Interpretive Educational Scheme (iED)
Clinical Scenario 3/2025 – Transfusion/Platelet Immunology Case

Dispatched on 28th October 2025

Summary of Results

There were 33 responses received. 15 from laboratories based in the UK and Ireland (UK&I) and 18 from laboratories based in the rest of the World (RoW).

A 61-year-old male was admitted from accident and emergency on the 8th of September with a cough, diarrhoea and vomiting. The patient left before full investigations were performed but no significant cardiac issues were identified. The patient's platelet count was $250x10^9$/litre.

The patient was re-admitted to hospital on the 12th September with urosepsis with haematuria, thrombocytopenia and breathing difficulties. The patient's platelet count was recorded as $4x10^9$/litre.

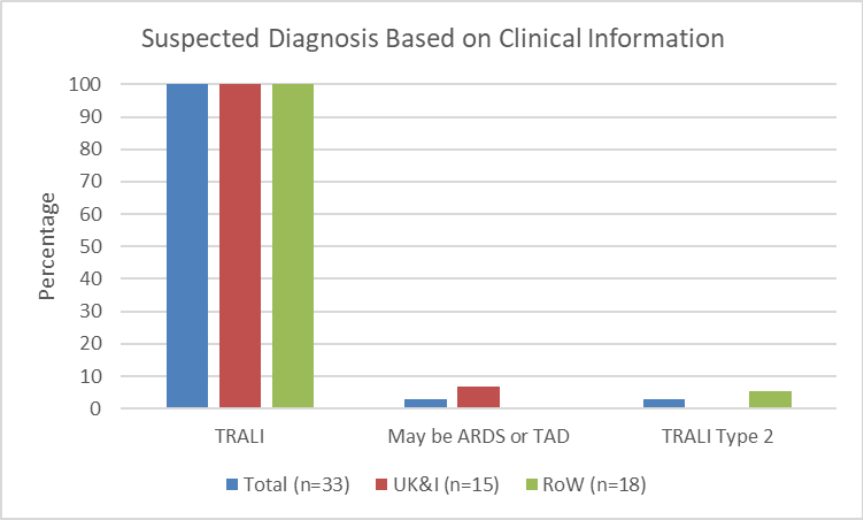
The patient was transfused with two units of platelets: pool A at 14:00 and pool B at 15:30. After the second unit was transfused the patient became increasingly breathless to the point where the patient was started on non-invasive ventilation, moving to high flow oxygen. Blood tests showed that urea and creatinine levels were significantly deranged and the patient had raised inflammatory markers.

On the 15th September the patient was transfused with two further units of platelets (pool C and pool D) without incident. The patient underwent a chest X-ray which showed widespread bilateral ground glass changes.

On the 16th September the patient was transfused with one unit of red cells. The case was reviewed by a multi-disciplinary team and samples were referred to the H&I laboratory for investigation.

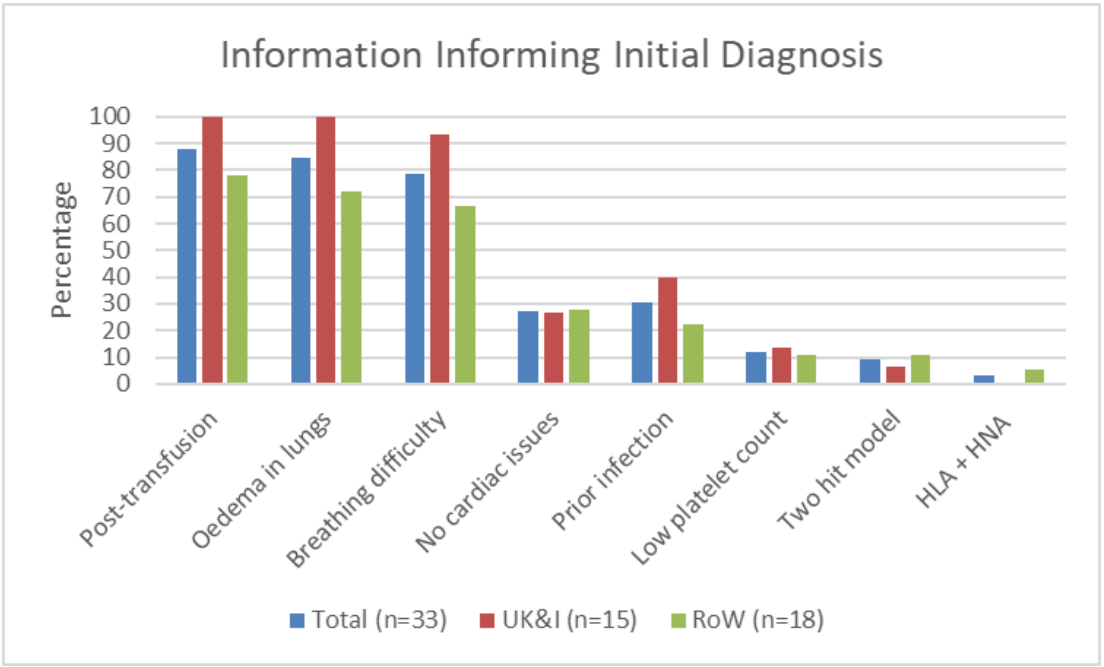
Q1.1. What diagnosis would you suspect based on this information?

