1913 DGVS
Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten

VISZERAL MEDIZIN 2024

A prospective post-market clinical follow-up registry to evaluate real-world effectiveness and patient satisfaction after duodenal mucosal resurfacing in patients with type 2 diabetes

Torsten Beyna, Thomas Veiser, Hui Zhang, Emily Cozzi, Kelly White, Stephan Martin

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Disclosure Statements and Revita System™ Indication for Use

Authors:

Torsten Beyna is a consultant for Olympus, Boston Scientific, Microtech, and Fractyl Health and received lecture honoraria from Olympus, Boston Scientific, Cook, Fujifilm, Pentax, ERBE, Microtech, Falk Foundation, and Medtronic. Stephan Martin is a consultant for Fractyl Health and Almased and received lecture honoraria from Lilly, MedUpdate, MerdTRix, Marpionion, and Bayer. Thomas Veiser is a consultant for ERBE, Microtech, Cook, Boston Scientific, Fractyl Health, and Falk. Hui Zhang, Emily Cozzi, and Kelly White are employees and shareholders of Fractyl Health, Inc.

Data shown in this presentation 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.

Revita is for Investigational use only in the US under Federal law and has been granted Breakthrough Device designation in T2D patients on insulin and for weight maintenance after GLP-1 discontinuation in obesity; and CE mark obtained from EU and UK in 2016 for Revita for the improvement of glycemic control in patients with inadequately controlled T2D despite oral and/or injectable glucose lowering medications and/or long-acting insulin.

Indications for Use:

As an adjunct to diet and exercise, the Revita System is intended for hydrothermal ablation of the duodenal mucosa to:

Improve glycemic control in patients with Type 2 Diabetes who have preserved pancreatic beta cell function and whose diabetes is inadequately controlled despite oral and/or injectable glucose lowering medications and/or long-acting insulin therapy.

Reduce liver fat in patients with Type 2 Diabetes and Non-Alcoholic Fatty Liver Disease.

DMR=duodenal mucosal resurfacing

The Rationale for Duodenal Mucosal Resurfacing (DMR)

