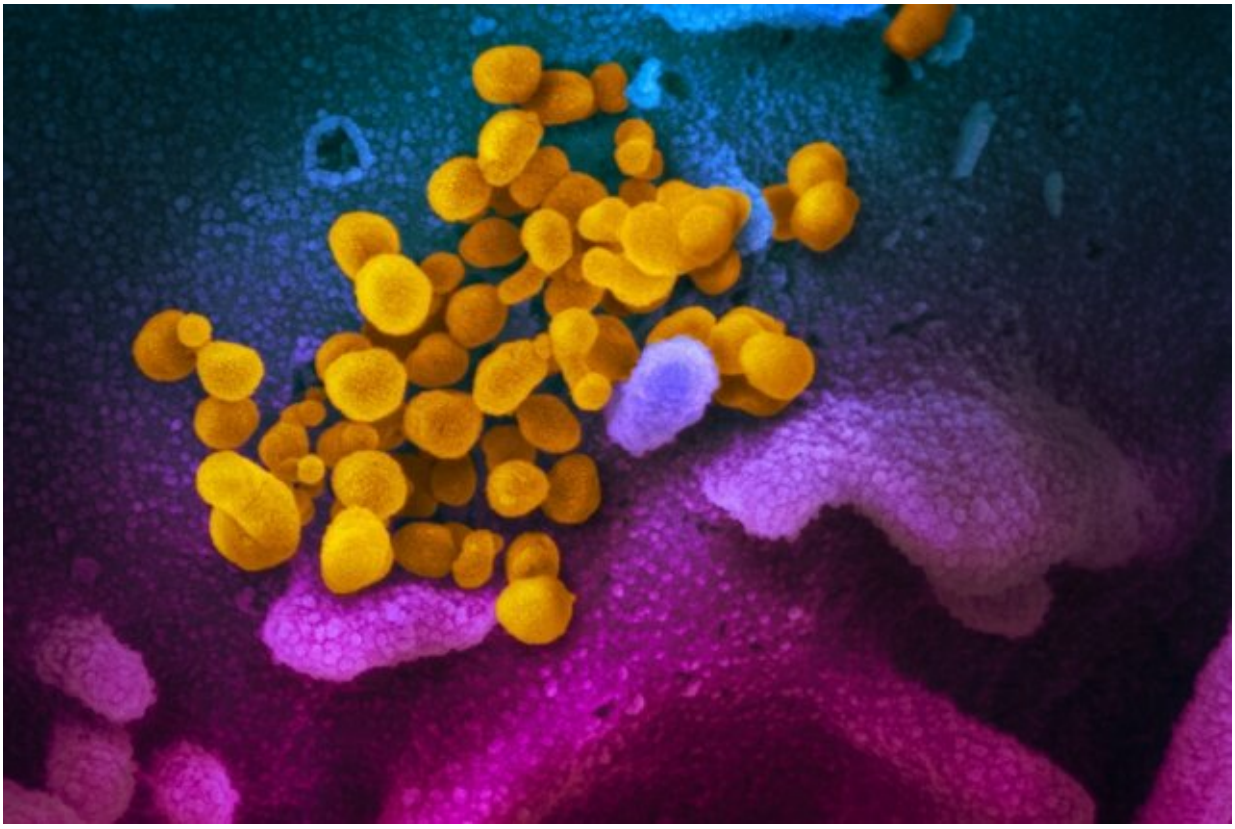
Investigational therapy gaining reputation as promising antiviral drug to fight COVID-19

April 16 2020



This scanning electron microscope image shows SARS-CoV-2 (yellow)—also known as 2019-nCoV, the virus that causes COVID-19—isolated from a patient, emerging from the surface of cells (blue/pink) cultured in the lab. Credit: NIAID-RML

COVID-19 patients in a clinical trial at Houston Methodist Hospital are

responding quickly to the antiviral drug Remdesivir. The trial's criteria allows for the treatment of patients early in their clinical course and, in some cases, at times where they might have otherwise been intubated.

