Semaglutide (GLP-1 analogue) and lanifibranor (pan-PPAR agonist) have both showed promising therapeutic efficacy in recent phase 2 clinical trials for NASH. The present study aimed to evaluate the metabolic, biochemical, histopathological and transcriptomic effects of semaglutide and lanifibranor combination treatment using low doses, as compared to maximal dose monotherapy in the GAN (Guba-Amylin NASH) diet-induced obese (DIO) mouse model of NASH with hepatic fibrosis.

### Improvement in NAFLD Activity Score

![Figure 2: Semaglutide and lanifibranor combination improves NAFLD Activity Score in GAN DIO-NASH mice](image)

Histopathological scores were determined by digital histopathological Objective Scoring Technique (GHOST™) deep learning-based image analysis. (A) NAFLD Activity Score (NAS). (B) Fibrosis stage. (C) Comparison of individual pre-post NAS. (D) Comparison of individual per-post NAS. 

**Conclusions:**
- Combined low-dose semaglutide and lanifibranor treatment demonstrate similar therapeutic effects as compared to high-dose monotherapy:
  - Reduction in body and liver weight
  - Reduction in plasma ALT and liver lipids.
  - 22-point significant improvement in NAFLD Activity Score.
  - Reduction in quantitative histological markers of steatosis, inflammation and stellate cell activation.
  - Suppression in fibrosis-associated genes.
  - These findings highlight the use of the GAN DIO-NASH mouse model for exploring novel combinatorial therapies for the treatment of NASH.

### Improvement in transcriptomic profile for fibrosis

![Figure 3: Semaglutide and lanifibranor combination improves quantitative liver transcriptomics in GAN DIO-NASH mice](image)

Intracellular pharmacodynamic assessments were performed by GHOST™ deep learning-based image analysis on scoring associated variables (panels A-C) and conventional histologic image analysis (panel C). 

**Conclusions:**
- Semaglutide and lanifibranor combination improve liver transcriptomics in GAN DIO-NASH mice by reducing expression of genes associated with fibrosis.

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**Background & Aim**

**Conclusion**

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