Diagnosis	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
TRALI	33	**100**	15	**100**	18	**100**
May be ARDS or TAD	1	**3**	1	**7**	0	**0**
TRALI Type 2	1	**3**	0	**0**	1	**6**



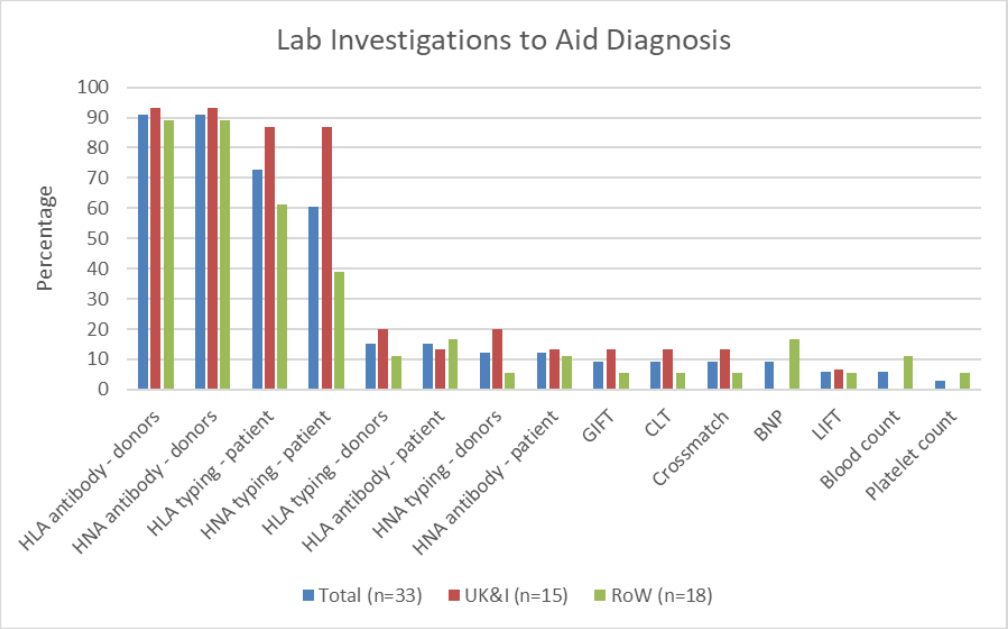
Q1.2. What information have you based this decision on?

Basis of Decision	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
Post-transfusion	29	**88**	15	**100**	14	**78**
Oedema in lungs	28	**85**	15	**100**	13	**72**
Breathing difficulty / oxygen support	26	**79**	14	**93**	12	**67**
Absence of cardiac issues	9	**27**	4	**27**	5	**28**
Prior infection	10	**30**	6	**40**	4	**22**
Low platelet count	4	**12**	2	**13**	2	**11**
Two hit model	3	**9**	1	**7**	2	**11**
HLA + HNA typing and antibody detection	1	**3**	0	**0**	1	**6**



Q1.3. What laboratory investigations would you perform to aid diagnosis and why?

Laboratory Investigations	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
HLA antibody - donors	30	**91**	14	**93**	16	**89**
HNA antibody - donors	30	**91**	14	**93**	16	**89**
HLA typing - patient	24	**73**	13	**87**	11	**61**
HNA typing - patient	20	**61**	13	**87**	7	**39**
HLA typing - donors	5	**15**	3	**20**	2	**11**
HLA antibody - patient	5	**15**	2	**13**	3	**17**
HNA typing - donors	4	**12**	3	**20**	1	**6**
HNA antibody - patient	4	**12**	2	**13**	2	**11**
GIFT	3	**9**	2	**13**	1	**6**
CLT	3	**9**	2	**13**	1	**6**
Crossmatch	3	**9**	2	**13**	1	**6**
Brain Natriuretic Peptide (BNP)	3	**9**	0	**0**	3	**17**
LIFT	2	**6**	1	**7**	1	**6**
Blood culture / blood count / Coomb's Test	2	**6**	0	**0**	2	**11**
Patient platelet count	1	**3**	0	**0**	1	**6**



The two implicated platelet units were platelet pools each consisting of donations from four separate donors (*note: M denotes male donor, F denotes female donor*):

Pool A: Donor 1 (F), Donor 2 (M), Donor 3 (F), Donor 4 (F)
Pool B: Donor 5 (F), Donor 6 (F), Donor 7 (M), Donor 8 (F)

Samples were screened by LABScreen Multi assay for HLA-class I, HLA-Class II and HNA antibodies. The granulocyte immunofluorescence test (GIFT), lymphocyte immunofluorescence test (LIFT) and

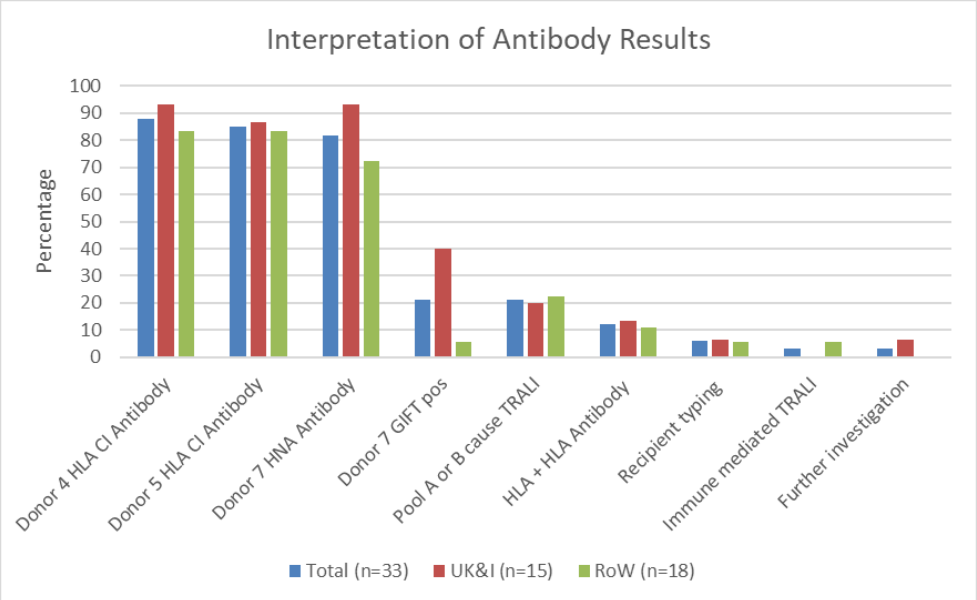
chemiluminescence test (CLT) were used to test for Granulocyte specific antibodies. Results are summarised in Table 1.

Table 1: Summary of Laboratory Testing for HLA, HNA and Granulocyte Specific Antibodies.

