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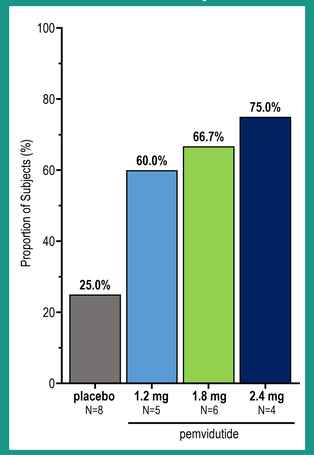
Pemvidutide improved MASH NITs associated with histologic response

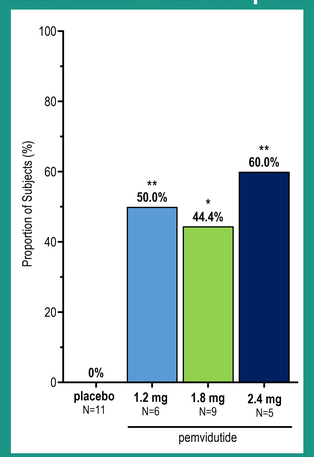
FAST Score Responders



Baseline Characteristic (FAST ≥0.35)		Treatment			
		Placebo (n=8)	1.2 mg (n=7)	1.8 mg (n=6)	2.4 mg (n=6)
AST, IU/L	mean (SD)	34.1 (8.9)	29.4 (6.7)	30.3 (6.1)	43.3 (13.6)
CAP, dB/m	mean (SD)	356.4 (33.4)	361 (21.7)	353.7 (41.8)	364.8 (37.6)
LSM, kPa	mean (SD)	7.1 (0.8)	7.2 (1.9)	6.6 (1.4)	7.4 (1.9)
FAST score[1]	mean (SD)	0.8 (0.5)	0.6 (0.2)	0.6 (0.1)	1.4 (0.6)

Figure 1. Proportion of subjects with an Intermediate-to-High risk FAST score at baseline who achieved a FAST score <0.35 at Week 24

Combined MRI + ALT Responders



Baseline Characteristic (ALT ≥30 IU/L)		Treatment			
		Placebo (n=11)	1.2 mg (n=6)	1.8 mg (n=9)	2.4 mg (n=5)
LFC, %	mean (SD)	26.7 (10.4)	25.5 (8.4)	23.0 (7.1)	24.1 (6.3)
ALT, IU/L	mean (SD)	52.5 (18.1)	47.5 (11.7)	41.9 (10.3)	56.3 (23.4)

Figure 2. Proportion of subjects with baseline ALT ≥30 IU/L who achieved simultaneous reductions in MRI-PDFF ≥30% and ALT ≥17 IU/L at Week 24. Cochran-Mantel-Haenszel: *p<0.05, **p<0.005, vs. placebo

Pemvidutide treatment is associated with improvement in noninvasive tests indicating greater likelihood of histologic response in subjects with metabolic dysfunction-associated steatotic liver disease: a 24-week, randomized, double-blind, placebo-controlled trial

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altimmune

Introduction

- Approximately 70% of individuals with obesity have metabolic dysfunction-associated steatotic liver disease (MASLD), a condition of excess liver fat
- 20-30% of MASLD subjects may advance to metabolic dysfunction-associated steatohepatitis (MASH), an inflammatory form of MASLD
- Fibroscan-AST (FAST) score combines liver stiffness measure (LSM), controlled attenuated parameter (CAP), and aspartate aminotransferase (AST) to detect elevated NAS and fibrosis
- FAST scores >0.35 indicates patients at risk of developing MASH (Newsome et al. 2020)
- A 30% relative reduction in LFC correlates with ≥2-point reduction in NAFLD activity score (NAS)
- Alanine aminotransferase (ALT) reductions of 17 IU/L are positive predictors of histologic improvement
- Pemvidutide is a balanced GLP-1/glucagon dual receptor agonist under development for the treatment of MASH and obesity

Aim

- Examine the effects of pemvidutide on non-invasive tests (NITs) that have been shown to predict the likelihood of histologic response

Method

Study Design

- Sixty-four subjects with MASLD treated with pemvidutide or placebo by subcutaneous injection weekly for 24 weeks (NCT05292911)

Study Population – Key Eligibility Criteria

- BMI ≥28 kg/m² and LFC by MRI-PDFF ≥10%
- FibroScan® LSM <10kPa
- HbA1c <9.5%
- ALT and AST ≤75 IU/L

Outcome Measures

- Proportion of subjects who achieved a FAST score <0.35 at week 24
- Proportion of subjects with ALT ≥30 IU/L at baseline who achieved a simultaneous reduction in MRI-PDFF (≥30%) and ALT (≥17 IU/L) at week 24

