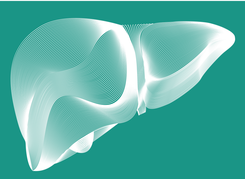

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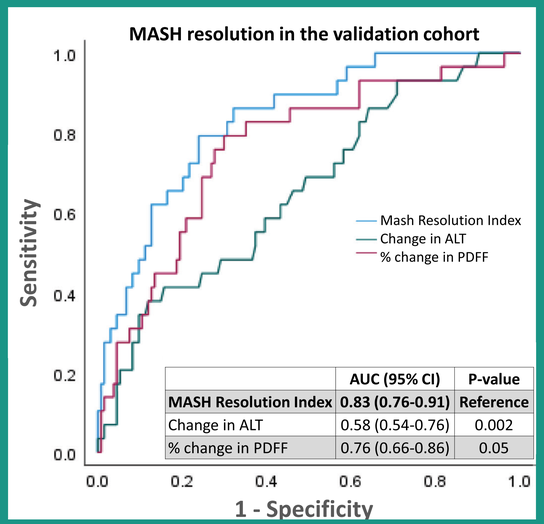
MASHResInd Cut-off of 0.67 yielded an AUC of 0.83 for prediction of MASH resolution without worsening of fibrosis (Loomba, *Gut 2024*)



	AUC (95% CI)	P-value
MASH Resolution Index	0.83 (0.76-0.91)	Reference
Change in ALT	0.58 (0.54-0.76)	0.002
% change in PDFF	0.76 (0.66-0.86)	0.05

Pemvidutide resulted in significantly higher MASHResInd response rates in MASLD subjects

MASH Resolution Index Responders

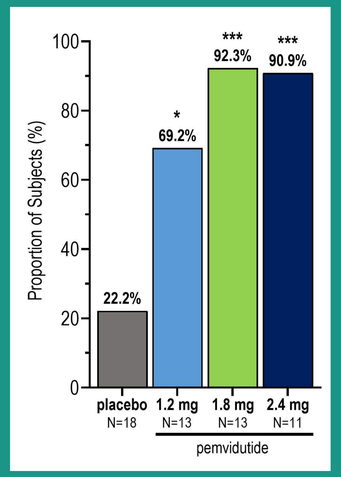


Figure 1. Proportion of responders achieving MASHResInd ≥-0.67 at Week 24. Cochran-Mantel-Haenszel: *p<0.05, ***p<0.001, vs. placebo.

MASH resolution index, a novel, highly sensitive non-invasive measure of histologic improvement, predicts high rates of MASH resolution with pemvidutide treatment of metabolic dysfunction-associated steatohepatitis (MASH)

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altimmune

Introduction

- Pemvidutide is a balanced GLP-1/glucagon dual receptor agonist under development for the treatment of MASH. An ongoing 24-week Phase 2b biopsy-driven trial (IMPACT: NCT05989711) is expected to read out in Q2 2025
- The MASH resolution index (MASHResInd) combines changes in the non-invasive tests (NITs) of MRI-PDFF liver fat content (LFC) and alanine aminotransferase (ALT) with baseline aspartate aminotransferase (AST) to predict MASH resolution without worsening of fibrosis (Loomba, *Gut 2024*)
- A MASHResInd cut-off of ≥-0.67 yielded an area under the curve (AUC) of 0.83, exceeding the AUC for either MRI-PDFF or ALT
- Separately, corrected T1 imaging (cT1) is an MRI modality that assesses hepatic fibroinflammatory activity. An 80 ms reduction has been associated with a 2-point reduction in NAFLD activity score (NAS) (Alkhouri, *J Hepatol 2024*)

Aim

- Examine the effects of pemvidutide on MASHResInd to predict the likelihood of MASH resolution

Method

Study Design

- Sixty-four subjects with metabolic dysfunction-associated steatotic liver disease (MASLD) treated with pemvidutide or placebo by subcutaneous injection weekly for 24 weeks (NCT05292911)

Study Population – Key Eligibility Criteria

- BMI ≥28 kg/m^2 and LFC by MRI-PDFF ≥10%
- FibroScan® Liver stiffness measurement <10kPa
- HbA1c <9.5%
- ALT and AST ≤75 IU/L

Outcome Measures

- Proportion of subjects who achieved a MASHResInd score ≥-0.67 at week 24
- Proportion of subjects who achieved a MASHResInd score ≥-0.67 and a cT1 reduction of ≥80 ms at week 24

Conclusions

- Pemvidutide treatment of subjects with MASLD resulted in significant reductions in MASH NITs (LFC and ALT) and MASHResInd response rates of greater than 90% within 24 weeks of treatment at the 1.8 and 2.4 mg doses
- In a subset of subjects assessed by cT1 imaging, pemvidutide treatment resulted in up to 100% of subjects achieving a combined MASHResInd and cT1 response compared with 0% in placebo
- Achievement of both MASHResInd and cT1 responses occurred in the majority of subjects receiving pemvidutide (77% for pooled pemvidutide vs. 0% for placebo; p=0.0031; Fisher's exact test)
- Based on these findings, high rates of MASH resolution are predicted to be observed in the upcoming IMPACT trial readout

