Interpretive Educational Scheme (iED)
Clinical Scenario 2/2023 – Haematopoietic Stem Cell Transplant Case

Dispatched on 29th August 2023

Summary of Responses

A total of 42 responses were received. 13 responses were from participants based in the UK and Ireland (UK&I) and 29 from participants from the rest of the world (RoW).

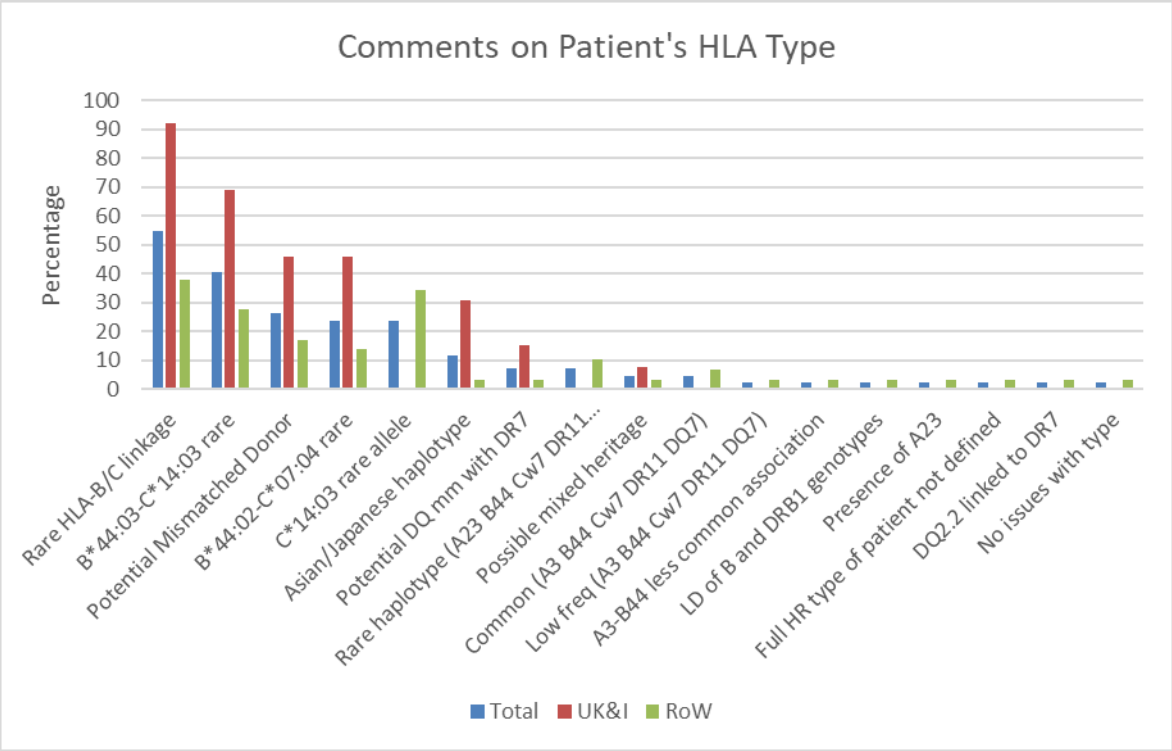
A 53-year-old female patient with acute myeloid leukaemia requires a haematopoietic stem cell transplant. The patient is CMV negative, ABO O RhD positive and weighs 84kg.

The patient's HLA type is detailed below:

HLA-A	A*03:01	A*23:01
HLA-B	B*44:02	B*44:03
HLA-C	C*07:04	C*14:03
HLA-DRB1	DRB1*07:01	DRB1*11:01
HLA-DRB3	DRB3*02:02	-
HLA-DRB4	DRB4*01:01	-
HLA-DQA1	DQA1*02:01	DQA1*05:05
HLA-DQB1	DQB1*02:02	DQB1*03:01
HLA-DPA1	DPA1*01:03	-
HLA-DPB1	DPB1*04:01	DPB1*04:02

Q1. Comment on the HLA type. What aspects may cause issues when trying to find a suitable match for this patient?

Comment	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
Rare HLA-B/C linkage	23	**55**	12	**92**	11	**38**
B*44:03-C*14:03 rare association	17	**40**	9	**69**	8	**28**
Potential Mismatched Donor	11	**26**	6	**46**	5	**17**
B*44:02-C*07:04 rare association	10	**24**	6	**46**	4	**14**
C*14:03 rare allele	10	**24**	0	**0**	10	**34**
Asian/Japanese haplotype	5	**12**	4	**31**	1	**3**
Potential DQ mismatch with DR7	3	**7**	2	**15**	1	**3**
Rare haplotype (A23 B44 Cw7 DR11 DQ7)	3	**7**	0	**0**	3	**10**
Patient has possible mixed heritage	2	**5**	1	**8**	1	**3**
Common haplotype (A3 B44 Cw7 DR11 DQ7)	2	**5**	0	**0**	2	**7**
Low freq haplotype (A3 B44 Cw7 DR11 DQ7)	1	**2**	0	**0**	1	**3**
A3-B44 less common association	1	**2**	0	**0**	1	**3**
LD of B and DRB1 genotypes	1	**2**	0	**0**	1	**3**
Presence of A23	1	**2**	0	**0**	1	**3**
Full HR type of patient not defined	1	**2**	0	**0**	1	**3**
DQ2.2 linked to DR7 in West African Population	1	**2**	0	**0**	1	**3**
No issues with type	1	**2**	0	**0**	1	**3**



There are no related donor options available for this patient.

An unrelated search is carried out. The potential donors are shown in Table 1.

