EASL (European Association for the Study of the Liver) Congress 2025

May 7-10, 2025; Amsterdam, the Netherlands; Day #2 Highlights – Draft

Executive Highlights

- **The EASL (European Association for the Study of the Liver) Congress continued with Day #2.** Speakers reiterated a similar message across the day: the importance of treating MASLD as a metabolic disease and providing interdisciplinary care cannot be overstated. Sessions featured discussion of how comorbid T2D affects MASLD and MASH therapeutic outcomes, as well as more data on risk assessment.
- **A popular afternoon symposium sponsored by Novo Nordisk** focused on risk factors for MASH, which include obesity, T2D, hypertension, and dyslipidemia. The panel, chaired by Prof. Elizabeth Powell (University of Queensland, Australia), featured Profs. Philip Newsome (King's College London, England) and Faeiz Zannad (University Henri Poincaré, France). T2D plays an essential part in MASLD risk due to insulin resistance, which is a key driver of free fatty acids circulating in blood, eventually causing fat accumulation in the liver (steatosis). T2D is also a strong predictor of increased severity of fibrosis in affected patients. Profs. Powell, Newsome, and Zannad called for interdisciplinary care teams involving hepatologists, cardiologists, endocrinologists, nutritionists, and more, to address all aspects of metabolic disease.

For the latest from Amsterdam, be sure to monitor our resource hub. Check out our preview for a look at what's coming over the remaining two days of the conference.

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Top Highlights

1. Cardiometabolic perspectives on MASH therapy: Clinical approaches and holistic management

A Novo Nordisk-sponsored symposium, chaired by Prof. Elizabeth Powell (University of Queensland, Australia), included Profs. Philip Newsome (King's College London, England) and Faeiz Zannad (University Henri Poincaré, France). Prof. Powell began by describing MASH as a truly metabolic disease, which was echoed by other speakers in the session. Risk factors include obesity, T2D, hypertension (HTN), and dyslipidemia. MASH also has high prevalence in at-risk populations: 66% of people with T2D and MASLD have inflammation associated with MASH, 34% of people with obesity have MASH, as well as nearly half (49%) of people with hypertension. Prof. Newsome noted that T2D plays an essential part in MASLD risk due to insulin resistance, which is a key driver of free fatty acids circulating in blood, eventually causing fat accumulation in the liver (steatosis). T2D is a strong predictor of increased severity of fibrosis in affected patients.

- **Prof. Powell described the MASLD treatment landscape as rapidly evolving.** Her discussion reviewed resmetirom, a THR-beta agonist currently approved in the US, as well as phase 3 trials of GLP-1 RA, GIP/ GLP-1/RA, and GRA/GLP-1 RA in MASH, and FGF-21 therapy in phase 2 trials. In February 2025, Novo Nordisk submitted once weekly semaglutide 2.4 mg to US and EU regulatory authorities for the treatment of MASH with moderate to advanced fibrosis (F2 to F3). The FDA accepted Novo Nordisk's NDA and granted priority review with a decision expected in 2H25.

- **Resmetirom achieved primary endpoints of MASH resolution and fibrosis improvement** in the 52-week phase 3 MAESTRO-NASH trial (n=966). 26% of patients taking resmetirom 80 mg and 30% of those taking resmetirom 100 mg achieved MASH resolution compared to 10% in placebo. 24% of participant showed fibrosis improvement using 80 mg, and 26% of patients taking 100 mg, compared to 14% in placebo.
- **In comparison, semaglutide also demonstrated strong performance in primary and secondary endpoints when used for MASH treatment.** In part one of the 72-week phase 3 ESSENCE trial recently published in NEJM, 63% of participants taking semaglutide 2.4 mg demonstrated resolution of steatohepatitis, compared to 34% in placebo. 37% of patients demonstrated a reduction in liver fibrosis, compared to 22% in placebo. Semaglutide demonstrated strong performance in other cardiometabolic metrics, resulting in 11% body weight loss compared to 2% in placebo. A 0.4% reduction in A1c from a baseline of 5.8% was observed in people without T2D, compared to an increase of 0.1% in placebo. In people with T2D, A1c decreased by 1.1% from a baseline of 7.1% in the intervention group, with no change observed in the placebo group.
- **Profs. Powell, Newsome, and Zannad discussed a broad range of clinical practice guidelines related to T2D.** Prof. Newsome described his "heightened awareness" when working with patients with T2D, given the tendency for this population to develop MASLD later in life. In people without T2D who demonstrate no signs of MASLD by age 30-40, risk of developing the condition is quite low, but this does not apply to people with T2D. Prof. Zannad encouraged broad use of statins, saying that he prescribes the drugs as part of a diabetes management portfolio due to their anti-inflammatory properties. All panelists emphasized the need for interdisciplinary care teams involving hepatologists, cardiologists, endocrinologists, and nutritionists, to address all aspects of metabolic disease overall.

