Bulevirtide in Combination With PegInterferon Results In Undetectable Hepatitis D RNA Post-Treatment

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Bulevirtide (Hepcludex; Gilead Sciences) combined with pegylated interferon alfa-2a showed superiority to bulevirtide monotherapy in achieving undetectable hepatitis D virus (HDV) RNA at 24 weeks post-treatment, according to results of a study published in the *New England Journal of Medicine.*[1,2]

“HDV is the most severe form of viral hepatitis. For people living with HDV, bulevirtide 2 mg has been proven to be a successful long-term treatment approach, as highlighted in clinical trials and real-world data. These new data support the potential for bulevirtide as a finite treatment option, demonstrating that almost half of people treated with bulevirtide 10 mg in combination with [pegylated interferon alfa-2a] remained undetectable for HDV RNA 1 year after treatment cessation,” Tarik Asselah, MD, PhD, professor of Hepatology in the Hôpital Beaujon APHP at Université Paris-Cité and head of Viral Hepatitis at UMR1149 Inserm, said in the news release. “These long-term data are the highest post-treatment response rates ever reported for HDV.”[2]

According to the study authors, the only treatment available for HDV was off-label therapy with pegylated interferon alfa recommended by clinical practice guidelines; however, it has been associated with early discontinuation due to adverse events and late relapse after treatment cessation. Bulevirtide became the first approved treatment for HDV and compensated liver disease in Europe, but no therapies have been approved in the United States.[1]

Investigators of the study used the MYR 204 study to evaluate bulevirtide in combination with pegylated interferon alfa for 96 weeks as a potential treatment for individuals with chronic HDV, according to the study authors. Individuals aged 18 to 65 years old with chronic HDV were included in the multicenter, open-label, randomized study. Treatment was randomized 1:2:2:2 into 4 treatment groups, including: subcutaneous pegylated interferon alfa-2a at 280 µg per week for the first 48; subcutaneous bulevirtide at 2 mg per day for 96 weeks with subcutaneous pegylated interferon alfa-2a at 280 µg per week for the first 48 weeks; subcutaneous bulevirtide at 10 mg per day for 96 weeks with pegylated interferon alfa-2a at 280 µg per week for the first 48 weeks; or subcutaneous bulevirtide at 10 mg per day for 96 weeks. All individuals in the study were followed for an additional 48 weeks after treatment ended.[1]

The primary end point included undetectable HDV RNA level at week 24 post-treatment. The secondary end points included undetectable HDV RNA at week 48 and week 96 (in the bulevirtide group) during treatment and at week 48 post-treatment, according to the study authors. Safety assessment included adverse events (AEs) and elevations in bile acid levels.[1]

Investigators included a total of 175 individuals were included in the study with 25 patients being assigned to the pegylated interferon alfa-2a monotherapy arm and 50 to each other arm. In the 2 mg bulevirtide group, 44% of individuals achieved HDV RNA that was undetectable compared with 70% in the 10 mg group, 21% in the pegylated interferon alfa-2a monotherapy, and 22% in the bulevirtide monotherapy at the end of treatment. At the primary endpoint, the rates were 32%, 46%, 17%, and

12%, respectively. At 48 weeks post-treatment, the rates were 26%, 46%, 25%, and 12%, respectively.[1]

About The Trial

Trial Name: Study to Assess Efficacy and Safety of Bulevirtide in Combination With Pegylated Interferon Alfa-2a in Participants With Chronic Hepatitis Delta (CHD)

ClinicalTrials.gov ID: NCT03852433

Sponsor: Gilead Sciences

Completion Date: September 2022

As for safety, the most frequent AEs included leukopenia, neutropenia, and thrombocytopenia at rates that were mostly mild to moderate, according to the news release.[2]

“Chronic HDV can greatly impact those affected due to its rapid progression to liver failure, liver cancer and liver-related death. With these promising finite data for bulevirtide, we have the opportunity to support healthier futures for people living with HDV,” Anu Osinusi, vice president of Clinical Research for Hepatitis, Respiratory, and Emerging Viruses at Gilead Sciences, said in the news release. “In addition to highlighting the curative potential of combination therapy for some people with chronic HDV, these final data support the safety profile of bulevirtide.”[2]

References

1. Asselah T, Chulanov V, Lampertico P, et al. Bulevirtide Combined with Pegylated Interferon for Chronic Hepatitis D. N Engl J Med. Published online June 6, 2024. doi:10.1056/NEJMoa2314134
2. Gilead Announces New England Journal of Medicine Publication of Data that Demonstrate Bulevirtide with PegIFN Achieved Post-Treatment Undetectable HDV RNA. News release. Gilead Sciences. June 6, 2024. Accessed June 10, 2024. https://www.gilead.com/news-and-press/press-room/press-releases/2024/6/gilead-announces-new-england-journal-of-medicine-publication-of-data-that-demonstrate-bulevirtide-with-pegifn-achieved-post-treatment-undetectable-hdv

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