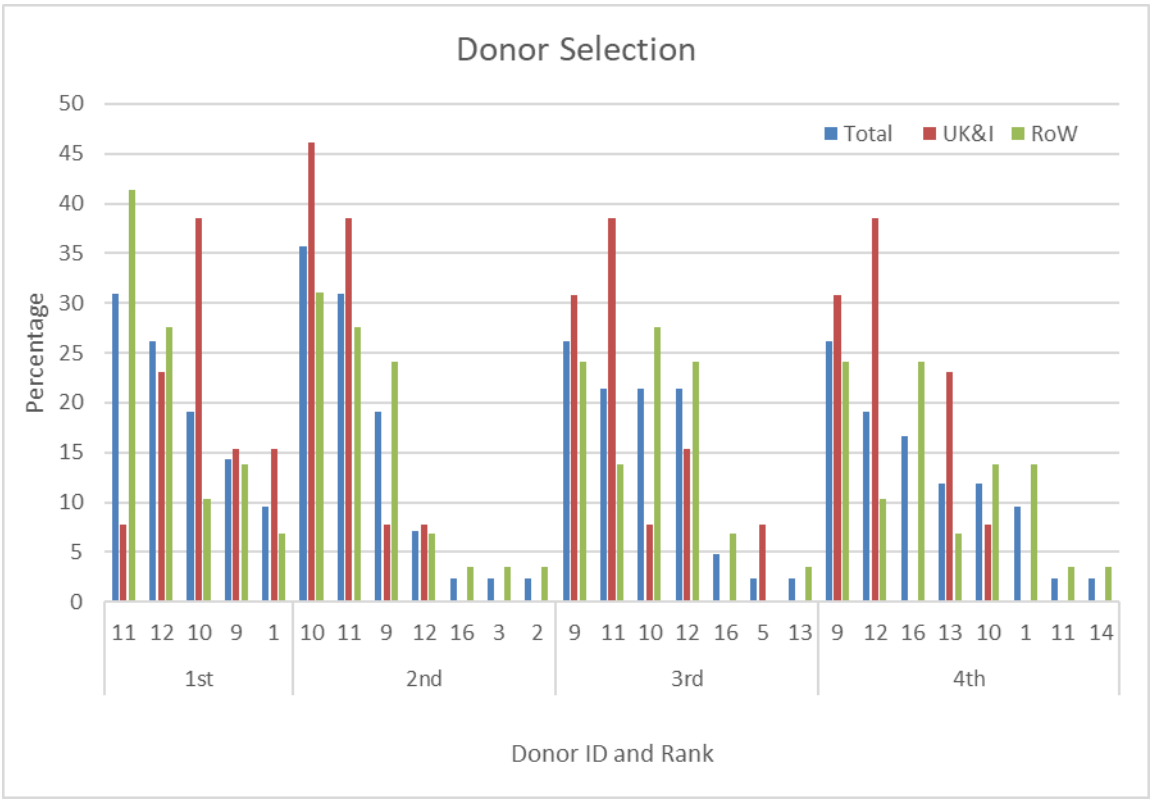
Table 1: Unrelated Donor Search Results

Donor	Registry	M/F	Age	ABO	CMV	HLA-A*	HLA-B*	HLA-C*	HLA-DRB1*	HLA-DQB1*	HLA-DPB1*
Patient Details		**F**	**53**	**O+**	**Neg**	**03:01 23:01**	**44:02 44:03**	**07:04 14:03**	**07:01 11:01**	**02:02 03:01**	**04:01 04:02**
1	BR-REDOME	M	26y	O+		03:01; 23:01	44:02; 44:03		07:01; 11:01		
2	BR-REDOME	F	32y			03:01; 23:01	44:02; 44:03		07:01/03/05; 11:01		
3	US-NMDP	F	49y			03:01; 23:01	44:02; 44:03		07:01; 11:01		
4	DE-ZKRD	F	33y			03:XX; 02:XX	44:XX		07:XX; 11:XX		
5	BR-REDOME	M	35y			03:01; 23:01	44:02; 44:03		07:01; 11:01		
6	DE-ZKRD	F	37y	O+		3; 23	44		07:01; 11:01		
7	DE-ZKRD	F	40y	O+		03:01; 23:01	44:02; 44:03		07:01; 11:01		
8	BR-REDOME	M	41y	O+		03:01; 23:01	44:02; 44:03		07:01; 11:01		
9	CL-DKMS	M	21y	B+	Neg	03:01; 23:01	44:02; 44:03	04:01; 07:04	07:01; 11:01	02:02; 03:01	02:01; 15:01
10	GB-ANT	M	26y		Neg	23:01; 68:01	44:02; 44:03	07:04; 14:03	07:01; 11:01	02:01/02; 03:01	02:01; 04:02

11	DE-DKMS	M	27y	O-	Neg	03:01; 23:01	44:02; 44:03	04:01; 07:04	07:01; 11:01	02:02; 03:01	02:01; 02:01
12	GB-BBMR	M	38y	O+		03:01; 23:01	44:02; 44:03	04:09N; 07:04	07:01; 11:01	02:02; 03:01	04:01; 04:01
13	US-NMDP	F	34y	A+		23:01; 68:01	44:02; 44:03	07:04; 14:03	07:01; 11:01	02:02; 03:01	02:01; 02:01
14	DE-DKMS	F	39y			03:01; 23:01	44:02; 44:03	07:04/11; 16:01	07:01; 11:01	02:02; 03:01	
15	US-NMDP	M	38y			03:01; 23:01	44:02; 44:03	07:01; 16:01	07:01; 11:01		
16	FR-FGM	F	36y	B+	Neg	03:01; 23:01	44:02; 44:03	04:01; 07:04	07:01; 11:01	02:02; 03:01	04:01; 17:01

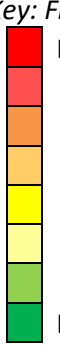
Q2. Which 4 donors would you consider as a transplant option for the patient and why?

Donor Choice	Donor ID	Total (n=42)		UK&I (n=13)		RoW (n=29)	
		Count	%	Count	%	Count	%
1	**11**	13	**31**	1	**8**	12	**41**
	12	11	**26**	3	**23**	8	**28**
	10	8	**19**	5	**38**	3	**10**
	9	6	**14**	2	**15**	4	**14**
	1	4	**10**	2	**15**	2	**7**
2	**10**	15	**36**	6	**46**	9	**31**
	11	13	**31**	5	**38**	8	**28**
	9	8	**19**	1	**8**	7	**24**
	12	3	**7**	1	**8**	2	**7**
	16	1	**2**	0	**0**	1	**3**
	3	1	**2**	0	**0**	1	**3**
	2	1	**2**	0	**0**	1	**3**
3	**9**	11	**26**	4	**31**	7	**24**
	11	9	**21**	5	**38**	4	**14**
	10	9	**21**	1	**8**	8	**28**
	12	9	**21**	2	**15**	7	**24**
	16	2	**5**	0	**0**	2	**7**
	5	1	**2**	1	**8**	0	**0**
	13	1	**2**	0	**0**	1	**3**
4	**9**	11	**26**	4	**31**	7	**24**
	12	8	**19**	5	**38**	3	**10**
	16	7	**17**	0	**0**	7	**24**
	13	5	**12**	3	**23**	2	**7**
	10	5	**12**	1	**8**	4	**14**
	1	4	**10**	0	**0**	4	**14**
	11	1	**2**	0	**0**	1	**3**
	14	1	**2**	0	**0**	1	**3**



ID	Most Common Reasons Given for Donor Selection																				
	Male	Female	Young	CMV match	ABO compatible	Trusted Registry	Permissive DP	Non-permissive DP	C mismatch	A mismatch	HR Typing	6/6	9/10	10/10	11/12	GvH	Bi-directional MM	B-C Match	Ethnically Diverse	Full HLA Type	Lower PIRCHE	Null Allele
1	✓		✓		✓							✓		✓					✓			
2																			✓			
3																						
4																						
5	✓											✓										
6																						
7																						
8																						
9	✓		✓	✓		✓	✓		✓		✓		✓				✓			✓		
10	✓		✓	✓		✓	✓			✓	✓		✓	✓			✓	✓		✓		
11	✓		✓	✓	✓	✓	✓		✓		✓		✓				✓			✓		
12	✓			✓	✓	✓	✓		✓				✓	✓	✓	✓				✓		✓
13		✓	✓			✓	✓			✓			✓									
14						✓			✓													
15																						
16		✓		✓				✓	✓				✓								✓	

Key: Frequency of Donor Selection



Most Popular

Least Popular

An HLA antibody screen is performed using One Lambda Single Antigen Bead kits, see Table 2. The patient did not have any Class II antibodies.

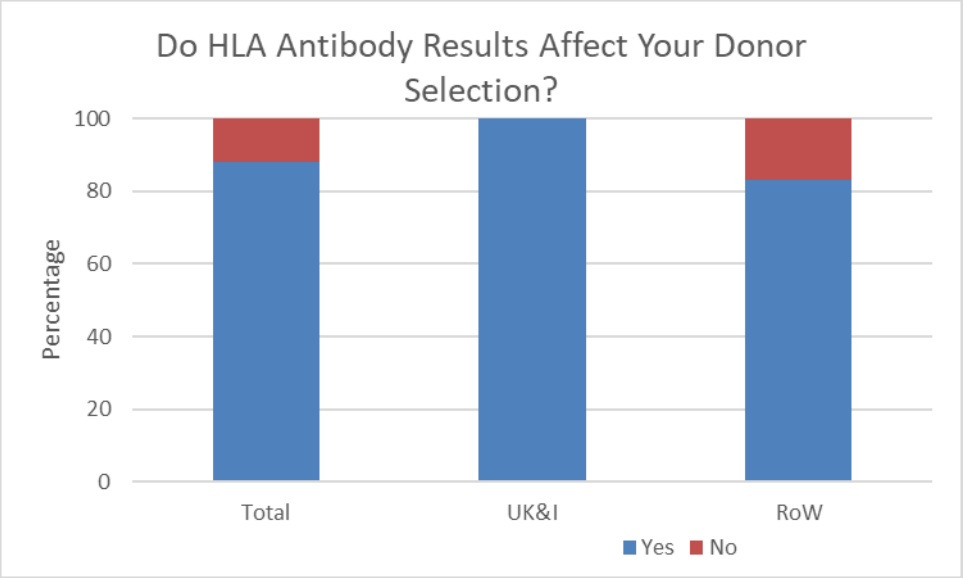
Table 2: Results from HLA Single Antigen Bead Testing, Sample Bled 09/05/23, Positive Beads Only Displayed

HLA Specificity	MFI		HLA Specificity	MFI
A2	17878		B51	23881
A11	8758		B52	20583
A*24:03	2005		B53	22810
A25	13660		B54	23998
A26	10026		B55	23833
A29	5931		B56	23640
A*30:01	2927		B57	23692
A31	2287		B58	21793
A32	1992		B59	21873
A33	9693		B60	23769
A34	9082		B61	23829
A36	4051		B62	24222
A43	5631		B63	23351
A66	15213		B64	16112
A68	11784		B65	10643
A69	14045		B67	24290
A74	1885		B71	23778
B7	24468		B72	23892
B8	23810		B73	19391
B13	19674		B75	22869
B18	24121		B76	23373
B27	21242		B77	20816
B35	24184		B78	23489
B37	18394		B81	24179
B38	23045		B82	20227
B39	23916		Cw2	9572
B41	23271		Cw5	3620
B42	24210		Cw6	3453
B45	7634		Cw9	9326
B46	22418		Cw10	7622
B47	17339		Cw15	21264
B48	23601		Cw17	3243

