Recommended Referral Timing for Cellular Therapy Treatment

A RESOURCE FOR PHYSICIANS
Cellular therapies aim to improve the immune system’s ability to fight cancer. There are many types of cellular therapy being explored to fight cancer: CAR T cells, genetically and non-genetically-modified T cells, NK cells, and vaccines.

Dana-Farber Brigham Cancer Center offers all FDA-approved CAR T products as well as numerous clinical trials of CAR T and other cellular therapies. This guide can help inform when it may be appropriate to refer a patient for evaluation for cellular therapy treatment.

Commercial CAR T-Cell Therapy

CAR T-cell therapy is FDA approved for some forms of non-Hodgkin lymphoma, multiple myeloma and adult and pediatric B-cell acute lymphoblastic leukemia.

Aggressive Non-Hodgkin Lymphoma

For diffuse large B-cell lymphoma (DLBCL), primary mediastinal B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma

Eligibility Criteria:

- Confirmed diagnosis of DLBCL, primary mediastinal large B-cell lymphoma, high-grade B-cell lymphoma, or transformed follicular lymphoma to DLBCL that has relapsed or not responded to at least two prior lines of systemic therapy, if the initial response to first-line therapy was longer than 12 months. Patients with these diagnoses who do not achieve remission or relapse within 12 months of first-line therapy are eligible for CAR T as a second-line therapy.

Recommended Referral Timing

Refer for evaluation at first relapse, before initiating salvage therapy.

For mantle cell lymphoma

Eligibility Criteria:

- Histologically confirmed diagnosis of mantle cell lymphoma that has either not responded to, or has relapsed after, first line therapy.

Recommended Referral Timing

Refer for evaluation at first relapse, preferably before initiating salvage therapy.
Select Indolent Lymphomas

For follicular lymphoma

Eligibility Criteria:

• Histologically confirmed diagnosis of follicular lymphoma that has relapsed or not responded after two prior lines of treatment.

• No history of malignancy expected to shorten one’s life expectancy, other than lymphoma.

Recommended Referral Timing

Refer for evaluation at first relapse, preferably before initiating salvage therapy.

Multiple Myeloma

Eligibility Criteria:

• Confirmed diagnosis of multiple myeloma that has relapsed or not responded (refractory) after four or more prior lines of treatment.

• Prior therapy must have included a proteasome inhibitor, an immunomodulatory drug, and an anti-CD38 monoclonal antibody.

Recommended Referral Timing

Refer for evaluation after 2 prior of lines of therapy for multiple myeloma or after treatment with a proteasome inhibitor, immunomodulatory agent, and an anti-CD38 monoclonal antibody.

B-Cell Acute Lymphoblastic Leukemia

Eligibility Criteria:

• Confirmed diagnosis of B-cell ALL that has either not responded or relapsed after at least two lines of prior treatment.

• Adequate organ, cardiac, and pulmonary function (must meet established criteria/measures).

Recommended Referral Timing

Refer for evaluation post allogeneic stem cell transplant or once determined to be ineligible for allogeneic stem cell transplant.

Note: Patients younger than 18 years are evaluated through our pediatric program, Dana-Farber/Boston Children’s Cancer and Blood Disorders Center.
Typical Process for Patients Receiving CAR T-Cell Treatment

CAR T-cell therapy is a complex, lengthy process with the risk of serious side effects. It is important that you and your patients understand what’s involved with this advanced treatment.

**Evaluation:** Physical exam and review of medical records and medical history as well as several screening tests including but not limited to laboratory studies, EKG, TTE, and CXR.

**If CAR T is determined to be an appropriate treatment:**

**Cell Collection:** We collect patient’s T cells using leukapheresis. This process takes place at the Kraft Family Blood Donor Center at Dana-Farber Cancer Institute and Brigham and Women’s Hospital.

**Manufacturing:** The T cells are sent to a lab, either a Dana-Farber or off-site, to be engineered to express the target specific for the patient’s cancer. This manufacturing process generally takes two to three weeks.

**Conditioning:** In the days prior to their CAR T-cell infusion, patients may receive lymphodepleting chemotherapy to make room in their immune system for the CAR T cells to expand and proliferate.

**Infusion:** Most patients receive their CAR T cells in the hospital. Most remain in the hospital for one to three weeks to monitor for side effects. Some patients may receive their CAR T cells in the outpatient clinic and be monitored for 14 days in the outpatient setting. Potential serious side effects may include fevers, chills, low blood pressure, difficulty breathing, confusion, difficulty speaking or understanding language, or stupor. Our teams are specially trained to address these side effects, though patients may be quite ill for a period of time while in the hospital.

**Discharge and Recovery:** After discharge, patients must remain within two hours of Dana-Farber/Brigham and Women’s for 30 days after their CAR T-cell infusion for rapid management of side effects. A caregiver is required to stay with the patient during this period.

Clinical Trials

**CAR T-Cell Therapy**

Researchers are exploring ways to improve CAR T-cell therapies and extend it to other types of cancer. Our program offers several trials of CAR T for other types of blood cancers as well as new studies of CAR T in solid tumors. Trials are also exploring combining CAR T with other therapies, giving CAR T earlier in the treatment cycle, and minimizing side effects.

**Other Cellular Therapies**

Studies are also exploring other types of cellular therapies across a range of cancer types.

- Engineered T-cell receptor (eTCRs) therapy is currently in clinical trials for patients with myeloma or sarcoma, or cervical or head and neck cancers caused by infections by the human papilloma virus, HPV.
- Tumor Infiltrating Lymphocyte (T-IL) therapy is being evaluated for several solid tumors such as cervical and lung cancer.
- NK cell therapies for head and neck cancer and to address relapse after stem cell transplant.

Visit [dana-farber.org/cartclinicaltrials](http://dana-farber.org/cartclinicaltrials) for an up-to-date list of trials, eligibility criteria, and contact information.

Refer a Patient

To discuss or refer a patient, call 877-801-CART (2278) or email cartinquiries@dfci.harvard.edu.