

Semaglutide, but not lanifibranor, promotes tumor regression in the GAN diet-induced obese and biopsy-confirmed mouse model of NASH with advanced fibrosis and HCC

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Background & Aim

Non-alcoholic steatohepatitis (NASH) is emerging as a major cause of hepatocellular carcinoma (HCC). Semaglutide (glucagon like peptide-1 (GLP-1) receptor agonist) and lanifibranor (pan peroxisome proliferator activated receptor (pan-PPAR) agonist) are currently in late-stage clinical development for NASH. The present study aimed to evaluate the efficacy of semaglutide and lanifibranor monotherapy on disease progression in the translational Gubra Amylin NASH (GAN) diet-induced obese (DIO) and biopsy-confirmed mouse model of advanced fibrosing NASH and HCC.

Methods

Male C57BL/6J mice were fed the GAN diet high in fat, fructose, and cholesterol for 54 weeks prior to treatment intervention. Only animals with liver biopsy-confirmed NAFLD Activity Score (NAS ≥ 5) and advanced fibrosis (stage F3) were included and stratified into study groups. DIO-NASH-HCC mice received vehicle, semaglutide, or lanifibranor for 14 weeks. Vehicle-dosed chow-fed C57BL/6J mice served as lean healthy controls. Untreated DIO-NASH-HCC mice (n=10) were terminated at baseline.

Conclusion

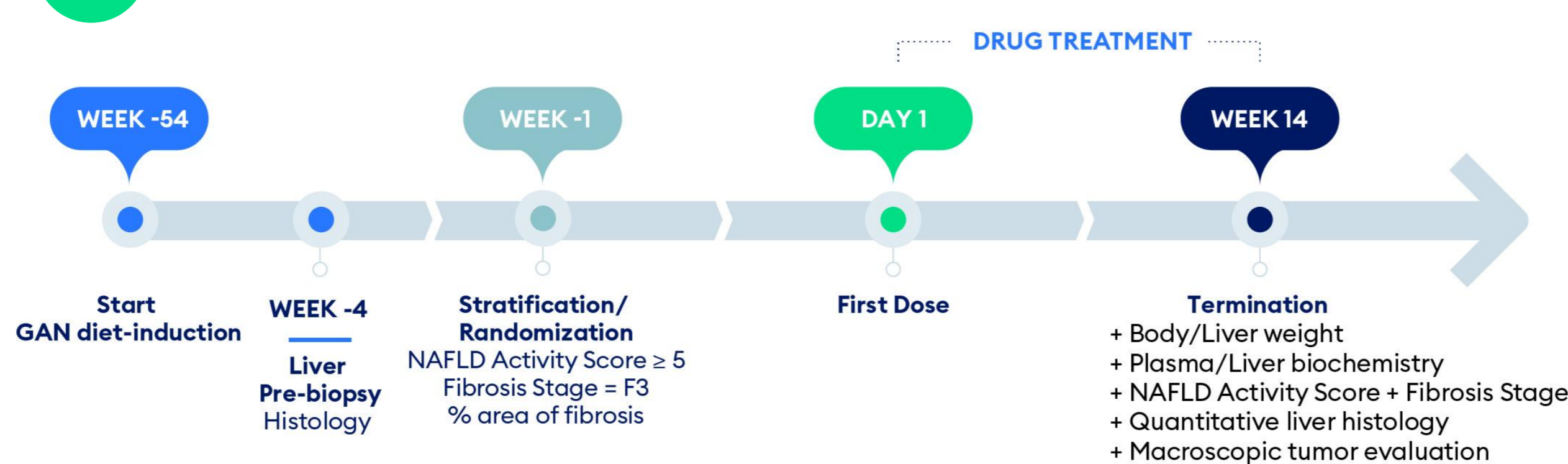
- + Both semaglutide and lanifibranor promotes ≥ 2 -point improvement in NAFLD Activity Score
- + Lanifibranor improves fibrosis histology
- + Semaglutide reduces HCC burden
- + The GAN DIO-NASH-HCC mouse is highly applicable for profiling novel drug therapies targeting NASH with advanced fibrosis and HCC

