UK NEQAS Histocompatibility & Immunogenetics

UK NEQAS H&I

Educational Scheme (iED) Scenario 3: Platelet/Transfusion Scenario Feedback

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@UKneqasHI @UK_NEQAS

	Our	iED	Sch	emes
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Re denois to formade, for yours all and Add Delois degrees. Re denois to formade, for yours (BALA), ALI; 427; Curi; CHEL, DELDIS; CHEL, CHEL, DELDIS; CHEL, DELDI	Please consider the potential ca questions 1	-5 using a <u>maxim</u>		complete your ansi swer	wers to
Lightly AD Organ Req'4 Articlearly Development Development <thdevelopment< th=""> Development <thdevelopm< th=""><th>The donor is Female, 64 years old a The donor HLA type is: HLA-A2, A11</th><th>nd ABO blood grou 1; -B27; -Cw1; -DR1</th><th>5, DR103; DR51; -DQ6, DQ7; -DP</th><th>B1*03:01, DPB1*10:0 sts have the same clir</th><th>1 lical</th></thdevelopm<></thdevelopment<>	The donor is Female, 64 years old a The donor HLA type is: HLA-A2, A11	nd ABO blood grou 1; -B27; -Cw1; -DR1	5, DR103; DR51; -DQ6, DQ7; -DP	B1*03:01, DPB1*10:0 sts have the same clir	1 lical
Image: Second	urgency: ABO Organ Req A A Heart B O Heart C O Double Lu D A Heart E O Single Lu C O Single Lu	rd Antibody Positive Yes Yes No No Yes Yes	Donor Directed (Peak MFI) Yes (DR15 - 12500) No	Date of Last Sample 26/11/2019 03/01/2020 27/11/2019 14/10/2019 26/11/2019 03/01/2020	
	Rest Rest 1.1. Rank the 3 most suitable Rest like 3 most suitable 14 Rest Resignent 14 G 2 ⁵⁴ Choose an Item	Reason Click or tap h m. Click or tap h	a the information provided and the to enter text. ere to enter text.	give reasons for the d	hoices made

3 clinical scenarios a year

Solid organ, HSCT,
 platelet/transfusion

- Based on patient cases
 - Provide relevant clinical details and test results
 - Questions on interpretation of results and clinical advice
- Not assessed
- Provided free of charge

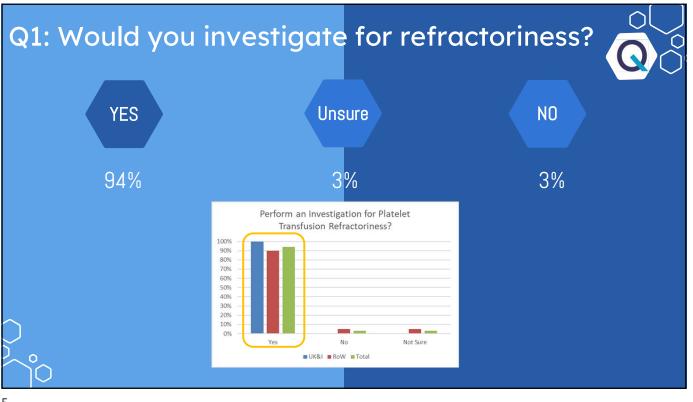
iED3 Sce	enarios		Q
Year	Transfusion/Platelet	Returns	
	Matched platelet selection		
	Platelet Refractoriness		
	TRALI		
2018	NAIT		
	Platelet Refractoriness then HSCT		
	TRALI		
	 Dispatched on 11th January 2022 36 Responses 15 from UK and Ireland (UK&I) 21 from the Rest of the World (RoW) 		