Intervening at a potential root cause of type 2 diabetes and obesity

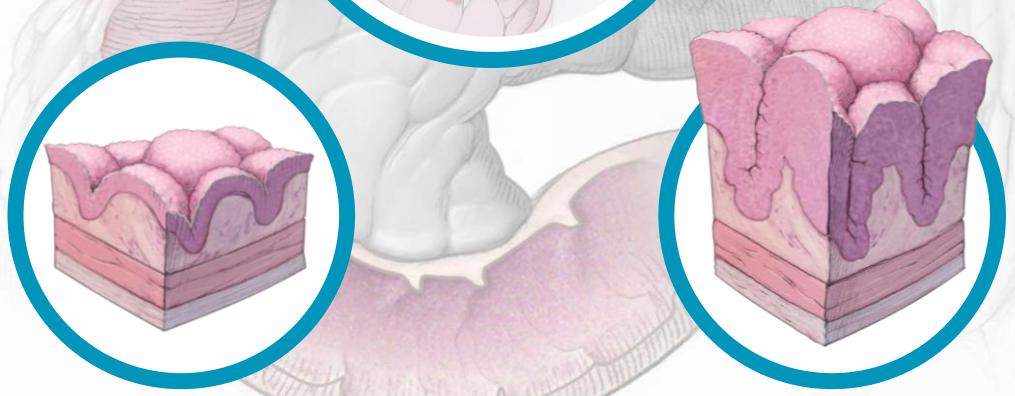
High-fat and high-carbohydrate diets

Nutrient-induced maladaptation

Duodenal Dysfunction

Impaired nutrient sensing and signaling

Metabolic Impairment



Healthy

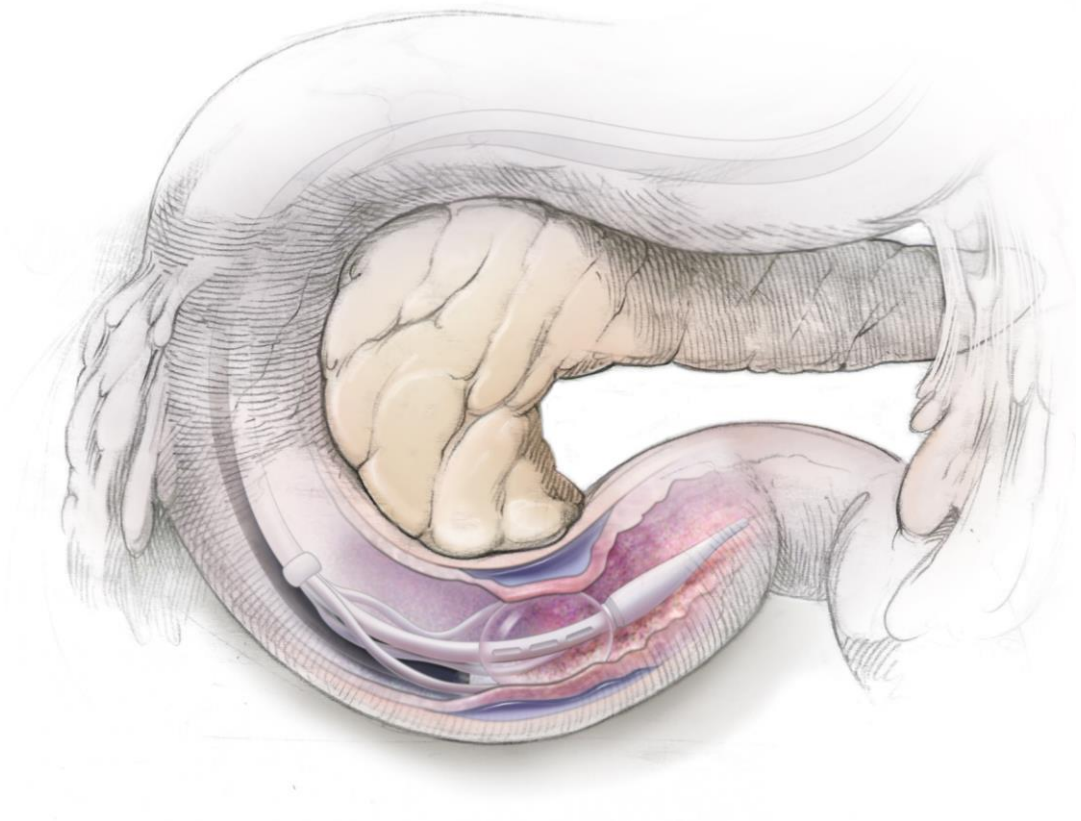
Dysfunctional

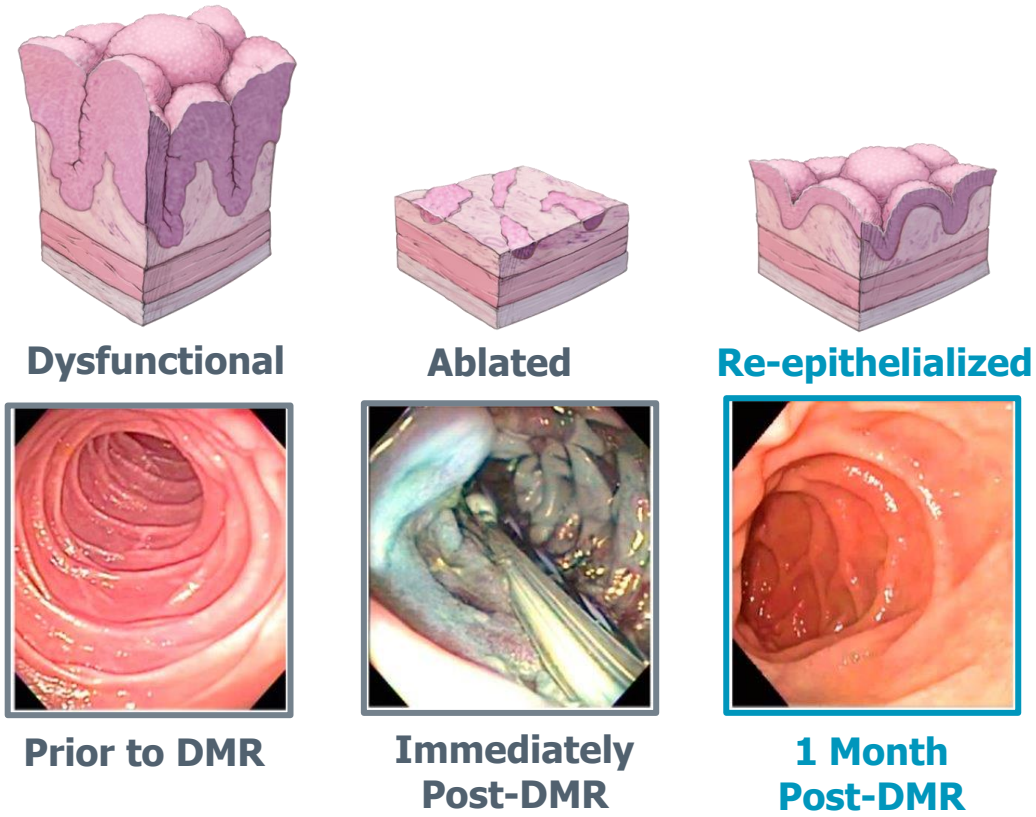
1. Mah AT et al. Endocrinology. 2014;155:3302-3314. 2. Baldassano S et al. J Endocrinol. 2013;217:11-20. 3. Mao J et al. Diabetes. 2013;62:3736-3746. 4. Aliluev A et al. Nat Metab. 2021;3:1202-1216. 5. Dailey MJ. Physiol Behav. 2014;136:74-78. 6. Theodorakis MJ et al. Am J Physiol Endocrinol Metab. 2006;290:E550-559. 7. Verdam FJ et al. J Clin Endocrinol Metab. 2011;96:E379-E383. 8. Gniuli et al. Diabetologia. 2010;53:2233-40. 9. Fiorentino et al. Obesity (Silver Spring). 2023;31:724-731. 10. Dyer J et al. Am J Physiol Gastrointest Liver Physiol. 2002;282:G241–G248. 11. Fiorentino et al. Clin Endocrinol Metab. 2017;102:3979–3989. DMR=duodenal mucosal resurfacing

