HEPATITIS

A new re-treatment regimen for persistent HCV infection?

Including the NS3 protease inhibitor telaprevir in the re-treatment regimen for patients with persistent HCV infection is more effective than re-treatment with only pegylated interferon α 2a and ribavirin, the findings of a multinational phase II study published in the *New England Journal of Medicine* suggest. "There is a great unmet need to develop more effective therapies for the 170 million people infected with HCV worldwide," says John McHutchison of Duke University Medical Center, USA, the study's corresponding author, "particularly those ... for [whom] no effective treatment options exist"—namely, patients who do not demonstrate

a durable response to standard first-line treatment.

The current treatment strategy for patients with HCV genotype 1 infection combines pegylated interferon α 2a injections with oral ribavirin for 24 or 48 weeks. Up to 50% of patients respond to this therapy. For those who do not respond, re-treatment options are currently limited to a second course of the same medications, which is associated with high levels of morbidity and a low rate of success.

The researchers randomly assigned 453 patients (from 53 international sites) infected with HCV genotype 1 who had either not responded to or who had relapsed after first-line therapy to one of four treatment groups: 24 weeks of pegylated interferon and ribavirin, plus telaprevir for the first 12 weeks; telaprevir with pegylated interferon and ribavirin for 24 weeks; 48 weeks of pegylated interferon and ribavirin, plus telaprevir for the first 24 weeks; or pegylated interferon and ribavirin for 48 weeks (control group).

Across the three telaprevir groups, "We cured 50% of patients," says McHutchison—a rate fourfold or more higher than that achieved in the control group. Interestingly, patients' responses to first-line therapy influenced the efficacy of second-line treatment with telaprevir, as 39% of patients who had previously not responded to first-line therapy responded to re-treatment with telaprevir. By contrast, more than 70% of patients who relapsed after first-line treatment had a durable response to telaprevir therapy.

However, patients who received telaprevir were more likely than controls to discontinue treatment because of treatment-related adverse effects, such as fatigue, rash and pruritus (15% versus 4% of patients, respectively). Rash was the most common adverse event, experienced by 51% of patients, and was more severe in patients receiving telaprevir than in

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patients from the control group. Treatment with telaprevir was also associated with a decrease in hemoglobin levels, which resulted in anemia in a few patients. This effect was reversed on discontinuation of therapy.

A phase III study is currently being conducted to evaluate a second-line treatment regimen of short-term telaprevir in combination with an extended duration of pegylated interferon α 2a and ribavirin. The results are expected in late 2010; if they are favorable, this treatment could be approved as soon as 2011.

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Original article McHutchison, J. G. *et al.* Telaprevir for previously treated chronic HCV infection. *N. Engl. J. Med.* 362, 1292–1303 (2010)