Additive hepatoprotective effects of DA-1241, a novel GPR119 agonist, in combination with semaglutide in the GAN diet-induced obese and biopsy-confirmed mouse model of MASH

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Background & Aim
The G protein-coupled receptor 119 (GPR119) and glucagon-like peptide 1 receptor (GLP1R) are promising therapeutic targets for metabolic dysfunction-associated steatohepatitis (MASH).

The aim of this study was to evaluate the metabolic, biochemical, histological and transcriptomic effects of DA-1241 (GPR119 agonist, Phase 2a) and semaglutide (GLP-1R agonist) combination therapy in the GAN diet-induced obese (DIO) and biopsy-confirmed mouse model of MASH with moderate-severe liver fibrosis.

**Study outline**

**Metabolic and biochemical parameters**

**Histological markers of steatosis, inflammation and fibrosis**

**Liver transcriptome analysis**

**Conclusion**

- DA-1241 + semaglutide exhibited only body weight loss caused by semaglutide.
- Combination therapy further improves NAS compared to monotherapy. Driven by anti-inflammatory effects were likely attributed to DA-1241 treatment.
- Benefits on NAS is supported by quantitative histological markers.
- Combination therapy improves hepatic gene expression markers of lipid metabolism, inflammation and fibrogenesis.
- DA-1241 and semaglutide show no effect on fibrosis score after 8-week treatment.
- Combined GPR119 and GLP1R agonist treatment shows promise in MASH.