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Immunotherapy Side Effects CAR T-Cell Therapy



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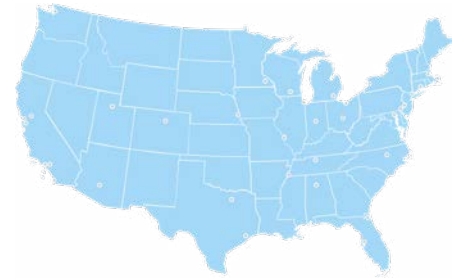
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Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Management of Immunotherapy-Related Toxicities, Version 1.2024 — December 7, 2023.

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CAR T-cell therapy basics

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While most side effects of CAR T-cell therapy can be managed with expert care and improve over time, some side effects may be severe or life-threatening.

What is CAR T-cell therapy?

CAR T-cell therapy is a type of immunotherapy. Immunotherapy uses the immune system to fight cancer. Chimeric antigen receptor (CAR) T-cell therapy works by changing your own immune cells in a way that allows them to find and kill cancer cells.

CAR T is currently used to treat certain blood cancers that did not respond to other treatment, or that have come back after treatment. This includes some forms of lymphoma, leukemia, and multiple myeloma.

CAR T products

At this time there are 6 CAR T-cell therapies approved by the U.S. Food & Drug Administration (FDA) for cancer treatment:

- Tisagenlecleucel (Kymriah)
- Axicabtagene ciloleucel (Yescarta)
- Brexucabtagene autoleucel (Tecartus)
- Lisocabtagene maraleucel (Breyanzi)
- Idecabtagene vicleucel (Abecma)
- Ciltacabtagene autoleucel (Carvykti)

The first 4 therapies listed bind to a protein called CD19. They are used to treat B-cell leukemias and lymphomas. The last 2 products listed target B-cell maturation antigen (BCMA). They are used to treat multiple myeloma, a cancer of plasma cells.

Serious side effects

A common, serious side effect of CAR T is cytokine release syndrome (CRS). In CRS, inflammation-causing proteins appear in the bloodstream, causing the immune system to go into overdrive.

The other main side effect of CAR T is a range of problems affecting the brain and nervous system. Together this group of symptoms is called neurotoxicity. Immune effector cell-associated neurotoxicity syndrome (ICANS) is a way to describe some but not all of these effects.

Another possible side effect is Immune Effector Cell-Associated Hemophagocytic Lymphohistiocytosis-Like Syndrome (IEC-HS). Until recently, this syndrome was thought to be part of CRS. Now it is considered a separate condition. In IEC-HS, immune messengers called cytokines are over-produced, leading to organ damage. It tends to occur in people who have already had treatment for CRS. Signs and symptoms include high ferritin (iron) levels, low blood cell counts, blood clotting problems, high liver enzyme levels, and organ failure.

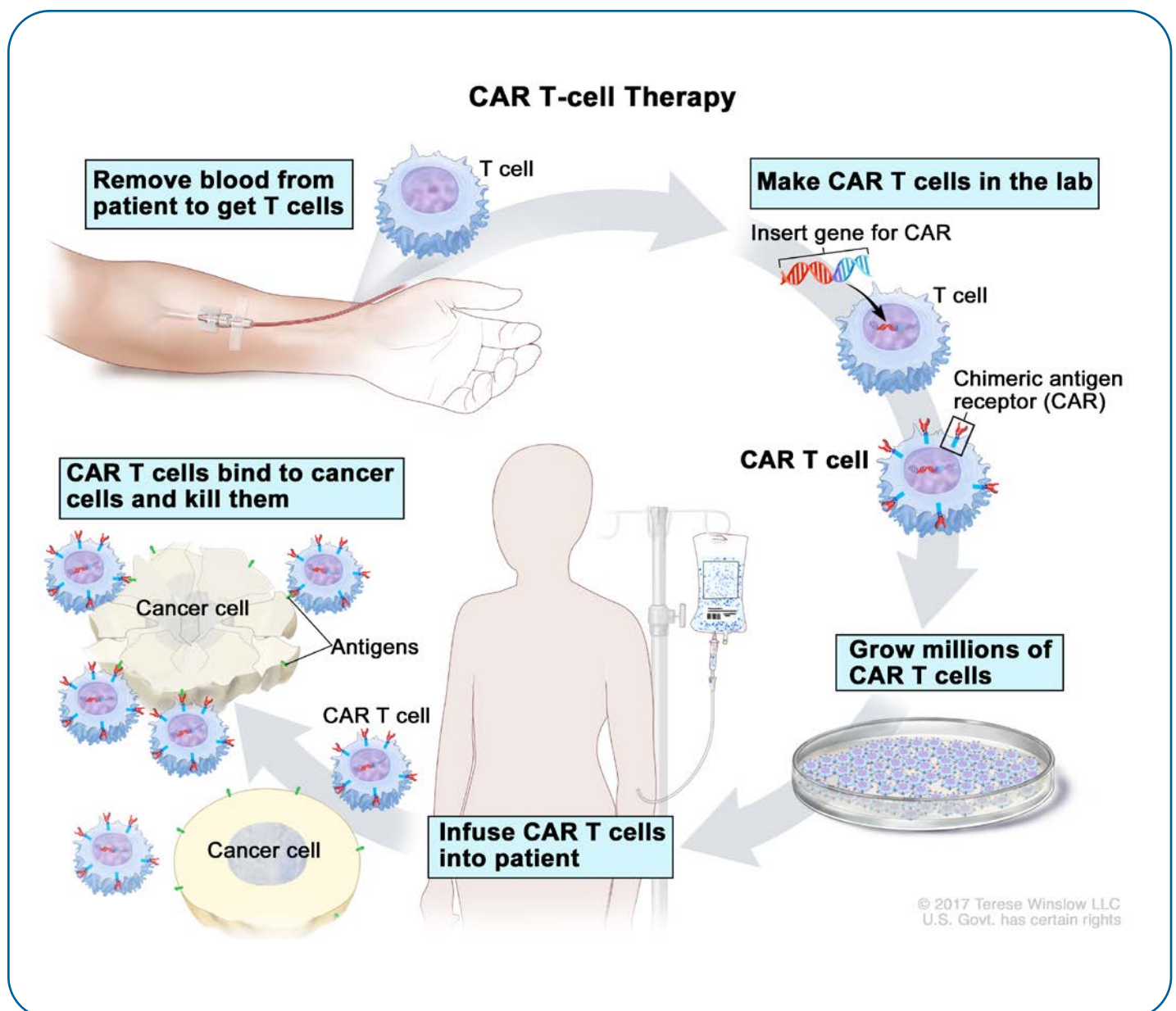
The FDA requires that makers of drugs or cell therapy products with very serious risks develop a Risk Evaluation and Mitigation Strategy (REMS). The purpose is to ensure that the benefits of a drug outweigh its

