UK NEQAS
International Quality Expertise

Histocompatibility & Immunogenetics

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Interpretive Educational Scheme (iED)
Clinical Scenario 3/2023 – Transfusion/Platelet Immunology Case

Dispatched on 9th January 2024

Summary of Submitted Responses

A total of 30 responses were received, 15 from UK & Ireland (UK&I) based laboratories and 15 from Rest of the World (RoW) based laboratories.

Background:

A 21-year-old female patient weighing 66 kg was referred with an acute thrombocytopenia noted two weeks post-transfusion. The patient had no history of thrombocytopenia.

The patient has been transfused with one red cell unit on the 11th September. Her platelet count pre-transfusion was 210 x 10^9/L.

Patient's post-transfusion platelet counts:

Date	Patient Platelet Count
30th September	1 x 10^9/L
1st October	21 x 10^9/L
2nd October	114 x 10^9/L

Serum and EDTA samples were provided for investigation.

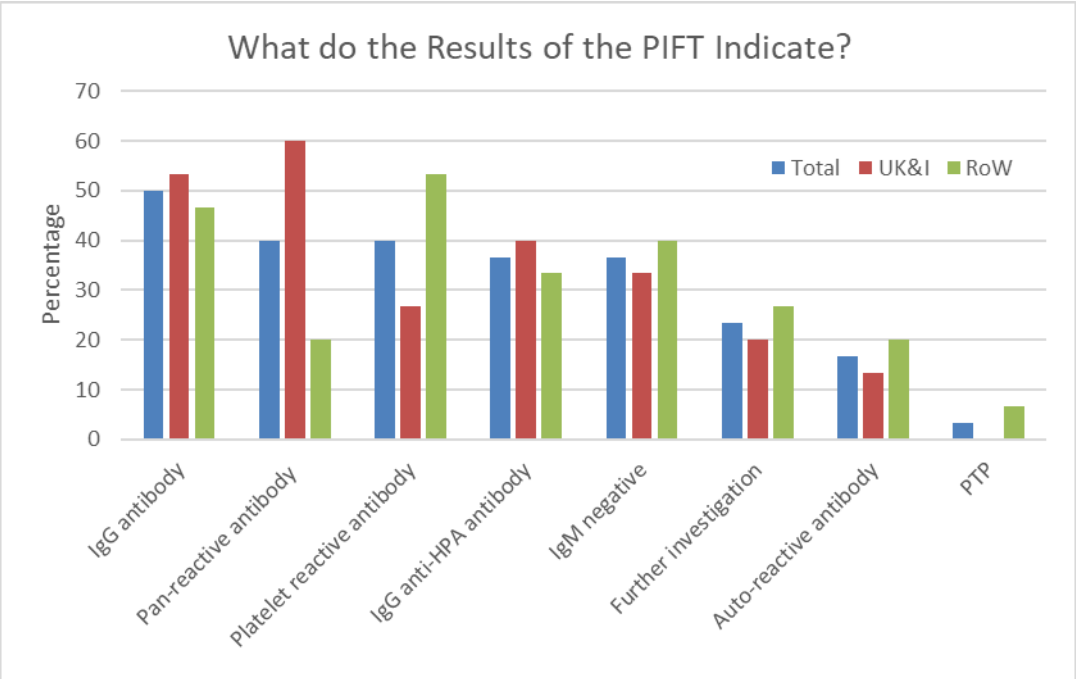
The patient's serum was screened using the Platelet Immunofluorescence Test (PIFT), see Table 1.

Table 1: Results of the PIFT

Plt Donor ID	1	2	3
HPA	1a1a 2a2a 3a3a 5b5b	1a1a 2b2b 3a 3b 5a5a	1b1b 2a2a 3b3b 5a5a
PIFT IgG	POS	POS	POS
PIFT IgM	NEG	NEG	NEG

1. What does do the results of the PIFT indicate?

Results from PIFT	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
IgG antibody	**50**	15	**53**	8	**47**	7
Pan-reactive antibody (anti-HLA/HPA/ABO)	**40**	12	**60**	9	**20**	3
Platelet reactive antibody	**40**	12	**27**	4	**53**	8
IgG anti-HPA antibody	**37**	11	**40**	6	**33**	5
IgM negative	**37**	11	**33**	5	**40**	6
Further investigation required	**23**	7	**20**	3	**27**	4
Possible auto-reactive antibody	**17**	5	**13**	2	**20**	3
PTP	**3**	1	**0**	0	**7**	1



