Glycemic Improvement, Insulin Reductions, and Improved Body Weight 48 Weeks after Revita Duodenal Mucosal Resurfacing in T2D patients with Previously Inadequately Controlled Glucose Despite Multiple Glucose-Lowering Agents Including Insulin

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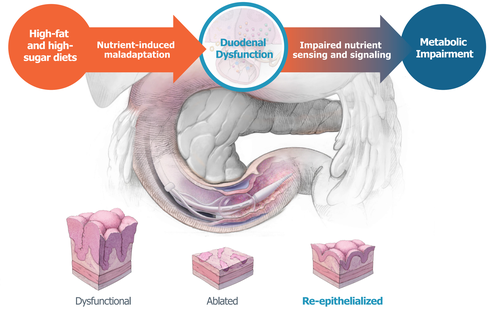
BACKGROUND AND METHODS

- The duodenal mucosa plays a key role in regulating glucose homeostasis and is known to be impaired early in type 2 diabetes (T2D) progression (Figure 1).
- Duodenal mucosal resurfacing (DMR) is an outpatient endoscopic procedure utilizing hydrothermal ablation to remove potentially dysfunctional duodenal mucosa and allow regeneration (Figure 1).[1-4]
- Previous studies with >300 patients treated with DMR have shown favorable safety and metabolic efficacy.[4-8]

Figure 1. Rationale for Targeting Duodenal Dysfunction with DMR

Watch the full procedure.



DMR is for investigational use only in the United States.

- **Here, we present initial data from the open-label training phase of an ongoing, multicenter, double-blind, sham-controlled, randomized study assessing safety and efficacy of DMR in insulin-treated T2D patients with inadequately controlled hyperglycemia.**

Key Inclusion Criteria

21–70 years of age

Body mass index (BMI) of 24–40 kg/m^2

HbA1c 7.5%–9.5%

Fasting plasma glucose (FPG) ≥180–<270 mg/dL

On insulin (20–60 U/day)

≥2 additional glucose-lowering agents (GLAs)

Before DMR

GLAs other than metformin and basal insulin were washed out for ≥8 weeks followed by a 4-week run-in period.[9]

After DMR

Insulin, if needed, was reinstated by a pre-specified treat-to-target design with preexisting metformin and de novo empagliflozin (DMR+Empa).[9]

RESULTS

Table 1. Demographics and Baseline Characteristics

Nine patients from the open-label training phase, who received DMR+Empa, were assessed. Demographics and baseline characteristics were consistent with inadequate control of T2D. Seven of nine patients completed a 48-week follow-up with two early-study discontinuations unrelated to the DMR procedure at weeks 4 and 23, respectively.

Demographics	N=9
Male, n (%)	6 (67)
Age (years), median (min, max)	60 (45, 68)
Race, n (%)	
White	8 (89)
Black or African American	1 (11)
Ethnicity, not Hispanic or Latino, n (%)	9 (100)
Region, n (%)	
US	3 (33)
Europe	6 (67)

Baseline Characteristics	N=9
Diabetes duration (years), median (min, max)	13 (7, 24)
HbA1c (%), median (min, max)	8.5 (7.6, 9.1)
FPG (mg/dL), median (min, max)	205 (171, 221)
Body weight (kg), median (min, max)	96 (85, 128)
BMI (kg/m^2), median (min, max)	32.2 (28.4, 40.7)
C-peptide (ng/mL), median (min, max)	1.73 (0.70, 3.21)
Insulin dose (U/day), median (min, max)	32 (20, 60)

Figure 2. HbA1c, FPG, and Insulin Change from Baseline at Week 48

All seven patients in whom glycemic parameters were evaluated showed improvements in HbA1c and FPG despite reductions in insulin usage (**A**,**B**, and **C**). The median (min, max) reduction in HbA1c at 48 weeks post-DMR procedure was 1.6% (0.4%, 1.8%) from a baseline of 8.5% (7.6%, 9.1%) to 7.1% (6.3%, 7.6%). The reduction in FPG was 77 mg/dL (49, 104 mg/dL) from a baseline of 205 mg/dL (171, 221 mg/dL). Insulin usage was reduced in six out of seven patients with a median (min, max) reduction in total daily dose of 44% (-20%, 100%) from a baseline dose of 32 U/day (20, 60 U/day). Two out of seven patients completely discontinued their insulin usage during the study (**C**).