potential risks, and that providers are educated in treating related side effects. All FDA-approved CAR T products have a REMS.

The CAR T process

CAR T-cell therapy is a combination of chemotherapy, gene therapy, and immunotherapy. White blood cells called T

cells are first taken from your blood and sent to a lab. There they are modified by adding a gene to produce a receptor called chimeric antigen receptor (CAR). Once made, the CAR T cells are allowed to multiply to achieve the required dose. Most people receive a short course of chemotherapy, after which the cells are put back into the bloodstream. CAR guides the T cells to find and kill cancer cells using a



“search and destroy” approach. CAR T cells are one type of immune effector cell (IEC).

Before and during infusion

Central venous access

CAR T products are given intravenously. This means they are put directly into the bloodstream through a vein. A type of catheter called a central venous catheter is often used when long-term (weeks or months) vein access is needed. A thin tube is inserted into your vein, usually below the collarbone or in the upper arm. The tube is guided into a large vein above the right side of the heart. When needed, this catheter will be accessed to draw blood, give fluids or medicines, or administer CAR T-cell therapy.

Heart check

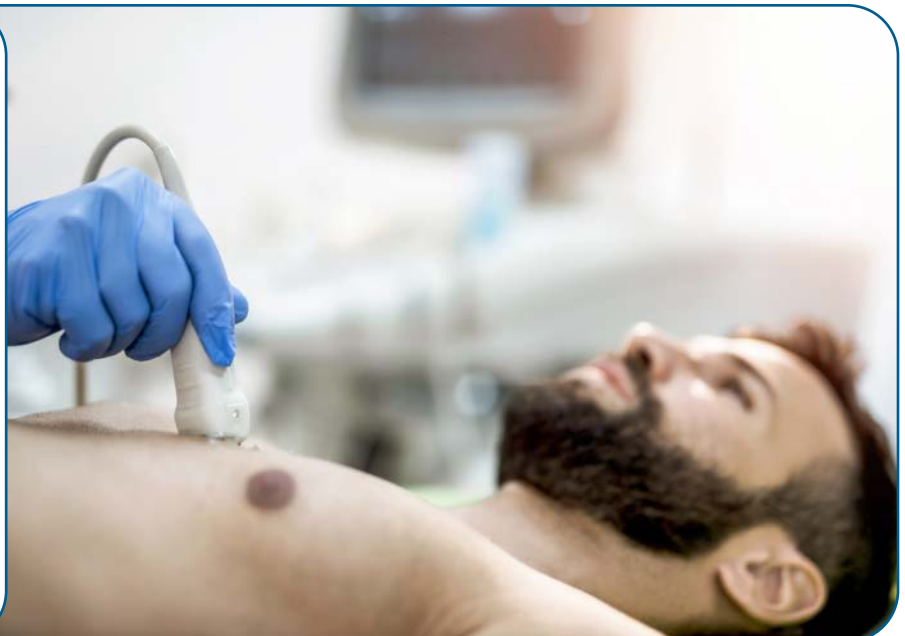
CAR T-cell therapy can cause changes in heartbeat and other problems. Before receiving CAR T, your doctor will want to check your heart. This will provide a baseline (starting) picture of its structure and function. A heart ultrasound (echocardiogram) is often ordered. This noninvasive test is performed using a handheld wand placed on your chest. It does not use radiation. If you have a history of heart problems, your doctor will consult with a heart expert (cardiologist).