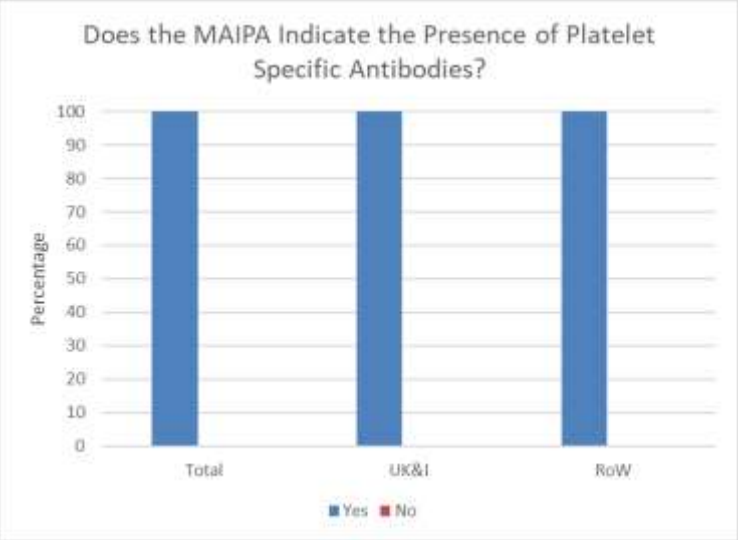
The patient was tested using the Monoclonal Antibody Immobilisation of Platelet Antigen (MAIPA) assay (see Table 2) to identify potential HPA antibody specificities.

Table 2: Results of the MAIPA Assay

Plt Donor ID	A	B	C	D	E	F	G	H	I	J
HPA	1a1a 2a2a 3a3a 5b5b	1a1a 2a2a 3b3b 5a5a	1b1b 2a2a 3a3a 5a5a	1b1b 2a2a 3b3b 5a5a	1a1a 2b2b 3a 3b 5a5a		1a1a 2b2b 3a3a 5a5a	1a1a 2a2a 3b3b 5b5b	15a15a	15b15b
GPIIb/IIIa	NEG	NEG	NEG	NEG						
GPIa/IIa	POS	NEG					NEG	POS		
GPIb/IX		NEG			NEG					
CD109									NEG	NEG
HLA						NEG				

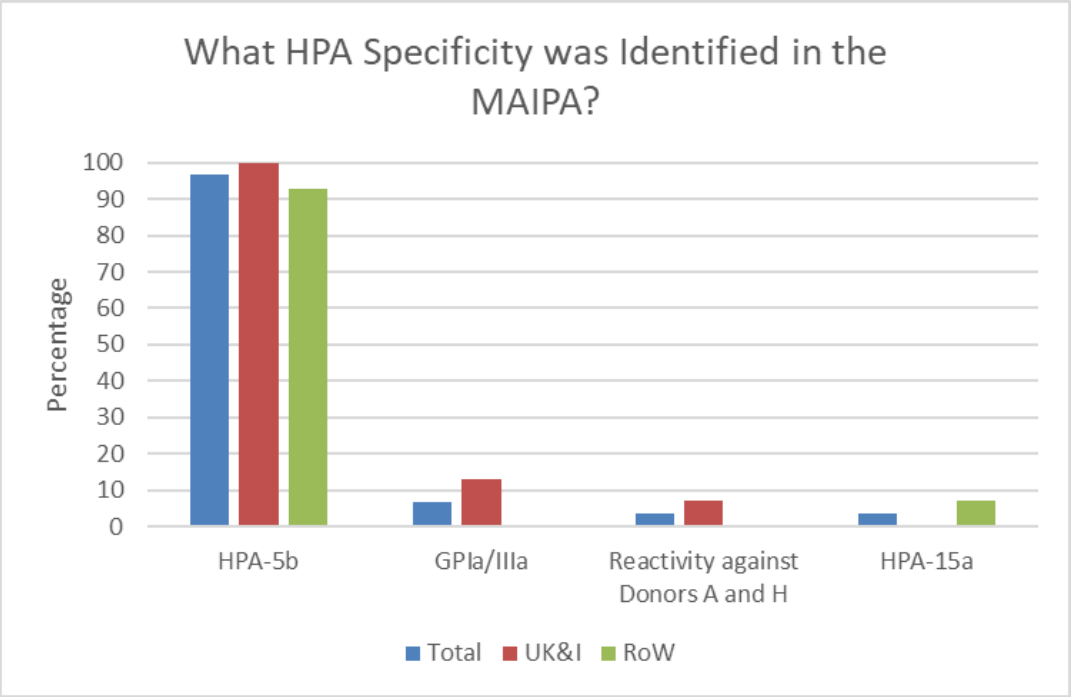
2. Do the results of the MAIPA test indicate that platelet specific antibodies are present?

