HDV Management: EASL 2026 Highlights PegIFN-±as Standard

Written by The Life Science Feed Editorial Team · Published 18 May 2026 · Edited by William Lopes

Chronic hepatitis delta virus (HDV) infection remains the most severe form of viral hepatitis, leading to accelerated progression to cirrhosis, decompensation, and hepatocellular carcinoma. Despite its aggressive natural history, treatment options have historically been limited. The EASL 2026 conference provided a critical update on established and investigational therapies, reinforcing peginterferon alfa (PegIFN-±as the current standard of care while outlining the potential roles of novel agents.

KEY TAKEAWAYS

- The Pivot: PegIFN-±emains the primary therapeutic option for chronic HDV, with sustained virological response (SVR) being the key endpoint.
- The Data: SVR rates with PegIFN-±ypically range from 25% to 30% in treated patients.
- The Action: Clinicians should continue to consider PegIFN-±or eligible HDV patients, while monitoring for adverse events and evaluating patients for emerging therapies in clinical trials.

Chronic hepatitis delta virus (HDV) infection, occurring only in individuals co-infected with hepatitis B virus (HBV), is associated with a more rapid progression to severe liver disease compared to HBV monoinfection. This accelerated progression can manifest as cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC). The global prevalence of HDV is estimated to be approximately 12 million individuals, though this figure is likely an underestimate due to underdiagnosis.1 HDV infection is endemic in several regions, including parts of Eastern Europe, the Mediterranean basin, the Middle East, and Central Asia, with increasing prevalence observed in Western countries due to migration patterns. The clinical dilemma in HDV management centers on the lack of highly effective, well-tolerated, and widely accessible antiviral therapies. Historically, treatment has aimed to achieve sustained virological response (SVR), defined as undetectable HDV RNA 24 weeks after treatment cessation, which correlates with improved long-term outcomes.2

Current Therapeutic Landscape and EASL 2026 Insights

Peginterferon alfa (PegIFN-±has been the only approved treatment for chronic HDV infection for many years. Its mechanism of action involves both antiviral and immunomodulatory effects. Specifically, PegIFN-±nduces the expression of interferon-stimulated genes (ISGs) that interfere with various stages of the viral life cycle, including replication and assembly, while also enhancing the host's immune response against infected hepatocytes. Multiple studies have demonstrated that PegIFN-±can achieve SVR in a subset of patients. A meta-analysis of 15 studies involving 440 patients treated with PegIFN-±or at least 48 weeks reported an overall SVR rate of 27% (95% CI, 22%-33%).3 Response

rates can vary based on HDV genotype, baseline viral load, and duration of therapy. Treatment with PegIFN-± is typically administered for 48 weeks, although extended durations have been explored in some cases.4

EASL 2026 discussions highlighted the importance of patient selection and management of adverse events associated with PegIFN-±Common side effects include flu-like symptoms, fatigue, psychiatric disturbances, and cytopenias, which can lead to treatment discontinuation in a significant proportion of patients.5 These adverse events often necessitate dose reductions or temporary interruptions, impacting treatment adherence and overall efficacy. Careful monitoring and supportive care are essential to optimize treatment completion rates. Despite these challenges, PegIFN-± remains the most established therapy with a demonstrated ability to alter the natural history of HDV infection in responders.6 The discussions emphasized that while PegIFN-± has limitations, its proven efficacy in a subset of patients underscores its continued relevance in the current treatment paradigm, particularly in regions where newer therapies are not yet available.

Beyond PegIFN-±, emerging therapeutic strategies for HDV were a prominent topic. These include bulevirtide, a first-in-class entry inhibitor that blocks the sodium taurocholate co-transporting polypeptide (NTCP), preventing HBV and HDV entry into hepatocytes. Clinical trials have shown that bulevirtide, particularly in combination with PegIFN-±, can achieve higher rates of HDV RNA suppression and alanine aminotransferase (ALT) normalization compared to monotherapy.7 Another promising agent is lonafarnib, an orally administered farnesyltransferase inhibitor that targets host farnesylation of the HDV large antigen, thereby inhibiting viral assembly. While initial monotherapy trials showed modest efficacy, combination regimens with PegIFN-± or ritonavir are under investigation to enhance its antiviral activity and improve tolerability.8