Neurologic (neuro) exam

CAR T-cell therapy can cause brain and nervous system problems. Expect to have a neurologic (“neuro”) exam before receiving your cells. Neurologic means having to do with the nervous system. This check provides a point of comparison for testing done after infusion.

Echocardiogram

CAR T can cause heart problems. It is important for your doctor to know how your heart looks and works before you receive CAR T cells. An echocardiogram (“echo”) is often ordered. It is a painless ultrasound of the heart.



The extent of the exam will vary between providers. At a minimum, the exam will check your level of awareness and ability to interact with your surroundings. The Immune Effector Cell-Associated Encephalopathy (ICE) Assessment Tool is often used. This screening test measures your ability to carry out simple tasks, such as writing and counting. Other tests and tools may be used to check your:

- Motor (movement) and sensory skills
- Balance and coordination
- Reflexes
- Nerve function

Your doctor may also order magnetic resonance imaging (MRI) of your brain. This can be helpful to compare with brain images taken if neurotoxicity develops after infusion.

Tumor lysis syndrome

Cancer cells break apart when they die. The contents of the dead cells enter the bloodstream. They disrupt the chemical balance of the blood. This is called tumor lysis syndrome (TLS). It is a serious potential side effect of cancer treatment. It can lead to organ damage and be life-threatening. TLS most often occurs after treatment of large tumors or fast-growing cancers. If this applies to your cancer, your doctor will take steps to prevent TLS. You will be monitored closely.

Preventing seizures

Some CAR T therapies are more likely to affect the brain than others. On the day of infusion, or anytime after, your doctor may start you on a medication to prevent seizures. A drug called levetiracetam is often given. It is an anticonvulsant. Anticonvulsants reduce abnormal overactivity in the brain. Levetiracetam is usually taken as a pill every 12 hours for up to 30 days.

After infusion

Expect to stay at or close to the hospital after infusion. This allows for close monitoring and treatment of urgent side effects. Early signs of CRS or nervous system problems will be easier to spot while being monitored in the hospital.

If hospital (inpatient) care is not needed, close monitoring by a center with CAR T experience may be an option. At the first sign of CRS or neurologic toxicity, hospitalization is needed.

You will have ongoing blood testing while in the hospital. Testing will look for any deficiencies or problems. Blood tests you are likely to have include:

- Complete blood count (CBC)
- Comprehensive metabolic panel (CMP)
- Blood clotting tests
- C-reactive protein (CRP)
- Ferritin (a protein that stores iron for the body to use)

After leaving the hospital, you will continue to be closely monitored for side effects. Expect to be watched closely for at least 4 weeks after infusion, and possibly up to 6 months. This will depend on the CAR T product you received. Your care team will instruct you not to drive or do anything else potentially dangerous for at least 8 weeks after infusion.

Low blood cell counts

For weeks to months after CAR T-cell therapy your levels of red and white blood cells and platelets may be lower than normal. Low blood

cell counts raise your risk of infection. One or both of the following may be used to try to lower the risk of infection:

- Blood and platelet transfusions
- Growth factors

Blood transfusions can raise the levels of red blood cells or platelets. In a transfusion, cells donated by healthy volunteers are put into your bloodstream through a vein.

Growth factors are medications that drive bone marrow to make more blood cells. They are given by injection or intravenously. Colony-stimulating growth factors such as filgrastim can also help your body make more white blood cells.

Low numbers of B cells

CAR T-cell therapy is most often used to treat B-cell non-Hodgkin lymphomas. In the process of killing cancer cells, normal B cells are also destroyed. Absence of B cells is called B-cell aplasia. It is a common side effect of CAR T. Depending on the type of CAR T received, it may last a long time. Having too few B cells can mean that the CAR T cells continue to fight the cancer. But it also means that you have fewer immune cells to protect you from infection.

Preventing infections

Medications to prevent certain infections is recommended for at least 3 to 6 months after CAR T. Pneumocystis jiroveci pneumonia is a fungal infection of the lungs. It can be prevented by taking an oral antibiotic. The varicella-zoster virus causes chickenpox

and shingles, a painful skin rash. It can be prevented with oral antiviral medications.

Some people will have frequent infusions of a particular therapy called intravenous immunoglobulin therapy (IVIG). The antibodies used for the IVIG infusions come from different people. These donated antibodies help strengthen your immune system and fight infection. IVIG is typically only given if you are getting serious or repeated infections.

Key points

What is CAR T-cell therapy?

- CAR T-cell therapy is a type of immunotherapy. Immune cells are modified in a facility and put back in the body.
- The modified immune cells find and kill cancer cells using a “search and destroy” approach.

Serious side effects

- Cytokine release syndrome (CRS) is one of the most common side effects of CAR T-cell therapy.
- Immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS) is similar to CRS but typically starts later and may be more severe.
- Nervous system problems can occur after CAR T-cell therapy. Immune effector cell-associated neurotoxicity syndrome (ICANS) describes some but not all of these side effects.

After infusion

- Expect to stay at or close to the hospital after infusion. This allows for close monitoring and treatment of urgent side effects.
- You will be instructed not to drive or do any other hazardous activities for at least 8 weeks after infusion.
- Low blood cell counts are common after CAR T. You may receive blood transfusions and/or growth factors to help prevent infection.
- Having low numbers of B cells is called B-cell aplasia. It is a common, long-term side effect of CAR T therapy.
- Intravenous immunoglobulin (IVIG) may be used to strengthen your immune system and fight infection after CAR T-cell therapy.