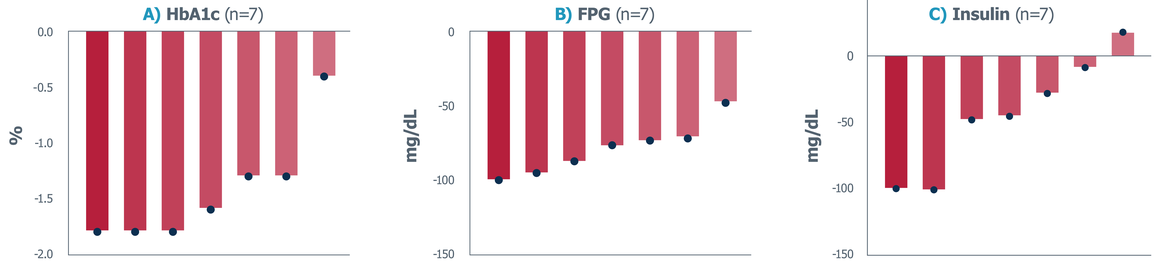


Figure 3. Percent Weight Change from Baseline at Week 48

All seven patients that were evaluated showed reductions in body weight at 48 weeks post-DMR procedure. The median (min, max) reduction in total body weight at 48 weeks was 9.3% (2.9%, 16.8%) from a baseline of 96 kg (85, 128 kg).

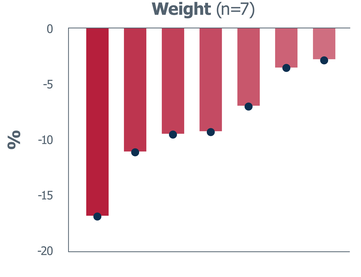


Table 2. Overall Safety Summary

No device- and/or procedure-related serious adverse events (AEs) or unanticipated adverse device effects were observed. Device- and/or procedure-related AEs were mild to moderate, did not require treatment, and resolved without sequelae. Two patients discontinued early from the study, unrelated to the DMR procedure: euglycemic ketoacidosis (related to sodium-glucose cotransporter-2 inhibitor usage [SGLT2i]) and protocol nonadherence (unrelated to safety).

	# Subjects with ≥ 1 Event (N=9)	# of AEs
Device/Procedure Related Adverse Events	**2 (22%)**	**2**
Abdominal pain	1 (11%)	1
Diarrhea	1 (11%)	1
Treatment Emergent Serious Adverse Events	**3 (33%)**	**3**
Device/Procedure Related	0	0
Non-Device/Procedure Related*	**3 (33%)**	**3**
COVID-19	1 (11%)	1
Hypertension	1 (11%)	1
Euglycemic ketoacidosis (discontinued study)	1 (11%)	1
Unanticipated Adverse Device Effects	**0**	**0**

*Non-Device/Procedure Related serious AEs: Euglycemic ketoacidosis associated with SGLT2i; hypertension and COVID-19 both required hospitalization. These were 3 separate patients with 1 serious AE each. Note: The data presented in this table are preliminary and based on an ongoing study. The study database has not been locked, and the data are subject to further cleaning and validation.

CONCLUSIONS

- **Initial data from an open-label training phase show promising safety and efficacy of DMR+Empa in patients with inadequately controlled T2D.**
- **Improvements in HbA1c, FPG, and weight are consistent with the broad metabolic benefit demonstrated in prior DMR clinical studies.**
- **The overall safety and AE profile is consistent with DMR device and procedural findings to date.**
- **Given 1 episode of euglycemic ketoacidosis, the study protocol has been modified to remove use of de novo SGLT2i.**
- **Further results are forthcoming from the currently enrolling Revitalize 1 study (NCT04419779).**

Disclosures: VF—employee of Tulane University School of Medicine. JJGHMB—Amsterdam University Medical Centres. ZS—employee of Indiana University and shareholder of Buclid LLC. HR, BS, KW, and HZ—employees and shareholders of Fractyl Health, Inc. GM—employee of Fondazione Policlinico Universitario A. Gemelli IRCCS - Università Cattolica del Sacro Cuore.

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Contact information: To learn more about the presented research and/or Fractyl Health, Inc., please visit our website at **www.fractyl.com** or contact us at info@fractyl.com.

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