

## Clinical trials present results to guide care of severely ill COVID-19 patients using routinely available drugs

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The Global Coalition for Adaptive Research (GCAR) in collaboration with the University of Pittsburgh and UPMC, on behalf of the REMAP-



CAP Investigator Network, announce clinical trial results examining the use of vitamin C and simvastatin to treat severely ill patients with COVID-19.

Published in JAMA and NEJM, and presented at the European Society of Intensive Care Medicine in Milan, the studies are part of the ongoing Randomized Embedded Multifactorial Adaptive Platform for Community Acquired Pneumonia (<u>REMAP-CAP</u>) trial.

Simvastatin, a widely available and inexpensive drug that is included on the <u>WHO list of essential medicines</u>, was shown to have a high probability (96%) of improving outcomes (a combination of survival and length of time patients need support in an <u>intensive care unit</u>) when started as a treatment for critically ill patients with COVID-19, and a 92% chance of improving survival at three months. This equates to one life saved for every 33 patients treated with simvastatin. A total of 2,684 critically ill patients were included at 141 hospitals across 13 countries.

"These results are really encouraging as they have shown that treatment with simvastatin is highly likely to improve outcomes in critically ill patients with COVID-19," said Professor Danny McAuley, Professor and Consultant in Intensive Care Medicine at the Royal Victoria Hospital and Queen's University Belfast and lead investigator for the Simvastatin Domain of REMAP-CAP. "This research will help health care professionals internationally to improve the treatment of patients with COVID-19."

Vitamin C is widely available around the world and was used in some settings for the treatment of COVID-19. Through harmonizing two <u>clinical trials</u>—REMAP-CAP and <u>LOVIT-COVID</u>—over 2,500 patients in 20 countries took part, including both critically ill and non-<u>critically ill</u> <u>patients</u> with COVID-19 in hospital.



It was shown that high dose vitamin C did not improve outcomes for patients. This is the largest trial examining high-dose vitamin C in COVID-19 and provides evidence that high-dose vitamin C is not beneficial and suggests a high probability that it may be harmful.

"Harnessing the power of global collaboration, the harmonized REMAP-CAP and LOVIT-COVID trials have investigated vitamin C, a potential therapy for COVID-19, and have shown it to be ineffective and probably harmful," said Dr. Neill Adhikari, co-lead investigator for the LOVIT-COVID trial and of the Vitamin C Domain of REMAP-CAP, and of Sunnybrook Health Sciences Center.

"The results from this trial suggest that the use of vitamin C in hospitalized COVID-19 patients should be de-adopted." Dr. François Lamontagne, co-lead investigator of these trials and of Université de Sherbrooke, added, "The results underscore the health and <u>economic</u> <u>benefits</u> of identifying and abandoning readily available interventions that are ineffective and potentially harmful to patients."

Through this global initiative, combining clinical trial data and recruiting patients from countries around the world, this model of research continues to produce important evidence for the clinical communities.

"The beauty of these trials is in connecting doctors across continents to provide the best possible treatment for the sickest patients with COVID-19, while learning from each other to arrive at evidence-based answers to improve standard of care for patients worldwide," said Derek Angus, MD, MPH, FRCP, U.S. principal investigator of REMAP and chair of critical care medicine at UPMC and the University of Pittsburgh School of Medicine.

"To have both of these results from REMAP-CAP published simultaneously is testament to the ability of this trial to efficiently



evaluate multiple interventions. Through this horrific pandemic, we've pioneered a new way to rapidly address some of the biggest treatment questions, caring for patients today and preparing to respond more nimbly in the future. It has been personally rewarding to be a part of this process and see our aspirational goal become reality."

REMAP-CAP is a global adaptive platform trial investigating multiple treatments for hospitalized patients with respiratory tract infection. The trial mobilized to evaluate specific treatments for COVID-19 patients in ICUs in early March 2020, and continues to evaluate multiple interventions for COVID-19, influenza, and other causes of severe respiratory infection.

A total of 290 U.S. patients participated in the <u>vitamin</u> C domain at UPMC, the Ohio State University Wexner Medical Center, and Oregon Health & Science University.

**More information:** Intravenous Vitamin C for Patients Hospitalized With COVID-19 Two Harmonized Randomized Clinical Trials, *JAMA* (2023). DOI: 10.1001/jama.2023.21407

Simvastatin in Critically Ill Patients with COVID-19, *New England Journal of Medicine* (2023). DOI: 10.1056/NEJMoa2309995

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