# FDA Grants Breakthrough Therapy Designation to Tobevibart With Elebsiran for Treatment of Chronic Hepatitis Delta

## Key Takeaways

- Tobevibart and elebsiran received breakthrough therapy and PRIME designations for CHD, based on positive phase 2 SOLSTICE trial data.
- Tobevibart is a monoclonal antibody targeting hepatitis B surface antigen, while elebsiran is an RNA-targeting agent, both administered subcutaneously.

*The treatments are currently undergoing evaluation in the SOLSTICE*

The FDA granted a breakthrough therapy designation to tobevibart (VIR-3434; Vir Biotechnology) and elebsiran (VIR-2218; Vir Biotechnology) for the treatment of patients with chronic hepatitis delta (CHD). The designation comes after positive safety and efficacy data from the phase 2 SOLSTICE trial (NCT05461170), which were presented at the 2024 American Association for the Study of Liver Diseases (AASLD) The Liver Meeting, which was held in San Diego, California from November 15 to November 19. Additionally, the combination treatment was also granted a European Medicines Agency Priority Medicines designation.[1]

Tobevibart is an investigational broadly neutralizing monoclonal antibody that targets the hepatitis B surface antigen. It is designed to inhibit the entry of hepatitis B and hepatitis delta viruses into hepatocytes, as well as reduce the levels of circulating viral and subviral particles in the blood. The agent is administered subcutaneously and is currently under clinical development for the treatment of patients with chronic hepatitis B and patients with chronic hepatitis delta.[1]

Elebsiran is an investigational hepatitis B virus-targeting small interfering RNA designed to degrade hepatitis B virus RNA transcripts and limit the production of the hepatitis B surface antigen. According to current data, it has the potential to have a direct antiviral activity against hepatitis B virus and hepatitis delta virus.Like tobevibart, it is administered subcutaneously, and it is currently in clinical development for the treatment of patients with chronic hepatitis B and patients with chronic hepatitis delta.[1]

“Chronic hepatitis delta has devastating effects on liver and overall health, yet people living with this condition are still waiting for highly effective therapeutic options,” Mark Eisner, MD, MPH, executive vice president and chief medical officer, Vir Biotechnology, said in a news release. “The phase 2 SOLSTICE trial data suggests that tobevibart and elebsiran can rapidly and deeply suppress the hepatitis delta virus, driving it to undetectable levels.”[1]

Tobevibart and elebsiran are currently undergoing evaluation in the SOLSTICE trial (NCT05461170), a randomized, open-label, multicenter phase 2 trial assessing the safety, tolerability, and efficacy of tobevibart alone (300 mg) every 2 weeks or in combination with elebrsiran (200 mg) every 4 weeks in patients with chronic hepatitis delta. The study’s primary end points are proportion of participants with undetectable hepatitis delta virus RNA (HDV RNA; $\geq 2$ $\log_{10}$ decrease from baseline or below limit of detection) up to week 24, alanine aminotransferase (ALT) normalization (defined as ALT below upper limit of normal) up to week 24, and treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) up to 118 weeks. Additionally, secondary end points include proportion of participants with undetectable HDV RNA and different timepoints and up to 192 weeks.[1-3]

According to findings presented at AASLD The Liver Meeting, all patients achieved an HDV RNA greater than or equal to 2 $\log_{10}$ decrease or below limit of detection at week 24. This rate was sustained over time in all patients

at weeks 36 (n = 22 of 22) and those in the rollover cohort who reached week 60 (n = 5 of 5). Further, HDV RNA target not detected was achieved in approximately 41% (n = 13) of patients receiving the combination regimen at week 24, and this increased to 64% (n = 14) at week 36.[3]

In addition, approximately 90% of participants receiving the combination achieved reductions in hepatitis B surface antigen (HBsAg) values below 10 IU per mL at week 24, with sustained responses at later time points, indicating suppression of the key biologic mechanisms that HDV require for viral replication. ALT had also decreased in most participants between day 1 and week 24, normalizing in about 47% (n = 15) of participants in the combination cohort and 56% (n = 5) in the rollover cohort by week 24. These were sustained at week 36.[3]

According to the investigators, the safety profiles of tobevibart and elebsiran were consistent with previous studies. TEAEs were considered mild or moderate and transient across all treatment groups, with influenza-like illness being the most common. No ALT flares were observed and there were no discontinuations because of the study drugs. Additionally, no treatment-related SAEs were reported.[3]

"Receiving FDA breakthrough therapy and European PRIME designations recognizes this combination's potential to transform the lives of people living with CHD. We look forward to advancing the phase 3 ECLIPSE program as quickly as possible," said Eisner in the news release.[1]

### About the Trial

**Trial Name:** SOLSTICE: Combination Therapy for the Treatment of Chronic Hepatitis D Infection.

**ClinicalTrials.gov ID:** NCT05461170

**Sponsor:** Vir Biotechnology, Inc.

**Completion Date (Estimated):** August 2029

## REFERENCES


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