Immune and Cholestatic Liver Disease at the EASL Congress 2026

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THIS YEAR, at the European Association for the Study of the Liver (EASL) Congress, there were exciting new developments in immune and cholestatic liver disease, with two packed abstract sessions fully devoted to primary biliary cholangitis (PBC), primary sclerosing cholangitis (PSC), and autoimmune hepatitis (AIH).

PRIMARY BILIARY CHOLANGITIS

PBC, and specifically the role of bile acids, was on full display during the Karl Wilhelm von Kupffer Basic Science lecture. This state-of-the-art lecture series showcases key opinion leaders, and this year, Ulrich Beuers, Amsterdam UMC, the Netherlands, was the laureate. His lecture focused on the biology of bile acids, which is of relevance for PBC. Beuers highlighted how the therapeutic strategy for PBC will eventually move beyond the current treatment sequence of ursodeoxycholic acid (UDCA), followed by a farnesoid X receptor agonist (e.g., obeticholic acid) and a peroxisome proliferator-activated receptor (PPAR) agonist (e.g., elafibranor). Future therapies are expected to directly target bile acid signalling networks, cholangiocyte function, and immune responses. He highlighted that bile acids serve as hormone-like signalling molecules with pleiotropic mechanism of action, and that they have the potential to become future therapies for PBC.

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There were also novel developments in the therapeutic arena. During the late-breaker session, the results of the double-blind RCT evaluating saroglitazar, a dual PPARα/γ agonist, were presented.[1] The target population was patients with PBC who had an inadequate response to or intolerance to UDCA. Patients were treated with saroglitazar 1 mg daily (n=97) or placebo (n=51) for 52 weeks. Saroglitazar managed to lower alkaline phosphatase (ALP) in 56.7% below the pre-set barrier for biochemical response (<1.67x ULN), compared with 9.8% in the placebo group.

PRIMARY SCLEROSING CHOLANGITIS

Next on the list is PSC, a disease for which there is currently no approved drug available, representing a clear unmet need. Antonio Molinaro, University of Gothenburg, Sweden, set out to identify targets that are potentially druggable in PSC. Extensive metabolic profiling across a wide set of human and experimental models allowed identification of the gut microbial metabolite imidazole propionate (ImP) as a key factor associated with PSC.[2] ImP was consistently elevated in PSC, remained high after transplantation, and predicted poorer transplant-free survival. They provided evidence that ImP originates from the gut and mediates pro-inflammatory and pro-fibrotic responses. These sets of experiments suggest that targeting ImP production or its downstream pathway may represent a novel therapeutic strategy for PSC. Then, Michael Trauner, University of Vienna, Austria, presented the NUC-5 trial that examined norucholic acid (NCA), a bile acid derivative, in PSC.[3] NCA demonstrated superiority over placebo. Trauner dug deeper and examined the effect of the use of UDCA as a covariate. He used a combined endpoint (no worsening in histological disease stage and reduction of ALP to <1.5x ULN). At the primary analysis, assessed at 96 weeks, 12.7% of NCA patients and 5.1% of placebo patients taking UDCA met the primary endpoint (p=0.08), compared to 23.4% and 0% in the population without UDCA (p<0.001). Histologic disease stage improvement was observed for 23.4% of NCA+UDCA versus 11.9% of placebo+UDCA patients (p=0.18), compared with 30.3% of patients with NCA alone versus 6.7% with placebo alone (p=0.13) among patients with paired biopsies. These findings reinforce the efficacy signal observed in the overall NUC-5 trial and suggest that the therapeutic effects of NCA may be most pronounced when used without concomitant UDCA. A large Norwegian study addresses the major challenge of predicting liver transplantation or death in PSC.[4] The investigators developed a multi-biomarker model integrating markers of fibrosis, extracellular matrix turnover, inflammation, and gut microbial metabolism, and demonstrated that it outperformed individual biomarkers and conventional

clinical risk scores. They also tested a simplified pragmatic model incorporating these key biological pathways and found similar predictive performance comparable to the full model.

The findings suggest that combining disease mechanism biomarkers may improve risk stratification in PSC.