B49	22013		Cw18	3472
B50	20257			

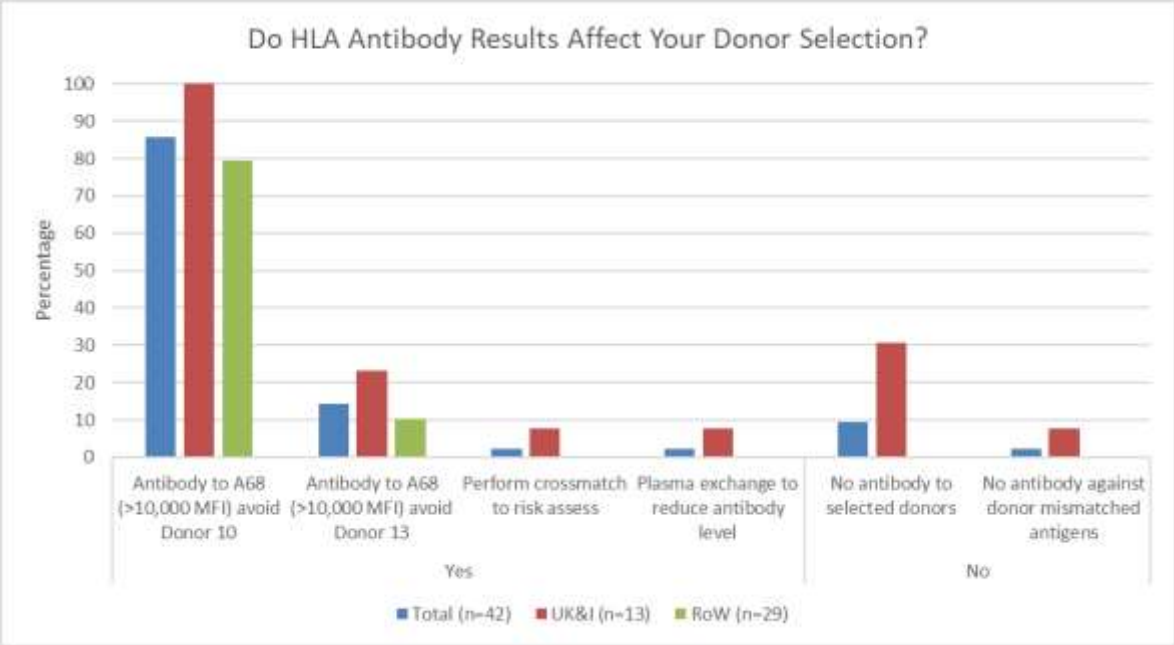
Q3.1. Do these results affect the donors you have selected in question 3?

Response	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
Yes	37	**88**	13	**100**	24	**83**
No	5	**12**	0	**0**	5	**17**



Q3.2. Explain your answer?

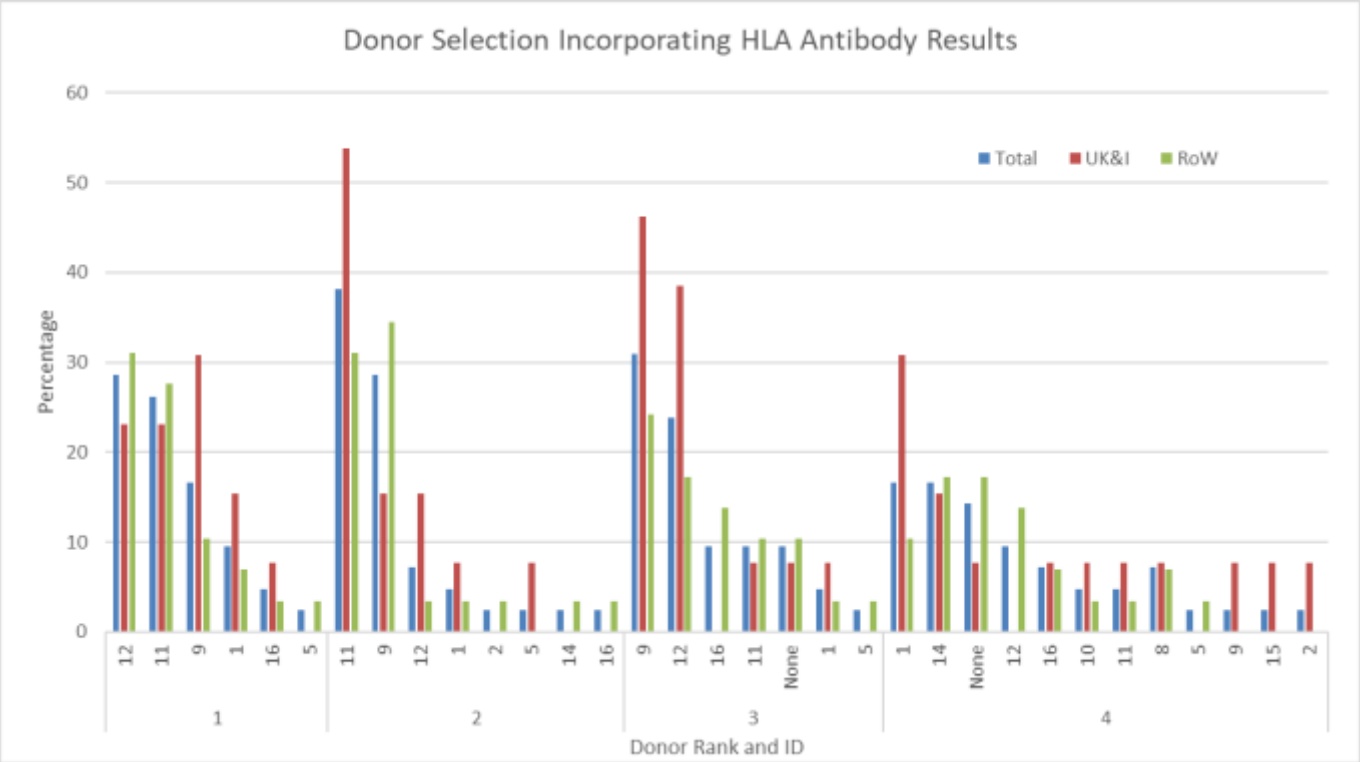
Response	Reason	Total (n=42)		UK&I (n=13)		RoW (n=29)	
		Count	%	Count	%	Count	%
Yes	**Antibody to A68 (>10,000 MFI) avoid Donor 10**	36	**86**	13	**100**	23	**79**
	Antibody to A68 (>10,000 MFI) avoid Donor 13	6	**14**	3	**23**	3	**10**
	Perform crossmatch to risk assess	1	**2**	1	**8**	0	**0**
	Plasma exchange to reduce antibody level	1	**2**	1	**8**	0	**0**
No	**No antibody to selected donors**	4	**10**	4	**31**	0	**0**
	No antibody against donor mismatched antigens	1	**2**	1	**8**	0	**0**



Q3.3. If yes, which donor(s) would you now consider in your selection?

Donor Choice	Donor ID	Total (n=42)		UK&I (n=13)		RoW (n=29)	
		Count	%	Count	%	Count	%
1	**12**	12	**29**	3	**23**	9	**31**
	11	11	**26**	3	**23**	8	**28**
	9	7	**17**	4	**31**	3	**10**
	1	4	**10**	2	**15**	2	**7**
	16	2	**5**	1	**8**	1	**3**
	5	1	**2**	0	**0**	1	**3**
2	**11**	16	**38**	7	**54**	9	**31**
	9	12	**29**	2	**15**	10	**34**
	12	3	**7**	2	**15**	1	**3**
	1	2	**5**	1	**8**	1	**3**
	2	1	**2**	0	**0**	1	**3**
	5	1	**2**	1	**8**	0	**0**
	14	1	**2**	0	**0**	1	**3**
	16	1	**2**	0	**0**	1	**3**
3	**9**	13	**31**	6	**46**	7	**24**
	12	10	**24**	5	**38**	5	**17**
	16	4	**10**	0	**0**	4	**14**
	11	4	**10**	1	**8**	3	**10**
	None	4	**10**	1	**8**	3	**10**
	1	2	**5**	1	**8**	1	**3**
	5	1	**2**	0	**0**	1	**3**
4	**1**	7	**17**	4	**31**	3	**10**
	14	7	**17**	2	**15**	5	**17**
	None	6	**14**	1	**8**	5	**17**

