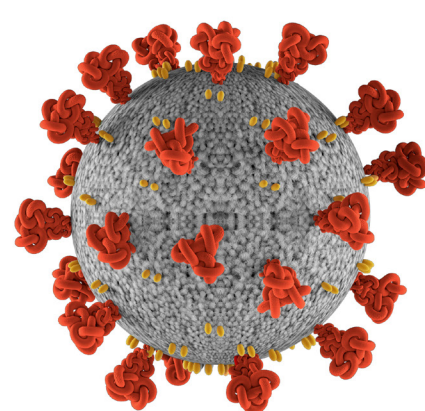


Cytokine Storm

About COVID-19

COVID-19 is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).¹ Coronaviruses are part of a larger family of viruses that can cause illness ranging from the common cold to more severe diseases.¹

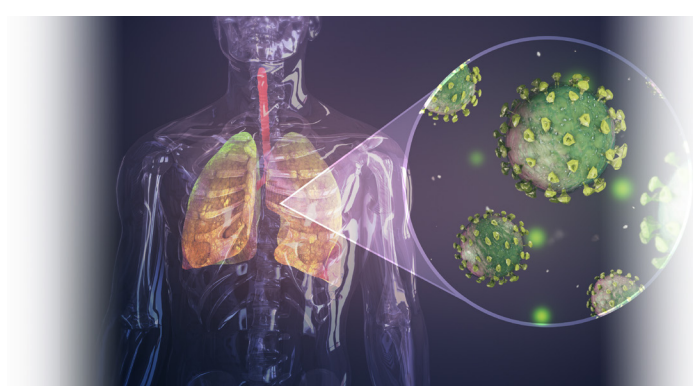
Since emerging in humans for the first time in late 2019, COVID-19 has developed into a public health crisis and global pandemic,² due to its novel disease type and high rates of transmissibility between humans.³



Balancing the Immune System

When the body is exposed to a viral infection, the immune system is the first line of defense. As part of this response, cytokines—small proteins released from cells—work to help maintain the immune system’s balance of pro- and anti-inflammatory mechanisms to preserve systemic homeostasis—or balance—and aid in pathogen clearance following an infection.^{2,4}

In some patients with active COVID-19 infections, a dysregulation of the immune system’s response may occur, leading to the overactivation of pro-inflammatory pathways. This response is known as a “cytokine storm” or “cytokine release syndrome,” and is believed to lead to more severe forms of the disease.²



What is the Cytokine Storm?

A cytokine storm can result from the overproduction of early response pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-6 (IL-6) and interleukin-1 β (IL-1 β), in response to a wide variety of infectious and noninfectious diseases.^{4,5}

Signs and symptoms of a cytokine storm may include:⁴



Fever



Rash/Redness



Muscle and joint aches or swelling



Difficulty breathing or loss of lung function

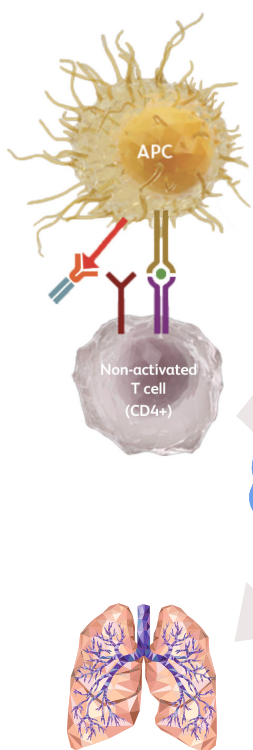
Patients who develop severe cases of COVID-19 as a result of a cytokine storm may progress to acute respiratory distress syndrome (ARDS) and multiple-organ failure that requires intensive care unit (ICU) care.^{2,3} In some cases, life-threatening complications including severe infections can occur, and may lead to death.^{2,4}

Potential Therapeutic Benefit of Targeting the Cytokine Storm

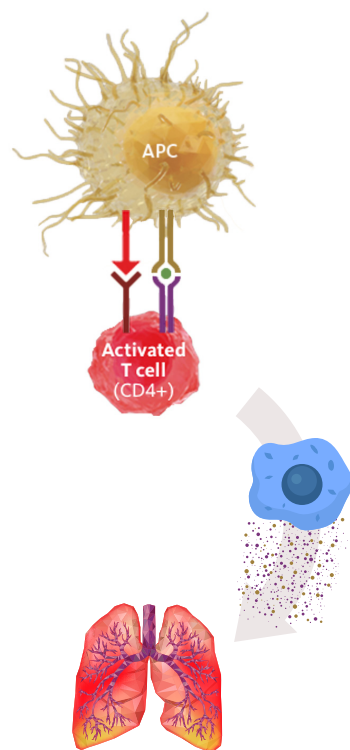
One potential target for treating a cytokine storm involves therapeutically inhibiting cell activation central to this process. This includes targeting cells that may be contributing like helper T cell (CD4+), B cells or macrophages.

Inhibiting these may prevent the excessive release of TNF, IL-6, IL-1 β and other cytokines and mediators of inflammation associated with severe COVID-19. This may prevent or reduce the cytokine storm driving most severe disease.^{2,4}

Inhibition of T cells to Prevent Cytokine Storm



Activated T cells Lead to Cytokine Storm/Pro-inflammatory Cytokine Release



Bristol Myers Squibb is committed to researching and pursuing treatment options and innovative development approaches to help deliver transformational medicines for patients.

To learn more about Bristol Myers Squibb’s efforts in COVID-19 research, please visit <https://www.bms.com/about-us/responsibility/coronavirus-updates.html>

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 2. Qing Y, Wang B and Mao J. The Pathogenesis and Treatment of the ‘Cytokine Storm’ in COVID-19. *J Infect.* 2020; 80(6):607-613.
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