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Case History

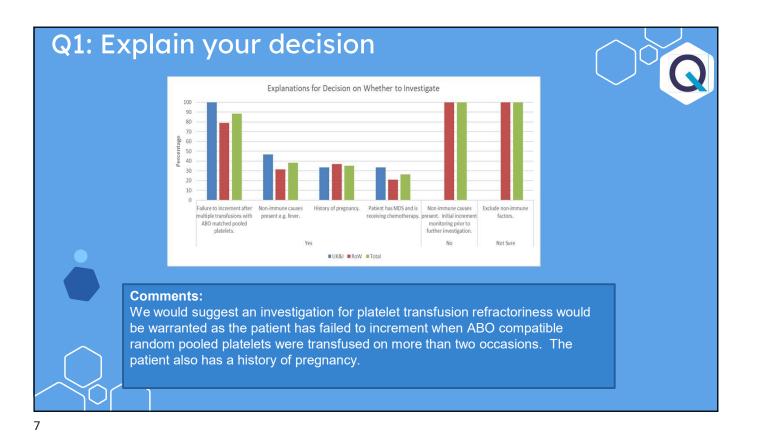
A 59-year old female with a history of pregnancy was previously diagnosed in May 2017 with Myelodysplastic Syndrome (MDS) which transformed to Acute Myeloid Leukaemia (AML) in November 2019. The patient was started on induction chemotherapy using a combination of Daunorubicin and Ara-C.

The patient was admitted to hospital with a fever and beginning on the 13/06/2020, the patient received three fresh ABO compatible random pooled platelets, but the platelet count failed to increment above $10x10^9$ /L.



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Investigate	Explanation	UK8	kl 🛛	RoV	v	Tota	l I
investigate	Explanation	Number	%	Number	%	Number	%
	Failure to increment after multiple transfusions with ABO matched pooled platelets.	15	100	15	79	30	88
Yes	Non-immune causes present e.g. fever.	7	47	6	32	13	38
	History of pregnancy.	5	33	7	37	12	35
	Patient has MDS and is receiving chemotherapy.	5	33	4	21	9	26
No Non-immune causes present. Initial increment monitoring prior to further investigation.		0	0	1	100	1	100
Not Sure	Exclude non-immune factors.	0	0	1	100	1	100



Further information

The patient was HLA typed and screened for Class I HLA antibodies using a LabScreen single antigen bead kit:

Antigen Specificity	MFI Value
A3	2686
A31	1272
A34	1147-1275
A74	1082
A68	1075-1352
A30	1060-1232
A11	5000-5356

HLA class I type: A*01, -; B*08, B*41; C*07, C*17 Blood Group: O Rh positive CMV Status: Negative

Q2: Sel	lect two	donors
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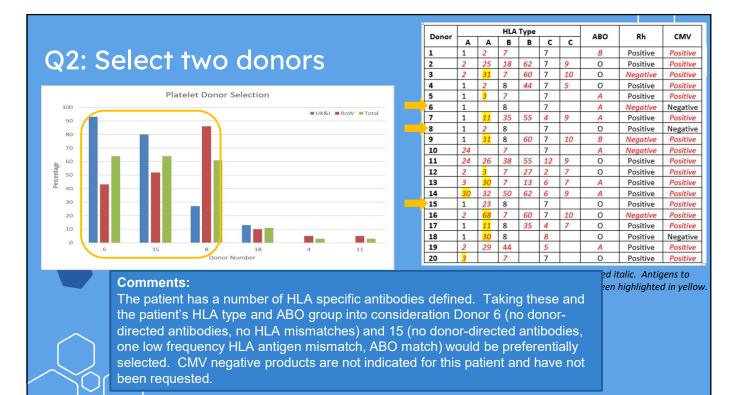
	UK&I		RoW	1	Tota	Total	
Donor ID	Number	%	Number	%	Number	%	
6	14	93	9	43	23	64	
15	12	80	11	52	23	64	
8	4	27	18	86	22	61	
18	2	13	2	10	4	11	
4	0	0	1	5	1	3	
11	0	0	1	5	1	3	

Reasons for Selection
No donor specific antibodies.
HLA matched at A and B.
CMV match.
ABO incompatible.
No donor specific antibodies. Single
antigen mismatch.
ABO match.
CMV mismatch.
A23 mm low frequency.
No donor specific antibodies.
Single antigen mismatch.
ABO match.
CMV match.
A2 mm may cause sensitisation and limit
further matches.
Low level donor specific antibody to A30.
Single antigen mismatch.
ABO match.
CMV match.
A30 mm low frequency.
ABO compatible.
HLA antigen donor to avoid patient
antibody.
ABO match. CMV status is not taken into
account.
Avoidance of antigens with positive MFI
and A2 typing in the platelet unit.

