Pemvidutide Significantly Reduces Liver Fat, Non-invasive Markers of Fibro-inflammation, and Body Weight in Patients with NAFLD: Results of a Randomized, Placebo-controlled Trial

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NASH-TAG, Park City, UT, January 2023
PEMVI: GLP-1/GLUCAGON RECEPTOR DUAL AGONIST
Optimized for weight loss and NASH

Designed for significant reductions in:

- BODY WEIGHT
- LIVER FAT, INFLAMMATION, & RESULTING FIBROSIS
- GLUCAGON effects on liver
  - energy expenditure
  - adipose browning
  - lipolysis
  - mobilization of liver fat
- GLP-1 Indirect effects on liver
  - appetite
  - inflammation

MIMICS
- EXERCISE
- DIETARY INTAKE
Pemvidutide NAFLD Trial Design

• 12-week, randomized, placebo-controlled study

• Completers were invited to participate in a 12-week extension to receive a total of 24 weeks of treatment

• **Primary endpoint**: Reduction in liver fat content by MRI-PDFF at Week 12

• **Secondary endpoints**: Hepatic inflammation (serum ALT, cT1) and body weight

• No caloric restriction or lifestyle intervention
Study Population

Key Eligibility Criteria

- MRI-PDFF ≥ 10%
- FibroScan® LSM < 10kPa
- Non-diabetes or non-insulin dependent diabetes with HbA1c< 9.5%
- Serum ALT ≤ 75 IU/L

Baseline Characteristics

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>placebo (n = 24)</td>
</tr>
<tr>
<td>Age, years mean (SD)</td>
<td>47.9 (14)</td>
</tr>
<tr>
<td>Gender, female, n (%)</td>
<td>14 (58.3%)</td>
</tr>
<tr>
<td>Ethnicity, Hispanic, n (%)</td>
<td>14 (58.3%)</td>
</tr>
<tr>
<td>BMI, kg/m² mean (SD)</td>
<td>36.9 (4.7)</td>
</tr>
<tr>
<td>Body weight, kg mean (SD)</td>
<td>105.1 (20.8)</td>
</tr>
<tr>
<td>Diabetes status, T2D, n (%)</td>
<td>6 (25.0%)</td>
</tr>
<tr>
<td>Liver fat content, % mean (SD)</td>
<td>23.8 (9.2)</td>
</tr>
<tr>
<td>Serum ALT, IU/L mean (SD)</td>
<td>39.5 (21.4)</td>
</tr>
</tbody>
</table>
Reduction in Liver Fat Content at Week 12

Relative Reduction

**30% Reduction** | **50% Reduction** | **Normalization (≤5% LFC)**

![Bar charts showing mean relative reduction in liver fat content for placebo and pemvidutide at 1.2 mg, 1.8 mg, and 2.4 mg doses.](image)

<table>
<thead>
<tr>
<th>Group</th>
<th>1.2 mg</th>
<th>1.8 mg</th>
<th>2.4 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Reduction</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo</td>
<td>4.4%</td>
<td>68.5%</td>
<td>57.1%</td>
<td>4.4%</td>
</tr>
<tr>
<td>1.2 mg</td>
<td>46.6%</td>
<td>65.0%</td>
<td>94.4%</td>
<td>94.4%</td>
</tr>
<tr>
<td>1.8 mg</td>
<td>****</td>
<td>72.2%</td>
<td>85.0%</td>
<td>85.0%</td>
</tr>
<tr>
<td>2.4 mg</td>
<td>****</td>
<td>70.0%</td>
<td>70.0%</td>
<td>70.0%</td>
</tr>
</tbody>
</table>

*** p < 0.001 vs placebo, ANCOVA, LS mean ± SE

* p < 0.05, *** p < 0.001, ****, p < 0.0001 vs placebo, Cochran-Mantel-Haenszel
Reduction of Serum ALT at Week 12

All Subjects

Subjects w/ Baseline ALT ≥ 30 IU/L

Mean Δ from Baseline ± SE (IU/L)

placebo
1.2 mg
1.8 mg
2.4 mg

N=24
N=23
N=23
N=24

placebo
1.2 mg
1.8 mg
2.4 mg

N=15
N=10
N=15
N=12

* p < 0.05 vs placebo, mixed model repeated measures, LS mean ± SE
cT1 Responder Rates at Week 12

RESPONDER DEFINED AS A SUBJECT WITH AN 80ms REDUCTION IN cT1 FROM BASELINE

- 80ms reduction in cT1 has been associated with a 2-point reduction of NASH Activity Score (NAS)\(^1\)
- Elevated cT1 levels have been associated with increased risk of major adverse cardiac events (MACE) and major adverse liver outcomes (MALO)\(^2,3\)

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\(^1\)Dennis A, Front Endocrinol 2021; \(^2\)Jayaswal, A. Liver Int 2020; \(^3\)Roca-Fernandez A, MedRxiv 2022;
Additional Reduction in Liver Fat Content at Week 24

**Relative Reduction**

![Bar chart showing relative reduction in liver fat content across different treatment groups.]

**30% Reduction**

- Placebo: 14.0% (N=18)
- 1.2 mg: 56.3% (N=14)
- 1.8 mg: 75.2% (N=13)
- 2.4 mg: 76.4% (N=11)

**50% Reduction**

- Placebo: 0% (N=18)
- 1.2 mg: 76.9% (N=14)
- 1.8 mg: 92.3% (N=13)
- 2.4 mg: 100.0% (N=11)

**Normalization (≤5% LFC)**

- Placebo: 0% (N=18)
- 1.2 mg: 53.8% (N=14)
- 1.8 mg: 45.5% (N=13)
- 2.4 mg: 45.5% (N=11)

*** p < 0.001 vs placebo, ANCOVA, LS mean ± SE

* p < 0.05, *** p < 0.001, ****, p < 0.0001 vs placebo, Cochran-Mantel-Haenszel

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial
Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial

**Weight Loss at Week 24**
DIFFERENTIATES PEMVIDUTIDE FROM NASH DRUGS WITH COMPARABLE LEVELS OF LIVER FAT REDUCTION

** p < 0.005, ** p < 0.001 vs placebo, mixed model with repeated measures, LS mean ± SE
Reduction in Liver Volumes at Week 24

Comparison to Week 0 (Baseline) of the Phase 1b NAFLD trial, LS mean ± SE
Safety Summary

- GI intolerability comparable to other drugs in the GLP-1 class of agents
- Low rates of AEs leading to treatment discontinuation, no serious/severe AEs related to pemvidutide
- Cardioprotective reductions in blood pressure without increases in heart rate
- Glycemic control maintained with trends toward improvements in fasting glucose and HbA1c in subjects with diabetes
- No significant ALT elevations
PEMVIDUTIDE REDUCES LIVER FAT, INFLAMMATION AND BODY WEIGHT
RAPID EFFECTS ON ALL THREE THERAPEUTIC OBJECTIVES

• Potent reduction in liver fat content, with >50% achieving normalization
• Potent reduction in serum ALT/ cT1 (inflammation)
• Significant reduction in body weight
Thank you