Memorial Sloan Kettering Cancer Center

PATIENT & CAREGIVER EDUCATION

About Cytokine Release Syndrome (CRS) and Neurotoxicity Syndrome

This information explains what cytokine (SY-toh-kine) release syndrome and neurotoxicity (NOOR-oh-tok-SIH-sih-tee) syndrome are. It also describes common causes, symptoms, and treatments for each condition.

Neurotoxicity syndrome is also called immune effector cell-associated neurotoxicity syndrome (ICANS).

What are cytokine release syndrome and neurotoxicity syndrome?

CRS and neurotoxicity syndrome are side effects of some immunotherapies. Immunotherapy is a type of cancer treatment that uses your immune system to attack cancer cells.

Chimeric antigen receptor (CAR) T cell therapy and bispecific antibody therapy are examples of common immunotherapies.

- **CAR T cells** are modified (changed) T cells that attach to cancer cells. T cells are a type of white blood cell in your immune system. Once a CAR T cell attaches to a cancer cell, your body sends other types of immune cells to kill the cancer cell. Talk with your healthcare provider to learn more about CAR T cells and the type of therapy you may get. You can also read *CAR T Cell Therapy: A Guide for Adult Patients & Caregivers* (www.mskcc.org/pe/car-t-guide).
- **Bispecific antibodies** are antibodies made to help T cells find and fight cancer cells. Antibodies are molecules your immune system makes when it notices something in your body that can make you sick. Bispecific

antibodies make a “bridge” between your T cells and the cancer cells. This helps your T cells kill the cancer cells. Talk with your healthcare provider to learn more about bispecific antibodies and the type of therapy you may get.

Cytokine release syndrome

CRS is a group of symptoms that can happen when T cells attack cancer cells.

Normally, T cells release signaling molecules called cytokines. They send messages to other parts of your immune system. CRS can happen if T cells release too many cytokines too fast. The rush of cytokines can cause inflammation that harms your healthy tissues and organs.

Your chance of having CRS depends on:

- The type of immunotherapy you get.
- The type of cancer you have.
- If you have other health issues. This includes autoimmune diseases and some genetic conditions.

Neurotoxicity syndrome

Neurotoxicity syndrome is a group of symptoms that can happen when a substance harms your nervous system. It’s a very bad side effect that may change how your brain works. This can affect how you think, move, and talk.

Your chance of having neurotoxicity syndrome depends on:

- The type of immunotherapy you get.
- The type of cancer you have.
- If you have other health issues, such as CRS or a neurological (nerve) disorder.

We do not know exactly how some immunotherapies can cause neurotoxicity syndrome. More research is needed to better understand this.

What are the symptoms of cytokine release syndrome and neurotoxicity syndrome?

Symptoms of CRS and neurotoxicity syndrome are listed below. They can happen as soon as a few hours after immunotherapy or as long as a few weeks. How soon you have symptoms and how strong they are depend on the type of immunotherapy you had.

CRS and neurotoxicity syndrome can happen alone or together. If you have both conditions, neurotoxicity syndrome often starts a few days after CRS. Sometimes, it can start at the same time as CRS.

Call your healthcare provider right away if you have any of the symptoms listed below. If their office is closed, follow the prompts to reach MSK's After-Hours Telephone Triage (AHTT) call center. You also can call the MSK operator at 212-639-7900. The AHTT lets you talk with a healthcare provider when your medical problem cannot wait until your care team is available. To learn more about the AHTT, read *About After-Hours Telephone Triage at MSK* (www.mskcc.org/pe/after-hours-triage).

If you have a life-threatening emergency, always call 911 or go to the nearest emergency room.

Symptoms of cytokine release syndrome

Common symptoms of CRS include:

- A fever of 100.4 °F (38 °C) or higher
- Flu-like symptoms, such as:
  - Muscle aches
  - Headaches
  - Chills
  - Fatigue (feeling more tired and weak than usual)
  - Nausea (feeling like you're going to throw up)

    - Vomiting (throwing up)
    - Diarrhea (loose, watery poop)
- A faster heart rate than usual
- Feeling dizzy or lightheaded
- Low blood pressure
- Swelling in your face, neck, arms, or legs
- Trouble breathing or catching your breath

CRS symptoms can be different depending on the type of immunotherapy you had. Most people have mild, flu-like symptoms. In rare cases, some people have severe (very bad), life-threatening symptoms. Symptoms can get worse very fast once they start.

Symptoms of neurotoxicity syndrome

Common symptoms of neurotoxicity syndrome include:

- Confusion or agitation (feeling easily annoyed or bothered).
- Changes in consciousness (level of alertness).
- Feeling restless (like you cannot relax or get comfortable).
- Headaches.
- Seizures (shaking or stiffening of your body that you cannot control).
- Shaking or twitching (tremors).
- Numbness and tingling (feeling of “pins and needles”).
- Trouble speaking or understanding speech. You may feel confused, slur your words, or have trouble understanding what people are saying to you.
- Loss of coordination (control of your body movements).
- Trouble walking. You may stumble, lose your balance, or feel dizzy.
- Vision changes. You may have double vision (when you see 2 images of the same thing), blurry vision, or vision loss.

- Changes in handwriting.
- Muscle weakness in your body or face.

Symptoms of neurotoxicity syndrome can range from mild to severe. In rare cases, symptoms can be life-threatening.

What are the treatments for cytokine release syndrome and neurotoxicity syndrome?

It's important to get treatment right away if you have CRS, neurotoxicity syndrome, or both. Getting treatment as soon as symptoms start can help prevent serious health problems.

Treatment for CRS and neurotoxicity syndrome depends on:

- How bad your symptoms are.
- The type of immunotherapy you had.
- If you have other serious medical conditions.

Treatment is not the same for everyone. Your healthcare provider will focus on treating your exact symptoms.

The amount of time it takes for symptoms to get better or go away is different for everyone. Symptoms often get better within hours of treatment, but it can take up to a few weeks.

Medicine

Your healthcare provider may prescribe medicine to treat your exact symptoms. Or, they may suggest an over-the-counter medicine you can buy at your local pharmacy without a prescription.

Do not take any medicine to treat CRS or neurotoxicity syndrome without talking with your healthcare provider. Taking certain medicines may mask (hide) your symptoms and cause more harm.

Urgent care or shared care

Your healthcare provider may tell you to get medical care right away. This is called urgent care.

If you live near Manhattan, your healthcare provider may tell you to go to MSK's Urgent Care Center (UCC). The UCC is open 24 hours a day, 7 days a week. To learn more about the UCC, read *About the Urgent Care Center at Memorial Sloan Kettering* (www.mskcc.org/pe/ucc).

If you don't live near Manhattan, your healthcare provider may tell you to go to one of MSK's partner hospitals. MSK has relationships with many high-quality healthcare providers at partner hospitals in New Jersey, Westchester, and on Long Island. These are doctors and other experts who MSK doctors know, trust, and work with closely.

You may be admitted to the hospital, depending on your symptoms. If you're admitted to an MSK partner hospital, your MSK care team will work with them to coordinate your care. This is called shared care.

If you have questions or concerns, contact your healthcare provider. A member of your care team will answer Monday through Friday from 9 a.m. to 5 p.m. Outside those hours, you can leave a message or talk with another MSK provider. There is always a doctor or nurse on call. If you're not sure how to reach your healthcare provider, call 212-639-2000.

For more resources, visit www.mskcc.org/pe to search our virtual library.

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