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Cytokine release syndrome (CRS)

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Cytokine release syndrome (CRS) is a common, serious side effect of CAR T-cell therapy. Although CRS is often mild, it can be severe.

What is CRS?

Cytokines are proteins. They carry out different immune-related jobs in the body. Some types cause inflammation. Other types help to reduce it.

In the days after a CAR T infusion, immune cells affected by the treatment may release many inflammation-causing cytokines into the blood. This causes your immune system to go into overdrive. A number of signs and symptoms are possible as a result. They include:

- Fever
- Low blood pressure
- Low tissue oxygen level
- Chills
- Rapid heartbeat
- Trouble breathing
- Nausea
- Rash
- Headache
- Muscle and joint aches

CRS usually starts 2 to 4 days after infusion and lasts about a week. However, it can start as early as hours after infusion and as late as 10 to 15 days afterward.

CRS can lead to damage to major organs. The heart, liver, kidneys, and/or lungs may be affected. While most people experience CRS, you do not need it for CAR T to work. Your cancer type and the specific CAR T medicine you are treated with play a role in how likely you are to get CRS.

Serious CRS problems

CRS is mild for most people, but serious and possibly deadly problems are possible. These are described next.

Low blood pressure

Blood pressure is the strength of blood pushing against the sides of blood vessels. CRS can cause blood pressure to drop. Low blood pressure (hypotension) is dangerous. It reduces blood flow to the heart, brain, and other vital organs. In severe cases, low blood pressure can be life-threatening. Severely low blood pressure is treated with vasopressors. These medicines raise blood pressure by contracting (tightening) blood vessels.

Lack of oxygen to tissues

Hypoxia is a dangerous condition. It happens when there is not enough oxygen reaching the cells and tissues of the body. The brain, liver, and other organs can be damaged in minutes if they do not get enough oxygen.

Oxygen therapy is used to make sure that your tissues and organs are getting enough oxygen. Oxygen may be given through noninvasive nose tubes or a mask that covers your nose and mouth. The method used to give oxygen will depend on how low the level is.

In severe cases, intubation may be needed. Intubation refers to putting a tube through the mouth and into the airway. The tube is connected to a respirator that moves air in and out of your lungs. This is called mechanical ventilation.

Effects on the heart

CRS can cause changes in the way the heart beats. It may beat faster, slower, or at abnormal intervals. Atrial fibrillation (“A-fib”) refers to a fast and irregular heartbeat. In ventricular tachycardia (“V-tach”) the heart beats quickly but regularly. Changes in heartbeat like these can be dangerous. Extra medications and other treatments may be needed.

CRS can also cause your heart to not work as well. This is often temporary. While uncommon, the heart can also suddenly stop working after CAR T. This is called cardiac arrest. It causes you to stop breathing and pass out. It can be life threatening, but this is very rare.

Poor kidney function

The kidneys filter waste from the blood. CRS can cause the kidneys to suddenly stop filtering blood. This is called acute kidney injury (AKI). It is not common. If it occurs, the effects are usually reversible (not permanent).

Capillary leak syndrome

This syndrome is a condition in which fluid and proteins leak out of the bloodstream. They leak out through tiny blood vessels (capillaries). It can lead to dangerously low blood pressure, organ failure, and shock. Shock is a life-threatening problem. It occurs when there is a sudden drop in blood flow in the body.

How severe is it?

Doctors use a grading system to assign CRS a grade from 1 (mildest) to 4 (most severe). The grade helps guide treatment decisions.

- **Grade 1** – Fever above 38 degrees Celsius (100.4 degrees Fahrenheit)
- **Grade 2** – Fever + slightly low blood pressure or slightly low oxygen level
- **Grade 3** – Fever + more severe low blood pressure or moderately low oxygen level
- **Grade 4** – Fever + low blood pressure requiring very aggressive support or severely low oxygen level

Treatment

Tocilizumab (Actemra)

Interleukin-6 (IL-6) is a cytokine released during CRS. This leads to very high levels of it in the blood. Tocilizumab is a prescription medicine that blocks interaction between IL-6 and its receptors. Intravenous tocilizumab is essential for treating moderate to severe CRS (grades 2, 3, and 4).

It is also used to treat milder (grade 1) CRS in certain cases. It may be given for mild CRS lasting longer than 3 days (or less, depending on the specific CAR T therapy). It may also be given to treat mild CRS in the elderly, those with nervous system symptoms, and/or other health problems.

Steroids

Corticosteroids (steroids for short) are drugs that reduce the activity of the immune system. They are not the same as steroids used to build muscle mass (anabolic steroids).

Intravenous steroids are used together with tocilizumab to treat more severe CRS, and sometimes milder CRS. They are also used to treat more severe neurologic side effects. Dexamethasone and methylprednisolone are commonly used steroids.

Anakinra (Kineret)

For severe CRS that does not improve with tocilizumab and high-dose steroids, treatment with anakinra (Kineret) may be considered. It is given as an injection under the skin. Anakinra blocks the activity of interleukin-1, a cytokine that causes inflammation.



