Circulating total and intact GDF-15 levels are not altered in response to weight loss induced by liraglutide and/or lorcaserin treatment in humans with obesity and/or diabetes

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Background

- It is unclear whether Growth differentiation factor 15 (GDF-15) is a hormone that regulates Body Weight, Energy Expenditure, Cachexia, Anorexia, or whether it is mainly a Stress-response Cytokine
- Anti-obesity effects have been proposed

Objectives

- Investigate changes of Intact and Total GDF-15 in response to GLP-1-RA and 5-HT2C-RA in obese patients with and without T2DM.
- Correlate GDF-15 levels with clinical, hormonal, and metabolo-lipidomic parameters

Methods

Randomized, double-blinded, cross-over trials:

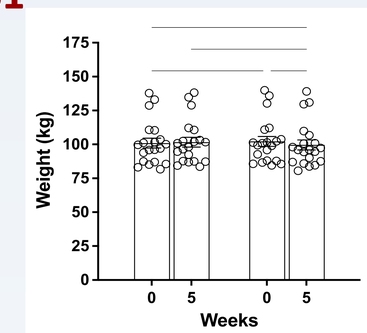
- **S1**: Liraglutide vs. placebo for 5 weeks, starting at 0.6 mg/day week 1 and increasing weekly, up to 3.0 mg/day.
- **S2**: Liraglutide vs. placebo for 14 days, followed by the opposite one, at 0.6mg, to 1.2mg and 1.8mg on day 14.
- **S3:** Lorcaserin 20mg/day vs. placebo for 12-weeks

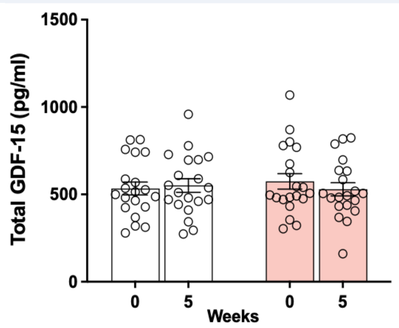
Measurements:

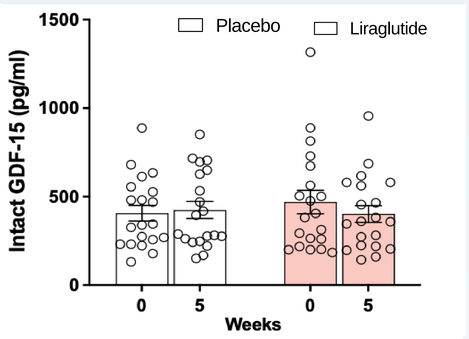
Novel Total and nonH202D GDF15 ANSH ELISAs. NMR spectroscopy for Omics.

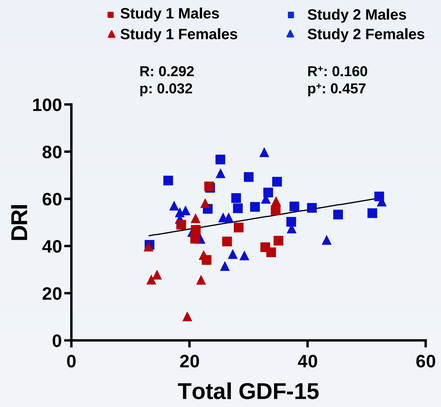
Results

S1









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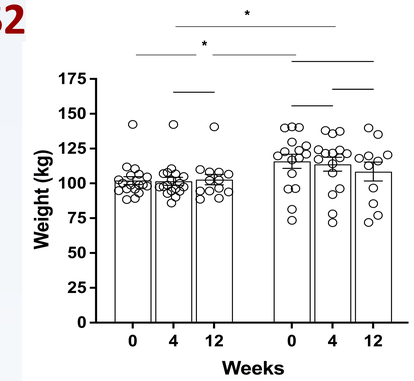

