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# Pemvidutide Treatment Results in Concurrent Reductions in Multiple Non-Invasive Tests for Hepatic Inflammation and Fibrosis: 48-Week Responder Analyses of the IMPACT Phase 2b Trial in Metabolic Dysfunction-Associated Steatohepatitis

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## INTRODUCTION

### Background

- Metabolic dysfunction-associated steatohepatitis (MASH) is a progressive liver disease characterized by hepatic fat accumulation, inflammation, and fibrosis and is a leading cause of liver transplantation in the U.S. and of advanced liver disease globally[1]
- MASH affects an estimated ~5% (16-17 million) of the U.S. population and is projected to reach 7.9% (23.2 million) by 2050[2,3]
- Pemvidutide is a balanced 1:1 glucagon/GLP-1 dual receptor agonist, that provides direct liver effects through glucagon specificity, including liver fat reduction, leading to reductions in inflammation and fibrosis[4]
  - Its GLP-1 specificity mediates metabolic effects, such as appetite suppression, decreased alcohol cravings and consumption, and drives weight loss[4]
  - The EuPort sidechain allows for weekly dosing and may contribute to tolerability[4]
- In the IMPACT Phase 2b trial, pemvidutide demonstrated significant improvements in histology and individual non-invasive tests (NITs) of hepatic inflammation and fibrosis within 24 weeks[5]
- While individual NITs may be indicators of therapeutic effect, composite analyses using multiple, overlapping NITs may provide a more rigorous assessment of therapeutic improvement as they increase diagnostic accuracy and stringency

### Aim

- This study evaluated composite NIT responses after 48 weeks of pemvidutide in the IMPACT Phase 2b trial, using thresholds associated with MASH and/or fibrosis improvement

## METHODS

### Study Design

- In this Phase 2b, randomized, double-blind, placebo-controlled trial (NCT05989711) of pemvidutide, composite NIT responses were assessed at Week 48 in the placebo, pemvidutide 1.2 mg, and pemvidutide 1.8 mg groups
  - Patients were included if they had biopsy-confirmed MASH with fibrosis stage 2 or 3 (F2/F3), liver fat content (LFC) ≥8%, liver stiffness measurement (LSM) ≥8.5 kPa, body mass index (BMI) ≥27.0 kg/m$^2$, and hemoglobin A1c (HbA1c) ≤9.5%
  - A total of 212 patients were randomized 1:2:2 to once-weekly subcutaneous pemvidutide 1.2 mg (n=41), pemvidutide 1.8 mg (n=85), or placebo (n=86) for 48 weeks, administered without dose titration
  - NITs assessed as secondary endpoints included LFC, alanine aminotransferase (ALT), enhanced liver fibrosis (ELF) score, and LSM
- NIT responses were defined using thresholds associated with MASH and/or fibrosis improvement
  - LFC: ≥30-50% reduction[6]; ALT: ≥17 IU/L reduction[7]; ELF score: ≥0.5 reduction[8]; LSM: ≥30% reduction[9]
- Three composite endpoints were evaluated, each requiring concurrent responses across all component NITs at 48 weeks
  - MASH improvement: LFC ≥30%, ALT ≥17 IU/L, and LSM ≥30%
  - Fibrosis improvement: ELF ≥0.5 and LSM ≥30%
  - Disease remission: LFC ≥50%, ELF ≥0.5, and LSM ≥30%
- The proportion of patients achieving each composite response was compared between each pemvidutide dose and placebo using the Cochran-Mantel-Haenszel (CMH) test, stratified by type 2 diabetes status and fibrosis stage

## RESULTS

### Baseline Characteristics

- Demographic and baseline clinical characteristics were similar across groups
- Overall, the mean age was 53.4 years, and the mean BMI was 38.7 kg/m$^2$
- 123 (58%) patients were female, and 91 (43%) had type 2 diabetes
- The mean baseline LFC was 19.4%

### Composite NIT responses at 48 weeks

- Response rates for the MASH improvement composite were more than 10-fold higher with both pemvidutide doses than with placebo (Figure 1A)
- Concurrent responses in both fibrosis markers were 9- to 10-fold more frequent with pemvidutide than with placebo (Figure 1B)
- For the disease remission composite NITs, up to one in four pemvidutide-treated patients responded, while no placebo-treated patient did (Figure 1C)

