# Understanding the Role of CAR T-Cell Therapy in Treating Cancer

# CANCERCARE CONNECT® BOOKLET SERIES





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Chimeric antigen receptor (CAR) T-cell therapy is a type of immunotherapy that uses a person's own T-cells (a type of white blood cell) to treat certain blood cancers.

Our immune system is a complex network of organs, cells and molecules that protects us from foreign substances that can cause infection, such as bacteria, fungi and viruses. In addition to finding and destroying foreign substances, the immune system can also locate and attack abnormal cells.

There are two main parts of the immune system:

- Innate immunity, a defense system we are born with, is the ability of the body to immediately protect itself against cancer, foreign organisms and toxins.
- Adaptive immunity is a learned defense system that develops in response to exposure to a specific foreign substance. The adaptive immune system works in one of two ways:
  - Cell-mediated, in which T-cells identify and destroy abnormal cells, including cancer cells.
  - Humoral, also called antibody-mediated, in which B-cells (a type of white blood cell called a lymphocyte) make antibodies (specific blood proteins) that identify and destroy foreign substances.

## Cancer-Targeting Immunotherapies

The purpose of cancer-targeting immunotherapy is to modify the immune system to recognize that the cancer is foreign to the body and needs to be attacked. This can be difficult, because the differences between cancer cells and healthy cells are often quite small and hard to detect.

In addition to CAR T-cell therapy, immunotherapy approaches fall into the following main categories:

- Checkpoint inhibitors are designed to block "immune checkpoint" molecules that shield cancer cells. These drugs are designed to remove the shield so that the immune system can attack cancer cells.
- Monoclonal antibodies are lab-generated proteins that target specific tumor antigens (substances that the immune system sees as being foreign or dangerous). Some monoclonal antibodies help the immune system recognize and destroy cancer cells.
- Bispecific antibodies are lab-generated proteins that target specific tumor antigens (as do monoclonal antibodies) but also bind proteins on the surface of T-cells. This allows the T-cells to get close to and destroy the cancer cells.
- Therapeutic vaccines can boost the immune system and have the potential to treat cancer or prevent it from recurring (coming back) after treatment. The U.S. Food and Drug Administration (FDA) has approved vaccines for certain cancers. Additionally, a number of types of vaccines are being studied in clinical trials.

### **CAR T-Cell Therapy**

CAR T-cell therapy is currently approved by the FDA for certain types of relapsed (recurred) or refractory (not responding to treatment) lymphomas:

- Diffuse large B-cell lymphoma
- · Primary mediastinal B-cell lymphoma
- · High grade B-cell lymphoma
- · Transformed follicular lymphoma
- · Mantle cell lymphoma

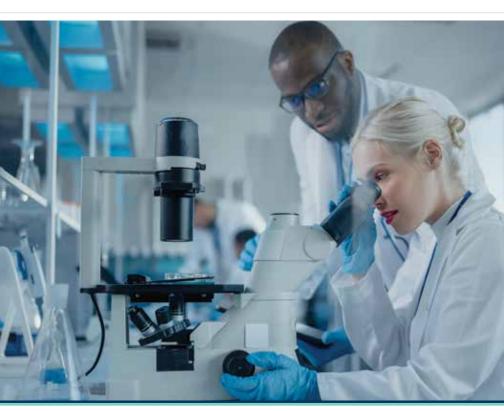
It is also approved for the treatment of acute lymphoblastic leukemia in patients up to age 25 and, as of March 2021, for the treatment of relapsed or refractory multiple myeloma.

Based on a person's individual circumstances, CAR T-cell therapy may be conducted on an outpatient basis or require a hospital admission. The process is similar regardless of the drug used or the specific type of cancer:

- Blood is drawn from the patient via an intravenous catheter (a flexible tube).
- T-cells are isolated from the rest of the blood.
- In a laboratory, the T-cells are genetically re-engineered by adding a chimeric antigen receptor to their surface.
- The modified T-cells (which are now CAR T-cells) are expanded to number in the hundreds of millions.
- The CAR T-cells are infused back into the patient where they target and destroy cancer cells.

