

CAR T Cell Immunotherapy



A “LIVING DRUG” TO FIGHT CANCER

One new cancer treatment being studied is CAR T cell (Chimeric Antigen Receptor T cell) therapy. CAR T cell therapy uses a patient’s own cells and “re-engineers”

them to fight cancer. It is a very complex treatment. Collecting and altering the cells is difficult, and CAR T cell therapy often causes very severe side effects. To date, most of the patients treated with CAR T cell therapy have been people with blood cancers.

WHAT DOES CAR T STAND FOR?

CAR T cell therapy, or chimeric antigen receptor T cell therapy, is one way to use the body's natural defenses to fight cancer. It is called CAR T cell therapy because a lab-made protein, a CAR protein, is added into the patient's own T cells. The CAR protein helps T cells target cancer cells to be killed. CAR stands for:

CHIMERIC

The CAR protein is called "chimeric" because scientists engineer it using different components in order to get the T cell to do what they want. (In Greek mythology, a chimera was a monster with a lion's head, a goat's body and a serpent's tail.)

ANTIGEN

Antigens are proteins on the cancer cell that the T cells are engineered to target. In general, the immune system works by recognizing cells with abnormal antigens and attacking them.

RECEPTOR

The CAR protein, which is added to the surface of the engineered T cell, functions as a receptor. These receptors then search for the matching antigen on a cancer cell so the T cell can destroy it.

T CELLS

Re-engineered T cells are this therapy's primary weapons.

This booklet provides basic information about CAR T cell therapy. If you think that this treatment might be right for you or your loved one, you should discuss this with your doctor.

What is Immunotherapy?

Immunotherapy is a new way to treat many kinds of cancer. There are many approaches to immunotherapy, but they all work by using the body's own defenses to identify and attack cancer cells. Immunotherapy can try to boost your body's overall immune response or it can enable your immune system to recognize and fight cancer. The drugs or agents used can be substances made by your own cells or agents made in the lab.

Your immune system works in many ways to identify unhealthy cells and foreign invaders (such as viruses and bacteria) and attack them. Researchers have known for years that our bodies can recognize cancer cells as abnormal and then destroy them. But our immune system often either doesn't do so, or the effort falls short.

The idea of using the body's own defenses to fight cancer is not new, but earlier attempts to develop immunotherapies were not very successful. That is changing fast. Researchers now better understand the complex interaction between the immune system and cancer.

Doctors are developing new ways of using the immune system to fight cancer. They include:

- Monoclonal antibodies that target specific features of cancer cells.
- Adoptive T cell therapy (such as CAR T cell therapy) that uses the patient's re-engineered immune cells to help the immune system work better.
- Checkpoint inhibitors that stop cancer cells from turning off the immune system.
- Cancer vaccines that help the body's defenders recognize and destroy cancer cells.
- Oncolytic viruses that use modified viruses to kill cancer cells.

What is CAR T Cell Therapy?

CAR T cell therapy removes some of a patient's T cells and alters them to make them better able to fight cancer. The altered T cells are then returned to the patient's body to go to work. Some researchers have called these re-engineered cells "a living drug."

Every patient who is undergoing CAR T cell therapy receives CAR T cells created in the lab just for them. It works like this:

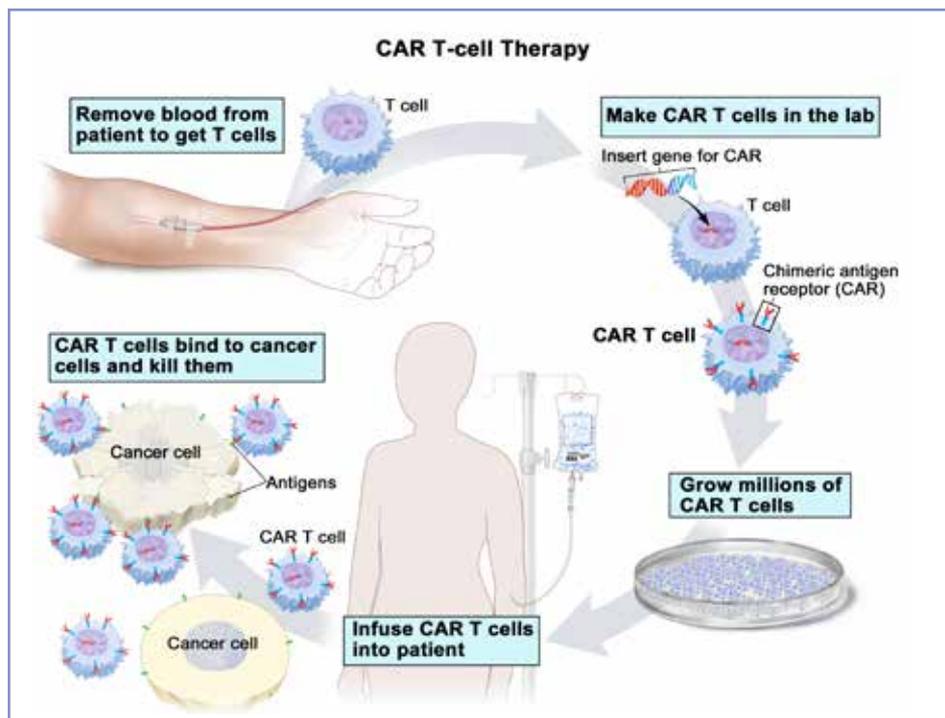
- T cells are collected from your bloodstream in a fairly simple procedure called apheresis. The T cells may be frozen until you are ready to receive treatment.
- CARs, which act like a cancer-cell tracking device, are added to your T cells in a complex lab process. With the CAR added, your T cells become CAR T cells. They can more easily find and destroy cancer cells.
- The new CAR T cells are then grown in the lab. This process can take days to weeks.
- The CAR T cells are then infused back into you. Many patients receive a brief course of

chemotherapy before getting the CAR T cell infusion. This is done to destroy other immune cells and give the new cells more room to operate.

- Once they are back in your bloodstream, the CAR T cells attack your cancer.

CAR T cell therapy differs in several key ways from many other approaches to immunotherapy.

- Most immunotherapy uses drugs to help the immune system to work better. For example, checkpoint inhibitors prevent cancer cells from blocking the immune response, which reactivates T cells.
- Each patient's CAR T cell infusion is individual, created from the patient's own cells.
- CAR T cell therapy is designed to be a one-time treatment.
- CAR T cells can remain in the body and continue to be active for a long period of time. Some patients who have responded to CAR T cell therapy remain in remission after several years.



T cells are the immune system's fighters. They are white blood cells formed in the thymus gland. They circulate throughout the body seeking out and attacking any abnormal cells or substances. Many kinds of immunotherapy activate or boost T cell activity.



“First, we were hoping to get into the trial, then we hoped it would work. There were no alternatives. It was my last hope and I wanted to go out fighting.”

—Kristin, CAR T cell clinical trial patient, shown with David Maloney, MD, PhD, during her CAR T cell infusion

Kristin’s Story

In 2010, Kristin, then 36 years old, was diagnosed with acute lymphoblastic leukemia (ALL). After an initial remission, her leukemia came back, as she says “more stubborn” than ever. She had few options until she heard about a clinical trial in Seattle of CAR T cell therapy. The study was an early phase trial, one of very few in the nation, but for Kristin and her family it meant hope. In November 2014, her engineered T cells were infused into her body. The first weeks were rough as she went through cytokine release syndrome, experiencing fevers, chills, low blood pressure and full body aches and then was hospitalized again for a bacterial infection. One month later, she learned that she was in complete remission. She then underwent a stem cell transplant and has remained free of cancer since then. While Kristin has continued to face some serious physical challenges related to her treatment, she is optimistic about the future and enjoying life with her boyfriend, Benny. Kristin’s clinical trial included 29 patients with ALL that had stopped responding to other treatments. Of the 29 patients, 27 (93%) went into remission.

“This is just the beginning,” says Cameron Turtle, MD, of the Fred Hutchinson Cancer Research Center in Seattle. “There’s so much more work to do to make sure they are durable remissions, to work out who’s going to benefit the most and extend this work to other diseases.”

Is CAR T Cell Therapy Right for Me?

As of September of 2021, CAR T cell therapy is an approved treatment option for patients who have multiple myeloma and certain types of leukemia and lymphoma. These treatments are typically for patients where the cancer is refractory (the cancer has not responded to previous treatment) or relapsed (the cancer has returned) after having two or more prior treatments. Patients eligible for CAR T cell therapy include:

- Children and young adults up to 25 years old with certain kinds of acute lymphoblastic leukemia (ALL).
- Adults with large B-cell lymphoma or follicular lymphoma who have had 2 or more unsuccessful treatments where the cancer did not respond or has returned.
- Adults with mantle cell lymphoma (MCL) who have not responded to other kinds of treatments or whose cancer has returned after previous treatments.
- Adults with multiple myeloma who have had 4 or more unsuccessful treatments where the cancer did not respond or has returned.

There is great interest in treating other types of cancer, including solid tumors, with adoptive T cell therapies. Clinical trials are now enrolling patients with different tumor types. Over time, we will learn from these trials which CAR T cell therapies work best for which cancers.

If you are a patient or caregiver interested in learning more about CAR T cell therapy, talk to your doctor. Right now CAR T cell therapy is available at more than 150 cancer centers in the United States. If you do not live near one of these centers, you should ask whether there is a patient assistance program available to pay for travel costs.

Clinical trials using CAR T cell therapy are also available at cancer centers. If you are in a clinical trial, the trial may pay for your drug and/or travel costs.

CAR T Cells Target Specific Antigens

The immune system works by recognizing foreign, abnormal or toxic substances in our bodies. It can identify differences between normal cells and abnormal ones, such as cancer cells. These differences that are recognized are proteins called antigens that sit on the surface of cells. To be effective, the CAR T cells are engineered to identify and attack only those cells that have the same antigens your cancer cells have.

Cancer cells are not like viruses or bacteria that invade our body from the outside. Cancer cells arise from our own tissues and organs, and they are often very similar to normal cells. The challenge for CAR T cell researchers is to find targets that the engineered cells can attack without doing too much damage to normal cells.

So far, most of these targets have been those found on cancers that begin in B cells, a type of white blood cell. These include some acute and chronic leukemias and several types of non-Hodgkin lymphomas. B cells are normal cells that are part of the immune system. The most common target for CAR T cell therapy is a protein called CD19 which is found on both normal and cancerous B cells. The CAR T cells attack both the normal and cancerous B cells.

Side Effects of CAR T Cell Therapy

The side effects of CAR T cell therapy can be severe and very serious. This is a major reason why this treatment is done only in hospitals that have a team of physicians, nurses and support staff with the expertise to manage the potentially life-threatening effects. (A few patients have died because of their treatment.) Patients are very carefully monitored for side effects after their CAR T cell infusions.

- Cytokine release syndrome (CRS). This is by far the most serious side effect of CAR T cell therapy. After they are infused back into the body, the CAR T cells release a large amount of cytokines into the bloodstream. This can cause a wide range of problems. Patients at first experience high fevers, and sometimes nausea, fatigue, and muscle aches. Unfortunately, the CRS can progress to more serious life-threatening situations with difficulty in breathing and low blood pressure.
- Patients who have more cancer in their bodies are more likely to have severe CRS than patients with less cancer in their bodies. It's a sign that the treatment is working and that there is a positive response. The worst symptoms usually occur in the first days or weeks of treatment. As the number of cancer cells goes down, the symptoms tend to go down as well. Doctors use a variety of medicines to help manage these issues and get patients through the first phase of treatment. These include steroids and drugs that can directly block the action of cytokines. Researchers are also working on ways to minimize the chances of CRS occurring.
- Nervous system side effects. Some patients become delirious, hallucinate or have seizures from CAR T cell therapy. Problems affecting the brain and nervous system can be very severe and life-threatening, lasting from days to weeks for some patients.
- Loss of normal B cells (B cell aplasia). Many CAR T cells target a specific protein, called CD19. The protein is found on both normal and cancerous B cells. This means some normal B cells can also be destroyed. This can reduce the body's ability to protect itself from infections. Doctors use injections of immunoglobulin (immune defense proteins made by healthy B cells) to help prevent infection. B cell aplasia can continue as long

as the CAR T cells persist in the body. So far, this side effect seems to be well managed with immunoglobulin infusions.

Patients who start CAR T cell therapy will be told about all of the side effects they might have. It is very important that patients tell their doctors about any side effects they experience. Most side effects can be managed if they are treated early.

Patients who do respond to CAR T cell therapy and get beyond the initial side effects often have few or no long lasting side effects. However, patients may have long lasting side effects from their other treatments. Some patients respond to CAR T cell and then relapse with time. This is a new treatment. Researchers have much to learn about it.

COSTS

Right now, CAR T cell therapy is a very complex and expensive cancer treatment. Ask if your insurance will cover the drug and hospital costs. Ask if you qualify to get this therapy as part of a clinical trial where the drug cost is covered. You may have to travel long distances to get this therapy. Ask if you can get assistance to cover travel, lodging, and food costs for you and a caregiver. Call 888-793-9355 or visit www.CancerSupportCommunity.org/Cost for more help on coping with cancer costs.

