

# CAR-T Cell Therapy: Process and Clinical Considerations

CAR-T=chimeric antigen receptor-T cell.

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# Objectives



Introduction to **CAR-T**



Describe the **CAR-T patient journey**



Highlight the **importance** of **care partners** in providing **patient support** throughout the **CAR-T process**



Illustrate the **safety considerations** of CAR-T cell therapy and the importance of the **monitoring period**

CAR-T=chimeric antigen receptor-T cell.

# The CAR-T Patient Care Team

The referring oncology practice and CAR-T Treatment Center share an important partnership.

## Referring oncology practice

Educating patients about CAR-T treatment

Educating patients on and coordinating referrals to a CAR-T Treatment Center

Screening patients for potential CAR-T eligibility

Long-term monitoring of patients after CAR-T treatment



## CAR-T Treatment Center

Educating patients about CAR-T treatment

Coordinating intake of patients for consultations and treatment

Managing treatment logistics

Determining bridging therapy options with input from referring practice

CAR-T administration

Monitoring patients after CAR-T treatment

Coordinating return of patients to referring oncology team

CAR-T=chimeric antigen receptor-T cell.



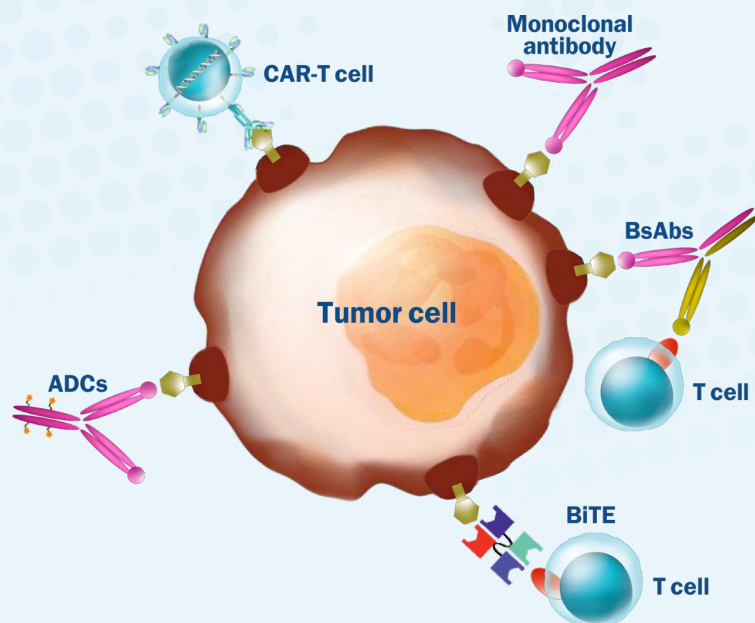
# Immunotherapy



# Select Immunotherapy Strategies: Understanding Bispecific Antibodies (BsAbs), Antibody Drug Conjugates (ADCs), and Chimeric Antigen Receptor-T Cell (CAR-T)

Over the past few decades, immunotherapies have been developed to help the immune system recognize and attack cancer cells more effectively. Some immunotherapies include BsAbs, ADCs, and CAR-T cell therapy.<sup>1</sup>

## Immunotherapy targeted to antigens on tumor cells<sup>2</sup>



## Immunotherapy mechanisms and differences

### BsAbs<sup>3,4</sup>

BsAbs have 2 distinct binding domains. One binds to tumor-associated antigens and the other attaches to a T cell. This allows the T cell to attack the tumor cell directly.

BiTEs are a subset of BsAbs.

### ADCs<sup>5,6</sup>

ADCs consist of a mAb linked to a cytotoxic drug. Once the antibody binds to its target antigen on the tumor cell, it delivers the cytotoxic drug that is released and typically, through DNA damage, leads to cell death.

### CAR-T<sup>7</sup>

CAR-T cell therapy involves genetically modifying a patient's own T cells to express a specialized receptor (CAR) that recognizes a specific antigen on cancer cells, enabling the T cells to identify and eliminate them.

BiTE=bispecific T-cell engager; CAR=chimeric antigen receptor; DNA=deoxyribonucleic acid; mAb=monoclonal antibody.

**References:** 1. Lancman G et al. Bispecific antibodies in multiple myeloma: present and future. *Blood Cancer Discov.* 2021;2(5):423-433. doi:10.1158/2643-3230.BCD-21-0028 2. Rodríguez-Lobato LG et al. Why immunotherapy fails in multiple myeloma. *Hemato.* 2021; 2(1):1-42. <https://doi.org/10.3390/hemato2010001> 3. Research C for DEA. Bispecific antibodies: an area of research and clinical applications. U.S. Food And Drug Administration. Published February 14, 2024. <https://www.fda.gov/drugs/spotlight-cderscience/bispecific-antibodies-area-research-and-clinical-applications> 4. Verkleij CPM et al. T-cell redirecting bispecific antibodies targeting BCMA for the treatment of multiple myeloma. *Oncotarget.* 2020;11(45):4076-4081. doi:10.18632/oncotarget.27792 5. D'Agostino M et al. Monoclonal antibodies to treat multiple myeloma: a dream come true. *Int J Mol Sci.* 2020;21(21):8192. doi:10.3390/ijms21218192 6. Swan D et al. The evolving status of immunotherapies in multiple myeloma: the future role of bispecific antibodies. *Br J Haematol.* 2022;196(3):488-506. doi:10.1111/bjh.17805 7. Shah NN et al. Multi targeted CAR-T cell therapies for B-cell malignancies. *Front Oncol.* 2019;9:146. doi:10.3389/fonc.2019.00146

