

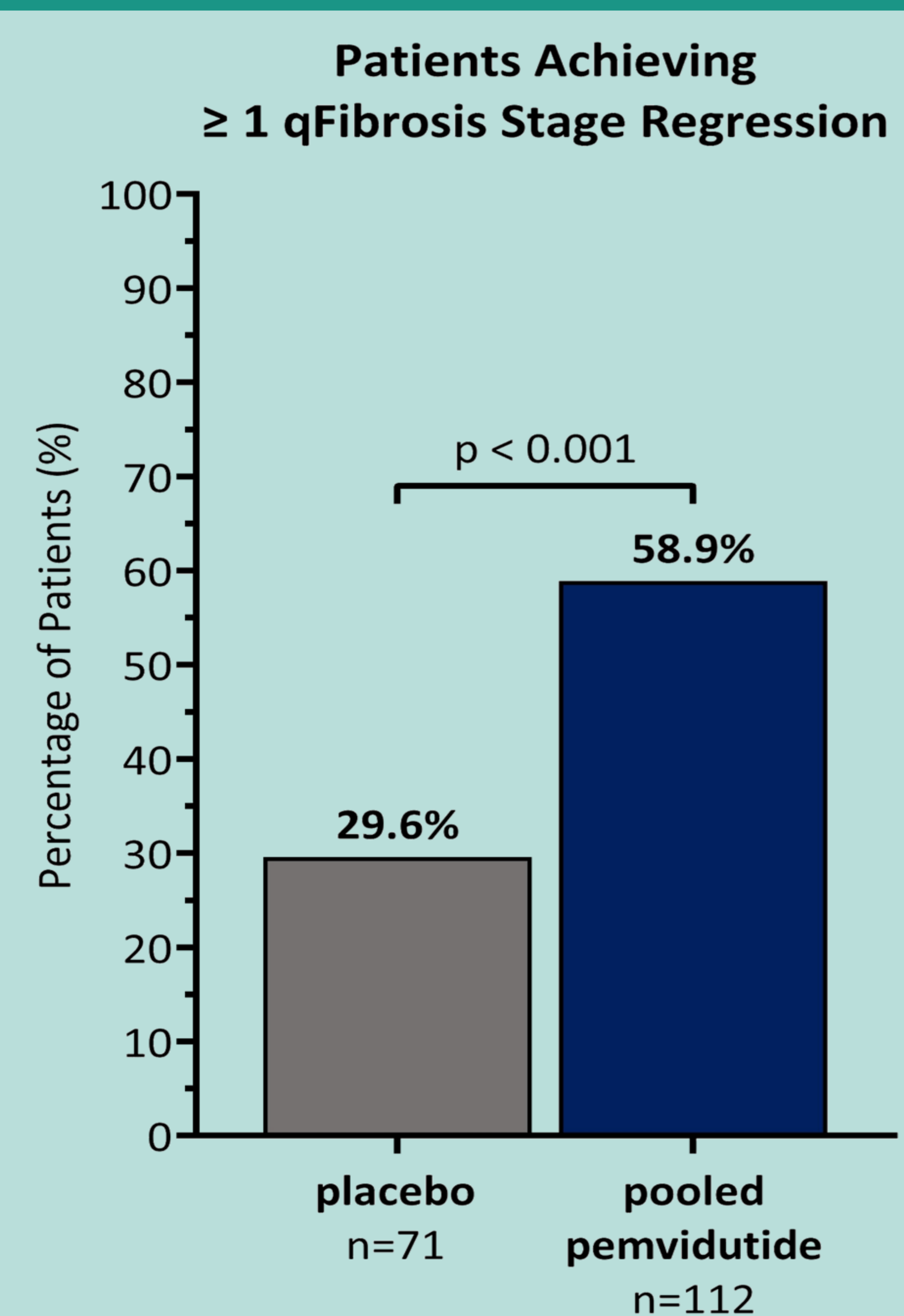


Pemvidutide treatment led to fibrosis regression after 24 weeks in patients with metabolic dysfunction-associated steatohepatitis: Quantitative digital pathology analysis from the IMPACT phase 2b, multicenter, randomized, placebo-controlled trial

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More patients receiving pemvidutide had ≥ 1 qFibrosis stage regression at 24 weeks compared to placebo



Percentage of patients ≥ 1 qFibrosis stage regression after 24 weeks of treatment. Pemvidutide patients were pooled across the doses. Statistical analysis was assessed by Cochran–Mantel–Haenszel test.