Damas			HLA	Type			ABO	Rh	CMV
Donor	A	A	В	В	С	С	ABU	Kn	CIVIV
1	1	2	7		7		В	Positive	Positive
2	2	25	18	62	7	9	0	Positive	Positive
3	2	<mark>31</mark>	7	60	7	10	0	Negative	Positive
4	1	2	8	44	7	5	0	Positive	Positive
5	1	3	7		7		A	Positive	Positive
6	1	1	8		7		A	Negative	Negative
7	1	11	35	55	4	9	A	Positive	Positive
8	1	2	8		7	-	0	Positive	Negative
9	1	31	8	60	7	10	В	Negative	Positive
10	24		7		7		Α	Negative	Positive
11	24 2		38	55	12	9	0	Positive	Positive
12	2	3	7	27	2	7	0	Positive	Positive
13	3	<mark>30</mark>	7	13	6	7	A	Positive	Positive
14	30	32	50	62	6	9	A	Positive	Positive
15	1	23	8		7		0	Positive	Positive
16	2	68	7	60	7	10	0	Negative	Positive
17	1	11	8	35	4	7	0	Positive	Positive
18	1	30	8		8		0	Positive	Negative
19	2	29	44		5		A	Positive	Positive
20	3		7		7		0	Positive	Positive

*Mismatches have been highlighted in red italic. Antigens to which the patient has antibodies have been highlighted in yellow.

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Further information

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Following the transfusion of two ABO compatible HLA matched (no HLA-A, B or Cw mismatches) platelets 7 days earlier, and with a platelet count of $2x10^{9}$ /L, the patient presented with a retinal haematoma, bleeding in the lungs with haemoptysis, bleeding round the knee joint and purpura.

These symptoms could indicate Post Transfusion Purpura (PTP)

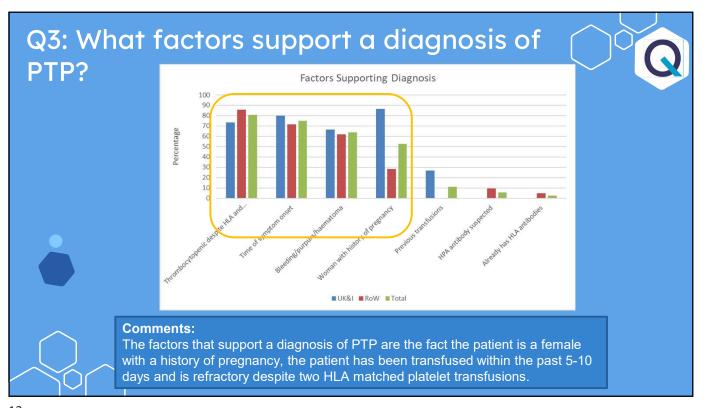


Figure 1): Purpuric skin rash (a, b) red to purple discoloration spots on the skin that are raised and do not stand on applying pressure.

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Q3: What factors support a diagnosis of PTP?

	U	K&I	R	οW	Total	
Factors Supporting Diagnosis	Number	%	Number	%	Number	%
Thrombocytopenic despite HLA and ABO matched platelets	11	73	18	86	29	81
Time of symptom onset	12	80	15	71	27	75
Bleeding/purpura/haematoma	10	67	13	62	23	64
Woman with history of pregnancy	13	87	6	29	19	53
Previous transfusions	4	27	0	0	4	11
HPA antibody suspected	0	0	2	10	2	6
Already has HLA antibodies	0	0	1	5	1	3



Q3: What further testing would you recommend?

%
97%
69%
8%
3%
3%
3%
3%
3%

Q3: What further testing would you recommend?

Comments:

Screening the patient for the presence of HPA antibodies and performing HPA genotyping of the patient would be recommended.

