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Global study to test malaria drug to protect health workers from COVID-19

COVID-19 Therapeutics Accelerator to fund international trial of chloroquine

An international group of physicians and scientists, including the University of Cape Town (UCT) and the University of the Witwatersrand, is establishing a research network to evaluate promising therapies for COVID-19 with a boost of \$9 million in philanthropic support.

The group, called the COVID-19 Research Outcomes Worldwide Network (CROWN) Collaborative, is testing whether the antimalaria drug chloroquine can prevent COVID-19 infection or decrease its severity in front-line health-care workers. Up to 55 000 such workers from across the globe will participate in the clinical trial, which the collaborative is calling the CROWN CORONATION trial.

The collaborative and the trial are funded by the COVID-19 Therapeutics Accelerator, an initiative with contributions from an array of public and philanthropic donors, intended to support research and development to bring effective, accessible COVID-19 treatments to market as quickly as possible.

Professor Bruce Biccadd, Deputy Head of the Department of Anesthesia and Second Chair in Anaesthesia at UCT, said: "This trial is important for many reasons. It repurposes a drug which has a long track record of safety in the management of malaria. It is a drug that is cheap and accessible in Africa. Importantly, if we can prevent COVID-19 infection or decrease the severity of the infection in healthcare workers, it means that we can ensure that our healthcare workforce can continue to provide care during this pandemic."

Washington University School of Medicine in St. Louis is the clinical coordinating center for this ambitious international trial. The investigators comprising the CROWN Collaborative are from prominent research organisations in African, European, North American and South American countries, including Cameroon, Canada, Ireland, Ghana, Peru, South Africa, United Kingdom, United States, and Zambia. The Medicines for Malaria Venture, a nonprofit foundation in Geneva, Switzerland, is also partnering with the group.

"Because of their repeated close contacts with infected patients, front-line health-care workers in all parts of the world have a higher risk of contracting COVID-19 than most members of the general public," said one of the study's principal investigators, Michael S. Avidan, MD, the Dr. Seymour and Rose T. Brown Professor and head of the Department of Anesthesiology at Washington University. "In some places, more than 10% of those who have become infected are health-care workers. There is an urgent need to identify drugs that are effective at preventing infection or mitigating its severity."

The study will recruit front-line health-care workers globally, including those from lower- and middle-income countries. That's important because in many such countries there are relatively few health-care workers per capita and protecting them from severe COVID-19 infection would provide a substantial public health benefit.

"An important way to protect the public at large is to do our best to protect the health-care workers," Avidan said. "It is very important that there is a global effort to protect health-care workers because when it comes to COVID-19, we're all in this together. Finding ways to keep health-care workers from getting seriously ill is one of the most important ways to protect vulnerable people everywhere."

This new trial will be important because of its immense size and global reach, as well as its use of three different but well-established chloroquine dose schedules in healthy people. Health-care workers in the trial will be divided randomly into four groups. Three of the groups will receive chloroquine at various doses. The fourth group will receive an inactive placebo. The researchers want to learn whether the drug can prevent health-care workers from developing COVID-19 disease or decrease the severity of illness for those who do become infected.

The researchers also want to determine the lowest dose required to provide a benefit. Health-care workers in the study will receive lower doses of chloroquine than have been given in most other trials that have focused on treating patients already sick with COVID-19. That is important because lower doses of chloroquine should have fewer side effects. Plus, with a limited supply of chloroquine globally, if a lower dose turns out to be just as effective as a higher dose, many more people could benefit from the drug.

"When people have to travel to parts of the world where malaria is a problem, they often take low doses of chloroquine to help prevent infection," said Avidan, also a professor of psychiatry and of surgery. "We want to learn whether this drug might work in a similar fashion in the case of COVID-19, or at the very least, whether low-dose chloroquine might help prevent the severe and life-threatening complications associated with the illness."

The study will last five months. Health-care workers who participate will take chloroquine or a placebo for the first three months and will be monitored for another two months. Those previously infected with COVID-19 or those who have underlying medical problems that might make it unsafe to take chloroquine, such as heart ailments, will not be eligible to participate.

Data from the trial sites will be compiled at University College London. Laurence Lovat, a professor of gastroenterology and biophotonics, is the study leader in the United Kingdom. "Our hypothesis is that chloroquine may decrease the COVID-19 burden by decreasing entry of the novel coronavirus into host cells and by inhibiting viral replication," Lovat said. "Furthermore, with its anti-inflammatory properties, chloroquine might

dampen the exaggerated and unregulated immune response in the host, which often is responsible for the unpredictable and severe complications of COVID-19.”

The CROWN CORONATION trial’s other principal investigators are Ramani Moonesinghe, a professor of perioperative medicine at University College London, and Professor Helen Rees, executive director of the Wits Reproductive Health and HIV Institute in Johannesburg. “In the African region, the healthcare workforce is under-resourced and overstretched, and the impact of the COVID-19 pandemic will make this situation worse,” Professor Rees said. “If an inexpensive drug such as chloroquine could help protect our health workers it would provide important insurance for many countries whose health-care systems could collapse if large numbers of health-care workers were to become infected and could not care for others who were sick with COVID-19.”

“There is quite a bit of interest in chloroquine for both the prevention and treatment of COVID-19 infection,” Avidan said. “It has shown promise treating patients with COVID-19, but the only way to determine accurately whether this drug actually works is to conduct rigorous, large-scale, randomized trials in multiple locations.”

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