiled by subject matter experts from the UK NEQAS for H&I 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. UK 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.