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Procedure Apheresis Collection of Allogeneic Mononuclear Cells for the Manufacturing of Cytotoxic T-Cells for Clinical Protocols NYMC 579, NYMC 580, NYMC 581 and NYMC 590

I. PURPOSE

This SOP details the steps for collection of the MNC apheresis products for NYMC 579, NYMC 580, NYMC 581, and NYMC 590.

II. SCOPE

This procedure applies to the collection of allogeneic MNCs for patients enrolled on IRB Protocols for NYMC 579, NYMC 580, NYMC 581, and NYMC 590. This procedure is performed by trained Apheresis Registered Nurses under the direction of an Apheresis Physician.

III. STATEMENTS/REQUIREMENTS

A. Any exceptions to this policy must be approved by the Apheresis Collection Facility Director. Any exceptions that deviate from the study protocol must be approved by the Study PI.

B. This procedure is used to support:

- A Pilot Study in the Treatment of Refractory Adenovirus (ADV) Infection with Related Donor ADV Cytotoxic T-Lymphocytes (ADV-CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 579
- A Pilot Study in the Treatment of Refractory BK Infections with Related Donor BK Specific Cytotoxic T-cells (CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 590
- A Pilot Study in the Treatment of Refractory Cytomegalovirus (CMV) Infections with Related Donor CMV Specific Cytotoxic T-cells (CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 580
- A Pilot Study in the Treatment of Refractory Epstein-Barr Virus (EBV) Infection with Related Donor EBV Cytotoxic T-Lymphocytes in Children, Adolescents and Young Adult Recipients – NYMC 581

C. No study specific forms are required for collection.

D. Allogeneic donor eligibility and labeling rules must be followed.

1. Refer to DR 012 Procedure: Allogeneic Donor Eligibility and Suitability for eligibility requirements.

2. Refer to AP 066 Procedure: HPC(A) and MNC(A) Product Labeling for labeling.

E. Any deviation that has the potential to impact the quality, purity, safety or testing of the MNC product must be reported to Apheresis QA, the PI, and the Riley Research Coordinator within 24 hours.

IV. DEFINITIONS

AABB: Association for the Advancement of Blood & Biotherapies
BMT: Bone Marrow Transplant
CMNC: Continuous Mononuclear Cell Collection
CTL: Cellular Therapy Laboratory
FACT: Foundation for the Accreditation of Cellular Therapy
FDA: Food and Drug Administration
IRB: Institutional Review Board
ISBT: International information standard for coding and labeling of cell therapy products
MNC: Mononuclear Cells
MNC(A): Mononuclear Cells by Apheresis
PI: Principal Investigator
SOP: Standard Operating Procedure

V. EQUIPMENT/RESOURCES

1. Refer to SOP AP 020 Adult Continuous Mononuclear Cell Collection by Apheresis Using Spectra Optia® for a list of current materials and supplies.

VI. PROCEDURE

A. The Riley Research Coordinator will notify Apheresis to schedule the MNC collection procedure.

1. Apheresis will reserve an outpatient bed for the day of collection.

B. The Riley Research Coordinator will provide Apheresis with the following paperwork:

1. Donor Evaluation Checklist F-CL-2.04-7
2. Allogeneic Recipient Pre-Transplant Evaluation Checklist F-CL-2.00-3
3. Request for Processing Order (Allogeneic Products and NMDP Outgoing Products) F-CL-2.04-1
   a. The subject study ID will be documented on this request.
4. Copy of the Informed Consent to participate in the study.

C. Patient Identity Verification Day of Procedure

1. Positive patient/donor identification must be assured.
   a. The information on the hospital account label/armband is verified by the patient/donor.
   b. All patients/donors (inpatients and outpatients) must have an armband with their name, medical record number, and date of birth.
   c. Ask donor/patient to state their name and DOB.

d. Verify correct MRN on armband.

2. The F-344 Allogeneic Donor Registration Form HPC/MNC will be completed each day of collection by the patient/donor and assigns a DIN for the collection.
3. Subject identifiers on the confirmation of the Study ID must exactly match the verification source.
    a. If there is a discrepancy, DO NOT proceed. Immediately contact the Riley Research Coordinator for further guidance.

