Long-term Entecavir Therapy Reverses Fibrosis and Cirrhosis in Chronic Hepatitis B Patients

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Substantial Histologic Improvement Achieved in 96% of Patients with Advanced Disease

Researchers from this international study found that patients with chronic hepatitis B virus (HBV) infection who received at least 3 years of cumulative entecavir (antiviral) therapy achieved substantial histologic improvement and regression of fibrosis or cirrhosis. Full details of the study appear in the September issue of Hepatology, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases (AASLD).

According to the Centers for Disease Control and Prevention (CDC), chronic hepatitis B afflicts an estimated 800,000–1.4 million people in the U.S. It is an even greater problem globally, affecting approximately 350 million people. An estimated 15%–25% of people with this chronic disease develop serious liver problems, including liver damage, cirrhosis, liver failure, or liver cancer, and an estimated 620,000 persons worldwide die from HBV-related liver disease each year.

Viral replication is now recognized as the key driver of liver injury and disease progression, and the primary aim of treatment is long-term suppression of hepatitis B viral replication to undetectable levels. Entecavir is a potent HBV antiviral drug that in previous trials has demonstrated superior virologic, histologic and biochemical outcomes in nucleoside-naïve patients after treatment periods ranging from 48 weeks to 3 years, with minimal emergence of resistance. The present study confirms these results.

The study evaluated nucleoside-naïve patients from two Phase III entecavir studies—HBeAg-positive and HBeAg-negative—who subsequently entered an open-label rollover study and received entecavir for a total duration of at least 3 years. HBeAg is found in serum during acute and chronic HBV infection and indicates that the virus is replicating and the infected person has high levels of HBV DNA.

Sixty-nine patients (50 HBeAg-positive; 19 HBeAg-negative) receiving entecavir therapy underwent long-term liver biopsies (median time of biopsy was 6 years; range: 3–7 yrs). Histologic improvement was analyzed for 57 patients who had an adequate baseline biopsy, a baseline Knodell necroinflammatory score ≥2, and an adequate long-term biopsy. At the time of long-term biopsy, all patients in the cohort had HBV DNA <300 copies/mL and 86% had normalized ALT. Histologic improvement, defined as ≥2-point decrease in Knodell necroinflammatory score and no worsening of Knodell fibrosis score, was observed in 96% of patients and a ≥1 point improvement in Ishak fibrosis score was found in 88% of patients, including all ten patients with advanced fibrosis or cirrhosis at Phase III baseline.

The lead author, Professor Ting-Tsung Chang explains, “These data support the conclusion that in most nucleoside-naïve patients, long-term entecavir therapy leads to potent suppression of HBV DNA, normalization of ALT and improvement in liver histology with accompanying regression of fibrosis, including those with advanced fibrosis or cirrhosis at baseline. Substantially more patients demonstrated histologic improvement at the time of the long-term biopsy compared to week 48, confirming the value of long-term treatment for chronic HBV infection. The safety profile, potent suppression of HBV replication, and low potential for antiviral drug resistance in nucleoside-naïve patients make long-term treatment of chronic HBV infection with entecavir monotherapy possible.”

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During the Phase III program, patients received an entecavir dose of 0.5 mg daily and during the long-term rollover study, all patients received 1.0 mg of entecavir daily. Some patients received concurrent lamivudine (100 mg daily) for a brief period of time early in the rollover study before continuing on entecavir monotherapy (1.0 mg daily) after the protocol was amended.

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