Platelet Pool	Donor	HLA Luminex Class I	HLA Luminex Class II	HNA Luminex	GIFT	LIFT	CLT
A	1	Neg	Neg	Neg	Neg	Neg	Neg
	2	Neg	Neg	Neg	Neg	Neg	Neg
	3	Neg	Neg	Neg	Neg	Neg	Neg
	4	Pos	Neg	Neg	Neg	Neg	Neg
B	5	Pos	Neg	Neg	Neg	Neg	Neg
	6	Neg	Neg	Neg	Neg	Neg	Neg
	7	Neg	Neg	Neg	Pos	Neg	Neg
	8	Neg	Neg	Neg	Neg	Neg	Neg

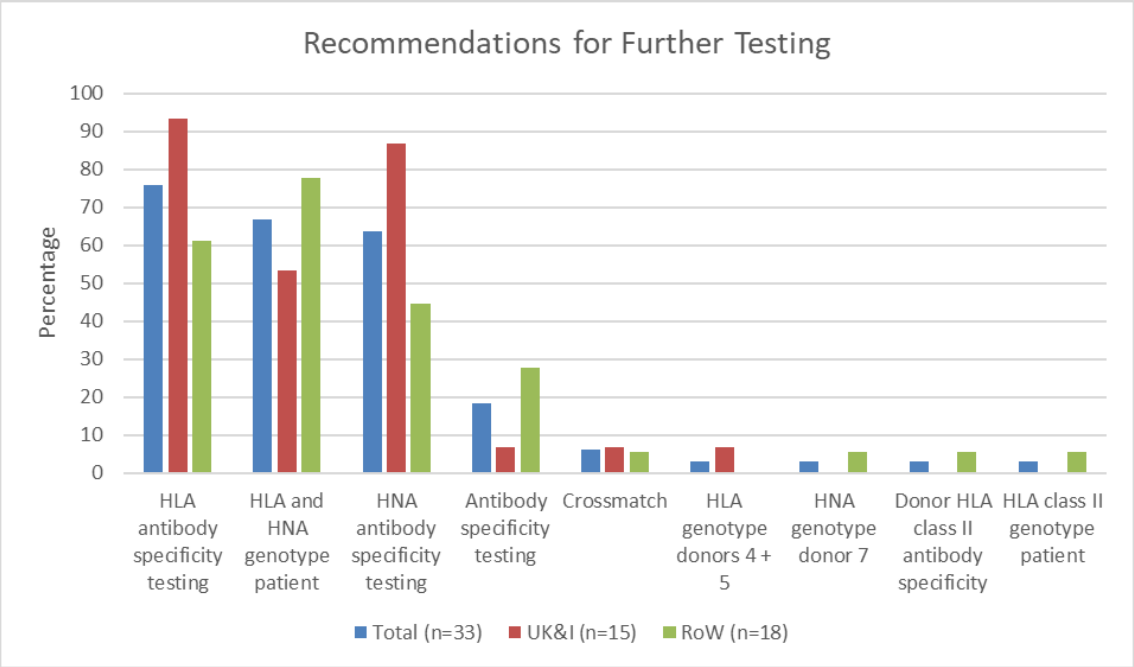
Q2.1. What do the results presented in Table 1 indicate?

Interpretation of Results	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
Donor 4 (Pool A) HLA CI Antibody	29	**88**	14	**93**	15	**83**
Donor 5 (Pool B) HLA CI Antibody	28	**85**	13	**87**	15	**83**
Donor 7 (Pool B) HNA Antibody	27	**82**	14	**93**	13	**72**
Donor 7 GIFT only positive	7	**21**	6	**40**	1	**6**
Pool A or B could cause TRALI	7	**21**	3	**20**	4	**22**
HLA + HLA Antibody in donor pools	4	**12**	2	**13**	2	**11**
Recipient HLA + HNA typing required	2	**6**	1	**7**	1	**6**
Immune mediated TRALI	1	**3**	0	**0**	1	**6**
Further investigation required	1	**3**	1	**7**	0	**0**



Q2.2. What further testing, if any, would you recommend and why?

Further Testing	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
HLA antibody specificity testing	25	**76**	14	**93**	11	**61**
HLA and HNA genotype patient	22	**67**	8	**53**	14	**78**
HNA antibody specificity testing	21	**64**	13	**87**	8	**44**
Antibody specificity testing	6	**18**	1	**7**	5	**28**
Crossmatch	2	**6**	1	**7**	1	**6**
HLA genotype donors 4 + 5	1	**3**	1	**7**	0	**0**
HNA genotype donor 7	1	**3**	0	**0**	1	**6**
Donor HLA class II antibody specificity	1	**3**	0	**0**	1	**6**
HLA class II genotype patient	1	**3**	0	**0**	1	**6**



Testing was performed on Donors 4, 5, and 7. The results are displayed in Table 2a, 2b and 2c, please note that Donor 4 and 5 had no HLA Class II antibodies present. Also, Donor 7 was negative for Class I and II HLA antibodies.

Table 2a: Summary of LABScreen Class I Single Antigen Bead Testing of Donor 4 for HLA Antibodies

Allele Specificity	MFI Value
A*02:01	3393
A*02:06	3118
A*02:03	3046
A*30:02	987
A*69:01	983
A*68:01	982
B*82:01	978
A*31:01	976
A*68:02	974
B*08:01	969
B*41:01	967
B*58:01	949
B*57:01	911
B*48:01	905
B*57:03	873
B*44:03	855
B*42:01	855
B*38:01	845
B*54:01	841
A*29:02	809
B*81:01	801
B*78:01	786
B*59:01	744
B*40:01	735
B*39:01	734
B*13:02	699
B*40:02	668
A*29:01	668
B*13:01	641
B*55:01	607
A*30:01	599
B*50:01	581
B*27:08	574

Allele Specificity	MFI Value
B*15:02	552
B*51:01	527
B*44:02	514
B*27:05	513
B*15:03	499
B*51:02	487
B*45:01	477
A*24:03	467
B*56:01	465
B*37:01	464
A*24:02	453
B*15:12	451
B*35:01	439
B*15:01	427
B*49:01	413
B*67:01	402
C*05:01	401
C*03:03	389
B*40:06	389
B*52:01	386
B*53:01	379
A*34:02	376
A*23:01	375
C*18:02	373
A*80:01	350
B*15:10	345
C*08:01	340
B*47:01	334
B*15:11	334
B*07:02	333
C*15:02	331
A*74:01	327
B*18:01	319

