intervention in Latino youth with obesity and impaired glucose tolerance (IGT).

Methods: Present analysis included 9 Latino youth with obesity (age 15.3 ± 1.1 [SEM], 5F/4M; BMI % 97.5 ± 0.7) and IGT defined as a 2-hour post-challenge glucose ≥140 mg/dL. All participants underwent two 2-hr OGTTs with 30-min blood samples collected for the measurement of glucose, insulin, and incretin hormones pre and post a 12-week lifestyle in intervention that included nutrition education and 180 minutes of moderate-vigorous exercise weekly.

Results: Despite no change in total GLP-1 response, a reduced total GIP area under the curve (AUC) during the OGTT was observed (5499.1 ± 715.3 vs. 4085 ± 389.5 pg/mL), with a 1% reduction in BMI % (both, $p \leq 0.05$) from pre to post intervention. Accompanying these reductions was an improvement in insulin dynamics, measured by insulin and glucose AUC (31,987.6 ± 11,524.4 vs. 23,309.5 ± 12,932.5 uU/mL, $p = 0.08$; 19,052.5 ± 1610.9 vs. 16,395.0 ± 2614.1 mg/dL, $p = 0.05$, respectively). Furthermore, glucose tolerance was significantly improved as measured by reductions in 2-h glucose (147.0 ± 1.7 vs. 115.0 ± 9.4 mg/dL, $p = 0.01$).

Conclusions: In Latino youth with obesity and IGT, a 12-week lifestyle intervention reduced total GIP AUC and 2-hr glucose concentrations. We speculate that changes in GIP concentration correspond to an increased β-cell sensitivity to GIP. It will be critical to examine how decrease or increase in incretin hormones by lifestyle changes translates to clinical improvement in metabolic health in youth with obesity and IGT.

Poster-311

Baseline Characteristics Associated with Time to Weight Plateau with Tirzepatide in SURMOUNT-1

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Background: The rate of intentional weight reduction declines over time with a plateau observed eventually. In SURMOUNT-1, tirzepatide (TZP), a glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist, resulted in significantly greater weight reduction than placebo after 72 weeks of treatment in participants with overweight or obesity (without type 2 diabetes). We sought to identify baseline characteristics associated with the time to weight plateau (TTWP) in SURMOUNT-1.

Methods: Data from TZP-treated participants with ≥1 weight measurement at or after week 24 who received ≥75% doses were included in the analysis. Weight plateau was defined as a weight change of <5% over a 12-week interval and all subsequent 12-week intervals. TTWP was defined as the time from randomization to the start of the first 12-week interval with <5% weight change. Multivariate linear regression models were used to assess baseline characteristics associated with TTWP. Each model had dose, age, sex, and race as independent variables and one of the 3 anthropometric measures: (1) BMI category (<30, ≥30 to <35, ≥35 to <40, ≥40 kg/m^2), (2) waist circumference (WC, cm), and (3) WC category (<median, ≥median).

Results: Across the three models, higher doses of TZP, younger age, and female sex were associated with longer TTWP ($p < 0.05$). Mean TTWP was 4.2 and 6.4 weeks longer with TZP 10 and 15 mg, respectively, compared with 5 mg, 0.6 weeks longer with every 10-year decrease in age, and 3.8 weeks longer in females vs. males. None of the anthropometric measures were associated with TTWP. Race was significantly associated with TTWP in models (2) and (3) with mean TTWP about 2.5 weeks longer in White vs. Asian participants.

Conclusions: In SURMOUNT-1, higher doses of TZP (10 and 15 mg), younger age, and female sex were associated with longer TTWP. Understanding how individual characteristics influence patterns of weight loss may assist in informing treatment decisions with TZP for chronic weight management.

Poster-312

Intestinal Mucus Complexation by an Oral Duodenal Exclusion Treatment for T2DM and Obesity

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Background: GLY-200 is an oral, non-absorbed polymer therapeutic designed to enhance the intestinal mucus layer by covalently cross-linking mucin (a major component of mucus) to mimic the effects of metabolic surgery and duodenal exclusion devices. In healthy volunteers, GLY-200 lowered postprandial glucose and enhanced GLP-1, PYY, and bile acids, indicating a pharmacological effect in the proximal small intestine. This study aimed to demonstrate the formation of a durable polymer-mucus complex resistant to repeat rinsing and to evaluate the extent of coverage at various doses using ex-vivo imaging modalities.

Methods: Complexation of GLY-200 and Dextran 70 K (negative polymer control) with mucus on rat and porcine explanted intestinal tissue was evaluated through staining and fluorescent imaging using an in vivo imaging system (IVIS). Tissues were incubated with the polymer solution followed by rinsing to remove unbound polymer. The extent of FITC-conjugated polymer retention was quantified using IVIS. Mucin complexation and coverage of porcine intestine by 1 and 5 wt% GLY-200 solutions were also visualized by staining with indigo carmine.

Results: In both species, a majority of dextran was removed following rinsing (<30% retention). In comparison, GLY-200 complexed with mucus and retention was robust following sequential rinses (>90%

retention). Coverage of porcine intestine, as visualized by indigo carmine, appeared to be concentration dependent, with GLY-200 forming more uniform staining at higher concentrations.

