

Concurrent responses in multiple non-invasive tests for hepatic inflammation and fibrosis following pemvidutide treatment: 24-week responder analyses of the phase 2b IMPACT trial in metabolic dysfunction-associated steatohepatitis

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Pemvidutide yielded significant increases in the percentage of patients achieving concurrent responses in NITs of MASH fibrosis improvement

Introduction

- Pemvidutide is a balanced 1:1 glucagon/GLP-1 dual receptor agonist in development for the treatment of MASH
- IMPACT was a phase 2b, randomized, placebo-controlled, trial in patients with biopsy-confirmed F2 or F3 MASH (NCT05989711)¹
- Pemvidutide treatment resulted in statistically significant MASH resolution and high rates of fibrosis improvement at 24 weeks¹
- Reductions in individual NITs have been used as indicators of therapeutic effect
- Overlapping NITs may provide a clearer assessment of therapeutic improvement as they increase stringency of the response and lower placebo response rates compared to individual NITs

Aim

- Examine the percentage of patients achieving concurrent reductions in key NITs of MASH improvement and fibrosis improvement

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 $< 9.5\%$

Conclusions

- Pemvidutide treatment resulted in significant percentages of patients achieving concurrent reductions in LFC, ALT and LSM compared to placebo, consistent with MASH improvement
- Pemvidutide treatment resulted in significant improvements in non-invasive markers of fibrosis activity at 24 weeks compared to placebo¹
- Pemvidutide treatment resulted in significant percentages of patients achieving concurrent reductions in ELF and LSM compared to placebo, consistent with fibrosis improvement
- Pemvidutide treatment resulted in significant percentages of patients achieving concurrent reductions in LFC, ELF, and LSM compared to placebo, consistent with fibrosis improvement
- The data suggest that the 1:1 ratio of glucagon/GLP-1 in pemvidutide may contribute to the rapid reduction in steatosis, yielding early and potent effects on hepatic inflammation and fibrosis in patients with MASH