Allele Specificity	MFI Value
A*66:02	299
C*03:02	298
A*11:01	277
B*46:01	276
C*02:02	257
A*43:01	245
A*36:01	234
B*15:13	232
A*03:01	231
C*06:02	226
B*15:16	215
A*34:01	212
C*17:01	211
A*66:01	207
A*26:01	201
A*25:01	198
C*07:02	198
A*33:03	191
C*01:02	184
A*11:02	181
A*01:01	179
C*12:03	170
C*03:04	166
A*32:01	163
B*73:01	153
C*04:01	146
A*33:01	144
C*14:02	136
C*16:01	115
B*14:01	55
B*14:02	37
001 NC	15
002 PC	14257

Table 2b: Summary of LABScreen Class I Single Antigen Bead Testing of Donor 5 for HLA Antibodies

Allele Specificity	MFI Value
B*40:01	3437
B*08:01	3296
B*15:02	2448
B*44:03	999
B*13:02	998
B*35:01	996
B*82:01	996
B*15:01	994
A*29:02	993
B*57:03	991
B*57:01	990
B*15:03	990
B*15:12	989
B*67:01	988
B*50:01	988
A*29:01	987
B*46:01	985
B*56:01	984
B*37:01	980
B*41:01	980
B*45:01	980
B*54:01	978
B*47:01	977
B*27:08	976
B*13:01	974
B*18:01	974
B*42:01	973
B*44:02	972
B*59:01	971
B*58:01	969
B*15:11	968
B*15:10	966
B*38:01	966

Allele Specificity	MFI Value
B*27:05	964
B*55:01	963
C*05:01	962
B*39:01	962
C*08:01	937
A*30:02	914
A*24:03	910
B*49:01	901
A*68:02	893
B*07:02	885
B*40:02	876
B*40:06	840
B*51:02	833
B*53:01	824
B*81:01	820
C*03:02	814
B*15:16	796
A*24:02	766
C*03:03	766
B*15:13	762
A*02:01	757
B*48:01	735
B*78:01	727
A*23:01	703
A*02:06	698
B*73:01	684
A*66:02	683
A*80:01	667
A*31:01	665
C*15:02	654
B*51:01	646
A*02:03	632
C*18:02	631

Allele Specificity	MFI Value
C*02:02	599
C*07:02	596
A*30:01	594
C*06:02	571
A*11:02	568
A*34:02	537
A*74:01	534
C*01:02	522
A*11:01	521
C*03:04	504
A*25:01	502
C*12:03	500
A*66:01	491
A*33:03	485
A*69:01	477
C*14:02	446
A*32:01	446
A*33:01	441
A*34:01	440
A*36:01	437
A*01:01	420
A*26:01	415
A*68:01	399
A*43:01	394
A*03:01	381
B*52:01	365
C*16:01	319
B*14:01	280
C*04:01	268
C*17:01	232
B*14:02	198
001 NC	22
002 PC	10516

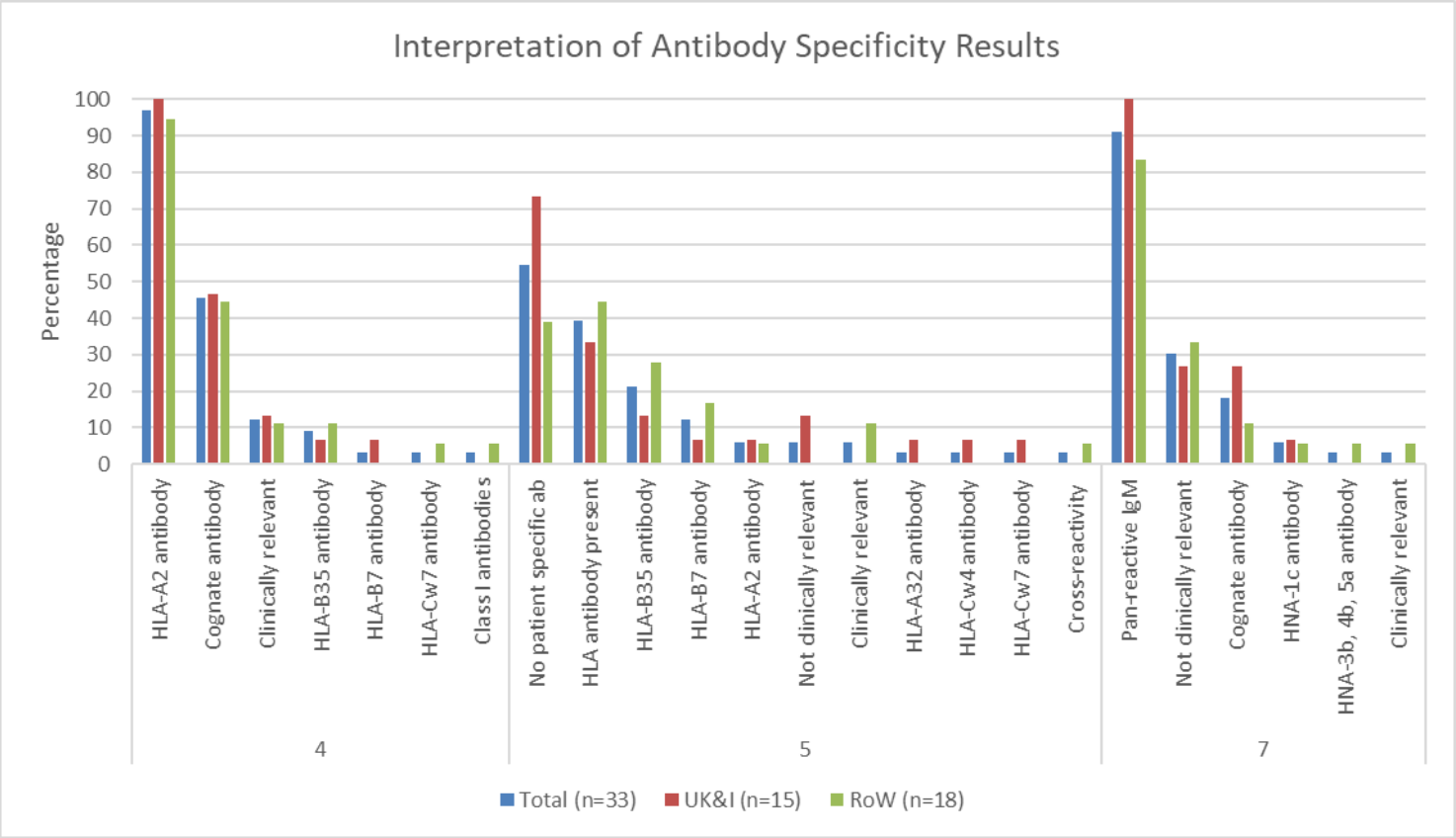
Table 2c: Summary of HNA Antibody Testing for Donor 7