	12	4	**10**	0	**0**	4	**14**
	16	3	**7**	1	**8**	2	**7**
	10	2	**5**	1	**8**	1	**3**
	11	2	**5**	1	**8**	1	**3**
	8	3	**7**	1	**8**	2	**7**
	5	1	**2**	0	**0**	1	**3**
	9	1	**2**	1	**8**	0	**0**
	15	1	**2**	1	**8**	0	**0**
	2	1	**2**	1	**8**	0	**0**



Donor ID	Most Common Reasons Given for Donor Selection																		
	No Antibodies to [redacted]	Male	Female	Young	CMV match	ABO compatible	Trusted Registry	Permissive DP	C mismatch	A mismatch	HR Typing	6/6	9/10	10/12	11/12	Potential 10/10	Bi-directional MM	? Similar Heritage	Null Allele
1		✓		✓		✓						✓				✓			
2				✓												✓		✓	
3																			
4																			
5		✓										✓				✓			
6																			
7																			
8																✓			
9	✓	✓		✓	✓			✓	✓		✓		✓				✓		

10		✓		✓	✓			✓		✓							✓		
11	✓	✓		✓	✓	✓	✓	✓	✓		✓		✓				✓		
12	✓	✓				✓	✓	✓	✓				✓	✓	✓				✓
13																			
14	✓		✓						✓		✓		✓						
15		✓		✓			✓		✓										
16	✓		✓	✓	✓				✓				✓	✓					

Key: Frequency of Donor Selection

Most Popular

Least Popular

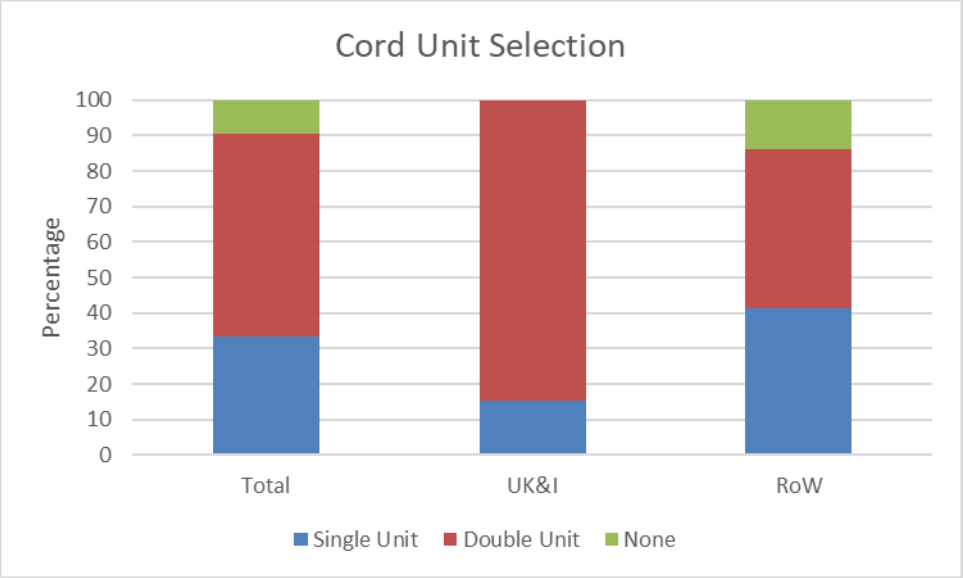
The clinical team request the cord options for this patient. The following units are identified, see Table 3.

Table 3: Potential Cord Units Identified for the Patient

Donor	Cord bank	HLA-A*	HLA-B*	HLA-C*	HLA-DRB1*	HLA-DQB1*	TNC ($x10^7$)	CD34 ($x10^5$)	Vol (ml)	ABO	AABB/FACT accredited
Patient Details		**03:01 23:01**	**44:02 44:03**	**07:04 14:03**	**07:01 11:01**	**02:02 03:01**	**weight 84kg**			**O+**	
1	DE-AKB	03:01; 23:01	44:02; 44:03		07:01; 11:01/30		84	13	55	O+	No
2	IT-Bologna	23:XX; 25:XX	44:XX		07:01; 11:01		264	139	160		FACT
3	ES-Valencia	03:01; 23:XX	44:XX; 44:03		07:01; 07:01		190	106	24	O+	No
4	US-St Louis	03:01; 23:01	44:02; 44:03	04:01; 07:04	07:01; 07:01		179	58	33	O+	AABB
5	US-Cleveland	03:01; 68:01	44:02; 44:03	07:04; 16:01	07:01; 11:01	02:02; 03:01	137	56	25	B+	FACT/AABB
6	FR-FGM	02:01; 23:01	44:02; 44:03	04:01; 07:04	07:01; 11:01		233	48	25	A+	No
7	RU-Samara	03:01; 23:XX	35:03; 44:03		07:01; 11:01		186	74	22	AB+	No
8	DE-DUS	23:01; 24:02	44:02; 44:03		07:XX; 11:XX	02:XX; 03:XX	147	51	42	A+	FACT
9	ES-Barcelona	03:XX; 23:XX	44:XX	04:XX; 16:XX	07:01; 11:03		193	93	25	A-	FACT
10	US-St Louis	03:01; 23:01	44:02; 44:03		04:01; 07:01		162	29	58	B+	AABB

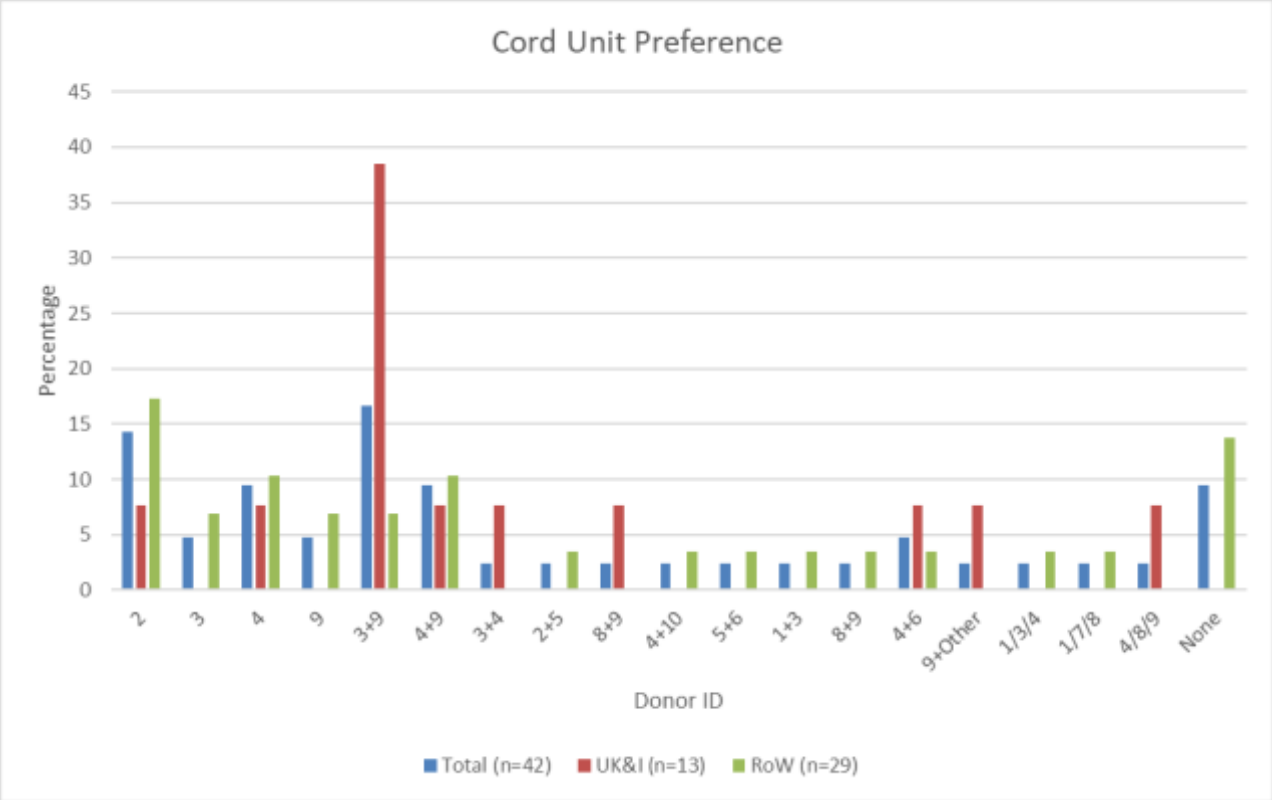
Q4. Which of the units would you propose as the best option for this patient and why?

