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International Quality Expertise

Histocompatibility
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Interpretive Educational Scheme (iED)
Clinical Scenario 3/2022 – Transfusion/Platelet Immunology Case

Dispatched on 10th January 2023

Summary of Submitted Responses

A total of 35 responses were received, 15 from UK & Ireland (UK&I) based laboratories and 20 from Rest of the World (RoW) based laboratories.

Background:

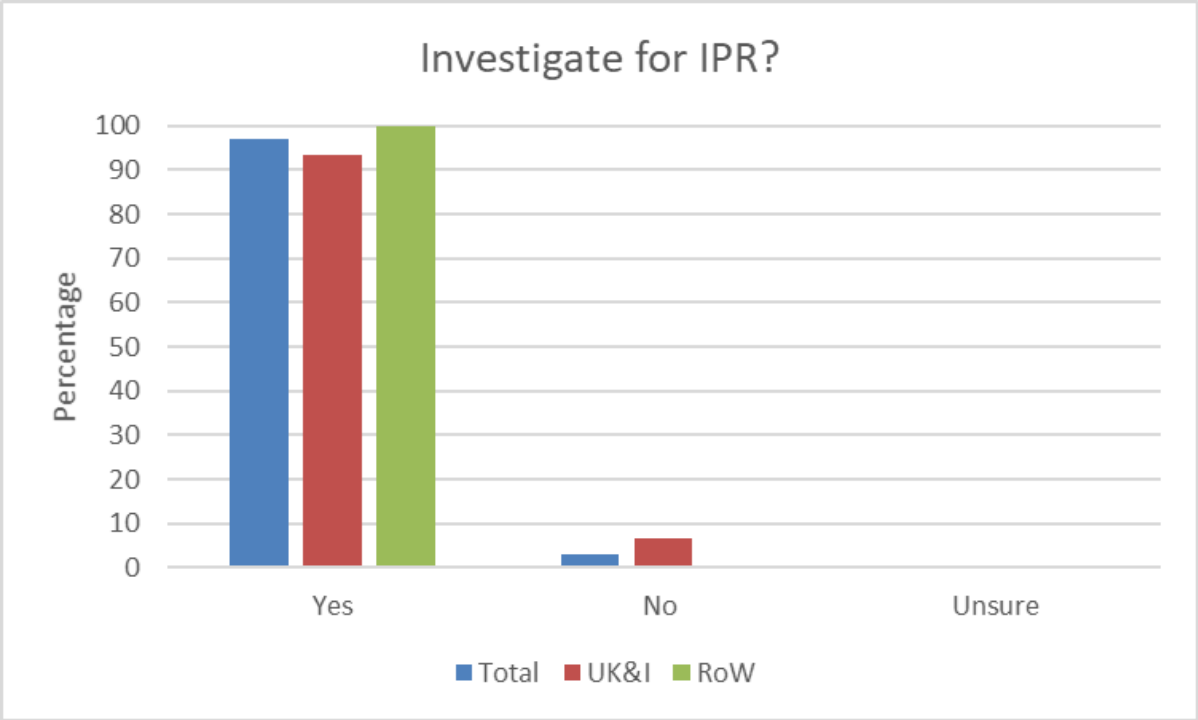
The patient was referred to the laboratory on the 1st of June 2022 with Acute Myeloid Leukaemia (AML) requiring platelet support during chemotherapy prior to haematopoietic stem cell transplant. A failure to increment to Random Donor Platelets (RDP) was noted on a number of occasions. The patient suffered an intracranial haemorrhage (ICH) as well as having an ongoing infection.

Patient Details:

Patient ID	**LD70**
Gender	Female
Age	52
ABO Group	O+
CMV Status	Positive
Diagnosis	AML (monosomy 7)
Weight	70kg
Height	165cm
Clinical Details	Poor increment to RDP: ICH and infection

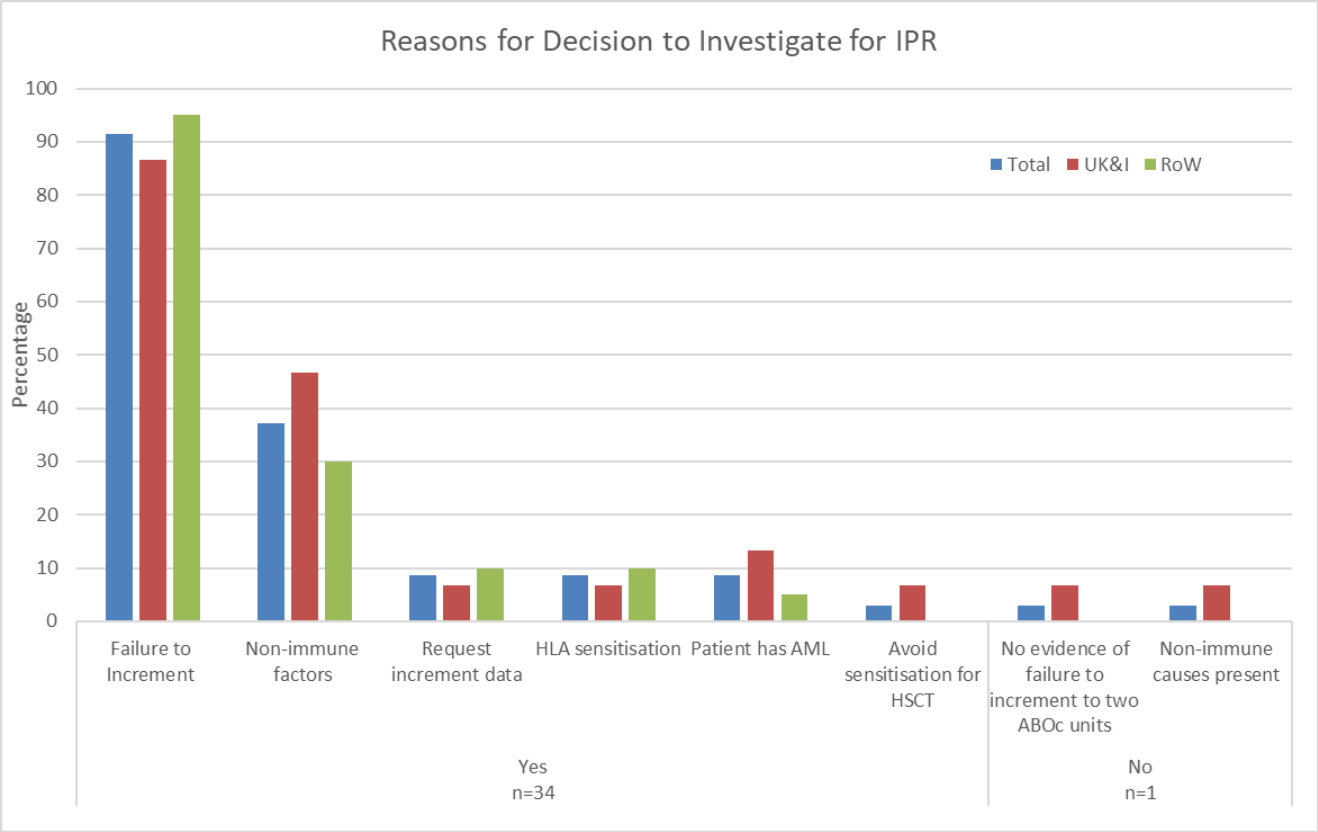
Question 1.1 – Would you investigate this patient for Immune Platelet Refractoriness (IPR)?

