MedicalXpress

Investigational oral regimen for hepatitis C shows promise in NIH trial

August 27 2013

In a study of an all-oral drug regimen, a majority of volunteers with liver damage due to hepatitis C virus (HCV) infection were cured following a six-month course of therapy that combined an experimental drug, sofosbuvir, with the licensed antiviral drug ribavirin. The results showed that the regimen was highly effective in clearing the virus and well tolerated in a group of patients who historically have had unfavorable prognoses.

Scientists from the National Institute of Allergy and Infectious Diseases (NIAID) and the NIH Clinical Center, parts of the National Institutes of Health, led the Phase II trial. The findings appear in the Aug. 28 issue of the *Journal of the American Medical Association* (*JAMA*).

More than 3 million Americans have chronic HCV infection, a condition that is a major cause of cirrhosis (liver tissue scarring) and liver cancer, and a leading reason for liver transplantation. Deaths from HCV-related liver disease number about 15,000 every year. Standard treatment for HCV can last up to a year and usually involves weekly injections of pegylated interferon-alpha given with the oral drug ribavirin and an HCV protease inhibitor. Side effects from this treatment can be severe, notably from interferon-alpha, and can include depression, flu-like symptoms and anemia.

"There is a pressing need for hepatitis C virus treatments that are less burdensome to the patient, have fewer side effects and take less time to complete. Building on previous work, this trial provides compelling

evidence that interferon-free regimens can be safe and effective," said NIAID Director and study co-author Anthony S. Fauci, M.D.

The current study involved 60 volunteers with genotype-1 HCV, which tends to be less responsive to interferon-based treatment. Fifty of the 60 participants were African-American.

"While African-Americans make up about 13 percent of the U.S. population, they represent more than 22 percent of people with chronic HCV infection and, compared to whites, have lower cure rates with traditional HCV therapy," said NIAID researcher Shyam Kottilil, M.D., Ph.D., the principal investigator of the trial. "Several recently completed trials testing interferon-free regimens have yielded promising results, but most volunteers in those studies were white."

The new study also differs from many previous trials because it enrolled people with severe liver damage as well as those with mild or moderately scarred livers.

The study was divided into two parts. The first part enrolled 10 people with mild or moderate liver fibrosis. Volunteers received oral ribavirin at a dosage based on their weight along with the experimental drug sofosbuvir, also in pill form, taken daily for six months. Gilead Sciences, Inc., of Foster City, Calif., manufactures sofosbuvir and supplied it to the study physicians.

Nine volunteers completed the course of therapy. Virus was undetectable in all nine volunteers 12 weeks after the end of therapy and continued undetectable when they were tested again 24 weeks after finishing therapy. HCV does not integrate itself into human DNA. If the virus cannot be detected for a period of 12 weeks after stopping therapy, the patient is considered cured, Dr. Kottilil said.

The second part of the trial enrolled 50 volunteers, 13 of whom had liver damage rated as serious. Twenty-five received ribavirin based on their weight, and 25 received a low dose (600 milligrams per day). All received sofosbuvir.

"Because ribavirin can cause serious side effects, including anemia, we wanted to compare response rates in patients taking low-dose ribavirin with results from patients on a weight-based dosage," said Dr. Kottilil.

At four, 12 and 24 weeks after the end of treatment, volunteers were tested for the presence of HCV. HCV levels were undetectable in 24 of the volunteers in the weight-based arm when treatment ended. Of those, 17 continued to have undetectable virus levels 24 weeks later and were considered cured of infection. In the low-dose arm, three volunteers dropped out of the study. Of the remaining 22, all responded to the treatment, but only 12 were considered cured at 24 weeks after the end of treatment.

"We saw an overall cure rate of about 70 percent using regimens that did not include interferon," said Dr. Kottilil. "This is an encouraging result, especially considering the proportion of volunteers who had characteristics—such as being male, having HCV genotype-1 infection, being African-American and having advanced liver damage—that are recognized as predictors of poor response to treatment."

Additional trials are underway to further determine if regimens without interferon or ribavirin can help people with chronic HCV infection, particularly those who have both HIV and HCV infections, said Dr. Kottilil. These trials include two studies in which volunteers with or without HIV infection take a combination of HCV drugs (but no interferon or ribavirin) for periods of three months or less. Information about these trials is available at clinicaltrials.gov using the identifiers NCT01805882 and NCT01878799.

More information: A Osinusi et al. Sofosbuvir and ribavirin for hepatitis C genotype 1 in patients with unfavorable treatment characteristics: A randomized clinical trial. *JAMA* DOI: 10.1001/JAMA.2013.109309 (2013).

Provided by NIH/National Institute of Allergy and Infectious Diseases