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Key points

What is CRS?

- CRS is the release of inflammation-causing cytokines into the blood after an infusion of CAR T-cell therapy.
- It is the most common, serious side effect of CAR T-cell therapy. Although CRS is often mild, it can be severe.

Signs and symptoms

- Signs and symptoms include fever, low blood pressure, low tissue oxygen, chills, rapid heartbeat, nausea, rash, headache, and trouble breathing.
- Other possible side effects of CRS include heart problems, acute kidney injury, and capillary leak syndrome.
- CRS is similar to another condition called immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS).

Treatment

- Tocilizumab is a drug that blocks a cytokine released during CRS. It is essential for treating moderate to severe CRS.
- Steroids are used together with tocilizumab to treat moderate to severe CRS.
- Anakinra may be used to treat severe CRS that does not improve with other treatment.

3

Nervous system side effects

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CAR T-cell therapy can cause brain and nervous system problems. While the most common symptoms are mild, very serious problems can occur. These side effects are usually reversible if treated promptly.

About nervous system side effects

The brain, the spinal cord, and nerves make up the nervous system. This complex system controls everything the body does. Movement, sensation, and breathing are all guided by the nervous system. It is the hub of all things mental including thought, memory, and learning.

Doctors call nervous system side effects, including those caused by immunotherapy, "neurotoxicity." Immune effector cell-associated neurotoxicity syndrome (ICANS) is a term used to describe some but not all of these effects. Immune effector cell (IEC) is another term for a CAR T cell.

Common, mild symptoms include:

- Headache
- Dizziness
- Trouble sleeping
- Shaking
- Confusion
- Memory issues
- Anxiety
- Trouble finding words or speaking
- Feeling very sleepy

In more severe cases, seizures, brain swelling, and coma can occur. These may be life-threatening. These and other possible symptoms are described below.

Nervous system side effects, if they occur, typically start 4 to 10 days after treatment. They tend to last about 2 weeks but can last as long as 4 to 8 weeks.

Delirium

Delirium is a sudden change in brain function. It causes confusion, disorientation, and changes in behavior or emotions. It can also cause agitation and hallucinations (seeing things that aren't there). Delirium comes on quickly, often in a matter of hours to days.

Nerve problems

Your autonomic nervous system is always working behind the scenes. It regulates your basic body functions. This includes your heart rate, digestion, breathing rate, and body temperature. ICANS can cause this system

to not work as well. This causes symptoms such as dizziness upon standing up, sweating too much or too little, and bowel and bladder problems.

Language problems

Aphasia is the loss of ability to understand or express speech. It is caused by injury to the brain. Aphasia is a language disorder—it does not affect intelligence. People with aphasia are still able to formulate thoughts in the same way. They are just unable to express them as they did before. This can be very frustrating. Aphasia typically only lasts a few hours or days.

Serious problems

The uncommon but serious nervous system side effects of CAR T-cell therapy are described next.

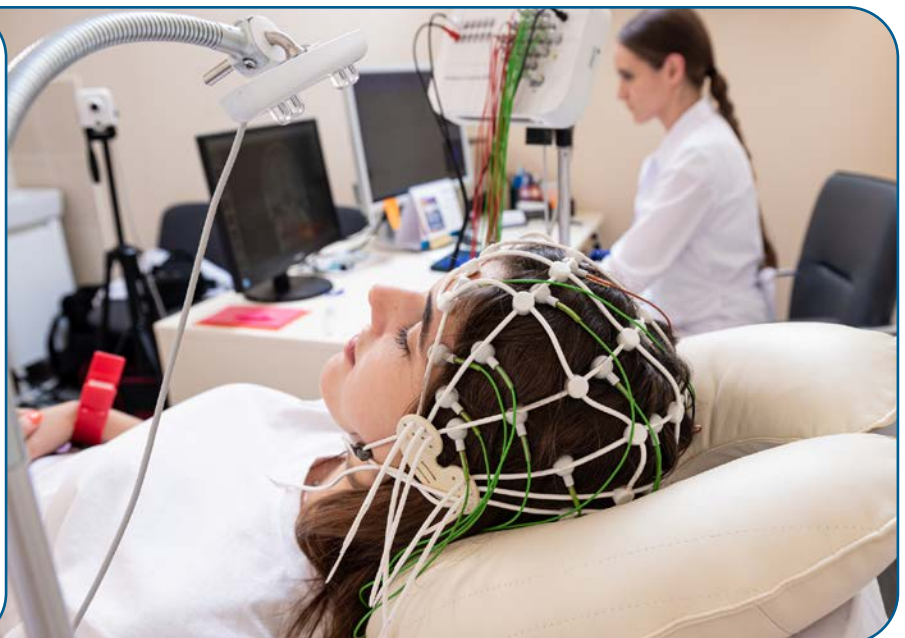
Seizures

Abnormal electrical signals in the brain can cause sudden and uncontrolled body movements. Shaking in particular is common. These are called seizures. Other symptoms include behavior changes, loss of awareness, and loss of muscle control.

Status epilepticus is the medical term for having one long (5 minutes or more) seizure, or several shorter seizures in a row. This is a medical emergency that can occur in severe ICANS. Hospital treatment typically includes use of several different types of drugs.

