Annals of Hepatology

Treatment of hepatitis C patients who do not respond to treatment or relapse after treatment

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Responses to therapy with pegylated interferon plus ribavirin vary according to the hepatitis C virus (HCV) genotype present.[1] Patients with HCV genotype 1a have a sustained response rate of 42%–52%,[2] and patients with genotypes 2 and 3 have a sustained response rate of 76%–84%.[3] If viral load is not reduced by 2 $\log_{10}$ by week 12 of treatment, the patient is considered a nonresponder.[4] If the virus is undetectable at the termination of treatment (week 24 for genotypes other than type 1 and week 48 for genotype 1) but reappears 6 months to a year after treatment, the patient is deemed to have relapsed.[5]

Management of nonresponders depends on the treatment they received previously.[6] Patients who received treatment with regular interferon alone or in combination with ribavirin may benefit from pegylated interferon plus ribavirin (response rate = 30%–40%). If a patient previously received pegylated interferon plus ribavirin, the possibility of a response with a repeat of the same regimen is very low and is not recommended.[7] The duration of treatments and drug dosages for repeat treatments are similar to those of treatment-naïve patients.

A review of the literature revealed that there are few data about the management of nonresponders or relapsed patients. No recommendations can be made regarding maintenance therapy until the results of large multicenter clinical trials are known. Patients with advanced fibrosis represent a major problem because they rapidly develop cirrhosis, portal hypertension, and hepatocellular carcinoma.[8]

We suggest that any patient for whom standard treatment has failed should be considered a prospect for maintenance therapy, because therapy may reduce or stop the progression of the disease. However, studies have shown that the disease progresses slowly in patients with initially benign biopsies and slightly elevated aminotransferase levels. In such cases, we recommend that they be maintained with vigilance pending development of more efficient therapeutic alternatives.[9] Therefore, we recommend carrying out liver biopsies to determine the status of the liver.[10]

As triple therapies (pegylated interferon plus ribavirin plus timosin[11] or pegylated interferon plus ribavirin plus amantadite[12]) have not had any additional effect on patients who do not respond to pegylated interferon plus ribavirin or on relapsed patients, they are not recommended.

Slow responders, in whom viral loads become undetectable at week 48 instead of week 12, are difficult to treat. It is recommended that treatment of these patients be extended to 72 weeks, because the relapse rate of treatment for 48 weeks (27%) is reduced to 19% by 72 weeks' treatment.[13]

Recommendations of the consensus panel

Is retreatment recommended for relapsed patients or those who do not respond to pegylated interferon and ribavirin?

There was no consensus on this. However, most panel members considered that retreatment should not be recommended until alternatives to pegylated interferon and ribavirin are available. However, most panel members felt that retreatment with standard interferon and ribavirin should be recommended for relapsing patients or nonresponders. Standard interferon plus ribavirin treatments for periods similar to those for the corresponding HCV genotypes in treatment-naïve patients were considered the regimens of choice for retreatment.

Evidence quality: 1

In patients with low virological responses (2 $\log_{10}$ decrease with detectable viral load at week 12, but an undetectable viral load at week 24), would you recommend that treatment be continued for longer than 48 weeks?

The panel of consensus highly recommends extending the duration of treatment in view of the high relapse rates.

Evidence quality: 3

Is the criterion of early viral response applicable to this group of patients?

No consensus was reached on this; more studies of viral kinetics are needed before recommendations can be made.

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Are repeat biopsies recommended for these groups of patients?

A second biopsy is recommended before initiating retreatment with pegylated interferon plus ribavirin.

Evidence quality: 3

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