MORPHOMETRIC DIGITAL PATHOLOGY CONFIRMS CLINICAL TRANSLATABILITY FOR LANIFIBRANOR AND SEMAGLUTIDE IN BIOPSY-CONFIRMED GAN-DIO-NASH MICE

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OBJECTIVES

- To assess Lanifibranor and Semaglutide effects on fibrosis and steatosis in the Gubra's Amylin NASH (GAN) diet-induced obese (DIO) and biopsy-confirmed mouse model with advanced fibrosis using morphometric digital pathology.

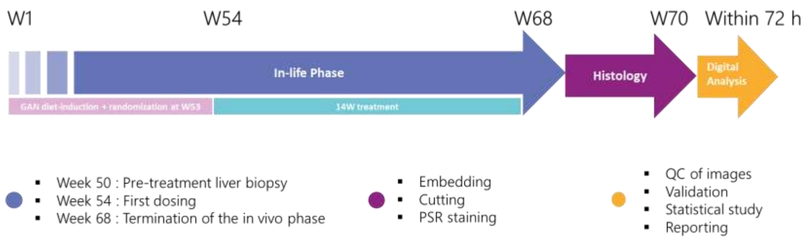
MATERIALS AND METHODS

- GAN-DIO-NASH mice were treated with either vehicle, lanifibranor or semaglutide, and lean chow-fed animals served as control group.
- pre- and post-treatment liver biopsies were stained with picrosirius red (PSR) and hematoxylin and eosin (H&E) and scanned at the magnification of X20.
- Histopathological NAFLD Activity Score (NAS) and fibrosis stage were evaluated by Gubra Histopathological Objective Scoring Technique (GHOST) AI-deep learning-based image analysis.
- MorphoQuant, a fully automated and deterministic artificial intelligence was developed to assess steatosis and fibrosis.
- Effects of treatments were compared.

CONCLUSION

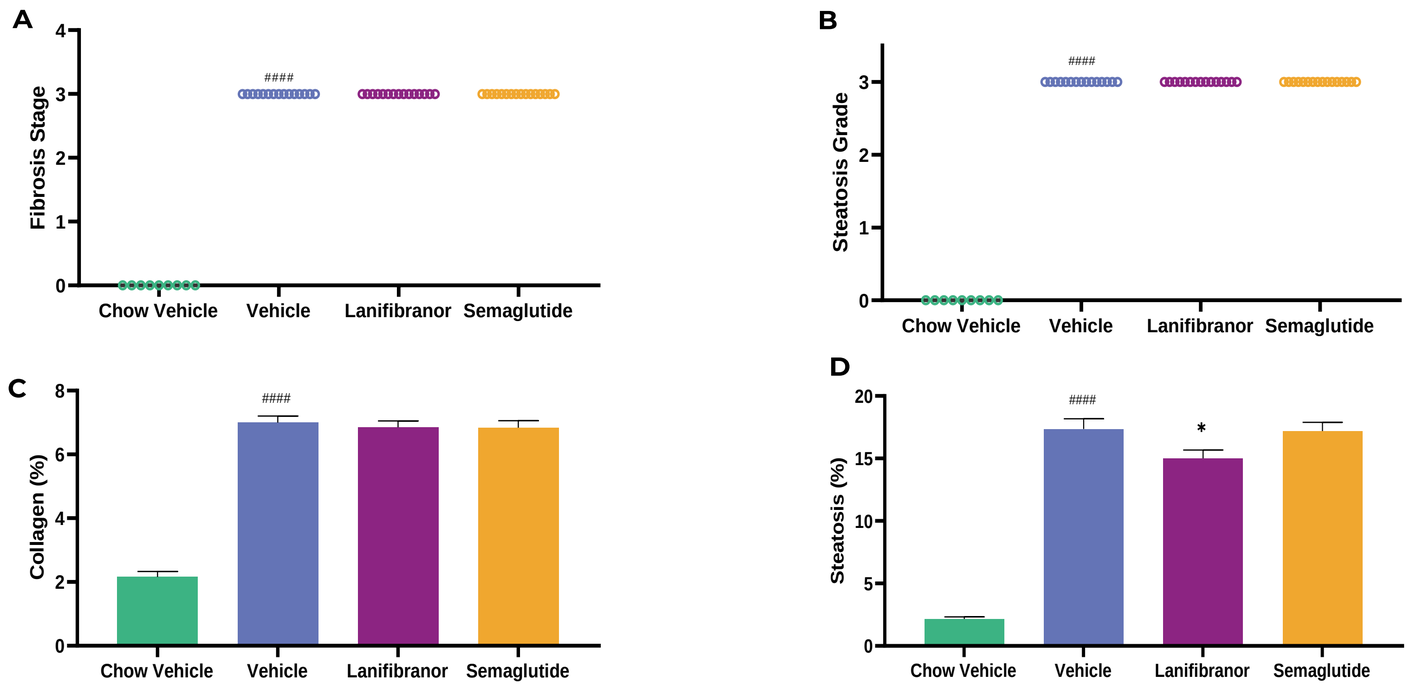
Morphometric AI-digital pathology showed superior anti-steatotic action for lanifibranor, compared to semaglutide. In addition, anti-fibrotic effect of lanifibranor, but not semaglutide, was demonstrated, in alignment with the Phase 2 clinical trial data. Lastly, digital quantification showed more granularity in the assessment of fibrosis.

