Bristol Myers Squibb®

CAR T ACADEMY

Patient Considerations for CAR T Cell Therapy

Journey Through the CAR T Cell Therapy Process

Icon indicates areas of collaboration between the non-CAR T and CAR T treatment teams

Manufacturing

Patient identification[1,2]

- Appropriate patients are identified for treatment at qualified treatment sites or referring sites
- Early collaboration may facilitate timely referral and eligibility evaluation
- Once a patient is confirmed as eligible, leukapheresis is scheduled

Apheresis[1-4]

- Before apheresis, patients undergo a washout of prior medications that may affect T cell health to ensure optimal collection
- Physicians, APPs, and nurse coordinators all play a role in ensuring a proper washout occurs before apheresis
- Patients then undergo apheresis, which involves collection of white blood cells
- The collected apheresis product is then sent to the manufacturer

Bridging[1,3]

- Bridging therapy may be given to maintain disease control during CAR T cell manufacturing
- Appropriate bridging therapy should be discussed and coordinated between the referring physicians and those treating with CAR T cell therapy

LDC and Infusion[1-3]

- LDC is administered prior to CAR T cell infusion to deplete endogenous T cells and create an environment for CAR T cell expansion
- Infusion will then occur at the qualified treatment center

Monitoring and long-term follow-up[1,2,5]

- After infusion, patients are closely monitored for at least 2 weeks at the CAR T cell therapy treatment site, and side effects are promptly managed
- After at least 2 weeks, patients may be discharged back to the referring physician's care
- Communication continues between the CAR T cell therapy treatment center and the primary hematologist/ oncologist as patients are monitored long-term

APP, advanced practice provider; CAR, chimeric antigen receptor; LDC, lymphodepleting chemotherapy.

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. **4**. Qayed M, et al. *Cytotherapy*. 2022;S1465-3249(22)00641-7. **5.** US Food and Drug Administration. Accessed June 27, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor

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Coordination Between Primary Hematologist and CAR T Cell Treatment Team

Primary Hematologist

Refers the patient for CAR T cell therapy

- Patient assessment begins with the primary hematologist[1]
  - It is important that primary physicians be knowledgeable of the eligibility criteria for CAR T cell therapy[2]
- 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[3]

CAR T Cell Treatment Team

The clinical staff at a qualified treatment facility

- Referred patients meet with members of the CAR T treatment team to determine if CAR T cell therapy is right for them[3]
- 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[3]

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

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

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 CAR T cell therapy:

- Have a disease as defined in commercial indication or in clinical trial[1]
- Adequate marrow and organ function, as well as patient fitness and performance status[2,3]
- Do not administer to patients with active infections or inflammatory disorders[3,4,a]
- Prior chemotherapy exposure may adversely affect quality of circulating T cells[2]
- Allogeneic stem cell transplant before CAR T cell therapy may increase the risk of graft-versus-host disease (GVHD)[5]

These considerations are typically part of the general workup conducted and do not necessarily disqualify patients from CAR T cell therapy

Additional considerations:

- Socioeconomic factors[1]
- Caregiver support[6]
- Social work evaluation[7]
- Stay in close proximity of treating institution for at least 2 weeks after CAR T cell infusion[8]

Centers and manufacturers may have resources to assist eligible patients

Precise criteria for eligibility vary by malignancy, treatment regimen or protocol, and CAR T cell product[3]

[a] Including hepatitis B, hepatitis C, HIV, and CMV.
CMV, cytomegalovirus; HIV, human immunodeficiency virus.

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. 2022. **4.** Hill JA, Seo SK. *Blood* 2020;136(8):925-935. **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. **8.** US Food and Drug Administration. Accessed June 27, 2025. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/fda-eliminates-risk-evaluation-and-mitigation-strategies-rems-autologous-chimeric-antigen-receptor

Considerations For CAR T Cell Therapy May Differ From Criteria For Stem Cell Transplants[1]

General considerations for candidates for stem cell transplant:

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

It is important to recognize that eligibility for CAR T cell therapy may differ from criteria for stem cell transplants[1]

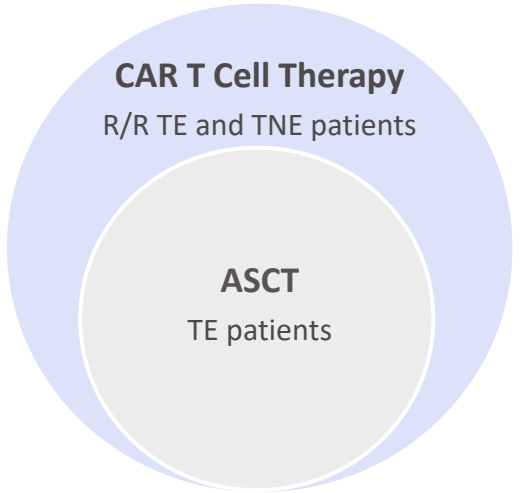
Real-world data has estimated that only approximately **25%** of eligible patients have **received CAR T cell therapy**[6]

Additional considerations:

- Socioeconomic factors[2]
- Caregiver support[2]
- Social work evaluation[2]

CAR T cell therapy is appropriate for a broader patient pool than ASCT[7,8]

- Poor performance status
- No upper age limit (≥18 years)
- Regardless of SCT eligibility (comorbidities)
- Chemosensitive or chemorefractory



ASCT, autologous stem cell transplant; R/R, relapsed/refractory; SCT, stem cell transplant; TE, transplant eligible; TNE, transplant non-eligible.

