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New drug combination offers hope to patients with currently untreatable Hepatitis C

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Hepatitis C is a viral infection which, if left untreated, can lead to severe and potentially fatal liver damage. Existing treatments consist of a combination of drugs, usually ribavirin, pegylated interferon and a protease inhibitor, which together inhibit viral replication and enhance the body's immune response to eradicate the virus. These drugs can place a substantial burden on the patient, with complicated pill and injection regimens, which can last for up to 48 weeks, and unpleasant side-effects for some patients, including anaemia, depression, and loss of appetite.

Although hepatitis C can be curable, different genetic strains of the virus respond differently to drug treatment, and a significant number of patients with genotype 1 hepatitis C (the most common strain of the virus in the United States and Europe) do not respond to existing treatments. Patients whose infection cannot be cured run the risk of sustaining substantial damage to their livers (such as cirrhosis), and patients in this group currently have no further treatment options.

A team of researchers from the Texas Liver Institute in San Antonio, Texas, USA, and Gilead Sciences, Inc., a biopharmaceutical company based in Foster City, California, USA, recruited 100 patients with genotype 1 hepatitis C virus who had either never received treatment (60 patients), or who had been treated unsuccessfully using existing drugs (40 patients). Of patients in the latter group, just over half (22, 55%) had cirrhosis.

All trial participants took a new combination pill consisting of the investigational drugs sofosbuvir and ledipasvir. Patients took the combination pill for either 8 weeks or 12 weeks, and some patients in the study also received ribavirin as part of their regimen. Participants were stratified into different groups according to whether they had previously received treatment for hepatitis C, their length of treatment, and whether they received the new combination pill alongside ribavirin or not.

At 12 weeks following the completion of therapy, nearly all (97 or 97%) of the patients in the study had achieved a sustained virological response (SVR) – essentially a functional cure for hepatitis C, where the virus is eliminated, and prevented from replicating.

Just under half of the patients in the study experienced at least one adverse event, with the highest rates observed in the groups of patients who were receiving ribavirin as part of their treatment regimen. No patient in any group discontinued treatment because of an adverse event.

According to Professor Eric Lawitz, of the Texas Liver Institute, who led the study, "To our knowledge, this trial is the first to report data for cirrhotic genotype 1 hepatitis C patients who did not respond to prior treatment with a protease inhibitor regimen, a population without treatment options at present. The results of this trial suggest that the fixed-dose combination of sofosbuvir and ledipasvir could offer patients a short, all-oral treatment that might be highly effective and safe in patients who tend not to respond well to existing therapies, including individuals with cirrhosis or black race, resistant strains of the virus, and those who have not responded to standard-of-care regimens that include protease inhibitors."

According to Professor Margaret Hellard, of the Burnet Institute, Melbourne, Australia, co-author of a linked Comment, "As a proof of

concept study, [this] demonstrates very high response rates, regardless of the presence of cirrhosis, prior treatment failure, or [resistant] genotype. However, this was a small, single-centre study with only short follow-up, raising concerns about the representativeness of the sample and whether early clinical trial results can be easily generalised to real-world settings. Whilst giving cause for optimism, the full implications of these results need to be tempered for now."

More information: www.thelancet.com/journals/lan … (13)62121-2/abstract

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