.01 STUDY DESIGN AND OUTLINE



Name	Animal Model	Treatment	Subject Number
Chow Vehicle	Chow	Vehicle	9
Vehicle	GAN-DIO-NASH	Vehicle	15
Lanifibranor	GAN-DIO-NASH	Lanifibranor 30 mg/kg	15
Semaglutide	GAN-DIO-NASH	Semaglutide 30 nmol/kg	16

.02 SIGNIFICANT INDUCTION OF STEATOSIS AND FIBROSIS IN GAN-DIO-NASH MOUSE MODEL AT BASELINE



*: p ≤ 0.05, ** : p ≤ 0.01, *** : p ≤ 0.001, ****: p ≤ 0.0001
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Figure 1. Fibrosis and steatosis in pre-treatment liver biopsies from GAN-DIO-NASH mice after 50 weeks of diet-induction. A. Fibrosis score by GHOST. **B.** Steatosis score by GHOST. **C**. Digital quantification of collagen by MorphoQuant. **D.** Steatosis quantification by MorphoQuant. # = t-test between chow vehicle and vehicle, * = Fisher's LSD test between vehicle and treatments

.03 SIGNIFICANT STEATOSIS REDUCTION IN LANIFIBRANOR- AND SEMAGLUTIDE-TREATED ANIMALS

