



# 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 patients are 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.

