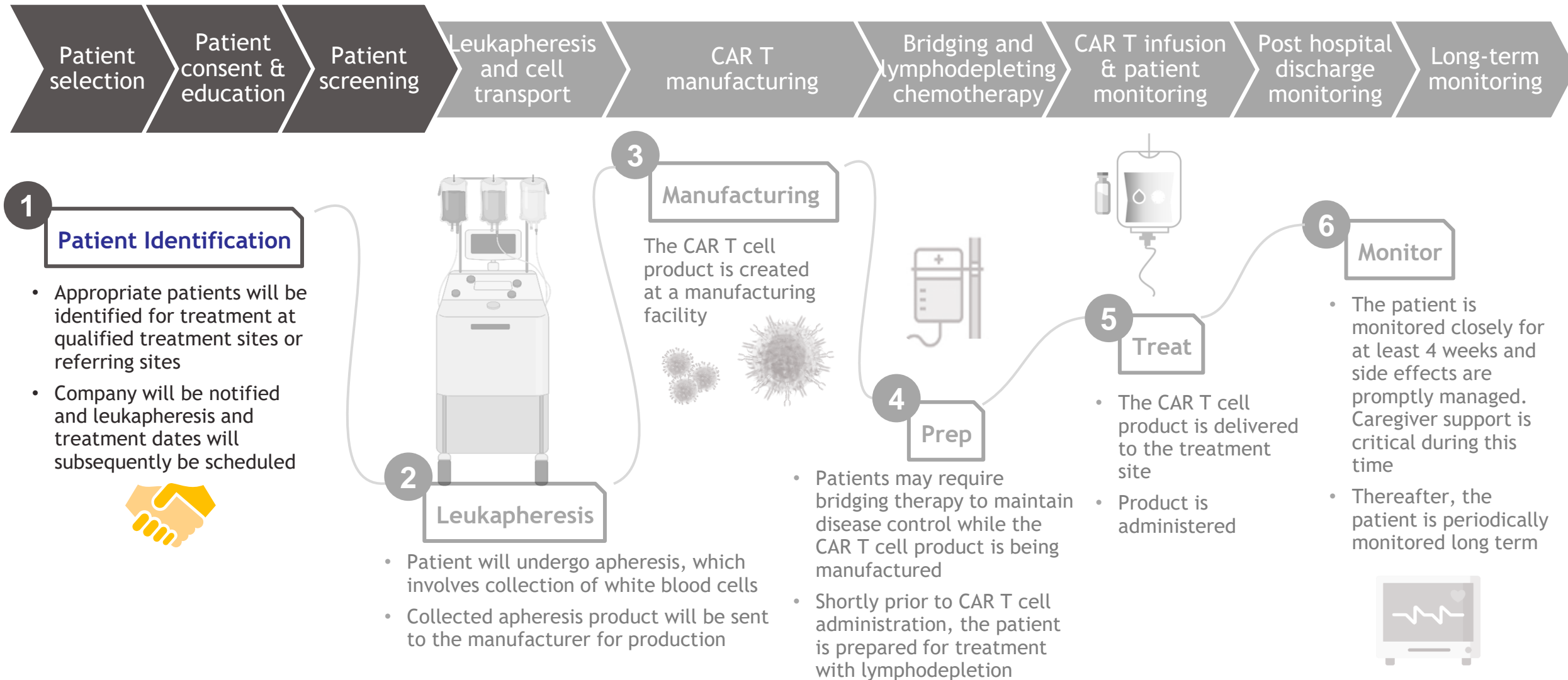




# Patient Considerations for CAR T Cell Therapy

# Patient Journey Through the CAR T Cell Therapy Process



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

# Patient Considerations for CAR T Therapy



01 Patient Evaluation

02 Select Considerations Around CAR T Cell Infusion

03 Patient Characteristics and Outcomes

04 Bridging Therapy and Prior Treatment Effects on Patient Outcomes

# Coordination Between Primary Hematologist and CAR T Cell Treatment Team

## Primary Hematologist



Refers the patient  
for CAR T cell  
therapy

## CAR T Cell Treatment Team



The clinical staff at  
a qualified treatment  
facility

- Patient assessment begins with the primary hematologist<sup>1</sup>
  - It is important that primary physicians be knowledgeable of the eligibility criteria for CAR T cell therapy<sup>2</sup>
- Medical records, including pathology reports, historical imaging, laboratory values, treatment history, and other salient information should be provided by the referring provider for consideration by the CAR T cell treatment team<sup>3</sup>

- Referred patients meet with members of the CAR T treatment team to determine if CAR T cell therapy is right for them<sup>3</sup>
- Efficient pre-screening of patients can expedite the next step in therapy for the patient, whether that be undergoing apheresis for CAR T cell therapy or receiving another therapeutic option<sup>3</sup>

**References:** 1. Beaupierre A, et al. *J Adv Pract Oncol*. 2019;10(Suppl 3):29-40. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34. 3. McGuirk J, et al. *Cytotherapy*. 2017;19(9):1015-1024.

