



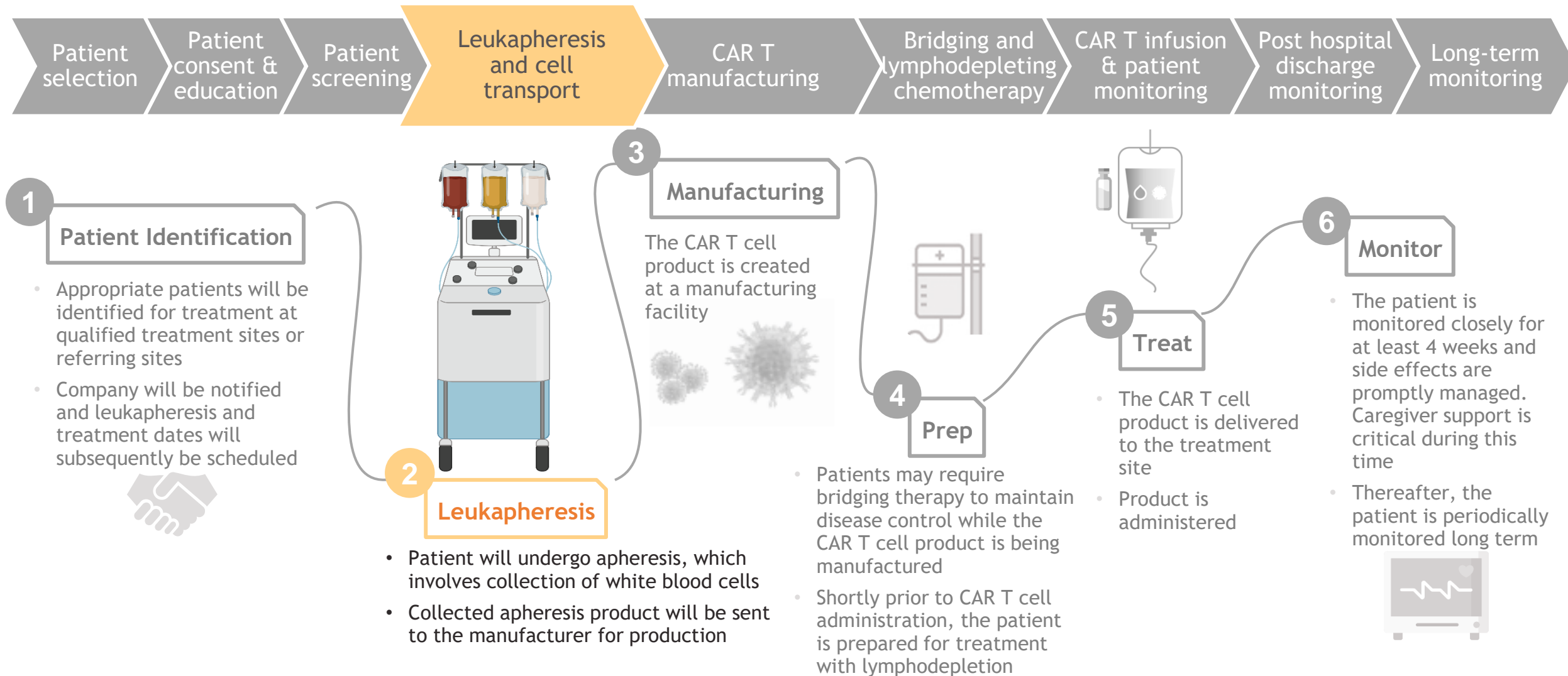
Apheresis

CAR T Academy: Apheresis



- 01 Procedure Overview
- 02 Collection Considerations
- 03 Technical Considerations
- 04 Scheduling and Shipping

