Tocilizumab cuts mortality risk in severely ill COVID-19 patients finds new trial conducted in India

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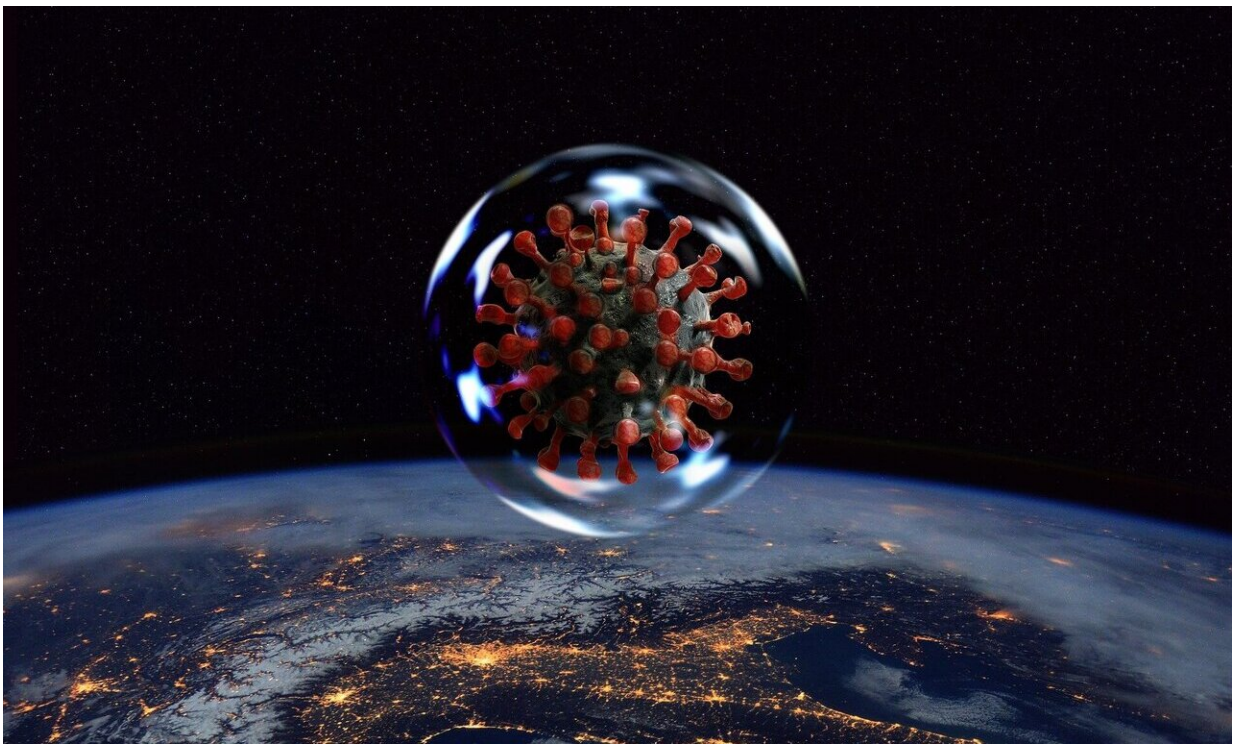

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Tocilizumab, an anti-inflammatory drug used to treat rheumatoid arthritis, improves outcomes in severely ill COVID-19 patients, finds the results of a new trial conducted in hospitals across India—one of the

world's most ethnically diverse countries. Researchers from the University of Bristol and Medanta Institute of Education and Research in India who led the study, published in *The Lancet Respiratory Medicine*, say it adds to existing evidence supporting the drug's use in critically ill patients.

Conducted in 12 public and private hospitals across India, the COVID India Tocilizumab (COVINTOC) phase 3 randomized controlled trial aimed to investigate whether tocilizumab could prevent disease progression and mortality in hospitalized patients with moderate to severe COVID-19.

The study team recruited 180 patients (age 18-years and over) who had been hospitalized with moderate to severe COVID-19. Of these, 89 patients were randomized to receive standard care, and 91 patients were randomized to receive standard care plus tocilizumab.

Patients were followed up over a 28-day period to record any clinical improvement markers and assess disease progression from moderate to severe or from severe to death. The team also recorded whether patients experienced adverse events, serious adverse events, and post-treatment infections, and requirement for renal replacement drugs.

Analysis of the data revealed a subset of patients with severe disease in whom tocilizumab might have a reduced risk for progression to death if treated with tocilizumab in addition to standard care. However, clinical parameters or biomarkers to reliably identify these patients and the optimal timing of treatment during COVID-19 progression remain unknown. The authors conclude that while the study does not support the routine use of tocilizumab in adults with COVID-19 it adds to the growing evidence suggesting it may help some severely ill patients.

The trial's lead co-author, Professor A. V. Ramanan from the University

of Bristol's School of Clinical Sciences, and Consultant Paediatric Rheumatologist at Bristol Royal Hospital for Children, said: "Our study suggests tocilizumab might still be effective in patients with severe COVID-19 and so should be investigated further in future studies. It adds to existing evidence from the RECOVERY and REMAP-CAP studies which demonstrate that tocilizumab does have a significant impact on reducing mortality in those with COVID-19 requiring oxygen or being ventilated.

"After dexamethasone (steroids), this is still the most significant advance in the treatment of COVID that has an impact in reducing deaths."

Lead co-author Dr. Arvinder Soin, Chairman of the Medanta Liver Transplantation Institute at Gurugram, India, said: "While there were no differences in mortality and the need for ventilation among the two groups of patients when moderate and severe categories of patients were considered together, a subgroup analysis of the severe patients in the two groups showed a lower mortality at 28 days (8/50; 16 per cent) among those who received tocilizumab compared to those who did not (14/41; 34 per cent). The reported adverse events did not differ between the tocilizumab and standard care arms.

"Given the conflicting results of the previous studies, millions were wasted last year on the indiscriminate use of tocilizumab, as the precise stage of the disease in which to use the drug was not clear. This study plugs an important gap in knowledge on COVID treatment and clarifies that tocilizumab should be administered to patients in the severe category. Incidentally, last month, two major studies from the UK—the RECOVERY Trial and the REMAP-CAP study—have revealed similar findings, that tocilizumab reduces mortality among patients with severe COVID-19."

The trial was conducted against incredible odds across multiple sites

under difficult conditions in a country that has the second highest COVID-19 caseload in the world.

Professor Ramanan added: "Challenges to conducting randomized controlled trials during the COVID-19 pandemic are exacerbated in low- and middle-income countries, and several hurdles were encountered during this trial in India. Patients treated with drugs not licensed for the condition they have or compassionate use of treatments in patients with COVID-19 is common and can impede enrolment into clinical trials. Ensuring follow-up is challenging for patients who are likely to be discharged early because of the high demand on hospital resources and for patients who might have logistical difficulty traveling for return visits. We believe it is important that all potential therapies be trialed across diverse settings, not only in North America and Europe."

More information: Arvinder S Soin et al. Tocilizumab plus standard care versus standard care in patients in India with moderate to severe COVID-19-associated cytokine release syndrome (COVINTOC): an open-label, multicentre, randomised, controlled, phase 3 trial, *The Lancet Respiratory Medicine* (2021). DOI: 10.1016/S2213-2600(21)00081-3

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