Scan the QR code to see the poster



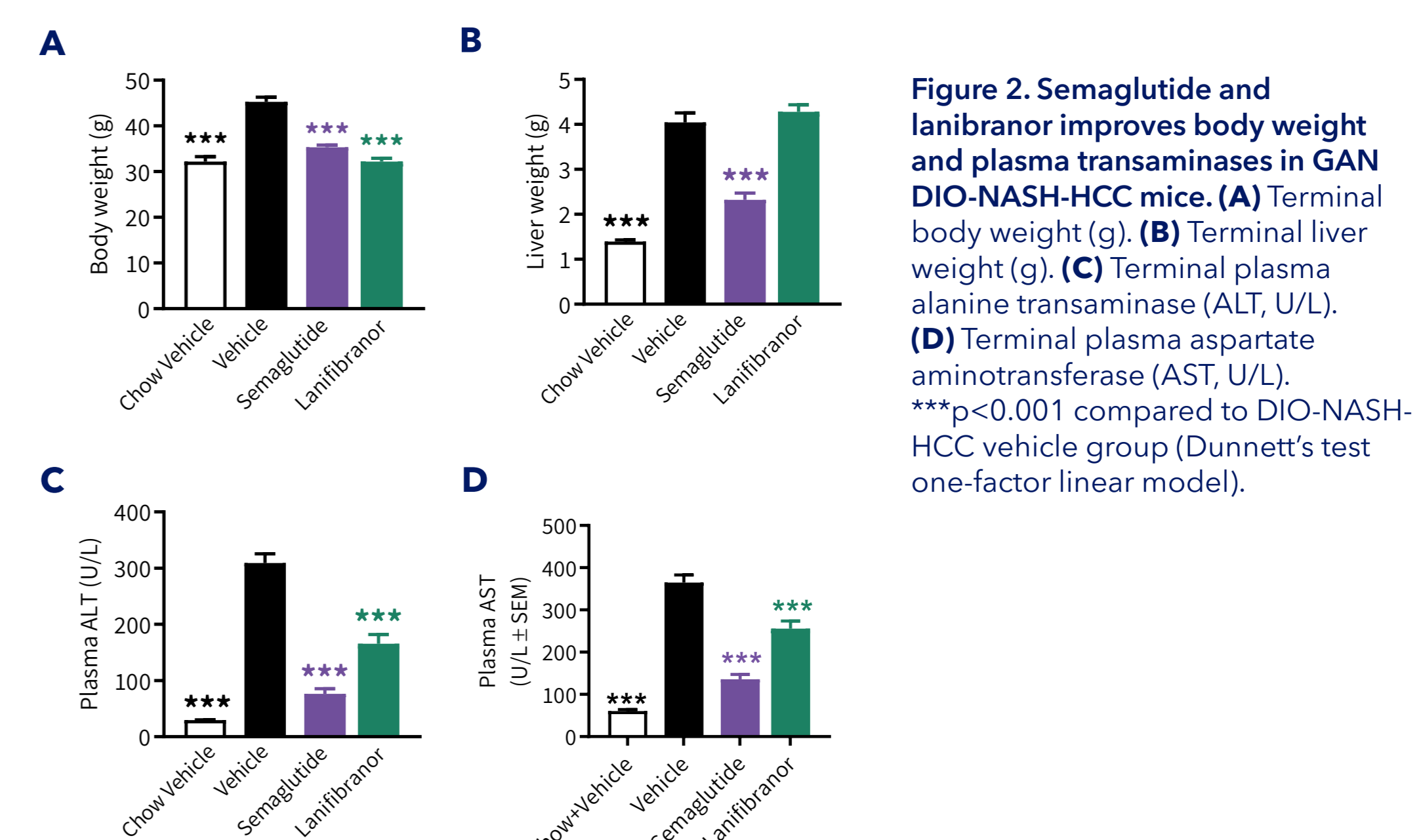
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1 Study outline

