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Procedure Receipt and Administration of CD4CAR Investigational Product for Protocol CTO-IUSCCC-ICG122-101

Printed copies are for reference only. Please refer to the electronic copy for the latest version.

I. PURPOSE

To provide guidelines to receive, prepare and distribute autologous CAR-T products for patients receiving the CTO-IUSCCC-ICG122-101 CD4CAR investigational product.

II. SCOPE

This procedure applies to the receipt and dose preparation of CD4CAR for patients approved for this CAR-T therapy. All CTL Technologists will comply with this procedure.

III. STATEMENTS/REQUIREMENTS

A. Any exceptions to this procedure require approval by CTO-IUSCCC-ICG122-101 Protocol and CTL Processing Facility Medical Director.

B. This procedure is used in conjunction with the CTO-IUSCCC-ICG122-101 Protocol for CD4CAR, a CD4- directed chimeric antigen receptor engineered T-cells (CD4CAR) in patients with Relapsed or Refractory CD4+ Lymphoid Hematological Malignancies.

C. Always contact the CTO-IUSCCC-ICG122-101 Protocol Site Manager for any questions or concerns.

D. CD4CAR will be thawed bedside by CTL Technologists and the product will be infused by BMT Nursing Staff or MD.

E. Any deviation from the protocol must be reported to Site Manager.

   i. Deviations must be reported within 24 hours of discovery.

F. All CTO-IUSCCC-ICG122-101 Protocol forms (referred to appendixes) are attached at the end of the current edition of the CD4CAR Cellular Therapy Manual (CTM). The CTM is maintained in the protocol folder on the secure drive.

IV. DEFINITIONS

AABB: Association for the Advancement of Blood and Biotherapies

AWB: Air Waybil

CD4CAR Investigational CAR-T Product. CD4CAR is an CD4- directed chimeric antigen receptor engineered T-cells (CD4CAR) in patients with Relapsed or Refractory CD4+ Lymphoid Hematological Malignancies.

BMT: Bone Marrow Transplant

CAR: Chimeric Antigen Receptor

CIT: Center for Cell Immunotherapy and Transduction

COC: Chain of Custody

COI: Chain of Identity

CTL: Cellular Therapy Laboratory

CTM: Cellular Therapy Manual – Manual published by the CTO-IUSCCC-ICG122-101 Protocol to guide the workflow for collection, shipment, receipt, and infusion of the CD4CAR Investigational Product.

DIN: Donation Identification Number DOB: Date of Birth

FACT: Foundation for the Accreditation of Cellular Therapy

FDA: Food and Drug Administration

IP: Investigational Product

LN2: Liquid Nitrogen

MRN: Medical Record Number

PI: Primary Investigator

PPE: Personal Protective Equipment

SOP: Standard Operating Procedure

V. EQUIPMENT/RESOURCES

Equipment:

CTO-IUSCCC-ICG122-101 Protocol LN2 Shipper LN2

Vapor Phase Freezer

CTL LN2 Shipper charged for transport

Water Bath

Materials:

CD4CAR Investigational Product

0.9% NaCl Injection, USP (normal saline) in pre-warmed water bath, 2L

Alcohol swabs

BD Alaris Pump Infusion Burette Set (or equivalent)

Non-sterile gloves and masks (on unit)

LN2 PPE (cryogenic gloves, lab coat, safety glasses) Approved hospital disinfectant

OriGen Sterile overwrap bag

Forceps (both sterile and non-sterile)

CH-7755 Form (Stem Cell Infusion Assessment)

CH-2046 Form (Infusion of Hematopoietic Progenitor Cells)

VI. PROCEDURE

A. **Product Receipt:**

1. CTL will be notified in advance of delivery and will record the shipment date on the CTL calendar.
2. CTL will follow all instructions for receipt as described in the most current version of the CTO-IUSCCC-ICG122-101 CD4CAR Cellular Therapy Manual.

3. Appendix 9.5 Cell Product Receipt Form will be filled out at the time of unpacking of the LN2 dewar.
    a. This form will be kept in the recipients CTL chart.
    b. Follow the emailing instructions on the form once completed.
4. Ensure that all the required documents were sent along with the product.
5. Examine the attached data logger as described in the CTO-IUSCCC-ICG122-101 CD4CAR Cellular Therapy Manual
6. Any temperature excursions or product integrity deviations will be reported to the CTL Medical Director, CTL QA and to CTO-IUSCCC-ICG122-101 Protocol immediately.
    a. In the case of a temperature deviation, complete transfer of the product to a functioning LN2 freezer prior to initiating any notifications.
    b. The CTL Medical Director and CTO-IUSCCC-ICG122-101 Protocol PI will decide if the product is suitable or needs to be replaced.
7. Ensure that the lid of the shipper is sealed upon arrival. Remove the lid (if necessary) and confirm the temperature of the container and record on Cryopreserved Product Receipt Checklist (Appendix 9.5).
8. Remove the product from the plastic bag and visually inspect it. Ensure there are no clots and the bag itself is intact. Record the products condition on Cryopreserved Product Receipt Checklist (Appendix 9.5)
    a. In case of bag integrity issue, notify the CTL Medical Director, CTL Facility Director, CTL QA and the Protocol Coordinating Center immediately.
9. Read the product label with a second technologist according to PST-005 Procedure Receipt of Cellular Therapy Products.
10. The investigational product must be stored according to the conditions on the label, in a secure location with limited access.
    a. Store in vapor phase of the liquid nitrogen freezer.
    b. Temperature must remain at <150°C.
        i. In case of a temperature excursion notify the CTL Medical Director, CTL Facility Director, CTL QA and the Protocol Coordinating Center immediately.
            1. Transfer the IP to a freezer that is in the proper temperature range prior to reporting the excursion.
    c. The IP must be stored in a continuously monitored freezer.
11. Log the product into the F-001 CTL Activity Log.
12. Log each bag received into the F-414 Cellular Therapy Laboratory Investigational Product Dispensing and Accountability Log.