Donor	GD1	GD2	GD3	GD4	GD5	GD6
HNA type	1a+1b-1c- 1d- 2+ 3a+3b- 4a+4b- 5a+5b-	1a+1b-1c- 1d- 2- 3a+3b+ 4a+4b- 5a+5b-	1a+1b-1c- 1d- 2+ 3a+3b- 4a+4b- 5a-5b+	1a-1b+1c- 1d+ 2+ 3a-3b+ 4a+4b- 5a+5b-	1a-1b+1c- 1d+ 2+ 3a+3b- 4a+4b- 5a-5b+	1a-1b+1c- 1d+ 2+ 3a+3b- 4a-4b+ 5a+5b-
CLT	Neg	Neg	Neg	Neg	Neg	Neg
GIFT IgG	Neg	Neg	Neg	Neg	Neg	Neg
GIFT IgM	Pos	Pos	Pos	Pos	Pos	Pos
LIFT IgG	Neg	Neg	Neg	Neg	Neg	Neg
LIFT IgM	Neg	Neg	Neg	Neg	Neg	Neg

The patient was HLA typed as HLA-A*02:01, A*32:01; B*07:02, B*35:01; C*04:01, C*07:02
The patient's interpreted HNA type was: HNA 1a+,1b+,1c+,1d+;3a+,3b-;4a+,4b-;5a-5b+

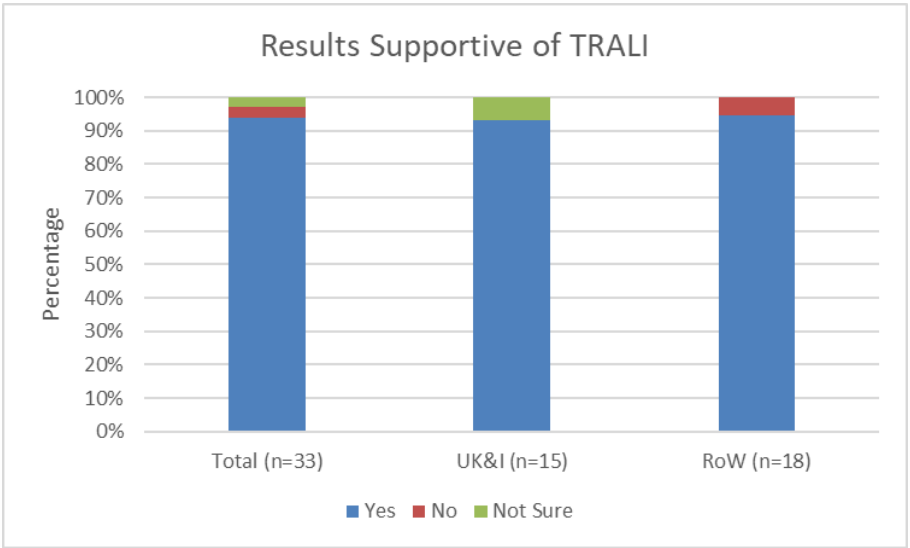
Q3.1. What do the results presented in Tables 2a, 2b and 2c indicate?

Donor	Result Interpretation	Total (n=33)		UK&I (n=15)		RoW (n=18)	
		Count	%	Count	%	Count	%
4	HLA-A2 patient specific antibody	32	**97**	15	**100**	17	**94**
	Antibody cognate to patient genotype	15	**45**	7	**47**	8	**44**
	Clinically relevant for TRALI	4	**12**	2	**13**	2	**11**
	HLA-B35 patient specific antibody	3	**9**	1	**7**	2	**11**
	HLA-B7 patient specific antibody	1	**3**	1	**7**	0	**0**
	HLA-Cw7 patient specific antibody	1	**3**	0	**0**	1	**6**
	Class I antibodies	1	**3**	0	**0**	1	**6**
5	No patient specific antibodies	18	**55**	11	**73**	7	**39**
	HLA antibody present	13	**39**	5	**33**	8	**44**
	HLA-B35 patient specific antibody	7	**21**	2	**13**	5	**28**
	HLA-B7 patient specific antibody	4	**12**	1	**7**	3	**17**
	HLA-A2 patient specific antibody	2	**6**	1	**7**	1	**6**
	Not clinically relevant to TRALI	2	**6**	2	**13**	0	**0**
	Clinically relevant for TRALI	2	**6**	0	**0**	2	**11**
	HLA-A32 patient specific antibody	1	**3**	1	**7**	0	**0**
	HLA-Cw4 patient specific antibody	1	**3**	1	**7**	0	**0**
	HLA-Cw7 patient specific antibody	1	**3**	1	**7**	0	**0**
	Potential cross-reactivity with patient antigen	1	**3**	0	**0**	1	**6**
7	Pan-reactive IgM antibody	30	**91**	15	**100**	15	**83**
	Not clinically relevant to TRALI	10	**30**	4	**27**	6	**33**
	Antibody cognate to patient HNA genotype	6	**18**	4	**27**	2	**11**
	HNA-1c patient specific antibody	2	**6**	1	**7**	1	**6**
	HNA-3b, 4b, 5a patient specific antibody	1	**3**	0	**0**	1	**6**
	Clinically relevant for TRALI	1	**3**	0	**0**	1	**6**



