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Editorial: evolution of GLP-1 receptor agonists as pharmacotherapy for NASH beyond diabetes mellitus and obesity – authors' reply


We thank Professor Kim for his editorial in response to our recent study^{1,2} of the imaging response associated with semaglutide treatment in patients with NAFLD. We agree that larger and longer-term studies are needed to further assess the effect of semaglutide on long-term clinical outcomes in NASH. A phase III trial is underway to examine the role of semaglutide in improving the risk of progression to cirrhosis and long-term clinical outcomes (NCT04822181). This trial is global in outlook and will recruit patients from several Asian as well as Western countries.


Also, as noted in the editorial, it remains unclear to what extent the anti-steatotic efficacy of semaglutide is a direct effect or an indirect effect mediated by weight loss. In addition to weight reduction, semaglutide is associated with improvements in insulin resistance, lipid dysfunction, and hepatic inflammation. In pre-clinical models, improvements in hepatic lipotoxicity and inflammation with the GLP-1 receptor agonist liraglutide were shown to be independent of weight reduction, as was the prevention of initiation of fibrosis.³ Mediation analyses to investigate the extent to which the effects of semaglutide on liver steatosis are mediated by weight reduction are planned.

The authors' declarations of personal and financial interests are unchanged from those in the original article.²

LINKED CONTENT

This article is linked to Flint et al papers. To view these articles, visit <https://doi.org/10.1111/apt.16608> and <https://doi.org/10.1111/apt.16641>

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