# What Is CAR-T?

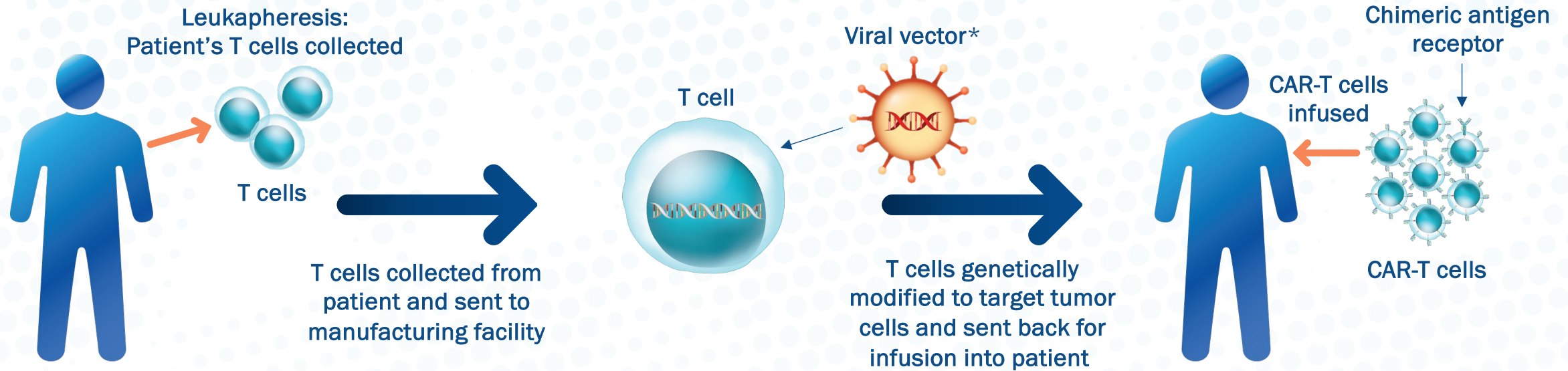
CAR-T=chimeric antigen receptor-T cell.

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# CAR-T Cell Therapy: A Personalized Immunotherapy for Tumor Cell Targeting<sup>1,2</sup>



CAR-T cell therapy uses the immune system to find and attack targets that are expressed on the surface of tumor cells by modifying isolated T cells collected from the patient to express CARs<sup>1,3</sup>



The specificity of antibodies and the activation of T cells are a combined process in CAR-T cell therapy<sup>1,3</sup>

CAR=chimeric antigen receptor; CAR-T=chimeric antigen receptor-T cell.

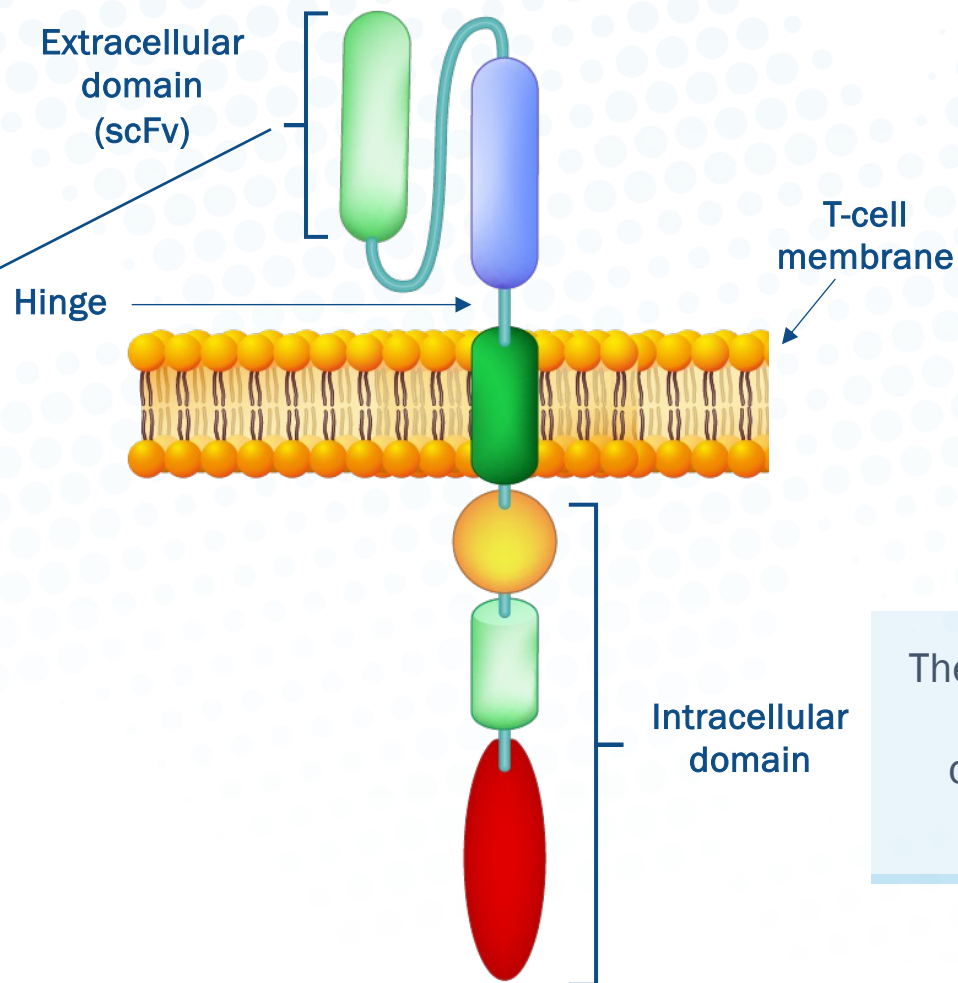
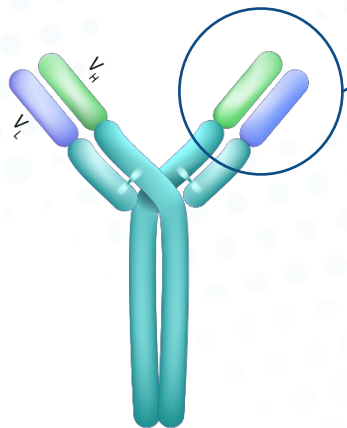
\*Some manufacturing methods use alternatives to viral vectors for modifying T cells.

