

## Commonly Asked Questions

### How is CAR-T cell therapy different from stem cell transplantation?

Both stem cell transplantation and CAR-T cell therapy are cellular therapies, and many of the steps in the procedures are similar, such as collecting cells from the patient, conditioning chemotherapy, and reinfusion of the cells. However, CAR-T cell therapy and stem cell transplantation differ in many ways. A transplant is not *immunotherapy* (promoting the body's own immune response), but rather gives a patient a new immune system to rebuild after chemotherapy. Patients who receive stem cells from a matched donor may require immunosuppressants to control rejection of the graft or experience graft-versus-host disease. Since the CAR-T cells are your own genetically altered cells, your body should not reject these new cells. Additionally, the chemotherapy is less intense, with fewer side effects, and the side effects caused by cytokine release syndrome (CRS) are unique to CAR-T cell therapy.

### Is the procedure covered by insurance?

Before undergoing this procedure, check with your medical insurance provider to see what costs the provider will cover and what costs you will be responsible for paying. If there is a dispute about coverage or if coverage is denied, ask your insurance carrier about their appeals process. If a claim is repeatedly denied, contact your state's insurance agency.

CAR-T cell therapy should only be performed at certified centers, which may require travel and lodging near the treatment center. Be sure to consider these costs and ask your provider if they cover these expenses.

If you need financial assistance, talk with your doctor and social worker about available options to enroll in an appropriate program. Cancer organizations like the Lymphoma Research Foundation (LRF) offer limited financial assistance to patients who qualify. Some pharmaceutical companies may have patient assistance programs in place that help to provide drugs to qualified patients, as well.

For additional information on financial aid resources, view LRF's *Resources for Financial Assistance* fact sheet available at [lymphoma.org/publications](http://lymphoma.org/publications), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

### Which symptoms should I call my healthcare provider about or go to the emergency room?

You will need to seek immediate attention for any of the following:

- Signs or symptoms associated with CRS including fever, chills, fatigue, rapid heartbeat, nausea, feeling short of breath, and feeling faint or dizzy upon standing.
- Signs or symptoms associated with neurologic events including altered mental state, sleepiness, memory loss, or personality changes, seizures, changes in your level of consciousness, difficulty writing, speech disorders, tremors, and confusion.
- Signs or symptoms associated with infection such as fever or chills.
- Signs or symptoms associated with bone marrow suppression including feeling overtired, bleeding that does not stop, or fever.

### How can I be sure that I am getting my own CAR-T cell therapy?

There are several quality control checks throughout the process to make sure that you only receive your own CAR-T cells. Your T cells are labeled with a unique identifier that stays with them during the entire process, and the identifiers are carefully matched to your identity before the cells are infused.

### How long do I need to be near the certified treatment center?

You will need to plan to be near the certified treatment center for at least four weeks after the infusion of your CAR-T cells.

### Can I take other medications at the same time as CAR-T cell therapy?

Before receiving the CAR-T cell therapy, tell your healthcare provider about all the medications, including the dosages, you currently take. Be sure to include prescription and over-the-counter medicines, as well as vitamins and herbal supplements. It is also important to tell your healthcare provider about all your medical history, including if you have or have had:

- Neurologic conditions (such as seizures, stroke, or memory loss)
- Lung or breathing conditions
- Heart conditions
- Liver conditions
- Kidney conditions
- A recent or active infection

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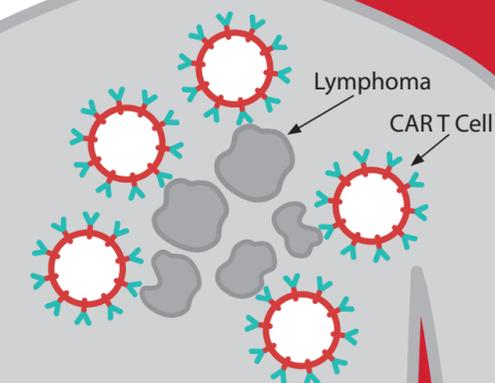
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# CAR-T Cell Therapy for Lymphoma

Immunotherapy enhances the power of a patient's immune system to attack tumors. An immunotherapy approach, called chimeric antigen receptor (CAR) T cell therapy, uses patients' own immune cells to treat their cancer.