B. **Product Infusion:**

1. Infusion will be scheduled by the BMT treating physician, BMT providor or by the protocol research nurse.
2. The BD Alaris Pump Infusion Burette Set (or equivalent) will be kept in the Cellular Therapy Laboratory and delivered to the nurse on the day of the infusion.
    a. Coordinate with the nurse prior to the infusion to see if the Burette is required prior to arrival with the investigational product.
3. Complete Appendix 9.3 Investigational Product Thaw Record.
4. Follow all applicable steps as described in SOP PM-003 Procedure Infusion of Cryopreserved Products with the following exceptions:
    a. Obtaining infusion advice from the CTL Medical Director is not required.
        i. The dose is determined by the protocol and the PI.
    b. Cellular dose calculations are not required.

i. Enter “n/a” on the CH-2046 Infusion of Hematopoeitic Progenitor Cells “E21” in appropriate section.

c. If the manufacturer gives a total dose on the COA, enter onto the CH-2046 Infusion of Hematopoeitic Progenitor Cells accordingly.

d. If the manufacturer gives the amount of DMSO, enter the DMSO on volume the and DMSO dose in the Cerner order.

i. If the DMSO volume is not provided enter “n/a”.

e. If the CD4CAR T cell product appears to have a damaged or leaking bag, or otherwise appears to be compromised, it should not be infused, and should be returned to the site’s cell processing facility. The site coordinator should contact the multicenter project manager immediately to facilitate shipment of back up bag to site.

f. Prior to the infusion, two individuals will independently verify all this information in the presence of the subject and confirm that the information is correctly matched to the participant.

g. Thaw temperature will be 37±1°C.

h. Instructions PM-003 Procedure Infusion of Cryopreserved Products for Infusion Set-Up and product infusion will not apply.

i. A sterile field will be set up, but the CTL technologist will only perform the thaw and then hand the IP off to the nurse for infusion.

i. Document the time and temperature for each bag thawed on a separate line of the LN2 Shipper and Water Bath QC form.

i. Ensure that all times recorded are from a synchronized source so that the times of each step are in sequential order (for example, the thaw cannot be documented to occur after the infusion is started).

j. If the CD4CAR T cell product appears to have a damaged or leaking bag, or otherwise appears to be compromised, it should not be infused, and should be returned to the Cellular Therapy Laboratory.

i. Notify the provider covering the infusion, CTL QA and CTO-IUSCCC-ICG122-101 Protocol PI immediately.

k. Massage the bag gently until just thawed.

l. A label will be generated for the thawed IP

i. Label will include at a minimum the following information for the IP Infusion Bag post thaw:

1. Maintain thawed IP at room/ambient temperature and light conditions.
2. Avoid direct sunlight exposure
3. Expiry*:
    a. Preferred format: dd / MON / yyyy HH:MM
    b. * Expiration time is 6 hours after the IP infusion bag has been thawed

ii. Attach this label usind a toe tag prior to handoff to the nursing personell.

m. If applicable, thawing of the subsequent bags must not start until the previous bag is completely infused.

n. The IP bag will be saved after infusion and submitted to microbiology by nursing personel for sterility testing.

13. Document on form 9.3 INVESTIGATIONAL PRODUCT THAW RECORD according to the current version of the CTO-IUSCCC-ICG122-101 CD4CAR Cellular Therapy Manual

a. Keep in the patient’s CTL chart.

b. Scan a copy of the completed form to the site coordinator.

VII. CLINICAL SIGNIFICANCE/ SPECIAL CONSIDERATIONS

A. Investigational Product return or destruction will only be performed in accordance with the CTO-IUSCCC-ICG122-101 Protocol and upon the written approval of the PI or study protocol representative.

B. CD4CAR T cells may require return to the site's cell processing facility for a variety of reasons, including but not limited to: 1) Mislabeled product; 2) Condition of patient prohibits infusion/injection, and 3) Subject refuses infusion/injection; any unused frozen product will be returned to the coordinating center for disposal or storage as per facility policy.

C. There will be an ongoing reconciliation of drug shipped, drug consumed, and drug remaining, performed by the BMT lab. This information is submitted on an annual basis to the FDA in annual reports. Drug destroyed on site will be documented in the study files.

D. All deviations must be reported to the protocol within 24 hours of discovery.

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

CTO-IUSCCC-ICG122-101 Protocol Cell Therapy Manual, current version

CTO-IUSCCC-ICG122-101 Protocol, current version

IX. FORMS/APPENDICES

F-001 CTL Activity Log

LN2 Shipper and Water Bath QC

F-410 CAR T Cryopreserved Product Receipt Checklist

F-414 Cellular Therapy Laboratory Investigational Product Dispensing and Accountability Log

CH-2046 Cellular Therapy Lab Infusion Form

CTO-IUSCCC-ICG122-101 Protocol Forms located in the current version of the CD4CAR Cellular Therapy Manual:

X. APPROVAL BODY

None

PROCEDURE #:

RCTL 025