Semaglutide and Kidney Function: Analysis of Three Randomised Trials in Metabolic Dysfunction-Associated Steatotic Liver Disease

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Semaglutide may preserve kidney function in patients with MASLD and eGFR <75 mL/min/1.73 m²

eGFR<75 mL/min/1.73 m²

Change at 1 year semaglutide 5.91 mL/min/1.73 m²

Change at 1 year placebo −1.53 mL/min/1.73 m²

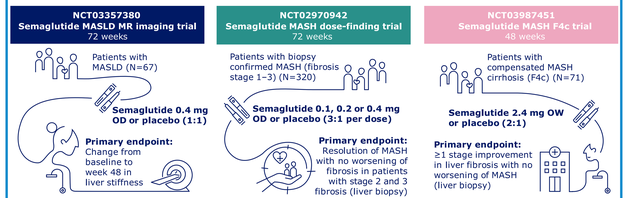
Background and Aim

- Chronic kidney disease (CKD) often co-occurs with metabolic dysfunction-associated steatotic liver disease (MASLD) with a prevalence of 16% in patients with MASLD versus 12% in patients without MASLD.[1]
- MASLD covers a range of conditions caused by a build up of fat in the liver, ranging from steatosis to steatohepatitis and cirrhosis.[2,3]
- Semaglutide, a glucagon-like peptide-1 agonist, is being investigated for the treatment of metabolic dysfunction-associated steatohepatitis (MASH), a severe form of MASLD, as well as other conditions including CKD.[4,5]
- We used pooled data from three randomised, placebo-controlled, phase 1 or 2 MASLD/MASH trials to investigate the effects of semaglutide on kidney function post-hoc.

Methods

- Trials included patients from Europe, North America, and Japan (see Trial Design graphic):
  - NCT03357380 (semaglutide [s.c] 0.4 mg once daily [OD] for 72 weeks in MASLD);
  - NCT02970942 (semaglutide [s.c] 0.1, 0.2, or 0.4 mg OD for 72 weeks in MASH with fibrosis stage 1–3);
  - NCT03987451 (semaglutide [s.c] 2.4 mg once weekly [OW] for 48 weeks in MASH and compensated liver cirrhosis).
- Placebo arms were pooled; the semaglutide 0.4 mg OD arms in NCT02970942 and NCT02970942, and 2.4 mg OW arm in NCT03987451, were also pooled.
- Change at 1 year in estimated glomerular filtration rate (eGFR) was analysed for semaglutide 0.4 mg OD/2.4 mg OW versus placebo.
- Results were analysed by baseline eGFR <75 and ≥75mL/min/1.73 m2 based on a random slope model.
- Patients with eGFR <30 were excluded.

Trial design graphic: Individual trial design for each of the three trials

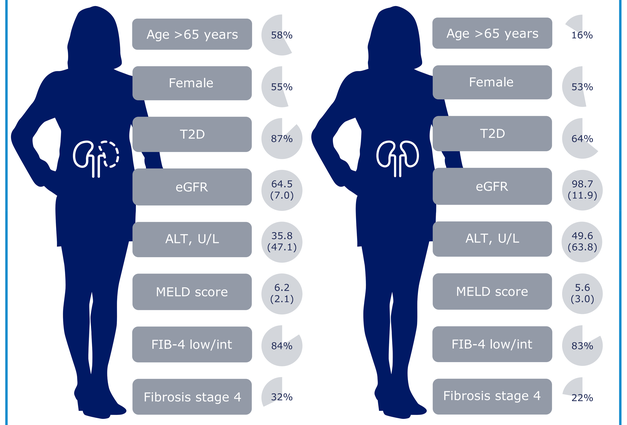


MASLD, metabolic dysfunction-associated steatotic liver disease; MASH, metabolic dysfunction-associated steatohepatitis; MR, magnetic resonance; OD, once daily; OW, once weekly.

Key results

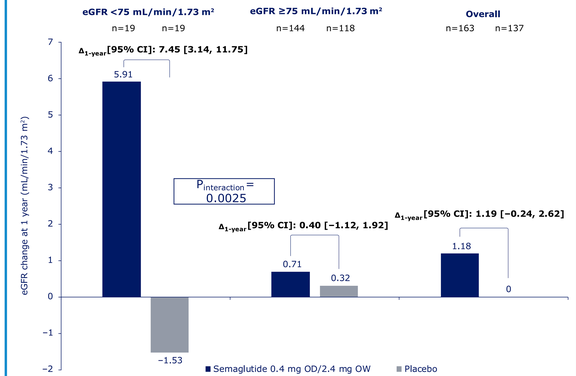
- Patients with eGFR <75 mL/min/1.73 m² were generally older with more advanced liver fibrosis, and more of these patients had type 2 diabetes than patients with eGFR ≥75 mL/min/1.73 m² (**Figure 1**).
- Within each eGFR group, baseline characteristics were generally balanced between the semaglutide and placebo arms.
- In patients with eGFR <75 mL/min/1.73 m², semaglutide appeared to have a beneficial effect on eGFR (**Figure 2**).
- In patients with eGFR ≥75 mL/min/1.73 m² there was no significant treatment difference between semaglutide and placebo (**Figure 2**).
- The test for interaction between the <75 and ≥75 mL/min/1.73 m² groups was significant.
- Semaglutide did not affect annual change in eGFR versus placebo in the overall population (**Figure 2**).

Figure 1. Baseline characteristics by eGFR group



Data are presented as percentages (%) except for eGFR and MELD score, for which mean (SD) values are given, and ALT, for which geometric mean (CV) values are shown.
ALT, alanine aminotransferase; CV, coefficient of variation; eGFR, estimated glomerular filtration rate; FIB4, fibrosis-4 score; MELD, model for end-stage liver disease; SD, standard deviation; T2D, type 2 diabetes.

Figure 2: Analysis of change in eGFR from baseline to 1 year **Key Results**



In-trial data based on all randomized participants. CI, confidence interval; eGFR, estimated glomerular filtration; OD, once daily; OW, once weekly.

Conclusions

- A potential protective effect of semaglutide on eGFR was seen in patients with MASLD and eGFR <75 mL/min/1.73 m².
- Although this post-hoc analysis had a small sample size, the results support further studies of semaglutide in MASLD with low eGFR.

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