Large clinical trial to study repurposed drugs to treat COVID-19 symptoms

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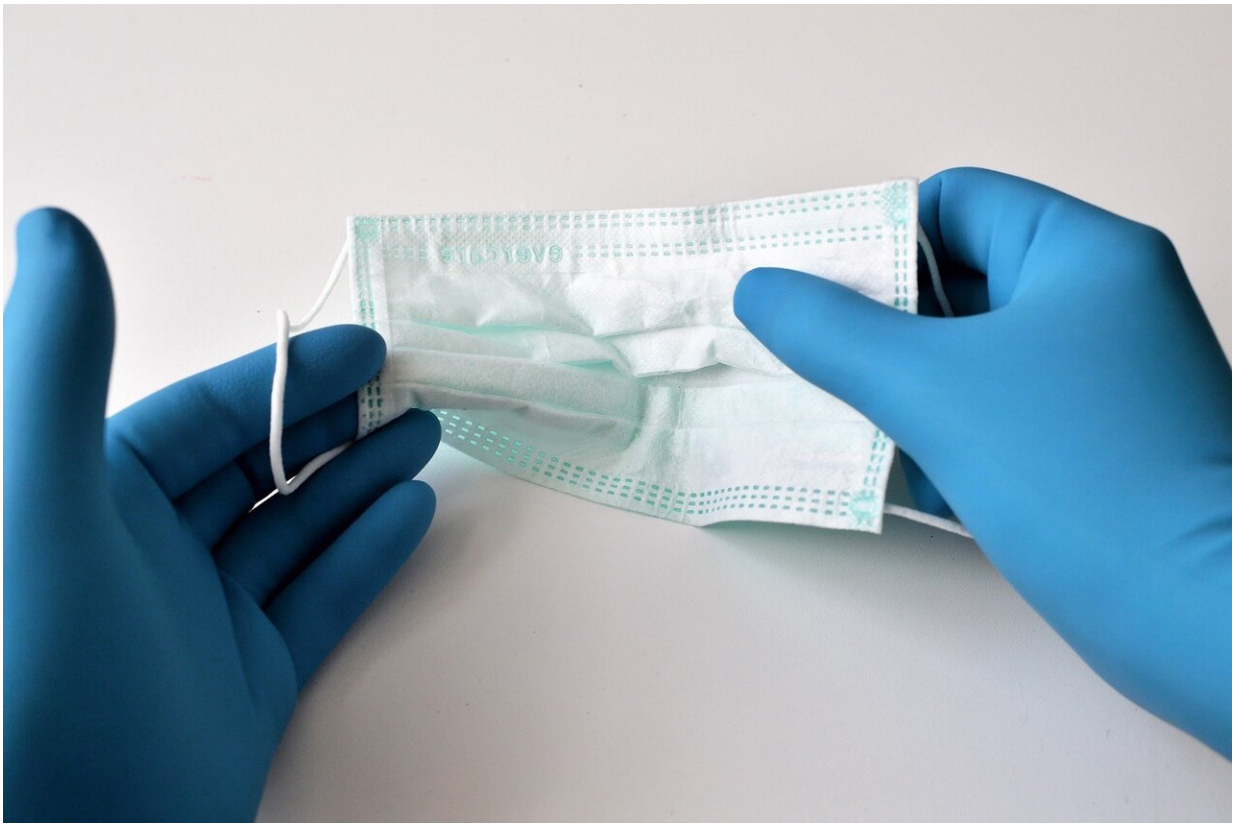

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Using an ACTIV master protocol, the trial will focus on potential interventions for mild-to-moderate illness.

The National Institutes of Health will fund a large, randomized, placebo controlled Phase 3 clinical trial to test several existing prescription and over-the-counter medications for people to self-administer to treat symptoms of COVID-19. Part of the Accelerating COVID 19 Therapeutic Interventions and Vaccines (ACTIV) public-private partnership, the ACTIV-6 trial aims to provide evidence-based treatment options for the majority of adult patients with COVID-19 who have mild-to-moderate symptoms and are not sick enough to be hospitalized. NIH will provide an initial investment of $155 million in funding for the trial.

"While we're doing a good job with treating hospitalized patients with severe disease, we don't currently have an approved medication that can be self-administered to ease symptoms of people suffering from mild disease at home, and reduce the chance of their needing hospitalization," said NIH Director Francis S. Collins, M.D., Ph.D. "ACTIV-6 will evaluate whether certain drugs showing promise in small trials can pass the rigor of a larger trial."

Several drugs currently are recommended for the treatment of hospitalized patients with moderate to severe COVID-19, including the antiviral drug remdesivir, the anti-inflammatory baricitinib, and corticosteroids. Additionally, the U.S. Food and Drug Administration authorized emergency use of intravenous monoclonal antibodies in non-hospitalized patients with mild to moderate COVID-19 who are at high risk for severe disease. However, medications that can be self-administered at home to reduce COVID-19 symptoms are critically needed.

The ACTIV-6 protocol will explore a pool of up to seven drugs approved by FDA for other conditions—an approach called drug repurposing—and test their safety and effectiveness in treating mild to moderate COVID-19. Because the drugs under consideration already have been tested in humans, repurposing could deliver COVID-19

treatment options sooner. Drugs will be administered orally or by inhaler and will be easy for participants to take at home. Participants will be assigned randomly to receive either a placebo or one of the treatments, which will be sent to them by mail.

Enrollment is expected to open in a few weeks to up to 13,500 participants who are at least 30 years old, have tested positive for SARS-CoV-2 infection and have experienced two or more mild-to-moderate symptoms of COVID-19 for no more than seven days. Researchers plan to assess changes in patients' symptoms over a 14-day period, as well as hospitalizations and deaths over a 28-day period. They also will assess long-term COVID-19-related symptoms at 90 days after treatment begins. The list of drugs that will be added to the study arms is still being finalized. All the drugs will have established safety records and early indications from smaller or less controlled studies of effectiveness against COVID-19.

The trial will focus on enrollment of people within minority, rural and other communities that are significantly affected by COVID-19 but lack access to major academic medical centers, where large clinical trials usually take place.

With funding provided by the American Rescue Plan Act, NIH's National Center for Advancing Translational Sciences (NCATS) will oversee the trial. The Duke Clinical Research Institute, Durham, North Carolina, an NCATS-funded Clinical and Translational Science Awards (CTSA) Program hub, will serve as the clinical coordinating center, and the Vanderbilt Institute for Clinical and Translational Research CTSA Program hub at Vanderbilt University Medical Center, Nashville, Tennessee, will serve as the trial's data coordinating center.

To expedite enrollment in ACTIV-6, NCATS and its Duke-Vanderbilt Trial Innovation Center will partner with the Patient-Centered Outcomes

Research Institute (PCORI), an independent nonprofit research funding organization. PCORnet, the National Patient-Centered Clinical Research Network, which is funded by PCORI, will support the ACTIV-6 governance and operations. In addition, PCORnet sites will enroll participants from a broad range of communities.

"Getting approval for a new drug to come to market usually takes years," said Joni Rutter, Ph.D., NCATS acting director. "By leveraging drug repurposing and existing national clinical trial networks, ACTIV-6 aims to speed the delivery of definitive answers about available drugs that could help people manage COVID-19 symptoms at home."

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