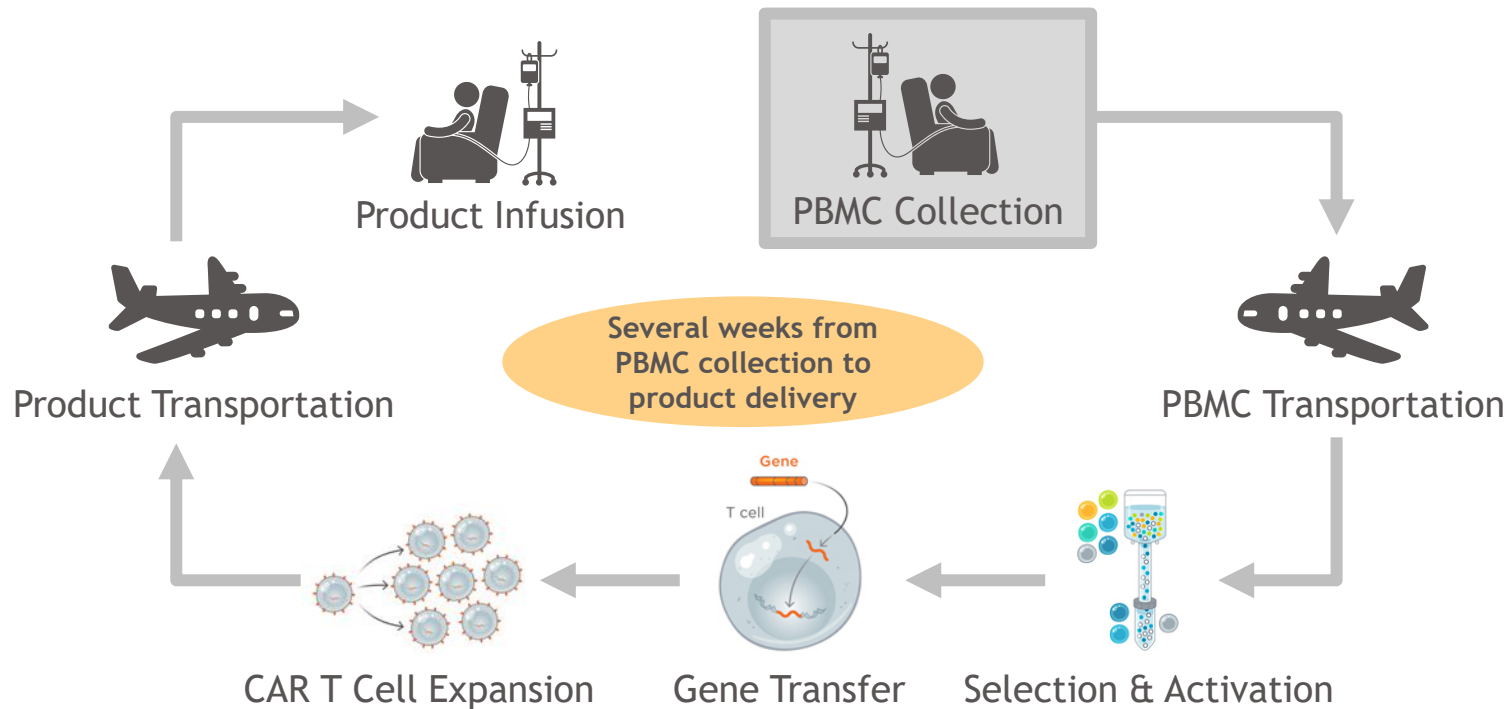
Patient Journey Through the CAR T Cell Therapy Process



Reference: 1. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34.

Importance of Apheresis

Apheresis is a critical step in the autologous CAR T cell manufacturing process in which the starting material used to produce the CAR T cell therapy is collected^{1,2}



The manufacturing process cannot continue without successful collection of the patient's white blood cells

