GUIDELINES FOR THE MANAGEMENT OF PATIENTS REFRACTORY TO PLATELETS

REASON FOR ISSUE: Addition to Scenarios "c" and "f" and Management – Table 1. Update to NZTIL name. Addition of DWR1210.

1. PURPOSE

The purpose of this document is to define how patients who are truly refractory to platelet transfusions should be managed. It is based on reviews of the literature and currently accepted practice.

2. BACKGROUND

When a patient does not have a satisfactory response to platelet transfusions it is important to find out why and in particular whether or not the failure is due to immunological or non-immunological (e.g. clinical) causes. For example, in recent year's clinical factors such as sepsis, DIC, splenomegaly, have largely surpassed alloimmunisation as the major cause of refractoriness.

Identifying patients with white cell (HLA) or platelet (HPA) antibodies is important since the use of HLA-matched (or HPA-matched) platelet components may result in improved transfusion responses. Similarly, the identification of patients with other allo- and (rarely) autoantibodies is also important as it may be possible to find serologically ('crossmatch') compatible platelets in these situations.

However, in deciding how to treat a refractory patient there may be a number of appropriate strategies for improving the response to platelet transfusions such as matching for HLA or HPA, identifying donors based on antibody specificity prediction (single antigen matching) and very rarely resorting to cross-match compatible platelets.

3. DEFINITIONS

- **Alloimmunisation** is defined as the development of HLA or HPA antibodies
- **HLA antibodies** are antibodies to HLA antigens (only HLA class I antibodies are considered in platelet refractoriness).
- **HPA antibodies** are antibodies to Human Platelet Antigens
- **Refractoriness** is a failure to obtain a satisfactory response to transfusion of random donor platelets on two or more occasions. A poor platelet response is defined by a platelet increment of $<10x10^9$/L or (more accurately) a Corrected Count Increment (CCI) of <5000/uL
- **Platelet increment** is the difference between pre- and post-transfusion platelet counts. This may be a reasonable measure of refractoriness or used to calculate the CCI (see below). The post transfusion platelet count should be performed 10 to 60 minutes after the transfusion.
- **Corrected Count Increment** is determined using the following formula (where BSA represents the patient's Body Surface Area):

  $$CCI = \frac{\text{Platelet Increment } (10^9/L) \times BSA\ (m^2)}{10^{11} \text{ platelets transfused}}$$

- **Body Surface Area** is determined using the following formula (also known as the 'Mosteller' formula):

  $$BSA = \sqrt{\frac{\text{Height (cm)} \times \text{Weight (Kg)}}{3600}}$$

- **HAPU** is the application used to find compatible donors based on HLA antibody specificity or genotype.

- DWR1210 is the data warehouse report which provides a list of donors in stock, booked in the next 14 days, or eligible to donate. DWR1210 also allows the selection of donors based on HPA type.

- Labscreen single antigen bead assay is used to identify Class I HLA antibodies

- Pak Lx assay is used to identify HPA antibodies

- MAIPA assay is used to identify HPA antibodies (sent abroad)

4. KEY RESPONSIBILITIES

NZBS TMS (or MO)
Liaison with the patient's physician. Initiates the request for 'special platelets' and coordinates the provision of suitable platelet components.

DHB Clinicians
Responsible for the patient and ensuring that the correct samples and tests are requested.

New Zealand Transplantation and Immunogenetics Laboratory (NZTIL)
HLA and/or HPA typing of potential platelet recipients; testing for the presence of HLA and/or HPA antibodies; and the identification of suitable platelet donors using HAPU and DWR1210.

NZBS Donor Services staff
Calling in and bleeding the appropriate platelet donors as identified by the NZTIL and DWR1210.

NZBS Manufacturing Services
Processing of the collected platelet donation.

NZBS Logistics and Customer Services
Ensuring that the appropriate platelet components are sent to the relevant location (e.g. hospital blood bank).