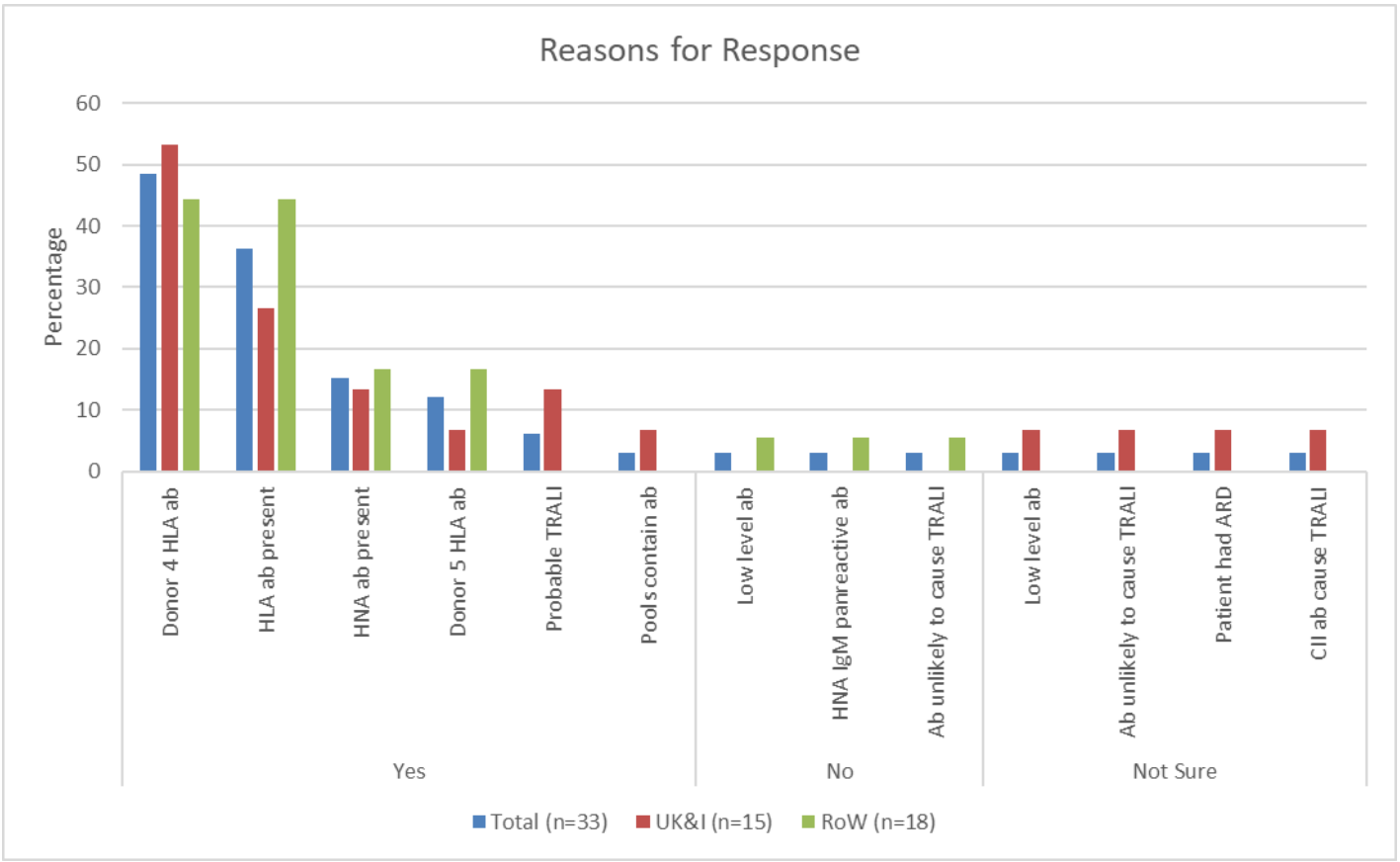
Q3.2. Do these results support your suspected diagnosis (question 1.1)?

Support Diagnosis	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
Yes	31	**94**	14	**93**	17	**94**
No	1	**3**	0	**0**	1	**6**
Not Sure	1	**3**	1	**7**	0	**0**