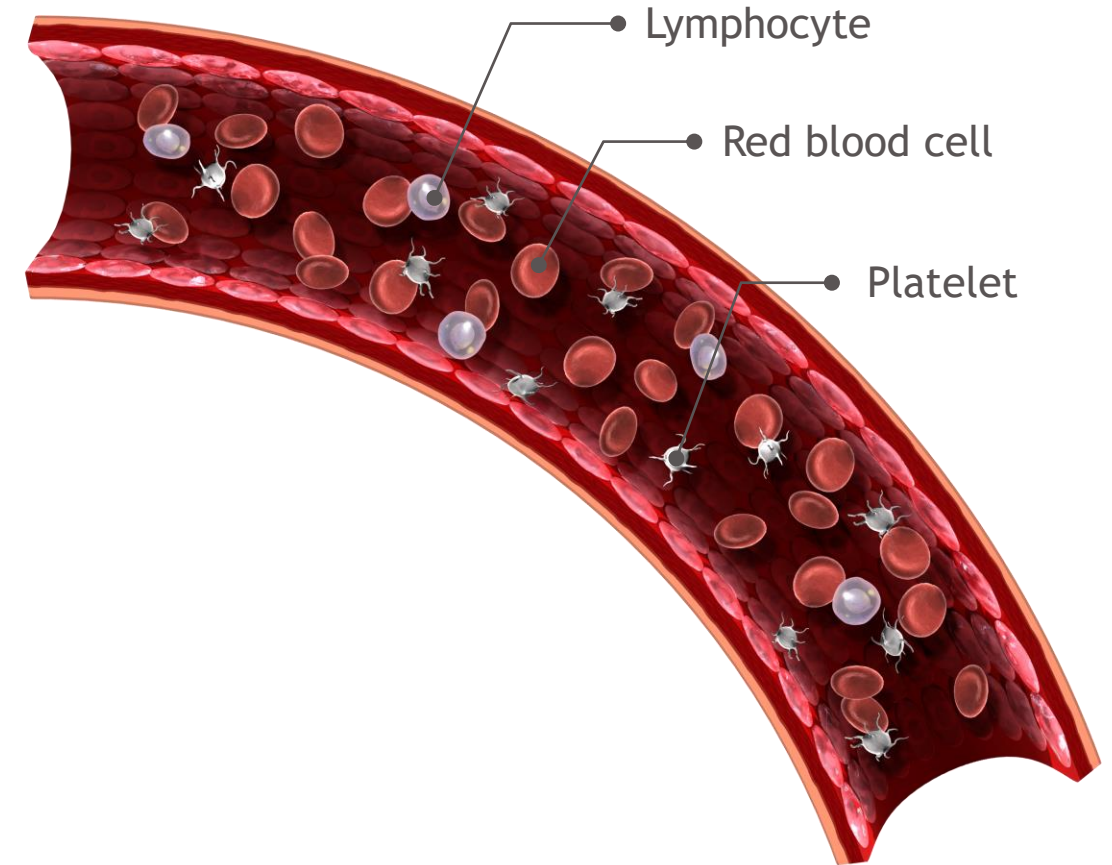
PBMC, peripheral blood mononuclear cell.

References: 1. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34. 2. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024.

Apheresis


Greek word root: “to take away”

- Apheresis begins with whole blood removal
- Blood is separated into different layers by centrifugation using specific gravity of cellular components (plasma, platelets, leukocytes, erythrocytes)
- Certain cellular components or plasma can be removed, replaced, or treated in-line and returned
- Remaining blood components are returned to the body



Reference: Chegini A, et al. *Transfus Apher Sci.* 2019;58(3):266-272.