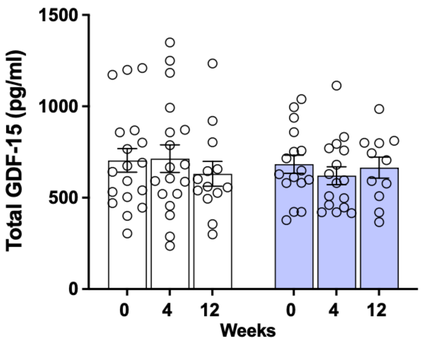

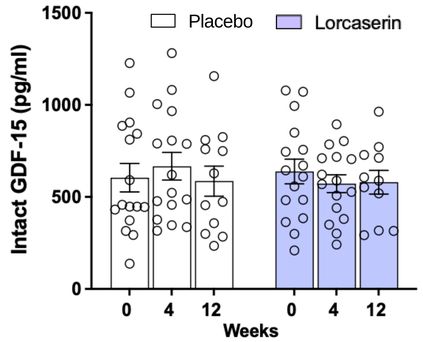

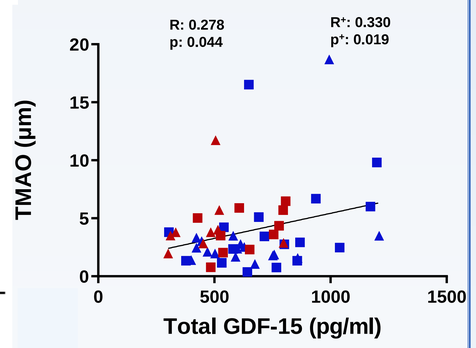

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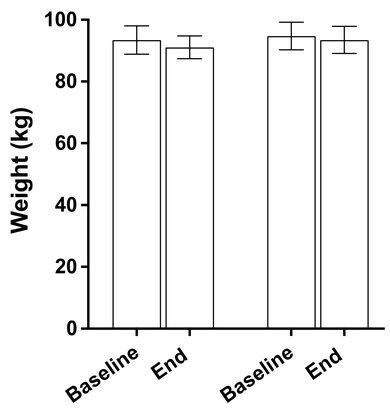

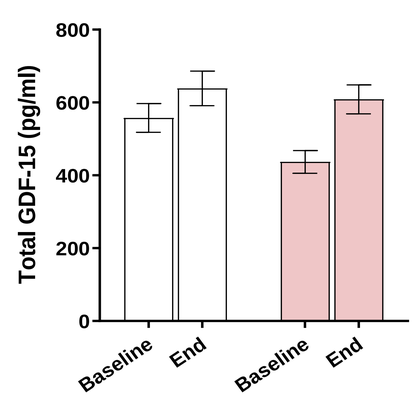

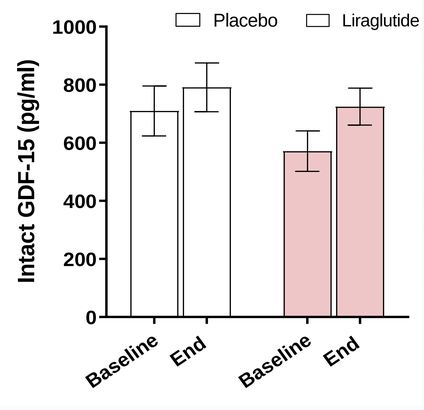

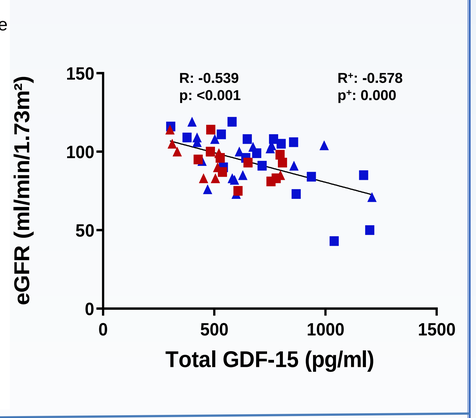

Discussion and Conclusions

- GDF-15 is not altered in response to Liraglutide or Lorcaserin in subjects with obesity with and without T2DM; it may thus not be directly involved in the metabolic feedback loop pathways downstream of GLP1 or 5-HT2C
- GDF-15 is positively correlated with diabetes risk index (DRI) and TMAO and negatively with total cholesterol and eGFR.

Poster presentation at the 20th World Congress on Insulin Resistance, Diabetes and Cardiovascular Disease, Los Angeles, California USA (2022)