



# Effect of pemvidutide on cardiovascular risk factors in patients with metabolic dysfunction-associated steatohepatitis: 48-week results from the phase 2b, IMPACT trial



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## Introduction

- Pemvidutide is a balanced 1:1 glucagon/GLP-1 dual receptor agonist in development for the treatment of MASH
- Cardiovascular disease is prevalent in patients with MASH and is the most common cause of mortality in patients with non-cirrhotic MASH<sup>1</sup>
- Obesity is a primary driver of MASH, and weight loss is central to the treatment of MASH as it is associated with both MASH resolution and improvement in hepatic fibrosis
- Waist circumference (a measure of visceral adiposity), elevated serum lipids, and high blood pressure are risk factors for cardiovascular disease
- IMPACT was a phase 2b, randomized, placebo-controlled, trial in patients with biopsy-confirmed F2 or F3 MASH (NCT05989711)<sup>2</sup>
- Pemvidutide treatment resulted in statistically significant MASH resolution and high rates of fibrosis improvement at 24 weeks<sup>2</sup>

## Aim

- Examine the effects of pemvidutide on cardiovascular risk factors in patients with F2 or F3 MASH

## 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  $\geq 27$  kg/m<sup>2</sup>
- Histological diagnosis of MASH by liver biopsy within the preceding 6 months
  - A NAS  $\geq 4$  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 reductions in body weight and BMI, with weight loss appearing to continue at the end of treatment
- Pemvidutide treatment resulted in significant reductions in waist circumference at the 1.8 mg dose. Increased waist circumference is a predictor of cardiovascular disease<sup>3</sup>
- Pemvidutide treatment yielded significant reductions in serum lipids with elevated baseline levels which may be a result of glucagon's established direct effects on hepatic lipid metabolism
- Significant reductions in body weight, waist circumference, serum lipids, and blood pressure may be indicative of broad improvements in cardiovascular disease
- The data suggest that the 1:1 ratio of glucagon/GLP-1 in pemvidutide may contribute to rapid reductions in body weight, visceral adipose tissue, and serum lipids in patients with MASH

## References and Abbreviations

<sup>1</sup>Sanyal et al. Am Heart J Plus. 2024 Mar 24;41:100386;

<sup>2</sup>Noureddin et al. Lancet. 2025 Dec 6;406(10520):2644-2655

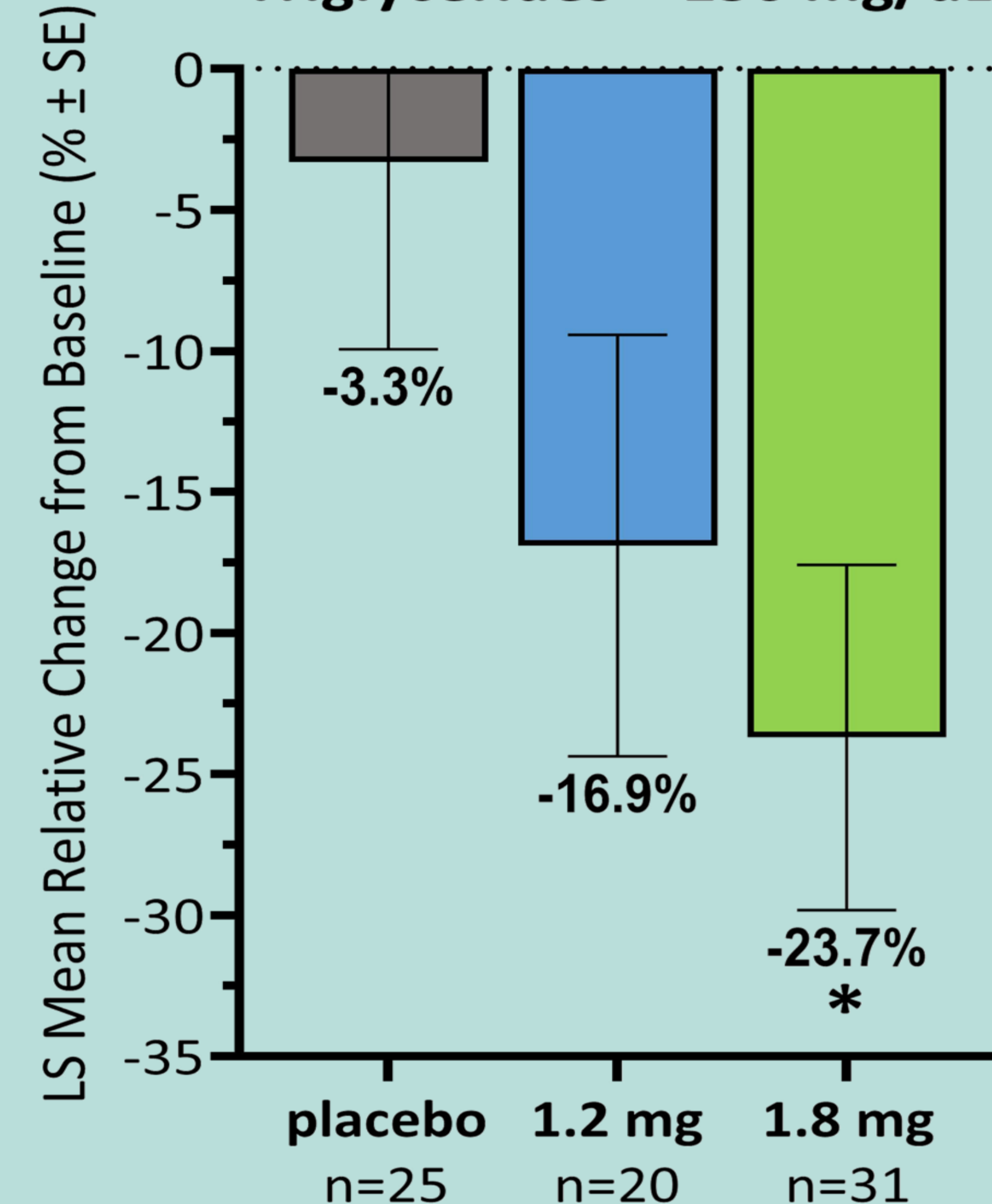
<sup>3</sup>Siren et al. BMC Public Health. 2012 Aug 9;12:631