2. Fibrosis progression prevention in patients with advanced MASH

A lively panel debated challenges in preventing fibrosis progression among patients with advanced MASH. Panelists Dr. Homie Razavi (Center for Disease Analysis Foundation), Prof. Elisabetta Bugianesi (University of Torino, Italy), Dr. Onno Holleboom (Amsterdam UMC, the Netherlands), and chair Dr. Arun Sanyal (Virginia Commonwealth University) first discussed challenges with "traditional" lifestyle-modification-based approaches to fibrosis progression. The speakers expressed their support for highly effective therapies like GLP-1 RAs, which can cause up to 20% body weight loss. They framed this result in terms of similarity to the weight loss provided by bariatric surgery, noting that bariatric surgery is very effective, but underused due to access issues and understandable patient hesitancy.

- **Combination therapy, including anti-inflammatory, anti-fibrotic, and metabolic therapy, is ideal for treating different stages of MASH.** Drugs that target fibrosis alone may not be sufficient, as systemic inflammation may continue to cause a reoccurrence of fibrosis if not addressed. In further support of GLP-1 RAs, Dr. Holleboom said that the drug class is known to improve liver steatosis. Newer combination therapies may also target both fat tissue and fibrotic tissue in the liver.
- **Raising awareness, training providers, and embedding liver screening into diabetes and obesity care are essential measures for preventing fibrosis progression.** Panelists noted that a majority of primary care settings do not screen for liver health. The speakers also agreed that the treatment for liver fibrosis in patients with liver disease must be prioritized as fibrosis strongly predicts risk of long-term complications. While panelists agreed that awareness, training, and screening efforts are likely to have large impact upon liver disease treatment efforts, pharmacotherapies presented more controversy. Dr. Sanyal presented the results of an in-session audience poll showing that a majority of the audience believed that it was somewhat likely that weight loss therapies alone would "solve" the MASH epidemic. The panelists disagreed, again returning to the importance of lifestyle modifications and combined treatment regimens in conjunction with pharmacotherapy. In all, panelists agreed that preventing fibrosis progression remains a key challenge for the treatment of MASH and urged further attention to the issue.

3. Sustained improvements with survodutide, a novel dual glucagon/ GLP-1 receptor agonist

Dr. Mazen Noureddin (Houston Methodist Hospital) presented new phase 2 data showing sustained improvements in outcomes (as measured by biomarkers) with survodutide (Boehringer Ingelheim), a dual glucagon/ GLP-1 RA for use in the treatment of MASH and fibrosis. MASH is a progressive liver disease with limited therapeutic

options currently available. Survodutide is currently being explored for its potential to address the underlying disease as opposed to related symptoms, such as weight loss, alone.

- **Enhanced liver fibrosis (ELF) scores improved significantly in the survodutide group compared to placebo.** ELF scoring uses an algorithm incorporating measurements of three extracellular matrix components involved in liver fibrosis. A score <9.80 indicates lower risk of disease progression, between ≥9.80 and <11.30 indicates mid-level risk, and ≥11.30 indicates higher risk. The average decrease through the use of survodutide was 0.57-0.62, occurring rapidly and persisting throughout the course of treatment. The control group demonstrated a marginal reduction of 0.05. This result reflects rapid and sustained change in fibrosis-related signals through the use of survodutide.
- **PRO-C3 values also decreased rapidly and demonstrated continued improvement.** PRO-C3 is a relatively new biomarker that indicates type III collagen formation. Estimated relative change in PRO-C3 was 0.71-0.74 with survodutide versus 1.01 with placebo. The biomarker's direct association with fibrotic and collagen turnover activity and the consistent decline shown here indicate that survodutide is likely targeting the fibrotic process itself.
- **In an intriguing finding, non-responders also showed improvement as measured by biomarkers.** Patients who failed to achieve biopsy-proven improvement nonetheless had biomarker changes indicative of disease improvement. This suggests widespread drug activity and may be an early indication of therapeutic response prior to confirmation based on histological grounds.
- **Given the speed and uniformity of changes, particularly in PRO-C3, Dr. Noureddin believed that the observed effect is more likely to be caused by glucagon receptor stimulation versus to GLP-1 RA stimulation**. This observation provides insight into the potential mechanisms through which the drug operates at the molecular level. The observed biomarker responses of survodutide are significant, long-lasting, and present even in those patients who do not show histological improvement. This evidence supports further clinical research and promotes incorporating these non-invasive markers into our evaluation of treatment effectiveness in future studies, which may reduce reliance on liver biopsies.

--by Nour Khachemoune, Andrew Serrano, Monica Oxenreiter, and Kelly Close