

Superior Efficacy and Clinical Translatability of CagriSema Compared to Cagrilintide and Semaglutide in the DIO Rats

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Background & Aim

Long-acting amylin analogues offer mechanistic complementarity to incretin-based therapies for obesity. Accordingly, CagriSema, a fixed-dose combination of the amylin analogue Cagrilintide and the GLP-1 analogue Semaglutide, has demonstrated superior weight loss compared with either agent alone in recent clinical trials. The present study aimed to compare the efficacy of CagriSema, Cagrilintide and Semaglutide on metabolic, adipose and skeletal muscle endpoints in diet-induced obese (DIO) rats.

Methods

DIO Sprague-Dawley rats (n=9-10 per group) were randomized according to baseline body weight and administered subcutaneously once daily with vehicle, Cagrilintide (10 nmol/kg), Semaglutide (10 nmol/kg), or CagriSema (10 nmol/kg + 10 nmol/kg) for four weeks. Endpoints included body weight, food intake, EchoMRI, and muscle histomorphometrics.

Conclusion

- + CagriSema demonstrates greater body weight loss efficacy than Cagrilintide and Semaglutide alone.
- + CagriSema preferentially mobilizes metabolically harmful visceral fat.
- + CagriSema reduced intramuscular adipocyte load.
- + CagriSema induced skeletal muscle remodelling commensurate with reduced body mass.

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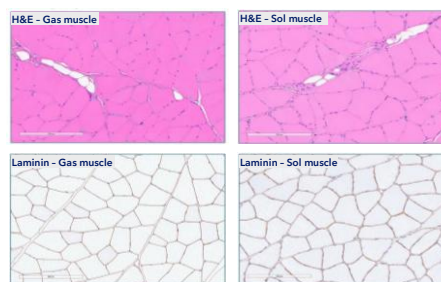
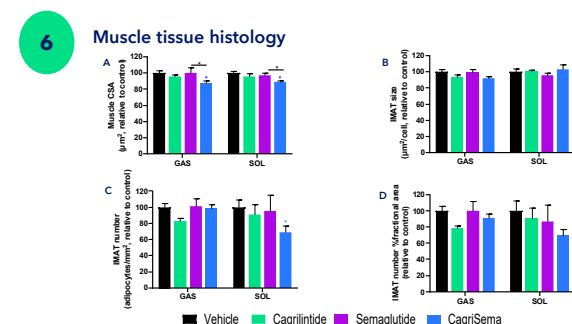
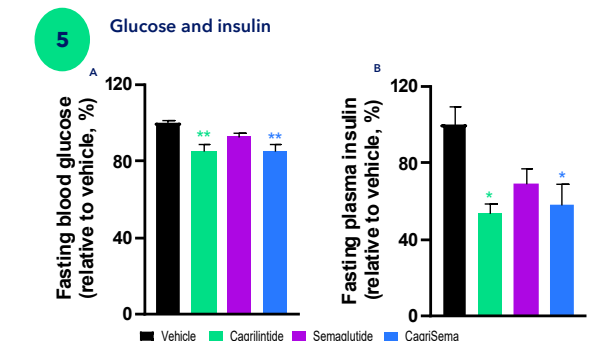
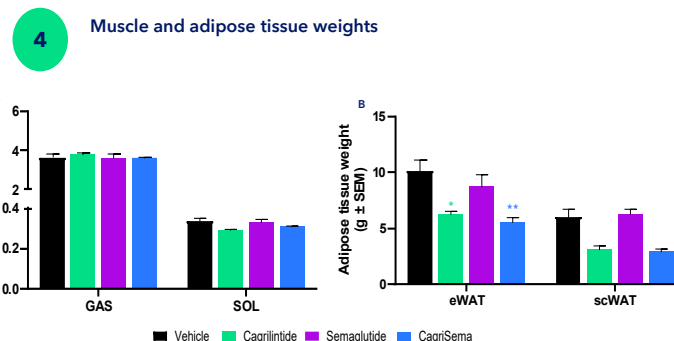
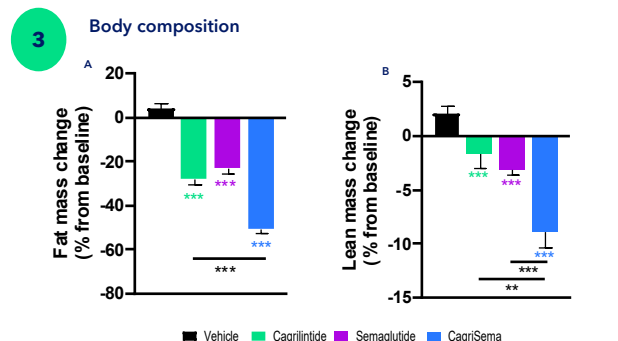
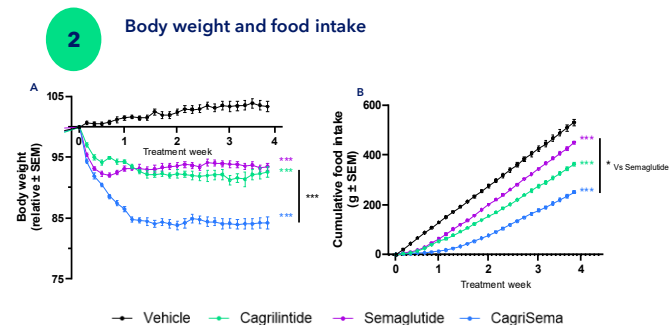


Figure 6. Histomorphometric assessment of muscle fiber cross-sectional area (CSA, proxy for plasticity) and muscle lipid content. Gastrocnemius (GAS) and soleus (SOL) skeletal muscle quantification for (A) CSA (μm^2 , laminin staining), (B) intramuscular adipocyte (IMAT) size ($\mu\text{m}^2/\text{cell}$, H&E staining), (C) intramuscular adipocyte (IMAT) number (cells/ mm^2 , H&E staining) and (D) intramuscular adipocyte (IMAT) number % fractional area (H&E staining). Data shown as mean % change from vehicle $\pm$ SEM. *p<0.05.

