

EASL: Telaprevir and Boceprevir Effective but Cause Serious Side Effects in Patients With Cirrhosis

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A real-world study of recently approved hepatitis C protease inhibitors in the group of patients who have been told they should not wait for newer, experimental antivirals has shown a much higher rate of serious adverse events and treatment discontinuations than in clinical trials, Christophe Hézode reported on behalf of the French Compassionate Use of Protease Inhibitors in Cirrhotics (CUPIC) cohort study at the 47th International Liver Congress (EASL 2012) in Barcelona on Thursday.

However, rates of virological response after 16 weeks of treatment were high in this group of patients who had previously relapsed or failed to respond to pegylated interferon and ribavirin.

The French program and cohort study were established prior to the licensing of telaprevir (Incivo/Incivek) and boceprevir (Victrelis) in Europe in order to provide early access to the new drugs in patients with hepatitis C judged to be in urgent need of treatment. Under French law experimental drugs may be made available prior to licensing to patients with urgent clinical needs, if data on safety are collected.

The cohort study sought to evaluate outcomes in patients who received the drugs, and in particular to evaluate the tolerability and efficacy of the new drugs in patients with hepatitis C mono-infection and compensated cirrhosis with a previous history of non-response or relapse after standard treatment with pegylated interferon and ribavirin.

Early access was provided to telaprevir or boceprevir for 655 patients at 55 hospitals in France; 455 were eligible for inclusion in the cirrhosis analysis (296 taking telaprevir, 149 taking boceprevir).

The telaprevir regimen consisted of 12 weeks of telaprevir in combination with standard hepatitis C treatment, followed by a further 36 weeks of pegylated interferon and ribavirin. The boceprevir regimen comprised 4 weeks of lead-in treatment with pegylated interferon and ribavirin, followed by 44 weeks of boceprevir with pegylated interferon and ribavirin. This study did not report on sustained virological response after completion of treatment, and efficacy and adverse event data cover the first 16 weeks of treatment. However, week 16 on-treatment virologic response data showed that 86% (177 of 205 patients) of telaprevir-treated patients and 71% (89 of 126) of boceprevir-treated patients had undetectable HCV viral load.

There was no randomization, which precluded any comparison between the safety profiles of the 2 drugs.

Most of the patients were male and their mean age was 57 years.

Just under half (48.6%) of patients receiving telaprevir experienced a serious adverse event, as did 38% of those treated with boceprevir. This high prevalence of serious side effects contrasted to rates of between 9% and 14% observed in the Phase 3 studies which led to the licensing of the drugs. 14.5% of the telaprevir-treated patients and 7% of the boceprevir-treated patients discontinued treatment as a result of serious adverse events.

"The safety profile of telaprevir or boceprevir with pegylated interferon/ribavirin in cirrhotic patients was poor," comment the investigators.

Grade 2 anemia (8.0 - < 10.0 g/dl) developed in 19.6% of telaprevir-treated patients and 22% of individuals receiving boceprevir-based therapy. Grade 3-4 anemia (< 8.0 g/dl) was observed in 10% of those taking telaprevir and 10% of patients treated with boceprevir.

Erythropoietin (EPO) therapy for anemia was provided to 56% of telaprevir patients and 66% of boceprevir patients. One-fifth of individuals taking telaprevir and 10% of those treated with boceprevir required a blood transfusion.

Serious (grade 3-4, < 50,000/mm³) thrombocytopenia was also common. It developed in 13% and 7% of telaprevir- and boceprevir-treated patients, respectively. Neutropenia grade 3-4 (< 1000/mm³) was observed in 5% of telaprevir and boceprevir-treated patients.

Although serious infections were rare (1%-2%), a large proportion of patients developed "other" grade 3-4 adverse events (53% taking telaprevir; 32% taking boceprevir).

"These data strongly suggest that triple therapy must be administered cautiously with intensive safety monitoring in...patients [with cirrhosis]," concluded the investigators.

C Hezode, C Dorival, F Zoulim, et al. Safety of Telaprevir or Boceprevir in Combination with Peginterferon alfa/Ribavirin, in Cirrhotic Non Responders. First Results of the French Early Access Program (ANRS CO20-CUPIC). 47th Annual Meeting of the European Association for the Study of the Liver (EASL 2012). Barcelona, April 18-22, 2012. Abstract 8.