**References:** 1. Majzner RG, Mackall CL. *Nat Med.* 2019;25(9):1341-1355. 2. Wang X, Rivière I. *Mol Ther Oncolytics.* 2016;3:16015. 3. June CH, Sadelain M. *N Engl J Med.* 2018;379(1):64-73.



# Chimeric\* Antigen Receptors (CARs): Combining Antibody and T Cell Domains<sup>1-3</sup>

The single-chain variable fragment (scFv) is the part of the antibody that will recognize a specific tumor protein<sup>1,2</sup>



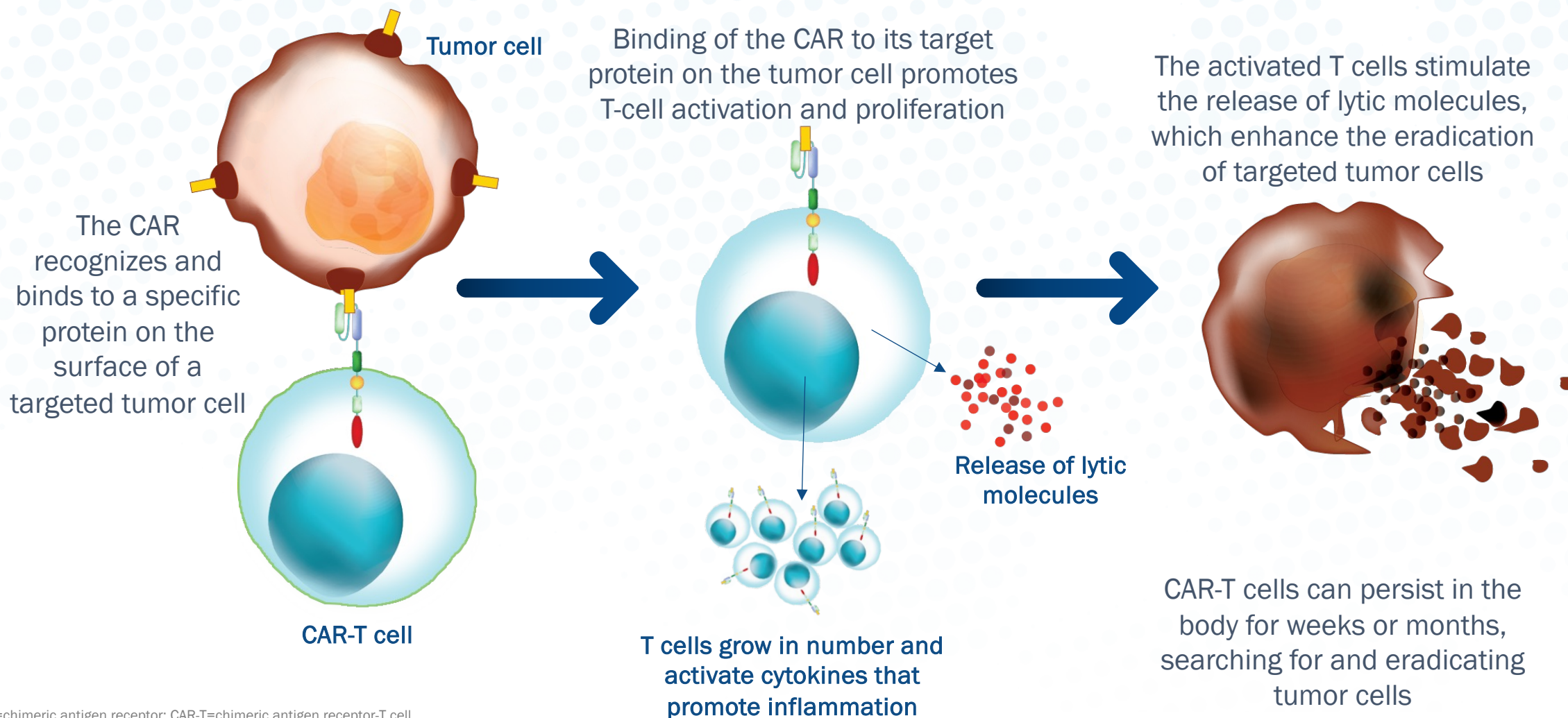
T cells collected from patients are genetically modified to express the CAR<sup>2</sup>

The intracellular domain includes costimulatory and signaling domains that help the T cells grow and fully activate<sup>1</sup>

\*Composed of parts from different origins.