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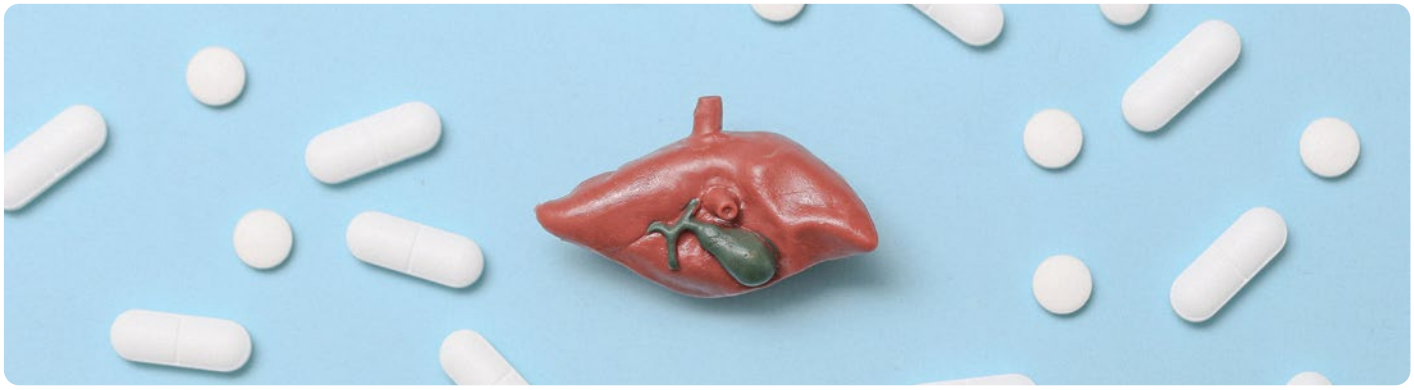
AUTOIMMUNE HEPATITIS

Lastly, for AIH, Lotte Slooter, Amsterdam UMC, presented the 3-year follow-up of the CAMARO-trial.[5] This trial established mycophenolate mofetil (MMF) plus prednisolone as an effective first-line treatment for treatment-naïve AIH, demonstrating superior tolerability and better biochemical response rates at 24 weeks compared with azathioprine (AZA) plus prednisolone. To assess whether these early advantages were sustained over time, Slooter spearheaded a 3-year follow-up study and evaluated outcomes in patients from the original CAMARO trial. This, in essence, confirmed the durability of MMF therapy, with a numerically higher proportion of patients maintaining on trial-assigned treatment and achieving normal transaminase levels at 3 years compared with AZA (78% versus 57%; p=0.067). Importantly, MMF led to a substantially faster biochemical remission, with a median time to normalisation of liver enzymes of 16 weeks versus 64 weeks for AZA (p<0.05). While rates of treatment discontinuation after the initial 24-week study period, loss of response, steroid-free remission, and prednisolone withdrawal were comparable between groups, the faster achievement of remission and higher long-term normalisation rates on trial-assigned treatment support MMF as the clinically superior strategy. These data were confirmed in a retrospective study from Spain that found that with MMF, complete biochemical remission was seen in 90% (6 months) and 97% (12 months).[6] MMF came with rapid disease control and allowed for a corticosteroid sparing strategy. Relapses were rare and treatment discontinuation due to adverse events was uncommon. All in all, MMF has been included as a valid first-line alternative to AZA in the updated 2025 EASL Clinical Practice Guidelines on AIH, given its efficacy and lower rate of adverse events.[7]

The central concept in AIH is to reach complete biochemical remission with immunosuppression to protect patients from a poor prognosis. The question is whether we are successful there. A single-centre study from the UK (496 patients) suggests that the mortality in AIH exceeds that of the general population, and that extrahepatic cancer, infection, and vascular disease are the main drivers.[8] Indeed, there are worries that the immunosuppressive regimens used may be associated with an increased incidence of cancer. A number of studies presented at the EASL Congress tried to quantify this risk. In a Swedish registry study (SweHep), data were collected for 1,086 patients with AIH (follow-up time of 18,091 patient-years).[9]



The standardised incidence ratio (SIR) for any cancer was 2.60 and was significantly higher in men. Specifically, the risk for hepatobiliary cancer among patients with cirrhosis was high (SIR: 24.39). Moreover, 12% of those who progressed to cirrhosis on follow-up developed hepatocellular carcinoma, compared to 5% with cirrhosis at diagnosis. The increased risk appears not to be confined to the hepatobiliary tract. An Israeli cohort study amongst 685 patients with AIH (83.5% female; mean age: 53.1 years; mean follow-up: 7.5 years), found that nine patients developed non-Hodgkin lymphoma, corresponding to a SIR of 36.5.[10] However, it remains difficult to disentangle the effect of the disease itself from those of long-term immunosuppressive treatment. Some of the cancers are clearly related to thiopurines, such as non-melanoma skin cancers and non-Hodgkin lymphoma, whereas others such as hepatocellular carcinoma are more likely to be related to (development of) cirrhosis.

CONCLUSION

Across the PBC, PSC, and AIH sessions, EASL 2026 highlighted a clear shift towards mechanism-based therapies. We witnessed promising advances in bile acid signalling, microbial-metabolic targets, and immunosuppression strategies. While important efficacy signals emerged for several novel treatments, improving long-term outcomes remains a key priority across these rare immune and cholestatic liver diseases.

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