	Total		UK&I		RoW	
Option	**Number**	**%**	**Number**	**%**	**Number**	**%**
Yes	34	**97**	14	**93**	20	**100**
No	1	**3**	1	**7**	0	**0**
Unsure	0	**0**	0	**0**	0	**0**



Question 1.2 – Please state your reasons for making this decision.

IPR?	Reason	Total		UK&I		RoW	
		Number	%	Number	%	Number	%
Yes n=34	Failure to Increment multiple times	32	**91**	13	**87**	19	**95**
	Non-immune factors present	13	**37**	7	**47**	6	**30**
	Request increment data	3	**9**	1	**7**	2	**10**
	Potential sensitisation to HLA (pregnancy)	3	**9**	1	**7**	2	**10**
	Patient has AML	3	**9**	2	**13**	1	**5**
	Avoid further sensitisation if required HSCT	1	**3**	1	**7**	0	**0**
No n=1	No evidence of failure to increment to at least two ABO compatible single apheresis units	1	**3**	1	**7**	0	**0**
	Non-immune causes present	1	**3**	1	**7**	0	**0**



The sample was tested for the presence of Class I HLA antibodies by One Lambda Luminex Single Antigen Bead kit:

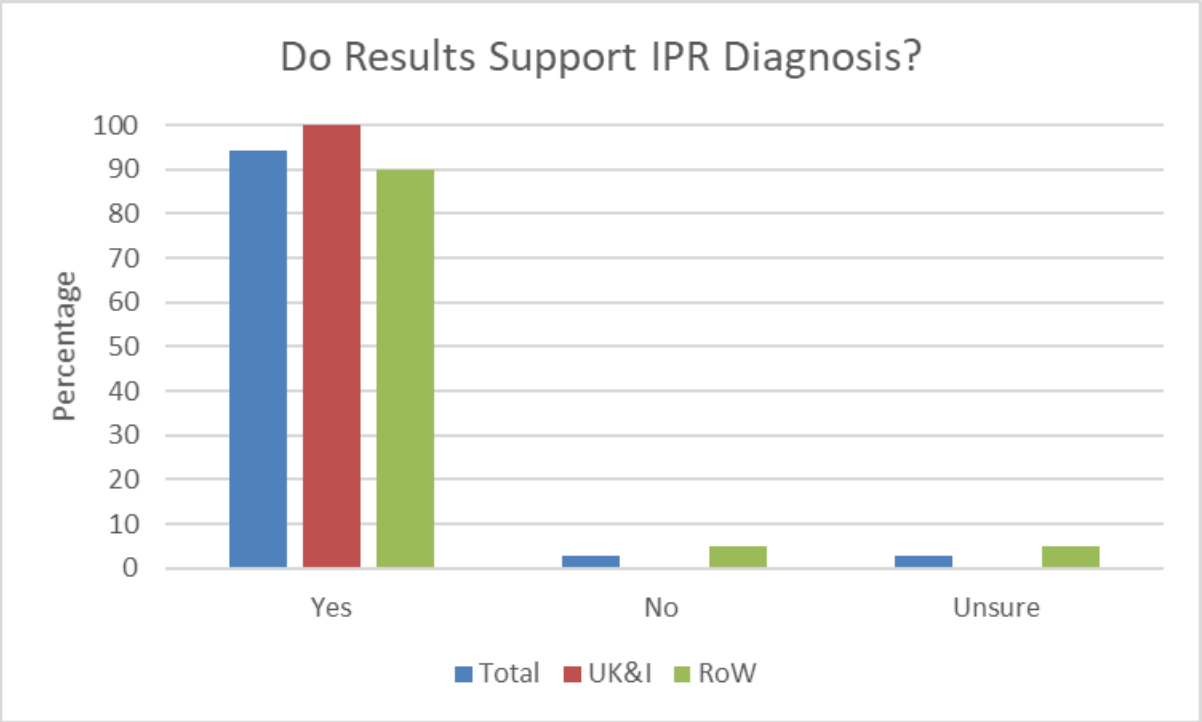
HLA Class I Antibodies (positive cut off >1000 MFI)	**Detected at (MFI Range):**	
	>20,000	A2, A3, A25, A31, B13, B35, B38, B39, B41, B44, B45, B47, B49, B50, B51, B53, B57, B60, B61, B62, B71, B72, B76, B77, Cw2, Cw9, Cw10, Cw12, Cw16
	15,000-19,999	A11, A25, A26, A29, A30, A32, A33, A43, A66, A68, A74, A80, B18, B27, B2708, B37, B46, B48, B52, B58, B59, B63, B75, B78, B82, Cw1, Cw2, Cw5, Cw6, Cw8, Cw14, Cw15
	10,000-14,999	A34, A36, B64, A66, A69, B54, B56, B67, B73, Cw17, Cw18
	5,000-9,999	A23, B55, B65, B81
	1,000-4,999	A2403, B42, Cw4

HLA Class I genotyping was also performed using PCR-SSO:

Patient ID	**LD70**
HLA Type	HLA-A*01, A*24; B*07, B*08; C*07, C*-

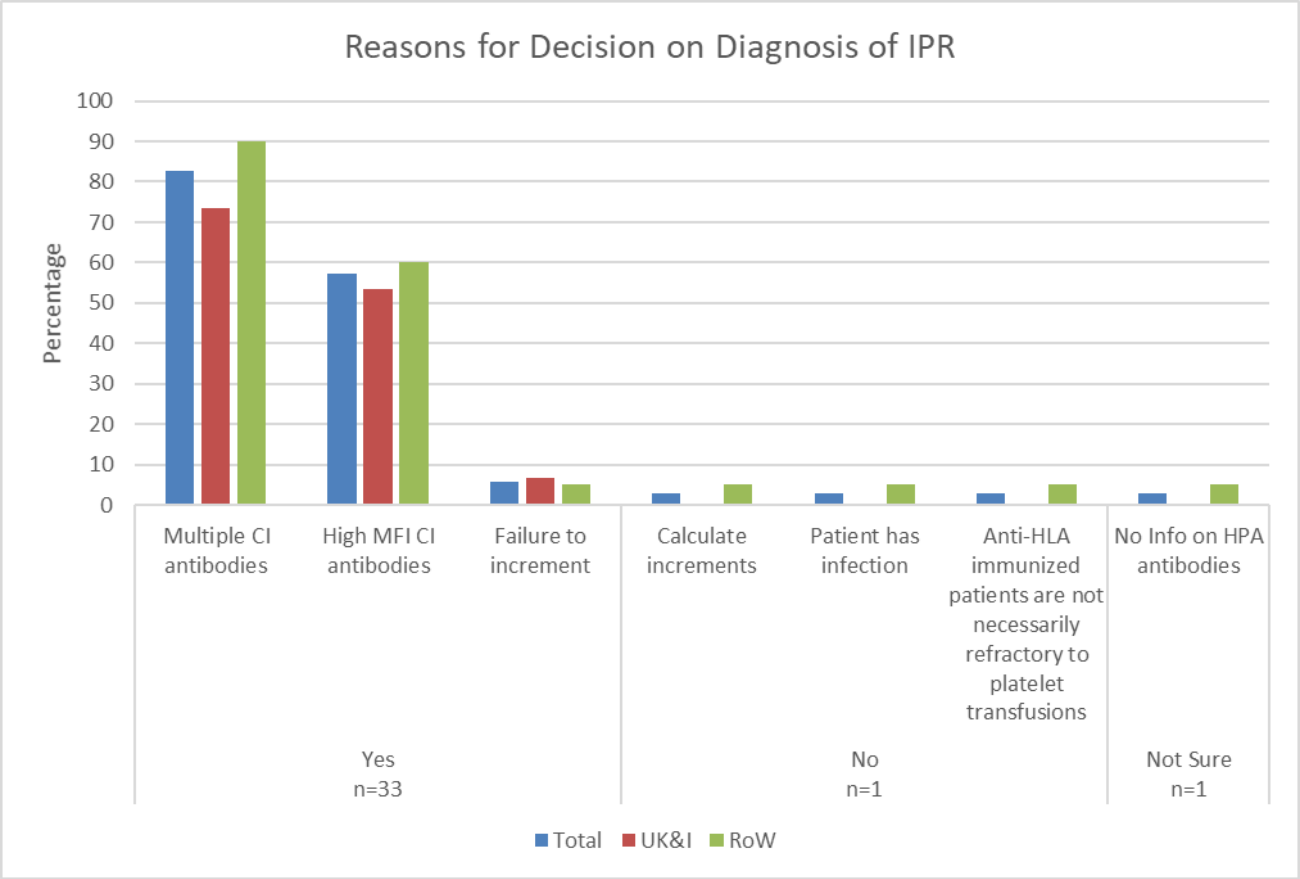
Question 2.1 – Do these results support a diagnosis of Immune Platelet Refractoriness?