References: 1. June CH, Sadelain M. *N Engl J Med*. 2018;379(1);64-73. 2. Majzner RG, Mackall CL. *Nat Med*. 2019;25(9):1341-1355. 3. Dwivedi A et al. *Front Immunol*. 2019;9:3180.

# CAR-T Cell Activation: Tumor Recognition and Cell Death<sup>1-6</sup>



CAR=chimeric antigen receptor; CAR-T=chimeric antigen receptor-T cell.

**References:** 1. Zhao L, Cao YJ. *Front Immunol.* 2019;10:2250. 2. Neeson P et al. *Gene Ther.* 2010;17(9):1105-1116. 3. Darcy PK et al. *J Immunol.* 2000;164(7):3705-3712. 4. June CH, Sadelain M. *N Engl J Med.* 2018;379(1):64-73. 5. Benmeharek M-R et al. *Int J Mol Sci.* 2019;20(6):1283. 6. Fan M et al. *J Hematol Oncol.* 2017;10(1):151.

# CAR-T Cell Therapies Are Currently in Development for a Variety of Diseases and Illnesses<sup>1-5</sup>

This may not be a comprehensive list, as research is ongoing for CAR-T

1

## Cancers (solid tumors)

- Glioblastoma
- Colorectal cancer
- Pancreatic cancer
- Gastric cancer
- Hepatocellular carcinoma
- Prostate cancer
- Ovarian cancer
- Breast cancer
- Lung cancer

2

## Cancers (hematologic malignancies)

- Non-Hodgkin lymphomas
- T-cell malignancies
- Multiple myeloma
- B-cell ALL

3

## Viruses

- Human immunodeficiency virus
- Hepatitis B virus
- Hepatitis C virus
- Human cytomegalovirus
- Epstein-Barr virus

4

## Other infectious diseases

- *Aspergillus fumigatus* (fungal infection)

5

## Autoimmune conditions

- Systemic lupus erythematosus
- Refractory antisynthetase syndrome
- Myasthenia gravis

ALL=Acute Lymphoblastic Leukemia; CAR-T=chimeric antigen receptor-T cell.

References: 1. Zhao L, Cao YJ. *Front Immunol.* 2019;10:2250. 2. June CH, Sadelain M. *N Engl J Med.* 2018;379(1):64-73. 3. Seif M et al. *Front Immunol.* 2019;10:2711.

4. Dana H et al. *Acta Pharm Sin B.* 2021;11(5):1129-1147. 5. Blache U et al. *RMD Open.* 2023;9:e002907. doi:10.1136/rmdopen-2022-002907



# Summary: What Is CAR-T?

## How does CAR-T cell therapy work?<sup>1-7</sup>

- CAR-T cells are T cells that have been collected from a patient, genetically modified to find a target expressed on the surface of tumor cells, and returned to the patient in a single infusion
- CARs include an extracellular domain that recognizes specific targets on malignant cells and an intracellular domain that activates T cells to expand and eliminate targeted tumor cells

CAR=chimeric antigen receptor; CAR-T=chimeric antigen receptor-T cell.

**References:** 1. June CH, Sadelain M. *N Engl J Med.* 2018;379(1):64-73. 2. Zhao L, Cao YJ. *Front Immunol.* 2019;10:2250. 3. Neeson P et al. *Gene Ther.* 2010;17(9):1105-1116. 4. Darcy PK et al. *J Immunol.* 2000;164(7):3705-3712. 5. Majzner RG, Mackall CL. *Nat Med.* 2019;25(9):1341-1355. 6. Benmeharek M-R et al. *Int J Mol Sci.* 2019;20(6):1283. 7. Seif M et al. *Front Immunol.* 2019;10:2711.



# CAR-T Treatment Process

CAR-T=chimeric antigen receptor-T cell.

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# What Type of Patient Is Generally Eligible for CAR-T Cell Therapy?<sup>1-4</sup>



- ✓ Disease is controllable while they wait for CAR-T cell therapy to be ready
- ✓ Meets trial criteria or use is consistent with product labeling
- ✓ In general good health with good ECOG performance status
- ✓ Has a support system for patient journey
- ✓ Diagnosed with one of the hematologic cancers for which CAR-T is currently a treatment option

CAR-T=chimeric antigen receptor-T cell; ECOG=Eastern Cooperative Oncology Group.

**References:** 1. Dave H et al. *Curr Hematol Malign Rep.* 2019;14(6):561-569. 2. Perica K et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. 3. Beaupierre A et al. *Clin J Oncol Nurs.* 2019;23(2):27-34. 4. CAR T cells: Engineering immune cells to treat cancer. *Cancer.gov.* Published March 10, 2022. <https://www.cancer.gov/about-cancer/treatment/research/car-t-cells>

# Logistical Considerations<sup>1-3</sup>



What is the distance to the closest CAR-T Treatment Center?



Can the patient and their care partner travel or remain close to the CAR-T Treatment Center for an extended period of time (~4 weeks)?

Timing may depend on patient and on CAR-T Treatment Center.



Does the patient need any resources to assist them with access to treatment?

Many CAR-T manufacturers have robust patient support programs that address lodging, travel support, and other resources.



Where can the patient receive leukapheresis and bridging therapy if necessary?

CAR-T=chimeric antigen receptor-T cell.

References: 1. Dave H et al. *Curr Hematol Malig Rep*. 2019;14(6):561-569. 2. Perica K et al. *Biol Blood Marrow Transplant*. 2018;24(6):1135-1141. 3. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34.