The following chimeric antigen receptors are approved by the FDA:

- Axicabtagene ciloleucel (Yescarta) for the treatment of certain types of B-cell lymphoma.
- **Tisagenlecleucel (Kymriah)** for the treatment of certain types of B-cell lymphoma and for the treatment of acute lymphoblastic leukemia in patients up to age 25.
- Brexucabtagene autoleucel (Tecartus) for the treatment of mantle cell lymphoma.
- Lisocabtagene maraleucel (Breyanzi) for the treatment of large B-cell lymphoma.
- Idecabtagene vicleucel (Abecma) for the treatment of multiple myeloma after four or more prior lines of therapy.
- Ciltacabtagene autoleucel (Carvykti), also for the treatment of multiple myeloma after four or more prior lines of therapy.



### The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of individuals as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know.

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Many clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

# Side Effects of CAR T-Cell Therapy

Immunotherapy, including CAR T-cell therapy, travels through the bloodstream to help prompt what is called an "immune response." Because immunotherapy can affect healthy cells as well as cancer cells, certain side effects may be experienced, including digestive tract symptoms, loss of appetite, fatigue and flu-like symptoms. (See the "General Side Effects" section of this booklet for tips on managing these potential side effects.)

Report any side effects that you experience to your health care team right away so they can help you manage them. The side effects can range in severity; reporting them early can minimize their intensity and seriousness. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

CAR T-cell therapy has its own specific potential side effects, including:

- Cytokine-Release Syndrome (CRS). The infusion of CAR T-cells into the body results in the production of large numbers of cytokines (molecules that help cells communicate), which can cause the immune system to become excessively active. This can lead to CRS, with symptoms such as high fever and flu-like symptoms. These side effects can be controlled and reversed with cytokine-blocking drugs and steroids.
- **B-Cell Aplasia.** The FDA-approved CAR T-cell therapy products destroy normal as well as cancerous B-cells, which can cause B-cell aplasia (low numbers of B-cells), in which the body is less able to make the antibodies that protect against infection. Immunoglobulin replacement, administered intravenously, can be used to treat or prevent infection.

- Tumor Lysis Syndrome (TLS). When cancer cells break down
  (are destroyed) very quickly, they release large amounts of
  potassium, phosphate and uric acid into the blood. This can
  result in TLS, a group of conditions that can cause neurological,
  heart or kidney problems. TLS is managed by medicines that
  decrease potassium and uric acid levels in the blood. Medicines may
  also be prescribed that help increase urination.
- Changes in cognition. Some changes in cognition (thought processes) ranging from mild to severe can occur within several days of CAR T-cell therapy. The symptoms are often treated with steroids and are almost always reversible.

Because of these possible side effects, people who have undergone CAR T-cell therapy should stay close to their treatment location for at least four weeks, so they can be closely monitored by their healthcare team.

# Side Effects of Chemotherapy

People being treated with CAR T-cell therapy receive a low dose of chemotherapy, which gives the CAR T-cells a better chance to fight the cancer. Because of this, certain side effects may be experienced, including:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

### General Side Effects

### **Managing Digestive Tract Symptoms**

### Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.



### Constipation

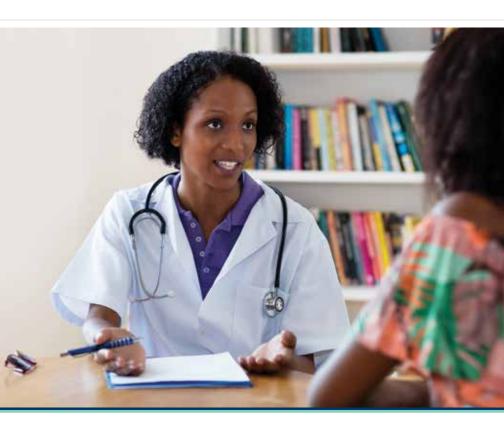
- As hydration is important to avoid constipation, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your health care team on the level of physical activity that is right for you.
- If your doctor has prescribed a "bowel regimen," make sure to follow it exactly.

### Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

### **Managing Loss of Appetite**

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight.
   Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.



### **Managing Fatigue**

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. Here are a few tips that may help reduce fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

There are also prescription medications that may help. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis or depression. Be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

It can also be beneficial to speak with an oncology social worker or oncology nurse to help manage your fatigue. These professionals can work with you to manage any emotional or practical concerns that may be causing symptoms and help you find ways to cope.

### **Managing Flu-Like Symptoms**

The fever and aches that may occur with immunotherapy treatments can be managed with a combination of rest and medication. Acetaminophen (such as Tylenol) is often a doctor's first choice to treat these symptoms. Nonsteroidal anti-inflammatory drugs (NSAIDs) can also help, but should be taken only if recommended by your doctor, as they can cause other side effects. NSAIDs include aspirin, ibuprofen (Motrin and others) and naproxen (Naprelan, Midol, Aleve and others).



# Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

**Start a health care journal.** Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Bring someone with you to your appointments or have them be present during telehealth sessions. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person you bring may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

**Write down your doctor's answers.** Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

**Record your visit if your doctor allows it.** Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

### Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that they can consult with your primary care physician or your specialist if needed.
- Ask your oncologist to send a summary of your visits to your primary care physician and all doctors involved in your care.

Remember, there is no such thing as over-communication.



# Cancer *Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer Care® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and offer information on support groups and other resources.

To learn more about how Cancer Care helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

## MORE ABOUT UNDERSTANDING THE ROLE OF CAR T-CELL THERAPY IN TREATING CANCER

# Frequently Asked Questions

# Q: What questions should I ask my oncologist about CAR T-cell therapy as a possible treatment approach?

A: Specific questions to discuss with your oncologist include:

- Does CAR T-cell therapy have a role in treating my type of cancer, alone or in combination with other treatments?
- Is there an FDA-approved CAR T-cell therapy for my type of cancer?
- Is there anything I need to do to prepare for CAR T-cell therapy?
- · Will I have to stay in the hospital for any period of time?
- Will receiving CAR T-cell therapy have an effect on future treatment decisions?
- · What side effects am I most likely to experience?
- · How will the effectiveness of the CAR T-cell therapy be monitored?

# Q: What research is currently being conducted on CAR T-cell therapy?

A: There are a number of areas of CAR T-cell therapy research, including:

- Using CAR T-cell therapy as a treatment approach for other types of cancer.
- Collecting T-cells from donors, which eliminates one step in the process for the patient.
- · Creating CAR T-cells inside the body.
- Developing CAR T-cells that have "off switches" to help limit side effects.
- Using gene-editing technology to more precisely engineer the T-cells.
- Combining chimeric antigen receptors with other immunotherapies.

### Q: What is a treatment summary and why is important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your cancer diagnosis and treatment. A treatment summary should include:

- · Your name and date of birth.
- · Date of diagnosis.
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate.
- Dates and types of baseline and post-diagnosis testing and the results of these tests.
- · Other medications and supplements you are taking.
- Names, affiliations and contact information of all members of your health care team.

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.





### Resources

#### CancerCare®

800-813-HOPE (800-813-4673) www.cancercare.org

### **American Cancer Society**

800-227-2345 www.cancer.org

### Cancer.Net

Patient information from the American Society of Clinical Oncology 888-651-3038 www.cancer.net

### **Cancer Support Community**

888-793-9355 www.cancersupportcommunity.org

#### **CLINICAL TRIALS WEBSITES**

### ClinicalTrials.gov

www.clinicaltrials.gov

### **Emerging Med**

www.emergingmed.com

### **National Cancer Institute**

800-422-6237 www.cancer.gov

### National Comprehensive Cancer Network

215-690-0300 www.nccn.org

### **Medicine Assistance Tool**

www.medicineassistancetool.org

**National Cancer Institute** 

www.cancer.gov

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