

Re-treating Patients With Chronic Hepatitis C Who Have Not Responded to Peginterferon- α 2b

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The full report is titled "Re-treatment of Patients With Chronic Hepatitis C Who Do Not Respond to Peginterferon- α 2b. A Randomized Trial." It is in the 21 April 2009 issue of *Annals of Internal Medicine* (volume 150, pages 528-540). The authors are D.M. Jensen, P. Marcellin, B. Freilich, P. Andreone, A. Di Bisceglie, C.E. Brandão-Mello, K.R. Reddy, A. Craxi, A. Olveira Martin, G. Teuber, D. Messinger, J.A. Thommes, and A. Tietz.

What is the problem and what is known about it so far?

Hepatitis C is inflammation of the liver caused by the hepatitis C virus (HCV). This disease is transmitted primarily by blood-to-blood contact. Risk factors include body piercing, intravenous drug use, and needlestick accidents. Most people cannot get rid of HCV on their own. More than 80% keep the virus in their blood for longer than 6 months and get chronic hepatitis C.

Chronic hepatitis C progresses slowly over 10 to 30 years. It causes inflammation and scarring of the liver. If untreated, it can lead to liver failure and liver cancer. Treatment clears HCV from the blood and prevents further liver damage. Doctors treat chronic hepatitis C with powerful antiviral drugs. They often combine a long-acting immunity-boosting protein (pegylated interferon) with another antiviral drug (ribavirin). However, the virus does not clear after initial treatment in about 20% to 30% of patients. We do not know whether re-treating them improves outcomes.

Why did the researchers do this particular study?

To see whether any of 4 regimens improves viral outcomes in patients with chronic hepatitis C who had not responded to previous combination therapy.

Who was studied?

950 patients with chronic hepatitis C. None had responded to previous treatment with peginterferon- α 2b plus ribavirin.

How was the study done?

Researchers randomly assigned patients to 1 of 4 groups. The groups received peginterferon- α 2a for 48 or 72 weeks and either fixed-dose induction or standard-dose peginterferon regimens. The fixed-dose induction was 360 μ g/wk for 12 weeks followed by standard 180- μ g/wk doses. All patients took standard doses of ribavirin (1000 to 1200 mg) by mouth daily. The researchers measured levels of virus in the blood regularly during re-treatment and 24 weeks after re-treatment ended. They routinely did blood tests, physical examinations, and interviews to check for side effects. They then assessed which re-treatment regimen got rid of the virus most often.

What did the researchers find?

Patients who were re-treated for 72 weeks had sustained virologic response after treatment ended more often than did those who were re-treated for 48 weeks (16% vs. 8%). The dose of peginterferon- α 2a that was given during the first 12 weeks of re-treatment did not affect response rates much. Undetectable virus levels at week 12 seemed to identify the patients who were most likely to respond to re-treatment. More patients in the longer-duration treatment groups withdrew from the trial because of adverse events or illnesses than did those in the shorter-duration treatment groups (12% vs. about 5%).

What were the limitations of the study?

Researchers and patients knew which therapies the patients received. Only nonresponders to a peginterferon- α 2b plus ribavirin regimen were studied.

What are the implications of the study?

Re-treating patients who had not responded to previous therapy for chronic hepatitis C for a longer rather than a shorter duration improved viral response. Sustained virologic response rates, however, were low. A positive aspect is that responders could be identified as early as week 12.

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