Response	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
Single Unit	14	**33**	2	**15**	12	**41**
Double Unit	24	**57**	11	**85**	13	**45**
None	4	**10**	0	**0**	4	**14**



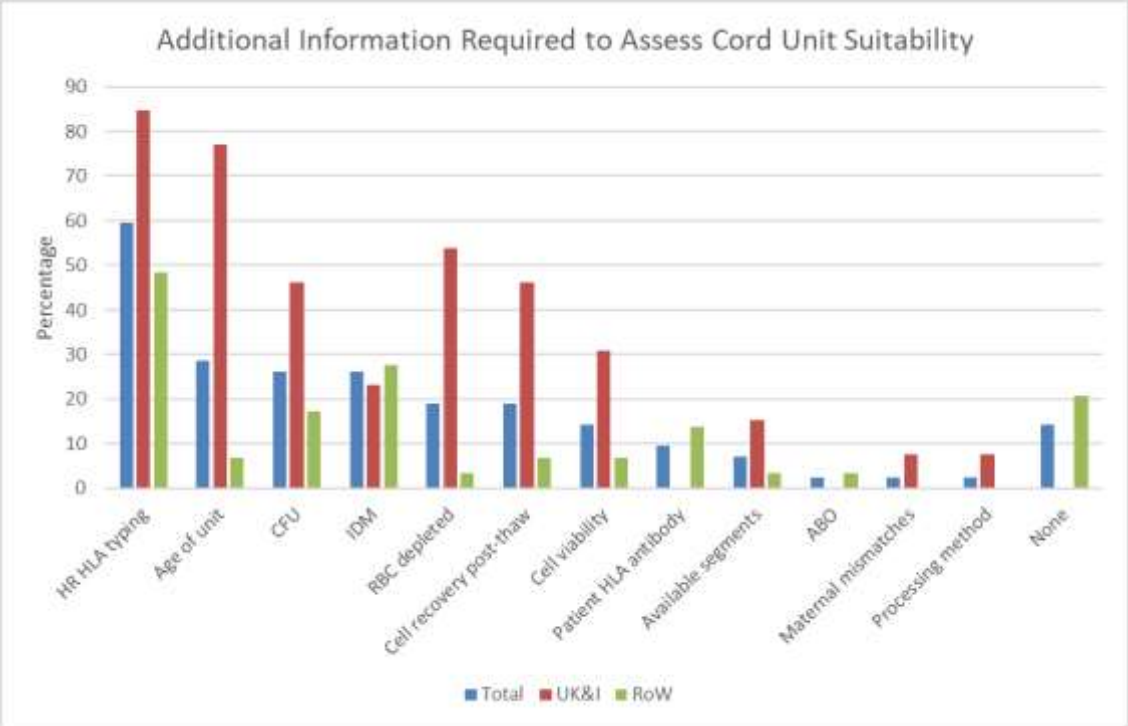
Donor ID	Total (n=42)		UK&I (n=13)		RoW (n=29)		Most Common Reasons Given for Donor Selection						
	Count	%	Count	%	Count	%	Accredited Bank	HLA Match	Cell Dose	Cell Volume	No DSA to Mismatched HLA	ABO match	Comments
2	6	**14**	1	**8**	5	**17**	✓	✓	✓				**DSA to A25 mismatch**
3	2	**5**	0	**0**	2	**7**		✓		✓		✓	
4	4	**10**	1	**8**	3	**10**	✓	✓			✓	✓	
9	2	**5**	0	**0**	2	**7**	✓	✓	✓		✓		
3+9	7	**17**	5	**38**	2	**7**			✓		✓		**Unit 3 not accredited**
4+9	4	**10**	1	**8**	3	**10**	✓	✓	✓		✓		
3+4	1	**2**	1	**8**	0	**0**			✓		✓		
2+5	1	**2**	0	**0**	1	**3**	✓	✓			✓		
8+9	1	**2**	1	**8**	0	**0**							
4+10	1	**2**	0	**0**	1	**3**	✓		✓		✓		
5+6	1	**2**	0	**0**	1	**3**		✓	✓		✓		
1+3	1	**2**	0	**0**	1	**3**					✓		
8+9	1	**2**	0	**0**	1	**3**	✓	✓	✓		✓		
4+6	2	**5**	1	**8**	1	**3**	✓	✓	✓		✓	✓	

9+Other	1	**2**	1	**8**	0	**0**							
1/3/4	1	**2**	0	**0**	1	**3**							
1/7/8	1	**2**	0	**0**	1	**3**		✓					
4/8/9	1	**2**	1	**8**	0	**0**	✓	✓	✓				
None	4	**10**	0	**0**	4	**14**							



Q5. Is there any additional information you would require to assess the suitability of a cord blood unit for transplant?

Information Requested	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
High resolution HLA typing	25	**60**	11	**85**	14	**48**
Age of unit	12	**29**	10	**77**	2	**7**
CFU	11	**26**	6	**46**	5	**17**
Infectious disease markers	11	**26**	3	**23**	8	**28**
RBC depleted	8	**19**	7	**54**	1	**3**
Cell recovery post-thaw	8	**19**	6	**46**	2	**7**
Cell viability	6	**14**	4	**31**	2	**7**
Patient HLA antibody status	4	**10**	0	**0**	4	**14**
Available segments	3	**7**	2	**15**	1	**3**
ABO	1	**2**	0	**0**	1	**3**
Maternal mismatches	1	**2**	1	**8**	0	**0**
Processing method	1	**2**	1	**8**	0	**0**
None	6	**14**	0	**0**	6	**21**



A further HLA antibody screen on a second sample date is performed, see Table 4.

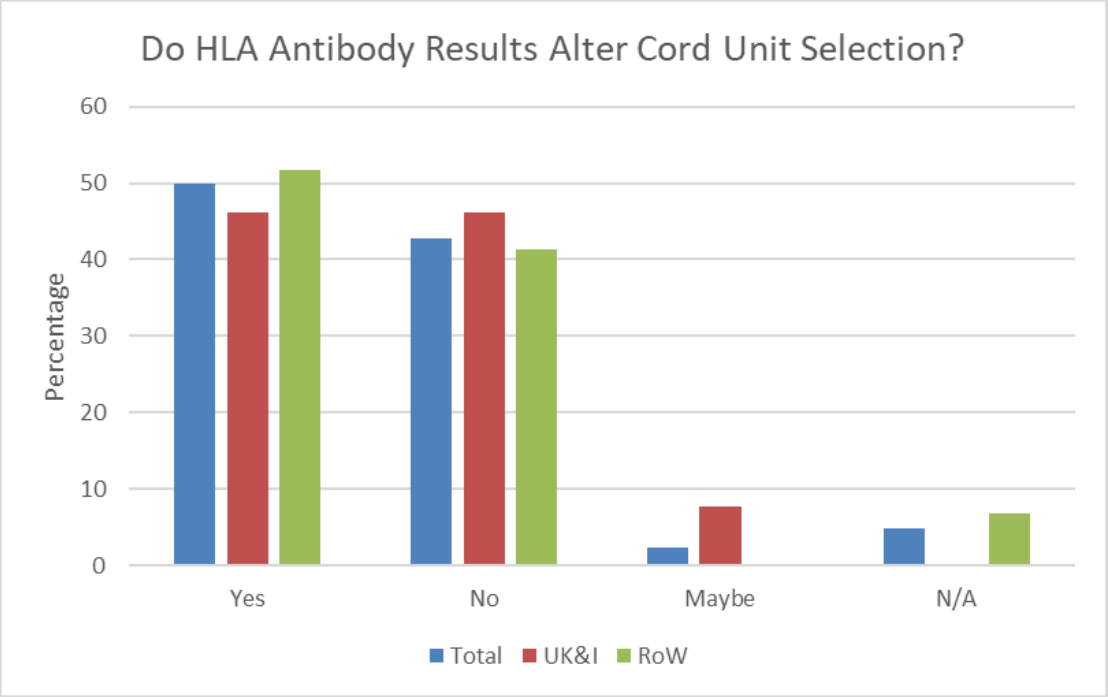
Table 4: Results from HLA Single Antigen Bead Testing, Sample Bled 25/07/23, Positive Beads Only Displayed