LS mean, Least-squares mean; MRI-PDFF, Magnetic Resonance Imaging-Proton Density Fat Fraction; MASH, metabolic dysfunction-associated steatohepatitis; NAS, NAFLD activity score; T2D, type 2 diabetes

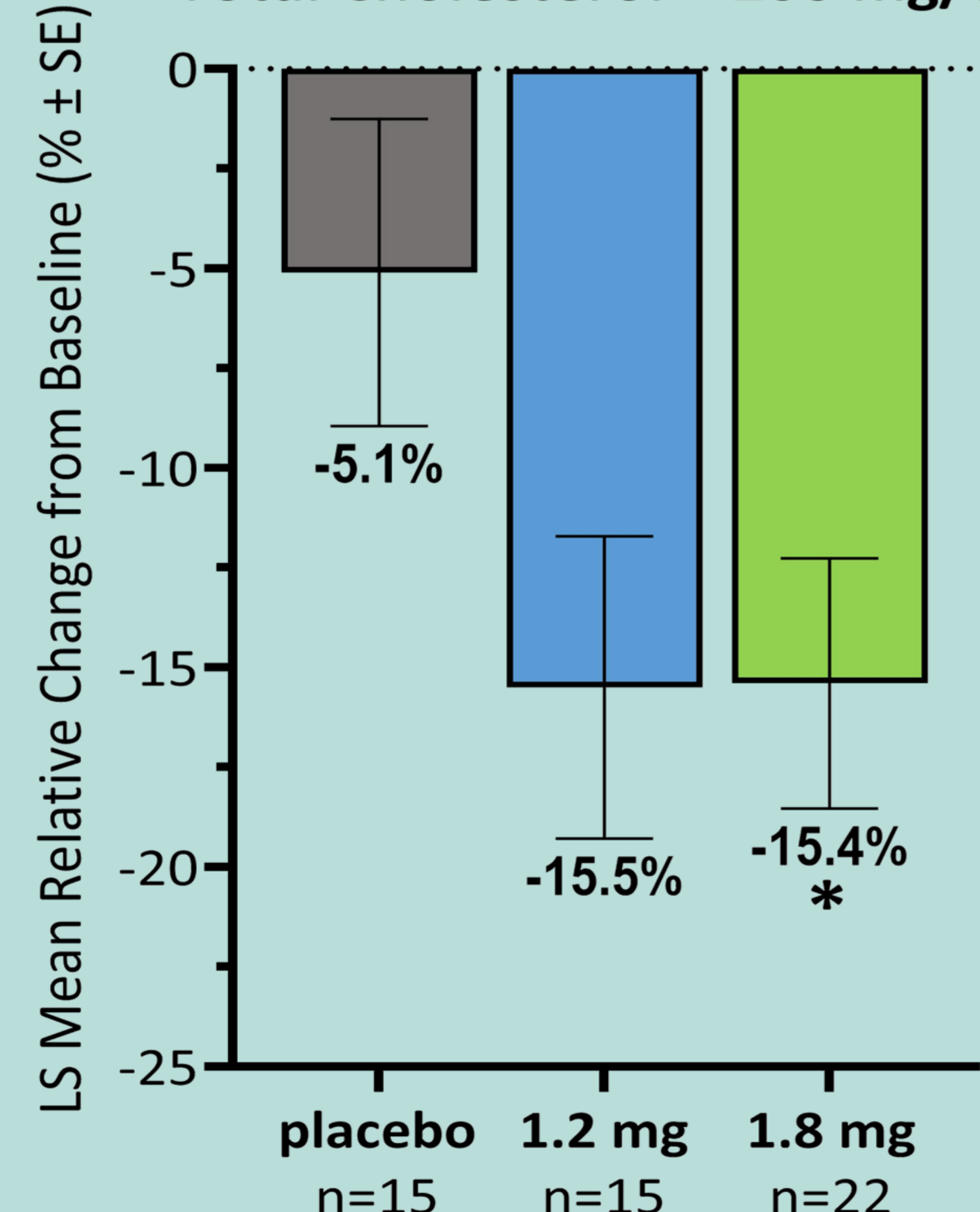
## Pemvidutide significantly reduced lipids in patients with MASH

