



InfoSheet

MANAGING IMMUNE EFFECTOR CELL-ASSOCIATED NEUROTOXICITY SYNDROME (ICANS) ASSOCIATED TO TREATMENT

Immunotherapies used to treat myeloma, more specifically Chimeric Antigen Receptor (CAR) T-cell therapies and bispecific antibodies, are T-cell-engagers that have the ability to target and destroy myeloma cells.

While they play an important role with the cells in your immune system, they unfortunately come with their load of side effects. These may include, among others: infusion or injection-related reactions, cytokine release syndrome (CRS), immune effector cell-associated neurotoxicity syndrome (ICANS), other neurologic events, infections, gastrointestinal problems, damage to nerves (peripheral neuropathy), lower blood cell counts, abnormal levels of minerals, and other potential more specific side effects such as temporary vision or skin problems.

This InfoSheet informs how the healthcare team monitors for a potential case of neurotoxicity syndrome after an immunotherapy is administered to a patient. It helps recognize its signs and symptoms, and understand its management to make sure the patient is in a safe environment.

Definition and causes of ICANS

Immune effector cell-associated neurotoxicity syndrome, known under the acronym ICANS, is an inflammatory reaction of the immune system that is somewhat related to CRS, but it actually occurs when that inflammatory response goes into the nervous system. That happens when the immune proteins, cytokines and some of the immune cells, leak into the nervous system and cause damage and inflammation to the brain. In other words, they cross the blood brain barrier, which usually protects us from a lot of this kind of damage to the nervous system.

ICANS is less common than CRS, and severe ICANS is also less common than severe CRS. People who have a higher burden of disease (have more cancer in their body) and get higher dose of treatment, particularly older patients, are at higher risk of this toxicity. According to Dr. Joseph Mikhael, IMF Chief Medical Officer, in his presentation on the *Early Side Effects of Bispecific Antibodies*, less than 10% of patients receiving bispecific antibodies experience ICANS.

This neurological complication usually occurs in the days or weeks following a myeloma immunotherapy treatment that activates T-cells. It typically happens after or at the same time as CRS. Although it can be quite frightening and it needs to be treated aggressively, most patients do really well.

Signs and symptoms of ICANS

ICANS manifests itself as any of these neurological symptoms:

- Headaches or migraines
- Confusion
- Disorientation
- Loss of consciousness
- Vision impairment
- Partial loss of the ability to speak or write
- Concentration issues
- Tremor
- Lethargy
- Muscle weakness
- Seizures
- Cerebral edema

Close monitoring by the healthcare team and the caregiver is key. There are many ways to measure this toxicity as it develops. The healthcare teams uses a scoring system to determine how severe the ICANS is. The patient is being asked basic questions such as “what is your name” and “where are you”, and undergo simple mental tasks. The doctor will look if there are damages to their sensations and how they move, as well as evidence of seizure activity or swelling in the brain.

How is ICANS prevented and treated?

There is not really a great way to prevent ICANS.

Like for CRS, a step-up dosing strategy of bispecific antibodies may be considered to minimize the side effects and reduce the likelihood of ICANS by preventing an overreaction of the immune system. In this case, the patient receives an initial reduced dose of drug followed by a gradual increase in the dose to allow the immune system to slowly become familiar with the new medication that is being introduced to the body.

Though most ICANS cases are manageable, prompt diagnosis and management of symptoms are essential to prevent serious complications and improve patient outcomes.

Steroids (e.g. dexamethasone) often given in combination with myeloma treatments, alone or combined with anakinra (Kineret), help to control and regulate toxicity syndrome when mild.

Moreover, the doctor involves the neurologist to perform brain imaging (CT scan or MRI of the brain) or an electroencephalogram (EEG) to measure the electrical activity of the brain. This will help determine the need to start anti-seizure medication as prevention or if they see early signs of seizure in order to manage this condition. They may also order a lumbar puncture to ensure that there is no infection or underlying problem, or order tests to check that the patient is not suffering from epilepsy.

In more severe cases, the intensive care unit colleagues are involved early in the process in case the patient needs to be transferred to the ICU, where supportive care and intravenous fluids can be dispensed. The dose and frequency of steroids can be increased, such as those of anakinra, or other agents may be introduced to block inflammation in the brain and solve the problem when ICANS progresses.

Precautionary measures

- It is extremely important that you speak to your healthcare team if you suspect signs of neurotoxicity syndrome as complications can lead to neurological disorders such as convulsions and even paralysis.
- Caregivers must remain attentive to signs of confusion or unusual changes in the patient's behavior, and notify the medical team accordingly.
- Patients need to be monitored frequently for early indications of side effects and given rapid care and supportive treatment if needed.
- Your healthcare team may hold treatment in case of active infection or if significant CRS and/or ICANS occur.
- Do not stop or adjust medications without discussing it with your healthcare provider. They may change your dose or schedule of medication to help reduce your discomfort.

Use Myeloma Canada's **Myeloma Monitor** to help you store, organize, and track your symptoms. Access the Myeloma Monitor App [here](#).

To learn more about CAR-T cell and bispecific antigen therapies, consult Myeloma Canada's "**Myeloma Immunotherapy**" and "**Clinical Trials: are they an option for me?**" InfoGuides in the Resource library at www.myeloma.ca.

Your healthcare team and your pharmacist, are also there to support you. It's important to share your symptoms with them.

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