HLA Specificity	MFI		HLA Specificity	MFI
A1	7269		B52	16743
A2	24636		B53	21007
A11	7544		B54	22942
A24	9009		B55	23637
A25	11365		B56	23576
A26	8978		B57	24050
A29	4754		B58	22135
A30	3422		B59	18496
A31	3653		B60	23557
A33	4780		B61	22789
A34	5151		B62	23796
A36	3571		B63	22504
A43	7699		B64	8926
A66	9415		B65	5744
A68	18501		B67	24549
A69	23205		B71	23272
B7	24465		B72	21666
B8	23198		B73	8498
B13	17920		B75	21849
B18	23410		B76	20957
B27	15996		B77	17970
B35	24485		B78	22477

B37	8610		B81	23900
B38	19120		B82	19672
B39	23593		Cw2	7414
B41	22776		Cw4	4091
B42	24513		Cw5	8806
B45	5001		Cw6	8981
B46	19938		Cw9	5912
B47	12102		Cw10	4037
B48	21839		Cw12	3158
B49	18357		Cw15	19158
B50	17099		Cw17	7013
B51	22923		Cw18	9406

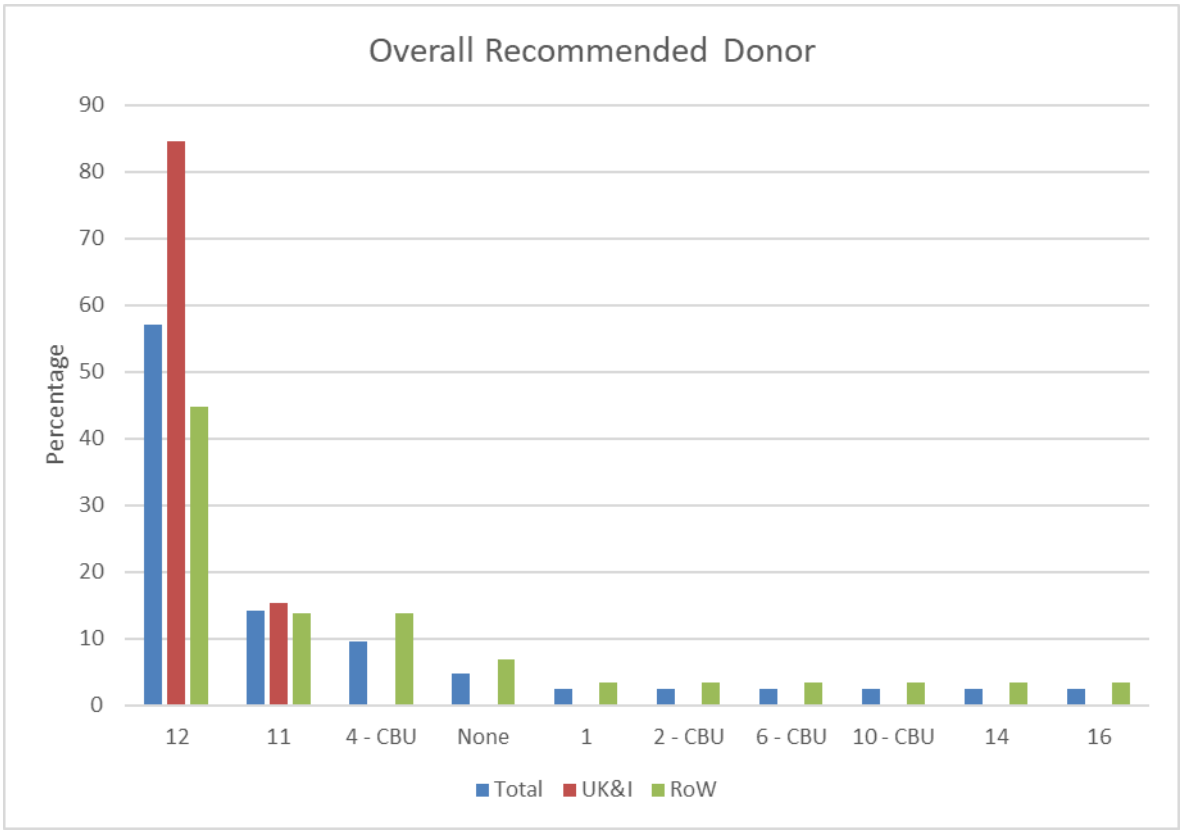
Q6. Does this information alter your selection of cord units selected in Q4?

Response	Total (n=42)		UK&I (n=13)		RoW (n=29)		Comments
	Count	%	Count	%	Count	%	
Yes	21	**50**	6	**46**	15	**52**	A24 antibody to Unit 8 Cw4 antibody to Units 4 and 9 A25 antibody to Unit 2 B35 antibody to Unit 7 Antibody to Units 5 and 6
No	18	**43**	6	**46**	12	**41**	Cw4 antibody <5,000 Cw HLA type of units unknown No suitable cord units
Maybe	1	**2**	1	**8**	0	**0**	Unknown clinical significance of Cw4 antibody
N/A	2	**5**	0	**0**	2	**7**	



Q7.1. Given all of the information above, which donor option would you propose as the best to the clinical team and why?

Donor ID (CBU = Cord Blood Unit)	Total (n=42)		UK&I (n=13)		RoW (n=29)		Most Common Reasons Given for Donor Selection															
	Count	%	Count	%	Count	%	Male	Young	no DSA	CMV match	ABO compatible	Trusted Registry/ Accred Bank	Permissive DP	C mismatch	HLA match	11/12	9/10	7/8	Null Allele	GvH	Cell Count	Potential DLI
12	24	**57**	11	**85**	13	**45**	✓				✓	✓	✓	✓		✓			✓	✓		
11	6	**14**	2	**15**	4	**14**	✓	✓		✓	✓	✓	✓	✓			✓					✓
4 - CBU	4	**10**	0	**0**	4	**14**			✓			✓									✓	
None	2	**5**	0	**0**	2	**7**																
1	1	**2**	0	**0**	1	**3**		✓			✓				✓							
2 - CBU	1	**2**	0	**0**	1	**3**															✓	
6 - CBU	1	**2**	0	**0**	1	**3**												✓			✓	
10 - CBU	1	**2**	0	**0**	1	**3**						✓									✓	
14	1	**2**	0	**0**	1	**3**			✓													
16	1	**2**	0	**0**	1	**3**			✓	✓			✓				✓					

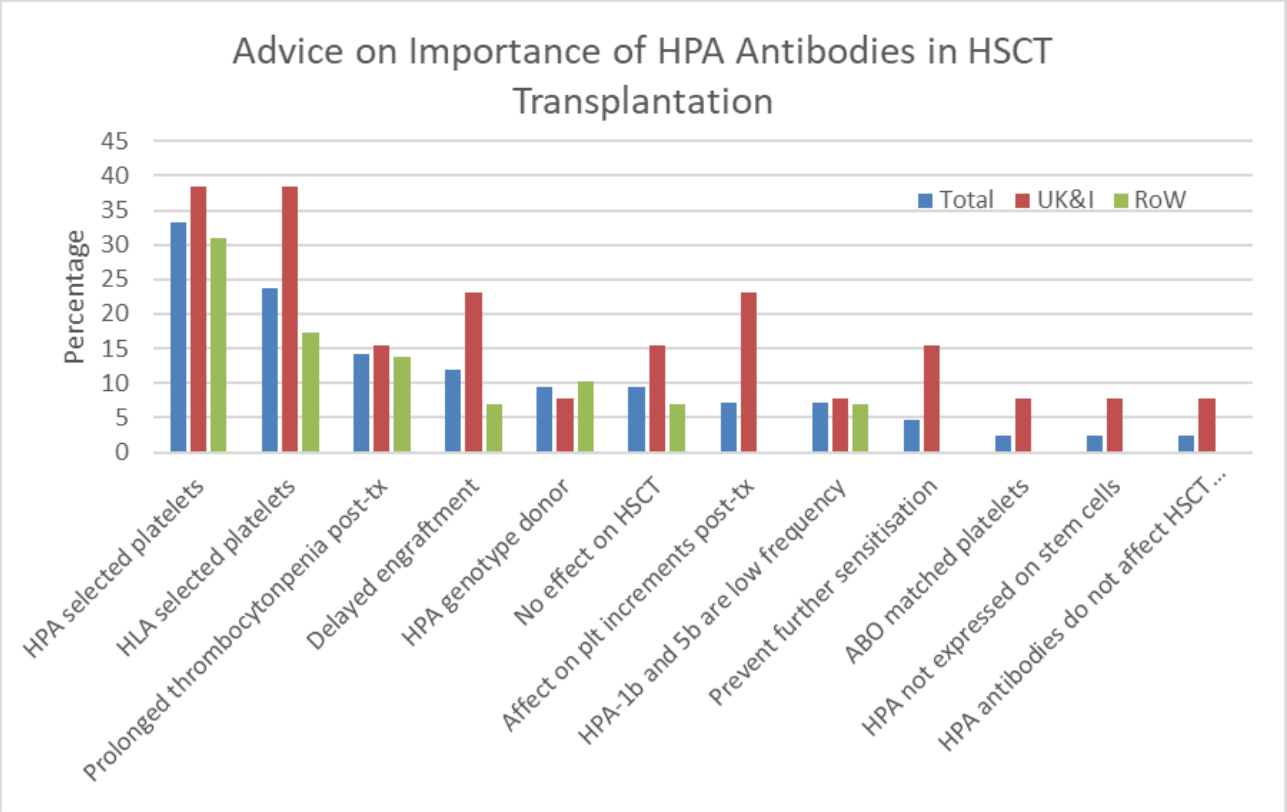


The patient was receiving platelet support and began refractory to random donor platelets. Further investigation reveals the patient also has HPA antibodies.