Baseline Demographics		Treatment		
		placebo	1.2 mg	1.8 mg
Triglycerides, mg/dL	mean (SD)	242.1 (96.8)	207.8 (53.3)	233.4 (88.4)
Total cholesterol, mg/dL	mean (SD)	234.9 (32.2)	232.8 (24.4)	227.3 (24.2)

### A. Patients with Baseline Triglycerides > 150 mg/dL



### B. Patients with Baseline Total Cholesterol > 200 mg/dL

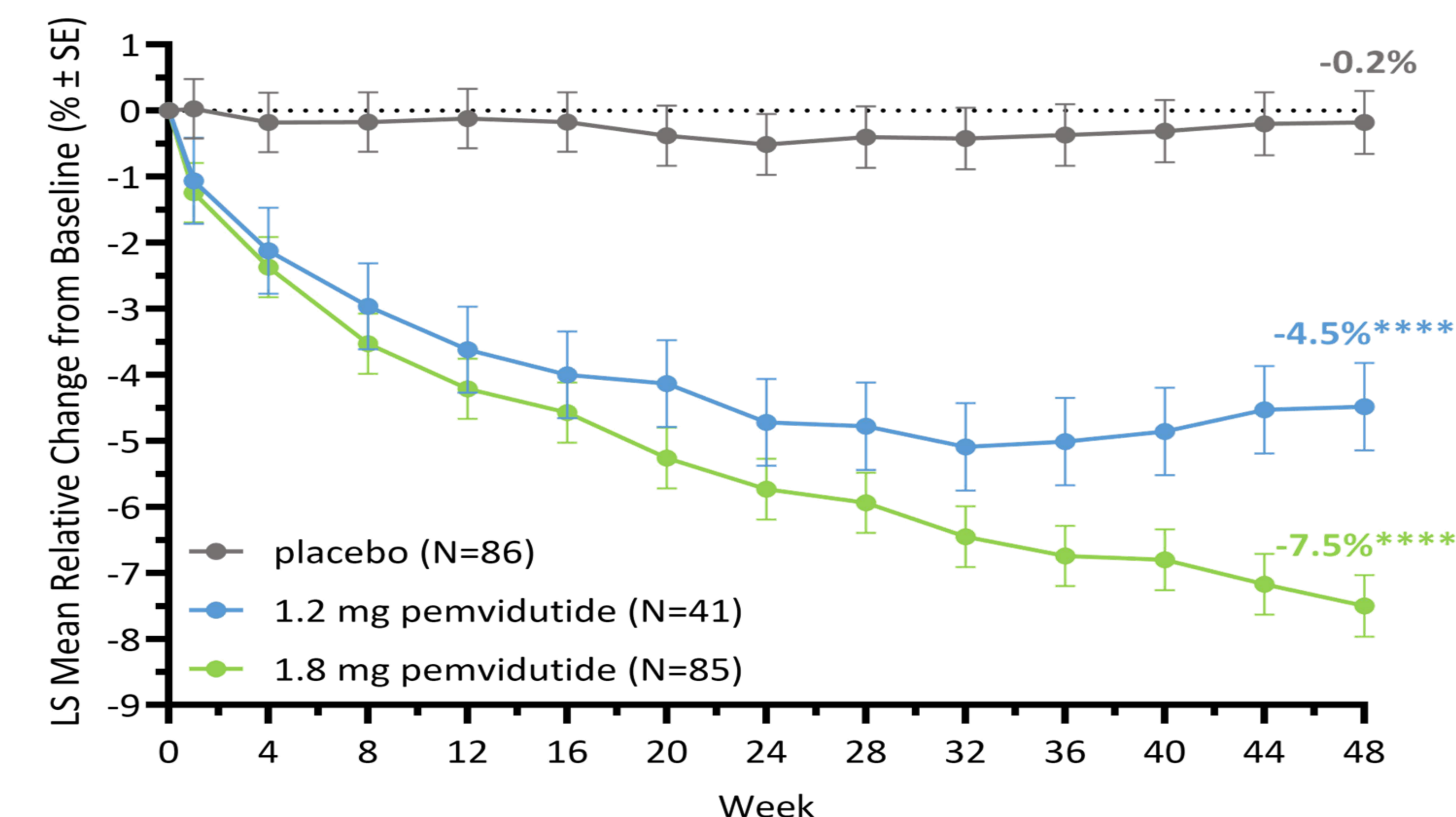


Change in elevated baseline lipids after 48 weeks of treatment. Relative LS mean (SE) change from baseline to week 48 in (A) triglycerides and (B) total cholesterol. Statistical analysis was assessed by analysis of covariance: \* p < 0.05 vs. placebo.

Disclosures: This study was sponsored by Altimmune, inc.

## 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)
Waist circumference, cm	mean (SD)	118.8 (18.8)	123.5 (16.9)	119.1 (14.3)
Body mass index, kg/m <sup>2</sup>	mean (SD)	38.3 (8.4)	39.2 (8.4)	38.7 (6.9)
Systolic blood pressure, mmHg	mean (SD)	125.7 (13.0)	125.3 (13.7)	124.2 (13.4)
Diastolic blood pressure, mmHg	mean (SD)	79.4 (7.3)	76.1 (8.4)	78.9 (7.8)
Liver Fat Content, %	mean (SD)	19.6 (6.4)	20.0 (7.1)	19.0 (6.8)
Triglycerides, mg/dL	mean (SD)	164.6 (91.6)	163.7 (63.6)	164.9 (84.8)
Total cholesterol, mg/dL	mean (SD)	179.5 (44.4)	191.4 (43.4)	180.2 (40.5)
Low-density lipoprotein cholesterol, mg/dL	mean (SD)	101.7 (38.9)	115.2 (40.5)	102.0 (36.5)



