Can Stopping Antivirals Lead to a Functional Cure for Hepatitis B?

Most people who stopped long-term nucleoside/nucleotide analogs did not need to restart treatment.

June 5, 2023 By Sukanya Charuchandra and Liz Highleyman

Some people with chronic hepatitis B virus (HBV) who received long-term antiviral therapy experienced sustained hepatitis B surface antigen (HBsAg) loss after stopping treatment, especially if they had low levels while on therapy, according to study findings published in the Journal of Hepatology. Although HBV viral load rebounded after treatment discontinuation, most did not need to restart antivirals.

“We were able to show that in some patients, discontinuing long-term therapy with nucleoside or nucleotide analogs after at least four years is more effective than continuing it, and that many patients no longer require antiviral therapy at all after discontinuation,” Florian van Bömmel, MD, of Leipzig University Medical Center in Germany, said in a news release. “In particular, patients who show low HBsAg levels when they discontinue treatment have a high chance of functional cure.”

Over time, chronic hepatitis B can lead to severe liver disease, including cirrhosis, liver cancer and the need for a liver transplant. Nucleoside/nucleotide antivirals, such as Viread (tenofovir disoproxil fumarate), Vemlidy (tenofovir alafenamide) or Baraclude (entecavir), are standard treatment for people with hepatitis B e antigen (HBeAg)-negative chronic hepatitis B.

However, patients rarely achieve HBsAg loss—which is considered a functional cure—so treatment usually continues for life. These drugs suppress viral replication and prevent liver disease progression, but they can cause impaired kidney function, bone loss and other side effects, and the cost of continuous treatment is high. If antivirals are stopped and viral replication resumes, this can lead to a flare-up of liver inflammation as the immune system fights the virus.

Van Bömmel and colleagues conducted a randomized controlled trial that included 166 people with HBeAg-negative chronic hepatitis B at 20 clinics in Germany. They were on long-term antiviral therapy with a low HBV DNA viral load (below 172 international units per milliliter or 1,000 copies) for at least four years.

Participants in the STOP-NUC trial were randomly assigned to either continue their antivirals or

stop treatment. After about two years, 158 people were ultimately assessed. The main outcome was sustained HBsAg loss up to week 96.

Eight people (10%) who stopped antiviral therapy consistently tested negative for HBsAg, indicating immune control of the virus. No one who continued treatment achieved a similar outcome. Sixteen people who stopped therapy (20%) experienced at least a 1-log HBsAg reduction compared with only one person who continued therapy (1.3%). Among those with low HBsAg levels (below 1,000 IU/mL) at the beginning of the trial, seven (28%) achieved HBsAg loss. Among those who stopped treatment, six (7.6%) experienced seroconversion, meaning antibodies against HBsAg (anti-HBs) made an appearance.

Everyone who stopped treatment saw a relapse in HBV DNA viral load, indicating that the virus resumed replication. But most did not need to start treatment again: 32 participants who stopped antivirals (41%) experienced sustained remission, meaning they had HBV levels below the threshold for resuming therapy, while only 11 people (14%) had to restart antivirals due to liver inflammation.

Three quarters of people who stopped treatment did not have elevated liver enzyme levels, a sign of inflammation. Stopping therapy did not lead to hepatitis decompensation (liver failure) or other serious adverse events, according to the researchers. However, prior studies have seen a few cases of severe liver inflammation after antiviral therapy discontinuation, so this should be done only under the supervision of an experienced physician, Van Bömmel said.

“Cessation of [nucleoside/nucleotide antiviral] treatment was associated with a significantly higher rate of HBsAg loss than continued [antiviral] treatment, which was largely restricted to patients with end of treatment HBsAg levels below 1,000 IU/mL,” the study authors wrote.

“The results of the STOP-NUC trial provide evidence for the concept of stopping [nucleoside/nucleotide antiviral] treatment as a therapeutic option that can induce functional cure,” they concluded.

Click here to read the study in the Journal of Hepatology.

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