F. Collection Procedure

1. All products will be collected using the Spectra Optia CMNC protocol according to SOP AP 020 Adult Continuous Mononuclear Cell Collection by Apheresis Using Spectra Optia® .
2. The cell collection target is 2 x 10^9 TNC for shipment to the manufacturing facility.
    a. If a minimum is not collected on the first attempt, a second collection may be attempted to attain this target. Product bags from multiple collections should not be combined, each apheresis collection should be performed with the goal of achieving the Total WBC target.
3. Leave the collect pump flow rate at 1.0 mL/min.

G. Product Labeling

1. Products will be labeled according to SOP AP 066 Procedure: HPC(A) and MNC(A) Product Labeling .
    a. Follow the instructions for **Allogeneic Matched Related Apheresis Products.**
        - Since this MNC product is for research purposes choose “Investigational Drug” rather than “Standard” under the product code.
        - Include the Donor Study ID next to the Donor MRN.
        - Include the Recipient Study ID next to the Recipient MRN.

H. Product Release and Documentation

1. All products collected in Apheresis will be released to CTL for final distribution according to AP 020 Adult Continuous Mononuclear Cell Collection by Apheresis Using Spectra Optia®.
    a. Notify CTL for product pick-up.
2. All products must be transferred to CTL within 60 minutes of collection end time.

H. Billing

1. Billing will be entered under the donor’s Cerner account according to AP 064 Procedure: Apheresis Billing and Computer Entry.

VII. CLINICAL SIGNIFICANCE/SPECIAL CONSIDERATIONS

Hematopoietic stem cell transplantation (HSCT) is curative therapy for many malignancies and non-malignant conditions. However, HSCT is associated with three major risks: graft rejection, graft-versus-host disease and opportunistic infections. Viral reactivation and infections remain a significant cause of morbidity and mortality in post-HSCT patients. These infections occur with delayed immune reconstitution, which may result from methods to reduce graft vs host disease (GVHD) such as in vivo serotherapy or ex vivo T depletion, and from GVHD itself. Although incidence and severity of viral infections/reactivations can be lowered by prophylactic and therapeutic antiviral antibiotics, the efficacy of this treatment is limited. Standard antiviral treatment does not lead to restored virus-specific immunity and thus, after therapy completion (usually day 100) new

reactivations or infections are frequent. In addition, standard anti-viral antibiotics, including ganciclovir, foscarnet and cidofovir, are associated with significant side effects including leukopenia and renal dysfunction. Historic results of therapy for infections caused by Epstein-Barr virus (EBV), adenovirus (AdV) and cytomegalovirus (CMV) post HSCT have been dismal.

VIII. REFERENCES

AABB Standards for Cellular Therapy Product Services, current edition.

FDA CFR Title 21, Part 1271 Human Cells, Tissues and Cellular and Tissue Based Products

FACT Standards, current edition

A Pilot Study in the Treatment of Refractory Adenovirus (ADV) Infection with Related Donor ADV Cytotoxic T-Lymphocytes (ADV-CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 579

A Pilot Study in the Treatment of Refractory BK Infections with Related Donor BK Specific Cytotoxic T-cells (CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 590

A Pilot Study in the Treatment of Refractory Cytomegalovirus (CMV) Infections with Related Donor CMV Specific Cytotoxic T-cells (CTLs) in Children, Adolescents and Young Adult Recipients – NYMC 580

A Pilot Study in the Treatment of Refractory Epstein-Barr Virus (EBV) Infection with Related Donor EBV Cytotoxic T-Lymphocytes in Children, Adolescents and Young Adult Recipients – NYMC 581

IX. FORMS/APPENDICES

Donor Evaluation Checklist F-CL-2.04-7

Allogeneic Recipient Pre-Transplant Evaluation Checklist F-CL-2.00-3

Request for Processing Order (Allogeneic Products and NMDP Outgoing Products) F-CL-2.04-1

F-344 Allogeneic Donor Registration Form HPC/MNC

X. APPROVAL BODY

None

PROCEDURE #:

RAP 012