

EASL Congress 2026: Key Trials to Watch in Liver Disease Management

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The management of chronic liver diseases remains a complex challenge, with significant unmet needs in non-alcoholic fatty liver disease (NAFLD) and its progressive form, non-alcoholic steatohepatitis (NASH), as well as in hepatitis B virus (HBV) infection and hepatocellular carcinoma (HCC).¹ The upcoming EASL Congress 2026 is anticipated to present data from several late-stage clinical trials that could offer new therapeutic options and refine existing treatment strategies across these critical areas.

KEY TAKEAWAYS

- ° The Pivot: Novel agents targeting fibrosis and metabolic pathways in NASH, alongside new HBV cure strategies, are expected to be presented.
- ° The Data: Look for primary endpoints such as histological improvement without worsening fibrosis in NASH, or functional cure rates in HBV.
- ° The Action: Clinicians should prepare for potential updates to treatment guidelines based on efficacy and safety profiles of emerging therapies.

The landscape of hepatology is continually evolving, driven by ongoing research into the pathophysiology and treatment of chronic liver diseases. NAFLD and NASH represent a growing global health burden, with an estimated prevalence of NAFLD affecting 25% of the global population and NASH affecting 3-5% of adults.¹ Current management primarily relies on lifestyle modifications, but pharmacological interventions are urgently needed for patients with advanced fibrosis. Similarly, despite effective antiviral therapies, a complete cure for chronic HBV infection remains elusive for most patients, necessitating lifelong treatment and surveillance.² In HCC, while systemic therapies have improved outcomes, there is still a need for more effective first-line and subsequent-line treatments, particularly for patients with advanced disease.³

Key Trials to Watch at EASL 2026

Several late-stage clinical trials are expected to report significant findings at EASL 2026, potentially influencing clinical practice. In NASH, attention will be focused on agents targeting distinct pathogenic pathways. For instance, trials evaluating GLP-1 receptor agonists, such as semaglutide, are exploring their efficacy in achieving histological improvement in NASH. The phase 3 STELLAR trials for resmetirom, a thyroid hormone receptor-beta agonist, have already demonstrated significant histological improvement in NASH, with a resolution of NASH and no worsening of fibrosis in 25.9% of patients receiving 80 mg and 36.6% of patients receiving 100 mg, compared to 9.7% on placebo ($p < 0.0001$ for both doses).⁴ Further data on long-term outcomes and safety profiles from similar agents will be critical.

Additionally, studies on farnesoid X receptor (FXR) agonists, like obeticholic acid, which showed a 24% histological improvement in NASH with fibrosis compared to 13% with placebo ($P=.0002$) in the REGENERATE trial, will be closely scrutinised for their benefit-risk profiles, particularly concerning pruritus and lipid alterations.⁵

For chronic HBV infection, research is moving beyond viral suppression towards functional cure, defined as HBsAg loss with or without anti-HBs seroconversion. Trials investigating novel therapeutic classes, including siRNA agents, capsid assembly modulators, and immunomodulators, are anticipated. For example, the REEF-1 study, a phase 2b trial evaluating the siRNA agent JNJ-3989 in combination with nucleos(t)ide analogues, has shown promising HBsAg reductions.⁶ Further data on sustained HBsAg loss rates post-treatment cessation will be crucial. The efficacy and safety of these agents, alone or in combination, in achieving durable HBsAg seroclearance will be a primary focus.⁷

In HCC, advancements in systemic therapy continue to be a priority. Trials evaluating novel immune checkpoint inhibitors (ICIs) in combination with anti-angiogenic agents or other targeted therapies are expected to report. The IMbrave150 trial established atezolizumab plus bevacizumab as a first-line standard of care for unresectable HCC, demonstrating a median overall survival of 19.2 months compared to 13.4 months with sorafenib (HR 0.66, 95% CI 0.52-0.85; $p < 0.001$).⁸ Subsequent trials are exploring similar combinations or novel agents in different lines of therapy. Data on biomarkers predicting response to ICIs and strategies to overcome resistance will also be of significant interest.⁹

Limitations and Future Directions

While these trials offer considerable promise, limitations often include patient selection biases, relatively short follow-up periods for chronic conditions, and the challenge of translating histological endpoints into clinically meaningful outcomes, particularly in NASH. The long-term impact of these novel therapies on liver-related morbidity and mortality, as well as their cost-effectiveness, will require further investigation. Future research will need to focus on real-world effectiveness, identifying optimal patient populations for specific therapies, and developing combination strategies to achieve more comprehensive and durable responses across these complex liver diseases. The integration of artificial intelligence and advanced imaging techniques in patient stratification and response monitoring also represents a significant area for future development.¹⁰

Whilst anticipating future trial results, a deeper understanding of liver pathophysiology and its management can be found in Sherlock's Diseases of the Liver and Biliary System.

CLINICAL IMPLICATIONS

The anticipated data from EASL 2026 will likely present a mixed bag of incremental gains and potentially transformative shifts. For NASH, the continued emergence of agents like resmetirom and other GLP-1 receptor agonists underscores a move towards targeted pharmacological intervention beyond lifestyle modification. Clinicians should be prepared to integrate these new options into their practice, particularly for patients with advanced fibrosis, but also to critically evaluate the long-term safety and cost implications. The high price point of many novel therapies will inevitably create access disparities, challenging healthcare systems and potentially widening the gap between guideline recommendations and real-world applicability.

In HBV, the pursuit of a functional cure is commendable, yet the data presented will need to demonstrate not just HBsAg reduction, but sustained HBsAg loss post-treatment cessation with acceptable safety profiles. The current standard of care, nucleos(t)ide analogues, offers effective viral suppression, and any new regimen

must significantly improve upon this benchmark to justify its adoption. The industry's focus on combination therapies for HBV, while scientifically sound, also raises concerns about polypharmacy and potential drug-drug interactions, which will require careful monitoring in clinical practice.

For HCC, the ongoing refinement of systemic therapies, particularly immune checkpoint inhibitor combinations, offers hope for improved survival. However, the challenge remains in identifying reliable biomarkers to predict response and manage immune-related adverse events. The sheer volume of new agents and combinations necessitates a more nuanced approach to treatment selection, moving beyond a one-size-fits-all model. Clinicians will increasingly rely on multidisciplinary teams and molecular profiling to guide therapy, a shift that demands continuous education and resource allocation. The ultimate goal remains to improve patient outcomes, but the path to achieving this must balance efficacy with safety, accessibility, and economic feasibility.

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