GETTING SUPPORT

Patients who get CAR T cell therapy and their caregivers receive a high level of support from their cancer centers during the process.

If you are considering CAR T cell therapy, you should:

- Have an open and honest discussion with your oncology team about your cancer and its treatment.
- Be willing to change doctors or travel to a different cancer center, if your current cancer center does not offer CAR T cell therapies or CAR T cell clinical trials.
- Have a caregiver who can provide physical and emotional support before, during and after the treatment.
- You can find support and additional materials about immunotherapy from the Cancer Support Community's Helpline and website as well as your local CSC or Gilda's Club. The Cancer Support Community's Open to Options® program offers help for asking questions of your health care team. See the last page of this booklet for more information on getting support.

THE FUTURE

CAR T cell therapy is still very new. There is still a lot we need to learn about which patients it works for, and why. The goals for the future of this therapy are ambitious, and they will take many studies, done over a period of years, to achieve.

Future goals include:

- Finding new targets so that CAR T cell therapies can be used to treat more cancer types, especially hard-to-treat tumors like brain and pancreatic cancer.
- Finding ways of maximizing the positive benefits of the treatment while reducing the side effects.
- Finding ways of turning the T cell activity off and on to fight the cancer.
- Making the process of engineering the CAR T cells less complex so that it can be used in more cancer centers and costs can be reduced.
- Making CAR T cells work even better for cancer types where it is already approved.

CAR T Cell Therapy and Clinical Trials Resources

Cancer Support Community's Clinical Trial Matching Service • 800-814-8927

CAR T Cancer Support Helpline • 844-792-6517 • www.CancerSupportCommunity.org/Helpline

Cancer Research Institute • 800-992-2623 • www.cancerresearch.org

Leukemia & Lymphoma Society • 800-955-4572 • www.lls.org

National Cancer Institute's CAR T Information • www.cancer.gov/about-cancer/treatment/research/car-t-cells

National Cancer Institute's Clinical Trials Registry • 800-422-6237 • www.trials.cancer.gov

National Library of Medicine's Clinical Trials Search • www.clinicaltrials.gov

Cancer Support Community Resources

The Cancer Support Community's (CSC) resources and programs are available free of charge. To access any of these resources below, call 888-793-9355 or visit www.CancerSupportCommunity.org.

Cancer Support Helpline[®] Whether you are newly diagnosed with cancer, a longtime cancer survivor, caring for someone with cancer, or a health care professional looking for resources, CSC's toll-free Cancer Support Helpline (888-793-9355) is staffed by licensed CSC Helpline Counselors available to assist you Mon-Fri 9am - 9pm ET.

Open to Options[®] If you are facing a cancer treatment decision, this research-proven program can help you. In less than an hour, our trained specialists can help you create a written list of specific questions about your concerns for your doctor. Appointments can be made by calling 888-793-9355, visiting www.CancerSupportCommunity.org or by contacting your local CSC or Gilda's Club providing this service.

Cancer Experience Registry[®] The Registry is a community of people touched by cancer. The Registry works to collect, analyze, and share information about the experience and needs of patients and their families. To join, go to www.CancerExperienceRegistry.org.

Frankly Speaking about Cancer[®] CSC's landmark cancer education series provides trusted information for cancer patients and their loved ones. Information is available through publications, online, and in-person programs.

Grassroots Network CSC's Cancer Policy Institute provides updates on policy issues that impact the health and well-being of cancer patients and survivors. Join the Network to make your voice heard by federal and state policy makers. www.CancerSupportCommunity.org/join-our-movement.

Services at Local CSCs and Gilda's Clubs Almost 50 locations plus 120 satellite locations around the country offer on-site support groups, educational workshops, and healthy lifestyle programs specifically designed for people affected by cancer at no cost to the member.

The Living Room, Online Here you will find support and connection with others on discussion boards, a special space for teens, and personal web pages to keep your family and friends up-to-date.

THIS PROGRAM WAS MADE POSSIBLE THROUGH GENEROUS SUPPORT FROM:



Bristol Myers Squibb

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This booklet is available to download and print yourself at www.CancerSupportCommunity.org/CART. For print copies of this booklet or other information about coping with cancer, visit Orders.CancerSupportCommunity.org.

The Cancer Support Community and its partners provide this information as a service. This publication is not intended to take the place of medical care or the advice of your doctor. We strongly suggest consulting your doctor or other health care professionals to answer questions and learn more.

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