

Telaprevir in HCV Treatment-Failure Patients

The 2009 Annual Meeting of the European Association for the Study of the Liver (EASL), held recently in Copenhagen, Denmark, included results from the PROVE 3 trial. In this randomized, double-blind, placebo-controlled phase IIb study, prior nonresponders, prior relapsers, and patients experiencing prior breakthrough while on peg-interferon (IFN) and ribavirin (RBV) therapy, including those with cirrhosis, were re-treated with regimens including telaprevir (Vertex; n=453). In intent-to-treat analysis, 51% and 52% of treatment-failure patients achieved sustained viral response (SVR) with 24- and 48-week telaprevir regimens, respectively, compared to 14% of patients randomized to 48 weeks of peg-IFN and RBV alone. Among prior relapsers, 69% and 76% in the 24- and 48-week telaprevir groups, respectively, achieved SVR compared to 20% in the control group, whereas among prior nonresponders, 39% and 38% in the 24- and 48-week telaprevir groups, respectively, achieved SVR compared to 9% in the control group. A subanalysis of patients with cirrhosis revealed that 53% and 45% in the 24- and 48-week telaprevir groups, respectively, achieved SVR compared to 8% in the control group, which was similar to the rates for patients without cirrhosis.

Overall in PROVE 3, 13% (10/76) of patients receiving 48 weeks of telaprevir relapsed compared to 53% (18/34) of patients in the control group. A third arm of the study, which assessed 24 weeks of telaprevir treatment, demonstrated a SVR rate similar to that achieved with 48 weeks, as well as an overall relapse rate of 30% (26/87). Based upon these results, the researchers noted that telaprevir regimens that include a total of 48 weeks of treatment with peg-IFN and RBV including 12 weeks of telaprevir may be warranted in treatment-failure patients.

Adverse events in this trial were consistent with those from prior telaprevir trials. Rash led to discontinuations in 5% of patients but was reversible upon treatment end. A 1% discontinuation rate due to anemia was seen, similar to the rate in the control arm.

Corticosteroid Usage in Severe Alcoholic Hepatitis

Recent meta-analysis evaluated steroid therapy in patients with severe alcoholic hepatitis based on 5 randomized, controlled trials consisting of 185 control patients and

202 patients receiving corticosteroids. Researchers found an overall 28-day survival rate of 79.2% for patients receiving steroids compared to 64.1% for control patients. Factors predictive of poor outcome included the patient's age, serum creatinine, leucocyte and albumin levels, and the presence of encephalopathy, as well as the Maddrey scale of discriminant function (Maddrey DF) and the Lille scale. The Maddrey DF scale considers prothrombin time and bilirubin measurements and suggested that a score of ≥ 32 is predictive of poor outcome. The Lille scale includes renal insufficiency, bilirubin, and change in bilirubin over 7 days, showing that 85% of patients with a score greater than 0.45 will die within 6 months, compared to 25% of patients with a score less than 0.45. According to the meta-analysis, after 7 days, bilirubin levels fell more sharply among patients receiving steroids compared to those who did not (73.1 vs 36.1 $\mu\text{mol/L}$). Lower Lille scores were seen in patients who received steroids (0.225) compared to control patients (0.391). Among patients who received steroids, 66.4% were considered responders to treatment (Lille scores < 0.45) compared to 54.6% in the control groups. Among patients with Lille scores less than 0.45 at baseline, the meta-analysis demonstrated a 94.1% 28-day survival for those who received corticosteroids compared to 78.6% among control patients ($P=.002$). Philippe Mathurin, MD, one of the study authors, noted that this analysis helps address the controversy of whether corticosteroids should be used in patients with severe alcoholic hepatitis, and demonstrates that among a subset of patients with better baseline Lille scores, steroid use could extend 28-day survival rates.

In Brief

Ulcerative colitis patients given prolonged-release oral mesalamine 2 g once daily had better remission rates, acceptability, and self-reported adherence to therapy compared to patients given oral mesalamine 1 g twice daily. *Clin Gastroenterol Hepatol.* 2009 Apr 15. [Epub ahead of print]

Researchers noted that argon plasma coagulation is an effective and safe endoscopic treatment for gastric antral vascular ectasia in patients with liver cirrhosis. *Digestion.* 2009;79:143-150.