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Introduction

- MASH is characterized by metabolic-dysfunction, hepatic steatosis and liver inflammation, a key driver of fibrosis
- Changes in fibrosis, especially intra-stage changes, can be difficult to quantify by traditional pathology methods
- AI-based digital pathology analyses can quantify continuous changes in hepatic fibrosis
- Glucagon acts directly in the liver to reduce lipid synthesis and increase lipid β -oxidation
- Pemvidutide, a balanced (1:1) glucagon/GLP-1 dual receptor agonist, was recently tested in a phase 2b trial of patients with biopsy-confirmed F2 or F3 MASH (IMPACT: NCT05989711)¹
- Pemvidutide treatment led to statistically significant improvements in MASH resolution with statistically significant reductions in NITs of hepatic fibrosis at 24 weeks¹

Aim

- To evaluate continuous and categorical fibrosis regression by second harmonic generation (SHG)/two-photon excited fluorescence (TPEF) microscopy imaging with the HistoIndex qFibrosis[®] quantitative AI-based image analysis algorithm,

Method

Study Design

- 212 patients were randomized (2:1:2) across 83 sites
 - Placebo (N=86); 1.2 mg pemvidutide (N=41); 1.8 mg pemvidutide (N=85)
- Patients stratified by fibrosis stage at baseline and the presence or absence of T2D

Study Population – Key Eligibility Data

- Men and women, ages 18-75 years with body mass index ≥ 27 kg/m²
- Histological diagnosis of MASH by liver biopsy within the preceding 6 months
 - A NAS ≥ 4 with a score of at least 1 on each component score
 - MASH fibrosis stages 2 through 3
- MRI-PDFF $\geq 8\%$
- No diabetes or T2D if on a stable dose of concomitant T2D medication and HbA1c $< 9.5\%$