# The CAR-T Treatment Process<sup>1,2</sup>

The patient's journey begins with the referring HCP identifying if a patient might benefit from CAR-T. Eligible patients are then referred to a CAR-T Treatment Center,\* where they are re-evaluated for eligibility. Continued communication between the referring and treating teams supports treatment success.



CAR-T=chimeric antigen receptor-T cell; HCP=healthcare provider.

\*Different CAR-T centers may offer different CAR-T products.<sup>1</sup>

†Patients may receive additional therapy for disease control before their CAR-T treatment at the discretion of the treating physician at either the CAR-T Treatment Center or referring oncology center.<sup>1,2</sup>

**References:** 1. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Beaupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl 3):29-40.



# The CAR-T Treatment Process

## 1 Leukapheresis<sup>1-3</sup>



T cells are collected during leukapheresis



The quality and quantity of T cells collected through leukapheresis impact the target number of T cells in the manufactured product



To ensure the quality of cells collected and reduce the likelihood of complications, certain medications should be stopped prior to leukapheresis\*

### Timeline for stopping medications prior to leukapheresis\*



These timelines may vary depending on the product/CAR-T cell therapy.

CAR-T=chimeric antigen receptor-T cell.

\*Depending on product Prescribing Information and treating physician recommendation.

References: 1. Beupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Dave H et al. *Curr Hematol Malig Rep*. 2019;14(6):561-569. 3. Perica K et al. *Biol Blood Marrow Transplant*. 2018;24(6):1135-1141.

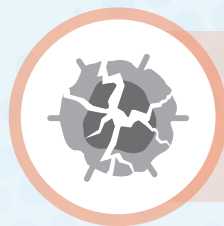
# The CAR-T Treatment Process

## 2 Bridging<sup>1,2\*</sup>

After leukapheresis and concurrent with manufacturing, bridging therapy may be appropriate for some patients.



Disease control



Reducing  
tumor burden



Maintaining  
performance  
status

Bridging therapies may vary among patients and patients are monitored for any adverse reactions

Continued communication across the multidisciplinary team is important to manage disease state during bridging therapy, and prior to lymphodepletion and CAR-T cell infusion

CAR-T=chimeric antigen receptor-T cell.

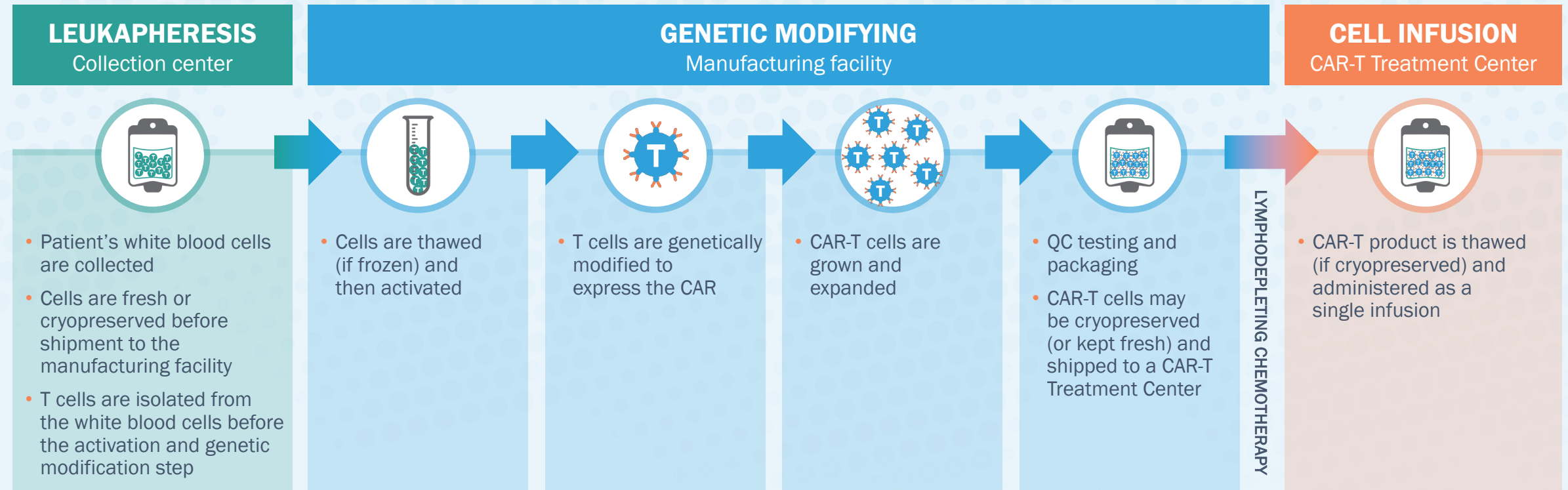
\*Patients may receive additional therapy for disease control before their CAR-T treatment at the discretion of the treating physician at either the CAR-T Treatment Center or referring oncology center.

References: 1. Beupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Beupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl 3):29-40.

# The CAR-T Treatment Process

## 3 Manufacturing

The manufacturing phase is a multistep process that can take between 3 and 6 weeks, but can vary per patient and product.<sup>1-6</sup>



Some patients may undergo bridging therapy between leukapheresis and infusion.\*

CAR=chimeric antigen receptor; CAR-T=chimeric antigen receptor-T cell; QC=quality control.