	Total		UK&I		RoW	
Option	Number	%	Number	%	Number	%
Yes	33	**94**	15	**100**	18	**90**
No	1	**3**	0	**0**	1	**5**
Unsure	1	**3**	0	**0**	1	**5**



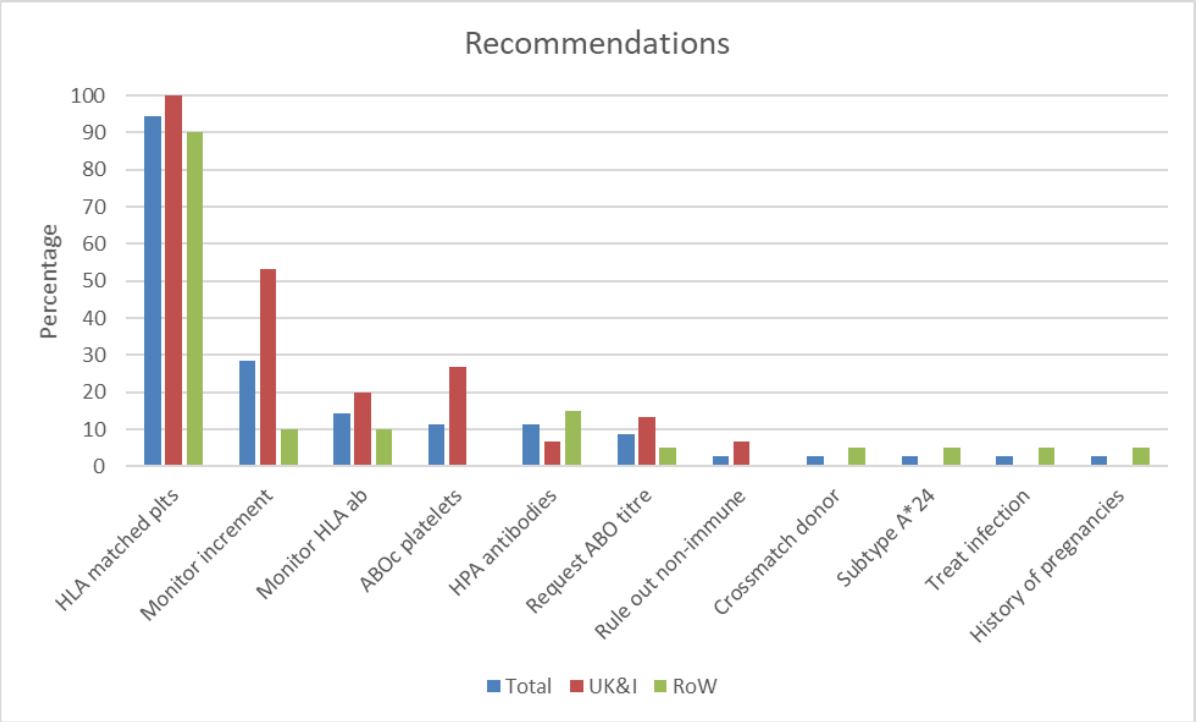
Question 2.2 – Please explain your answer.

IPR?	Reason	Total		UK&I		RoW	
		Number	%	Number	%	Number	%
Yes n=33	Patient has multiple CI antibodies	29	**83**	11	**73**	18	**90**
	High MFI CI antibodies	20	**57**	8	**53**	12	**60**
	Failure to increment	2	**6**	1	**7**	1	**5**
No n=1	Calculate platelet increments	1	**3**	0	**0**	1	**5**
	Patient has infection	1	**3**	0	**0**	1	**5**
	Anti-HLA immunized patients are not necessarily refractory to platelet transfusions	1	**3**	0	**0**	1	**5**
Not Sure n=1	No Info on presence of HPA antibodies	1	**3**	0	**0**	1	**5**



Question 2.3 – What would you recommend to the clinical team managing the patient?

Recommendations	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
Provide HLA matched platelets	33	**94**	15	**100**	18	**90**
Monitor increment	10	**29**	8	**53**	2	**10**
Monitor HLA antibodies	5	**14**	3	**20**	2	**10**
ABO compatible platelets	4	**11**	4	**27**	0	**0**
Screen for HPA antibodies	4	**11**	1	**7**	3	**15**
Request ABO titre	3	**9**	2	**13**	1	**5**
Rule out non-immune causes	1	**3**	1	**7**	0	**0**
Crossmatch donor	1	**3**	0	**0**	1	**5**
Subtype A*24	1	**3**	0	**0**	1	**5**
Treat infection	1	**3**	0	**0**	1	**5**
Investigate history of pregnancies	1	**3**	0	**0**	1	**5**