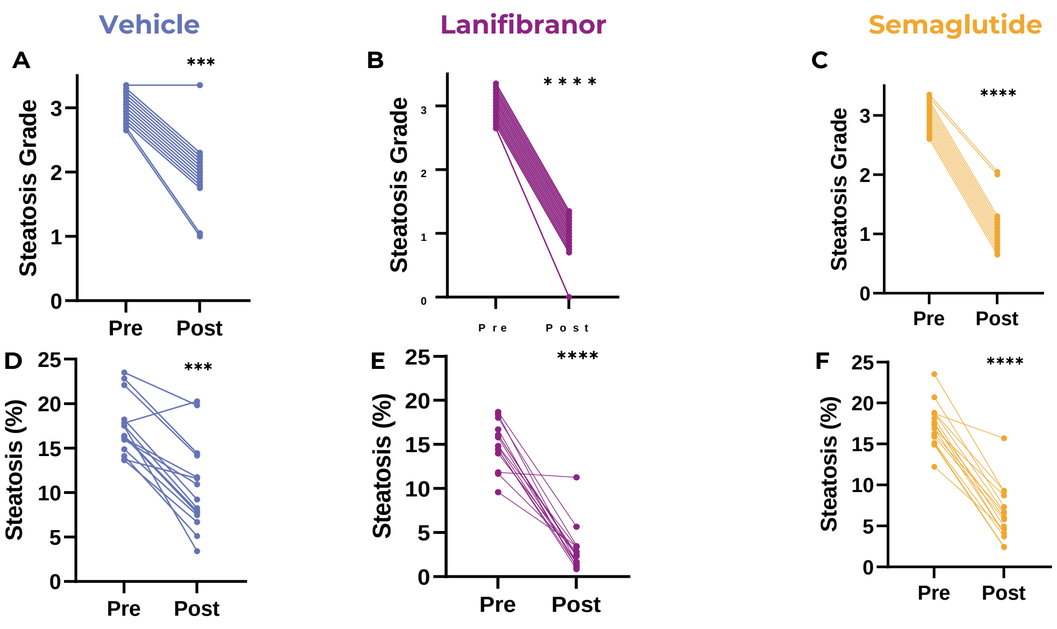

Figure 2. Assessment of steatosis response after 14-weeks treatment with Vehicle, Lanifibranor or Semaglutide in GAN-DIO-NASH mice using a Wilcoxon's test A-B-C. Steatosis score by GHOST for Vehicle-, Lanifibranor- and Semaglutide-treated animals, respectively . **D-E-F.** Steatosis quantification by MorphoQuant for Vehicle-, Lanifibranor- and Semaglutide-treated animals, respectively .

.04 SIGNIFICANT FIBROSIS REGRESSION IN LANIFIBRANOR-TREATED ANIMALS

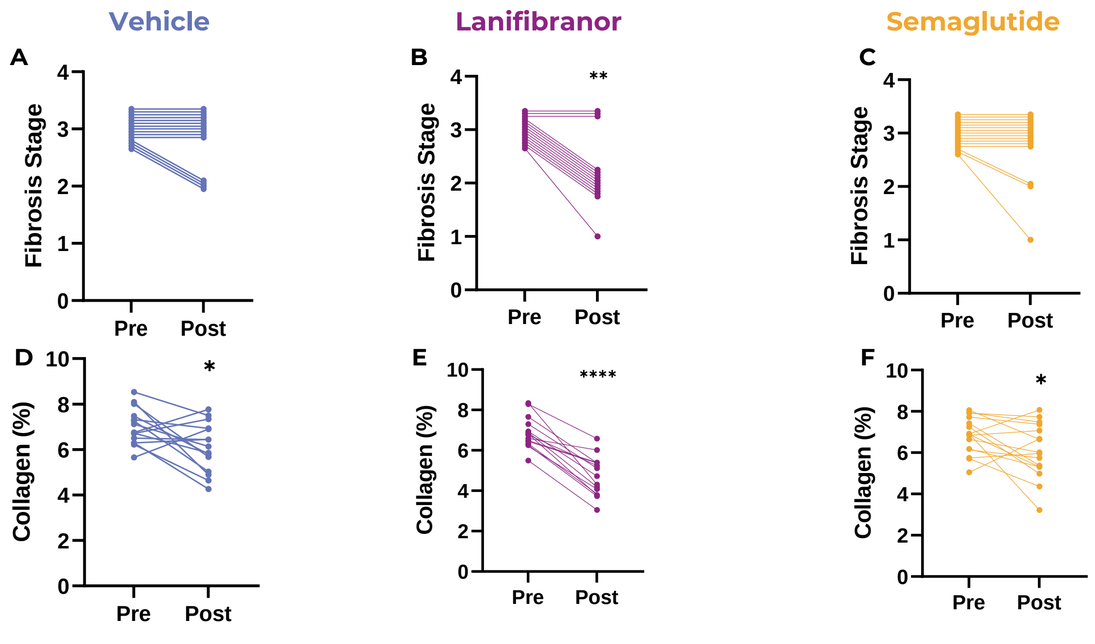

Figure 3. Assessment of fibrosis response after 14-weeks treatment with Vehicle, Lanifibranor or Semaglutide in GAN-DIO-NASH mice using a Wilcoxon's test A-B-C. Fibrosis score by GHOST for Vehicle-, Lanifibranor- and Semaglutide-treated animals, respectively . **D-E-F.** Collagen quantification by MorphoQuant for Vehicle-, Lanifibranor- and Semaglutide-treated animals, respectively .

