



# Humanigen

## FACTS ON CYTOKINE STORM

### ▶ What is “cytokine storm”?

Cytokine storm is an **immune hyper-response**. It takes place when the body's innate immune system over responds to a threat (often an infectious agent, such as a virus or a foreign body, as is the case with CAR-T) by suddenly releasing certain immune messengers known as cytokines into the bloodstream in quantities that can be out of proportion to the threat, and sometimes rapidly or long after the threat has disappeared.<sup>1</sup>

**This can lead to a potentially fatal hyperactive immune response that is often referred to as cytokine release syndrome (CRS), or cytokine storm.**

### ▶ Why is cytokine storm a problem?

The exaggerated release of cytokines into the bloodstream results in an immune response that can ultimately surpass the immune threat and cause the body to attack its own healthy tissues, including organs. The severe immune reaction brought on by a cytokine storm can damage the lungs, kidneys, heart, blood vessels, brain, nerves, liver, and lead to coagulation disorders which can result in the formation of blood clots and/or excessive bleeding.

**Cytokine storm can ultimately lead to multiple or individual organ failure and death.<sup>1</sup>**

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**Humanigen has developed a neutralizing, IgG1, monoclonal antibody against human GM-CSF, using proprietary Humaneered<sup>®</sup> technology.**





## ▶ What are the symptoms of cytokine storm?

The symptoms of cytokine storm may include fever, difficulty breathing, inflammation (redness and swelling), fatigue, nausea, tremors, rash, and/or bruising. Sometimes, dangerously low blood pressure, respiratory failure, heart rhythm or neurological abnormalities (like fatigue, headaches, hallucinations, or coma), and/or kidney and liver failure can occur.<sup>2</sup> A blood test can measure a number of inflammatory markers and indicate whether a patient is progressing into cytokine storm.

## ▶ When does cytokine storm occur?

Variations of this immune hyper-response can occur in a range of conditions, including as a result of treatment of certain blood-borne cancers with CAR-T therapy, and in graft versus host disease, which is sometimes seen with bone marrow and other stem cell transplants. It has also been known to play an important role in disease severity and mortality of viral diseases, including SARS and MERS, as well as COVID-19.<sup>3</sup>

## ▶ What is the connection of cytokine storm to COVID-19?

Some of the most critically ill COVID-19 patients have significantly elevated levels of certain inflammatory cytokines, such as GM-CSF, compared to other individuals who are infected but experience less severe symptoms.<sup>4</sup> Several studies analyzing cytokine profiles from COVID-19 patients suggest that cytokine storm is directly correlated with the worst clinical outcomes of the disease – acute respiratory distress syndrome (ARDS), lung injury, and multi-organ failure. Mortality in COVID-19 patients has been linked to the presence of cytokine storm induced by the virus.<sup>5</sup>

**Suppressing or preventing cytokine storm may be key to preventing the rapid deterioration of patients with COVID-19 infection, the need for mechanical ventilation and potentially saving patients' lives.<sup>6</sup>**

### Sources

1. Harvard Health Publishing. COVID-19 Basics. Updated August 21, 2020. Accessed August 27, 2020. <https://www.health.harvard.edu/diseases-and-conditions/covid-19-basics>
2. NIH National Cancer Institute. Cytokine Storm. Accessed August 27, 2020. <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cytokine-storm>
3. Tisoncik JR, et al. Microbiol Mol Biol Rev. 2012 Mar; 76(1): 16-32.
4. Costela-Ruiz VJ et al. Cytokine Growth Factor Rev. 2020 Jun 2.
5. Ragab D et al. Front Immunol. 2020; 11: 1446.
6. Ye Q, et al. J Infect. 2020 Jun; 80(6): 607-613.