### Helpline

(800) 500-9976  
[helpline@lymphoma.org](mailto:helpline@lymphoma.org)  
9:30am to 7:30pm EST  
(Monday - Friday)

### Website

[lymphoma.org](http://lymphoma.org)



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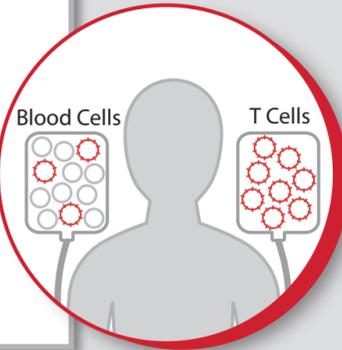


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# The Process

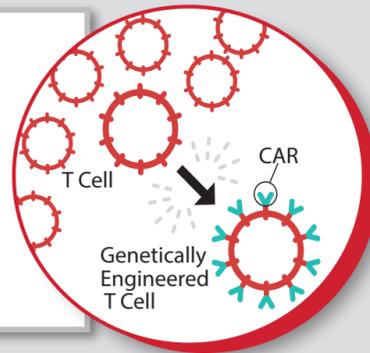
## 1 Leukapheresis

- The first step of CAR-T cell therapy is to obtain some of your T cells, a type of white blood cell. This process is called leukapheresis and usually takes three to four hours.
- During leukapheresis, your blood is removed through an IV.
  - Your blood is then passed through a machine that separates your T cells from the other blood cells
  - The rest of your blood cells are returned to your body.



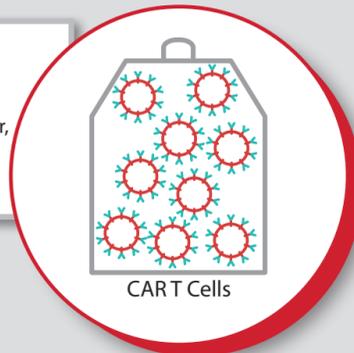
## 2 T-Cell Engineering

- The T cells are sent to a processing center where they are genetically engineered to target your lymphoma.
- The genetically enhanced cells now have chimeric antigen receptors (CAR) that allow the T cells to better recognize your cancer cells.
  - The CAR on the surface of the T cells specifically binds to a protein (for instance, CD19) on lymphoma cells.



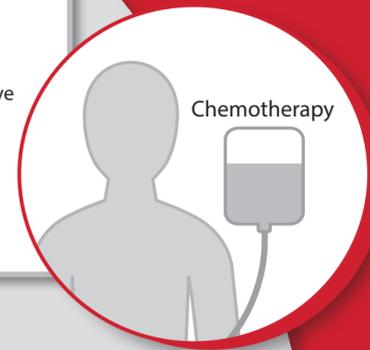
## 3 CAR T-Cell Transport

Once enough of the CAR-T cells are available at the processing center, the cells are frozen for transport to your certified treatment center.



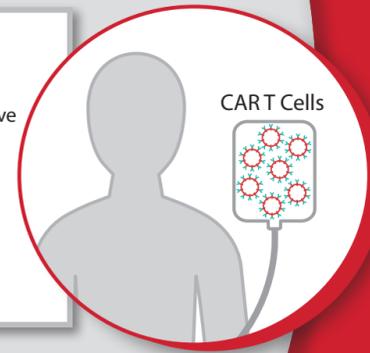
## 4 Chemotherapy

- A few days prior to your CAR-T cell infusion, you will receive low-dose chemotherapy.
- The chemotherapy suppresses the immune system slightly so that it does not react to your CAR-T cells.
  - It gives the CAR-T cells the chance to grow and fight your lymphoma.



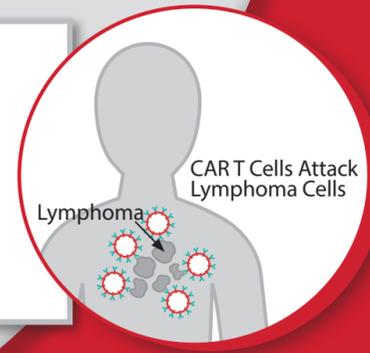
## 5 CART Infusion

- A few days after completing chemotherapy, you will receive your CAR-T cells at your certified treatment center.
- The infusion of CAR-T cells takes less than one hour.
  - You may be given acetaminophen (Tylenol) and/or diphenhydramine (Benadryl) before the infusion to prevent or relieve some of the possible side effects.