Platelet Specific Antibodies	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
Yes	100	30	100	15	100	15
No	0	0	0	0	0	0



If so, what is the HPA specificity?

What HPA Specificity is Present?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
HPA-5b	97	29	100	15	93	14
GPIa/IIIa	7	2	13	2	0	0
Reactivity against Donors A and H	3	1	7	1	0	0
HPA-15a	3	1	0	0	7	1

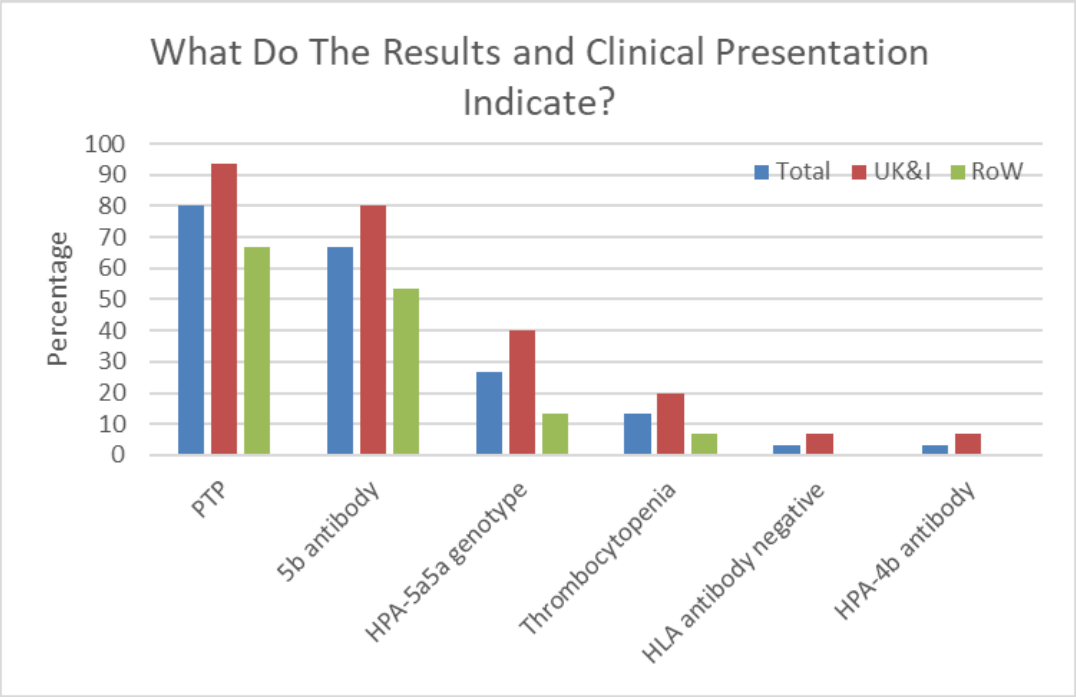


HPA typing was carried out on the patient sample:

HPA-1a1a; 2a2a; 3a3b; 4a4a; 5a5a; 6a6a; 9a9a; 15a15b

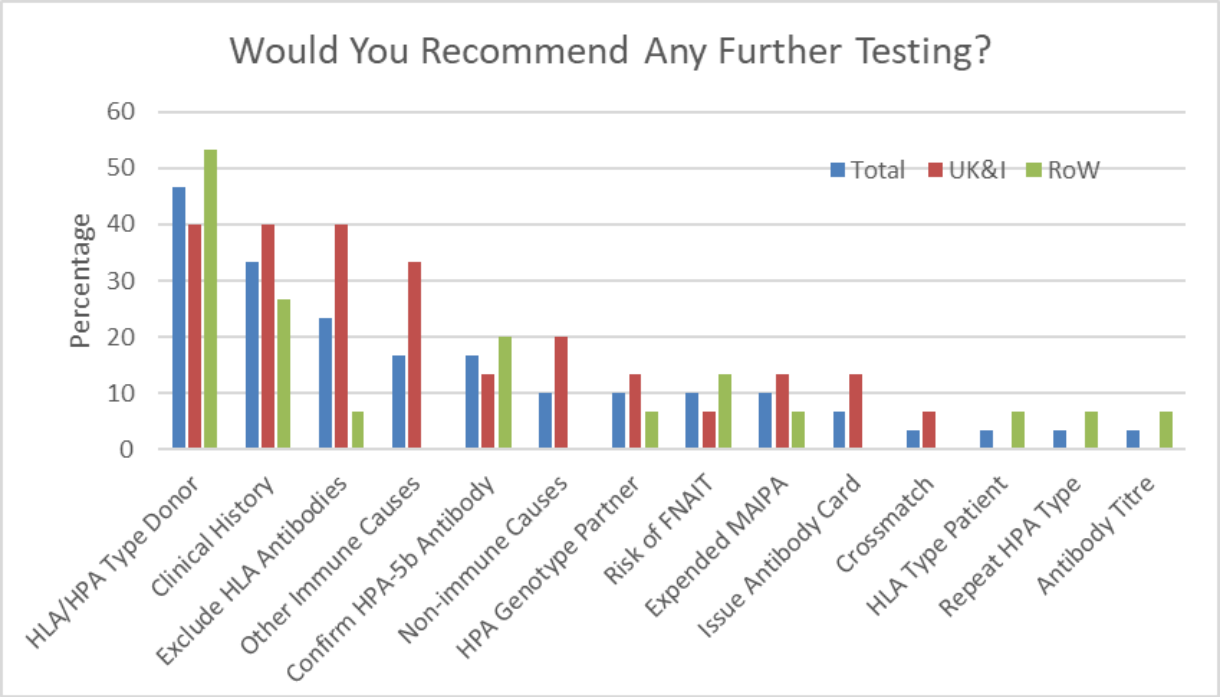
3. Given the **patient's presentation, what do these results suggest?**

What do the Results Suggest?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
Post-Transfusion Purpura	**80**	24	**93**	14	**67**	10
HPA-5b antibody	**67**	20	**80**	12	**53**	8
Patient HPA-5a5a genotype	**27**	8	**40**	6	**13**	2
Thrombocytopenia	**13**	4	**20**	3	**7**	1
HLA antibody negative	**3**	1	**7**	1	**0**	0
Cannot exclude HPA-4b antibody	**3**	1	**7**	1	**0**	0