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. **6**. Perales MA et al. *Transplant Cell Ther.* 2025;31(2):S391. 7. Sehgal A et al. *Lancet Oncol*. 2022;23:1066–1077**. 8.** Vic S et al. *Eur J Cancer.* 2022;175:246-253.

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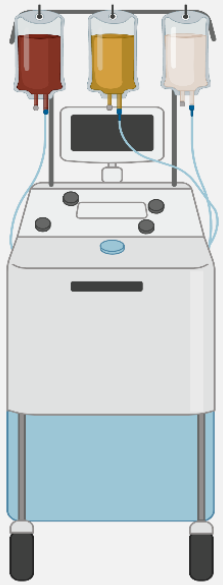
Washout Periods Prior to Apheresis

The washout period prior to apheresis is critical to ensure a sufficient number of cells can be collected for CAR T cell manufacturing[1]



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

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[1]
- Prophylactic systemic corticosteroids may interfere with activity of CAR T cell therapy and should be avoided[2,3]
- Access via peripheral or central line for infusion of CAR T cell product, as indicated by each product's prescribing information[4]
- Washout period between prior therapy (including bridging therapy) and CAR T cell infusion to avoid interference with CAR T cell activity[3]
- CAR T cell therapy should not be administered to patients with active uncontrolled infections or inflammatory disorders[5-11]

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 July 23, 2025. https://www.mskcc.org/pdf/cancer-care/patient-education/car-cell-therapy-guide-adult-patients-caregivers. **5.** National Institutes of Heath. 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 **9.** National Institutes of Health. DailyMed. Accessed July 7, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7d040b91-3fb8-41db-ba7f-60a36f06e2c2 **10.** National Institutes of Health. DailyMed. Accessed July 7, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=a16108c2-7ca7-45af-965e-54bda4713022 **11.** National Institutes of Health. DailyMed. Accessed July 7, 2025. https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=4fef6986-b988-45e4-8c20-b14f0ef1f538&audience=consumer

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Factors That May be Associated with Poor Outcomes[a]

- 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[b]
  - Total metabolic tumor volume (TMTV)[c]

- Elevated LDH and CRP, low lymphocyte count, low albumin, and high ferritin have been associated with poor survival following CAR T cell therapy

[a]Characteristics at time of treatment; [b]Measured via CT scan; [c]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[a]

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

Factors associated with increased risk for CRS and for neurotoxicity:[1,2]

- 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[3]
- Elevated baseline serum ferritin and CRP[3]

Factors associated with neurotoxicity:

- Elevated CRP after infusion[1]
- Select serum cytokines and proteins, including: IL-2, sIL-2Rα, IL-6, IL-8, IL-10, IL-15, INF-ϒ, TNF-α, granzyme B, soluble GM-CSF, and MCP-1[1]

Refer to the CRS and Neurotoxicity module for more information

ECOG, Eastern Cooperative Oncology Group; GM-CSF, granulocyte-macrophage colony-stimulating factor; IFN- ϒ, interferon gamma; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; PS, performance status; TNF-α, tumor necrosis factor alpha.
[a]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[1]
- Immunotherapeutic drugs with a longer half-life may interfere with expansion or persistence of infused CAR T cells[2]
  - Eg, alemtuzumab, daratumumab, check point inhibitors, and brentuximab vedotin[2]
- Bridging chemotherapy may contribute to development of cytopenias[3]

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[1,2]

Considerations for CAR T cell therapy include medical history and physical characteristics, as well as socioeconomic factors and caregiver support[1, 3-5]

Prior to apheresis, washout periods may be needed to ensure a sufficient number of cells can be collected for CAR T cell manufacturing[6]

Several factors have been found to be associated with risk of relapse and/or poor survival following CAR T cell therapy[7]

Select patient-specific characteristics and/or treatment-related factors have been associated with increased risk of toxicity following CAR T cell therapy[8-9]

Certain bridging therapies and prior treatments may affect the safety and/or efficacy of CAR T cell therapy[4,8,10]

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. **3.** Taylor L, et al. *Clin J Oncol Nurs.* 2019;23:20-26. **4.** Yakoub-Agha I, et al. *Haematologica*. 2020;105(2):297-316. **5.** Leukemia & Lymphoma Society. Facts about chimeric antigen receptor (CAR) T-cell therapy. 2020. **6.** Wall DA, Krueger J. *Curr Oncol.* 2020;27(suppl 2):S115-S123. **7.** Vercellino L, et al. *Blood Adv*. 2020;4(22):5607-5615. **8**. Brudno JN, Kochenderfer JN. *Blood Rev*. 2019;34:45-55. **9.** Siddiqi T, et al. *Blood*. 2017;130 (suppl_1):193. **10.** Yáñez L, et al. *Hemasphere*. 2019;3(2):e186.

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