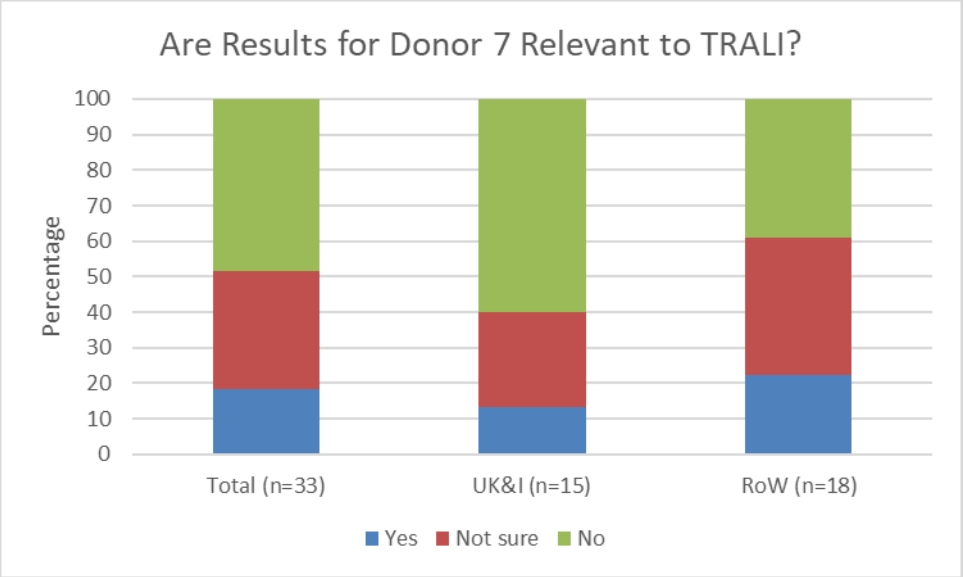
Q3.3. Give a reason for your answer

Decision	Reason for Response	Total (n=33)		UK&I (n=15)		RoW (n=18)	
		Count	%	Count	%	Count	%
Yes	Donor 4 HLA-A2 antibody	16	**48**	8	**53**	8	**44**
	HLA antibody present	12	**36**	4	**27**	8	**44**
	HNA antibody present	5	**15**	2	**13**	3	**17**
	Donor 5 HLA antibody	4	**12**	1	**7**	3	**17**
	Probable TRALI	2	**6**	2	**13**	0	**0**
	Pools contain antibodies to patient	1	**3**	1	**7**	0	**0**
No	Low level antibody	1	**3**	0	**0**	1	**6**
	HNA IgM pan-reactive antibody present	1	**3**	0	**0**	1	**6**
	Antibody unlikely to cause TRALI	1	**3**	0	**0**	1	**6**
Not Sure	Low level antibody	1	**3**	1	**7**	0	**0**
	Antibody unlikely to cause TRALI	1	**3**	1	**7**	0	**0**
	Patient had ARD	1	**3**	1	**7**	0	**0**
	CII HLA antibodies more likely to cause TRALI	1	**3**	1	**7**	0	**0**



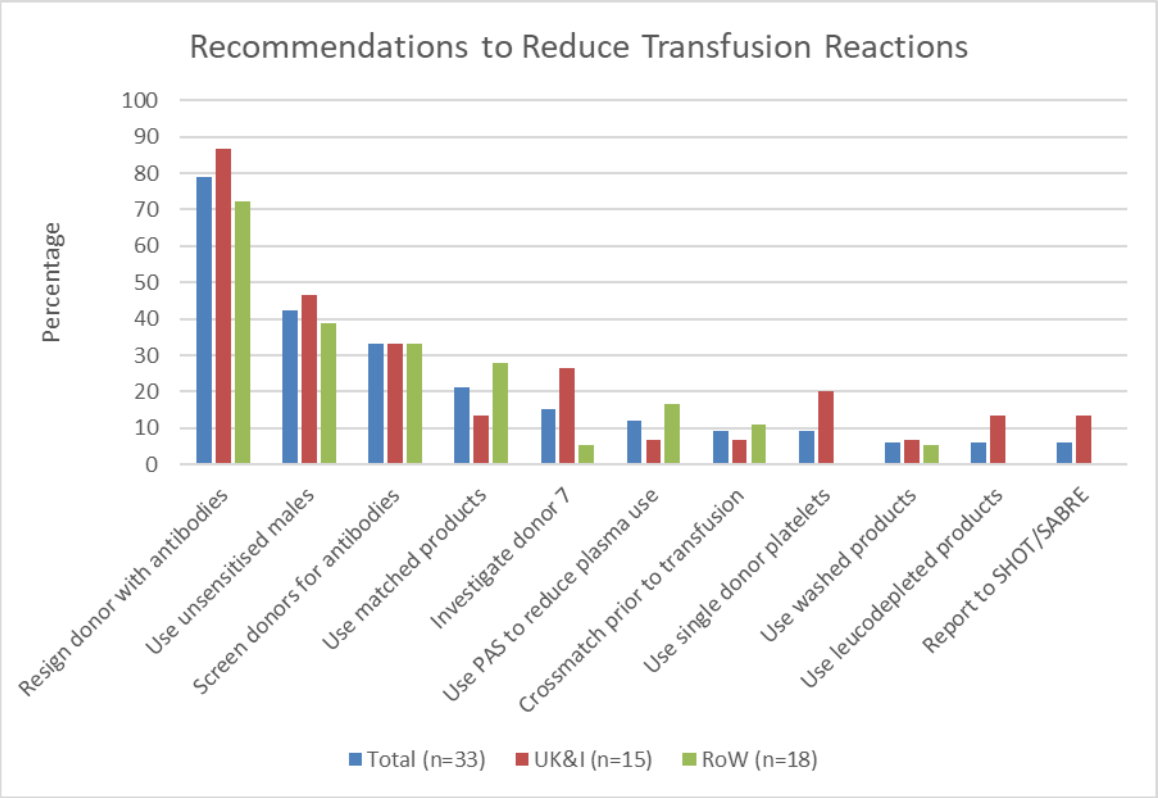
Q3.4. Are the results related to Donor 7 (Table 2c) relevant to the diagnosis?

Decision	Reasons for Response	Total (n=33)		UK&I (n=15)		RoW (n=18)	
		Count	%	Count	%	Count	%
Yes	IgM antibodies have been implicated in TRALI IgM antibodies can activate neutrophils	6	**18**	2	**13**	4	**22**
Not sure	Unclear if IgM antibodies can cause TRALI More laboratory investigations required	11	**33**	4	**27**	7	**39**
No	IgM antibodies not clinically relevant IgM pan-reactive / non-specific	16	**48**	9	**60**	7	**39**



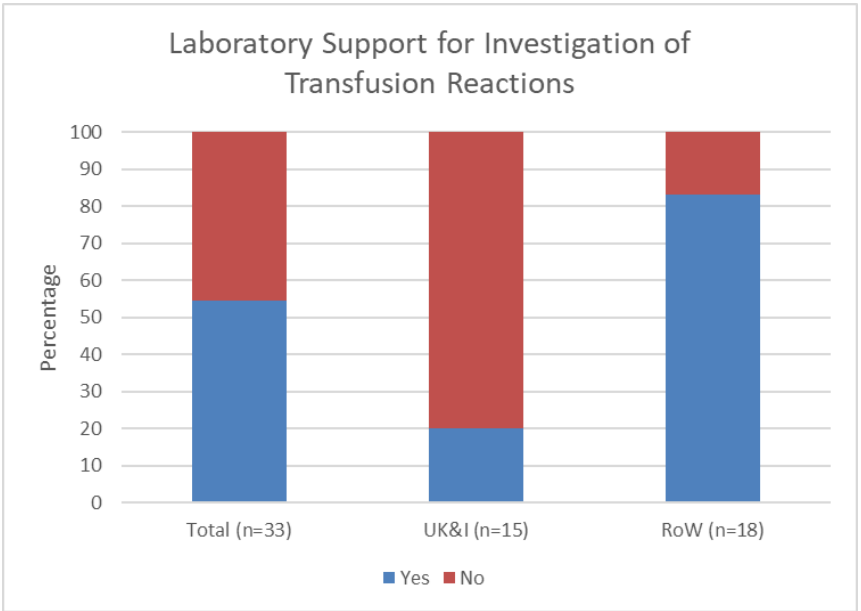
Q4.1. What steps would you take to reduce the risk of future transfusion reactions?

