Incivek, Victrelis Associated With Serious Side Effects in Cirrhotic Patients

April 24, 2012

Many people living with hepatitis C virus (HCV) can't wait until all-oral, potentially less toxic regimens become available. In these patients, notably those with cirrhosis of the liver and who didn't respond favorably to prior treatment with pegylated interferon and ribavirin, regimens containing Incivek (telaprevir) or Victrelis (boceprevir) may boost the likelihood of curing HCV, but with the risk of serious side effects.

The mixed good-news, bad-news data involving a population of people living with HCV who were not well studied in clinical trials leading to the approval of both protease inhibitors were reported Thursday, April 19, at the 47th Meeting of the European Association for the Study of the Liver (EASL) in Barcelona. They were presented at the conference by Christophe Hézode, MD, of the Hôpital Henri Mondor in Créteil, France, and his colleagues, and are based on the experiences of more than 450 people with HCV-related cirrhosis who participated in the country's Compassionate Use of Protease Inhibitors in Cirrhotics (CUPIC) program before the protease inhibitors were approved in France.

CUPIC, which ensured access to either Incivek (solid in France as Incivio) or Victrelis in combination with pegylated interferon and ribavirin (peg-IFN/RBV), enrolled 655 people living with HCV in the country. A total of 455—296 receiving Incivek and 149 receiving Victrelis—were confirmed to have cirrhosis and included in the analysis by Hézode's team.

Standard dosing schedules, in combination with peg-IFN/RBV, were used for both drugs.

Unfortunately, data were only available for those completing 16 weeks of treatment, thus only partial glimpses at the regimens' safety and efficacy are possible. And while some casual comparisons between those treated with Incivek or Victrelis are possible, the CUPIC program was not designed to determine which agent was safer or more effective.

After 16 weeks on treatment, 86 percent of those receiving Incivek plus peg-IFN/RBV and 71 percent of those receiving Victrelis plus IFN/RBV had undetectable viral loads—both strong indicators of eventual cures or sustained virologic responses 24 weeks after completing therapy (SVR 24).

Unfortunately, rates of serious side effects were high. Among those receiving Incivek plus peg-IFN/RBV, nearly 49 percent experienced at least one serious adverse event. Among those receiving Victrelis plus peg-IFN/RBV, 38 percent experienced at least one major side effect. Roughly one of every seven people in the Incivek group had to discontinue treatment prematurely because of serious side effects, compared with one of every 14 people in the Victrelis group.

Severe anemia occurred in 10 percent of patients in both treatment groups, and erythropoietin therapy to boost hemoglobin levels was required for more than half of patients receiving either Incivek or Victrelis. Moreover, 20 percent of Incivek recipients and 10 percent of Victrelis recipients required blood transfusions because of severe anemia-related fatigue.

Serious decreases in neutrophils—the most common type of white blood cell and primarily responsible for engulfing bacteria—occurred in 5 percent of patients receiving either Incivek or Victrelis. Serious decreases in platelets (thrombocytopenia) occurred in more than one in five CUPIC participants receiving Incivek and in 7 percent of those receiving Victrelis.

“The safety profile of [Incivek] or [Victrelis] with peg-IFN/RBV in cirrhotic patients was poor and associated with increased rates (30 to 51 percent) [of serious adverse events] compared to those reported in phase III trials (9 to 14 percent),” Hézode and his colleagues concluded. “These data strongly suggest that triple therapy must be administered cautiously with intensive safety monitoring in these patients.”