# Patient Workup at the CAR T Cell Treatment Center

After referral to a CAR T cell treatment center, patient workup may include:

- Review of medical and treatment history<sup>1,2</sup>
  - May require confirmatory biopsy of disease if not recently completed or reviewed<sup>2</sup>
- Assessment of organ function, comorbidities, and performance status<sup>1</sup>
- Laboratory studies<sup>2</sup>
  - CRP, ferritin, LDH, CBC with differential, comprehensive metabolic panel<sup>2</sup>
  - Screening for infections including hepatitis B, hepatitis C, and HIV<sup>3</sup>

Referring centers are often responsible for providing current patient records including diagnostic scans and pathology reports, along with a complete patient history and physical<sup>2</sup>



CBC, complete blood count; CRP, C-reactive protein; HIV, human immunodeficiency virus; LDH, lactate dehydrogenase.

**References:** 1. McDermott K, Spendley L. *J Adv Pract Oncol*. 2019;10(Suppl 3):11-20. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23:27-34. 3. Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316.

# Considerations for CAR T Cell Therapy

## General considerations for candidates for CAR T cell therapy:

- Have a disease as defined in commercial indication or in clinical trial<sup>1</sup>
- Adequate marrow function<sup>2</sup>
- Adequate patient fitness, performance status, and organ function<sup>3</sup>
- No active, uncontrolled infections, including hepatitis B, hepatitis C, or HIV<sup>3</sup>
- Absence of clinically relevant comorbidities (eg, select cardiovascular, neurologic, or immune disorders)<sup>3</sup>
- Cumulative chemotherapy exposure may adversely affect quality of circulating T cells<sup>2</sup>
  - Eg, bendamustine may adversely affect T cell numbers and function<sup>4</sup>
- Allogeneic stem cell transplant before CAR T cell therapy increases the risk of GVHD because the manufactured CAR T cells will be derived mostly from the engrafted donor T cells<sup>5</sup>

Precise criteria for eligibility vary by malignancy, treatment regimen or protocol, and CAR T cell product<sup>3</sup>



## Additional considerations:

- Socioeconomic factors<sup>1</sup>
- Caregiver support - a dedicated caregiver should be available 24 hours a day<sup>6</sup>
- Social work evaluation<sup>7</sup>
- Stay in close proximity of treating institution for at least 4 weeks after CAR T cell infusion<sup>6</sup>

GVHD, graft-versus-host disease.

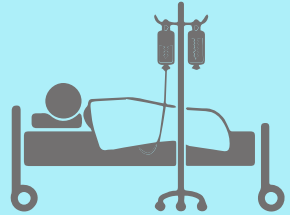
**References:** 1. Taylor L, et al. *Clin J Oncol Nurs*. 2019;23:20-26. 2. Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316. 3. Leukemia & Lymphoma Society. Facts about chimeric antigen receptor (CAR) T-cell therapy. 2020. 4. Fang PQ, et al. *Front Oncol*. 2021;11:648655. 5. Wall DA, Krueger J. *Curr Oncol*. 2020;27(suppl 2):S115-S123. 6. Beaupierre A, et al. *J Adv Pract Oncol*. 2019;10(Suppl 3):29-40. 7. Perica K, et al. *Biol Blood Marrow Transplant*. 2018;24(6):1135-1141.

# Considerations For CAR T Cell Therapy May Differ From Criteria For Stem Cell Transplants<sup>1</sup>

It is important to recognize that eligibility for CAR T cell therapy may differ from criteria for stem cell transplants<sup>1</sup>

## General considerations for candidates for stem cell transplant:

- Age<sup>2</sup>
- Adequate patient fitness, performance status, and organ function<sup>2</sup>
- Tolerant of high doses of chemotherapy<sup>3,4</sup>
- Chemosensitivity (precise recommendations may vary by institution)<sup>4,5</sup>



## Additional considerations:

- Socioeconomic factors<sup>2</sup>
- Caregiver support<sup>2</sup>
- Social work evaluation<sup>2</sup>



**References:** 1. Li C, et al. *JCI Insight*. 2019;4(16):e130195. 2. Tay J, et al. *Bone Marrow Transplant*. 2019;54:368-382. 3. Gisselbrecht C, Van Den Neste E. *Br J Haematol*. 2018;182(5):633-643. 4. Memorial Sloan Kettering Cancer Center. Autologous Stem Cell Transplant: A Guide for Patients & Caregivers. Accessed August 12, 2021. <https://www.mskcc.org/pdf/cancer-care/patient-education/autologous-stem-cell-transplant-guide-patients-caregivers>. 5. Gisselbrecht C, et al. *J Clin Oncol*. 2010;28(27):4184-4190.