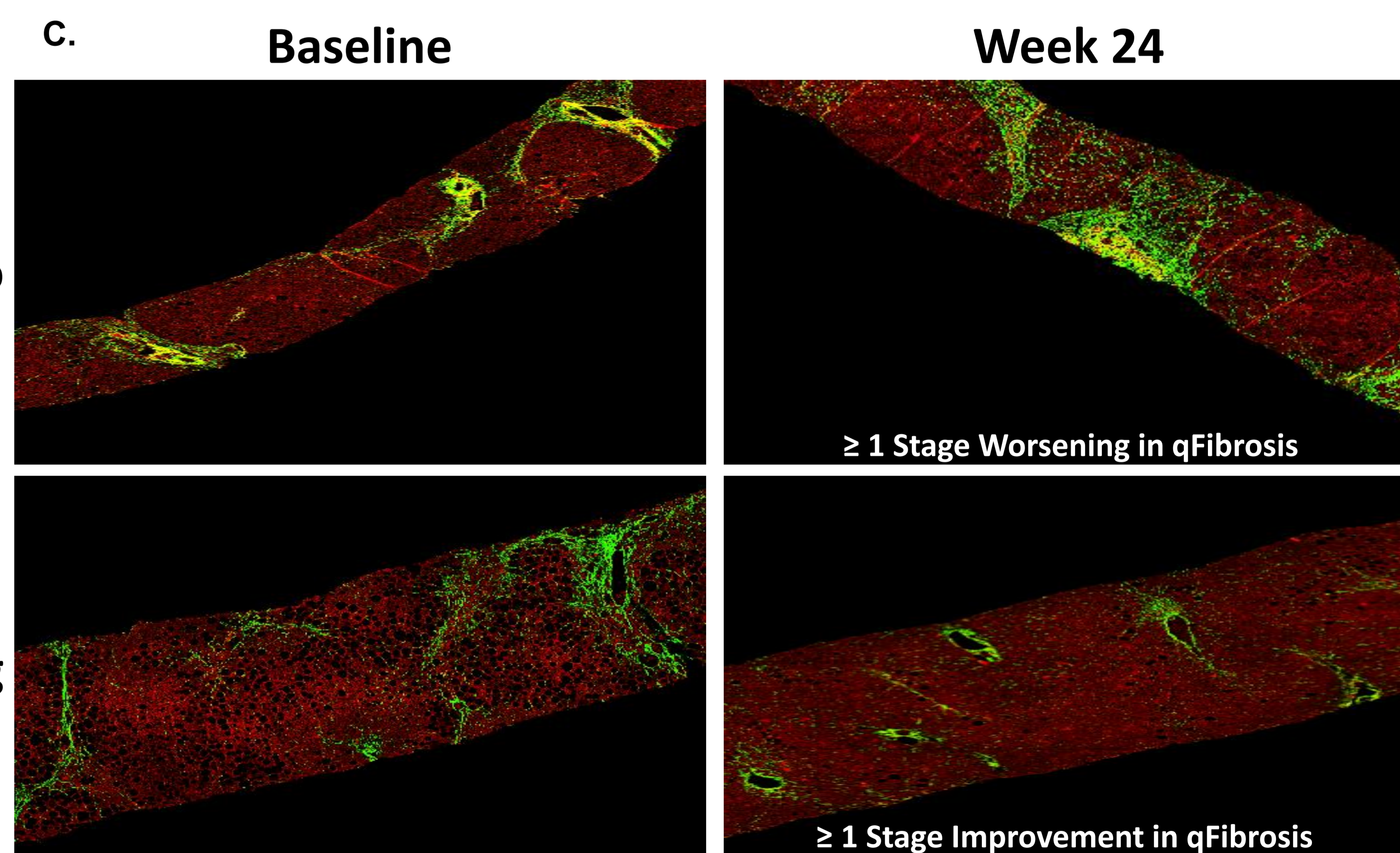
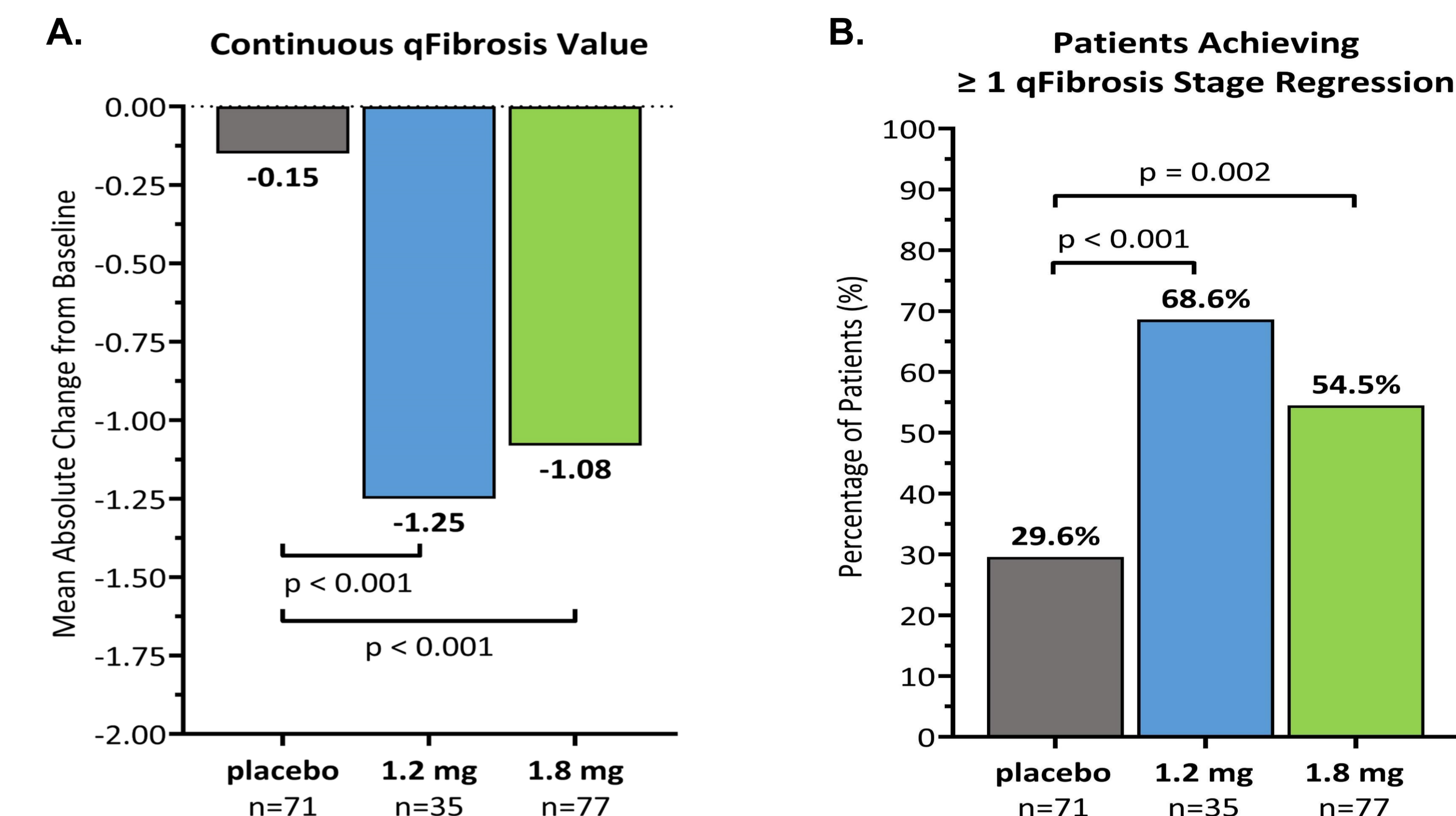
AI-based Digital Pathology