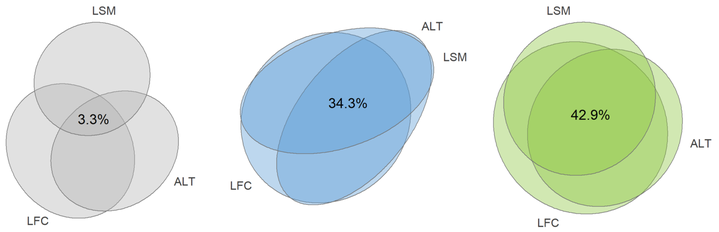
### Table 1. Demographic and baseline clinical characteristics across groups

| Characteristic | Placebo n=86 | Pemvidutide 1.2 mg n=41 | Pemvidutide 1.8 mg n=85 |
|---|---|---|---|
| Age, years, mean (SD) | 52.5 (12.2) | 55.2 (13.0) | 53.4 (12.4) |
| Female sex, n (%) | 48 (55.8) | 25 (61.0) | 50 (58.8) |
| 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) |
| Type 2 diabetes, n (%) | 36 (41.9) | 18 (43.9) | 36 (42.4) |
| F3 fibrosis, n (%) | 40 (46.5) | 17 (41.5) | 39 (45.9) |
| ELF, mean (SD) | 9.7 (0.8) | 10.0 (0.8) | 9.9 (1.0) |
| LSM, kPa, mean (SD) | 12.5 (4.4) | 12.3 (3.6) | 12.8 (4.4) |
| Liver fat content, %, 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) |

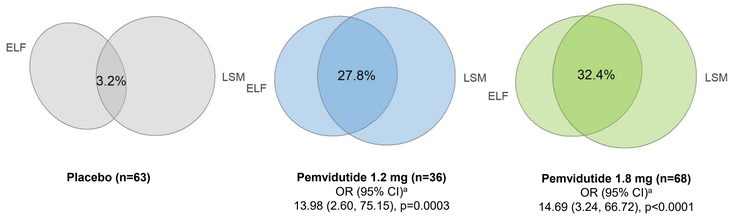
Treatment was completed by 85% of patients receiving pemvidutide and 77% of patients receiving placebo.

### Figure 1. Proportion of patients achieving concurrent responses across composite NITs at Week 48[a]

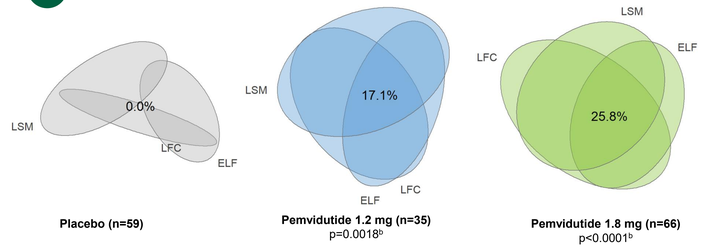
**A MASH Improvement Composite NITs at Week 48**




**B Fibrosis Improvement Composite NITs at Week at 48**




**C Disease Remission Composite NITs at Week at 48**




[a]p-values, ORs, and 95% CIs were calculated using the CMH test stratified by type 2 diabetes status and fibrosis stage; n values reflect the number of participants with evaluable data.
[b]OR and CI not estimable (no placebo responders).

## CONCLUSION

- Response rates were significantly higher with pemvidutide than placebo across all composite NIT endpoints
- 1.8 mg pemvidutide consistently achieved numerically higher response rates compared with 1.2 mg pemvidutide and placebo
- 48-week NIT findings align with trends in histologic MASH resolution and fibrosis improvement observed at 24 weeks[5]
- Collectively, these findings suggest that the balanced 1:1 glucagon/GLP-1 ratio of pemvidutide rapidly reduces liver fat, yielding potent downstream effects on hepatic inflammation and fibrosis

## NEXT STEPS

- The ongoing PERFORMA phase 3, global, randomized, placebo-controlled, double-blind, parallel-group trial evaluates pemvidutide in MASH, including:
  - Longer-term histologic and safety outcomes evaluation at 52 weeks and event-driven follow-up through ~60 months
  - Biopsy-confirmed and NIT-confirmed F2/F3 MASH cohorts
- Findings from PERFORMA are expected to expand the clinical evidence base for pemvidutide with longitudinal data across a broad MASH population, ultimately supporting regulatory approval

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### DISCLOSURES

This study was sponsored by Altimmune, Inc.
Pemvidutide is an investigational product candidate that has not been approved by the FDA or any other regulatory authority. Medical communications support was provided by Boston Strategic Partners, Inc., which was funded by Altimmune, Inc.

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**Abbreviations:** ALT, alanine aminotransferase; BMI, body mass index; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; ELF, enhanced liver fibrosis; F2/F3, fibrosis stage 2/3; FDA, US Food and Drug Administration; GLP-1, glucagon-like peptide-1; HbA1c, hemoglobin A1c; LFC, liver fat content; LSM, liver stiffness measurement; MASH, metabolic dysfunction-associated steatohepatitis; NAS, non-alcoholic fatty liver disease activity score; NITs, non-invasive tests; OR, odds ratio; SD, standard deviation.