Percent change in body weight after 48 weeks of treatment. LS mean (SE) percent reductions from baseline to week 48. Statistical analysis was assessed by mixed model repeated measures: \*\*\*\* p < 0.0001 vs. placebo at week 48.

Secondary Efficacy Endpoints		Treatment		
		placebo	1.2 mg	1.8 mg
Weight loss, kg <sup>†</sup>	LS mean (SE)	-0.1 (0.5)	-4.6 (0.8)****	-8.2 (0.5)****
Body mass index, kg/m <sup>2†</sup>	LS mean (SE)	-0.02 (0.2)	-1.7 (0.3)****	-3.0 (0.2)****
Waist circumference, cm <sup>†</sup>	LS mean (SE)	-1.9 (0.8)	-3.9 (1.1)	-5.3 (0.8)**
Systolic blood pressure, mmHg <sup>†</sup>	LS mean (SE)	1.3 (1.3)	-3.8 (1.8)*	-4.0 (1.3)**
Diastolic blood pressure, mmHg <sup>†</sup>	LS mean (SE)	0.8 (0.8)	-1.0 (1.1)	-2.2 (0.8)*
Triglycerides, % <sup>‡</sup>	LS mean (SE)	2.5 (4.2)	-11.2 (5.5)*	-12.4 (4.0)*
Total cholesterol, % <sup>‡</sup>	LS mean (SE)	-1.9 (1.9)	-5.2 (2.5)	-9.4 (1.7)**
Low-density lipoprotein cholesterol, % <sup>‡</sup>	LS mean (SE)	-0.8 (3.0)	-5.7 (3.9)	-8.2 (2.8)

Change in cardiovascular risk factors after 48 weeks of treatment. LS mean (SE) absolute or relative changes from baseline to week 48. <sup>†</sup>Statistical analysis was assessed by mixed model repeated measures. <sup>‡</sup>Statistical analysis was assessed by analysis of covariance. \* p < 0.05; \*\* p < 0.01, \*\*\*\* p < 0.0001 vs. placebo.

