

## European association for the study of the liver (EASL) congress 2024



The European Association for the Study of the Liver (EASL) congress, Europe's largest event in hepatology, took place in Milan, Italy from 5 to 8 June 2024 in a hybrid format. This four-day event welcomed 7807 attendees from 118 countries, fostering research, education, scientific exchange and collaboration concerning the liver. Hui Wu reports highlights from EASL 2024.

### New EASL-EASD-EASO clinical practice guidelines on metabolic dysfunction-associated steatotic liver disease (MASLD)

The new EASL-EASD-EASO clinical practice guidelines were launched at the one-year anniversary of the new nomenclature announced at EASL Congress 2023, introducing steatotic liver disease (SLD) as a new overarching term, with metabolic dysfunction-associated steatotic liver disease (MASLD) replacing non-alcoholic fatty liver disease (NAFLD). The new guidelines provide an update on definitions, prevention, screening, diagnosis, and treatment.

### Bulevirtide combined with pegylated interferon for chronic hepatitis delta

Prof. Tarik Asselah (France) reported the results of a phase 2b study, evaluating the efficacy and safety of bulevirtide (BLV) with or without pegylated interferon alfa-2a (PegIFN) in patients with compensated chronic hepatitis delta (NCT03852433). 174 participants were randomly assigned in a 1:2:2:2 ratio to one of four treatment groups: subcutaneous PegIFN (180 µg/week) for 48 weeks, subcutaneous BLV (2 mg/day) for 96 weeks with subcutaneous PegIFN (180 µg/week) for the first 48 weeks, subcutaneous BLV (10 mg/day) for 96 weeks with subcutaneous PegIFN (180 µg/week) for the first 48 weeks or subcutaneous BLV (10 mg/day) for 96 weeks. All the trial groups were followed for an additional 48 weeks after the end of treatment. The primary end point was an undetectable hepatitis D virus (HDV) RNA level at week 24 after the end of treatment. The primary comparison was between the 10-mg BLV plus PegIFN group vs. the 10-mg BLV monotherapy group. At 24 weeks after the end of treatment, HDV RNA was undetectable in 17% of the patients in the PegIFN monotherapy group, in 32% of those in the 2-mg BLV plus PegIFN group, in 46% of those in the 10-mg BLV plus PegIFN group, and in 12% of those in the 10-mg BLV monotherapy group. For the primary comparison, the between-group difference was 34 percentage points

(95% confidence interval, 15 to 50;  $P < 0.001$ ). The combination of 10-mg BLV plus PegIFN was superior to BLV monotherapy with regard to an undetectable HDV RNA level at 24 weeks after the end of treatment. The study was published in *The New England Journal of Medicine* (NEJM) on 6th June 2024 and presented on the same day at the congress.

### Survodutide for people with metabolic dysfunction-associated steatohepatitis (MASH) and fibrosis

Prof. Arun Sanyal (United States) reported a 48-week, phase 2, double-blind, dose-finding study, assessing survodutide, a novel dual agonist of glucagon receptor and glucagon-like peptide-1 (GLP-1) receptor in patients with MASH and fibrosis (NCT04771273). 293 participants were randomly assigned to a 1:1:1:1 ratio to receive once-weekly subcutaneous injections of survodutide at a dose of 2.4 mg, 4.8 mg, or 6.0 mg or placebo. A 24-week rapid-dose-escalation phase was followed by a 24-week maintenance phase. The primary end point was histologic improvement in MASH with no worsening of fibrosis. Secondary end points included a decrease in liver fat content by at least 30% and biopsy-assessed improvement in fibrosis by at least one stage. Improvement in MASH without worsening fibrosis occurred in 47%, 62%, and 43% of participants with 2.4 mg, 4.8 mg, and 6.0 mg survodutide, compared to 14% with placebo. A  $\geq 30\%$  decrease in liver fat content occurred in 63%, 67%, and 57% with 2.4 mg, 4.8 mg, and 6.0 mg survodutide, compared to 14% with placebo, while  $\geq 1$ -stage fibrosis improvement occurred in 34%, 36%, and 34%, compared to 22% with placebo. Adverse events that were more frequent with survodutide than with placebo included nausea (66% vs. 23%), diarrhea (49% vs. 23%), and vomiting (41% vs. 4%); serious adverse events occurred in 8% with survodutide and 7% with placebo. Survodutide was superior to placebo with respect to improvement in MASH without worsening of fibrosis, warranting further investigation in phase 3 trials. The study was published in NEJM on 7th June 2024 and presented on the same day at the congress.

### Tirzepatide for MASH with liver fibrosis

Prof. Rohit Loomba (United States) reported the results of the SYNERGY-NASH phase 2, multicenter, international trial that investigated the efficacy and safety of tirzepatide, a once-weekly glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptor agonist, vs. placebo in adults with biopsy-proven MASH with stage 2 or 3



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fibrosis (NCT04166773). 190 participants were randomly assigned in a 1:1:1:1 ratio to receive once-weekly subcutaneous tirzepatide (5 mg, 10 mg, or 15 mg) or placebo for 52 weeks. The primary end point was resolution of MASH without worsening of fibrosis at week 52 and a key secondary end point was an improvement of at least one fibrosis stage without worsening of MASH at week 52. For participants treated with 5 mg, 10 mg, and 15 mg tirzepatide, 44%, 56%, and 62% achieved MASH resolution (vs. 10% with placebo) and 55%, 51%, and 51% achieved  $\geq 1$ -stage fibrosis improvement without

worsening of MASH (vs. 30% with placebo). The most common adverse events with tirzepatide were gastrointestinal, and most were mild to moderate in severity. Treatment with tirzepatide for 52 weeks was more effective than placebo with respect to resolution of MASH without worsening of fibrosis. Larger and longer trials are needed for further investigation. The study was published in NEJM on 8th June 2024 and presented on the same day at the congress.

*Hui Wu*