

Cytokine Release Syndrome

WHAT PATIENTS & CAREGIVERS NEED TO KNOW



WHAT ARE CYTOKINES?

Cytokines are proteins that control the activity of the immune system, which works to fight off infections and prevent disease. Cytokines trigger the body's immune response by communicating with other cells, directing them to locate and target the lymphoma cells detected by the immune system.

CYTOKINE RELEASE SYNDROME (CRS)

Cytokine Release Syndrome (CRS) is a potential side effect of immunotherapy treatments, which harness the body's immune system to fight cancer.

Immunotherapies, such as CAR T-cell therapy, bispecific antibodies, and monoclonal antibodies, target T-cells in the immune system to help recognize and attack lymphoma cells. The thymus gland plays a key role in producing T-cells, which are crucial for fighting infected or abnormal cells. After immunotherapy, the heightened T-cell activity leads to the release of cytokines, which can cause an overactive immune response. This excessive cytokine release can lead to inflammation, potentially attacking healthy cells, tissues, and organs. In severe cases, this can result in life-threatening symptoms.

Symptoms of CRS can affect different organ systems, ranging from mild flu-like symptoms to severe, life-threatening reactions. See below for a list of symptoms. Your healthcare team will monitor for clinical signs of CRS, as symptoms may develop days or up to 1-2 weeks after immunotherapy.

WHO IS AT RISK FOR CRS?

CRS is most common in patients undergoing T-cell immunotherapy, as the therapy triggers a significant cytokine release when T-cells attack lymphoma cells. Patients with a higher disease burden are at greater risk for developing severe CRS. While higher doses of immunotherapy are often required for advanced stages of cancer, they also increase the risk of CRS.

While CRS cannot be prevented, reducing the cancer burden before immunotherapy—through chemotherapy or other treatments—can help minimize the risk and severity of CRS.

WHY IS IT IMPORTANT TO REDUCE THE RISK OF CRS?

An overactive immune system, which attacks both harmful and healthy cells, can lead to significant tissue damage and weakness. Left untreated, CRS can result in organ failure and potentially be life-threatening due to inflammation caused by the massive cytokine release. Timely treatment is essential for preventing serious complications.

TREATMENT OPTIONS FOR CRS

CRS severity varies, and treatment is tailored accordingly. Your healthcare team will grade CRS based on symptoms and their impact, helping determine the appropriate treatment.

- **Mild CRS** may only require supportive care, including monitoring and managing symptoms like fever, rash, and headaches.
- **Severe CRS** may require treatments such as high-dose vasopressors to support blood pressure, or immunosuppressors like tocilizumab and corticosteroids, which reduce immune activity. Tocilizumab, often the first line of treatment, blocks cytokines and can lead to rapid symptom improvement. If necessary, a second dose of tocilizumab or corticosteroids will be administered.

WHAT YOU CAN DO FOR YOURSELF

SIGNS AND SYMPTOMS OF INFECTION

If you experience any of the following symptoms after immunotherapy, contact your healthcare provider or seek emergency care immediately:

- Fever with temperatures close to or higher than 40°C (fever can be a crucial indicator of infection)
- Cough or shortness of breath
- Rash
- Chills
- Fatigue
- Muscle aches
- Nausea or vomiting
- Diarrhea
- Headache
- Low blood pressure
- Fast heart rate (over 100 bpm)
- Abnormal heart rhythm
- Reduced oxygen levels

Most side effects are short-lived, but some may persist for weeks or months after treatment. In rare cases, side effects can be permanent. Additionally, some side effects may not appear until long after treatment has ended, known as late side effects. Your doctor will discuss potential side effects with you before starting treatment. Any symptoms following immunotherapy should be taken seriously, and immediate evaluation is necessary. If you develop a fever after treatment, it could lead to life-threatening complications if not treated promptly. Seek medical attention as soon as possible.

QUESTIONS TO ASK YOUR DOCTOR

Consider taking notes on any side effects during or after treatment. This can help you communicate your symptoms and concerns with your doctor, improving understanding and reducing stress. Here are some questions you may also want to ask your doctor before treatment:

- What are the potential risks or side effects of this treatment, and how serious are they?
- How will my symptoms be monitored during and after treatment?
- What symptoms should I report immediately, and who should I contact if they occur?
- How long should I monitor for side effects, and when will they subside?
- Are there any foods or activities I should avoid during and after treatment?