Obesity No Hurdle to Combination HCV Therapy

BY DIANA MAHONEY
New England Bureau

BOSTON — Combination therapy with peginterferon α-2b and weight-based ribavirin produces consistent rates of sustained virologic response in obese patients with chronic hepatitis C virus in the largest U.S. hepatitis C virus study ever conducted.

In fact, the weight-based dosing regimen "produces sustained virologic response rates among obese patients similar to those seen in normal-weight individuals," Dr. Ira M. Jacobson reported at the annual meeting of the American Association for the Study of Liver Diseases.

Previous studies have shown that overweight patients with hepatitis C virus (HCV) infection are less likely to achieve a sustained virologic response (SVR) with antiviral therapy than are their normal-weight counterparts. And obese patients—those with a BMI greater than 30 kg/m^2—have a significantly reduced probability of attaining SVR, compared with normal-weight or overweight patients, said Dr. Jacobson of Weill Medical College of Cornell University, in New York.

Previously reported results from the current study—the WIN-R (Weight-Based Dosing of PEG-Intron and Rebetol) multicenter, prospective, open-label trial—showed that weight-based dosing of ribavirin is important in maximizing SVR rates in patients with chronic hepatitis C.

Across the study population, "SVR rates were significantly higher with peginterferon α-2b plus weight-based ribavirin than with flat-dose ribavirin," Dr. Jacobson said.

To evaluate the consistency of this effect in obese patients with HCV, Dr. Jacobson and his colleagues conducted a subanalysis of data from the 4,900-patient WIN-R trial, looking specifically at the outcomes of 51 chronic HCV patients in the study with a body weight of 125 kg or more.

All of the patients in the study were 18-70 years of age, were treatment naive, had elevated ALT levels within 6 months of study enrollment, had liver biopsy findings consistent with chronic HCV within 36 months of study enrollment, and had compensated liver disease. Patients who tested positive for hepatitis B surface antigen or HIV were excluded.

Patients were randomly assigned to receive subcutaneous peginterferon α-2b (PEG-Intron) at a dosage of 1.5 mcg/kg per week and either flat-dose (800 mg/day) or weight-based oral ribavirin (Rebetol) daily. The weight-based dosing was 800 mg/day for patients weighing less than 65 kg, 1,000 mg/day for patients weighing from 65 to 85 kg, 1,200 mg/day for patients weighing from 85 to 105 kg, and 1,400 mg/day for patients weighing more than 105 kg.

Patients infected with HCV genotype 1 were treated for 48 weeks, and patients infected with HCV genotype 2/3 were treated for 24 or 48 weeks. All patients were monitored for 24 weeks after treatment.

Of the 51 patients included in the subanalysis, 23 received flat-dose ribavirin, and 28 received weight-based doses. The mean body weight in the cohort was 131.2 kg, and the mean BMI was 41.0 kg/m^2. Twenty-seven patients had HCV genotype 1 infection, and 24 had HCV genotype 2/3.

Overall, 31of the 51 patients in the subanalysis responded to the treatment by the end of the study period, and SVR—defined as undetectable serum HCV RNA (less than 29 IU/mL) 24 weeks after treatment—was achieved by 25 patients (49%), Dr. Jacobson reported. The overall SVR rate for the WIN-R population was 44.3%, he said.

As with the general WIN-R trial population, "patients weighing more than 125 kg had a significantly increased probability of achieving an SVR with weight-based ribavirin than with flat-dose [ribavirin]," said Dr. Jacobson, noting that patients who received weight-based dosing were 3.5 times more likely to achieve SVR than were those on the flat-dose regimen. The differences in SVR rates between flat-dose and weight-based ribavirin were greater in patients in the subanalysis than they were in the WIN-R study population as a whole, he said.

In the subanalysis, 6% of patients had hemoglobin levels below 10 g/dL, and 6% had absolute neutrophil cell counts lower than 750/mm^3. In the larger study, the respective rates for these adverse events were 16% and 19%, said Dr. Jacobson.

The findings of this study suggest "that severe obesity should not preclude consideration of antiviral therapy for patients with chronic HCV," said Dr. Jacobson, who reported receiving research support for this study from Schering-Plough, manufacturer of PEG-Intron. ■

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