\*Patients may receive additional therapy for disease control before their CAR-T treatment at the discretion of the treating physician at either the CAR-T Treatment Center or referring oncology center.<sup>5,6</sup>

**References:** 1. Dave H et al. *Curr Hematol Malig Rep.* 2019;14(6):561-569. 2. Vormittag P et al. *Curr Opin Biotechnol.* 2018;53:164-181. 3. Panch SR et al. *Mol Ther.* 2019;27(7):1275-1285. 4. Professional CCM. CAR T-Cell Therapy. Cleveland Clinic. Published December 19, 2024. <https://my.clevelandclinic.org/health/treatments/17726-car-t-cell-therapy> 5. Beaupierre A et al. *Clin J Oncol Nurs.* 2019;23(2):27-34. 6. Beaupierre A et al. *J Adv Pract Oncol.* 2019;10(suppl 3):29-40.

# The CAR-T Treatment Process

## 4 Lymphodepletion<sup>1-6</sup>



Lymphodepletion before CAR-T cell therapy:

- Reduces regulatory T cells and myeloid-derived suppressor cells, making the environment more hospitable to CAR-T cells
- Suppresses host immune system and decreases immunogenicity
- Increases persistence of infused CAR-T cells

The patient is prepared for CAR-T cell therapy over the course of 3 to 4 days with lymphodepleting chemotherapy, which **typically** includes the following agents:

**CYCLOPHOSPHAMIDE\***

IV daily

**FLUDARABINE\***

IV daily

Dosing and regimen may vary according to the patient's cancer and renal function, as well as the CAR-T cell therapy prescribed.

CAR-T=chimeric antigen receptor-T cell; IV=intravenous.

\*Lymphodepleting agents other than cyclophosphamide or fludarabine may be used.

**References:** 1. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Yakoub-Agha I et al. *Haematologica*. 2020;105(2):297-316. 3. Cyclophosphamide. Prescribing Information. Baxter Healthcare Corporation. 4. Fludara®. Prescribing Information. Bayer HealthCare Pharmaceuticals Inc.. 5. Neelapu SS. *Blood*. 2019;133(17):1799-1800. 6. Wagner DL et al. *Nat Rev Clin Oncol*. 2021;18(6):379-393.



# The CAR-T Treatment Process

## 5 Infusion of CAR-T Cells<sup>1-6</sup>



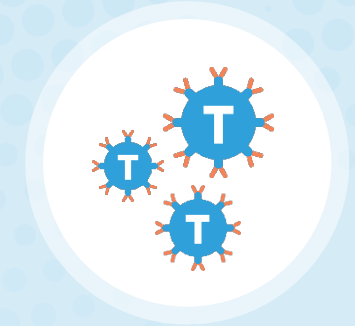
The process may vary depending on the manufacturer

- Medications may be administered preinfusion per protocols



CAR-T cells are usually cryopreserved and must be used shortly after thawing

- Fresh cells may be an option from some manufacturers



The CAR-T cell population will expand after infusion

- Adverse reactions can occur immediately after infusion or can be delayed

Some CAR-T cell therapies are available through a restricted program under the Risk Evaluation and Mitigation Strategy (REMS).<sup>1</sup>

Patients can receive their CAR-T cell infusion in the inpatient or outpatient setting, dependent upon the product and the CTC's discretion.

CAR-T=chimeric antigen receptor-T cell; CTC=CAR-T Treatment Center.

**References:** 1. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Perica K et al. *Biol Blood Marrow Transplant*. 2018;24(6):1135-1141. 3. Dave H et al. *Curr Hematol Malig Rep*. 2019;14(6):561-569. 4. Beaupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl 3):29-40. 5. Panch SR et al. *Mol Ther*. 2019;27(7):1275-1285. 6. Yakoub-Agha I et al. *Haematologica*. 2020;105(2):297-316.

# The CAR-T Treatment Process

## 6 Monitoring<sup>1-3\*</sup>

Patient at or near CAR-T Treatment Center

Patient under the care of referring oncologist

### CAR-T cell infusion



### MONITORING

~4 weeks after infusion

- Immediate post-infusion care is necessary to identify adverse reactions (primarily CRS and ICANS)
- Reevaluation may occur at 30 days after infusion; patient will transition back to referring oncologist when medically appropriate

### LONG-TERM MONITORING

~4+ weeks after infusion

- Patients should be monitored for disease progression or relapse
- Monitor for toxicities that may present over the long-term and manage as medically appropriate
- Patient monitoring requires continued collaboration between the CAR-T Treatment Center and the referring oncologist
- Patients may be required to return to the CAR-T Treatment Center at regular intervals for the first few years

CAR-T=chimeric antigen receptor-T cell; CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome.

\*Timing may vary among patients.

References: 1. Dave H et al. *Curr Hematol Malig Rep.* 2019;14(6):561-569. 2. Neelapu SS. *Hematol Oncol.* 2019;37(suppl 1):48-52. 3. Beaupierre A et al. *Clin J Oncol Nurs.* 2019;23(2):27-34.

