



# **HLA Selected Platelets**

Management of platelet refractory patients, why does your patient keep on bleeding ?

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### **Platelet Products**

Pooled Platelets (Buffy Coat Derived)

- Adult dose from 4 ABO-identical donors
- platelet count >240x10<sup>9/</sup>dose
- Leucocyte depleted
- leucocyte count <5x10<sup>6</sup>/dose
- Apheresis single donor (count as above)



## **Post Tx Increments**

#### Corrected count increment (CCI)

In a stable pt, the expected increment after 1 dose =  $30-40 \times 10^{9}/L$ 

$$CCI = \frac{P_1 - P_0 (10^9 L) \times Body \text{ Surface Area (m^2)}}{\text{platelets transfused } 10^{11}}$$

 $P_0$  = Platelet count before transfusion (10<sup>9</sup>/l)

 $P_1$  = Platelet count after transfusion (10<sup>9</sup>/l)



### **Platelet refractoriness**

• Poor increment (<10 x 10<sup>9</sup>/L or CCI <7.5) after at least two consecutive transfusions of random donor platelets

• Platelet count are taken 1hr post transfusion

## "Non-immune" refractoriness

- Old/poorly stored platelets, small dose
- Splenomegaly, hepatomegaly
- DIC (infection, septicaemia, malignancy)
- Infection (CMV)
- Fever
- Antibiotics, esp amphotericin B, ambisome, vancomycin, ciprofloxacin,



## Immunological causes of platelet refractoriness

- HLA class I specific antibodies
- HPA antibodies
  - incompatibility for HPA is uncommon
- ABO antibodies
  - Incompatible plts transfused into patients with high titre anti-A or anti-B have a decreased survival









## **Factors that predict alloimmune**

#### refractoriness

- Non leucodepleted blood
- History of pregnancy
- Receipt of multiple transfusions

Seftel et al 2004; Blood 103(1) : 333-339

# Management of alloimmunised platelet refractory patients

- Provide HLA/HPA compatible donors from an HLA/HPA typed apheresis donor panel
- Define HLA/HPA antibody specificity and select antigen compatible apheresis donors
- Cross-match random apheresis platelets to select compatible donors



Blood and Transplant

## The role of the H&I laboratory

- Detection of HLA specific antibody
- Definition of antibody specificity
- HLA typing of patients and donors
- Selection and issue of HLA compatible platelets
- Documentation of post-transfusion increments
- Advice on patient management



# Laboratory tests for immunological refractoriness

- HLA antibody screening and definition
- HLA class I typing
  - HLA-A, B , (& C)

## **HLA Polymorphism**

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	Alleles	Specificities
HLA-A	2,244	28
HLA-B	2,934	61
HLA-C	1,788	10
HLA-DRB1	1,317	21
HLA-DQB1	323	9
HLA-DPB1	185	6

**NHS** Blood and Transplant

#### **ANTIBODIES**



- A\*02:01 +
- A\*02:02 +
- A\*02:03 +
- A\*02:04 +
- A\*02:05 +



## **Patient Report**

```
HLA-A*25, A*26; B*18, B*38; C*07, C*12
HLA Antibody :
   Positive
     IgG + IgM
   Panel Reactive Antibodies
                                  90%
  Specificity
  A1, A2, A3, A11, A23, A24, A29, A30, A31, A68,
  A69, A80.
  B7, B8, B44, B45, B49, B50, B51, B52, B54, B55,
   B56, B57, B58, B59, B60, B61, B63.
```







### A match = No mismatch

The donor and patient are not serologically mismatched for the four antigens of the HLA-A and B loci.

donor	A*01-A*02 / B*08-B*44		
patient	A*01-A*02 / B*08-B*44		

donor*	A*01-A*01 / B*08-B*08		
patient	A*01-A*02 / B*08-B*44		

\*homozygous donor

## **B** match (**B**<sub>1</sub>-**B**<sub>4</sub>) = Mismatched

The donor and patient are mismatched

B1 donor:	A*01-A* <mark>02</mark>	/	B*08-B*27
patient:	A*01-A*68	/	B*08-B*27
B2 donor:	A*01-A* <mark>02</mark>	/	B*08-B* <mark>07</mark>

