



# InfoSheet

## MANAGING CYTOKINE RELEASE SYNDROME (CRS) ASSOCIATED TO TREATMENT

**Unlike chemotherapy, myeloma immunotherapy better targets myeloma cells and spares most healthy cells. It helps your immune system recognize and destroy myeloma cells.**

**Because of the way myeloma immunotherapy works in the body, some of the side effects that may occur are different from those seen in conventional myeloma treatments. 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 will give you more information about the cytokine release syndrome and the way it affects your body. We will learn how to recognize its signs and symptoms, better manage its undesirable effects on the body and limit the damages.**

### Definition and causes of CRS

Cytokine release syndrome, or namely CRS, is a severe and sudden inflammatory syndrome caused by a large, rapid and excessive release of cytokines into the blood. Cytokines are small proteins that play a crucial role to combat infections. However, the presence of too many cytokines can cause inflammation and an overreaction of the immune system.

This reaction often happens after an infection (e.g. COVID-19) but it is also observed with certain treatments associated with cancers. More precisely, such complication can occur after certain T-cell-engaging (TCE) immunotherapies such as Chimeric Antigen Receptor (CAR) T-cell therapies, like idecabtagene vicleucel and ciltacabtagene autoleucel, and bispecific antibody therapies, notably elranatamab, talquetamab and teclistamab, being investigated for myeloma. In this regard, the infusion of CAR-T cells or the injection of bispecific T-cell engagers trigger the activation of T-cells (also called T lymphocytes) binding them to the tumour cells.

CRS usually occurs within the first few doses of bispecifics or CAR-T (most frequently within the first 14 days) and typically happens before or at the same time as the neurotoxicity syndrome. The degree of CRS is graded on a scale of 1 to 4, based on the key symptoms and signs of fever and blood pressure. Grades 1 and 2 are considered

mild, while Grades 3 and 4 are severe to life-threatening and require admission to the hospital in an intensive care unit to ensure patients are given medications to boost their blood pressure. Fortunately, most cases of CRS are Grades 1-2, and generally respond very well to treatments designed to reduce inflammation while calming immune system activation.

### Signs and symptoms of CRS

You should inform your healthcare team if you experience any of the signs and symptoms below (particularly if you are currently on CAR-T cell or on a bispecific antigen treatment):

- Fever, chills and aches (similar to flu symptoms)
- Difficulty breathing
- Dizziness
- Nausea
- Tachycardia (fast heartbeat)
- Low blood pressure
- Low blood oxygen concentration (desaturation)
- Fatigue
- Multi-organ failure

Most often CRS is characterized by fever, a drop in blood pressure and/or a reduction in blood oxygen concentration (desaturation). These signs and symptoms will enable the healthcare team to establish a diagnosis of CRS.

The impact of CRS on the body can be visualized as:

