MANAGING
SIDE EFFECTS

LEUKEMIA & LYMPHOMA SOCIETY OF CANADA®

Immune effector cell-associated neurotoxicity syndrome ICANS

WHAT YOU NEED TO KNOW

You or your loved one has been diagnosed with a type of blood cancer. You may experience side effects from the therapy you receive. Immune effector cell-associated neurotoxicity syndrome (ICANS) is a side effect that can happen after some forms of immunotherapy treatment. It may cause you to experience serious neurological symptoms.

This fact sheet will help you:

- Learn about your immune system, immunotherapy, and ICANS
- Understand the symptoms, causes, and tests involved
- Manage this side effect and optimize your health and well-being
- Prepare a list of questions to ask your healthcare team

Managing side effects is an important part of cancer treatment. Be sure to talk to your healthcare team about any side effects you may have. They can help you manage these as you go through treatment.

Your immune system and immunotherapy

Your immune system

The immune system is your body's primary defence against infection and cancer. It recognizes the difference between cells that naturally belong in your body, and foreign and toxic cells (antigens).

An antigen can be from the environment, like a bacteria or a virus. An antigen, such as a cancer cell, can also be made inside your body. Having a foreign cell in your body causes your immune system to identify, target, and eliminate the cell.

Immunotherapy

Immunotherapy is a cancer treatment that improves your immune system's ability to detect and attack cancer cells. Doctors and researchers are learning to manage the immune system to destroy cancer cells. This approach is effective for certain blood cancers, but not all can be treated with immunotherapy.

The goal of immunotherapy is to detect and attack cancer cells.

Immune effector cell-associated neurotoxicity syndrome (ICANS)

T-cell-engaging bispecific antibodies (bispecifics) and chimeric antigen receptor T-cell (CAR T) are exciting immunotherapy approaches. Both are used as a standard line of therapy for some cancers. Two unique toxicities (harmful effects) can happen in the days or weeks after immunotherapy: cytokine release syndrome (CRS) and ICANS.

ICANS is a common and challenging side effect that is linked to bispecific antibodies and CAR T-cell therapy.

About ICANS

- ICANS disrupts the nervous system (known as neurological toxicity)
- It results from an overactive immune system
- It is common and usually reversible
- In rare cases, it can be life-threatening
- It may happen at the same time as CRS or soon after. (See our CRS factsheet on the LLSC website to learn more about cytokine release syndrome.)

Symptoms of ICANS

Your reaction to ICANS can be mild or moderate, or it can be severe or even life-threatening. The symptoms may vary. You will need treatment as soon as possible.

Common early symptoms can include:

- Difficulty finding words
- Trouble communicating verbally (aphasia)
- Difficulty writing (dysgraphia)
- Confusion
- Tremors and impaired attention
- Impaired fine motor skills
- Lethargy and headache

The prognosis for people living with ICANS is good. The majority of people fully recover without long-term effects.

It's important to get treated as soon as possible. Symptoms can worsen quickly.

Severe symptoms can include:

- Seizures
- Decreased level of consciousness
- Coma
- Brain swelling (cerebral edema)

ICANS can be divided into four grades (1 to 4), depending on how severe your symptoms are. The higher the number, the more serious ICANS is.

Causes of ICANS

ICANS can be caused by immunotherapy (bispecific antibodies or CAR T-cell therapy) used to treat blood cancer.

You are at higher risk for ICANS if:

- You are older
- You receive a specific type of bispecific antibodies or CAR T-cell therapy

Your diagnosis

ICANS is a complication of an underlying condition. It's usually diagnosed by ruling out other possible causes of brain function (cognition) problems. You may need to undergo some of the tests listed below if your medical team suspects ICANS:

Name of test	Description
Medical history and physical exam	The doctor reviews past illnesses, injuries, and symptoms, and examine your lungs, heart, and other organs.
Neurological consultation and ICE score	A neurological consultation includes tests of your coordination, balance, reflexes, and how you walk (gait). The 10-point immune effector cell encephalopathy (ICE) score assesses subtle changes in your cognition (thinking, attention, language, learning, memory, and perception). The higher the score, the lower the ICANS grade.
Imaging tests (neuroimaging)	A **computed tomography (CT) scan** uses a computer linked to an X-ray machine to make a detailed pictures of areas inside your body. **Magnetic resonance imaging (MRI)** uses magnetic fields and radio waves to create images of your body's organs and tissues.
Fundoscopy	A fundoscopy is an exam that uses a light and magnifying lens to check the back of your eye (fundus). This is a much less common test.
Electroencephalography (EEG)	An EEG measures electrical activity in the brain using small electrodes attached to your scalp. This is a much less common test.
Lumbar puncture	A thin, hollow needle is put into the lower part of the spine to collect a sample of cerebrospinal fluid. This is a much less common test.

Managing side effects

Learning about side effects helps you know what to expect and how to manage them. When the cause is cancer treatment, your doctor may recommend using smaller doses of the treatment drug. Recovery depends on what is causing ICANS and how severe it is. Many people recover somewhere between 4 and 14 days.

Treatment to manage ICANS

The treatment for ICANS depends on your symptoms, how severe they are, and your needs. Symptoms can become dangerous quickly, so you need to be treated as soon as possible.

Types of treatment

- Grade 1 ICANS: Supportive care
- Grades 2 to 4 ICANS: Supportive care, including a possible transfer to the intensive care unit, and treatment with corticosteroid and other drugs to suppress the immune system or help prevent and treat seizures

Questions to ask your healthcare team

- Is ICANS a possible side effect of my treatment?
- What symptoms should I watch for?
- What can I expect with ICANS?
- What can I do to manage or prevent this side effect?
- When and how should I contact you if I have ICANS symptoms?
- Can you reduce the medication dosage of my treatment if I start to have side effects?

Track your side effects with the
LLS Health Manager App
bloodcancers.ca/health-manager-app

Managing your side effects is an important part of cancer care. Tracking your medication, side effects, and food and nutrition intake allows you to share the information easily with your doctor to identify patterns and strategies.

Your healthcare team is there to support you throughout your treatment. Be sure to contact them if you have side effects so they can be managed quickly.

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