Monitoring for seizures

You may have electroencephalography (EEG) to monitor for seizures during ICANS. An EEG is a recording of electrical activity in the brain.



Brain swelling

Swelling due to trapped fluid is the body's response to many types of injury and illness. Swelling of the brain is a life-threatening reaction to CAR T. When the brain swells, it increases the pressure inside the skull.

Medicines are used to draw fluid out of the skull and injured brain. This is called osmotic therapy or hyperosmolar therapy. In severe cases of brain swelling, a lumbar puncture (described on the next page) or ventriculostomy may be needed. Ventriculostomy is a procedure that involves inserting a plastic tube into the skull. Excess fluid drains through the tube in order to lower the pressure.

Anti-BCMA CAR T side effects

The CAR T products listed below target B-cell maturation antigen (BCMA). They are used to treat multiple myeloma, a cancer of plasma cells.

- Idecabtagene vicleucel (Abecma)
- Ciltacabtagene autoleucel (Carvykti)

Anti-BCMA products can cause nervous system side effects that are not considered part of ICANS. Compared to ICANS, these effects start late. Symptoms can start between 10 and 110 days after infusion.

MNTs

Movement and neurocognitive treatment-emergent adverse events (MNTs) cause symptoms that are similar to those caused by Parkinson's disease. Symptoms include:

- Slowness of movement (bradykinesia)
- Shaking (tremor)
- Weak voice (hypophonia)
- Personality changes
- Impaired memory
- Trouble balancing (postural instability)

For mild symptoms, your doctor may prescribe an oral steroid. If you have severe or persistent symptoms and a high level of CAR T cells in your blood, chemotherapy may be given to reduce the number of CAR T cells.

There isn't much research on treatment for MNTs. Your care team will consider the possible benefits and risks of these therapies.

Nerve damage

Anti-BCMA CAR T products can damage nerves located outside of the brain and spinal cord, called peripheral nerves. Symptoms can include:

- Facial weakness or paralysis
- Problems moving eyes or eyelids
- Numbness, tingling, or pain in hands or feet
- Extreme sensitivity to touch
- Trouble balancing
- Muscle weakness or paralysis (if motor nerves are affected)

For mild symptoms, your doctor will consider treatment with steroids.

Acute inflammatory demyelinating polyneuropathy (AIDP) is a rare and severe peripheral nerve problem. It causes weakness that often starts in the feet and works its way up the body, eventually affecting all 4 limbs. If your symptoms suggest AIDP, your doctor will consider intravenous immunoglobulin therapy (IVIG).

Assessment and supportive care

Testing and care you may have while in the hospital are described next.

Neurologic exams

You will have frequent neurologic exams while in the hospital. These check your mental status and motor function. They also look for other signs of brain and nervous system problems.

Supportive care

You may receive fluids intravenously (an "IV drip") to keep you hydrated. Your care team will also take steps to prevent food or liquid from going into your airway instead of your food pipe (esophagus). Food or fluids in the airway is called aspiration. It can lead to infection (often pneumonia) and inflamed lungs.

Monitoring for seizures

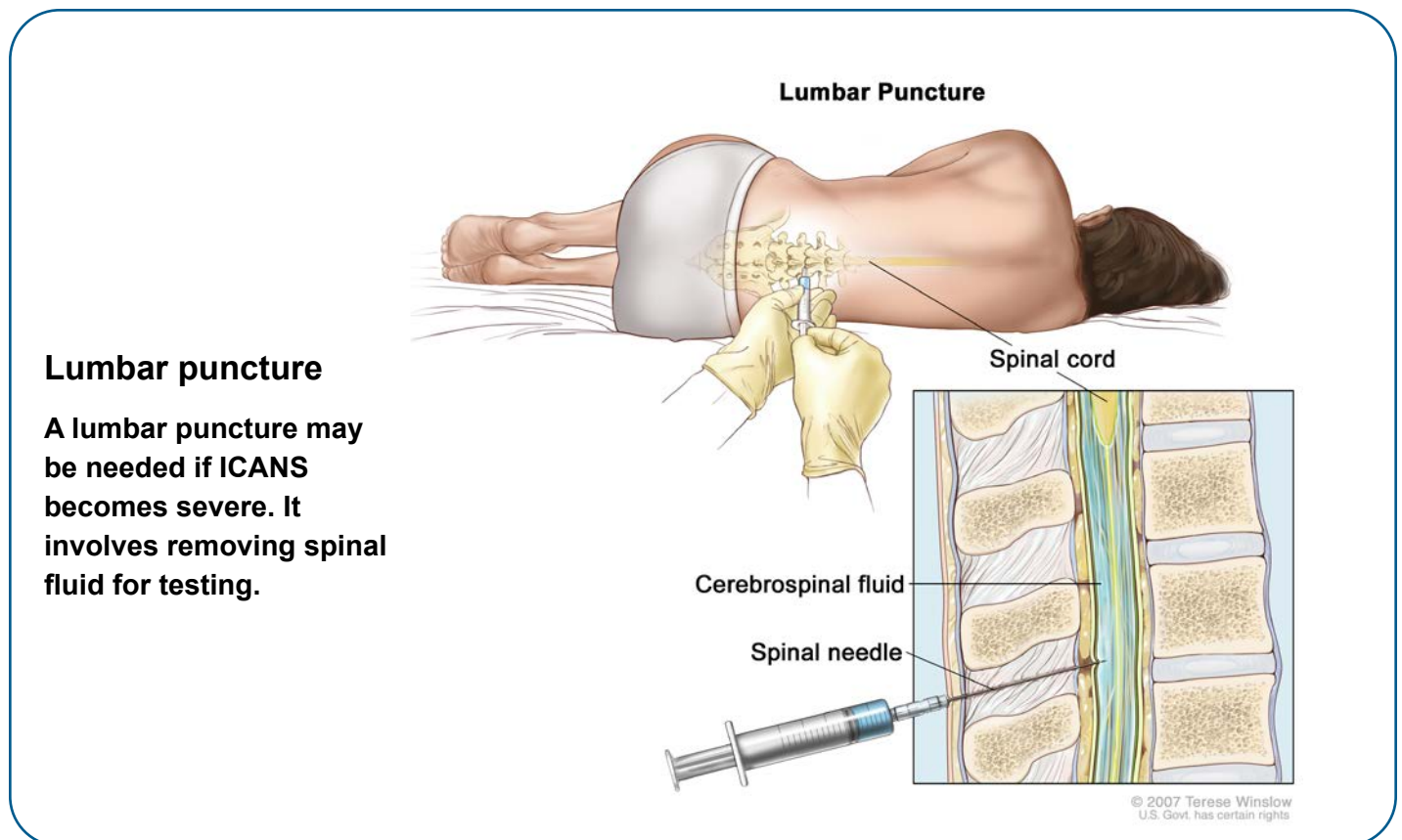
You may be monitored for seizures. An electroencephalogram (EEG) is used. An EEG is a recording of electrical activity in the brain. It tracks and records brain wave patterns. The patterns are relayed by small metal sensors placed on your scalp.

