Subject MIPLATE CTS-5030 Pathogen-Reduced Platelet Study

Method Clinical Effectiveness of Conventional Versus Mirasol-treated Apheresis Platelets in Patients with Hypoproliferative Thrombocytopenia (MIPLATE)

Purpose To describe the duties performed by the Blood Bank staff and Blood Bank Coordinators to manage patients in the Terumo MIPLATE Platelet Study

Policy Patients enrolled in the Terumo MIPLATE study are randomized to one of two arms:

- **ARM 1 (Investigational/Test Arm)** – receives **Mirasol-treated platelets** from Memorial Blood Centers. This is an unlicensed blood product and for **investigational use only**. Mirasol platelets have a 5 day expiration date and are stored at room temperature (20-24°C) with gentle agitation.
- **ARM 2 (Control Arm)** – receives only general inventory **plasma platelets**. Issuing a PAS (platelet additive solution) platelet to a study patient is not allowed for this trial and would be considered a protocol deviation.

All MIPLATE Study patients receive irradiated platelets.

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Procedure

I. Ordering Study Platelets

1. Study Coordinators order Mirasol-treated platelets from Memorial Blood Centers (MBC) based on anticipated need for patients on MIPLATE Study ARM 1.
2. Blood Bank staff order general inventory plasma platelets for use by MIPLATE Study patients on ARM 2 (Control) following standard ordering practices. See procedure **D5906 Blood Product Inventory and Ordering**.
3. If special platelet requests (crossmatched/HLA or washed platelets) are received, notify the BB MDs.
    a. If approved by the BB MDs, notify a Study Coordinator.
    b. The Study Coordinator will follow up with the BB MDs regarding the patient's study participation.

II. Receipt and Storage of Mirasol-Treated Platelets

1. Receive Mirasol-treated platelets from MBC per normal Blood Bank procedures. See procedure **D5843 Platelet Processing**.
    a. See Example 1 in Appendix A for an image of the packing slip.
    b. See Example 4 in Appendix A for an image of a Mirasol-treated platelet unit.
    c. Each shipment of Mirasol-treated platelets will contain 2 copies of the packing slip.
        i. One copy should be filed with the other blood component packing slips.
        ii. The second copy should be placed in the designated file at the processing desk for the Study Coordinators to pick up, next to the bin for all other platelets' purple yield tags.
2. Verify that each unit has a yellow study tag affixed.
    a. See Example 2 in Appendix A for a picture of the tag.
    b. If not attached, notify a Study Coordinator and MBC. Do not use the component until cleared by a Study Coordinator.
3. Inspect the unit for a free floating frangible. If still intact, break before placing product in storage.
    a. See Example 3 in Appendix A for pictures of intact vs. broken frangibles.
    b. To break the frangibles in the Mirasol bag:
        i. Hang the Mirasol bag so that the spike port is pointing down.
        ii. Hold the spike port as close to the bag as possible to hold the port steady, then pinch the frangible and move back and forth three times ensuring the frangible breaks away and separates completely from the port.

            NOTE: Do not attempt to break the frangible by pressing it against a hard surface (i.e. countertop), as this could result in compromising the integrity of the bag.
        iii. The frangible will remain in the Mirasol-treated product for the duration of storage and/or transfusion.
        iv. The component can still be issued, but the intact/unbroken frangible needs to be reported in an I Care. Also, notify a Study Coordinator.

            NOTE: Do NOT include patient information when reporting unbroken frangibles.
4. Affix a red Mirasol Platelet sticker on the unit label. Do not obscure any label text.

5. Enter all MBC Mirasol-treated platelets into computer inventory per LIS procedure **S5084-LIS Blood Product Entry**.
6. Verify that the unit has been irradiated by MBC.

a. If not, irradiate the platelet. Follow standard procedure. See **D5946 Irradiation of Blood Components**.

7. All group O Mirasol-treated platelets should be tested for high isohemagglutinins upon receipt following standard procedure. See **D5857 Titration of Apheresis Platelets and Granulocytes for Anti-A and Anti-B**.

   a. If needed for transfusion prior to completion of the titer, they may only be given to a group O recipient.

   b. Weekly incompatible plasma totals must be tracked to ensure incompatible plasma limit is not surpassed.

8. Store Mirasol-treated platelets at room temperature (20-24°C) with continuous agitation on the designated shelves of the platelet rotator.