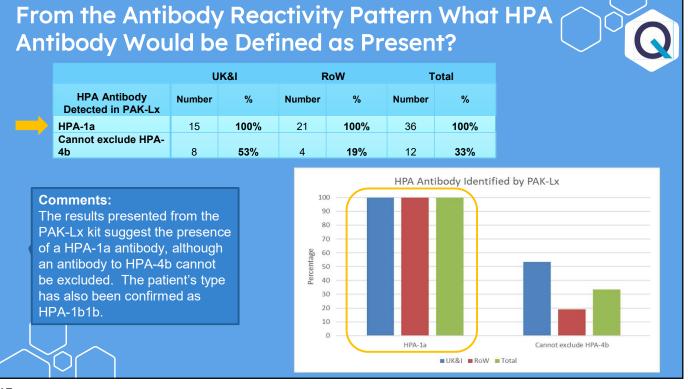


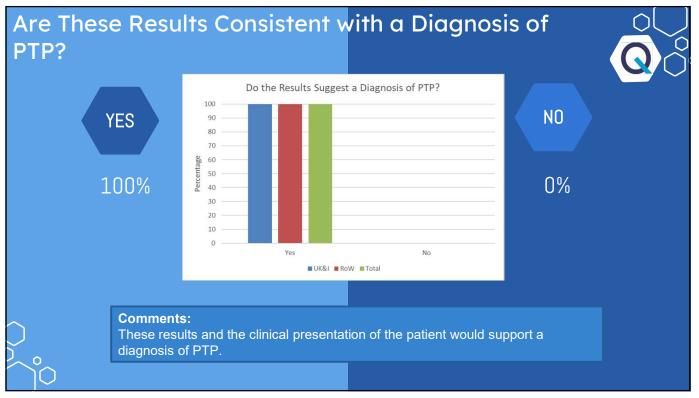
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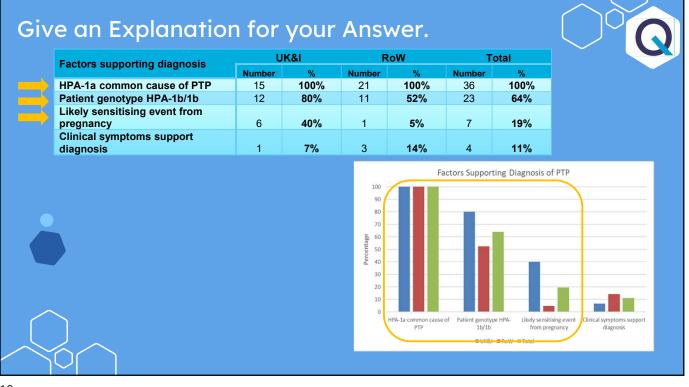
Further information

The patient's HPA type has been defined as HPA-**1b1b**, 2a2a, 3a3a, 4a4a, 5a5a, 15a15b Results from PAK-Lx testing have been provided:

Bead Region	Glycoprotein Group	Antigen	MFI	Bead Reactivity	Adjusted Ratio 1	Adjusted Ratio 2	Adjusted Ratio 3
13	Con1	Con1	29				
14	Con2	Con2	12				
18	Con3	Con3	40				
11	POS	POS	15766				
6	GPIV	GPIV	34	Negative	-3.06	-3.77	-2.66
10	HLA Class I	HLA Class I	20	Negative	-3.24	-4.15	-2.99
21	GPIIb-IIIa	- 1a 3a 4a	5745	Positive	54.52	53.52	55.08
22	GPIIb-IIIa	- 1a 3b 4a	5048	Positive	47.12	45.75	47.46
23	GPIIb-IIIa	HPA - Ib 3a 4a	97	Negative	-3.21	-4.01	-2.94
24	GPIIb-IIIa	P - 1b-3b-4a	89	Negative	-3.32	-4.19	-2.97
25	GPIIb-IIIa	- 1ap 3ap 4a	3727	Positive	34.33	33.29	34.72
26	GPIIb-IIIa	HPA - 1a Sap 4b	6953	Positive	66.55	64.97	67.17
27	GPIb/D	HPA - Za	59	Negative	-3.75	-4.38	-3.1
28	GPIb/IX	HPA - 2a	44	Negative	-3.56	-4.27	-2.98
29	GPIb/D	HPA - 2ab	30	Negative	-3.42	-3.92	-2.74
30	GPIb/IX	HPA - 2b	28	Negative	-3.43	-4.05	-2.8
32	GPIb/IX	HPA - 2b	31	Negative	-3.09	-3.59	-2.58







What Transfusion Support Would You Provide?

The clinician informs you the patient requires platelet and red cell transfusion support through the acute phase of this particular condition.