# The CAR-T Treatment Process

## Transition of Care Considerations<sup>1,2</sup>

After approximately 4 weeks of close monitoring following CAR-T cell therapy infusion and any adverse events have returned to Grade 1 or less, the CAR-T Treatment Center will notify the patient's referring physician about their CAR-T cell therapy experience and recovery. **Patient care is then transitioned from the CAR-T Treatment Center to the referring physician.**<sup>1</sup>

### TRANSFERRING CARE



The healthcare team at the CAR-T Treatment Center may relay the following to the referring physician upon transition of care<sup>2</sup>:

- ✓ A copy of the patient wallet card
- ✓ A copy of the CAR-T cell therapy Prescribing Information and Medication Guide
- ✓ An accurate medication list
- ✓ **Hospital records** (eg, pre-CAR-T cell therapy workup results, notes made during inpatient CAR-T cell therapy, the latest staging information, notes from the last ambulatory visit, discharge summary inclusive of any adverse events experienced after CAR-T cell therapy)
- ✓ Information on specific laboratory orders and how often they should be drawn
- ✓ Recommendations and guidelines for possible blood product administration, if required
- ✓ Outline of approximate dates when patient will follow up with CAR-T Treatment Center

CAR-T=chimeric antigen receptor-T cell; CRS=cytokine release syndrome.

References: 1. Beaupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl3):29-40. 2. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34.

# The CAR-T Treatment Process (cont'd)

## COMMUNICATION<sup>2</sup>



Ongoing close communication with the referring physician is essential for a smooth transition of care.

- > The healthcare team at the CAR-T Treatment Center should communicate with the referring physician's team about the toxicities associated with CAR-T cell therapy, steroid use, and long-term effects of treatment (ie, B-cell aplasia and hypogammaglobulinemia)
- > A point of contact should be provided to the referring physician (explain when and how to contact the oncologist who treated the patient with CAR-T cell therapy)

## PATIENT/CARE PARTNER KNOWLEDGE<sup>2</sup>



The patient needs to understand that they will be followed over time by their primary oncologist more often and by the CAR-T Treatment Center team less often.

Hand off procedures for transitioning patients from the treating provider to the referring provider ensure seamless continuity of care and include a clearly defined follow-up plan.

CAR-T=chimeric antigen receptor-T cell.

References: 1. Beaupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl3):29-40. 2. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34.



# CAR-T Safety

The adverse reactions discussed in the following slides are those most commonly reported for CAR-Ts and are not indicative of any specific treatment

CAR-T=chimeric antigen receptor-T cell.

# Adverse Reactions: Cytokine Release Syndrome (CRS)<sup>1-4</sup>

- Activation and proliferation of CAR-T cells initiates a cytokine cascade from lymphocytes and other immune cells
- Toxicity is characterized by high levels of serum cytokines and inflammatory markers; consensus toxicity grading criteria were introduced in 2019 to improve standardization in toxicity assessments
- Symptoms can appear within hours to 14 days following infusion



## SIGNS AND SYMPTOMS

Including, but not limited to:

- Fever
- Chills
- Hypotension
- Hypoxia
- Elevated liver enzymes
- Rigors
- May be associated with Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS)
- Multi-system organ dysfunction



## MANAGEMENT CONSIDERATIONS

Including, but not limited to:

- Supportive care
- Tocilizumab
- Steroids
- Vasopressors
- Oxygen

CRS, neurologic toxicities, and T-cell malignancies are currently in the Boxed Warnings for approved CAR-T products. Other adverse events are in the Warnings and Precautions for each CAR-T product.<sup>1-4</sup>

CAR-T=chimeric antigen receptor-T cell.

**References:** 1. Lee DW, Santomasso BD, Locke FL, et al. ASTCT consensus grading for cytokine release syndrome and neurologic toxicity associated with immune effector cells. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. 2. Brudno JN, Kochenderfer JN. Recent advances in CAR T-cell toxicity: mechanisms, manifestations and management. *Blood Rev*. 2019;34:45-55. 3. Neelapu SS. Managing the toxicities of CAR T-cell therapy. *Hematol Oncol*. 2019;37(suppl1):48-52. 4. Shimabukuro-Vornhagen A, Gödel P, Subklewe M, et al. Cytokine release syndrome. *J Immunother Cancer*. 2018;6(1):56.

# Adverse Reactions: Neurotoxicity, Including Immune Effector Cell–Associated Neurotoxicity Syndrome (ICANS)<sup>1-6\*</sup>

- Characterized by a pathologic response following any immunotherapy involving the central nervous system and resulting in the activation or engagement of endogenous or infused T cells and/or other immune cells
- Symptoms may appear simultaneously with CRS, after CRS has resolved, or in patients who did not experience CRS



## SIGNS AND SYMPTOMS

Including but not limited to:

- Aphasia
- Altered levels of consciousness
- Agitation
- Delirium
- Cognitive impairment
- Motor weakness



## MANAGEMENT CONSIDERATIONS

Including but not limited to:

- Supportive care
- Non-sedating seizure prophylaxis
- Corticosteroids
- Brain imaging and neurological testing
- Lumbar puncture



## LONG-TERM MONITORING

All patients receiving CAR-T cell therapy should be monitored lifelong for secondary malignancies.

Monitor for their underlying disease and symptoms of the long-term side effects of that disease, plus effects of CAR-T including CRS.

CRS=cytokine release syndrome.

\*ICANS is a neurologic toxicity seen with immune therapy that involves the activation of endogenous or infused immune effector cells such as T cells.<sup>1</sup>

**References:** 1. Lee DW et al. *Biol Blood Marrow Transplant*. 2019;25(4):625-638. 2. Siegler EL, Kenderian SS. *Front Immunol*. 2020;11:1973. 3. Neelapu SS. *Hematol Oncol*. 2019;37(suppl 1):48-52. 4. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55. 5. Borrega JG et al. *Hemasphere*. 2019;3(2):e191. 6. Dave H et al. *Curr Hematol Malig Rep*. 2019;14(6):561-569.