HPA genotype: 1a1a, 2a2a, 3a3a, 4a4a, 5a5a, 6a6a, 9a9a, 15a15b, 27a27a
HPA antibodies: HPA-1b and -5b

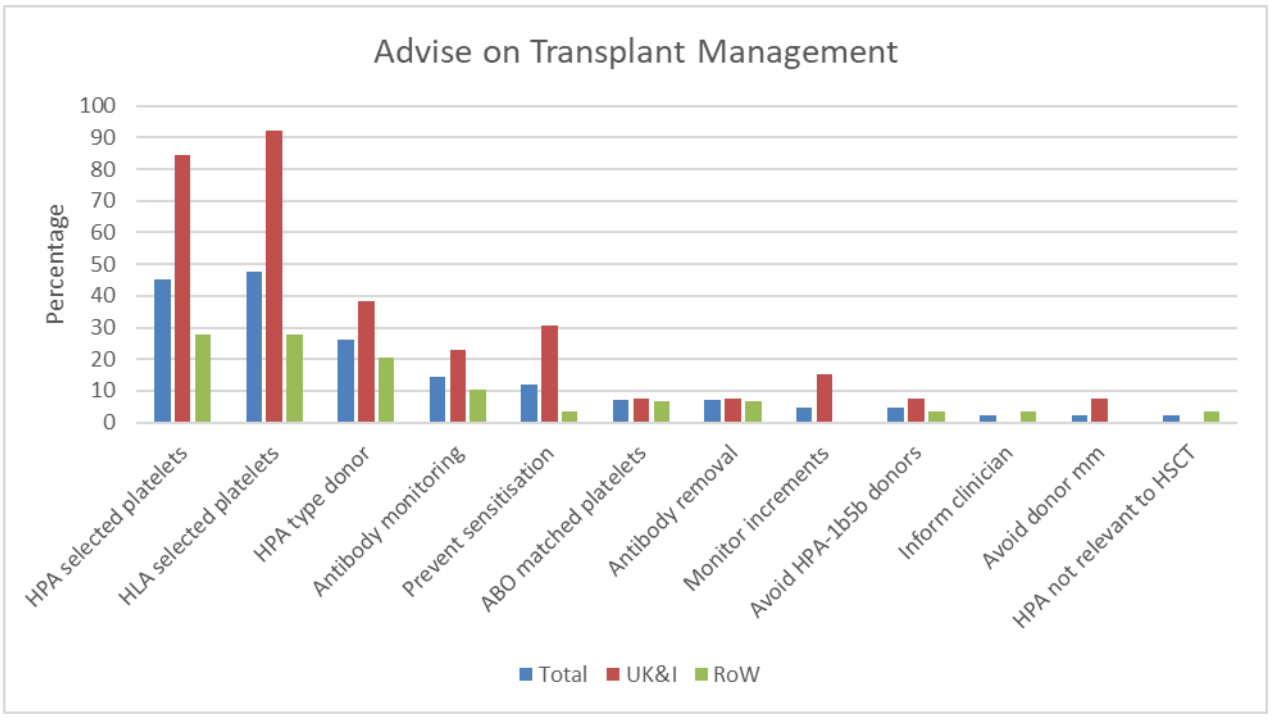
Q8.1. What advice would you give to the clinical team on the importance of these antibodies and the likely implications to transplant these antibodies may have?

Advice	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
HPA selected platelets	14	**33**	5	**38**	9	**31**
HLA selected platelets	10	**24**	5	**38**	5	**17**
Prolonged thrombocytopenia post-tx	6	**14**	2	**15**	4	**14**
Delayed engraftment	5	**12**	3	**23**	2	**7**
HPA genotype donor	4	**10**	1	**8**	3	**10**
No effect on HSCT	4	**10**	2	**15**	2	**7**
Affect on plt increments post-tx	3	**7**	3	**23**	0	**0**
HPA-1b and 5b are low frequency	3	**7**	1	**8**	2	**7**
Prevent further sensitisation	2	**5**	2	**15**	0	**0**
ABO matched platelets	1	**2**	1	**8**	0	**0**
HPA not expressed on stem cells	1	**2**	1	**8**	0	**0**
HPA antibodies do not affect HSCT donor selection	1	**2**	1	**8**	0	**0**



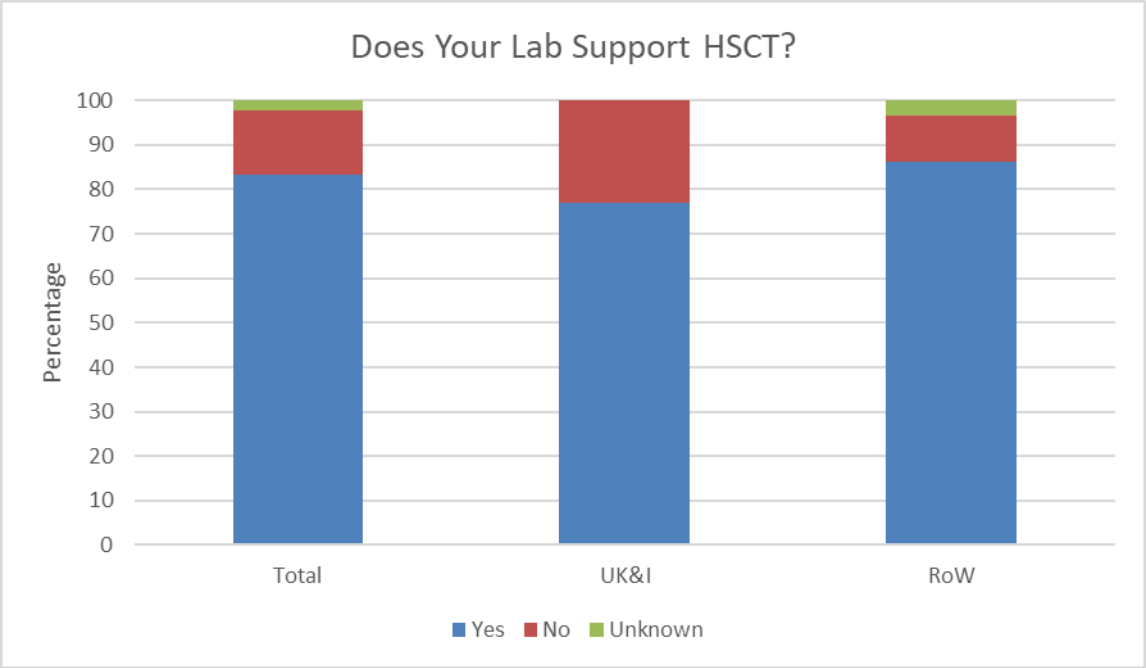
Q8.2. How would you suggest this is managed as part of the transplant work up?