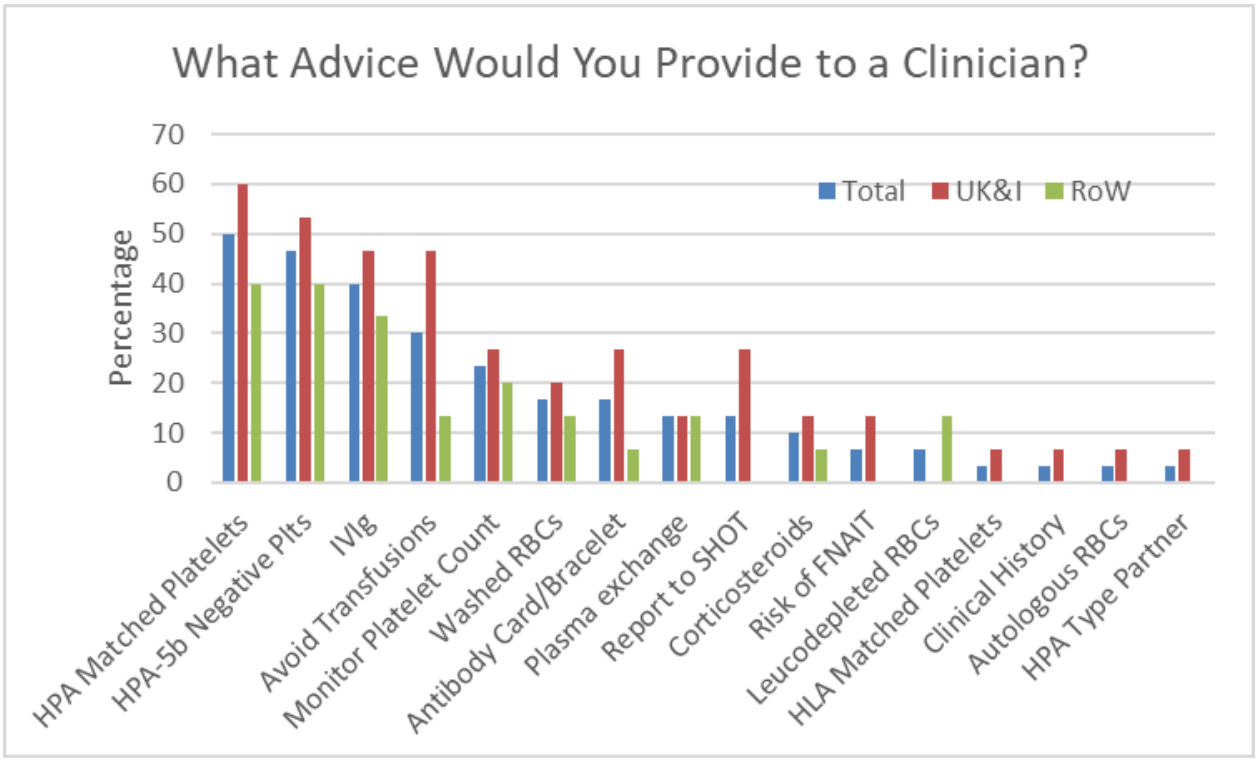
Given this diagnosis, is there any further investigation or testing that should be carried out?

Any Further Testing?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
HLA/HPA Type Donor	**47**	14	**40**	6	**53**	8
Clinical History (Sens Events)	**33**	10	**40**	6	**27**	4
Exclude HLA Antibodies	**23**	7	**40**	6	**7**	1
Check Other Immune Causes e.g. HIT	**17**	5	**33**	5	**0**	0
Confirm HPA-5b Antibody by Second Method	**17**	5	**13**	2	**20**	3
Investigate Non-immune Causes	**10**	3	**20**	3	**0**	0
HPA Genotype Partner	**10**	3	**13**	2	**7**	1
Risk of FNAIT	**10**	3	**7**	1	**13**	2
Expended MAIPA	**10**	3	**13**	2	**7**	1
Issue Antibody Card	**7**	2	**13**	2	**0**	0
Crossmatch	**3**	1	**7**	1	**0**	0
HLA Type Patient	**3**	1	**0**	0	**7**	1
Repeat HPA Type of Patient	**3**	1	**0**	0	**7**	1
Antibody Titre	**3**	1	**0**	0	**7**	1



What advice would you give to the referring Clinician?

