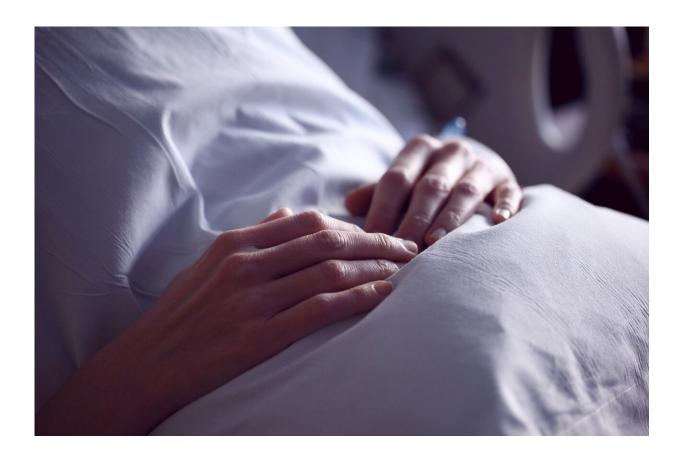


Better outcomes in severe COVID-19 patients administered interleukin-6 inhibitors early

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New research from Boston Medical Center found that patients experiencing severe COVID-19 symptoms had improved outcomes when administered an Interleukin-6 (IL6ri) inhibitor, sarilumab or tocilizumab, given to mediate severe systemic inflammatory responses.



The treatment was more effective when administered earlier in the disease course and reduced mortality rates and the need for intubation. Published in the *International Journal of Infectious Diseases*, the results show Interleukin-6 inhibitors appear to be a more effective treatment compared to other options, including remedesvir and dexamethasone, which are recommended and currently used in the pandemic.

Elevated IL-6 levels may mediate the severe systemic inflammatory responses that occur in patients with severe acute respiratory syndrome or a COVID-19 infection. The Boston Medical Center patients in this study were divided into two groups, stage IIB and stage III based on their fraction of inspired oxygen (FiO2). Patients requiring up to 45 percent FiO2 were considered to be stage IIB and those more severe who were requiring greater than 45 percent FiO2 were considered to be stage III. The discharge rate was higher for the stage IIB group compared to the stage III group, showing the impact that earlier administration can have throughout the progression of COVID-19. The average length of stay in the hospital was 12.9 days, but patients treated in stage IIB had a shorter average length of stay (11.3 days) than those in stage III (15 days). A total of 68 patients (26.7 percent) required mechanical ventilation, and of these patients, 44 were intubated 24 hours later, after receiving IL6ri.

"At a time where treatments are being tested with urgency throughout the COVID-19 pandemic, our study results offer some hope towards finding solutions to better treat patients throughout this disease," said Manish Sagar, MD, an infectious diseases physician and researcher at Boston Medical Center, and associate professor of medicine and microbiology at Boston University School of Medicine.

This observational study included 255 COVID-19-confirmed patients being treated with IL6ri during stage IIB (149 patients) and stage III of the disease (106 patients). An institutional treatment panel consisting of providers from departments of adult and pediatric infectious diseases, rheumatology and pulmonary/critical care, as well as clinical pharmacy



specialists collaborated to provide recommendations for or against treatment using IL6ri. Once an appropriate patient was identified, they were given IL6ri (sarilumab or tocilizumab) based on iteratively reviewed guidelines. The IL6ri was initially reserved for critically ill patients, but after review, the treatment was liberalized to patients with lower oxygen requirements.

The IL6ri recipients in this study had considerably higher supplementary oxygen requirements, indicating more advanced disease than patients in previous remdesivir and dexamethasone trials, and would have been expected to have a higher mortality rate. The study's sampling-with-replacement analysis found that the patients who received IL6ri had a lower mortality rate than patients in the intervention and control groups of the remdesivir and dexamethasone trials. The 22.9 percent mortality rate for the 105 BMC patients that required ICU care (41.1 percent) was considerably lower than previously published 45-50 percent mortality in other ICU studies.

"The greatest benefit with IL6ri use was seen in patients who received the drug in an earlier stage, prior to critical respiratory decompensation, showing the importance of prompt testing and treatment," said Pranay Sinha, MD, also an infectious diseases physician and researcher at Boston Medical Center. "We speculate that immunomodulatory drugs like IL6ri or dexamethasone may be more effective before immunemediated damage has occurred. We hope these findings can help guide physicians as we seek solutions to reduce mortality, increase extubation, reduce length of stay in the hospital, and have more patients discharged from the hospital alive."

More information: Pranay Sinha et al, Early administration of Interleukin-6 inhibitors for patients with severe Covid-19 disease is associated with decreased intubation, reduced mortality, and increased discharge, *International Journal of Infectious Diseases* (2020). DOI: 10.1016/j.ijid.2020.07.023



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