### **Triplets and Eplets**



From: Kostyu et al. Human Immunology 57, 1-18, 1997



# Traditional vs. molecular matching

Consider a platelet patient with HLA type A2, A30; B42, B53 and two potential donors D1 and D2 with types as listed

	НLА Туре	MM	Epitopes
Patient	A*02, A*30; B*42, B*53		
D1	A*02, A* <mark>29</mark> ; <mark>B*07</mark> , B*53	B2	
D2	A*30, A* <mark>69; B*08</mark> , B* <mark>35</mark>	B3	



# Eplet Mismatching and Increments







### **HLA Matched Platelets**





## **Value of increments**

- response may vary between different "A"-matched donors
- helps to differentiate immune from non-immune refractoriness



- Pt : PR 33 yr old Female
- Severe Aplastic Anaemia
- Poor response to pooled and single donor platelets
- Patient HLA Type : HLA-A\*02, A\*23; B\*44, B\*14:02
- Blood Group : O Rh pos
- HPA antibody negative
- HLA class I antibodies : positive multispecific
   A1,A3,A11,A24,A25,A26,A29,A30,A31,A32,A33,A34,A36,A43,A66,A68,A69,A74
   ,B7,B8,B13,B18,B35,B37,B38,B39,B41,B46,B47,B48,B49,B50,B51,B52,B53,B5
   4,B55,B56,B57,B58,B59,B60,B61,B62,B63,B71,B72,B72,B75,B76,B77,B78

		<u>Match</u>	Pre-	Post-
			<u>Count</u>	<u>Count</u>
Donor 1	<b>O+</b>	Random	7	6
Donor 2	0+	Random	4	2
 Donor 3	<b>B-</b>	<b>B1</b>	1	71
Donor 4	0+	Α	7	51
Donor 5	<b>A+</b>	Α	5	94
Donor 6	<b>O+</b>	<b>B1</b>	8	39

#### **Refractoriness due to HLA class I antibodies**



- Pt : RC 66 year old Female
- Aplastic Anaemia
- Poor response to pooled and single donor platelets
- Patient HLA Type : HLA-A\*02 ; B\*44, B\*45
- Blood Group : O Rh pos
- HLA class I antibodies : Multispecific

		<b>Match</b>	Pre-	Post-
			<u>Count</u>	<u>Count</u>
Donor 1	<b>O+</b>	Random	6	7
Donor 2	<b>O+</b>	Random	6	8
Donor 3	<b>A+</b>	<b>B1</b>	8	10
Donor 4	<b>A+</b>	Α	6	26
Donor 5	<b>A+</b>	Α	6	9
Donor 6	<b>O+</b>	<b>B1</b>	6	19
Donor 7	<b>A+</b>	Α	7	41

**Refractoriness due to HLA and HPA antibodies** 



- Pt : ID 50 yr old Male
- AML, 2nd course of chemotherapy
- Poor response to pooled and single donor platelets
- Patient HLA Type : HLA-A\*02, A\*11; B\*15:01,B\*15:17
- Blood Group : O Rh pos
- HLA class I antibodies : Multispecific
- HPA antibodies : Negative

		<b>Match</b>	<u>Pre</u>	<u>Post</u>
Donor 1	A+	Α	2	2
Donor 2	0+	<b>B1</b>	3	5
Donor 3	A+	<b>B2</b>	4	7
Donor 4	0+	Α	4	15*
Donor 5	A+	Α	4	5
Donor 6	0+	<b>B1</b>	2	8
Donor 7	<b>O+</b>	Α	2	27*

#### **Refractoriness due to HLA and ABO (anti-A) antibodies**



## **HLA selected platelets**

- Requires planning to obtain well matched platelets
- Post transfusion feedback can assist with patient management and the appropriate use of HLA selected platelets