	U	IK&I	R	loW	т	otal
Transfusion Support	Number	%	Number	%	Number	%
HPA and/or HLA matched platelets	9	60%	15	71%	24	67%
Random ABO matched platelets	7	47%	3	14%	10	28%
IVIg	2	13%	6	29%	8	22%
Washed RBCs	3	20%	5	24%	8	22%
HLA and/or HLA matched red cells	3	20%	3	14%	6	17%
Standard red cells	1	7%	3	14%	4	11%
Irradiated products if patient immunocompromised	1	7%	0	0%	1	3%
CMV neg products	0	0%	1	5%	1	3%
None	0	0%	1	5%	1	3%
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	U	K&I	R	oW	т	otal	
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IVIg	2	13%	6	29%	8	22%	
Washed RBCs	3	20%	5	24%		What Transfusi	on Support Would You Recommend?
HLA and/or HLA matched red cells	3	20%	3	14%	80 0 10	.lı	■UK&I ■RoW ■ Total
Standard red cells	1	7%	3	14%	Percentage		
Irradiated products if patient immunocompromised	1	7%	0	0%	- 0 6 - 0 - 0		l II II an an an an
CMV neg products	0	0%	1	5%	0	let ned as	1% 1885 d.c.1% d.c.1% cbutts abuts work
None	0	0%	1	5%	ed pla	ao mater	upped to red red ad red ad pool at produce
\sim					HPA I HAMACIN &	andon b	HALING SUPP WEDE CALL

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Reasons for Recommendation?

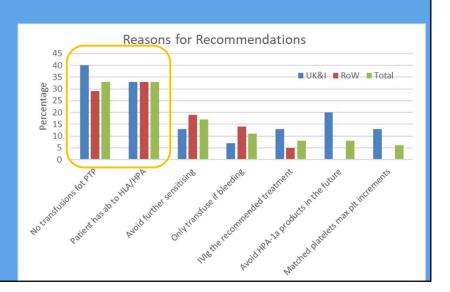
Reasons for Recommendations	U	IK&I	R	oW	Т	otal
Reasons for Recommendations	Number	%	Number	%	Number	%
Platelet transfusion not recommended to treat PTP	6	40%	6	29%	12	33%
Patient is refractory and has HLA and HPA antibodies so needs						
matched products	5	33%	7	33%	12	33%
Avoid further sensitising patient	2	13%	4	19%	6	17%
Avoid transfusion in PTP unless bleeding	1	7%	3	14%	4	11%
IVIg the recommended treatment	2	13%	1	5%	3	8%
Avoid HPA-1a products in the future to prevent re-occurrence of PTP	3	20%	0	0%	3	8%
Matched products will maximise platelet increment	2	13%	0	0%	2	6%

Reasons for Recommendation?



Comments:

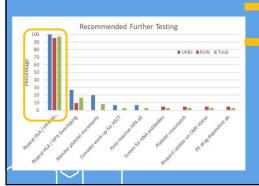
In terms of transfusion support for the patient, we would suggest discussing this requirement with the clinician. The BSH Guidelines (Estcourt et al., 2017), recommend treatment with IVIg and random donor platelets reserved to control severe bleeding if required.



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Q4 What Further Testing Would You Recommend?

In May 2021 the patient relapsed and was given FLAG-IDA and G-CSF, an effective remission-induction therapy for poor prognosis AML. During the treatment the patient required platelet support.



	Further Testing	UK&I	RoW	Total	Common Reasons Given
	· uniter · county	%	%	%	
	Repeat HLA / HPA Antibody Monitoring	100%	95%	97%	ALA/HPA-specific antibodies may change with time and impact efficacy of platelet transfusions. Select matched units to prevent further sensitisation. Recent sensitising events. Potential changes in immunosuppression levels. To inform platelet provision. Patient is homozygous at HLA-B locus and HPA 5b so could form additional anti HLA and HPA 5b antibodies. PTP is self-limiting but there is a recurrence potential so suggest receive a HPA compatible products.
Þ	Repeat HLA / HPA Genotyping	27%	10%	17%	If stem cell transplant is being considered, donors should be HPA typed also. Verification HLA types are essential for confirming patient types are correct.
	Monitor platelet increments	20%	0%	8%	To ensure successful increments achieved. Review which units produced best increments.
1	Consider work-up for HSCT if requested	7%	0%	3%	
	Test for auto-reactive HPA antibodies	7%	0%	3%	Development of autoreactive anti-platelet antibodies can continue to affect platelet increments.
	Screen for HNA antibodies	0%	5%	3%	The patient may develop new anti-HLA antibodies and anti-HNA after receiving blood products.
	Platelet crossmatch	0%	5%	3%	These findings will help to ensure no new allo- immunisation occurs and help ensure a compatible platelet transfusion
	Request update on CMV status	0%	5%	3%	The patient's CMV status may have changed, and could potentially increase the pool of donors available.
	Screen for platelet drug dependent antibodies	0%	5%	3%	The induction therapy may induce antibodies that cause thrombocytopenia