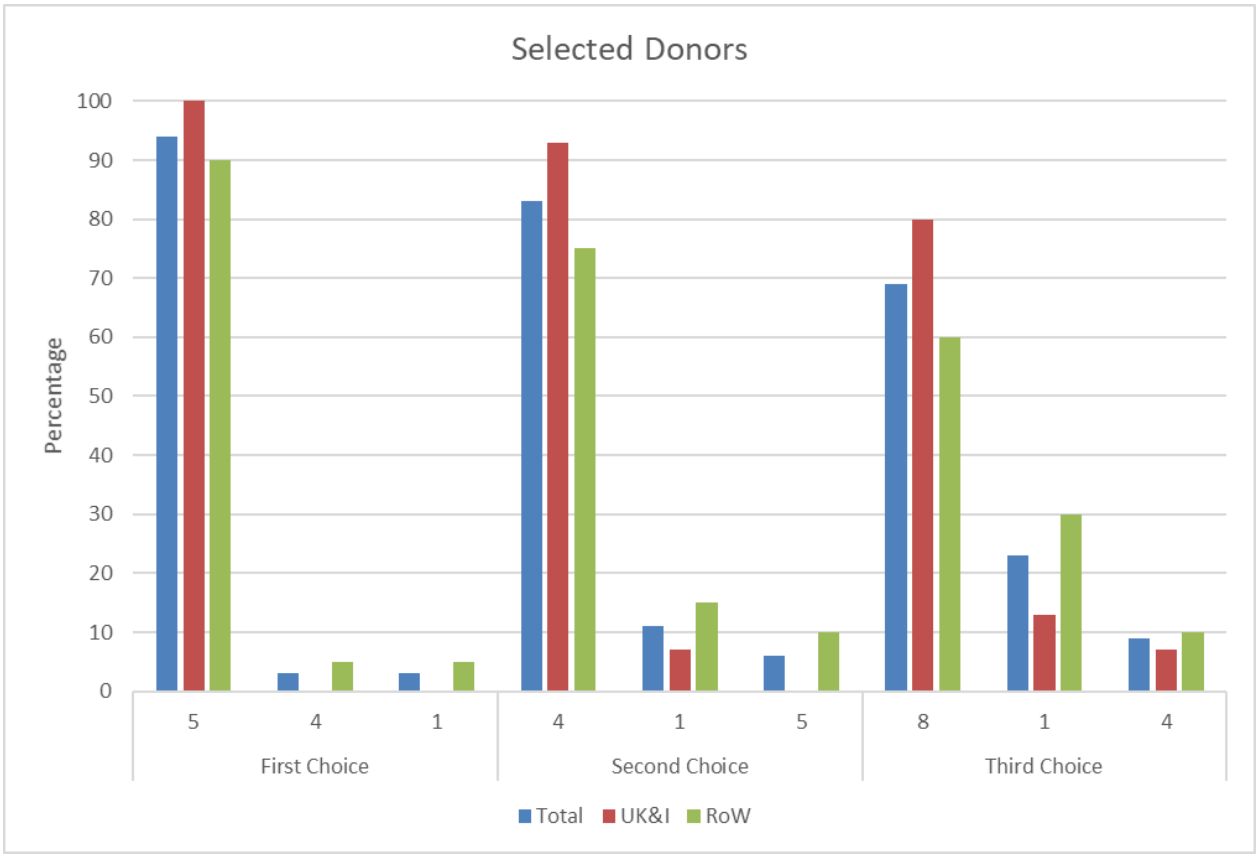


A search of local apheresis donors showed a number of potential donors available:

Patient Information	Patient ID	LD70								Comment
	Date of Matching Run	14/07/2022								
	Patient HLA Type	HLA Type						ABO Group	CMV Result	
		A1	A24	B7	B8	Cw7	Cw-	O+	Positive	
Donor ID	Donor 1	A2403		B7		Cw7		O+	Positive	Patient has antibody to A2403
	Donor 2	A1	A2	B8		Cw7		O+	Positive	Patient has antibody to A2
	Donor 3	A1	A33	B8	B44	Cw7		O+	Negative	Patient has antibody to B44
	Donor 4	A1		B7	B8	Cw7		B+	Negative	
	Donor 5	A1		B7		Cw7		O+	Positive	
	Donor 6	A1	A28	B8	B38	Cw7	Cw12	A-	Negative	Patient has antibody to B38 and Cw12
	Donor 7	A1	A23	B8		Cw7		B+	Negative	Patient has antibody to A23
	Donor 8	A1		B8		Cw7	Cw4	A+	Negative	Patient has antibody to Cw4

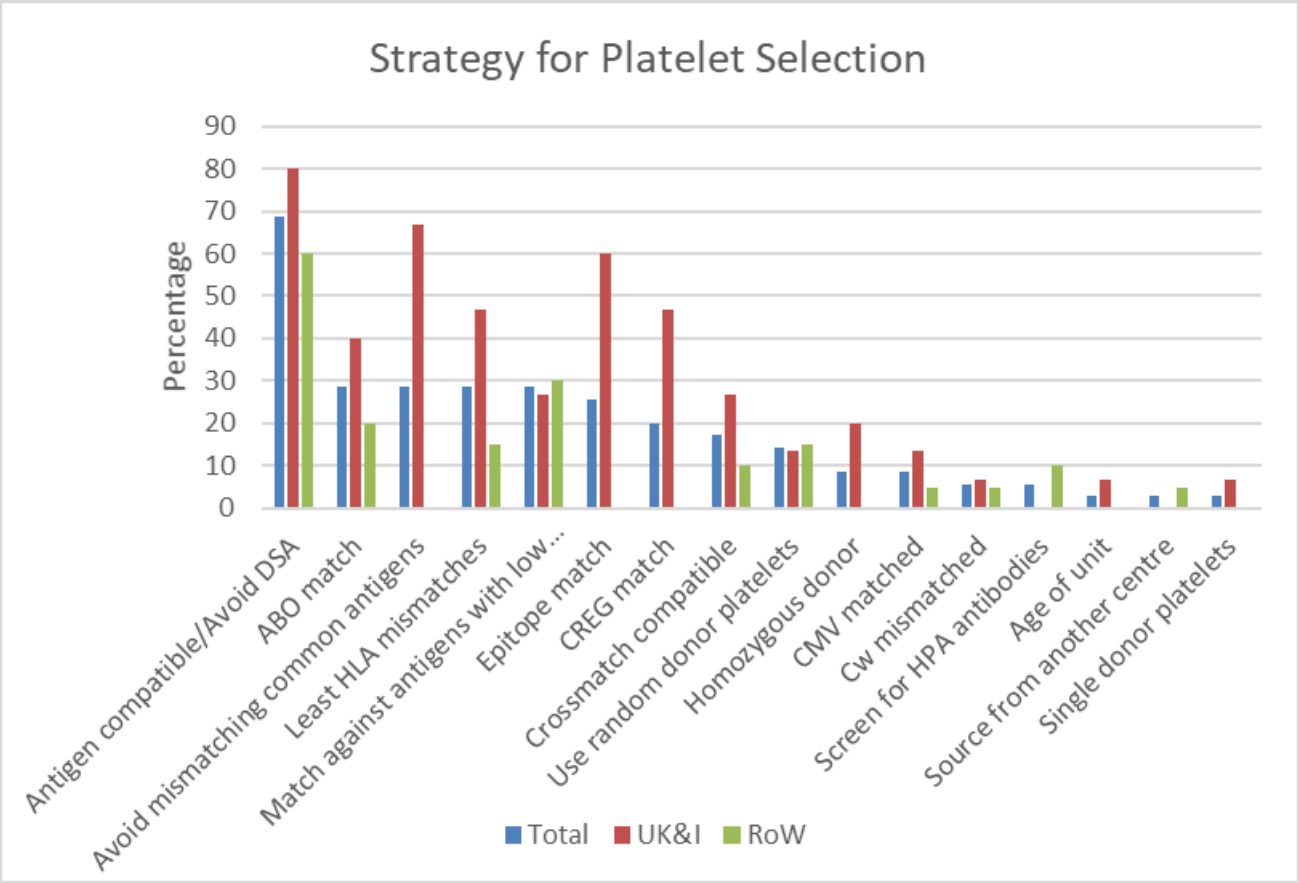
Question 3.1 – Which three donors would you select for this patient and give your reasons?

Priority	Donor ID	Total		UK&I		RoW		Reason for Selection
		Number	%	Number	%	Number	%	
First Choice	**5**	33	**94**	15	**100**	18	**90**	HLA matched ABO matched CMV matched Patient does not have any HLA antibodies against this donor No Cw mismatch
	4	1	**3**	0	**0**	1	**5**	HLA matched
	1	1	**3**	0	**0**	1	**5**	A2403 antibody (low MFI)
Second Choice	**4**	29	**83**	14	**93**	15	**75**	HLA matched ABO mismatched - test for anti-B titre if not incrementing CMV mismatched Patient does not have any HLA antibodies against this donor No Cw mismatch
	1	4	**11**	1	**7**	3	**15**	Good HLA match A2403 antibody (low MFI) ABO compatible CMV compatible
	5	2	**6**	0	**0**	2	**10**	HLA match No DSA
Third Choice	**8**	24	**69**	12	**80**	12	**60**	HLA match ABO mismatch – test for anti-A titre if not incrementing Cw4 antibody (low MFI) - HLA-C low expression on platelets
	1	8	**23**	2	**13**	6	**30**	HLA match - no Cw mismatch A2403 antibody (low MFI) ABO and CMV match
	4	3	**9**	1	**7**	2	**10**	No HLA mismatches ABO and CMV incompatible



Question 3.2 – If HLA identical platelets were not available, what strategies would you use to select platelets?

