About the NCCN Guidelines for Patients®

Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

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.


View the NCCN Guidelines for Patients free online NCCN.org/patientguidelines
Find an NCCN Cancer Center near you NCCN.org/cancercenters
Supporters

NCCN Guidelines for Patients are supported by funding from the NCCN Foundation®

NCCN Foundation gratefully acknowledges the following corporate supporters for helping to make available these NCCN Guidelines for Patients: Bristol Myers Squibb; Kite, a Gilead Company; Pfizer Inc.; Regeneron Pharmaceuticals, Inc.; and Sanofi Genzyme.

NCCN independently adapts, updates, and hosts the NCCN Guidelines for Patients. Our corporate supporters do not participate in the development of the NCCN Guidelines for Patients and are not responsible for the content and recommendations contained therein.

To make a gift or learn more, visit online or email

NCCNFoundation.org/donate  PatientGuidelines@NCCN.org
Contents

4  CAR T-cell therapy basics
11  Cytokine release syndrome (CRS)
16  Nervous system side effects
24  Resources
29  Words to know
31  NCCN Contributors
32  NCCN Cancer Centers
34  Index
1 CAR T-cell therapy basics

5 What is CAR T-cell therapy?
7 Before and during infusion
9 After infusion
10 Key points
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
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.
2

Cytokine release syndrome (CRS)

12 What is CRS?
12 Serious CRS problems
13 How severe is it?
14 Treatment
15 Key points
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.
Cytokine release syndrome (CRS) » How severe is it?

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.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response
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

17 About nervous system side effects
18 Serious problems
19 Anti-BCMA CAR T side effects
20 Assessment and supportive care
22 How severe is it?
22 Treatment
23 Key points
Nervous system side effects

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.

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 if ICANS becomes severe. It involves removing spinal fluid for testing.
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.
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

BMT InfoNet
bmtinfonet.org

Lymphoma Research Foundation
lymphoma.org

National Bone Marrow Transplant Link
nbmtlink.org

National Coalition for Cancer Survivorship
canceradvocacy.org

The Leukemia & Lymphoma Society
LLS.org/PatientSupport

Triage Cancer
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 CRS. 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.
Words to know

**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.
NCCN Contributors

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:

Dorothy A. Shead, MS
Senior Director
Patient Information Operations

Erin Vidic, MA
Senior Medical Writer, Patient Information

Laura Phillips
Graphic Artist

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Management of Immunotherapy-Related Toxicities, Version 1.2024 were developed by the following NCCN Panel Members:

*John A. Thompson, MD/Chair
Fred Hutchinson Cancer Center

Bryan J. Schneider, MD/Vice-Chair
University of Michigan Rogel Cancer Center

Julie Brahmer, MD, MSc/Vice-Chair
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Mohammad Abu Zaid, MBBS
Indiana University Melvin and Bren Simon Comprehensive Cancer Center

Amaka Achufusi, MD
University of Wisconsin
Carbone Cancer Center

*Philippe Armand, MD, PhD
Dana-Farber/Brigham and Women’s Cancer Center

Meghan K. Berkenstock, MD
The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins

Bonnie Bermas, MD
UT Southwestern Simmons Comprehensive Cancer Center

Tawnie Braaten, MD
Huntsman Cancer Institute at the University of Utah

Lihua E. Budde, MD, PhD
City of Hope National Medical Center

Saurin Chokshi, MD
St. Jude Children’s Research Hospital/
The University of Tennessee Health Science Center

Marianne Davies, DNP, RN, ACNP-BC, AOCNP
Yale Cancer Center/Smilow Cancer Hospital

Changchun Deng, MD
Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute

Yaron Gesthalter, MD
UCSF Helen Diller Family Comprehensive Cancer Center

Michael Jain, MD, PhD
Moffitt Cancer Center

Prantesh Jain, MD
Roswell Park Comprehensive Cancer Center

Benjamin H. Kaffenberger, MD, MS
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Maya Khalil, MD
O’Neal Comprehensive Cancer Center at UAB

Melissa G. Lechner, MD, PhD
UCLA Jonsson Comprehensive Cancer Center

Tianhong Li, MD, PhD
UC Davis Comprehensive Cancer Center

Alissa Marr, MD
Fred & Pamela Buffett Cancer Center

Suzanne McGettigan, MSN, CRNP, AOCN
Abramson Cancer Center at the University of Pennsylvania

Jordan McPherson, PharmD, BCOP, MS
Huntsman Cancer Institute at the University of Utah

Theresa Medina, MD
University of Colorado Cancer Center

Nisha A. Mohindra, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Anthony J. Olszanski, MD, RPh
Fox Chase Cancer Center

*Olabanke Oluwole, MBBS, MPH
Vanderbilt-Ingram Cancer Center

Sandip P. Patel, MD
UC San Diego Moores Cancer Center

Jason Prosek, MD
The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute

Sunil Reddy, MD
Stanford Cancer Institute

Pankti Reid, MD, MPH
The UChicago Medicine Comprehensive Cancer Center

John Ryan, MBA
Patient Advocate

Mabel Ryder, MD
Mayo Clinic Comprehensive Cancer Center

*Bianca Santomasso, MD, PhD
Memorial Sloan Kettering Cancer Center

Scott Shofer, MD, PhD
Duke Cancer Institute

Jeffrey A. Sosman, MD
Robert H. Lurie Comprehensive Cancer Center of Northwestern University

Yinghong Wang, MD, PhD
The University of Texas MD Anderson Cancer Center

Vlad G. Zaha, MD, PhD
UT Southwestern Simmons Comprehensive Cancer Center

Stephen Zucker, MD
Dana-Farber/Brigham and Women’s Cancer Center

* Reviewed this patient guide. For disclosures, visit NCCN.org/disclosures.

NCCN Guidelines for Patients®
Immunotherapy Side Effects: CAR T-Cell Therapy, 2024
'aphasia 18
B-cell aplasia 9
BCMA 5, 19–20
capillary leak syndrome 13
cardiac arrest 13
CD19 5
delirium 17
echocardiogram 7
electroencephalogram (EEG) 18, 20
IVIG 10, 20
immune effector cell-associated hemophagocytic lymphohistiocytosis-like syndrome (IEC-HS) 5
lumbar puncture 19, 21
movement and neurocognitive treatment-emergent adverse events (MNTs) 19–20
multiple myeloma 5, 19
nerve damage 20
seizures 8, 18, 20
supportive care 21, 22
tocilizumab 14, 23
vasopressor 12
wallet card 25
Immunotherapy Side Effects
CAR T-Cell Therapy
2024

To support the NCCN Guidelines for Patients, visit
NCCNFoundation.org/Donate