   NOTE: Avoid prolonged exposure to direct light. Store only on shelves labeled specifically for Mirasol platelets, and not on top of the rotator.

III. Receiving Orders and Identification of Study Patients

1. MIPLATE Study platelet patients will have comments in the Blood Bank Administrative Data (BAD) file indicating their study enrollment and treatment arm.

   a. ARM 1 – Investigational/test arm

      i. Problems field: MIRPLT (MIRASOL TREATED platelets only)

      ii. Comments field: "***MIPLATE PLATELET STUDY PATIENT*** ARM 1: Patient to receive MIRASOL TREATED platelets only. Contact MBC and Study Coordinator if product not available."

Blood Bank Administrative Data	
Problems	
MIRPLT -	MIRASOL TREATED platelets only
Antigens\Antibodies	
Comments	
-	;***MIPLATE PLATELET STUDY PATIENT*** ARM 1: Patient to receive MIRASOL TREATED platelets only. Contact MBC and Study Coordinator if product not available. 12/20/18 CLA
Transfusion Attributes	

   b. ARM 2 – Control arm

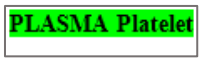
      i. Problems field: PLPLT (PLASMA platelets only)

      ii. Comments field: "***MIPLATE PLATELET STUDY PATIENT*** ARM 2 (Control): Patient to receive non treated PLASMA PLATELETS only."

Blood Bank Administrative Data	
Problems	
PLPLT -	PLASMA platelets only
Antigens\Antibodies	
Comments	
-	;***MIPLATE PLATELET STUDY PATIENT*** ARM 2 (control): Patient to receive non treated PLASMA platelets only. 12/20/18 CLA
Transfusion Attributes	

2. Receive the orders per normal protocol, and place a sticker on both the prepare and transfuse order indicating which treatment arm the patient is in:
   a. ARM 1 – Investigational arm: Add MIRASOL Platelet sticker.

   b. ARM 2 – Control arm: Add PLASMA Platelet sticker.



IV. Selecting and Allocating Platelets for Study Patients

1. Review patient history for each platelet request to identify and verify treatment arm.
   a. For **ARM 1** (investigational/test arm), select **MIRASOL** platelets only.

      NOTE: If no Mirasol platelets are available to fill orders, call MBC to see if they have platelets to send.

      i. If available, place an order with MBC as needed, and notify a Study Coordinator (M-F day shift) for awareness.

      ii. If no Mirasol platelets are available to order, notify a Study Coordinator immediately regardless of time of day.

   b. For **ARM 2** (control arm), select **PLASMA** platelets only.

      NOTE: If there is a platelet shortage, and no plasma platelets are available from either blood supplier to fill orders, contact a Study Coordinator.

2. Select products for ABO/Rh per standard Blood Bank policy. See procedure **D5883 Blood Type Selection Policies**.
3. Verify that the sticker on the order matches the sticker on the platelet selected.
4. Allocate platelet according to LIS procedure **S5067-LIS Allocating Blood Products**.

V. Issuing Platelet Product for Study Patients

1. Issue platelets according to procedure **D5909 Issue of Blood Components For Transfusion**.
2. Also, when issuing Mirasol-treated platelets, inspect the unit for a free floating frangible. If still intact, break before issuing.
   a. See Example 3 in Appendix A for pictures of intact vs. broken frangibles.

b. Refer to Step 3b in section II above for instructions on how to break frangibles.

3. For <u>all</u> MIPLATE Study patients (both ARM 1 and ARM 2), one hour post-platelet counts are required.
    a. Study Coordinators will prepare tubes and request slips for each patient.
    b. Attach a labeled tube and request slip to the platelet product using a plastic tie.
    c. If the patient is on a platelet drip, then the post-platelet count should be drawn 10 minutes after the end of each dose, just prior to the start of the next unit.
4. Do not send either Mirasol-treated (ARM 1) **<u>or</u>** control arm (ARM 2) platelets in the pneumatic tube system (PTS). **Call for pick up.**

