Boceprevir Effective in Advanced Fibrosis or Cirrhosis

April 8, 2011 By Tim Horn

Merck's HCV protease inhibitor boceprevir can be used safely and effective in people living with hepatitis C virus (HCV) with advanced fibrosis or cirrhosis, according to an analysis of data from two Phase III clinical trials reported Saturday, April 2, at the 46th annual meeting of the European Association for the Study of the Liver (EASL) in Berlin. To maximize the chance of a sustained virologic response (SVR)—a viral cure—it may be necessary to complete a full 48-week course of treatment, rather than stopping early based on encouraging early results.

Boceprevir, which is currently being reviewed for approval by the U.S. Food and Drug Administration, has been shown to increase SVR rates against difficult-to-treat genotype 1 HCV infection when used in combination with standard pegylated interferon/ribavirin (IFN/RBV). This was documented in the SPRINT-2 study involving people living with HCV starting therapy for the first time, as well as in RESPOND-2, which enrolled patients who didn't respond or relapsed during previous treatment with IFN/RBV.

At EASL, the SPRINT-2 and RESOND-2 researchers led by Savino Bruno, MD, of the Department of Internal Medicine at A.O. Fatebenefratelli e Oftalmico in Milan and his colleagues provided a closer look at boceprevir's efficacy in a subset of patients included in both studies: those with advanced fibrosis or cirrhosis—a liver biopsy Metavir score of F3 or F4—who tend to be less likely to experience SVRs and more likely to experience debilitating side effects than those with less severe fibrosis.

Both studies were similar in their design, with each trial comparing three treatment groups. All patients received four weeks of lead-in treatment of IFN/RBV alone. From there, one group in each study added boceprevir for a total of 24 weeks—those with undetectable viral loads through week 24 stopped treatment, whereas those with detectable virus continued IFN/RBV alone for the remainder of the 48-week studies (response-guided therapy). A second group in each study took boceprevir plus IFN/RBV for a total of 44 weeks. A third group in both studies took IFN/RBV, without boceprevir, for all 48 weeks of the trials.

In SPRINT-2, 100 of the 1,100 patients enrolled had Metavir scores of F3 or F4. In RESPOND-2, a total of 78 of 400 patients enrolled had advanced fibrosis/cirrhosis.

Boceprevir plus IFN/RBV was more effective than IFN/RBV alone in patients with advanced fibrosis

or cirrhosis upon entering the studies. Compared with those who received IFN/RBV alone for the duration of the study, study volunteers with F3–F4 scores were more likely to have an SVR if they used boceprevir as part of their treatment combination. Among F3–F4 patients in SPRINT-2, 41 percent of patients who underwent response-guided therapy and 52 percent of patients who took boceprevir plus IFN/RBV for 44 weeks had an SVR, compared with 38 percent who took IFN/RBV alone for 48 weeks. In RESPOND-2, SVR rates were 44, 68 and 13 percent, respectively.

The researchers noted, however, that patients with F3–F4 liver disease receiving boceprevir were less likely to experience an SVR, compared with their peers entering the studies with less pronounced fibrosis. Among first-time treatment takers for example, 67 percent of patients with a Metavir score of F0–F2 treated with either response-guided boceprevir or a full course of all three drugs experienced SVRs, compared with 41 to 52 percent of those with F3–F4 fibrosis/cirrhosis.

Encouragingly, the safety profile of boceprevir combined with IFN/RBV was relatively similar in both F0–F2 and F3–F4 groups. Serious adverse events were documented in 11 percent of those with F0–F2 fibrosis, compared with 14 percent of those with advanced fibrosis/cirrhosis. The rates of side effects leading to treatment discontinuation were 13 percent and 12 percent, respectively. The rates of side effects leading to dose modifications were slightly higher in the F3–F4 group: 41 percent versus 35 percent.

In conclusion, Bruno stressed that boceprevir plus IFN/RBV is both safe and effective in patients with a variety of treatment histories and advanced fibrosis or cirrhosis. However, he added, viral cure rates are lower compared with those with less advanced disease, and it may be necessary to further explore the optimal length of treatment when using boceprevir to treated patients with F3 or F4 fibrosis.

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