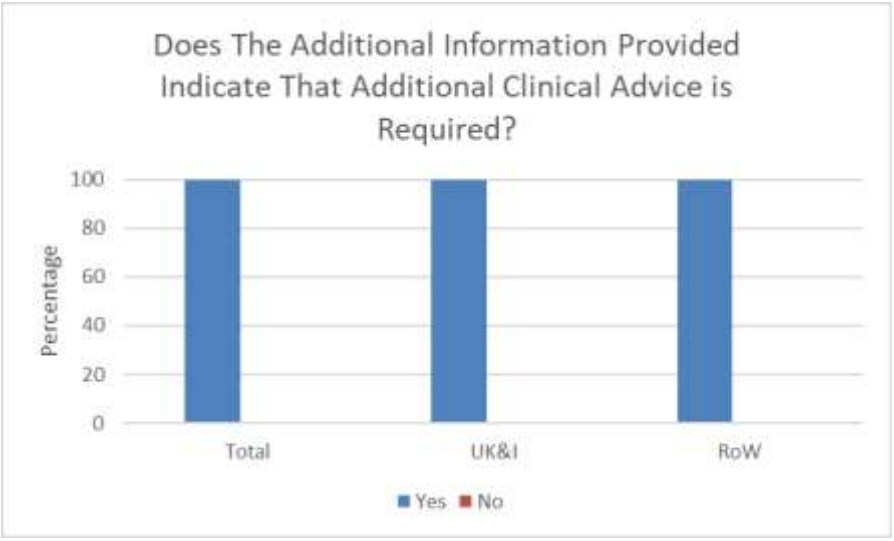
Advice for Clinician	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
HPA Matched Platelets	**50**	15	**60**	9	**40**	6
HPA-5b Negative Platelets	**47**	14	**53**	8	**40**	6
IVIg	**40**	12	**47**	7	**33**	5
Avoid Transfusions	**30**	9	**47**	7	**13**	2
Monitor Platelet Count	**23**	7	**27**	4	**20**	3
Washed RBCs	**17**	5	**20**	3	**13**	2
Antibody Card/Bracelet	**17**	5	**27**	4	**7**	1
Plasma exchange	**13**	4	**13**	2	**13**	2
Report to SHOT	**13**	4	**27**	4	**0**	0
Corticosteroids	**10**	3	**13**	2	**7**	1
Risk of FNAIT	**7**	2	**13**	2	**0**	0
Leucodepleted RBCs	**7**	2	**0**	0	**13**	2
HLA Matched Platelets	**3**	1	**7**	1	**0**	0
Clinical History	**3**	1	**7**	1	**0**	0
Autologous RBCs	**3**	1	**7**	1	**0**	0
HPA Type Partner	**3**	1	**7**	1	**0**	0



Subsequent information provided was that the patient had received the red cell transfusion during the delivery of her first child.

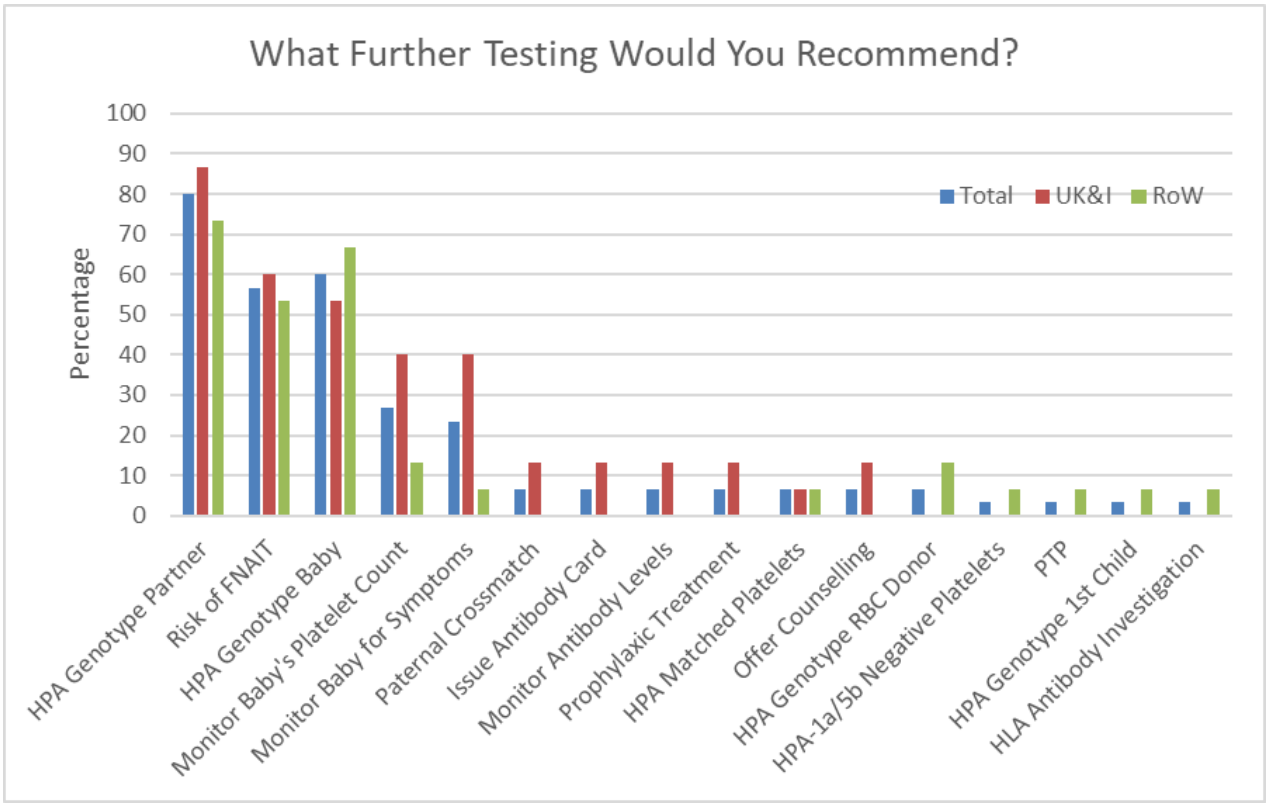
4. Does this information indicate that additional Clinical advice should be provided?