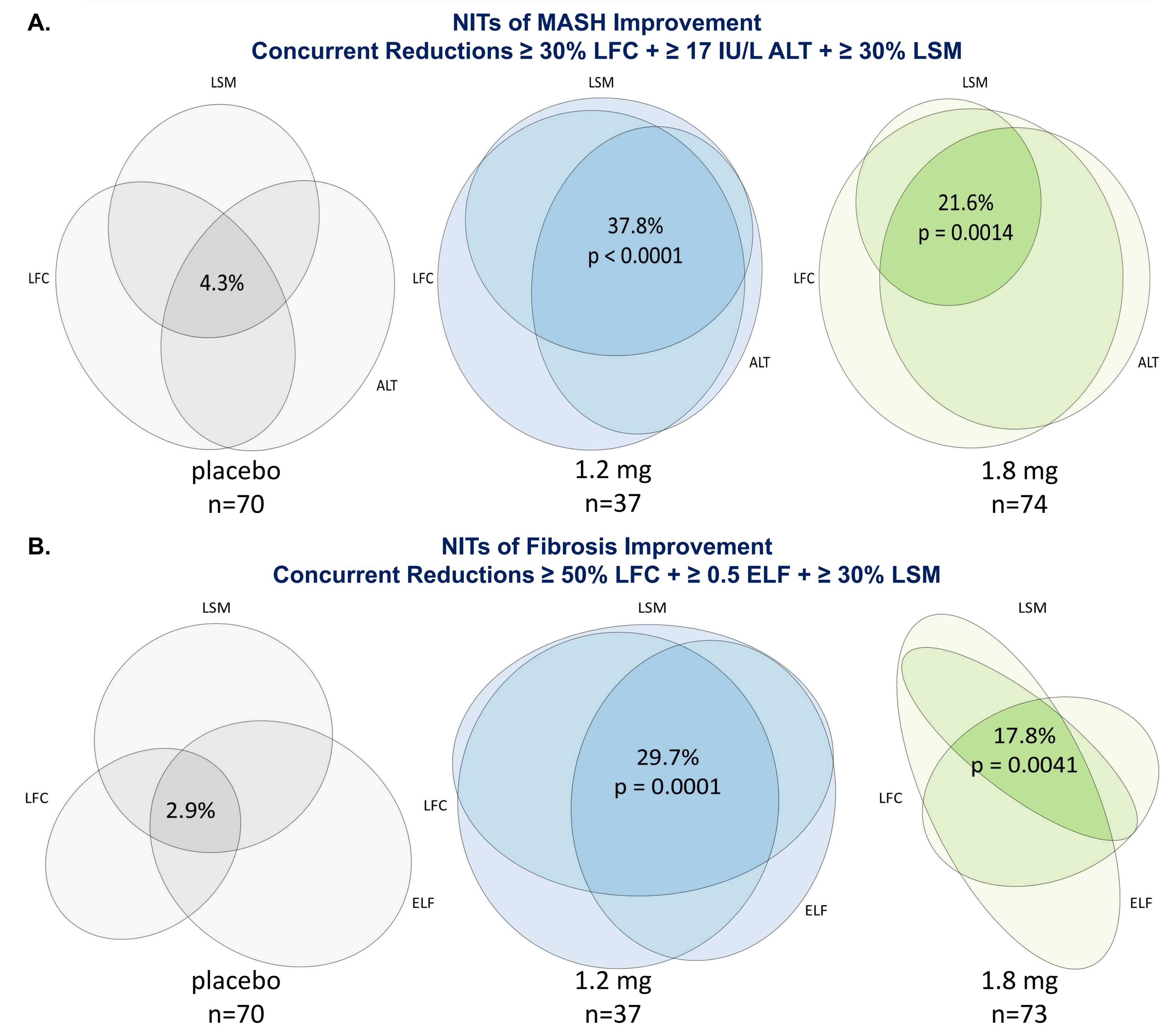
References and Abbreviations

¹Nouredin et al. Lancet. 2025 Dec 6;406(10520):2644-2655

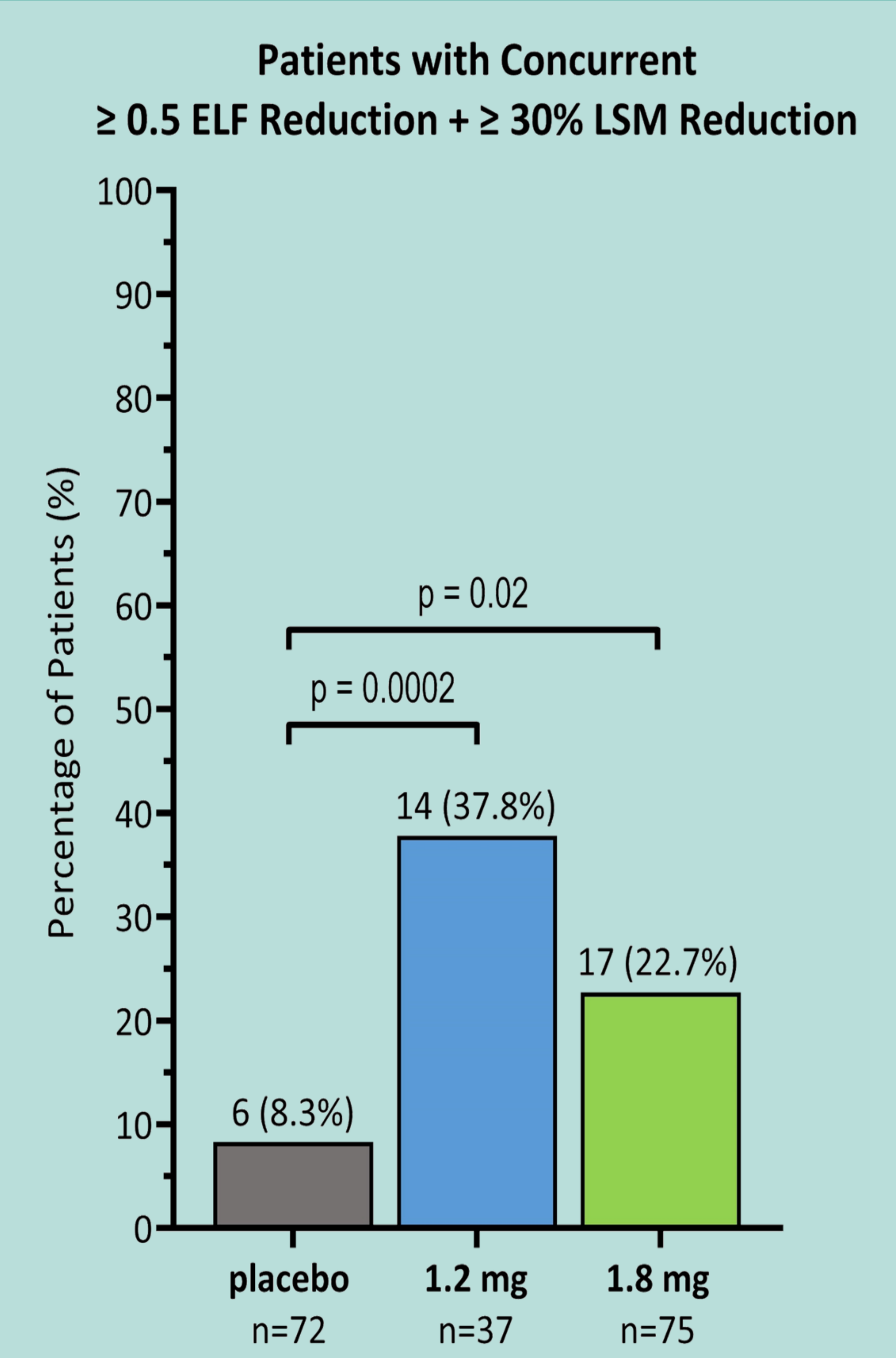
ALT, Alanine aminotransferase; ELF, Enhanced liver fibrosis; LFC, Liver fat content; LSM, Liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; MRI-PDFF, Magnetic Resonance Imaging-Proton Density Fat Fraction; NAS, NAFLD activity score; NIT, Non-invasive test; T2D, type 2 diabetes

Results

Baseline Demographics		Treatment		
		placebo (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 (56%)	25 (61%)	50 (59%)
F3 Fibrosis	n (%)	40 (47%)	17 (41%)	39 (46%)
Type 2 Diabetes	n (%)	36 (42%)	18 (44%)	36 (42%)
Body weight, kg	mean (SD)	109.7 (28.0)	110.7 (26.3)	107.7 (21.3)
Body mass index, kg/m ²	mean (SD)	38.3 (8.4)	39.2 (8.4)	38.7 (6.9)
LFC, %	mean (SD)	19.6 (6.4)	20.0 (7.1)	19.0 (6.8)
ALT, IU/L	mean (SD)	56.6 (32.7)	67.6 (54.6)	67.6 (43.0)
LSM, kPa	mean (SD)	12.5 (4.4)	12.3 (3.6)	12.8 (4.4)
ELF, score	mean (SD)	9.7 (0.8)	10.0 (0.8)	9.9 (1.0)



Percentage of patients with concurrent reductions in key NITs after 24 weeks of treatment. Percentage of patients achieving concurrent reductions in (A) NITs of MASH improvement and (B) NITs of fibrosis improvement. Statistical analysis was assessed by Cochran-Mantel-Haenszel. n values represent number of patients with reported values for all three respective NITs at week 24.



Percentage of patients with a concurrent ≥ 0.5 reduction in ELF and $\geq 30\%$ reduction in LSM after 24 weeks of treatment. Percentage of patients achieving reductions in both NITs of MASH fibrosis. Statistical analysis was assessed by Cochran-Mantel-Haenszel. n values represent number of patients with values for both respective NITs at baseline and week 24.