- Unstained slides available at baseline and week 24 were imaged by SHG/TPEF microscopy and analyzed using HistoIndex qFibrosis²
 - Fibrosis was measured across the entire tissue biopsy sample
 - qFibrosis analysis incorporated a correction for the steatotic area of each slide image³

Conclusions

- AI digital pathology analysis showed pemvidutide treatment led to significant reductions in qFibrosis continuous value
- AI digital pathology analysis showed pemvidutide treatment led to a significant percentage of patients achieving a ≥ 1 qFibrosis stage regression
- These data, combined with previous AI- and NIT-based analyses, are consistent with an antifibrotic effect at 24 weeks of treatment
- Overall, these data suggest that the balanced 1:1 ratio of glucagon/GLP-1 in pemvidutide may contribute to the rapid reduction in steatosis, yielding early and potent effects on hepatic fibrosis

Results



Significant improvement in qFibrosis continuous fibrosis scoring after 24 weeks of treatment. (A) Absolute change from baseline in continuous qFibrosis value. Statistical analysis was assessed by T-test. (B) Percentage of patients achieving ≥ 1 qFibrosis stage regression. Statistical analysis was assessed by Cochran–Mantel–Haenszel test. (C) Case examples. qFibrosis stages were corrected for steatosis area.

References and Abbreviations

- ¹Nouredin et al. Lancet. 2025 Dec 6;406(10520):2644-2655; ²Sun W, et al. Journal of Biomedical Optics, 2008, 13(6):7-0; ³Naoumov J Hepatol. 2022 Nov;77(5):1399-1409
- ALT, Alanine aminotransferase; ELF, Enhanced liver fibrosis; LFC, Liver fat content; LSM, Liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; MRI-PDFF, Magnetic Resonance Imaging-Proton Density Fat Fraction; NAS, NAFLD activity score; NIT, Non-invasive test; SHG, second harmonic generation; T2D, type 2 diabetes; TPEF, two-photon excitation fluorescence

