Duodenal Mucosal Resurfacing Durably Maintains Weight Loss in Metabolic Disease

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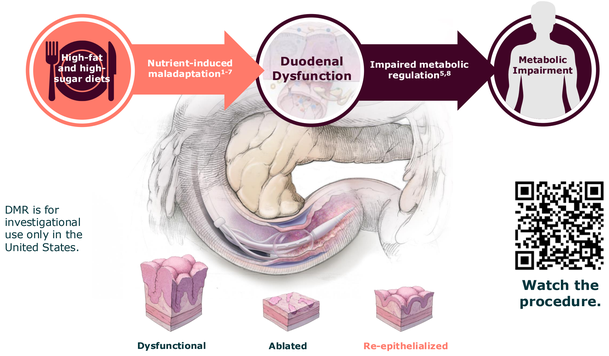
Introduction

- Drugs for obesity are effective for weight loss; however, discontinuation is frequent and results in weight rebound, underscoring the need for weight-maintenance therapies.
- The duodenal mucosa plays a key role in metabolic regulation and is known to be impaired in metabolic disease (Figure 1).[1-11]
- Duodenal mucosal resurfacing (DMR) is an investigational, non-drug, minimally invasive, endoscopic procedure that uses hydrothermal ablation to restore duodenal metabolic function (Figure 1).[12-13]
- Clinical trials with >300 patients have shown that DMR may safely improve multiple indices of metabolic health including glycemic control, insulin sensitivity, hepatic fat, and weight while reducing medication burden.[13-19]

The current pooled analysis was undertaken to evaluate the durability of DMR-induced, weight-related outcomes.

Figure 1. Rationale for Targeting Duodenal Dysfunction with DMR.



DMR is for investigational use only in the United States.

Watch the procedure.

Study Design

- Included pooled data from 5 clinical trials from N=118 participants in Europe or the United States followed for 48 weeks post-procedure.
- Trials were conducted from 2015 to 2023.
- No diet or lifestyle intervention changes were made after the DMR procedure.
- Participants in which an obsolete version of the DMR catheter (double catheter) was used were excluded.

Results

Table 1. Demographics and Baseline Characteristics. Participants had longstanding, inadequately controlled type 2 diabetes. Most had obesity (62%) or overweight (34%) at baseline.

Demographics	N=118
Male, n (%)	88 (75)
Age (years), mean (SD)	58 (8)

Baseline Characteristics	N=118
Diabetes duration (years), mean (SD)	10 (5)
HbA1c (%), mean (SD)	8.2 (0.7)
Body weight (kg), mean (SD)	93 (14)
BMI (kg/m^2), mean (SD)	31.1 (3.8)
With obesity (BMI>30 kg/m^2), n (%)	73 (62)
With overweight (BMI>25 and ≤30 kg/m^2), n (%)	40 (34)

Figure 2. DMR Led to Sustained Weight Loss in the Majority of Participants. Individual changes in body weight from baseline at 48 weeks post-DMR are shown (n=94).

Figure 3. DMR Durably Maintained Weight Loss Through 48 Weeks Post-Procedure. DMR induced a mean (SEM) weight loss of 3.4% (0.3%) at 4 weeks, 3.7% (0.4%) at 12 weeks, 3.9% (0.4%) at 24 weeks, 3.7% (0.4%) at 36 weeks, and 4.0% (0.5%) at 48 weeks (all p<0.0001 vs. baseline). Weight maintenance also was observed through 48 weeks after censoring participants who added any glucose-lowering agent that may have contributed to weight loss (e.g., GLP-1RA or SGLT2i, data not shown) during follow-up. Weight change from baseline was evaluated by paired t-test. Data are shown as mean ± SEM.

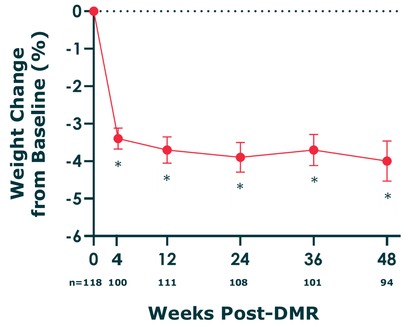


Table 2. The Majority of Participants Who Lost Weight at 4 Weeks Maintained Their Weight at 48 Weeks Post-Procedure. Of the participants who had weight data at both week-4 and -48 post-procedure visits (n=78), 90% achieved weight loss at week 4. Of these (n=70), 84% maintained their weight loss at week 48, and weight was stable from week 4 to week 48 in the cohort.

Category	n=78
Lost weight at 4 weeks post-DMR, % (n)	90 (70 of 78)
Maintained 4-week weight loss at week 48, % (n)	84 (59 of 70)
Mean change in weight from weeks 4 to 48, % (SEM)	0.2 (0.5)

Table 3. Overall Safety Summary. The DMR procedure was well tolerated. No serious device- or procedure-related AEs were observed.

	Participants with ≥1 Event (n=117*)
Device/Procedure-Related AEs, n (%)**	**45 (39)**
Most Common Device/Procedure-Related AEs, n (%)	
Abdominal pain	20 (17)
Oropharyngeal pain	12 (10)
Nausea	6 (5)
Diarrhea	5 (4)
Abdominal pain upper	3 (3)
Vomiting	3 (3)
Device/Procedure-Related Serious AEs, n	**0**

*N=118 in pooled ITT population; n=1 randomized to DMR but did not receive treatment.

**Device/Procedure Related AEs include definitely or probably related to procedure or device.

Conclusion and Next Steps

These data demonstrate that a single DMR procedure may safely result in durable weight maintenance through 48 weeks in patients with type 2 diabetes.

The impact of DMR on weight maintenance in patients with obesity, who discontinue GLP-1 therapy, will be assessed in the currently enrolling REMAIN-1 trial.

Publications and Presentations

Remain1study.com

Clinicaltrials.gov

Abbreviations: AE=adverse event, BMI=body mass index, DMR=duodenal mucosal resurfacing, GLP-1RA=glucagon-like peptide 1 receptor agonist, ITT=intent to treat, SD=standard deviation, SEM=standard error of the mean, SGLT2i=sodium-glucose cotransporter-2 inhibitor

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Disclosures: All authors are employees and shareholders of Fractyl Health, Inc. Harith Rajagopalan is a Board member of Fractyl Health, Inc.

Acknowledgments: Funded by Fractyl Health, Inc. The authors thank Edward Mahoney for writing and editorial support (Fractyl Health, Inc.) and Second Melody for design and creative support.

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