**#0087**

# Tirzepatide Improved Markers of Islet Cell Function (Fasting Glucagon and HOMA2-B) and Insulin Sensitivity (Fasting Insulin and HOMA2-IR) Compared to Semaglutide in People with Type 2 Diabetes

**Author/s:** Katelyn Brown[1], Laura Fernandez Landó[1], Brandon Bergman[1], Melissa K. Thomas[1], Bing Liu[1], Clare Lee[1], Amanda M. Giebel (Non-author Presenter)[1]

**Organizations/Affiliations:** [1]Eli Lilly and Company, Indianapolis, IN, USA

**Abstract**

**Background:** Tirzepatide (TZP) achieved significantly greater HbA1c and weight reductions with all doses (5, 10 and 15 mg) vs semaglutide 1 mg (SEMA) in a Phase-3 trial of 1879 people with type 2 diabetes (T2D) on background metformin (mean age 56.6 years; T2D duration 8.6 years; baseline HbA1c 8.3% [67 mmol/mol]; BMI 34.2 kg/m$^2$) (SURPASS-2).

**Objective:** To assess changes in markers of islet cell function (fasting glucagon and HOMA2-B) and insulin sensitivity (fasting insulin and HOMA2-IR) with tirzepatide, compared with semaglutide in patients with T2D in the SURPASS-2 study.

**Methods:** Changes in fasting markers of islet cell function and insulin sensitivity were assessed by mixed model repeated measures in the modified intent-to-treat population.

**Results:** At 40 weeks, all TZP doses improved HOMA2-B, calculated with C-peptide, as indicated by a significant increase by 97-120% on average with TZP vs 84% with SEMA. Fasting glucagon levels, adjusted for fasting serum glucose, significantly decreased by 53-55% on average with TZP 10 and 15 mg doses vs SEMA (48%). All TZP doses improved insulin sensitivity as reflected by a significant decrease by 16-24% on average of HOMA2-IR, calculated with insulin, compared to a decrease by 5% with SEMA. Fasting insulin levels were also significantly reduced by 9-21% on average with all TZP doses compared to an increase of 0.6% with SEMA.

**Conclusion:** The GIP/GLP-1 receptor agonist TZP significantly improved markers of islet cell function and insulin sensitivity compared to selective GLP-1 receptor agonist SEMA in people with T2D.

Previously presented at ADA 2022.

**Keywords:**

**Funding:** This study was funded by Eli Lilly and Company.

**Author Col: KB, LFL, BB, MKT, BL, CL and AMG** are employees and stockholders of Eli Lilly and Company.