# Patient Considerations for CAR T Therapy



01 Patient Evaluation

02 Select Considerations Around CAR T Cell Infusion

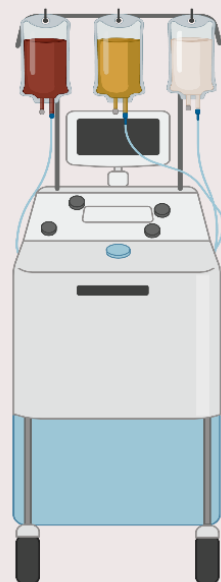
03 Patient Characteristics and Outcomes

04 Bridging Therapy and Prior Treatment Effects on Patient Outcomes



# Washout Periods Prior to Apheresis

The washout period prior to apheresis is critical to ensure a sufficient number of cells can be collected for CAR T cell manufacturing<sup>1</sup>



- Pre-apheresis washout periods may vary based on agent:
  - Chemotherapy (typically 2 weeks)<sup>2</sup>
  - Immunomodulatory drugs (typically 2 weeks)<sup>2</sup>
  - Immunosuppressants (typically earliest possible stop time)<sup>2</sup>
  - Steroids (typically greater than 72 hours)<sup>2</sup>
  - Radiation is lymphodepleting and should be delivered *after* apheresis. Radiation therapy is not recommended prior to apheresis<sup>3,4</sup>
  - Alkylating agents may require washout periods up to 6-9 months due to potential detrimental effects on apheresed PBMCs<sup>5</sup>
- Apheresis for CAR T cell therapy is discouraged within three months of allogeneic stem cell transplantation because of risk for GVHD<sup>2</sup>

GVHD, graft-versus-host disease; PBMC, peripheral blood mononuclear cell.

**References:** 1. Wall DA, Krueger J. *Curr Oncol*. 2020;27(suppl 2):S115-S123. 2. Beaupierre A, et al. *Clin J Oncol Nurs*. 2019;23(2):27-34. 3. Dreyfuss AD, et al. *Pract Radiat Oncol*. 2020;10(3):e155-e158. 4. Fang PQ, et al. *Front Oncol*. 2021;11:648655. 5. Rytlewski J, et al. Abstract 1405. Abstract presented at: American Society of Hematology Annual Meeting 2020. December 5, 2020.

# Select Considerations Prior to CAR T Cell Infusion

- Premedication with acetaminophen derivatives and antihistamines to reduce the risk of infusion site reactions from CAR T cell therapy<sup>1</sup>
- Prophylactic systemic corticosteroids may interfere with activity of CAR T cell therapy and should be avoided<sup>2,3</sup>
- Access via peripheral or central line for infusion of CAR T cell product, as indicated by each product's prescribing information<sup>4</sup>
- Washout period between prior therapy (including bridging therapy) and CAR T cell infusion to avoid interference with CAR T cell activity<sup>3</sup>
- CAR T cell therapy should not be administered to patients with active uncontrolled infections or inflammatory disorders<sup>5-8</sup>



**References:** 1. McDermott K, Spendley L. *J Adv Pract Oncol*. 2019;10(Suppl 3):11-20. 2. Yáñez L, et al. *Hemasphere*. 2019;3(2):e186. 3. Wall DA, Krueger J. *Curr Oncol*. 2020;27(suppl 2):S115-S123. 4. Memorial Sloan Kettering Cancer Center. CAR T Cell Therapy: A Guide for Adult Patients & Caregivers. Accessed April 12, 2021. <https://www.mskcc.org/pdf/cancer-care/patient-education/car-cell-therapy-guide-adult-patients-caregivers>. 5. National Institutes of Health. DailyMed. Accessed August 5, 2021. Available at <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=594bb413-af3b-4b97-afb3-bfe2b174f2ed>. 6. National Institutes of Health. Accessed August 5, 2021. DailyMed. Available at <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=b90c1fe7-f5cc-464e-958a-af36e9c26d7c>. 7. National Institutes of Health. DailyMed. Accessed August 10, 2021. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=aad3ba54-dfd3-4cb3-9e2b-c5ef89559189>. 8. National Institutes of Health. DailyMed. Accessed August 10, 2021. <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=9b70606e-b99c-4272-a0f1-b5523cce0c59>