Transplant Management Suggestions	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
HPA selected platelets	19	**45**	11	**85**	8	**28**
HLA selected platelets	20	**48**	12	**92**	8	**28**
HPA type donor	11	**26**	5	**38**	6	**21**
Antibody monitoring	6	**14**	3	**23**	3	**10**
Prevent sensitisation	5	**12**	4	**31**	1	**3**
ABO matched platelets	3	**7**	1	**8**	2	**7**
Antibody removal	3	**7**	1	**8**	2	**7**
Monitor increments	2	**5**	2	**15**	0	**0**
Avoid HPA-1b5b donors for HSCT	2	**5**	1	**8**	1	**3**
Inform clinician	1	**2**	0	**0**	1	**3**
Avoid mm for donor mm antigens	1	**2**	1	**8**	0	**0**
HPA not relevant to HSCT	1	**2**	0	**0**	1	**3**



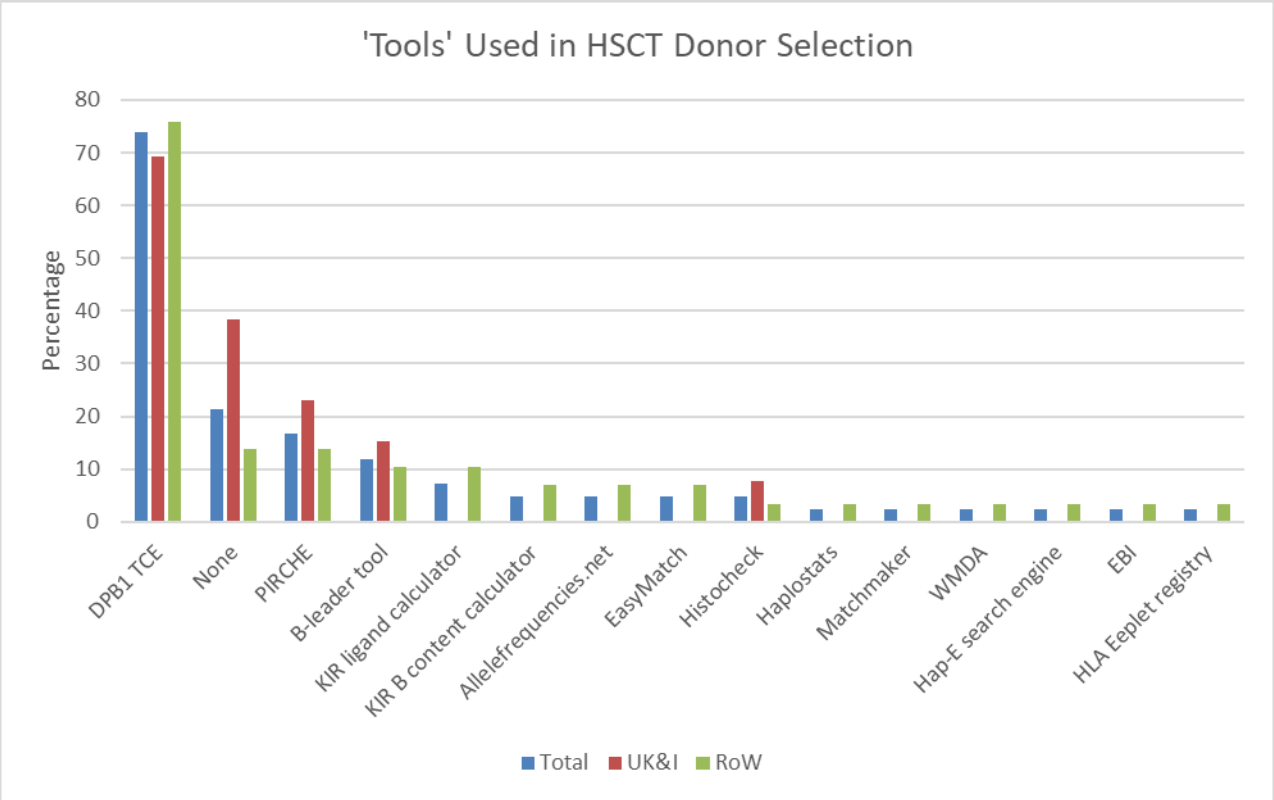
Q9.1. Does your laboratory support HSCT?

Response	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
Yes	35	**83**	10	**77**	25	**86**
No	6	**14**	3	**23**	3	**10**
Unknown	1	**2**	0	**0**	1	**3**



Q9.2. If so, what 'tools' (e.g. DPB1 T-Cell Epitope Algorithm, PIRCHE, etc.), if any, do you use to advise on donor options and why?

Tools	Total (n=42)		UK&I (n=13)		RoW (n=29)	
	Count	%	Count	%	Count	%
DPB1 T cell Epitope Algorithm	31	**74**	9	**69**	22	**76**
None	9	**21**	5	**38**	4	**14**
PIRCHE	7	**17**	3	**23**	4	**14**
B-leader tool	5	**12**	2	**15**	3	**10**
KIR ligand calculator	3	**7**	0	**0**	3	**10**
KIR B content calculator	2	**5**	0	**0**	2	**7**
Allelefrequencies.net	2	**5**	0	**0**	2	**7**
EasyMatch	2	**5**	0	**0**	2	**7**
Histocheck	2	**5**	1	**8**	1	**3**
Haplostats	1	**2**	0	**0**	1	**3**
Matchmaker	1	**2**	0	**0**	1	**3**
WMDA	1	**2**	0	**0**	1	**3**
Hap-E search engine	1	**2**	0	**0**	1	**3**
EBI	1	**2**	0	**0**	1	**3**
HLA eplet registry	1	**2**	0	**0**	1	**3**



Q10. Any constructive comments?

- We would not have considered a cord transplant as an option, we would prefer a haplo transplant, data supports this as a preferred option. Generation of good discussions around donor selection.
- Ethnicity of the patient would be useful for directing the donor search.
- Q7 is difficult to answer as incomplete HLA typing results on VUDs.
- Clinical direction from clinical team would be useful as this would happen routinely, in terms of progression to transplant and acceptance of mismatching.
- Our laboratory is not involved in the provision of platelet support.
- Difficult to answer Q7.1 given that we were not provided with additional information that would normally have been requested. Would have been good to know heritage of patient.
- When selecting the best suitable donor we would perform high resolution confirmatory typing and -in cases with antigenic/allelic mismatches on HLA-A*/B*/C*/DRB1*/DQB1*- screen the donor for patient-directed HLA-antibodies and perform a CDC-crossmatch (in HvG-direction); and in cases of DSAs we would also perform c1q-analysis in order to better qualify the significance of the antibodies.
- Usually, I would ask complementary typing for donors or CBU I plan to use before recruitment.
- Patient ethnicity would help a lot.
- We do not perform HPA testing in our lab.
- Thank you for such a rich challenging and fully described case.
- Looking forward to learn more on HSCT from UK NEQAS.
- Thank you.

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

Question 1
NEQAS felt the HLA-B-C linkage was unusual in this HLA type which may affect the likelihood of finding a fully HLA matched unrelated donor.

Question 2
UK NEQAS is based in the UK so we would follow the BSHI guidelines when selected an unrelated donor:
Little AM, Akbarzad-Yousefi A, Anand A, Diaz Burlinson N, Dunn PPJ, Evseeva I, Latham K, Poulton K, Railton D, Vivers S, Wright PA. BSHI guideline: HLA matching and donor selection for haematopoietic progenitor cell transplantation. Int J Immunogenet. 2021 Apr;48(2):75-109. doi: 10.1111/iji.12527. Epub 2021 Feb 10. PMID: 33565720.

The limited donor options for the patient has resulted in many different donor options selected with centres basing their decisions on the guidelines relevant to them locally and the requirements of their transplant centres.

Question 3
The impact of patient HLA antibodies has changed the donor selection for a number of participants. UK NEQAS would also consider avoiding donors to which the patient has high titre HLA antibodies where possible.

Question 4/5
For the selection of cord units, UK NEQAS would again follow local guidance contained in the BSHI guidelines. To achieve the recommended cell dose for the patient a double cord would be proposed.

Question 6
The impact of further HLA antibody testing on the patient limits the suitability of the available cord units as the patient has HLA antibodies to a number of mismatched antigens. If the transplant centre felt a cord transplant was the best option for this patient, then it may be prudent to consider antibody removal prior to transplantation.

Question 7
Overall participants favoured proceeding with a 11/12 unrelated donor. This donor had a mismatch at HLA-C but as the mismatch was a C*04:09N null allele. Participants felt that due to the lack of expression on the donor cell surface patient HLA antibodies directed toward Cw4 were not relevant.

It may also be worth exploring alternative donor options for this patient such as haplo-identical transplantation but this may also prove challenging due to the level of sensitisation to HLA.

Question 8
The impact of HPA antibodies on HSCT transplant produced mixed responses. Many felt the patient would benefit from HPA and HLA selected platelets. The impact of HPA antibodies on HSCT was more controversial and there is limited information in the literature to guide practice. Some felt there was no impact whilst others felt there could be delayed engraftment and prolonged thrombocytopenia post-transplant. Some participants mentioned HPA genotyping potential donors but due to the very limited donor options for this patient this may not be feasible. It may be prudent to provide HLA matched products to limit further sensitisation to HLA.

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.