Combination of oral drugs suppresses common type of hepatitis C

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A new combination of investigational drugs successfully suppressed hepatitis C genotype 1 infection in a high percent of patients who had not responded to previous treatment in a study led by a University of Michigan hepatologist.

The study, which will be published Jan. 19 in the New England Journal of Medicine, focused on hepatitis C genotype 1, which is predominant in the United States and the most difficult to treat. Hepatitis C is a virus that infects the liver and can cause liver cancer and liver cirrhosis. It is transmitted through direct contact with infected blood and blood products.

In this pilot study, patients with hepatitis C genotype 1 infection, who had not responded to previous treatment with PEG-interferon alfa and ribavirin, were given a combination of two investigational direct-acting antiviral agents (daclatasvir and asunaprevir) alone, or were given these two antiviral agents along with PEG-interferon alfa-2a and ribavirin. All the patients saw their hepatitis C viral load drop rapidly, says Anna S. Lok, M.D., professor of Internal Medicine, Division of Gastroenterology at the University of Michigan Medical School and lead author of the study.

All 10 patients given the four drug treatment -- two direct-acting antiviral agents (daclastasvir and asunaprevir) that block the NS3 and NS5A regions of the hepatitis C virus plus PEG-interferon alfa and ribavirin -- had sustained virologic response with undetectable virus at

the end of treatment and at 12 weeks after stopping treatment. Four of the 11 patients given the two direct-acting antiviral agents only also achieved sustained virologic response.

A sustained virologic response or SVR means there is no detectable Hepatitis C virus in a patient's blood after treatment is stopped. Achieving sustained virologic response is important, because research has shown that late relapse is rare.

"The two recently approved hepatitis C drugs – telaprevir or boceprevir -- combined with PEG-interferon alfa and ribavirin have limited success in patients who have not responded to previous treatment with PEG-interferon alfa and ribavirin. Because of this high unmet medical need, there is a necessity for new combination regimens that can increase response rates in that population," says Lok, who also is Director of Clinical Hepatology at U-M. "The high rate of sustained virologic response in patients who received the four drug regimen is very exciting. Although only four of 11 patients given the two direct-acting antiviral agents only achieved sustained virologic response, this is the first study to show that sustained virologic response can be achieved without the use of interferon or ribavirin. These data are very encouraging because PEG-interferon alfaand ribavirin are associated with many side effects and many patients with hepatitis C choose not to receive treatment for fear that they cannot tolerate those drugs."

An estimated 170 million people worldwide are infected with hepatitis C, with genotype 1 being the most prevalent genotype. Up to 80 percent of those infected with hepatitis C will become chronically infected. Twenty percent of people with chronic hepatitis C will develop cirrhosis and, of those, up to 25 percent may progress to liver cancer. Although there is no vaccine to prevent hepatitis C, it is a potentially curable disease.

In the Phase II clinical trial, Lok, along with a team of researchers including scientists from Bristol-Myers Squibb, studied patients with Hepatitis C genotype 1, who had not responded to prior therapy with PEG-interferon alfa and ribavirin. The study was funded by Bristol-Myers Squibb.

"Overall, these results suggest that further research into combinations of direct-acting antiviral agents, with or without PEG-interferon and ribavirin, should be encouraged," Lok says. "Caution must be exercised in selecting the right combination of direct-acting antiviral agents in studies of interferon-free regimens because in this study, all 7 patients who received only two direct-acting antiviral agents that did not achieve sustained virologic response had emergence of drug resistance variants to both drugs."

In this study there were no serious adverse events on treatment or discontinuations due to adverse events. Diarrhea was the most common adverse event in both groups, but it was mild or moderate in all cases.

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