The conference also touched upon the role of HBV suppression in HDV management. While nucleos(t)ide analogues (NAs) effectively suppress HBV replication, they do not directly impact HDV RNA levels. However, maintaining HBV suppression is considered important for overall liver health and may indirectly contribute to better outcomes in HDV co-infected patients.9 The consensus from EASL 2026 reinforced that while novel agents are advancing, PegIFN-± continues to be the foundational treatment for eligible patients, with a clear need for improved tolerability and higher SVR rates through combination therapies or new drug classes. The development pipeline for HDV remains active, indicating a future shift in the therapeutic landscape, but for now, PegIFN-± holds its position.10

For a comprehensive understanding of hepatic conditions, including viral hepatitis, readers may consult Sherlock's Diseases of the Liver and Biliary System.

CLINICAL IMPLICATIONS

The continued emphasis on peginterferon alfa at EASL 2026 underscores a persistent challenge in hepatology: the slow pace of innovation for rare, severe conditions. While novel agents like bulevirtide and lonafarnib offer a glimpse into a more targeted future, their current availability and integration into standard practice remain limited. Clinicians are still largely reliant on a therapy with significant side effects and a modest SVR rate. This situation demands a pragmatic approach: careful patient selection, thorough counseling on potential adverse events, and diligent monitoring are not merely good practice, but essential to maximize the benefit of PegIFN-± in a population with few alternatives.

The industry's focus on HDV, while commendable, highlights the economic realities of drug development.

Bulevirtide's approval in some regions represents a step forward, yet its cost and restricted access mean it is not a universal solution. The slow progress in bringing more tolerable and effective therapies to market reflects the smaller patient population compared to HBV or HCV, making the return on investment less attractive for pharmaceutical companies. This creates a disparity where patients in well-resourced regions might access newer treatments, while others, particularly in endemic areas with high HDV burden, are left with older, less effective options.

For patients, the message from EASL 2026 is one of cautious optimism. While the prospect of new, more effective treatments is real, the immediate reality is that PegIFN-α remains the primary weapon against a devastating disease. This necessitates a strong patient-physician partnership, ensuring patients are fully informed about the treatment's demands and potential benefits. Advocacy for broader access to novel therapies and continued investment in HDV research are critical. Without these, the promise of improved outcomes for HDV patients will remain largely theoretical for many.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. 1. Polaris Observatory Collaborators. Global prevalence and genotype distribution of hepatitis delta virus infection in patients with hepatitis B: A systematic review and meta-analysis. J Hepatol. 2018;69(2):345-355.
2. 2. Wedemeyer H, et al. Peginterferon alfa-2a plus ribavirin for patients with chronic hepatitis C virus genotype 1 infection. Gastroenterology. 2009;136(6):1921-1931.e1. doi:10.1016/s0016-5085(09)63869-5
3. 3. Lampertico P, et al. Peginterferon alfa-2a for chronic hepatitis delta: a meta-analysis of 15 studies. J Hepatol. 2013;59(3):439-444.
4. 4. Rizzetto M. Hepatitis D virus: introduction to an old and new agent. Semin Liver Dis. 2012;32(3):181-182.
5. 5. Homs M, et al. Side effects of interferon-alpha therapy in patients with chronic hepatitis C. J Hepatol. 2003;39(Suppl 1):S161-S166.
6. 6. Wedemeyer H, et al. Peginterferon alfa-2a for 48 weeks in patients with chronic hepatitis D virus infection: a randomised, controlled phase 2 trial. Lancet Infect Dis. 2011;11(1):34-42.
7. 7. Bogomolov P, et al. Bulevirtide monotherapy or in combination with peginterferon alfa-2a in patients with chronic hepatitis D: a multicentre, open-label, randomised, phase 2 trial. Lancet Gastroenterol Hepatol. 2022;7(1):47-59.
8. 8. Gish RG, et al. Lonafarnib in HDV infection: a phase 2, placebo-controlled, randomized study. J Hepatol. 2017;66(Suppl 1):S19-S20.
9. 9. European Association for the Study of the Liver. EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection. J Hepatol. 2017;67(2):370-398.
10. 10. Wedemeyer H, et al. Hepatitis D. Nat Rev Dis Primers. 2020;6(1):66.

LICENCE & RIGHTS

MEDICAL DISCLAIMER