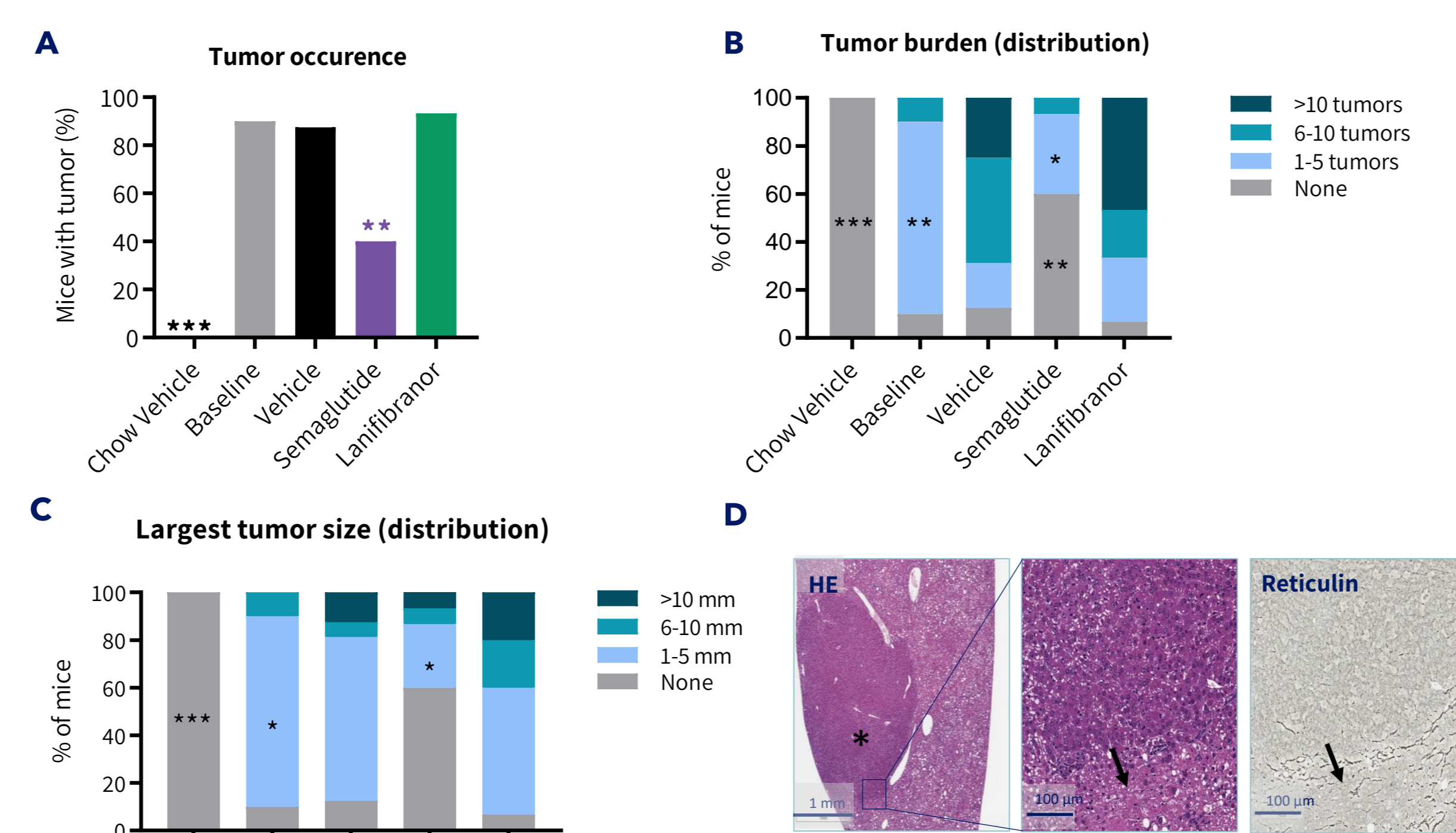


Group	Animal	Gender	Number of animals	Treatment	Administration route	Dosing Frequency	Dosing concentration
1	CHOW	Male	10	Vehicle	SC	QD	-
2	DIO-NASH-HCC	Male	16	Vehicle	SC	QD	-
3	DIO-NASH-HCC	Male	15	Semaglutide	SC	QD	30 nmol/kg
4	DIO-NASH-HCC	Male	15	Lanifibranor	PO	QD	30 mg/kg

