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Semaglutide and lanifibranor differentially alter NASH and liver fibrosis

in diet-induced obese hamsters with or without free access to alcohol.

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Abstract

Background: Chronic alcohol intake may aggravate liver lesions in NASH patients. Both GLP-1 and PPAR agonists reduce alcohol intake in mouse and rat, but these species are not truly alcohol dependent. Golden Syrian hamsters show high preference for alcohol and may represent a better animal model.

Objective: We tested semaglutide (SEMA) and lanifibranor (LANI) in diet-induced obese hamsters, a preclinical model with human-like NASH, with or without free access to 15% alcohol.

Methods: Obese NASH hamsters were maintained on high-fat diet with a choice between normal water or a 10% fructose water supplemented without or with 15% alcohol, and animals were simultaneously treated with vehicle, SEMA 0.06mg/kg s.c. QD or LANI 30mg/kg p.o. QD for 5 weeks.

Results: Without alcohol, SEMA induced a 17% body weight loss ($p<0.01$ vs. vehicle), a lower 10% fructose water intake and a higher normal water intake. SEMA did not reduce NAFLD Activity Score (NAS) and fibrosis, but reduced liver triglycerides levels (-25%, $p<0.01$). When alcohol was provided, SEMA significantly reduced fructose and alcohol intake but did not alter NAS and hepatic triglycerides levels. Without alcohol, LANI reduced 10% fructose water intake, increased normal water intake, and significantly reduced NAS and fibrosis score. As well, when alcohol was provided, LANI significantly reduced fructose and alcohol intake and NAS.

Conclusion: SEMA and LANI both reduced fructose and alcohol intake but had different effects on NASH and liver fibrosis in obese NASH hamsters. This preclinical model could help evaluating the potential benefits of drugs on alcohol intake.

Keywords:

nonalcoholic steatohepatitis, semaglutide, lanifibranor, alcohol intake

Abbreviations:

GLP-1, glucagon like peptide-1

NASH, nonalcoholic steatohepatitis

PPAR, peroxisome proliferator-activated receptors

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- François Briand and Thierry Sulpice are employees of Physiogenex and have shares in the company.
- Natalia Breyner and Estelle Grasset are employees of Physiogenex.