Conclusions

- Pemvidutide treatment resulted in reductions of up to 76.4% in relative LFC, and 15.2 IU/L in serum ALT at 24 weeks
- Reductions in LFC correlated with improvements in NITs
- In a subset of subjects with intermediate-to-high risk of MASH, pemvidutide treatment was associated with improvement in the FAST score
- In a subset of subjects with ALT ≥30 IU/L at baseline, pemvidutide treatment resulted in a significantly greater combined ALT/MRI-PDFF response rate compared to placebo, indicating greater likelihood of histologic response
- Pemvidutide is being evaluated in an ongoing 24-week Phase 2b biopsy-driven MASH trial (IMPACT: NCT05989711)

References

- Newsome et al. *Lancet Gastroenterol. Hepatol.* 2020 PMC7066580

Characteristics of 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/m²	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%)
Liver fat content (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)
CAP, dB/m	mean (SD)	342 (30)	333 (34)	347 (37)	347 (33)
LSM, kPa	mean (SD)	6.7 (0.9)	6.9 (2.0)	6.1 (1.3)	6.5 (1.8)
FAST score[1]	mean (SD)	0.4 (0.5)	0.4 (0.3)	0.3 (0.2)	0.7 (0.8)

[1]FAST = {exp (−1.65 + 1.07 × ln (LSM) + 2.66 × 10−8 × CAP3 − 63.3 × AST−1)}/{1 + exp (−1.65 + 1.07 × ln (LSM) + 2.66 × 10−8 × CAP3 − 63.3 × AST−1)}

Results

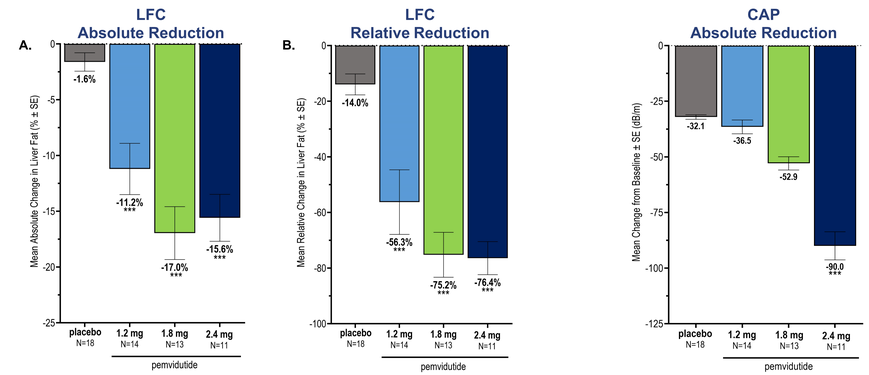

Figure 3. Reduction in LFC by MRI-PDFF at Week 24. (A) Absolute and (B) relative reductions in LFC from baseline. Analysis of Covariance: ***p<0.001 vs. placebo

Figure 4. Reduction in FibroScan CAP score at Week 24. Absolute reduction from baseline. Analysis of Covariance: ***p<0.001 vs. placebo

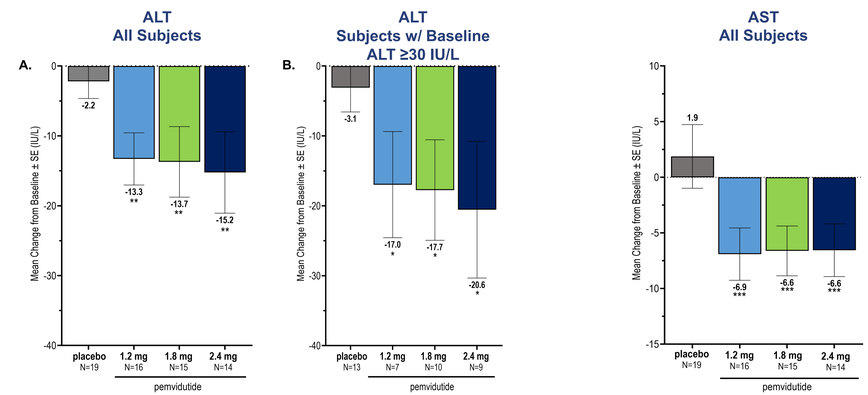

Figure 5. Reduction in ALT at Week 24. Absolute reductions from baseline in (A) all subjects and (B) subjects with baseline ALT ≥30 IU/L. Mixed model repeated measures: *p<0.05, **p<0.005, vs. placebo

Figure 6. Reduction in AST at Week 24. Absolute reduction from baseline in all subjects. Mixed model repeated measures: ***p<0.001 vs. placebo