References

- Loomba et al. *Gut 2024* PMID: 38418210
- Alkhouri et al. *J Hepatol 2024* PMID: 39326675

Characteristics of MASLD Study Participants

Baseline Characteristic		Treatment			
		Placebo (n = 19)	1.2 mg (n=16)	1.8 mg (n=15)	2.4 mg (n=14)
Age, years	mean (SD)	49.0 (15)	48.6 (11)	49.9 (10)	48.4 (8)
Gender	female, n (%)	11 (57.9%)	7 (43.8%)	8 (53.3%)	8 (57.1%)
BMI, kg/m^2	mean (SD)	37.1 (4.9)	36.7 (6.1)	36.0 (3.8)	37.0 (5.3)
Body weight, kg	mean (SD)	104.4 (21.2)	101.4 (16.3)	100.9 (13.2)	107.4 (17.2)
Diabetes status	T2D, n (%)	5 (26.3%)	3 (18.8%)	6 (40.0%)	3 (21.4%)
LFC, %	mean (SD)	24.0 (9.6)	20.1 (7.7)	23.9 (7.4)	20.5 (6.5)
ALT, IU/L	mean (SD)	41.0 (21.3)	32.4 (14.2)	35.3 (13.0)	39.6 (26.6)
AST, IU/L	mean (SD)	25 (10.5)	24.4 (6.6)	23.6 (6.9)	29.4 (15.4)
cT1[1], ms	mean (SD)	933.4 (114.7)	892.1 (96.3)	909.4 (162.0)	933.7 (21.9)

[1]A subset of study subjects were evaluated by cT1.

Results

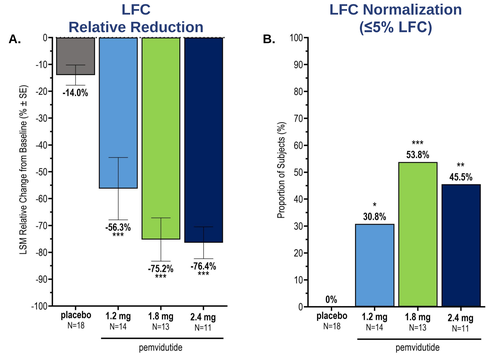

Figure 2. Reduction in LFC by MRI-PDFF at Week 24. (A) Relative reduction from baseline and (B) normalization of LFC to ≤5%. *p<0.05, **p<0.005, ***p<0.001, vs. placebo; ANCOVA and Cochran-Mantel-Haenszel, respectively.

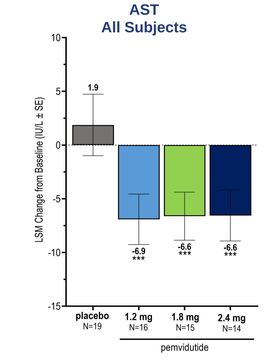

Figure 3. Reduction in AST at Week 24. Absolute reduction from baseline in all subjects. ***p<0.001 vs. placebo; MMRM.

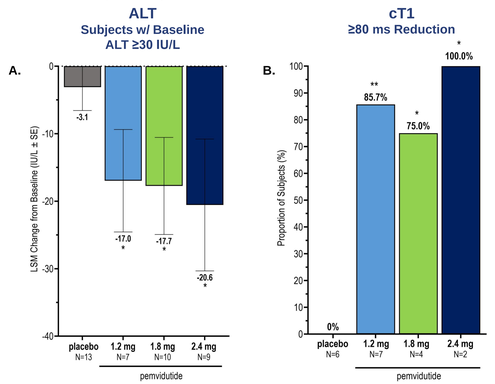

Figure 4. Reduction in ALT and cT1 at Week 24. (A) Absolute reductions in ALT from baseline in subjects with baseline ALT ≥30 IU/L; and (B) proportion of subjects with a ≥80 ms reduction in cT1 imaging. *p<0.05, **p<0.005, vs. placebo; MMRM and Fisher's exact test, respectively.

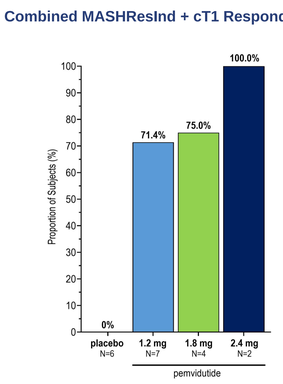

Figure 5. Proportion of subjects with combined MASHResInd and cT1 responses at Week 24. Proportion of subjects achieving MASHResInd ≥-0.67 and cT1 reductions ≥80 ms at Week 24.

Poster Session Online

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Metabolism, alcohol and toxicity
Shaheen Tomah

SAT-453
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