Blood Bank staff
Blood Bank staff may be required to locate matched platelets using the HAPU application on cornerstone.

5. RELATED DOCUMENT(S)

- 111M034 Requests for Matched Platelets
- 111F034 Matched Platelet Requisition and Record Form

6. POLICY

6.1 Request for Platelets

The first point of contact with NZBS will be a TMS (or MO). Samples may have been received by NZTIL without prior consultation. This will still necessitate communication between the TMS/NZBS MO and treating clinician.

6.1.1 Ascertain whether or not the patient is refractory i.e. has had a poor response to random donor platelets on two or more occasions (refer to figure 1: *Algorithm to Determine If Patient Is Refractory to Platelets*).

6.1.2 Determine the nature and urgency of the request in discussion with the patient's physician.

6.1.3 Discuss with the treating physician as to what testing of the patient is required and what samples should be collected.

6.1.4 Initiate and coordinate investigation(s) to determine whether the refractoriness is due to immunological or non- immunological causes.

6.1.5 Liaise with NZTIL regarding provision of appropriate platelets. Refer to document *Requests for Matched Platelets* (111M034).

6.2 Management of Refractory Patients

6.2.1 Refer to figure 2: *Algorithm for Management of Patients Refractory to Platelets*.

6.2.2 Depending on whether or not test results are available, the options shown below in (table 1) for managing the patient should be considered:

Table 1: Options for Managing Patients Refractory to Platelets

Scenario	Management
a. Patient's HLA ('tissue type') not known and serum sample(s) not yet available	Consider transfusing ABO-compatible, single donor platelets
b. Patient serum samples are available	Platelet antibody screen should be performed and serum sample retained for further testing
c. Patient's HLA type is known, anti-HLA antibody status is not known	HLA matched platelets should be considered particularly if HLA immunisation is suspected as the most likely cause of refractoriness. Request NZTIL to run HAPU and DWR1210 without the antibody profile to look for zero HLA mismatched donors which will allow an eProgesa search to find any donation in stock
d. The patient has HLA and/or HPA antibodies	HLA-matched (and/or HPA matched) platelets or matched platelets based on antibody specificity should be selected for transfusion using HAPU and DWR1210. Further antibody testing should be considered every 3 to 6 months or if refractoriness returns

e. The patient does not have HLA or HPA antibodies	The TMS (or MO) will advise the treating physician accordingly Consideration should be given to non-immunological causes for which the TMS (or MO) may advise suitable management options.
f. In highly alloimmunised patients there may not be an adequate number of eligible donors in the report generated by DWR1210 to support the transfusion needs of the patient. In these situations, the TMS or MO may request NZTIL for a modification to the HAPU run based on known limitations or the peculiarities of certain HLA antigens. These modifications must be carried out in a staged manner and not all at once and the report subsequently checked to see if more matched donors have appeared on the DWR1210 list.	• HLA-B44 and B45 are weakly expressed on platelets and if antibodies to these are present they could be dropped and a HAPU and DWR1210 re-run done. • Some individuals have undetectable HLA-B8, , and –B35 expression on their platelets and if antibodies to any of these are present they could be dropped and a HAPU and DWR1210 re-run done. • HLA antibodies showing low immunization between 1000 and 3000 MFI may not have an impact on platelet increments and these could be dropped and a HAPU and a DWR1210 rerun done.

6.3 Follow-up Post Transfusion

Following transfusion, the TMS (or MO) will:

6.3.1 Ascertain the patient's response to the platelet transfusion by requesting the treating physician to obtain a post transfusion platelet count (10-60 minutes, post transfusion).

6.3.2 Discuss with NZTIL the patient's response to possibly assist in future selection of appropriate donors.

6.3.3 If the response to matched platelets is poor, the TMS (or MO) will determine what further investigations are required in consultation with the treating clinician.