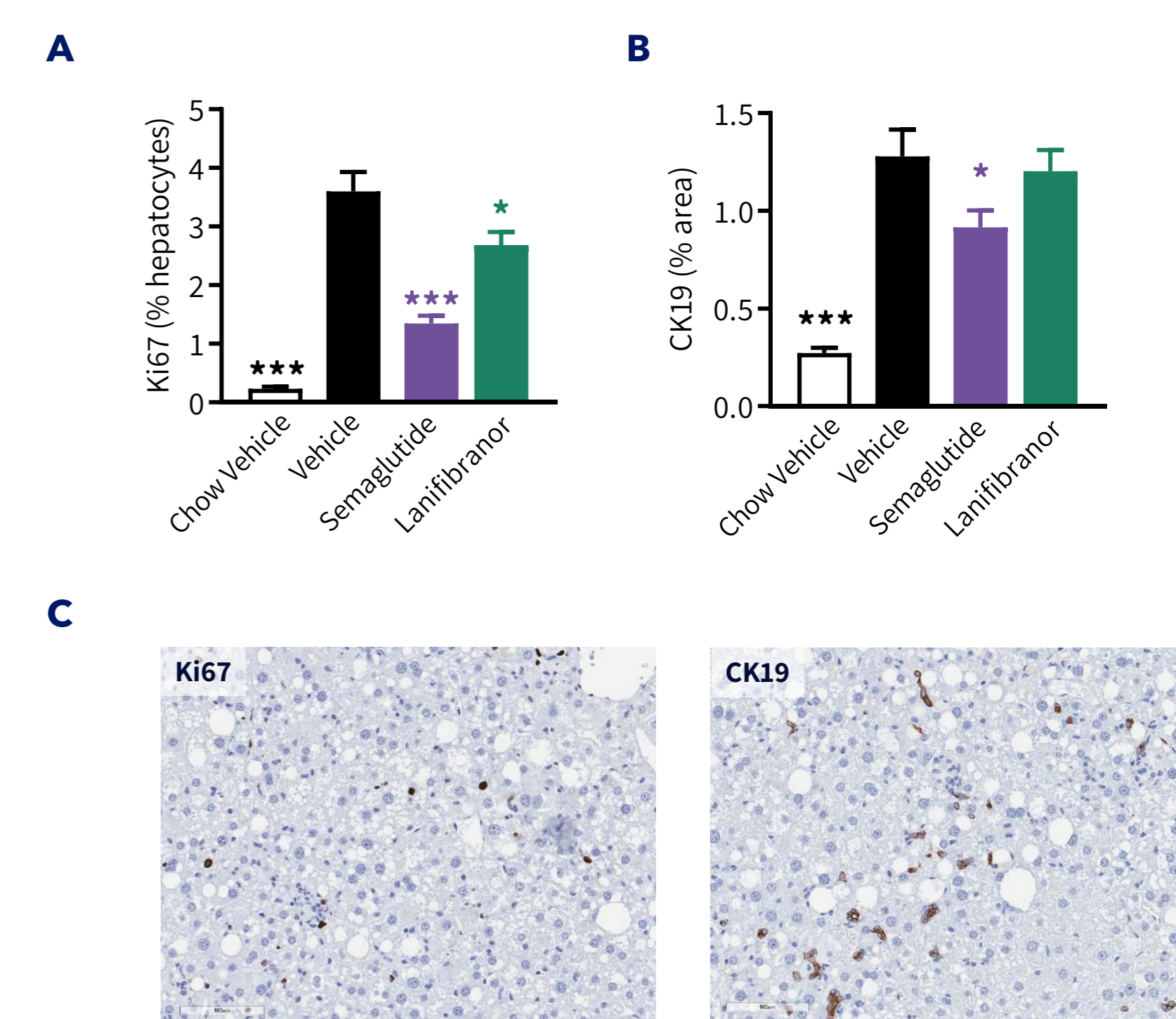
2 Metabolic and biochemical parameters



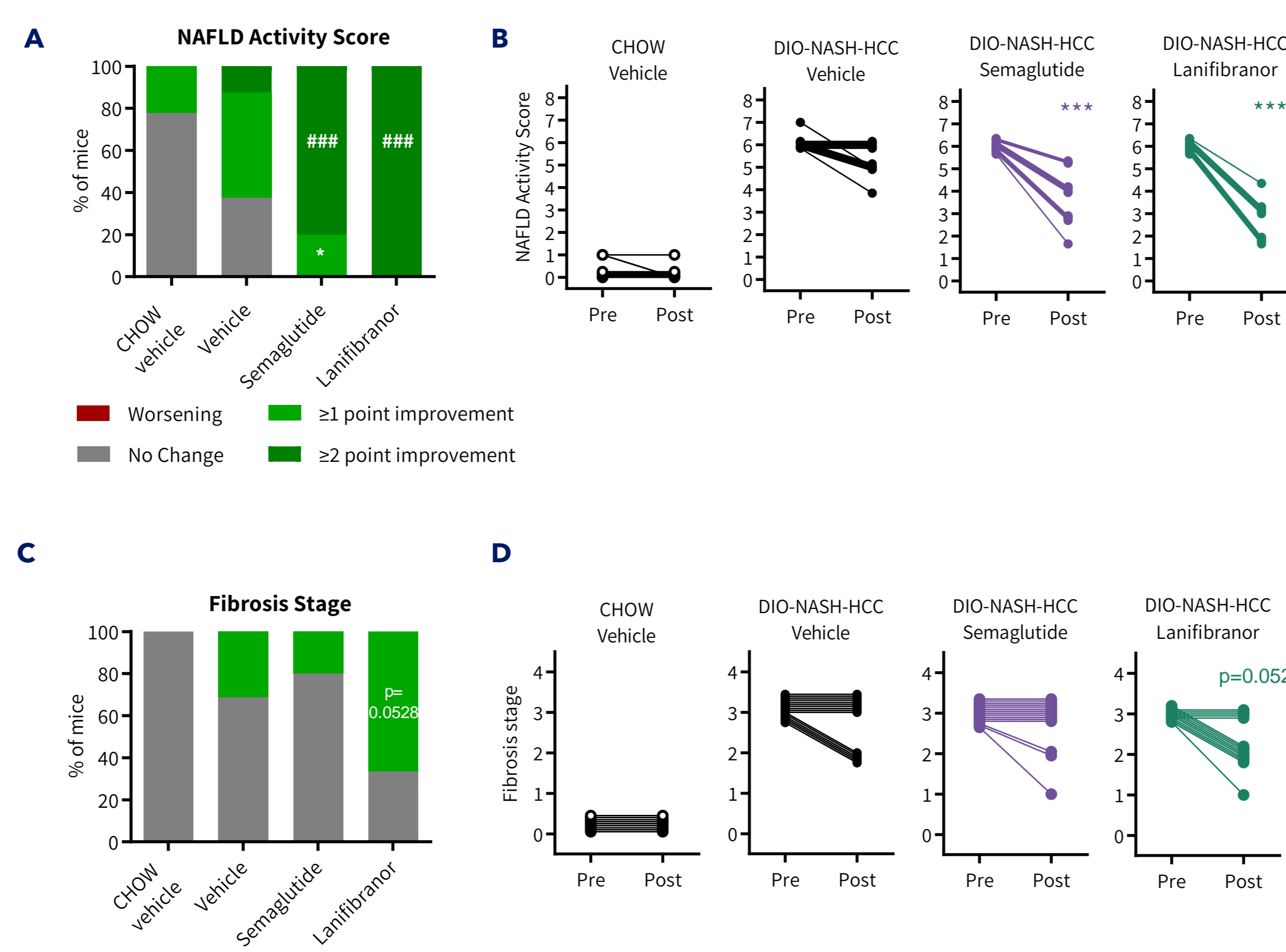
3 Hepatocellular carcinoma occurrence and burden



4 Histological markers of proliferation and progenitor cell activation



5 NAFLD Activity Score and Fibrosis Stage



6 Histological markers of steatosis, inflammation and fibrosis