Q4 What Further Testing Would You Recommend?

In May 2021 the patient relapsed and was given FLAG-		UK&I	RoW	Total	\bigcirc Q
	Further Testing	%	%	%	Common Reasons Given
IDA and G-CSF, an effective remission-induction therapy for poor prognosis AML. During the treatment the patient required platelet support.	Repeat HLA / HPA Antibody Monitoring	100%	95%	97%	HLA/HPA-specific antibodies may change with time and impact efficacy of platelet transfusions. Select matched units to prevent further sensitisation. Recent sensitising events. Potential changes in immunosuppression levels. To inform platelet provision. Patient is homozygous at HLA-B locus and HPA 5b so could form additional anti HLA and HPA 5b antibodies.
Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recommended Recom	t prior to receiving /HPA matched pla Post transfusion pl effectiveness of p	platele telets atelet	et sup for thi increr	oport. is pati nent c	It would also be confirming patient ent to prevent ea. data should also be and guide the future tantibodies can
² 30	antibodies	0%	5%	3%	anti-HNA after receiving blood products.
10	Platelet crossmatch	0%	5%	3%	These findings will help to ensure no new allo- immunisation occurs and help ensure a compatible platelet transfusion
new and the second	Request update on CMV status	0%	5%	3%	The patient's CMV status may have changed, and could potentially increase the pool of donors available.
and the second second second second	Screen for platelet drug dependent antibodies	0%	5%	3%	The induction therapy may induce antibodies that cause thrombocytopenia

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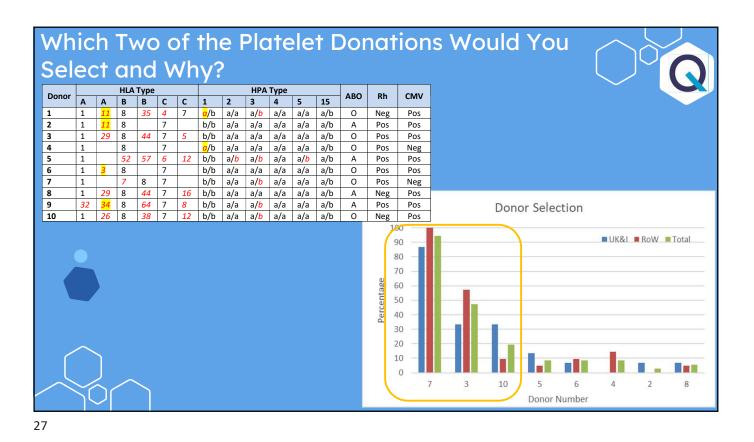
Further Information

The patient urgently required platelet support, with insufficient time for additional testing.

	Antigo Speci		,		Ν	/IFI Va	lue	
	A3				2	686		
	A31				1	272		D
	A34				1	147-1	275	Do
	A74				1	082		1
	A68				1	075-1	352	2
	A30				1	060-1	232	3
	A11				5	000-5	356	4
Bead Region	Glycoprotein Group	Artigen	MFI	Bead Reactive	Adjusted Ratio 1	Adjusted Ratio 2	Adjusted Ratio 3	5
3	Con1	Con1	29					~
4	Con2	Con2	12					6
8	Con3 POS	Con3 POS	40					7
1	POS GPDV	POS GPDV	15766	Negative	-3.04	-1.77	-2.66	/
	UP1V	GP2V	37	neyawe	-9-94	-3.57	2.00	•