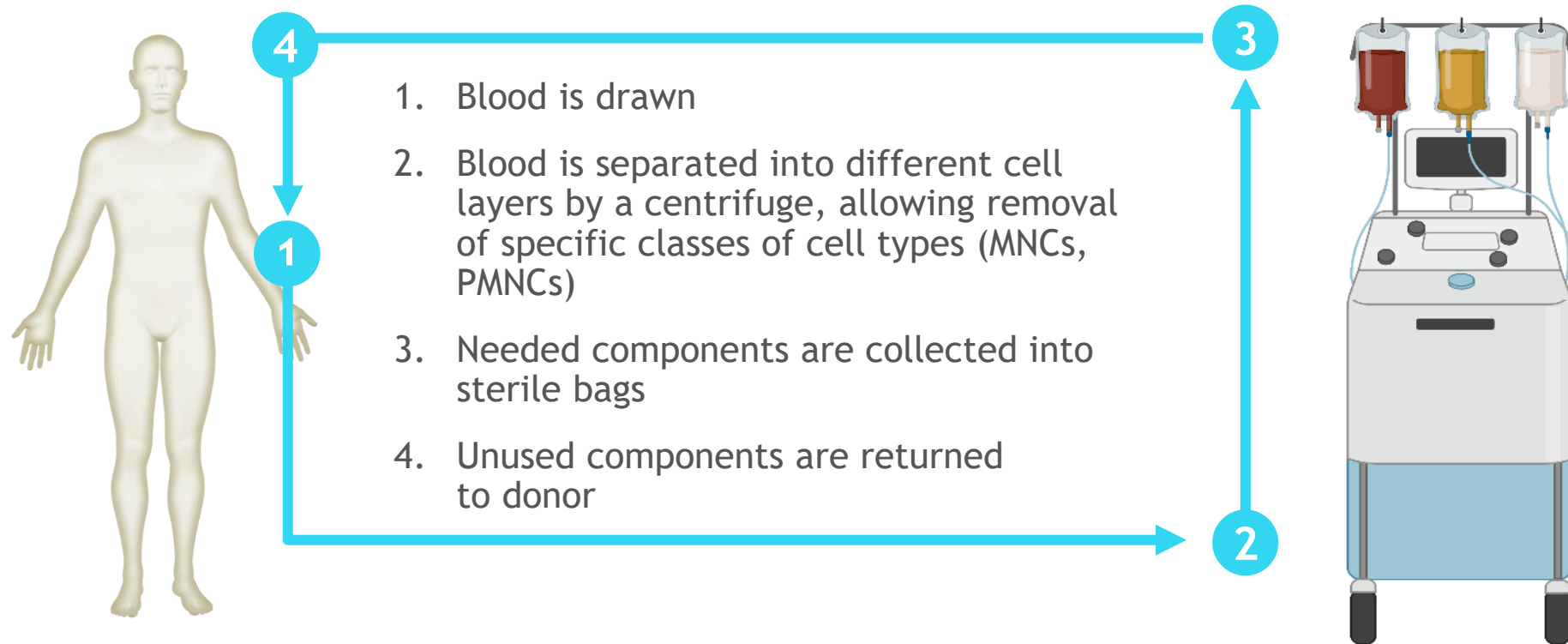
Types of Apheresis

Type of Apheresis	Examples
Therapeutic Apheresis ^{1,2}	<ul style="list-style-type: none"> • Plasma exchange (eg, for thrombotic thrombocytopenic purpura, Guillain-Barre Syndrome, myasthenia gravis) • Red blood cell exchange (eg, for sickle cell disease) • White blood cell depletion (eg, for select leukemias) • Platelet depletion • Low-density lipoprotein (LDL) apheresis • Photopheresis
Collection Apheresis ¹	<ul style="list-style-type: none"> • Platelets • Plasma • Red blood cells • White blood cells <p>  Collection of white blood cells from the peripheral blood is called leukapheresis¹ </p>

References: 1. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 2. Szczepiorkowski ZM, et al. *J Clin Apher*. 2010;25(3):83-177.

Apheresis Process

The apheresis process requires appropriate and approved collection devices, adherence to good clinical practice requirements and product-specific protocols, as well as trained personnel¹⁻³

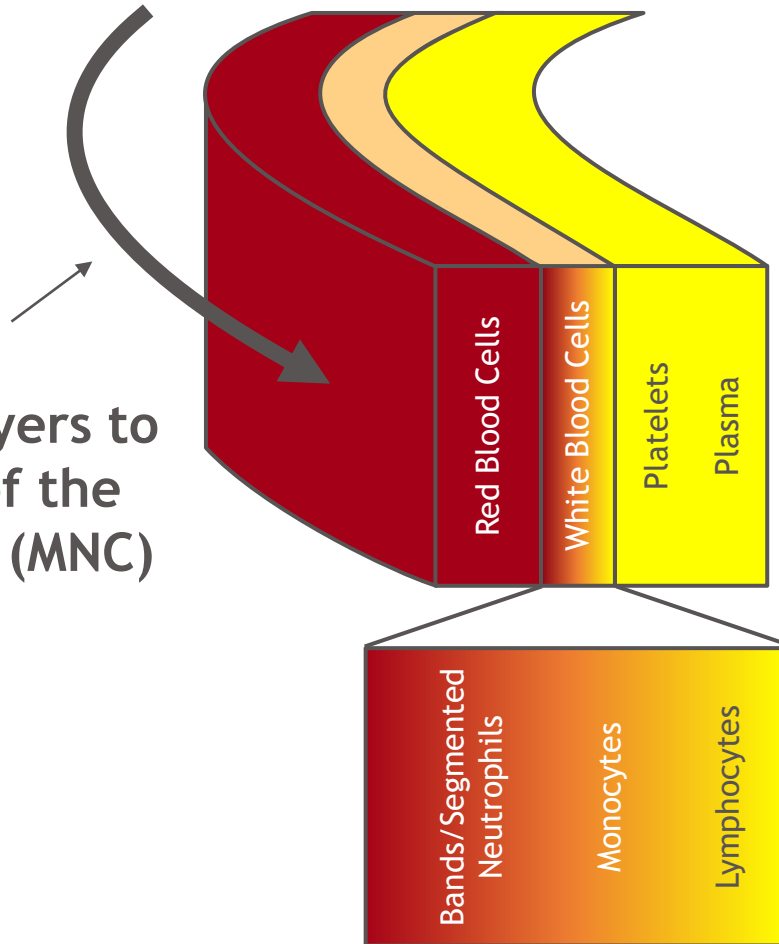


MNC, mononuclear cell; PMNC, polymorphonuclear cell.