Brain imaging

You may have magnetic resonance imaging (MRI) of your brain to look for swelling or damage. If MRI is not possible, you may have computed tomography (CT) instead.

Lumbar puncture

A lumbar puncture may be needed for more severe ICANS. The fluid that flows in and around the brain and spinal cord is called cerebrospinal fluid (CSF). Lumbar puncture is a simple bedside procedure to remove a sample of spinal fluid for testing. It can also be used to measure and relieve pressure from brain swelling.



How severe is it?

Doctors use a point system to assign ICANS a grade from 1 to 4. A score of 4 is the most severe (life threatening). The grade helps guide treatment decisions.

One key factor in the overall grade is the Immune Effector Cell-Associated Encephalopathy (ICE) score. The ICE Assessment Tool is an ICANS screening test. It provides a snapshot of your mental state. It measures your ability to carry out simple tasks, such as writing and counting. A score of 0 (critical emergency) to 10 (mild) is possible.

In addition to ICE score, the following information helps determine the overall severity of ICANS:

- How alert/responsive you are
- Whether you are having seizures
- Whether you have severe muscle weakness
- Whether there is brain swelling

The ICANS grading system was developed by the American Society of Blood and Marrow Transplantation, now the American Society for Transplantation and Cellular Therapy (ASTCT).

Treatment

For mild ICANS, supportive care is often all that is needed. Moderate or severe ICANS is treated with steroids given through a vein. Steroids are medicines that reduce immune system activity. They relieve inflammation in the body. Dexamethasone and methylprednisolone are widely used steroids.

For severe ICANS that is not improving with high-dose steroids, treatment with anakinra may be added.

Those with both ICANS (any grade) and cytokine release syndrome will also be given tocilizumab. See page 14 for more information on tocilizumab.

Key points

About nervous system side effects

- The nervous system side effects of CAR T-cell therapy are called neurotoxicities.
- They include immune effector cell associated neurotoxicity syndrome (ICANS) and some other symptoms.

Signs and symptoms

- Common symptoms include headache, delirium, dizziness, trouble sleeping, shaking, and anxiety.
- Language and nerve problems are also possible.
- Very serious nervous system side effects include seizures, brain swelling, and coma. These are usually reversible.
- Anti-BCMA products can cause nervous system side effects that are not considered part of ICANS and typically start later.

Treatment

- Supportive care may be all that is needed for mild nervous system side effects.
- Intravenous steroids are used to treat moderate to severe ICANS.
- Anakinra may be used to treat severe ICANS that does not improve with other treatment.



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4

Resources

25 Questions to ask your doctor

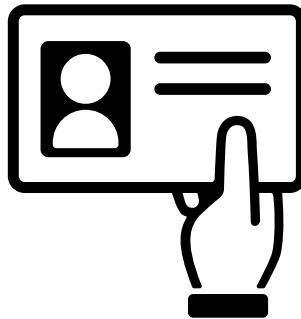
27 Resources

CAR T-cell therapy is a recent innovation in cancer treatment. This chapter includes resources for learning more about this type of immunotherapy and its effects.

Questions to ask your doctor

It is normal to have lots of questions about immunotherapy with CAR T-cell therapy. Possible questions to ask your doctor are listed on the following pages. Feel free to use these questions or come up with your own.