Donor			HLA	Туре					HPA	Туре			ABO	Rh	сму
Donor	Α	Α	В	В	С	С	1	2	3	4	5	15	ABO	- NII	CIVIV
1	1	<mark>11</mark>	8	35	4	7	<mark>a</mark> /b	a/a	a/ <mark>b</mark>	a/a	a/a	a/b	0	Neg	Pos
2	1	<mark>11</mark>	8		7		b/b	a/a	a/a	a/a	a/a	a/b	A	Pos	Pos
3	1	29	8	44	7	5	b/b	a/a	a/a	a/a	a/a	a/b	0	Pos	Pos
4	1		8		7		<mark>a</mark> /b	a/a	a/a	a/a	a/a	a/b	0	Pos	Neg
5	1		52	57	6	12	b/b	a/ <mark>b</mark>	a/ <mark>b</mark>	a/a	a/ <mark>b</mark>	a/b	A	Pos	Pos
6	1	<mark>3</mark>	8		7		b/b	a/a	a/a	a/a	a/a	a/b	0	Pos	Pos
7	1		7	8	7		b/b	a/a	a/ <mark>b</mark>	a/a	a/a	a/b	0	Pos	Neg
8	1	29	8	44	7	16	b/b	a/a	a/a	a/a	a/a	a/b	A	Neg	Pos
9	32	<mark>34</mark>	8	64	7	8	b/b	a/a	a/ <mark>b</mark>	a/a	a/a	a/b	A	Pos	Pos
10	1	26	8	38	7	12	b/b	a/a	a/ <mark>b</mark>	a/a	a/a	a/b	0	Neg	Pos

*Mismatches have been highlighted in red italic. Antigens to which the patient has antibodies have been highlighted in yellow.



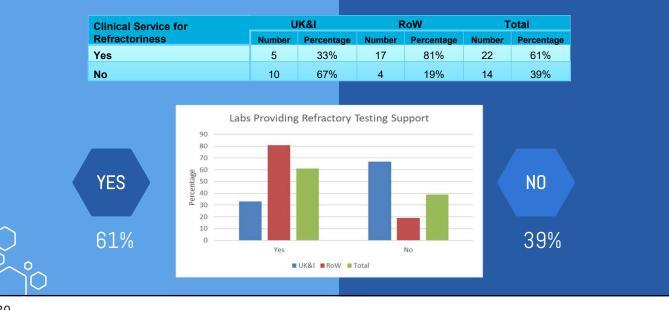
Which Two of the Platelet Donations Would You Select and Why?

	Donor	UK& Number	l %	Ro\ Number	N %	Tota Number	%	Reason for Selection
	7	13	87%	21	100%	34	94%	Single antigen HLA mismatch (B7 could cross-react with A2); HPA matched (HPA-1a negative); ABO matched; CMV match; No donor-directed HLA/HPA alloantibodies. Least immunogenic donor.
	3	5	33%	12	57%	17	47%	2 antigen mismatched (A29 low frequency and B44 high frequency but low expression);HPA matched; ABO matched.
	10	5	33%	2	10%	7	19%	2 antigen HLA mismatches (A26 and B38 lower frequency rather other mm units); HPA-3 mismatch; ABO matched; CMV mismatch (not relevant is unit is leucodepleted). No donor-directed HLA/HPA alloantibodies.
	5	2	13%	1	5%	3	8%	2 antigen HLA mismatch. No donor-directed HLA/HPA alloantibodies. Avoids HLA-A alleles in the A10 and A19 CREG to which the patient may have cross reactive HLA antibodies
	6	1	7%	2	10%	3	8%	HPA-1a negative, 1 antigen HLA mismatch; ABO matched; CMV mismatched
	4	0	0%	3	14%	3	8%	ABO match, no anti-HLA-DSA found in recipient; CMV match; HPA1a so there is a chance for reaction with patients HPA 1a Ab but all the other donors who are ABO compatible are CMV positive.
\langle	2	1	7%	0	0%	1	3%	HPA matched.
	8	1	7%	1	5%	2	6%	No comments received.
\sim	0	\frown						