.05 MORPHOQUANT ANALYSIS OF COLLAGEN WIDTH

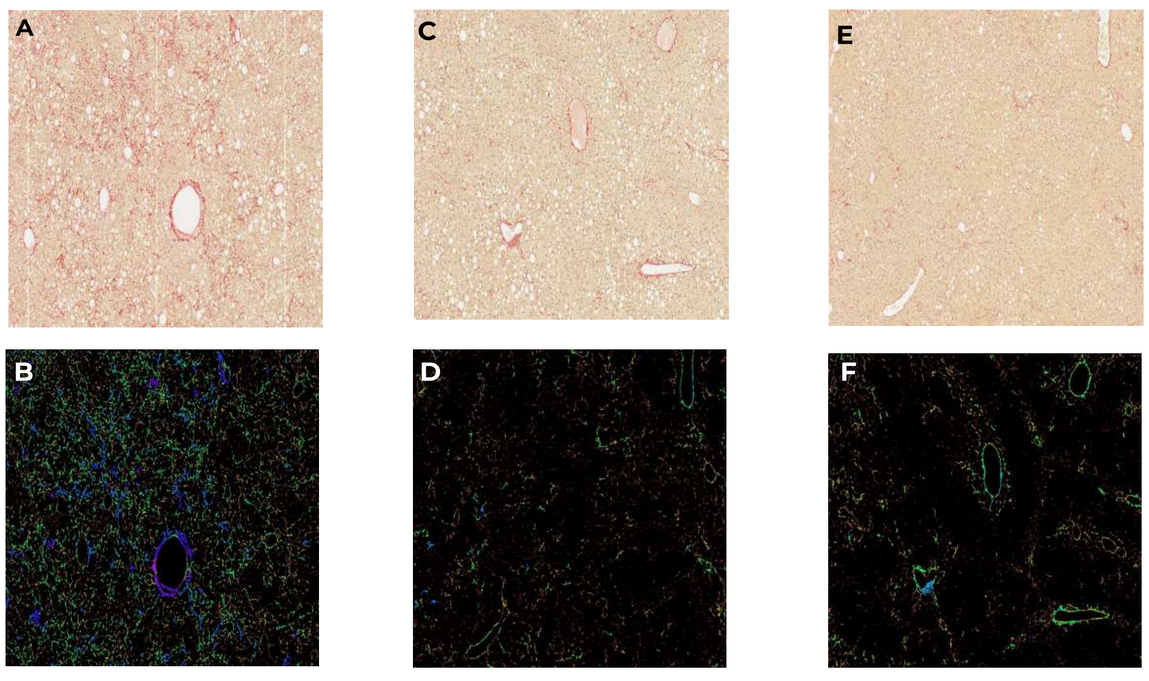

Figure 4. Rainbow color mapped images. A-B. Original image and collagen width recognition for Vehicle-treated animals. **C-D.** Original image and collagen width recognition for Lanifibranor-treated animals. **E-F.** Original image and collagen width recognition for Semaglutide-treated animals.

AT A GLANCE

- Lanifibranor and Semaglutide were investigated in GAN-DIO-NASH mouse model
- Liver biopsies were assessed for fibrosis and steatosis using GHOST and MorphoQuant (morphometric digital analysis)
- Both Lanifibranor and Semaglutide showed significant decrease of steatosis; Only Lanifibranor reduced significantly fibrosis.
- GAN-DIO-NASH mouse is a highly applicable model for the investigation of NASH treatments with advanced fibrosis
- Digital quantification showed more granularity in the assessment of fibrosis.