"Early results are promising, and that is important right now. Much of what we are learning about COVID-19 management is centered around preventing quick deterioration. Timing is everything. I can't say for certain they would have been intubated otherwise, but it's encouraging," said infectious diseases pharmacist Katherine K. Perez, Pharm.D.

One of the most challenging things with COVID-19 is the way this virus makes copies of itself once it finds its way into the body. This is how COVID-19 can ultimately take over and send someone into respiratory distress and in need of intubation if not stopped early enough. Remdesivir has demonstrated a potent ability to inhibit this viral replication in human cells and is now being tried in clinical trials of patients with the SARS-CoV-2 virus, which causes COVID-19. Houston Methodist is the only clinical trial site in Houston for this investigational new drug.

Working with pharmaceutical company Gilead Sciences, Remdesivir's manufacturer and sponsor of the studies, Houston Methodist Hospital was the fifth site in the U.S. to join the clinical trials and has been enrolling and treating patients since mid-March. Initially, five patients received early access to Remdesivir on a compassionate use basis, and since being activated as a clinical trial site, more than 35 patients have been enrolled.

The two Phase 3 clinical trials at Houston Methodist are randomized, open-label, multicenter studies and are treating patients with moderate to severe symptoms to evaluate the safety and efficacy of Remdesivir in adults diagnosed with COVID-19. One study is for patients with moderate COVID-19 and tests either a 5-day or 10-day Remdesivir

treatment. The second study is evaluating a 10-day course of Remdesivir for patients with severe COVID-19, including those on mechanical ventilation.

Infectious diseases physician Kevin A. Grimes, M.D., M.P.H., and Perez are leading efforts for both the clinical trials at Houston Methodist and say they've been encouraged by the results.

Perez says early results at Houston Methodist have been promising, courses have been well tolerated, and a number of COVID-19 patients who have undergone treatment with Remdesivir are showing signs of recovery and have been released from the hospital to go home. While it's too early to tell, she says there also are indications that treatment with Remdesivir can possibly stave off being intubated.

Grimes agrees that acting quickly is critical.

"If given early enough, we're hoping that Remdesivir interferes with the virus and blocks its ability to replicate in patients' cells," Grimes said. "The goal is that it staves off the deadly inflammatory cascade that leads to respiratory failure and the need to be intubated and put on a ventilator."

That crucial turning point is what makes COVID-19 become deadly. The main cause of death from this disease results from an extreme inflammatory response in the lungs brought on by the coronavirus. The immune system becomes hyperactive with its inflammatory disease-fighting processes going into overdrive, attempting to defeat the virus, but doing more harm than good by destroying cells in the lungs.

A broad-spectrum antiviral drug, Remdesivir was originally developed to treat Ebola more than a decade ago. It's known to be generally safe in humans and is backed by a large body of preclinical research, as well as

a number of studies that have shown it be quite successful in stopping SARS and MERS, the viral cousins of the new coronavirus strain. The testing stopped short of clinical trials, so its efficacy against SARS and MERS in patients is unknown.

Published in the journal *Nature*, a study in China earlier this year showed Remdesivir could successfully block COVID-19 from replicating in human cells. A paper in the *New England Journal of Medicine* chronicles the case of the man at ground zero in Washington state who was the first known U.S. COVID-19 patient. He received Remdesivir at the recommendation of the CDC and was said to have started improving within 24 hours.

On April 10, the first available results from one of Gilead's compassionate-use cohorts was published in the *New England Journal of Medicine*. The study showed clinical improvement in a two-thirds majority (68 percent) of patients hospitalized for severe COVID-19 who received compassionate-use Remdesivir.

Forthcoming data from several ongoing randomized, controlled clinical trials, including the ones at Houston Methodist, will provide more definitive, evidence-based conclusions regarding the safety and efficacy of Remdesivir for treating COVID-19. The clinical observations in this compassionate-use program are the only currently available data. The study authors expect results from some of Gilead's controlled clinical trial sites to potentially validate these findings in the coming weeks.

Provided by Houston Methodist