Strategy	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
Antigen compatible/Avoid DSA	24	**69**	12	**80**	12	**60**
ABO match	10	**29**	6	**40**	4	**20**
Avoid mismatching common antigens	10	**29**	10	**67**	0	**0**
Least HLA mismatches	10	**29**	7	**47**	3	**15**
Match against antigens with low level DSA	10	**29**	4	**27**	6	**30**
Epitope match	9	**26**	9	**60**	0	**0**
CREG match	7	**20**	7	**47**	0	**0**
Crossmatch compatible	6	**17**	4	**27**	2	**10**
Use random donor platelets	5	**14**	2	**13**	3	**15**
Homozygous donor	3	**9**	3	**20**	0	**0**
CMV matched	3	**9**	2	**13**	1	**5**
Cw mismatched	2	**6**	1	**7**	1	**5**
Screen for HPA antibodies	2	**6**	0	**0**	2	**10**
Age of unit	1	**3**	1	**7**	0	**0**
Source from another centre	1	**3**	0	**0**	1	**5**
Single donor platelets	1	**3**	1	**7**	0	**0**



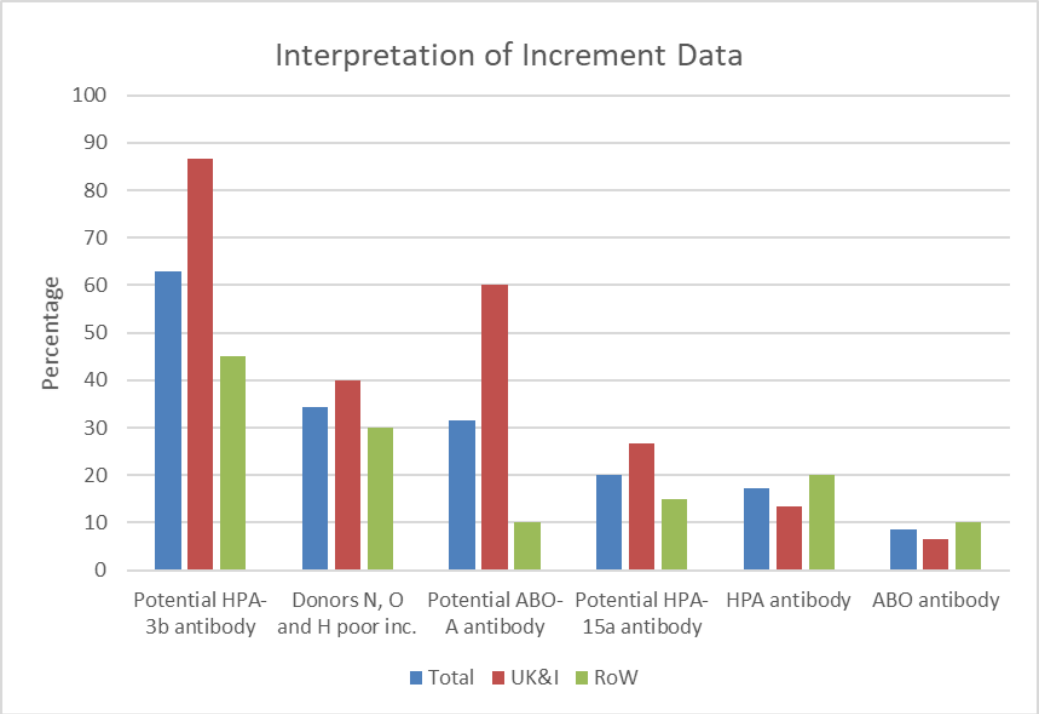
The patient received a number of platelet transfusions. A summary of the platelet increment data pre and post-transfusion can be found below:

Donor ID	HLA Match Grade*	Increment Data – Collected Pre-Transfusion and 24 hours Post-Transfusion				
		Pre	Post	HLA Class I Mismatches	HPA Mismatches	Blood Group
		Platelet Count ($x10^9$/l)				
Donor L	A	5	25	No mismatches	2b, 15a	A+
Donor F	A	28	54	No mismatches	1b, 3b, 15a	A+
Donor F	A	44	67	No mismatches	1b, 3b, 15a	A+
Donor P	A	58	85	No mismatches	1b, 15a	A-
Donor G	A	35	63	No mismatches	1b, 3b, 15a	B+
Donor G	A	38	66	No mismatches	1b, 3b, 15a	B+
Donor C	A	48	98	No mismatches	1b	O+
Donor E	A	68	92	No mismatches	15a	O+
Donor M	A	40	55	No mismatches	3b, 15a	A+
Donor B	A	37	53	No mismatches	15a	O+
Donor N	A	31	34	No mismatches	3b, 15a	A-
Donor O	A	18	14	No mismatches	3b, 15a	A+
Donor H	A	22	30	No mismatches	3b	A+
Donor H	A	18	23	No mismatches	3b	A+

**HLA Match Grade A denotes no HLA Class I mismatches between donor and patient*

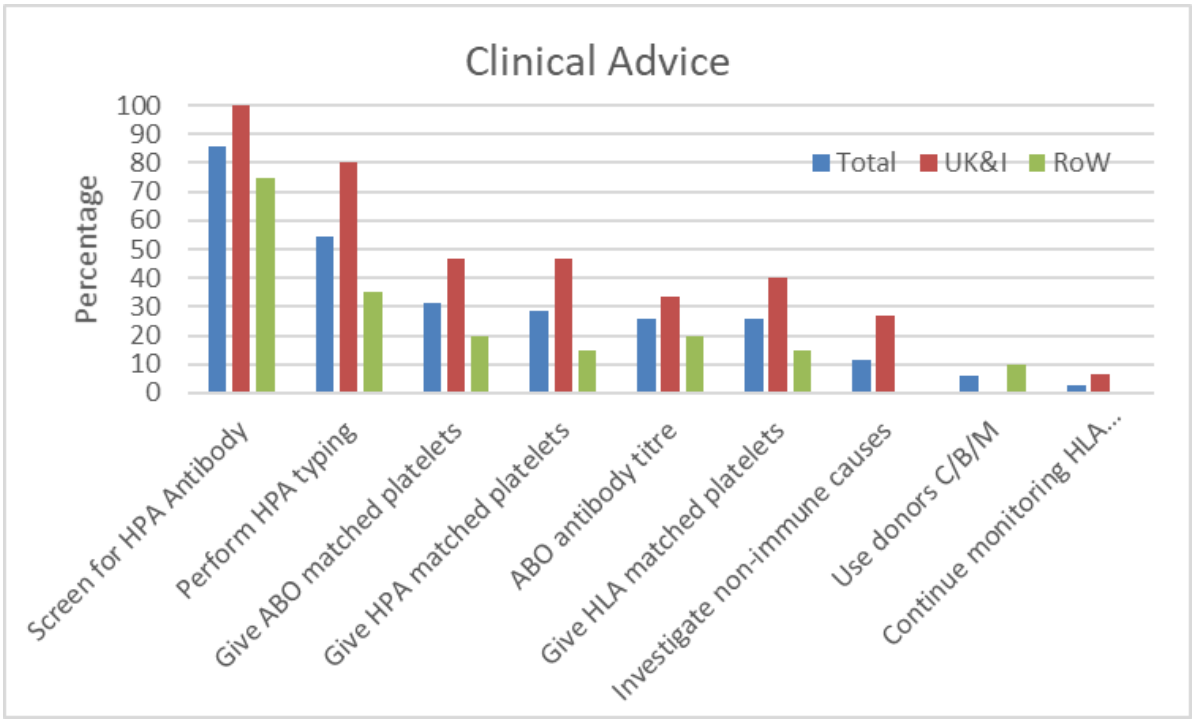
Question 4.1 – How would you interpret the increment data?