References: 1. Perica K, et al. *Biol Blood Marrow Transplant*. 2018;24:1135-1141. 2. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 3. Fesnak A, et al. *Transfus Med Rev*. 2016;30:139-145.

Leukapheresis

Centrifugal Force Separates Cell Layers to Enable Isolation of the Mononuclear Cell (MNC) Layer



- The apheresis process separates out general classes of cells, such as MNCs, PMNCs (polymorphonuclear cells), or blood components like plasma
- MNCs are located in the buffy coat which consists of lymphocytes + monocytes, PMNCs, and platelets. Red cells are the heaviest and will pack in the very bottom layer
- After apheresis, additional steps to isolate specific types of leukocytes (eg, T cells) are carried out in a cell processing laboratory

MNC, mononuclear cell; PMNC, polymorphonuclear cell.

Reference: Fesnak A, et al. *Transfus Med Rev.* 2016;30:139-145.

Apheresis: Possible Adverse Events



In a retrospective analysis of
15,763
apheresis procedures
at a single center
(2006-2009)¹:

The incidence of
moderate/severe
AEs was
0.37%

Possible AEs²:

- Fatigue
- Nausea
- Dizziness
- Chills
- Tingling/paresthesia (fingers, mouth)

Rare AEs^{1,2}:

- Abnormal heart rate
- Seizures
- Rash
- Burn (from heat pack application)
- Vascular access sequelae (eg, hematomas, nerve injuries after venipuncture)

AE, adverse events.

References: 1. Yuan S, et al. *Transfusion*. 2010;50:478-486. 2. Maus MV, Levine BL. *Oncologist*. 2016;21:608-617.

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- 
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Considerations Prior to Leukapheresis

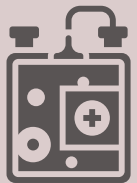
Assessments will determine the plan of care:



History and physical

- *Can the patient withstand the procedure?*
- *Are there any significant comorbidities?*

➤ Important to verify prior to initiating leukapheresis



Laboratory values^{1,2}

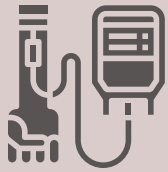
- *Does the patient have sufficient red blood cells, platelets, and white blood cells to begin the procedure?*

- Ensure that sufficient cells can be collected
- Reduce risk of possible complications (eg, syncope, bleeding)

References: 1. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34.

Considerations Prior to Leukapheresis (cont.)

Assessments will determine the plan of care:



Venous assessment²

- *Is there adequate venous access?*
- *Can peripheral veins be used or is there a need to place a central venous catheter?*

- In some cases, it may be necessary to place a temporary or permanent dialysis-grade catheter in pediatric patients or a central venous catheter in adolescent and adult patients²



Treatment history^{1,2}

- *Has the patient undergone stem cell transplantation (SCT) within 3 months?*
- *Are there other concomitant medications that might lead to low blood counts and/or complications?*

- Leukapheresis is discouraged within 3 months of allogeneic SCT due to the risk for graft-versus-host disease (GVHD)²

References: 1. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34.

Patient Education

The apheresis unit will counsel patients and provide instructions regarding the procedure, such as the following:

Pre-collection



Eat prior to the procedure, especially calcium-rich foods¹



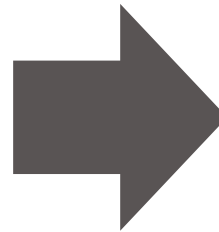
Increase fluid intake for 2 days, but limit fluids for 3 hours immediately before²



Hold certain medications prior to treatment, following HCP recommendations³



Bring entertainment!¹



Post-collection



Limit activity for 12 hours - mild fatigue or dizziness may occur. Contact your physician if you experience dizziness⁴



Continue to drink fluids to stay hydrated⁴

HCP, health care professional.