Reduce Transfusion Reactions	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
Resign donor with antibodies from therapeutic use/red cells only	26	**79**	13	**87**	13	**72**
Source products from unsensitised males	14	**42**	7	**47**	7	**39**
Screen donors for antibodies	11	**33**	5	**33**	6	**33**
Provide patient with matched products	7	**21**	2	**13**	5	**28**
Investigate donor 7	5	**15**	4	**27**	1	**6**
Use PAS to reduce plasma use	4	**12**	1	**7**	3	**17**
Crossmatch prior to transfusion	3	**9**	1	**7**	2	**11**
Use single donor rather than pooled platelets	3	**9**	3	**20**	0	**0**
Use washed products	2	**6**	1	**7**	1	**6**
Use leucodepleted products	2	**6**	2	**13**	0	**0**
Report to SHOT/SABRE	2	**6**	2	**13**	0	**0**



Q5.1. Does your laboratory support the investigation of transfusion reactions?

Support Testing	Total (n=33)		UK&I (n=15)		RoW (n=18)	
	Count	%	Count	%	Count	%
Yes	18	**55**	3	**20**	15	**83**
No	15	**45**	12	**80**	3	**17**



Any other comments on the scenario:

- Good educational case study, a rare case presented for discussion. We are interested to see what the experts will have to say about this case study.
- Timing of ventilation support not indicated.
- We will appreciate reading the summary to find out what MFI level of Luminex-defined HLA antibody is relevant in cases like this for our learning.
- Complex patient. Additional information required and advice would be sought from SHOT regarding investigation and classification.
- It would be interesting to see how SHOT defined this case, if it was from the UK. The clinical picture could point to TRALI or ARDS or TAD.
- Suspected transfusion reaction cases would be referred to National reference laboratory.
- HNA-1d not included on the LABScreen Multi Panel. Patient not typed at HNA-2.
- We would make some additional testing e.g. Luminex anti-granulocyte screening and anti HPA antibody screening.
- This case illustrates classic antibody-mediated TRALI associated with HLA class I antibodies from two different pooled platelet donors. Comprehensive haemovigilance and donor screening are essential to prevent recurrence.
- HNA antibody analysis is performed by a collaborating laboratory.
- We test for TRALI and anaphylactic transfusion reactions due to anti-IgA antibodies.
- In the clinical information, patient should undergo additional investigations-including PaO2/FiO2 testing or Spo2 testing, chest X-ray after incident occur.
- Transfusion is not without risk, only transfuse when necessary and clinically indicated.
- This is a classic TRALI case investigation.
- It effectively demonstrates the importance of donor antibody and patient antigen matching to identify the causative unit and inform preventative strategies. Document in transfusion records.

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

Question 1

The initial clinical details provided suggest that transfusion related acute lung injury (TRALI) or another transfusion reaction may be present. This is because an adverse reaction occurred within a 6-hour window post-transfusion, the patient experienced breathing difficulties, bilateral infiltrates where evident upon x-ray, there was a lack of cardiac issues and a low volume of transfused products (likely excluding transfusion-associated circulatory overload).

The patient had an underlying condition which may impact the decision to investigate further. However, such health issues could also contribute to the first phase in the two-hit model for the onset of TRALI, priming neutrophils.

In terms of laboratory investigations, it would be prudent to perform investigations for the presence of HLA and HNA antibodies. Donors in Pool 1 and Pool 2 pre-empt the adverse reaction and were given within a 6-hour window so would require further investigation. Pools 3 and 4 were post-reaction, without further effect on the patient, the red cells were also administered without incident. These products would not warrant further investigation. The investigation of suspected pools could primarily focus on screening female donors used in the pooled products for the presence of antibodies then determining the specificity of any antibodies detected. HNA and HLA typing of the patient should be performed to determine if any antibodies identified are cognate.

It may also be advisable to refer implicated blood products for bacterial testing to ascertain if non-immunological reasons for the adverse reaction are present. It would also be recommended to recall any unused blood products from these donors until the investigation is concluded.

Question 2

The initial antibody results suggest that Donor 4 (Pool A) and Donor 5 (Pool B) have HLA Class I antibodies. Donor 7 (Pool B) may have HNA antibodies. Further investigation is required to determine the specificity of these antibodies.

Question 3

The antibody specificity results suggest that Donor 4 has patient specific HLA-A2 antibodies. Donor 5 has HLA antibodies that are not patient specific. Donor 7 has pan-reactive IgM granulocyte antibodies.

The results from Donor 4 support a potential diagnosis of TRALI.

In relation to Donor 7, the role of IgM antibodies in TRALI is uncertain. There is little evidence that IgM antibodies are implicated in cases of TRALI, however, it may be advisable to defer donor 7 from therapeutic donation. Donor 7 could be re-tested for the presence of antibodies after a year to determine if these IgM antibodies were transient.

Question 4

Steps to reduce future transfusion reactions could include sourcing plasma products only from male donors or using plasma replacement products. The prospective screening of female platelet donors for HLA and HNA antibodies could also be considered.

Donors with antibodies could be informed. Donors with HLA antibodies could be deferred from therapeutic use or used for red cell products only. Donors with HNA antibodies could be deferred from therapeutic use.

If the patient required further support consideration could be given to using platelets sourced from one donor rather than use of a pooled product. Clinical teams should also practice responsible transfusion practice, giving blood products only when medically necessary.

Suggested reading

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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.