Following the questions is a listing of websites that provide information for patients about CAR T-cell therapy and its effects.



Immunotherapy Wallet Card

Ask your doctor for an immunotherapy wallet card. This card states that you have received CAR T-cell therapy. It also lists potential side effects and contact numbers for your cancer care team. Carry it with you at all times. If a card is not available, ask for a printable list of your treatment regimen.

Questions to ask about CAR T side effects

1. Which CAR T product will I be receiving?
2. Will I stay in the hospital afterward or can I be monitored from home?
3. Are there any long-term or permanent side effects?
4. When do they start? How long do they usually last?
5. How are they treated?
6. I didn't experience cytokine release syndrome (CRS). Is that bad?
7. How soon can I resume my normal activities after receiving CAR T-cell therapy?
8. After I leave the hospital, which symptoms should I report right away? How do I report them?
9. Can I report symptoms or communicate with my treatment team online?
10. Can you give me an immunotherapy wallet card?

Resources

Be the Match

[BeTheMatch.org/one-on-one](https://www.bethematch.org/one-on-one)

BMT InfoNet

[bmtinfonet.org](https://www.bmtinfonet.org)

Lymphoma Research Foundation

[lymphoma.org](https://www.lymphoma.org)

National Bone Marrow Transplant Link

[nbmtlink.org](https://www.nbmtlink.org)

National Coalition for Cancer Survivorship

[canceradvocacy.org](https://www.canceradvocacy.org)

The Leukemia & Lymphoma Society

[LLS.org/PatientSupport](https://www.lls.org/PatientSupport)

Triage Cancer

[triagecancer.org](https://www.triagecancer.org)



Words to know

aphasia

A language disorder caused by injury to the brain. A possible neurologic side effect of CAR T-cell therapy.

B-cell aplasia

Having low numbers of B cells. A common and sometimes long-term side effect of CAR T-cell therapy.

capillary leak syndrome

The escape of fluid and proteins from blood vessels into surrounding tissues. Results in dangerously low blood pressure.

cerebral edema

Brain swelling that causes an increase in pressure inside the skull. A possible side effect of CAR T-cell therapy.

chimeric antigen receptor (CAR) T-cell therapy

A type of immunotherapy in which T cells (a type of immune system cell) are modified in a way that allows them to find and kill cancer cells.

convulsive status epilepticus

A seizure lasting longer than 5 minutes, or having multiple seizures within a 5-minute period without fully recovering between them.

corticosteroids

Inflammation-reducing medicines. They reduce the activity of the immune system. Used to treat side effects of CAR T-cell therapy.

cytokine release syndrome (CRS)

A potentially serious side effect of CAR T-cell therapy. Caused by the release of inflammatory proteins into the blood from immune cells affected by the immunotherapy.

delirium

A mental state causing confusion, disorientation, and memory problems. May also cause agitation, hallucinations, and extreme excitement. A possible side effect of CAR T-cell therapy.

hypogammaglobulinemia

An immune system problem in which not enough antibodies are made, resulting in increased infection risk.

hypotension

Low blood pressure. A possible complication of cytokine release syndrome.

hypoxia

Decreased oxygen reaching body tissue. A possible complication of cytokine release syndrome.

immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS)

A serious problem in which too many of a type of white blood cell and T cells are made by the body. Previously known as macrophage activation syndrome (MAS).

immune effector cell-associated neurotoxicity syndrome (ICANS)

A group of nervous system-related side effects of CAR T-cell therapy.

intravenous immunoglobulin (IVIG)

A solution made from antibodies taken from the blood of healthy donors is given through a vein. Sometimes given to prevent infections after CAR T.

osmotic therapy

The use of medicines to draw fluid out of the skull and the brain, reducing pressure. Also called hyperosmolar therapy.

Risk Evaluation and Mitigation Strategy (REMS)

A strategy to ensure that the benefits of using a drug outweigh its serious potential risks. Required by the U.S. Food & Drug Administration (FDA) for currently available CAR T-cell therapies.

seizure

Sudden, uncontrolled body movements and changes in behavior caused by abnormal electrical activity in the brain.

tocilizumab (Actemra)

A prescription medicine used to treat severe or life-threatening cytokine release syndrome caused by CAR T-cell therapy.

tumor lysis syndrome (TLS)

A problem caused by treatment of large or fast-growing cancers. The contents of dead cancer cells are released into the blood. This causes problems and may cause organ damage.

vasopressor

Medicine that raises blood pressure by contracting (tightening) blood vessels. Used in emergency situations to treat severely low blood pressure.



We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

[NCCN.org/patients/feedback](https://www.nccn.org/patients/feedback)

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This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Immunotherapy-Related Toxicities, Version 1.2024. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • penmedicine.org/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • healthcare.utah.edu/huntsmancancerinstitute

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Robert H. Lurie Comprehensive Cancer Center
of Northwestern University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMLOW • yalecancercenter.org

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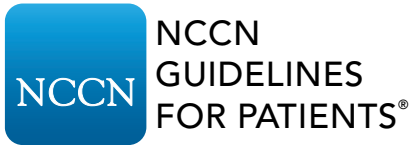
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