

# Prolonged treatment with peginterferon is not effective in advanced chronic hepatitis C

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**C**hronic hepatitis C infection affects over 170 million people worldwide and is a major cause of liver cirrhosis, end-stage liver disease and hepatocellular carcinoma. Treatment with pegylated interferon (peginterferon) leads to sustained virologic response in nearly half of all patients. However, few therapeutic options exist for the other half of patients who do not respond. Prolonged treatment with peginterferon might show improvement in these patients.

This hypothesis was tested in the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C) trial. This trial included 1050 patients with advanced chronic hepatitis C infection (all had liver fibrosis, and nearly half had cirrhosis) that have been non-responders to the standard treatment with peginterferon and ribavirin. The patients were randomized 1:1 to peginterferon 90 mcg/week for 3.5 years or no treatment. The primary end point was progression

of liver disease (death, hepatocellular carcinoma, hepatic decompensation, or an increase in the Ishak fibrosis score of  $\geq 2$  points for those with only liver fibrosis at baseline).

Although the level of serum aminotransferases, serum hepatitis C virus RNA, and histologic necroinflammatory scores were lower in the active treatment group ( $P < 0.001$ ), there was no significant difference between the groups in the rate of any primary outcome (34.1% in the treatment group and 33.8% in the control group; 95% CI, 0.81 to 1.27;  $P = 0.90$ ). The rate of serious adverse events during the study appeared to be slightly higher in the active treatment group compared with controls (38.6% vs. 31.8%;  $P = 0.07$ ).

In conclusion, long-term treatment with peginterferon is not effective in reducing the rate of progression of advanced chronic hepatitis C infection in patients that have been non-responders to the initial treatment with peginterferon and ribavirin.

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*Comment on the paper:*

Di Bisceglie AM, Shiffman ML, Everson GT, et al for the HALT-C Trial Investigators – Prolonged Therapy of Advanced Chronic Hepatitis C with Low-Dose Peginterferon. *N Engl J Med* 2008; 359:2429-2441