Interpretation	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
Potential HPA-3b antibody	22	**63**	13	**87**	9	**45**
Insufficient increment with Donors N, O and H	12	**34**	6	**40**	6	**30**
Potential ABO-A antibody	11	**31**	9	**60**	2	**10**
Potential HPA-15a antibody	7	**20**	4	**27**	3	**15**
HPA antibody	6	**17**	2	**13**	4	**20**
ABO antibody	3	**9**	1	**7**	2	**10**



Question 4.2 – What clinical advice would you recommend?

Clinical Advice	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
Screen for HPA Antibody	30	**86**	15	**100**	15	**75**
Perform HPA typing	19	**54**	12	**80**	7	**35**
Give ABO matched platelets	11	**31**	7	**47**	4	**20**
Give HPA matched platelets	10	**29**	7	**47**	3	**15**
ABO antibody titre	9	**26**	5	**33**	4	**20**
Give HLA matched platelets	9	**26**	6	**40**	3	**15**
Investigate non-immune causes	4	**11**	4	**27**	0	**0**
Use donors C/B/M	2	**6**	0	**0**	2	**10**
Continue monitoring HLA antibodies	1	**3**	1	**7**	0	**0**



A further serum sample was received from the patient on the 29th July 2022.

A monoclonal antibody immobilisation of platelet antigen (MAIPA) assay was performed on the two serum dates available:

Platelet	LD70 Sample 1	LD70 Sample 2
1a1a 3a3a	Negative	Negative
1a1a 3b3b	Negative	Positive
1b1b 3a3a	Negative	Negative
1b1b 3b3b	Negative	Positive
5a5a	Negative	Negative
5a5b	Negative	Negative
5b5b	Negative	Negative

An additional MAIPA with an expanded panel was performed:

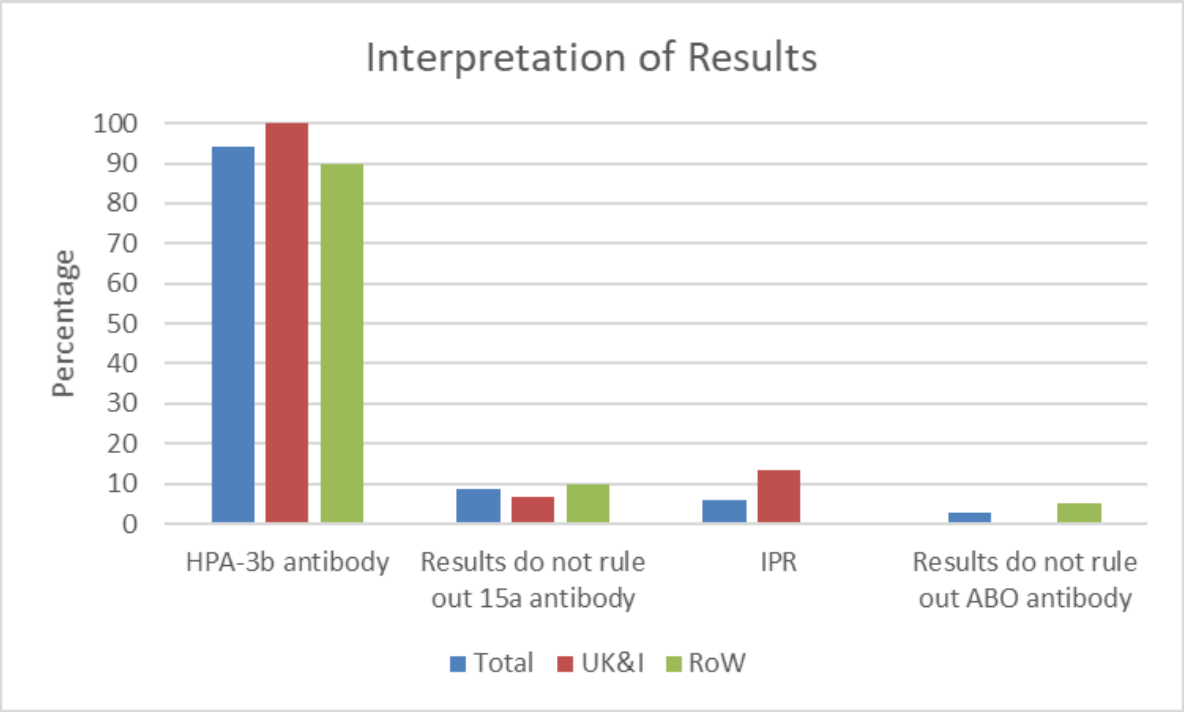
Platelet	LD70 Sample 2
1a1a 3a3a	Negative
1a1a 3b3b	Positive
1b1b 3a3a	Negative
1b1b 3b3b	Positive
1a1a 3a3b	Negative
1a1a 3b3b	Positive
1a1a 3b3b	Positive

HPA genotyping was also performed on the patient:

Patient ID	LD70
HPA Type	HPA-1a1a, 2a2a, 3a3a, 4a4a, 5a5b, 6a6a, 7a7a, 8a8a, 9a9a, 10a10a, 11a11a, 15b15b

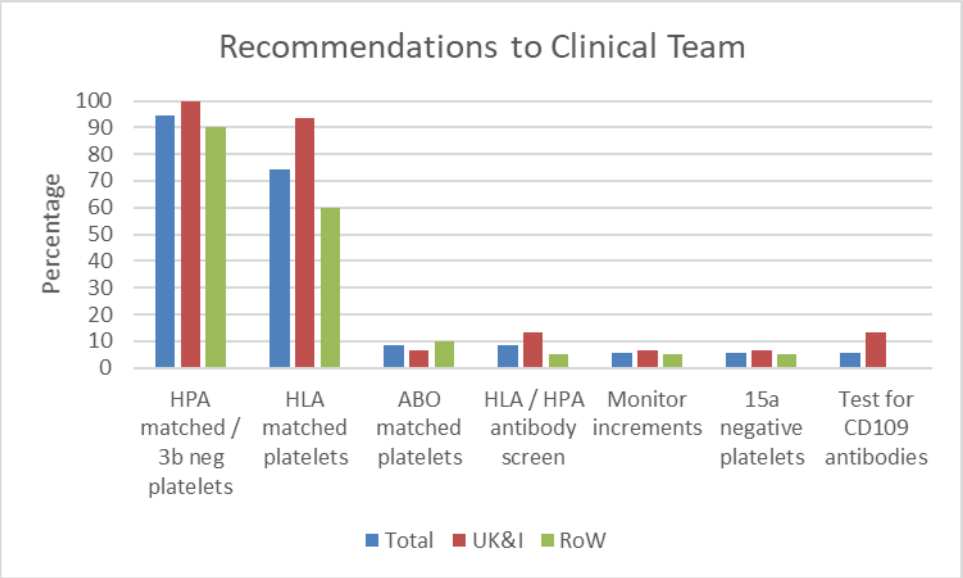
Question 5.1 – What do these results indicate?

Results Indicate	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
HPA-3b antibody	33	**94**	15	**100**	18	**90**
Results do not rule out 15a antibody	3	**9**	1	**7**	2	**10**
IPR	2	**6**	2	**13**	0	**0**
Results do not rule out ABO antibody	1	**3**	0	**0**	1	**5**



Question 5.2 – What would you recommend to the clinical team?

