New trial finds arthritis drug tocilizumab no better than standard care for severe COVID-19

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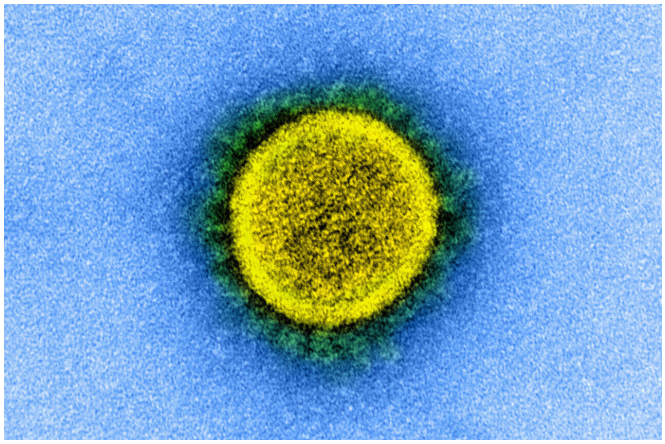

SARS-CoV-2 (shown here in an electron microscopy image). Credit: National Institute of Allergy and Infectious Diseases, NIH

Adding the arthritis drug tocilizumab to standard care for patients in hospital with severe or critical COVID-19 is no better than standard care alone in improving clinical outcomes at 15 days, finds a new trial published by *The BMJ* today.

There was an increased number of deaths at 15 days in patients receiving tocilizumab, resulting in the trial being stopped early.

Today's results contradict earlier observational studies suggesting a benefit of tocilizumab. However, observational effects are limited by a high risk that they may be due to other unknown (confounding) factors—and some studies have not yet been peer reviewed or published in a medical journal.

A randomised trial assessing tocilizumab in critically ill patients with COVID-19 (REMAP-CAP) published as a preprint earlier this month, found a beneficial effect of the drug on days free from organ support within 21 days and mortality. Reasons for these apparently contradictory effects, for example differences between patients' characteristics, need to be assessed in future analysis, say the researchers.

Tocilizumab blocks a specific part of the immune system (interleukin 6) that can go into overdrive in some patients with COVID-19. Doctors think this might help lessen the body's inflammatory response to the virus and avert some of the more dire consequences of the disease, but its effects are not well defined.

To test this theory, researchers based in Brazil conducted a randomised controlled trial comparing tocilizumab plus standard care with standard care alone in patients admitted to hospital with severe or critical COVID-19.

Their findings are based on 129 relatively young adults (average age 57 years) with confirmed COVID-19 at nine hospitals in Brazil between 8 May and 17 July 2020.

Patients were receiving supplemental oxygen or mechanical ventilation and had abnormal levels of at least two chemicals linked to inflammation in their blood.

Patients were randomly divided into two groups: 65 received tocilizumab plus standard care and 64 received standard care alone.

Other potentially important factors, such as underlying conditions and use of other medication, were taken into account and all patients were monitored for 15 days.

By day 15, 18 (28%) patients in the tocilizumab

group and 13 (20%) in the standard care group were receiving mechanical ventilation or died.

Death at 15 days occurred in 11 (17%) patients in the tocilizumab group compared with 2 (3%) in the standard care group.

The increased number of deaths in the tocilizumab group raised safety concerns and the trial was stopped early. In both groups, deaths were attributed to COVID-19 related acute respiratory failure or multiple organ dysfunction.

The researchers point to some limitations including the small sample size, which affects the chances of detecting a true effect. However, results were consistent after adjusting for levels of respiratory support needed by patients at the start of the trial, suggesting that the findings withstand scrutiny.

As such, the researchers conclude that in patients with severe or critical COVID-19, "tocilizumab plus standard care was not superior to standard care alone in improving clinical status at 15 days and might increase mortality."

And they say these results "raise questions about an anti-inflammatory approach in the treatment of COVID-19 beyond corticosteroids."

More information: Effect of tocilizumab on clinical outcomes at 15 days in patients with severe or critical coronavirus disease 2019: randomised controlled trial, *BMJ* (2021). DOI: 10.1136/bmj.n84

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