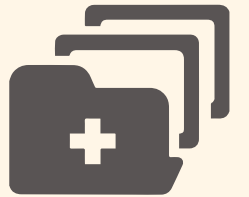
# Patient Considerations for CAR T Therapy



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# Factors That May be Associated with Poor Outcomes<sup>a</sup>

- Several baseline factors have been found to be independently associated with risk of relapse after CAR T cell therapy including:
  - Elevated LDH and CRP
  - Low albumin
  - High ferritin
  - Tumor burden<sup>b</sup>
  - Total metabolic tumor volume (TMTV)<sup>c</sup>
- Elevated LDH and CRP, low lymphocyte count, low albumin, and high ferritin have been associated with poor survival following CAR T cell therapy



<sup>a</sup>Characteristics at time of treatment; <sup>b</sup>Measured via CT scan; <sup>c</sup>TMTV computed with 41% maximum standardized uptake value threshold method.

CRP, C-reactive protein; LDH, lactate dehydrogenase; TMTV, total metabolic tumor volume.

**Reference:** Vercellino L, et al. *Blood Adv.* 2020;4(22):5607-5615.

# Factors That May be Associated with CAR T Cell Toxicity<sup>a</sup>

Factors that may impact toxicity following CAR T cell therapy may include patient-specific characteristics and/or treatment-related factors<sup>1</sup>

## Factors associated with increased risk for CRS and for neurotoxicity:<sup>1,2</sup>

- Higher CAR T cell doses and lymphodepletion regimens containing fludarabine
- Higher peak *in vivo* proliferation of CAR T cells
- Higher disease burden
- Baseline thrombocytopenia
- Baseline elevated markers of endothelial activation, including angiopoietin-2 and von Willebrand factor
- Poor ECOG status (PS 2)



### Factors associated with **CRS**:

- CAR T cells without selection of CD8+ central memory T cells<sup>3</sup>
- Elevated baseline serum ferritin and CRP<sup>3</sup>

### Factors associated with **neurotoxicity**:

- Elevated CRP after infusion<sup>1</sup>
- Select serum cytokines and proteins, including: IL-2, sIL-2R $\alpha$ , IL-6, IL-8, IL-10, IL-15, INF- $\gamma$ , TNF- $\alpha$ , granzyme B, soluble GM-CSF, and MCP-1<sup>1</sup>

ECOG, Eastern Cooperative Oncology Group; GM-CSF, granulocyte-macrophage colony-stimulating factor; INF- $\gamma$ , interferon gamma; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; PS, performance status; TNF- $\alpha$ , tumor necrosis factor alpha.

<sup>a</sup>The factors listed here are based on multiple different clinical studies, however research on factors that influence CAR T cell toxicity are ongoing and may vary by disease, specific product, or other factors.

**References:** 1. Brudno JN, Kochenderfer JN. *Blood Rev.* 2019;34:45-55. 2. Siddiqi T, et al. *Blood.* 2017;130 (suppl\_1):193. 3. Murthy H, et al. *Immunotargets Ther.* 2019:8.

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# Bridging Therapy and Prior Treatment Effects on CAR T Cell Therapy

Various therapies may potentially impact safety and efficacy of CAR T cell therapy

- Prophylactic use of corticosteroids may interfere with activity of CAR T cells<sup>1</sup>
- Immunotherapeutic drugs with a longer half-life may interfere with expansion or persistence of infused CAR T cells<sup>2</sup>
  - Eg, alemtuzumab, daratumumab, check point inhibitors, and brentuximab vedotin<sup>2</sup>
- Bridging chemotherapy may contribute to development of cytopenias<sup>3</sup>



GVHD, graft-versus-host disease.

**References:** 1. Yáñez L, et al. *Hemasphere*. 2019;3(2):e186. 2. Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316. 3. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55.

# Summary

- Evaluation of patients for CAR T cell therapy requires communication and coordination between the primary hematologist and the clinical care team at the CAR T cell therapy treatment site
- Considerations for CAR T cell therapy include medical history and physical characteristics, as well as socioeconomic factors and caregiver support
- Prior to apheresis, washout periods may be needed to ensure a sufficient number of cells can be collected for CAR T cell manufacturing
- Several factors have been found to be associated with risk of relapse and/or poor survival following CAR T cell therapy
- Select patient-specific characteristics and/or treatment-related factors have been associated with increased risk of toxicity following CAR T cell therapy
- Certain bridging therapies and prior treatments may affect the safety and/or efficacy of CAR T cell therapy



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