## 6 CAR-T Cells Attack the Lymphoma

- Once the CAR-T cells enter your body, they begin to multiply and attack the lymphoma cells.
- It is important to remain closely observed by your healthcare team so that you can be monitored for side effects.



## After Receiving the CAR-T Cells

After receiving the CAR-T cells, you may need to remain in or near the certified treatment center for at least four weeks to be monitored for side effects and treated, if needed. Some patients can receive their CAR-T cells as an outpatient with close surveillance in the clinic.

Side effects from CAR-T cell therapy usually range from mild to moderate in severity. Severe, life-threatening reactions are rare, but may be experienced by some patients. Be sure to ask your healthcare team which side effects you should contact them about, and when to call 911.

## Side Effects

### Cytokine Release Syndrome (CRS)

Cytokine release syndrome (CRS) is your body's response to the activation and growth of your CAR T cells. When the CAR-T cells attack the lymphoma cells, white blood cells are activated and release *cytokines* (chemicals in the body). Cytokines are part of the natural inflammatory response a person might have after a severe infection.

- The symptoms can include flu-like symptoms, fever, low blood pressure, and body aches.
- CRS usually occurs in the first few days to two weeks after the infusion of the CAR-T cells.
- Side effects will be treated with medications and other supportive treatments in the hospital.
- One medication used to treat CAR-T cell-induced CRS is tocilizumab (Actemra), which was approved by the U.S. Food and Drug Administration (FDA) in 2017. Corticosteroids can also be given for severe symptoms.

### Neurological Effects

Neurological effects may occur between two days and three weeks after receiving the CAR-T cells, and usually follow CRS. These may include:

- Altered mental state
- Anxiety
- Delirium
- Dizziness
- Headache
- Insomnia
- Seizures (rare)
- Speech conditions
- Tremor

The precise cause of these symptoms is unknown, but they appear related to effects of the cytokines within the central nervous system.

Because of the potential of these side effects, you should not drive or engage in hazardous occupations or activities, such as operating heavy or potentially dangerous machinery, for at least eight weeks after the procedure.

Neurological symptoms are treated with corticosteroids and anti-seizure medications such as levetiracetam, if needed.

### Other Side Effects

Hypersensitivity reactions can occur during the infusion. Other side effects may include severe or life-threatening infections, reactivation of hepatitis B viral infections, low white blood cell counts, and low platelets. As with many anti-cancer treatments, secondary malignancies are also possible.

### Long-Term Side Effects

In most patients, the number of CAR-T cells increase to a maximum level within two weeks then steadily decline. However, CAR-T cell therapy is unique in that the genetically modified cells can stay in your body for years, even if all the tumor cells are gone. Other normal healthy cells in your body can also be attacked and killed by your CAR-T cells; for example, healthy B cells also express CD19 and can be killed by CAR-T cells targeted to CD19. This situation is called "on-target, off-tumor" toxicity, and can result in temporarily having low levels of B cells. This condition may be treated with the administration of immunoglobulin to help keep you protected against infections.

## CAR-T Cell Therapies in Lymphoma

### Approved CAR-T Cell Therapies\*

Axicabtagene Ciloleucel (Yescarta)

- Treatment targeting CD19 for patients with certain types of large B-cell lymphoma who have not responded to or who have *relapsed* (cancer has returned after treatment) after at least two other kinds of treatment.
  - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified
  - Primary mediastinal large B-cell lymphoma
  - High grade B-cell lymphoma
  - DLBCL arising from follicular lymphoma

Tisagenlecleucel (Kymriah)

- Treatment targeting CD19 for patients with certain types of large B-cell lymphoma who have relapsed or were *refractory* (cancer does not respond to treatment) to two or more lines of systemic therapy.
  - DLBCL not otherwise specified
  - High grade B-cell lymphoma
  - DLBCL arising from follicular lymphoma

\*Neither axicabtagene nor tisagenlecleucel can be used in patients with primary central nervous system lymphoma.

### Investigational CAR-T Cell Therapies

CAR-T cell therapies that target CD19, CD20, CD22, and CD30 are in development for patients with lymphoma and chronic lymphocytic leukemia (CLL).

Several CAR-T cell therapies are in clinical trials, including lisocabtagene maraleucel (JCAR017).

For the most recent information on approved CAR-T cell therapies, visit [lymphoma.org/CART](http://lymphoma.org/CART).