Additional Clinical Advice?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
Yes	100	30	100	15	100	15
No	0	0	0	0	0	0



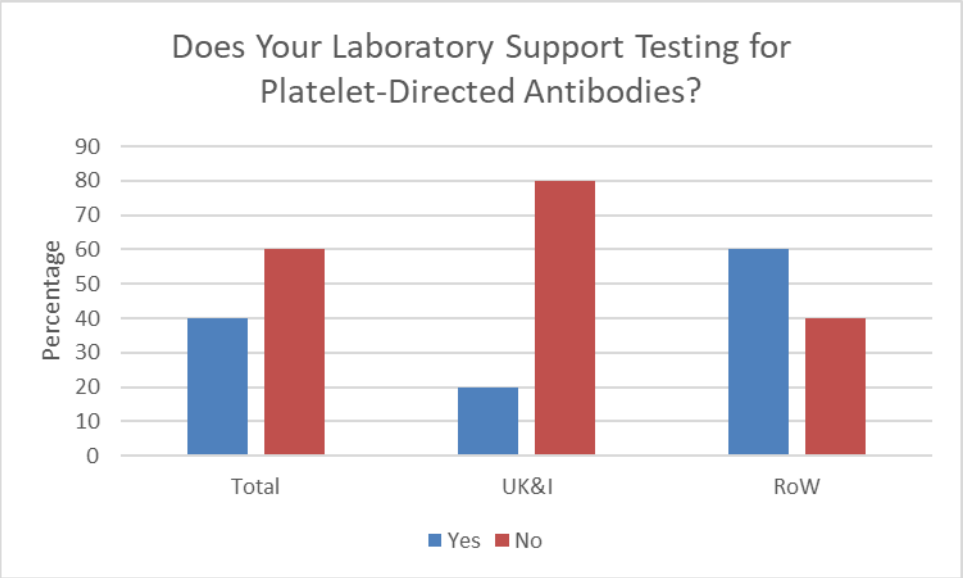
If so, what further testing would you recommend?

What Further Testing is Required?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
HPA Genotype Partner	80	24	87	13	73	11
Risk of FNAIT	57	17	60	9	53	8
HPA Genotype Baby	60	18	53	8	67	10
Monitor Baby's Platelet Count	27	8	40	6	13	2
Monitor Baby for Symptoms	23	7	40	6	7	1
Paternal Crossmatch	7	2	13	2	0	0
Issue Antibody Card	7	2	13	2	0	0
Monitor Antibody Levels	7	2	13	2	0	0
Prophylaxic Treatment	7	2	13	2	0	0
HPA Matched Platelets	7	2	7	1	7	1
Offer Counselling	7	2	13	2	0	0
HPA Genotype RBC Donor	7	2	0	0	13	2
HPA-1a/5b Negative Platelets	3	1	0	0	7	1
PTP	3	1	0	0	7	1
HPA Genotype 1st Child	3	1	0	0	7	1
HLA Antibody Investigation	3	1	0	0	7	1



5. Does your laboratory support testing for platelet-directed antibodies?

Platelet Testing?	Total (n=30)		UK&I (n=15)		RoW (n=15)	
	%	Count	%	Count	%	Count
Yes	40	12	20	3	60	9
No	60	18	80	12	40	6