VI. <u>Blood Component Preparation: Modifying Mirasol-Treated Platelets</u>

1. <u>Irradiation</u> – follow standard procedure. See **D5946 Irradiation of Blood Components**.
2. <u>Splitting</u> – Mirasol-treated platelets have strict rules about the volume remaining and what type of bag it's stored in:
    a. Each platelet must have ≥170 mL and still be stored in the original Mirasol bag to be able to maintain the original outdate. Otherwise, the outdate shortens to 4 hours.
    b. Follow standard operating procedures to make the split (see **D5902 Apheresis Platelet and Splitting Apheresis Platelets**), but make sure to update the expiration date as follows:
        i. <u>Parent unit (still in original Mirasol bag)</u>:
            1. If ≥170 mL left, outdate remains the same.
            2. If <170 mL left, shorten the outdate to 4 hours after the split was made.
        ii. <u>Split product (in transfer bag)</u>: Always shorten the outdate to 4 hours due to being stored in a non-Mirasol bag.
    c. Ensure that a yellow "Investigational Use Only" tie tag is attached to the split unit as well.
3. <u>Volume reduction</u> – Mirasol-treated platelets CANNOT be centrifuged in the Mirasol bag:
    a. Select a Mirasol-treated platelet with <300 mL and as little volume as possible.
    b. Prior to centrifugation, transfer the contents of the Mirasol bag into a 300mL transfer bag.
        i. Sterile connect a 300 mL transfer bag to the original Mirasol bag. Transfer the contents into the empty bag.
        ii. Using Sunquest function Blood Product Entry, change the outdate to 4 hours from the time the contents were transferred into the transfer bag.
        iii. Using Sunquest function Blood Bank Label Print, reprint a full-faced ISBT label.

iv. Ensure label printed correctly and attach to unit.

v. Write any pertinent information on new label that was on the original Mirasol bag label. (e.g. CMV negative status).

vi. Transfer the yellow "Investigational Use Only" tie tag to the new bag.

c. Then, follow the standard procedure for volume reduction. See **D5901 Volume Reduction of Platelets.**

VII. Discarding Mirasol-Treated Platelets

1. If outdated or late return, discard components per normal Blood Bank procedures.
2. If a Mirasol-treated platelet needs to be discarded for any other reason (leakage, insufficient labeling, etc.), follow instructions in "Reporting Product Issues" section below.

VIII. Reporting Product Issues

1. If a Mirasol-treated platelet is found to have any issues, a Study Coordinator should be notified, and the affected bag/unit should be saved.
2. If unacceptable for transfusion (leaking, insufficient labeling, positive bacterial culture result, etc.):
   a. Notify a Study Coordinator.
   b. Update the unit's status to "Discarded" in the LIS.
   c. Place the component in a plastic bag, place on quarantine shelf, and save for a Study Coordinator to review.
3. If transfusing staff reports any bag defects (hard to spike, etc.), but unit may still acceptable for transfusion:
   a. Request that the PCU/Clinic return the affected bag and administration set to the Blood Bank.
   b. Notify a Study Coordinator.
   c. Update the unit's status in the LIS, if applicable:
      i. If unit was not transfused, update the unit's status to "Quarantined."
      ii. If the unit was transfused, leave the unit in "Issued" status.
   d. Place the unit on quarantine shelf for a Study Coordinator to review.
   e. Report the issue in an ICare, including as much information about the incident as possible.
      i. Obtain as much information as possible from transfusing staff to describe any challenges with connecting or transfusing the product.
      ii. Include whether or not the issue resulted in a delay that affected the safety of the patient.

IX. Blinding

1. Blinded parties: patients, care providers, the study Principal Investigator (Dr. Claudia Cohn) and research nurse, and the BMT bleeding assessment team are not to know the Study Patient's assigned treatment arm. This is to ensure objectivity in the bleeding assessments and clinical care.
2. The patients and care providers may assume the transfusion of Mirasol-treated platelets due to the bright yellow color of the treated apheresis platelet product. They should make every effort to avoid revealing this assumption to the bleeding assessment team or physicians.
3. The Patient's MIPLATE treatment assignment is known (Unblinded) to the Study Coordinators and Blood Bank staff. Care must be taken to keep this information from the Blinded staff.

X. Contact Information

Unblinded Study Coordinators:

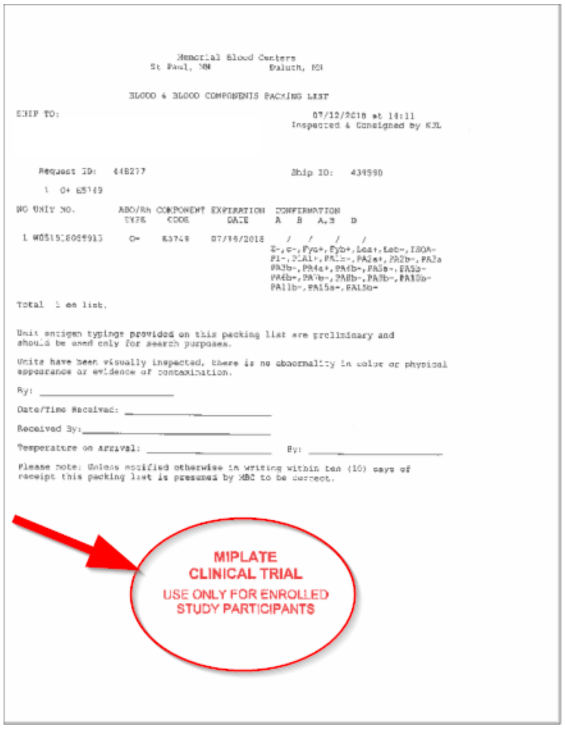
- Shelley Pulkrabek
- Connie Lien Adams

XI. Associated Documents

D5906 Blood Product Inventory and Ordering.
D5843 Platelet Processing
S5084-LIS Blood Product Entry
D5946 Irradiation of Blood Components
D5883 Blood Type Selection Policies
S5067-LIS Allocating Blood Products
D5909 Issue of Blood Components For Transfusion
D5902 Apheresis Platelet and Splitting Apheresis Platelets
D5901 Volume Reduction of Platelets

Appendix A: Examples for reference

Example 1: MBC Packing List – MIPLATE Study Platelets



Memorial Blood Centers
St Paul, MN Duluth, MN

BLOOD & BLOOD COMPONENTS PACKING LIST

SHIP TO:

07/12/2018 at 14:11
Inspected & Consigned by KJL

Request ID: 448277

Ship ID: 434590

1 O+ E5749

NO	UNIT NO.	ABO/Rh TYPE	COMPONENT CODE	EXPIRATION DATE	CONFIRMATION A B A,B D
1	W051518069913	O-	E5749	07/16/2018	/ / / /

Total 1 on list.

Unit antigen typings provided on this packing list are preliminary and should be used only for search purposes.

Units have been visually inspected, there is no abnormality in color or physical appearance or evidence of contamination.

By: ______

Date/Time Received: ______

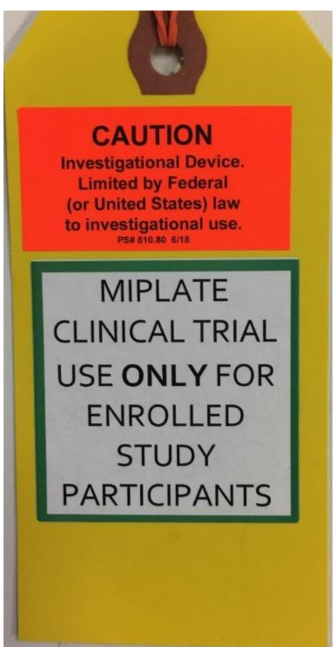
Received By: ______

Temperature on arrival: ______ By: ______

Please note: Unless notified otherwise in writing within ten (10) days of receipt this packing list is presumed by MBC to be correct.

Example 2: Investigational Use Only Tag

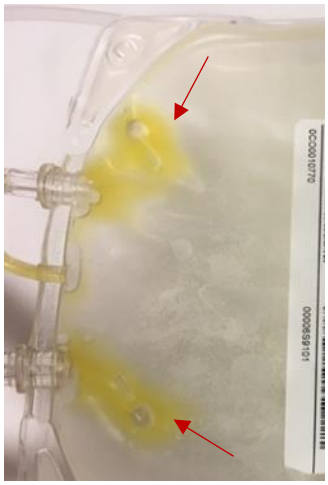
SIDE 1



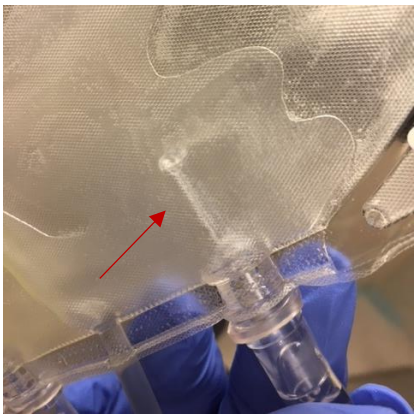
SIDE 2

Example 3: Frangible

Broken (Correct)



Intact (INCORRECT – Need to break!)



Breaking an intact frangible

Example 4: Mirasol-Treated Platelet Unit