Hepatitis C Treatment Should Last 24 Weeks

BY MIRIAM E. TUCKER
Senior Writer

Twenty-four weeks should be considered the routine duration of treatment with peginterferon α-2a and ribavirin for patients with hepatitis C virus genotypes 2 and 3, said Dr. Mitchell L. Shiffman, of the Virginia Commonwealth University Medical Center, Richmond, and his associates.

In a study comparing 24 weeks versus 16 weeks of treatment among 1,455 randomized patients with hepatitis C virus (HCV) genotypes 2 or 3, treatment lasting just 16 weeks resulted in a lower overall sustained response rate—primarily due to a higher subsequent relapse rate—compared with 24 weeks of treatment.

However, the data suggested that the shorter duration may be sufficient for certain subgroups. "Patients with a lower pretreatment viral load or a rapid virologic response appear to have the highest probability of having a sustained response with 16 weeks of therapy, and such therapy may be a reasonable option for these patients," the investigators said (N. Engl. J. Med. 2007;357:124-34).

In an accompanying editorial, Dr. T. Jake Liang, of the National Institute of Diabetes and Digestive and Kidney Diseases, wrote: "Patients with HCV genotype 3, high viral load, advanced fibrosis, and obesity who are black, older, and male should be treated for 24 weeks, and whites with HCV genotype 2 and with the opposite characteristics could be treated for a shorter duration."

The study, funded by Roche, was conducted at 132 centers worldwide between November 2003 and September 2005. Patients received either 16 or 24 weeks of treatment with 180 mcg of subcutaneous peginterferon α-2a once weekly plus 400 mg oral ribavirin twice daily. Investigators were blinded to their patients' treatment duration assignment until week 16.

The proportion with a sustained virologic response, defined as an undetectable serum HCV RNA level (less than 50 IU/mL) at 24 weeks after the end of treatment, was significantly lower among the patients treated for just 16 weeks versus 24 weeks in the per-protocol analysis (65% vs. 76%). The same was true in a more stringently modified intent-to-treat analysis, in which sustained virologic responses were seen in 62% of 732 patients treated for 16 weeks, compared with 70% of 731 treated for 24 weeks. The odds ratio for sustained virologic response for 24 weeks versus 16 weeks of treatment was 1.56, wrote the authors.

The virologic response rate immediately at the end of treatment was significantly higher in the 16-week treatment group, because more patients in the 24-week group had no response and were withdrawn prematurely. Thus, the significant difference in the sustained virologic response rate at 24 weeks post treatment reflects a higher relapse rate among the 16-week group (31% vs. 18%). "The trade-off in reducing the treatment duration is an increased relapse rate," the authors commented.

Within both treatment duration groups, the patients infected with HCV genotype 2 had higher virologic responses at the end of follow-up than did those with genotype 3. Relapse rates for those with genotype 2 were 30% among those treated for 16 weeks and 15% in the 24-week group. Among those with genotype 3, 31% of patients treated for 16 weeks relapsed during follow-up, compared with 22% of those treated for 24 weeks. Overall, the odds ratio of attaining a sustained virologic response with genotype 2 versus 3 was 1.88.

Other significant predictors of sustained virologic response included lower pretreatment HCV RNA level, younger age, lower weight, higher alanine aminotransferase quotient (the patient's alanine aminotransferase level divided by the upper limit of the normal range), and the absence of bridging fibrosis or cirrhosis.

A rapid virologic response, defined as an undetectable HCV RNA level by week 4 of treatment, was achieved in 67% of patients in the 16-week group and in 64% of the 24-week group. Sustained virologic response rates were consistently lower among patients who did not have rapid responses than among those who did. And, among those without a rapid response, sustained virologic response rates were consistently higher in the 24-week group than in the 16-week group.

Overall, the proportions of patients reporting adverse events and serious adverse events were similar in the two groups, and the rates of withdrawal were not significantly different. ■