Retreating patients with hepatitis C: Telaprevir boosts cure rate

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Adding the investigational drug telaprevir to standard treatment for hepatitis C infection cures about half the patients willing to give therapy a second try. That compares to a cure rate of just 14 percent among those who were retreated with the standard regimen, according to researchers at the Duke Clinical Research Institute (DCRI).

Standard treatment for hepatitis C is 48 weeks of a combination of two drugs, peginterferon alfa-2a plus the antiviral agent ribavirin. The treatment cures roughly 40 percent of who undergo it; for those who fail to respond, the only backup is a second round of therapy with the very same treatment.

The results of this study, appearing in the New England Journal of Medicine, suggest that telaprevir, a protease inhibitor that works by blocking an enzyme the hepatitis C virus needs to replicate itself, may greatly enhance many patients' chance of a cure, according to John McHutchison, MD, associate director for research for the DCRI and the lead author of the study.

The findings come from a DCRI-coordinated, multinational study of 453 patients who had failed to fully respond to initial treatment. All participants had the most common form of the virus, genotype 1, generally regarded as the most difficult type of hepatitis C to cure.

Investigators randomized the patients into one of four treatment groups. All participants received either peginterferon or peginterferon plus

ribavirin for 24 or 48 weeks. Researchers added the experimental drug telaprevir to three of the regimens for 12 or 24 weeks. Patients in a fourth arm of the study received a placebo plus peginterferon and ribavirin.

Telaprevir is made by Vertex Pharmaceuticals Incorporated, which funded the study, formally known as Protease Inhibition of Viral Evaluation 3 (PROVE3).

Researchers measured the amount of virus in the patients' blood at multiple points during the course of their therapy and then checked on their viral load six months after they had taken their last treatment. Those who did not have any detectable virus in their blood at that point were considered cured.

Investigators found that the addition of telaprevir to a treatment plan significantly improved cure rates across the board. "Fifty-two percent of patients who had originally failed to respond to standard treatment were cured of their disease when we added telaprevir to a retreatment regimen consisting of peginterferon alfa-2a and ribavirin" said McHutchison. "This is a major development in the field and may represent the single most significant efficacy finding in the treatment of prior non-responders."

Researchers also found that 24 percent of patients who received telaprevir and peginterferon - but no ribavirin - were virus-free at the end of the 6-month post- treatment period, a finding that confirms that ribavirin is a critical component of effective treatment, according to McHutchison. In contrast, only 14 percent of those who received standard treatment were virus-free at six months. Those in the latter group were offered treatment with telaprevir, peginterferon and ribavirin in a later study.

Data analysis also revealed an association between patients' prior experience with treatment and response to retreatment: Patients who had originally responded to standard therapy but who relapsed were more likely to have a sustained response to telaprevir than were original non-responders.

The benefit of adding telaprevir, however, was offset somewhat by significant side effects. About half of those receiving telaprevir developed a rash, and 5 percent of those who did so had to stop therapy because the rash was severe. Patients who received telaprevir-based therapy were also more likely to discontinue therapy (50 of 339, or 15 percent) than were patients who received standard therapy (5 of 114, or 4 percent).

"While it is true that patients receiving all three drugs were more likely to experience side effects, especially rash and anemia, the benefit of the regimen can be substantial," said McHutchison. "Adding telaprevir to standard treatment for hepatitis C is very helpful to large numbers of patients who originally failed to fully respond to previous treatment."

A phase III trial further evaluating telaprevir retreatment strategies for patients who didn't respond to initial therapy is currently under way.

Provided by Duke University