Figure 1: Algorithm to Determine If Patient Is Refractory to Platelets

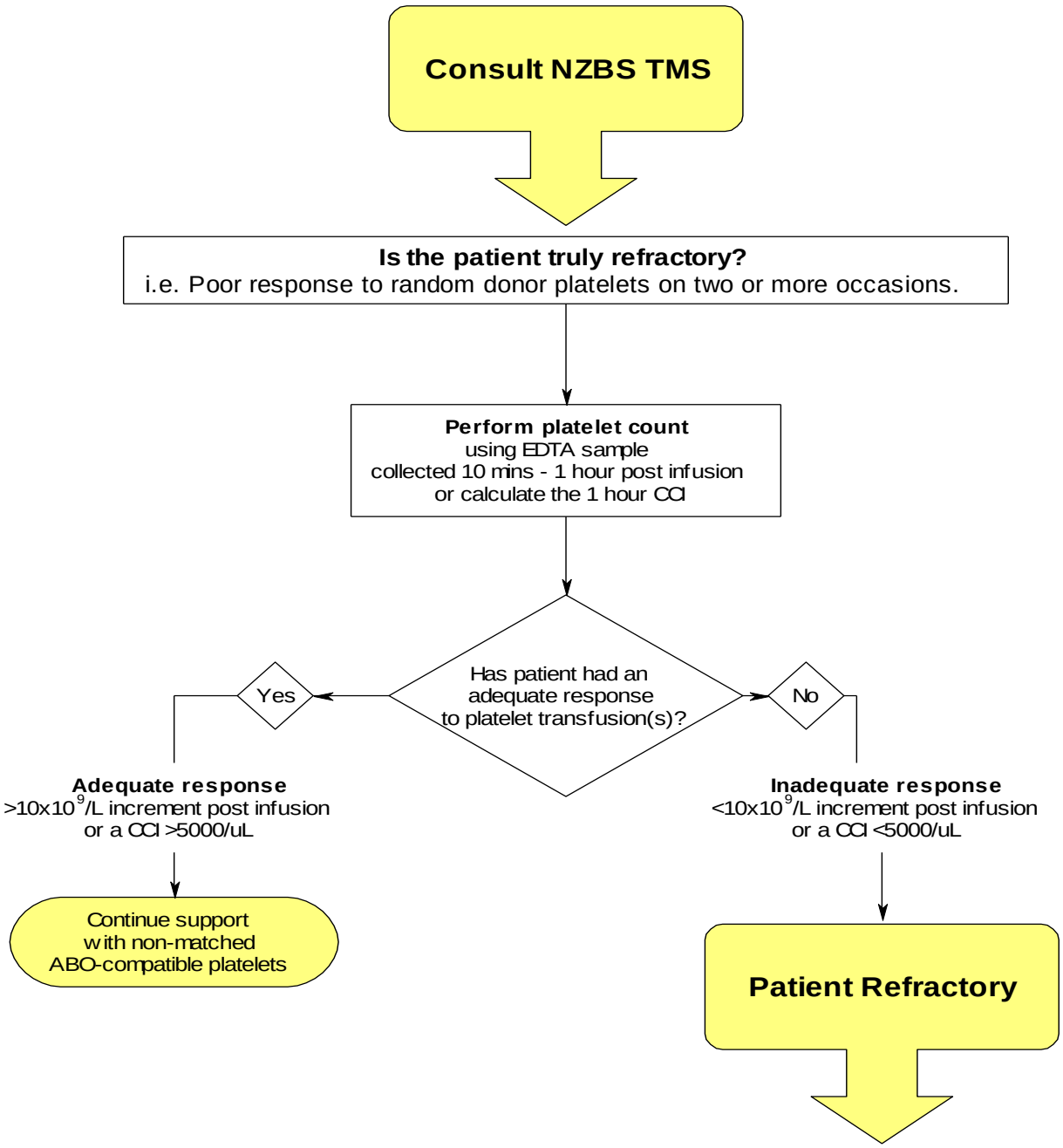

Figure 2: Algorithm for Management of Patients Refractory to Platelets

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