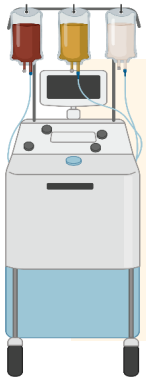
References: 1. Johns Hopkins. *A Guide to Apheresis*. Baltimore, MD; Johns Hopkins Medicine. 2. UC San Diego. *Plasmapheresis Patient Handout*. San Diego, CA: UC San Diego Health System. 3. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34. 4. Ohio State University. Apheresis. <https://healthsystem.osumc.edu/pteduc/docs/apheresi.pdf>.

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- 
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Leukapheresis for CAR T Cell Therapy

- CAR T cell manufacturers use collection protocols that target the MNC layer, which contains mature T lymphocytes¹
- Monocytes are selectively depleted to enrich for CD3+ T cells in the final leukapheresis product¹⁻³
- Mobilization (ie, use of growth factors to stimulate cells out of bone marrow) is not required since these cells are already in the blood^{2,3}



Each procedure takes several hours. A single collection is usually sufficient, but occasionally multiple collections may be required²

MNC, mononuclear cell.

References: 1. Juliano L, et al. *Cell Gene Ther Insights*. 2018;4:327-336. 2. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 3. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34.



Leukapheresis Instrumentation

There can be wide variation in leukapheresis training, collection protocols, and collection equipment across clinical sites¹

Spectra Optia®



Fenwal Amicus®



Two FDA-cleared machines commonly used to collect leukapheresis product in accordance with CAR T cell protocols and standards are the **Spectra Optia®** and **Fenwal Amicus®**²

References: 1. Juliano L, et al. *Cell Gene Ther Insights*. 2018;4:327-336. 2. Fesnak A, et al. *Transfus Med Rev*. 2016;30:139-145.

Technical and Quality Agreements for Leukapheresis




The product-specific protocols for collecting the leukapheresis product are aligned with the technical standards for CAR T cell production

- Pharmaceutical companies undergo a rigorous qualification and contracting process with apheresis facilities that can perform collections for its CAR T cell therapy products
- Additionally, on-site inspections may be performed
- Processes are defined for training personnel, tracking and verifying product identity, and many other aspects

Reference: Perica K, et al. *Biol Blood Marrow Transplant*. 2018;24:1135-1141.

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- 
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Scheduling

Whether leukapheresis will be conducted internal or external to the CAR T cell therapy treatment center is decided by the treating center and depends on its in-house capabilities. Sufficient time is needed to perform^{1,2}:



Close communication between the treating center, apheresis facility, and CAR T cell manufacturing facility is important throughout this process to deliver CAR T cell therapy to patients as safely and as quickly as possible¹

References: 1. McGuirk J, et al. *Cytotherapy*. 2017;19:1015-1024. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34.

Preservation, Storage, and Shipping



Cell therapy products are extremely sensitive to temperature excursions¹

- Cold preservation of the leukapheresis product is necessary immediately after collection¹
- There are 2 types of cold preservation, which may be product-specific¹
 - Short-term refrigerated storage (2° to 8°C), to slow down cellular metabolism and reduce physiologic stress that can damage or kill cells^{1,2}
 - Long-term cryopreservation (-80° to <-150°C), to help preserve cells in a stable state^{1,2}
- Once preserved, leukapheresis material is sent to the product manufacturer's central cell-processing facility in a validated shipping container that maintains product temperature³

References: 1. Juliano L, et al. *Cell Gene Ther Insights*. 2018;4:327-336. 2. Rafiq QA, et al. *Cell Gene Ther Insights*. 2017;3:335-344. 3. Better M, et al. *Cell Gene Ther Insights*. 2018;4:173-186.

Summary

- Leukapheresis is a specific type of apheresis that refers to the collection of white blood cells from the peripheral blood
- Before undergoing leukapheresis, patients must meet certain criteria per institutional protocols
- CAR T cell manufacturers use collection protocols that target the MNC layer and, more specifically, non-mobilized CD3+ T cells within that class of cells
- Different machines and techniques may be employed to collect and ship leukapheresis products in accordance with the manufacturer's CAR T cell product-specific apheresis protocols and standards
- Close communication between the CAR T cell therapy treating center, apheresis facility, and CAR T cell manufacturing facility is important throughout the leukapheresis process

Thank you for completing this module of CAR T Academy

We hope you found it informative and educational



- Follow this link to download a printable acknowledgment of completion:
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