Reduction of Liver Fibrosis by AI-Based Digital Pathology Analysis: Results from the Pemvidutide Phase 2b IMPACT Trial

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Background

- Metabolic dysfunction-associated steatohepatitis (MASH) is characterized by hepatic steatosis leading to liver inflammation, a key driver of fibrosis
- Non-invasive tests (NITs) can provide a comprehensive assessment of liver fibrosis progression
- Changes in fibrosis, especially intra-stage changes, can be difficult to quantify by traditional pathology methods
- Artificial intelligence (AI) digital pathology analysis provides granular quantification of hepatic fibrosis and measurements of fibrosis improvement
- Glucagon acts directly on the liver to reduce lipid synthesis and increase lipid oxidation
- Pemvidutide, a balanced 1:1 glucagon/GLP-1 dual receptor agonist, achieved MASH resolution in 55% of patients within 24 weeks in a phase 2b trial of patients with biopsy-confirmed F2 or F3 MASH (IMPACT: NCT05989711)

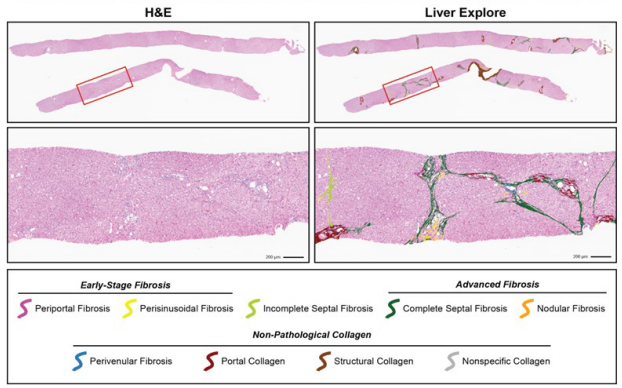
Aims

- To analyze the change in total, early, and advanced fibrosis by AI digital pathology in MASH patients following pemvidutide treatment at 24 weeks
- To analyze NITs of liver fibrosis from a planned 24-week efficacy analysis of the 48-week IMPACT MASH trial

Methods

- Digitized whole-slide images (WSIs) of H&E stained liver sections were generated with high resolution scanners
- Digitized slides were analyzed by Liver Explore™ (PathAI, Boston, MA)†
  - Fibrosis outputs were adjusted for steatotic area and quantified for the proportionate areas of total, early (periportal and perisinusoidal), and advanced fibrosis (bridging and nodular)

Quantification of Fibrosis from H&E-stained WSIs Using Liver Explore‡



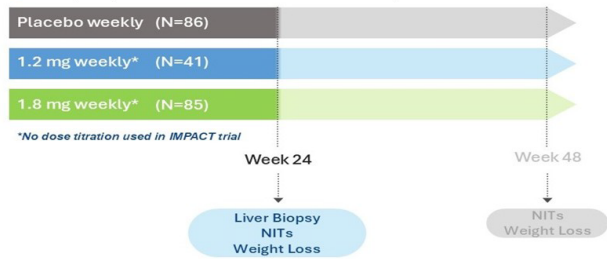
Study Design

Study Population – Key Eligibility Criteria

- Men and women, ages 18-75 years with BMI ≥27 kg/m^2
- 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 ≥8%
- No diabetes OR type 2 diabetes (T2D) if on a stable dose of concomitant T2D medication and HbA1c <9.5%

Phase 2b MASH Study Design

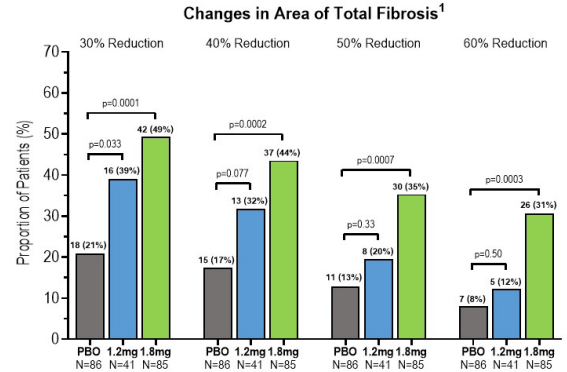
- 212 patients were randomized (2:1:2) across 83 sites to 1 of 3 treatment arms, stratified by fibrosis stage at baseline and the presence or absence of T2D
- Primary endpoints: MASH resolution or fibrosis improvement at Week 24

