# Hepatitis C Drugs Show Promise Against New Coronavirus

Sofosbuvir and daclatasvir were linked to faster recovery and improved survival in studies in Iran.

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A combination of two antiviral drugs commonly used to treat hepatitis C virus (HCV) were found to shorten the duration of hospitalization and improve survival for people with moderate or severe COVID-19 in a set of studies in Iran, researchers reported at the virtual International AIDS Conference last week.

If larger studies now underway confirm these findings, sofosbuvir and daclatasvir could offer an affordable and widely accessible treatment option, study coauthor Andrew Hill, MD, of Liverpool University said at a press briefing.

As the global COVID-19 pandemic continues unabated, scientists are studying a wide variety of existing medications as potential treatments for the new coronavirus, officially known as SARS-CoV-2.

Although not closely related, HCV and SARS-CoV2 are both enveloped single-stranded RNA viruses, suggesting that some of the same antiviral drugs might work against both of them. In fact, Gilead Sciences' COVID-19 frontrunner, remdesivir, was initially studied as a hep C candidate.

Sofosbuvir, marketed by Gilead as Sovaldi and a component of the Harvoni, Epclusa and Vosevi combination pills, is a HCV NS5B inhibitor that targets RNA-dependent RNA polymerase, an enzyme certain viruses use to copy their genetic material. Daclatasvir, marketed by Bristol Myers Squibb as Daklinza, is an HCV NS5A inhibitor.

In prior studies, sofosbuvir and daclatasvir have shown activity against SARS-CoV2 in laboratory cell lines; daclatasvir, in particular, appears to penetrate well into the lungs. The drugs have been shown to be safe and well tolerated for hepatitis C treatment.

Researchers have also found that several other HCV drugs are likely to bind to the new coronavirus, including elbasvir and grazoprevir (the drugs in the Zepatier combo), simeprevir (Olysio), paritaprevir (in the Viekira regimen) and velpatasvir (in Epclusa and Vosevi). The older hep C drugs interferon and ribavirin have also been studied for COVID-19.

Anahita Sadeghi, MD, of the Tehran University of Medical Sciences, presented findings from a randomized controlled trial comparing sofosbuvir plus daclatasvir with standard-of-care treatment versus standard-of-care alone for adult patients with moderate or severe COVID-19 at four university hospitals around Tehran.

At the time of the study, standard care in Iran consisted of lopinavir/ritonavir (the HIV combo Kaletra) with or without hydroxychloroquine, Sadeghi said. Studies of both of those drugs for COVID-19 have yielded mixed but mostly negative results.

This study enrolled 66 participants who had a fever and low oxygen levels and who tested PCR positive for SARS-CoV-2 and had lung CT scans that indicated COVID-19. About half were men and the median age was approximately 60. Comorbidities including diabetes, hypertension, chronic pulmonary disease and obesity were common, but they did not have hepatitis C. People who had poor kidney function or had progressed to multi-organ failure were excluded.

The researchers defined clinical recovery as normalization of fever, respiratory rate and oxygen saturation. They also looked at the duration of hospital stay, the need for mechanical ventilators and death from any cause.

Sadeghi reported that 88% of people taking sofosbuvir plus daclatasvir experienced clinical recovery within 14 days, compared with 67% of those taking standard therapy. In addition, 9% versus 21% required mechanical ventilation and three (9%) versus five (15%) patients died. Although none of these differences reached the threshold for statistical significance, the time to recovery was significantly shorter in the sofosbuvir plus daclatasvir group (six versus 11 days, respectively).

Sadeghi also presented findings from a small meta-analysis of three clinical studies, including this one, conducted in three Iranian cities. One, she noted, was not properly randomized due to changes in the standard therapy arm.

In the combined analysis, which included a total of 176 patients, the recovery rate was 94% for those taking sofosbuvir plus daclatasvir, compared with 70% for those taking various control regimens. The time to recovery was significantly faster in the sofosbuvir plus daclatasvir group, and the death rate was significantly lower (5% versus 20%).

Sadeghi noted that the studies lacked viral load data, which could show if the drugs were inhibiting SARS-CoV-2 replication, because the availability of PCR testing was limited in Iran at the time.

The researchers concluded that sofosbuvir plus daclatasvir was associated with faster recovery and improved survival, but larger studies are needed to confirm these findings.

To that end, a trial called DISCOVER will compare sofosbuvir plus daclatasvir with lopinavir/ritonavir versus lopinavir/ritonavir alone in 600 people in Iran with moderate to severe COVID-19. In addition, a network of five clinical trials has been set up to test sofosbuvir plus daclatasvir in over 2,000 patients with COVID-19 in Iran, Brazil, Egypt and South Africa. Results are expected by October.

Hill, who is well known for his research on drug pricing for HIV and hep C, emphasized the potential for this treatment to be affordable and widely accessible worldwide.

Although the sofosbuvir plus daclatasvir combination has a list price of more than $18,000 for a 14-day course in the United States, it is much less expensive elsewhere, for example about $7,600 in the United Kingdom and $4,300 in Brazil. A cheap generic version is available for about $7 in India. Around 2.5 million courses could be formulated with the current supply, according to Sadeghi.

Gilead recently announced that a 14-day course of remdesivir would cost about $2,000 to $3,000 in the United States, and the U.S. has bought up most of the available supply.

“This treatment is being developed with no support from large pharmaceutical companies, and all our funding is from governments, academia and donor agencies,” Hill said. “There is already enough generic sofosbuvir and daclatasvir mass produced to treat millions of people if this drug proves effective. We want this treatment to be affordable for anyone with COVID-19 in any country.”

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