Recommendations	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
HPA matched / 3b neg platelets	33	**94**	15	**100**	18	**90**
HLA matched platelets	26	**74**	14	**93**	12	**60**
ABO matched platelets	3	**9**	1	**7**	2	**10**
HLA / HPA antibody screen	3	**9**	2	**13**	1	**5**
Monitor increments	2	**6**	1	**7**	1	**5**
15a negative platelets	2	**6**	1	**7**	1	**5**
Test for CD109 antibodies	2	**6**	2	**13**	0	**0**
Investigate non-immune causes	1	**3**	1	**7**	0	**0**



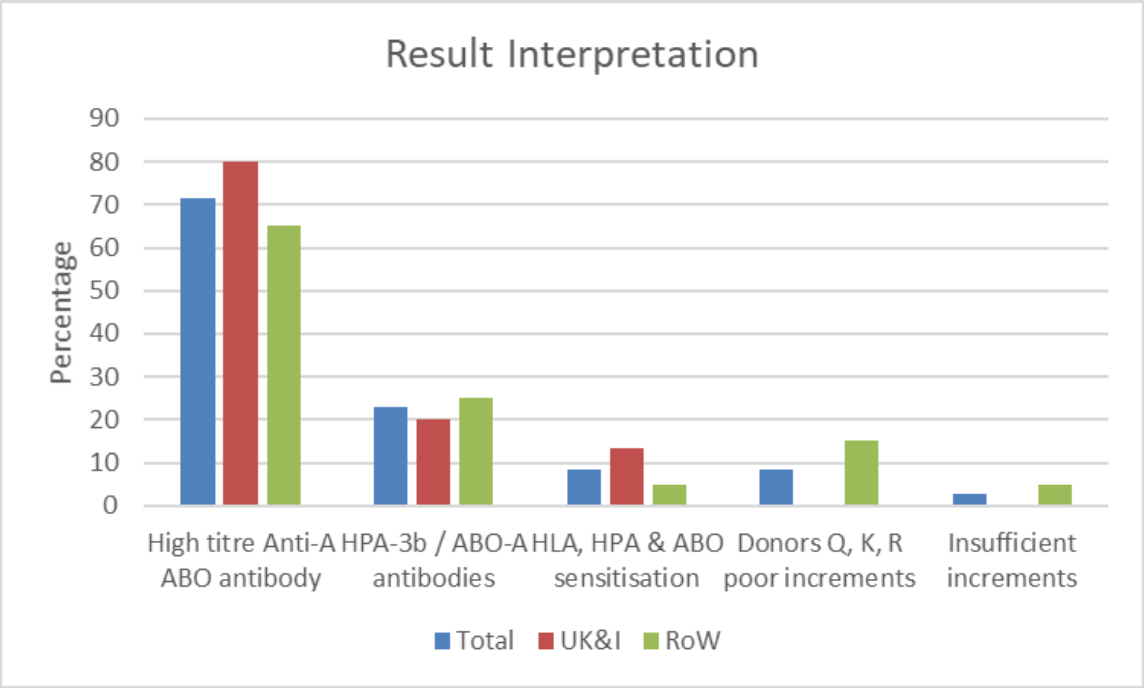
The patient received a second cycle of chemotherapy and prophylactic platelets were provided during treatment. A summary of the platelet increment data pre- and post-transfusion is provided:

Donor ID	HLA Match Grade*	Increment Data – Collected Pre-Transfusion and 24 hours Post-Transfusion				
		Pre	Post	HLA Class I Mismatches	HPA Mismatches	Blood Group
		Count (x10^9/l)				
Donor D	A	12	40	No mismatches	1b, 15a	B+
Donor D	A	19	32	No mismatches	1b, 15a	B+
Donor G	A	10	19	No mismatches	1b, 3b, 15a	B+
Donor Q	A	11	19	No mismatches	No mismatches	A+
Donor C	A	9	48	No mismatches	1b	O+
Donor C	A	23	64	No mismatches	1b	O+
Donor E	A	24	62	No mismatches	15a	O+
Donor K	A	23	26	No mismatches	15a	A+
Donor D	A	11	47	No mismatches	1b, 15a	B+
Donor D	A	30	57	No mismatches	1b, 15a	B+
Donor R	A	22	26	No mismatches	No mismatches	A+
Donor T	A	10	42	No mismatches	1b	O+
Donor E	A	28	57	No mismatches	15a	O+
Donor E	A	48	65	No mismatches	15a	O+
Donor R	A	44	52	No mismatches	No mismatches	A+
Donor B	A	22	60	No mismatches	15a	O+
Donor S	A	17	45	No mismatches	1b	O+
Donor E	A	24	60	No mismatches	15a	O+
Donor K	A	27	32	No mismatches	15a	A+
Donor B	A	15	65	No mismatches	15a	O+
Donor B	A	21	56	No mismatches	15a	O+
Donor T	A	13	85	No mismatches	1b	O+

**HLA Match Grade A denotes no HLA Class I mismatches between donor and patient*

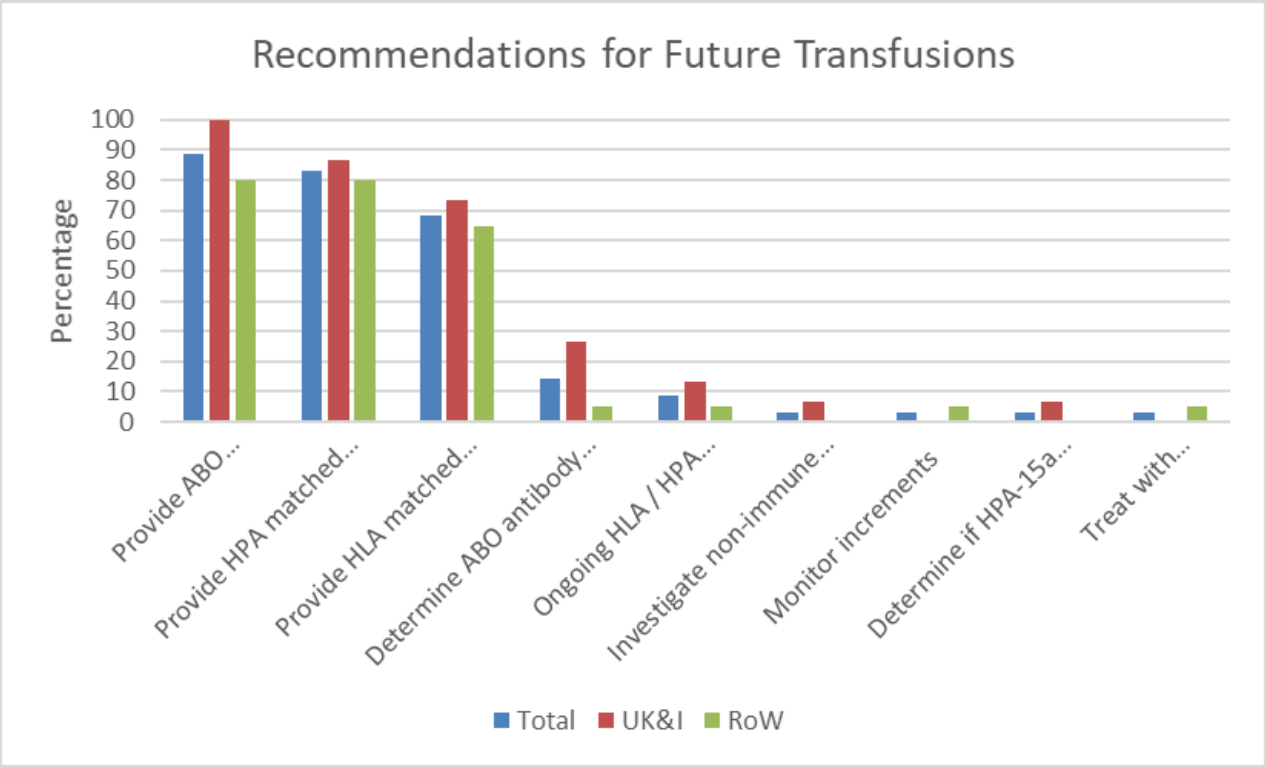
Question 6.1 – What do these results indicate?