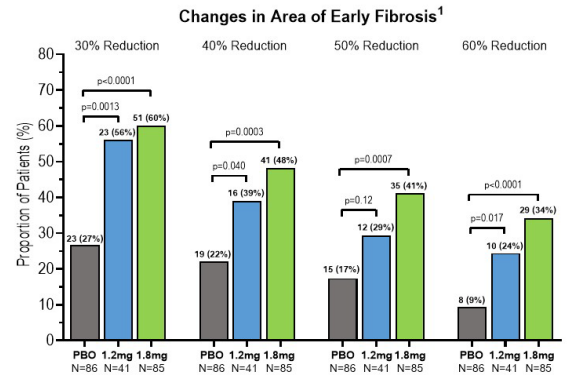


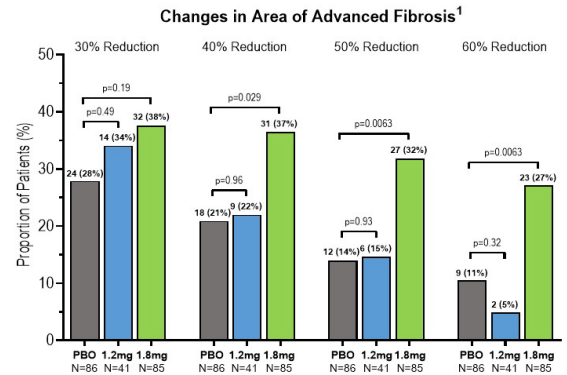
Results

Baseline Demographics		Treatment		
		PBO (N=86)	1.2 mg (N=41)	1.8 mg (N=85)
Age - years	mean (SD)	52.5 (12.2)	55.2 (13.0)	53.4 (12.4)
Sex	female, n (%)	48 (55.8)	25 (61.0)	50 (58.8)
Type 2 Diabetes	n (%)	37 (43.0)	19 (46.3)	36 (42.4)
Body weight, kg	mean (SD)	109.7 (28.0)	110.7 (26.3)	107.7 (21.3)
BMI, kg/m^2	mean (SD)	38.3 (8.4)	39.2 (8.4)	38.7 (6.9)
F3 Fibrosis	n (%)	40 (46.5)	17 (41.5)	39 (45.9)
Liver Fat Content, %	mean (SD)	19.6 (6.4)	20.0 (7.1)	19.0 (6.8)
Enhanced Liver Fibrosis	mean (SD)	9.7 (0.8)	10.0 (0.8)	9.9 (1.0)
Liver Stiffness Measurement, kPa	mean (SD)	12.5 (4.4)	12.3 (3.6)	12.8 (4.4)
Alanine Aminotransferase, IU/L	mean (SD)	56.6 (32.7)	67.6 (54.6)	67.6 (43.0)

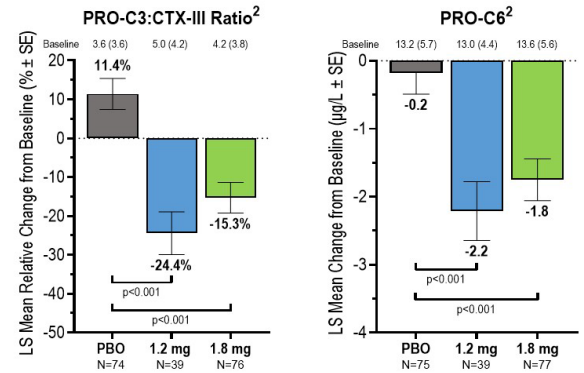
Significant Reductions in Hepatic Fibrosis by AI Digital Pathology

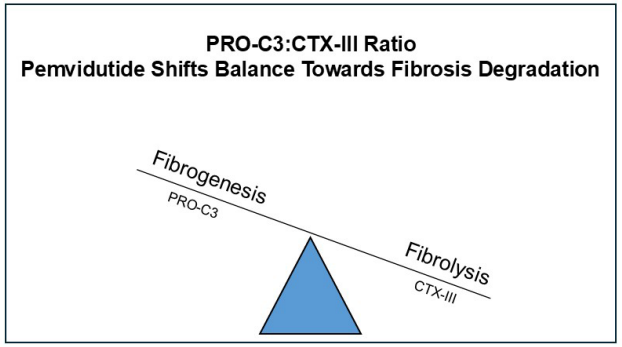






Significant Reductions in Non-Invasive Tests of Liver Fibrosis





Conclusions

- Pemvidutide treatment resulted in significant improvements in non-invasive markers of fibrosis activity at 24 weeks
- AI digital pathology analysis showed pemvidutide treatment led to significant reductions in the proportionate areas of total, early, and advanced liver fibrosis
- These data suggest that inter-stage improvements in fibrosis can be achieved in a trial of longer duration
- Overall, these data suggest that the 1:1 ratio of glucagon/GLP-1 in pemvidutide can rapidly reduce steatosis, yielding early and potent effects on hepatic fibrosis

Footnotes

† Liver Explore is For Research Use Only. Not for use in diagnostic procedures.
‡ Stanford-Moore, A., et al. (2025) medRxiv 2025.06.12.25328580.
[1]As measured by Liver Explore. Analysis by Cochran-Mantel-Haenszel test; PBO vs. treatment at Week 24
[2]Analysis of Covariance; PBO vs. treatment at Week 24

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