Vemlidy for Hepatitis B Is Safe and Effective for Up to 8 Years

Most study participants achieved viral suppression with minimal changes in kidney function or bone density.

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Vemlidy (tenofovir alafenamide, or TAF) works as well as the older Viread (tenofovir disoproxil fumarate, or TDF) for people with chronic hepatitis B, but the newer drug is easier on the kidneys and bones, according to eight-year follow-up data presented at the EASL Congress.

Nucleoside/nucleotide antivirals, such as Vemlidy, Viread and Baraclude (entecavir), can suppress hepatitis B virus (HBV) replication indefinitely, but they usually do not lead to a cure. This means many people stay on treatment for years, so long-term safety and effectiveness are important.

TDF and TAF are used to treat both HBV and HIV. TDF is sold alone as Viread and is a component of HIV coformulations including Truvada, Atripla, Complera, Stribild and Delstrigo. TAF is sold alone as Vemlidy (approved for HBV but not HIV) and is a component of combination pills including Descovy, Biktarvy and Symtuza.

TDF is generally safe and well tolerated, but it can cause bone loss and kidney problems in susceptible patients. TAF is a prodrug formulation that produces a high level of the active drug in target cells using a smaller dose than TDF, which means lower concentrations in the blood and less drug exposure for the kidneys, bones and other organs. (Click here to learn more about TAF and TDF.)

Maria Buti, MD, of Hospital Universitario Vall d'Hebron in Barcelona, presented final eight-year efficacy results from two pivotal Phase III studies that compared Vemlidy versus Viread in people with chronic hepatitis B.

Study 108 enrolled 425 hepatitis B e antigen (HBeAg)-negative participants, while Study 110 enrolled 873 HBeAg-positive patients in more than a dozen countries. In both studies combined, about two thirds were men, nearly 80% were Asian and the average age at the start of the study was about 40 years. Nearly a quarter had previously been treated for hepatitis B, and about 10% had liver cirrhosis.

Participants in both studies were randomly assigned to receive 25 milligrams of Vemlidy or 300 mg

of Viread once daily. After the initial blinded part of the study, participants in the Viread group switched to open-label Vemlidy at 96 or 144 weeks.

Researchers presented primary 48-week safety and efficacy results at the 2016 EASL Congress, showing that Vemlidy works as well as Viread but with better kidney and bone safety. In Study 108, 94% of Vemlidy recipients and 93% of Viread recipients had an undetectable HBV viral load, indicating that Vemlidy is noninferior to Viread. Among the more difficult-to-treat participants in Study 110, 64% and 67%, respectively, had undetectable HBV DNA at 48 weeks. However, hepatitis B surface antigen (HBsAg) loss and seroconversion—considered a functional cure—were rare, occurring in less than 1%. Follow-up reports showed continued equivalent effectiveness at 96 weeks and at 144 weeks.

At this year's conference, Buti reported final efficacy results at 384 weeks, or nearly eight years. This pooled analysis included 647 people initially assigned to Vemlidy and 327 people initially assigned to Viread who completed follow-up in the open-label part of the studies.

Among HBeAg-negative participants, 97% of people who took Vemlidy for the entire study and 98% of those who switched from Viread to Vemlidy had an undetectable HBV viral load at 384 weeks. Among HBeAg-positive patients, response rates ranged from 91% to 96%. Of the 29 participants (3%) eligible for viral sequencing, none developed resistance to Vemlidy.

Most participants experienced ALT liver enzyme normalization (70% to 89%, depending on the criteria used). Among people who started on Viread, ALT normalization increased after switching to Vemlidy.

Among the HBeAg-positive participants, about 45% experienced HBeAg loss and about 30% experienced HBeAg seroconversion at 384 weeks, with rates progressively increasing over the course of follow-up. But functional cure rates remained low. Just nine HBeAg-negative and 16 HBeAg-positive patients experienced HBsAg loss, and only six HBeAg-negative and 13 HBeAg-positive people experienced HBsAg seroconversion (5% or less across treatment groups).

This analysis had long enough follow-up to look at changes in liver cirrhosis. Of 78 participants with cirrhosis at baseline, more than 70% experienced regression and no longer had evidence of cirrhosis according to noninvasive FibroTest scores at 384 weeks.

"Treatment with TAF was highly effective in patients with chronic HBV," the researchers concluded. "These results provide continued support for TAF as the preferred treatment for chronic HBV infection."

In a second study presented as a poster, Young-Suk Lim, MD, PhD, of University of Ulsan College of Medicine in South Korea, and colleagues described pooled safety data from the two trials.

Consistent with earlier analyses, the overall incidence of adverse events was comparable across the groups. Rates of severe (Grade 3 or 4) treatment-related adverse events (less than 1%) and

events leading to discontinuation (1%) were low. People initially assigned to Viread experienced declines in estimated glomerular filtration rate (a measure of kidney function) and hip and spine bone mineral density, but these improved after switching to Vemlidy. About 5% of people who started on Vemlidy and 8% who switched had elevated LDL cholesterol.

Chronic hepatitis B infection can cause hepatocellular carcinoma (HCC), the most common type of primary liver cancer, but antiviral treatment reduces the risk. In this pooled analysis, 21 people developed HCC over eight years of follow-up.

“Long-term TAF treatment was safe and well tolerated, with minimal changes in [estimated glomerular filtration rate] and bone mineral density occurring over eight years,” the researchers concluded.

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