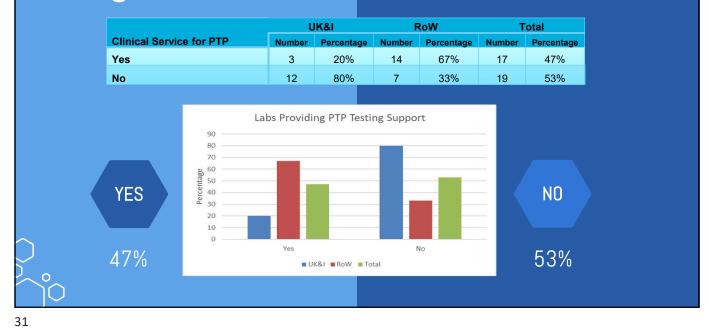
Donor	UK& Number	d %	RoV Number	N %	Tota Number	l %	Reason for Selection	
7	13	87%	21	100%	34	94%	Single antigen HLA mismatch (B7 could cross-react with A2); HPA matched (HPA-1a negative); ABO matched; CMV match; No donor-directed HLA/HPA alloantibodies. Least immunogenic donor.	
10 11	natched,	ABO	match	ed, no	donor-	direc	ingle HLA antigen mismatch, HPA cted antibodies) and Donor 10 (two low	
10 fr d	natched, equency irected a	ABO / HLA antibo	match antige	ed, no n misi or this	donor- matche patient	·direc s, HF	cted antibodies) and Donor 10 (two low PA matched, ABO matched, no donor- alloantibodies. Avoids HLA-A alleles in the A10 and A19	
10 m 10 fr	natched, requency	ABO / HLA	match antige	ed, no n misi	donor- matche	·direc s, HF	A matched, ABO matched, no donor- alloantibodies. Avoids HLA-A alleles in the A10 and A19 CREG to which the patient may have cross reactive HLA antibodies	
10 fr d	natched, equency irected a	ABO / HLA antibo	match antige	ed, no n misi or this	donor- matche patient	·direc s, HF	cted antibodies) and Donor 10 (two low PA matched, ABO matched, no donor- alloantibodies. Avoids HLA-A alleles in the A10 and A19 CREG to which the patient may have cross reactive	
10 fr d	natched, requency irected a 2	ABO / HLA antibo 13%	match antige odies) fo	ed, no n misi or this 5%	donor- matche patient 3	-direc s, HF 8%	alloantibodies, Avoids HLA-A alleles in the A10 and A19 CREG to which the patient may have cross reactive HLA antibodies HPA-1a negative, 1 antigen HLA mismatch; ABO	
10 m fr d 5	natched, requency irected a 2 1	ABO / HLA antibo 13% 7%	match antige odies) fo 1 2	ed, no on misi or this 5% 10%	donor- matche patient 3 3	direc s, HF 8% 8%	alloantibodies, Avoids HLA-A alleles in the A10 and A19 CREG to which the patient may have cross reactive HLA antibodies HPA-1a negative, 1 antigen HLA mismatch; ABO matched; CMV mismatched ABO match, no anti-HLA-DSA found in recipient; CMV match; HPA1a so there is a chance for reaction with patients HPA1 a Ab but all the other donors who are	

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Q5: Does Your Lab Provide Clinical Testing for Platelet Refractoriness?



Q5: Does Your Lab Provide Clinical Testing for PTP?



Patient Follow Up

During her second cycle of chemotherapy, the patient was admitted to the intensive care unit with respiratory difficulty, no formal diagnosis was made.

At day 31 and showing signs of neutrophil recovery and a general improvement in health, the patient was extubated.

Three weeks later, a bone marrow aspiration showed the patient to be in complete remission.

The patient was considered for a sibling allogeneic haematopoietic stem cell transplant but sadly died due to complications of AML before this could be realised.

Suggested Reading



Hawkins J, Aster RH, Curtis BR. Post-Transfusion Purpura: Current Perspectives. J Blood Med. 2019 Dec 9;10:405-415. doi: 10.2147/JBM.S189176. PMID: 31849555; PMCID: PMC6910090.

Estcourt LJ, Birchall J, Allard S, Bassey SJ, Hersey P, Kerr JP, Mumford AD, Stanworth SJ, Tinegate H; British Committee for Standards in Haematology. Guidelines for the use of platelet transfusions. Br J Haematol. 2017 Feb;176(3):365-394. doi: 10.1111/bjh.14423. Epub 2016 Dec 23. Erratum in: Br J Haematol. 2017 Apr;177(1):157. PMID: 28009056.