6. Do you have any further comments?
   - Discrepancy between the PIFT and the MAIPA could be due to lack of typing for HPA-4, could resolve if this is a HPA-4 antibody or a heparin induced thrombocytopenia.
   - Lack of information, additional info was required to be able to provide advice.
   - This scenario lacked the clinical background which would have been provided in a normal clinical scenario. More detail of patient's clinical condition would have been helpful, as well as platelet counts at dates more pertinent to typical PTP presentation. Detail regarding treatment course may have explained the rapid recovery of platelet count.
   - Other causes of thrombocytopenia need to be considered such as HIT. Was this patient given a dose of heparin during her hospital visit. Due to the severe drop in the PLT count, whereas HIT is often a milder PLT count drop, this case is more indicative of PTP. A helpful paper of PTP review can be found at 10.2147/JBM.S189176.
   - Cases of PTP should be reported to SHOT and MHRA. Elective caesarean for future pregnancies to be advised to reduce risk of bleeding. Future transfusions of HPA-5b negative products.
   - Information on the clinical symptoms would have been useful to confirm a diagnosis of PTP.
   - Atypical presentation for PTP due to HPA-5b antibodies, anti-HPA-1a are most frequently implicated. Typically affects middle-aged, multi-parous women.

- Would have been useful to know the precise date that patient samples were provided for the PIFT test.
- The description of the clinical case could have been more precise including the clinical context. Our clinicians do have to provide clinical info and indication when requesting platelet antibody screening. This fastens testing and clinical interpretation.
- Were the red cell units leucodepleted? Did patient receive blood transfusion earlier? Was this a first pregnancy?
- Post transfusion purpura is very rare with anti HPA5b antibodies. Differential diagnosis with anti-drug antibodies, reintroduced during delivery in an immunized woman.
- Should the patient receive future transfusions, screen for HLA antibodies. Patient may need HLA and HPA matched products to avoid complications.

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

Question 1

We would suggest that results from the PIFT indicate the patient has a platelet reactive IgG antibody. The PIFT is non-specific so the antibody may be directed against HLA, HPA, ABO or any other antigens expressed on the platelet surface.

Question 2

The results provided indicate that platelet glycoprotein (GP) Ia/IIa specific antibodies were detected, showing a specificity of HPA-5b.

Question 3

We feel the results of HLA genotyping and antibody testing support a diagnosis of Post-Transfusion Purpura (PTP): There was a drastic fall in platelets 7 to 10 days post-transfusion in a patient that was otherwise well and had no history of thrombocytopenia and the patient has an HPA specific alloantibody. While PTP due to HPA-5b is uncommon, other cases have been reported. HPA-1a is normally implicated.

We would consider further investigations such as confirming that the donor of the red cell unit has a HPA-5b genotype.

We would suggest to the clinical team that if platelet transfusion is required in the PTP crisis phase, the supply of antigen negative platelets is not indicated to be any more effective than random donor platelets. For future transfusions antigen negative products should be transfused as a preventative measure. Treatment of PTP usually consists of administering IVIg or steroids. In extreme cases plasma exchange may be considered. In the UK a platelet antibody card may be provided for the patient to keep.

Question 4

The supplemental information that the patient received the red cell transfusion during pregnancy would prompt us to offer further clinical advice.

A diagnosis of foetal neonatal alloimmune thrombocytopenia (FNAIT) should be investigated. A platelet count should be obtained from the child. If the child is thrombocytopenic and requires transfusion, HPA-5b negative platelets are recommended. In first pregnancies the child may not be affected or be subject to a milder thrombocytopenia. FNAIT due to HPA-5b tends to be less severe than that of HPA-1a. To aid risk assessment for future pregnancies HPA genotyping can be performed on the partner to determine his HPA-5 status and to investigate any other potential incompatibilities. The child may also be typed to complete the investigation.

Patient Update

This scenario was based on a real patient case. The child did not have a platelet count taken at birth and was asymptomatic. A platelet count taken 20 days later that was within normal range.

The patient received two doses of IVIg. When the patient did not respond to this, they were given prednisolone. They had a very quick response with a platelet count >700 x 10^9/L. Prednisolone was stopped and aspirin was prescribed. The full blood count was monitored on alternate days for two weeks after discharge. There was no relapse.

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. 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.