Integrated Analysis Supports Cardiovascular Safety And Risk Reduction With Pemvidutide Treatment

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Background

- Pemvidutide is a peptide-based GLP-1/glucagon dual receptor agonist in clinical development for the treatment of obesity and metabolic dysfunction-associated steatohepatitis (MASH)
- Overweight/obesity and elevated liver fat content (LFC) are strongly associated with hypertension, increased heart rate (HR), and increased risk of arrhythmias
- In subjects with overweight/obesity, pemvidutide treatment resulted in 15.6% reduction in body weight and significant reductions in serum lipids at 48 weeks (Figure 1A)
- In subjects with metabolic dysfunction-associated steatotic liver disease (MASLD), pemvidutide treatment resulted in significant reductions in LFC at 24 weeks (Figure 1B)

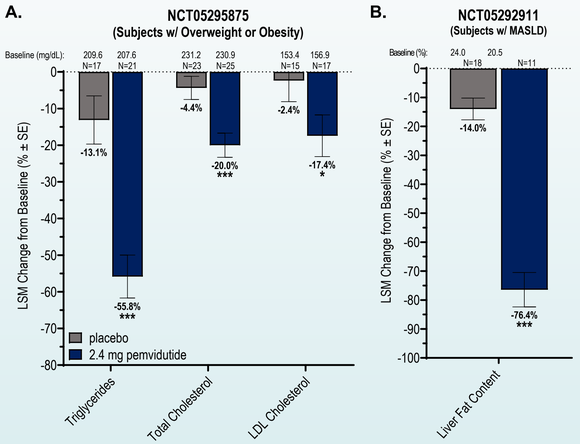

Figure 1: Pemvidutide improves multiple risk factors for CV disease. (A) Least-squares mean (LSM) change from baseline in serum lipids in subjects with elevated baseline levels at 48 weeks. (B) Change in LFC at 24 weeks. *p<0.05 ***p<0.001 vs. placebo; ANCOVA.

Objective

- Evaluate the effects of pemvidutide on additional cardiovascular (CV) safety parameters:
  - Systolic (SBP) and diastolic (DBP) blood pressure
  - HR and rate pressure product (RPP)
  - Frederica-corrected QT intervals (QTcF)

Methods

Study Population and Design

- Integrated analyses across 4 clinical trials (Table 1) to assess SBP, DBP, HR, and RPP
- Independent QT study in healthy volunteers receiving single ascending doses (SAD) up to 4.8 mg and multiple ascending doses (MAD) up to 3.0 mg once weekly for 12 weeks. Subjects underwent continuous electro-cardiogram (ECG) recordings and QTcF were assessed by linear time-matched concentration-QTc analysis

Results

- Pemvidutide led to reductions in SBP and DBP up to 11.3 mm Hg and 3.5 mm Hg, respectively
- There were no dose-related or clinically meaningful effects on HR or RPP or imbalances in cardiac adverse events
- In the independent QT study, Mean (90% CI) of predicted placebo-corrected change in QTcF (ΔΔQTcF) was <10 ms, an accepted threshold for safety, at all pemvidutide concentrations (Figure 2)

Conclusions

- Pemvidutide treatment reduces multiple risk factors for CV disease, including serum lipids, LFC, blood pressure, and RPP
- Pemvidutide treatment did not result in significant increases in HR as has been reported with some incretin-based treatments and did not increase QTcF

Study Number	Clinicaltrials.gov Identifier	Study Population	N	Treatment Duration	Change from Baseline			
					Systolic BP (mmHg) (± SE)	Diastolic BP (mmHg) (± SE)	HR (bpm) (± SE)	RPP* (± SE)
1	NCT04561245	Obesity/ overweight without T2DM	12	12 weeks	-11.3 (4.2)	-3.5 (3.3)	-4.0 (2.9)	-1157.2 (411.2)
2	NCT05006885	MASLD ± T2DM	24	0-12 weeks	-10.4 (2.8)	-4.8 (1.9)	2.6 (1.8)	-384.1 (306.0)
3	NCT05292911 (Extension of NCT05006885)	MASLD ± T2DM	14	12-24 weeks	-12.0 (3.5)	-3.8 (2.8)	-0.1 (1.8)	-737.7 (330.4)
4	NCT05295875	Obesity/ overweight without T2DM	97	48 weeks	-4.6 (2.3)	-2.9 (1.4)	2.5 (1.6)	-20.4 (238.8)

Table 1: Vital sign measurements in pemvidutide treated subjects at the highest delivered dose. T2DM, type 2 diabetes mellitus; *RPP = SBP x HR

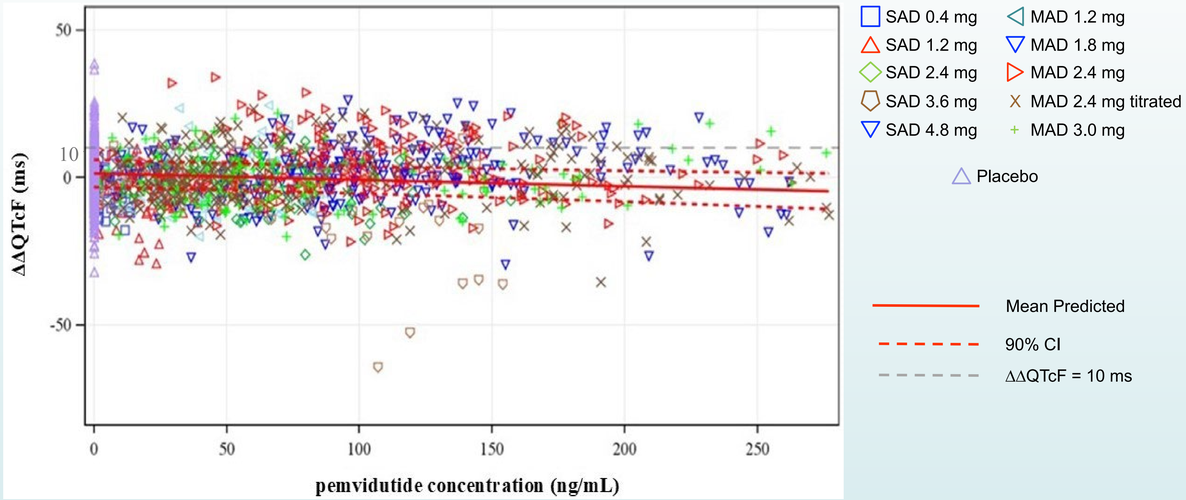

Figure 2: Observed pemvidutide plasma concentrations versus estimated placebo-corrected ΔQTcF. SAD cohorts ranged from 4-6 subjects. MAD cohorts ranged from 7-12 subjects receiving 12 weekly doses. The pooled placebo cohort was 23 subjects across both SAD and MAD arms.

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