# Adverse Reactions Monitoring the First 4 Weeks After Infusion<sup>1,2</sup>



Both the patient and their care partner should be educated on identifying signs and symptoms of potential side effects after CAR-T infusion and how and to whom to report them.

Care partners provide key support for patients, as they are often the first people to notice subtle changes in a patient's status.

For at least 4 weeks after infusion, side effects should be reported to the CAR-T Treatment Center. Early signs and symptoms may include:

- > Fever
- > Low blood pressure
- > Difficulty breathing
- > Tremors
- > Confusion

CAR-T=chimeric antigen receptor-T cell.

References: 1. Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 2. Beaupierre A et al. *J Adv Pract Oncol*. 2019;10(suppl3):29-40.



# Adverse Reactions Monitoring Beyond 4 Weeks and Long Term<sup>1-6</sup>

Some side effects may persist or appear 4 weeks or more after CAR-T cell infusion, such as:

➤ Guillain-Barré Syndrome	➤ Secondary malignancies
➤ Immune mediated myelitis	➤ Parkinsonism
➤ Cranial nerve palsies	➤ Peripheral neuropathy
➤ Cytokine release syndrome	➤ Prolonged and/or recurrent cytopenias
➤ Increased early mortality	➤ Serious infections including febrile neutropenia
➤ Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome	➤ Neurologic toxicity, including immune effector cell-associated neurotoxicity syndrome

Neurologic events may present in the 8 weeks following infusion and beyond. The patient should refrain from driving or engaging in hazardous activities for at least 8 weeks at the doctor's discretion, or if a new symptom appears.

Patients are typically being monitored by their local hematologist/oncologist at this point in the CAR-T journey.

CAR-T=chimeric antigen receptor-T cell.

**References:** 1. Abecma®. Prescribing Information. Celgene Corporation. 2. Yescarta®. Prescribing Information. Kite Pharma, Inc. 3. CARVYKTI®. Prescribing Information. Janssen Biotech, Inc. 4. Kymriah®. Prescribing Information. Novartis Pharmaceuticals Corporation. 5. Breyanzi®. Prescribing Information. Juno Therapeutics, Inc. 6. Tecartus®. Prescribing Information. Kite Pharma, Inc.

# Patient-Related Considerations

# Patient Support System



The patient should have access to a support system to provide assistance as needed through the CAR-T process



A care partner will be a valuable source of encouragement, emotional support, and daily assistance



Coach your patient's care partner on identifying signs and symptoms of side effects when they happen, and how to report them to healthcare professionals on the multidisciplinary team

CAR-T=chimeric antigen receptor-T cell.

Reference: Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34.

# Role of the Care Partner



## BEFORE TREATMENT

- Management of medications
- Household and general care (eg, cooking, cleaning, maintenance)
- Additional point of contact for the referring healthcare team



## DURING TREATMENT

- Transportation to/from the CAR-T Treatment Center or other appointments
- Management of medications
- Additional point of contact for the treating healthcare team



## AFTER TREATMENT

- **Help monitor the patient for signs and symptoms of side effects, especially during the first 28 days**
- Remain with the patient for extended periods of time in their home or outpatient facility
- Management of medications
- Household and general care (eg, cooking, cleaning, maintenance)
- Additional point of contact for transition back to referring healthcare team

Reference: Beaupierre A et al. *Clin J Oncol Nurs*. 2019;23(2):27-34.



# CAR-T Cell Therapy Summary<sup>1-7</sup>



## OVERVIEW OF CAR-T CELL THERAPIES

- Uses T cells that have been genetically modified to express a CAR that specifically targets and attacks tumor cells
- Requires coordination between a referring oncologist and a CAR-T Treatment Center



## CAR-T TREATMENT PROCESS AND ELIGIBILITY

- Assess the patient and discuss eligibility consistent with product labeling
- Treatment decision is made by the physician at the CAR-T Treatment Center in consultation with the referring oncologist and the patient
- Educate the patient on the need for a care partner and the care partner's role in long-term monitoring



## LONG-TERM SUPPORT

- Healthcare teams at both the CAR-T Treatment Center and the referring oncology center will continue to communicate regarding patients' disease status and safety



## CAR-T SAFETY

- Serious toxicities can occur after CAR-T treatment. Monitor for symptoms of side effects indicating CRS or ICANS
- Adverse reactions can occur soon after treatment or beyond 4 weeks. Patients should be monitored lifelong for secondary malignancies associated with CAR-T treatment

CAR=chimeric antigen receptor; CAR-T=chimeric antigen receptor-T cell; CRS=cytokine release syndrome; ICANS=Immune Effector Cell-Associated Neurotoxicity Syndrome.

**References:** 1. Jacoby E et al. *Immunol Rev.* 2019;290(1):39-59. 2. Vormittag P et al. *Curr Opin Biotechnol.* 2018;53:164-181. 3. Zhao L, Cao YJ. *Front Immunol.* 2019;10:2250. 4. Beaupierre A et al. *Clin J Oncol Nurs.* 2019;23(2):27-34. 5. Dave H et al. *Curr Hematol Malig Rep.* 2019;14(6):561-569. 6. Perica K et al. *Biol Blood Marrow Transplant.* 2018;24(6):1135-1141. 7. Beaupierre A et al. *J Adv Pract Oncol.* 2019;10(suppl 3):29-40.

# Questions