Conclusions: Imaging studies confirm that GLY-200 tightly complexes with mucus to coat the intestinal epithelium in a robust and dose-dependent manner. These data support the hypothesis that GLY-200 covalently binds to mucin to form a lining/barrier in the duodenum with the potential to form a non-invasive pharmacologic duodenal exclusion for the treatment of type 2 diabetes and obesity.

Poster-313

GLY-200 (Oral Pharmacologic Duodenal Exclusion) Reduces Appetite and Food Intake in Patients with T2D

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Background: GLY-200 is an oral non-absorbed polymer drug designed to bind to and enhance the barrier function of gastrointestinal mucus as a non-invasive alternative to metabolic surgery and duodenal exclusion devices. In healthy volunteers, GLY-200 lowered glucose and increased GLP-1, PYY, and bile acids, indicating pharmacologic effects of duodenal targeting. A 14-day Phase 2 study in patients with type 2 diabetes (T2D) demonstrated reductions in glucose and progressive body weight loss at the 2.0 g GLY-200 dose.

Methods: The Ph2 study was a randomized, double-blind, placebo (PBO)-controlled inpatient study in subjects with T2D washed off metformin, BMI 18–40. Treatments included 14 days (BID) of 2.0 g GLY-200 ($N = 13$, BMI 31.8 ± 4.09 kg/m^2, baseline HbA1c 7.18 ± 0.66%) or PBO ($N = 12$, BMI 31.7 ± 3.17 kg/m^2, baseline HbA1c 7.17 ± 0.73%). On Day −1, 1, and 13, assessments included food intake and appetite visual analog scale at standardized breakfasts and ad libitum dinners. Categorical food intake (0%–25%, 26%–50%, 51%–75%, 76%–100% consumed) was assessed at all other meals during the inpatient period.

Results: In the 2.0 g GLY-200 group, premeal overall appetite suppression scores were 18.9% ($p = 0.30$) and 49.5% ($p = 0.02$) higher than PBO at breakfast and dinner, respectively. Immediately and 60 min after a standardized breakfast, 2.0 g GLY-200 subjects reported significantly higher feelings of fullness and satisfaction and significantly lower feeling of hunger and amount they could eat. At ad libitum dinners, 2.0 g GLY-200 subjects had significantly lower food intake (↓16.7%, $p = 0.018$). During non-standardized inpatient meals, an average of 22.1%, 19.5%, and 28% of 2.0 g GLY-200 subjects consumed ≤75% of breakfast, lunch, and dinner, respectively, versus 0%, 4.8% and 6.8% of PBO subjects.

Conclusions: Results from this study suggest the body weight loss observed following 14 days of treatment with 2.0 g GLY-200 are, in part, due to reduced appetite, increased satiety, and better control of eating.

Poster-314

Patient Factors Associated with Metformin Concentrations in Youth-onset Type 2 Diabetes

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Background: Metformin monotherapy is suboptimal in ∼50% of youth with type 2 diabetes (Y-T2D). The reasons for non-responsiveness are unknown but may be related to patient-related social (adherence) or biological factors (age, glycemia, sex, diabetes duration, drug regimen, prior metformin use). Metformin concentrations reflect whole-body distribution but its and may predict personalized responses but no data are available in Y-T2D. We investigated the relationship between patient factors and metformin peak and trough concentrations during a short-term randomized metformin trial.

Methods: Peak and trough metformin were measured using LC–MS at baseline and after three-months of standard release metformin alone (Met, $n = 12$) versus metformin and liraglutide (Met+Lira, $n = 10$) in Y-T2D: age 15.3 ± 2.1 (12–20 years) mean ± SD (range), 68% female, BMI 40.4 ± 7.9 (22.8–54.4 kg/m^2). Metformin was assessed during a 30 h inpatient visit: troughs at 12 h and 18 h and peak at 2 h after direct observed administration. Adherence was assessed by pill count and glycemia as change in HbA1c.

Results: Glycemia improved in both groups, adherence was 79 ± 17% and did not vary by group or dosage. Trough levels were negligible at baseline (0.4 ± 1.4 ng/mL) and increased after 3 months but were variable (intra- and inter-individual variability was ∼3 and ∼20-fold, respectively). Peak levels were dose dependent (1 g/d: 671, 1.5 g/d: 739, 2 g/d: 1129, $p = 0.10$). Neither trough nor peak levels were associated with HbA1c, group, age, sex, diabetes duration but peak levels were lower in metformin naïve (566 vs 1232 ng/mL, $p = 0.02$). 18 h trough correlated with adherence ($r = 0.5$, $p = 0.02$). Concomitant liraglutide increased metformin distribution volume ($p = 0.04$).

Conclusions: The wide inter- and intra-individual variability in peak and trough metformin concentrations in Y-T2D preclude its use as a predictive glycemic biomarker. Concentrations were not related biological factors, but peak levels reflected prior metformin exposure and 18 h trough (an indicator red blood cell storage depots) may reflect adherence.

Poster-315

Broad Prescribing With Telemedicine-based Obesity Care Produces Clinically-significant Weight Loss

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