Results Indicate	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
High titre Anti-A ABO antibody	25	**71**	12	**80**	13	**65**
HPA-3b / ABO-A antibodies	8	**23**	3	**20**	5	**25**
HLA, HPA & ABO sensitisation	3	**9**	2	**13**	1	**5**
Donors Q, K, R poor increments	3	**9**	0	**0**	3	**15**
Insufficient increments	1	**3**	0	**0**	1	**5**



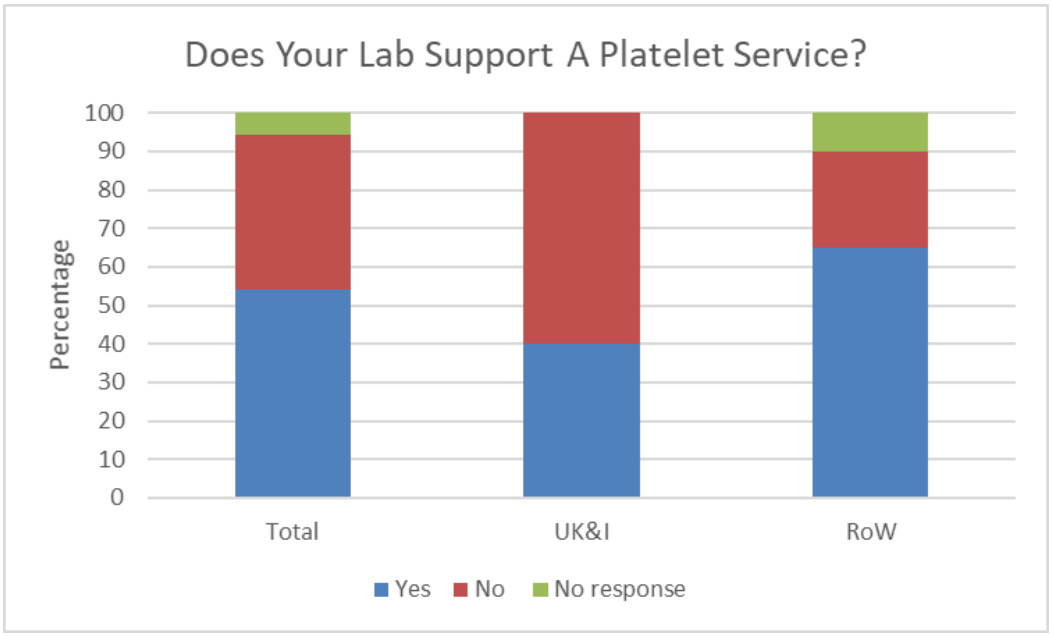
Question 6.2 – What recommendations would you make for future platelet transfusions?

Recommendations for Future Transfusions	Total		UK&I		RoW	
	Number	%	Number	%	Number	%
Provide ABO matched/compatible platelets	31	**89**	15	**100**	16	**80**
Provide HPA matched platelets	29	**83**	13	**87**	16	**80**
Provide HLA matched platelets	24	**69**	11	**73**	13	**65**
Determine ABO antibody titre	5	**14**	4	**27**	1	**5**
Ongoing HLA / HPA antibody monitoring	3	**9**	2	**13**	1	**5**
Investigate non-immune causes	1	**3**	1	**7**	0	**0**
Monitor increments	1	**3**	0	**0**	1	**5**
Determine if HPA-15a antibody	1	**3**	1	**7**	0	**0**
Treat with IVIg/corticosteroid	1	**3**	0	**0**	1	**5**



Question 7 – Does your lab support a platelet transfusion service?

	Total		UK&I		RoW	
Option	**Number**	**%**	**Number**	**%**	**Number**	**%**
Yes	19	**54**	6	**40**	13	**65**
No	14	**40**	9	**60**	5	**25**
No response	2	**6**	0	**0**	2	**10**



Question 8 – Do you have any general comments?

- Additional information on the type of infection, infection treatment to exclude non-immune causes for platelet refractoriness.
- Timelines for the platelet transfusions would have been a benefit.
- It is unlikely that this patient would receive a mismatched Class I stem cell donor due to having a common HLA type, but if this was the case, avoid platelets mismatched for any stem cell donor.
- It would be unlikely to see this combination of HLA, HPA and blood group antibodies in one patient – however, it was an interesting case study!
- The clinical team may want to consider finding an ABO matched HSCT donor given high-titre anti-A and/or -B antibodies.
- We do not match for CMV. Our donor typing only allows selection of HPA-1a negative donors if needed, whereas we can provide fully HLA-matched donors.
- Analysis of the titer of blood group isoaggluninines.
- The platelet dose in each platelet concentrate should be indicated to interpret the increments.
- Early BMT as the patient has AML and has become refractory to platelets on account of all possible immune causes including anti-HLA, anti-Blood group and anti-Platelet antibodies.

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

Question 1

We would suggest an investigation for Immune Platelet Refractoriness (IPR) would be warranted as the patient has failed to increment when random pooled platelets were transfused on multiple occasions and has suffered an intracranial haemorrhage. However, the patient also has an active infection which could indicate non-immune causes of refractoriness.

Question 2

We feel the results of HLA genotyping and antibody testing support a diagnosis of IPR. This is because the patient has a number of HLA Class I specific antibodies with high MFI levels. Class I HLA antibodies are known to cause IPR.

We would recommend that the patient received HLA selected platelets and that increment data is collected to monitor the therapeutic value of each transfusion.

Question 3

Our preference would be to select Donor 5 (HLA match, patient has no antibodies against donor), Donor 4 (HLA match, patient has no antibodies against donor) and then Donor 1 (A2403 mismatch, patient has antibody against A2403 MFI <5,000) or Donor 8 (Cw4 mismatch, patient has antibody against Cw4 MFI <5,000).

If HLA identical platelets were not available if may be prudent to use selected platelets which are compatible in terms of avoiding donors with antigen cognate to the patients HLA antibodies. Also, units with minimal HLA mismatches at HLA-A and -B should be prioritised.

Question 4

The increment data suggests the patient has developed an HPA-3b antibody. A fresh sample should be requested and tested for the presence of HPA antibodies. The patient should also be HPA genotyped.

Question 5

The results provided indicate the patient has a HPA-3b antibody. We would recommend that the patient receives HLA and HPA selected platelets.

Question 6

The increment data indicates the patient has more satisfactory platelet increment after receiving HLA and HPA matched products. The results also indicate that the patient may have an ABO-A antibody.

We would recommend that the patient receives HLA, HPA and ABO selected platelets.

Patient Update

This scenario was based on a real patient case. The patient was given HLA and HPA matched products and ABO matched products whenever possible to achieve satisfactory increments.

The patient went on to successfully receive a haematopoietic stem cell transplant from a 12/12 HLA matched, ABO group O+, CMV positive, HEV negative, 19 year old female donor. The patient only required transfusion support for the first two months post-transplant after which their platelet count was consistently >100 x 10^9/l.

Please note:

These comments have been 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.