

## **OR30-07: Mixed Meal Tolerance Test (MMTT) Results from Revita-2, the First Randomized, Sham-Controlled, Double-Blind, Prospective, Multicenter Study of Duodenal Mucosal Resurfacing (DMR) Safety and Efficacy in Patients with Sub-Optimally Controlled Type 2 Diabetes (T2D)**

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**Background:** The duodenum is a key metabolic signaling center and regulator of metabolic homeostasis. Duodenal mucosal hyperplasia is therefore a potential therapeutic target for metabolic diseases related to insulin-resistance. Previous reports demonstrated that DMR, a minimally invasive, endoscopic mucosal ablative procedure, safely improves hepatic and glycemic parameters. Primary endpoints from REVITA-2, the first randomized, sham-controlled, double-blind, prospective, multicenter study of DMR safety and efficacy in patients with T2D, were met and previously reported. Here we further explore mechanisms underlying the beneficial effects of DMR on hepatic and glucose metabolism by analyzing mixed meal tolerance test (MMTT) data from the REVITA-2 study.

**Methods:** Eligible patients (HbA1c 7.5-10%, BMI  $\geq 24$  to  $\leq 40$  kg/m<sup>2</sup>, on stable treatment with  $\geq 1$  oral anti-diabetic medication) received DMR or sham procedure (1:1). Exploratory endpoints included median change in fasting plasma glucose (FPG), MMTT glucose area under the curve (AUC) over 2 hours, and change in MMTT C-peptide and glucagon over 2 hours, from baseline to 12 weeks post-DMR. One-sided P value based on ANCOVA model on ranks without imputation assessed treatment difference at the 0.05 significance level. The modified intent to treat primary analysis population included randomized patients in whom study procedure was attempted.

**Results:** A total of 70 patients (DMR, N = 35; sham, N = 35) were included in the analysis, of which 57% and 54% (DMR, n = 20; sham, n = 19) had baseline FPG  $\geq 180$  mg/dL. Median MMTT AUC for glucose was significantly reduced post-DMR (-36.38 mg/dL) compared with sham (-4.94 mg/dL; P = 0.009), driven by a significant decrease in FPG (DMR, -41.0 mg/dL; sham, -15.0 mg/dL; P = 0.003) rather than median MMTT postprandial glucose excursion (DMR, -4.63 mg/dL; sham, 5.34 mg/dL; P = 0.209). AUC glucose reductions were more pronounced in patients with baseline FPG  $\geq 180$  (DMR, -63.03 mg/dL; sham, -20.31 mg/dL; P = 0.007) compared with baseline FPG < 180 (DMR, -26.81 mg/dL; sham, 13.81 mg/dL; P = 0.271). In patients with baseline FPG  $\geq 180$ , postprandial C-peptide excursion was significantly increased (DMR, 0.41 ng/mL; sham, 0.02 ng/mL; P = 0.012) and postprandial glucagon excursion was significantly decreased (DMR, -8.03 pg/mL; sham, 2.13 pg/mL; P = 0.027).

**Conclusion:** DMR markedly improves glucose responses to a mixed meal challenge, primarily driven by a decrease in FPG, suggesting a primary effect on insulin resistance. Increases in C-peptide and reductions in glucagon levels suggest improvement in beta cell function in addition to improvements in hepatic insulin sensitivity, and ratifies the position of the duodenum as both a culprit endocrine organ and therapeutic target for patients with T2D.