Duodenal Mucosal Resurfacing with the Revita System

Endoscopic procedure targeting dysfunctional duodenal mucosa

Revita DMR® is a minimally invasive, endoscopic procedure utilizing hydrothermal ablation to remove potentially dysfunctional duodenal mucosa, allowing for regeneration and return to metabolic function[1-7]





1. Duca FA, et al. Cell Metab. 2015 Sep 1;22(3):367-380. 2. Baldassano S, et al. J Endocrinol. 2013 Mar 15;217(1):11-20 3. Dailey MJ. Physiol Behav. 2014;136:74-78. 4. Mah AT et al. Endocrinology. 2014 Sep;155(9):3302-3314. 5. Mao J et al. Diabetes. 2013 Nov;62(11):3736-3746. 6. de Moura EGH et al. Endosc Int Open. 2019 May;7(5):E685-E690. 7. Haidry RJ, et al. Gastrointest Endosc. 2019 Oct;90(4):673-681.e2. DMR=duodenal mucosal resurfacing

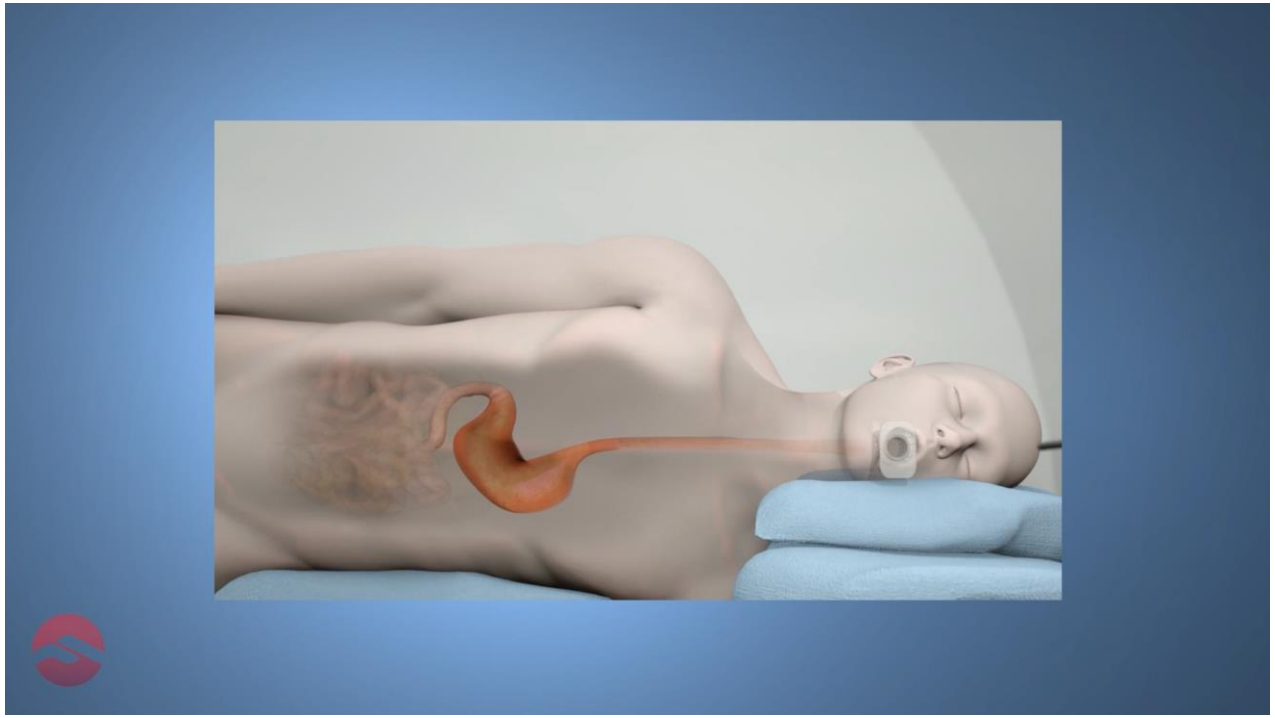
Duodenal Mucosal Resurfacing with the Revita System

Intuitive endoscopic procedural workflow

Carried out by a trained endoscopist in ~1 hour, progresses in 2 steps:

Step 1: circumferential **saline injection** of the duodenal submucosa to create a protective thermal barrier and uniform ablation surface[1,2]

Step 2: hydrothermal ablation of the duodenal surface via heated water circulating in the catheter balloon[2,3]



ESGE-aligned training[4] supports endoscopist proficiency in as little as 2 cases

1. van Baar ACG, et al. Endosc Int Open. 2020 Nov;8(11):E1683-E1689. 2. Galvao Neto M, et al. VideoGIE. 2016 Aug 11;1(1):10-11.; 3. Haidry RJ, et al. Gastrointest Endosc. 2019 Oct;90(4):673-681.e2; 4. Boškoski et al. Curriculum for bariatric endoscopy and endoscopic treatment of the complications of bariatric surgery: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy. 2023 Mar;55(3):276-293. ESGE=European Society of Gastrointestinal Endoscopy

Type 2 Diabetes Clinical Trial Findings to Date

Revita DMR improves multiple indices of metabolic function

Clinical trials in >300 patients have shown that Revita DMR may safely and durably improve:

- Glycaemic control & insulin sensitivity
- β-cell function
- Hepatic steatosis
- Weight maintenance
- Diabetes medication burden[1-7]

Commonly reported AEs include transient abdominal pain, distention, nausea, and diarrhea. SAEs related to the device and/or procedure are rare and have decreased in frequency over the course of the clinical development program with device optimisation and procedural training[3-6]

Will Revita DMR clinical trial findings translate to real-world effectiveness?

1. Haidry RJ, et al. Gastrointest Endosc. 2019;90:673-681.e2. 2. van Baar ACG, et al. Endosc Int Open. 2020;8:E1683-E1689. 3. Rajagopalan H, et al Diabetes Care. 2016;39:2254-2261. 4. van Baar ACG, et al. Gut. 2020;69(2):295-303. 5. Mingrone G, et al. Gut. 2022;71(2):254-264. 6. van Baar ACG, et al. Gastrointest Endosc. 2021;94(1):111-120.e3, 7. van Baar et al. Diabetes Res. Clin. Pract. 2022;184:109194. AEs= adverse events, DMR=duodenal mucosal resurfacing, SAEs=serious AEs

Assessing Real-World Effectiveness of Revita DMR

Study design: key participant criteria and assessments

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Ongoing, 5-year, non-interventional, prospective, observational study in ≤5 German centres

HbA1c, FBG, weight loss and maintenance, diabetes medications, and patient reported outcomes (PROs) were assessed

Single centre data from participants using Telemedical Lifestyle intervention Program (TeLiPro) standard of care[1] after Revita DMR

Key Inclusion Criteria
≥18 years of age
BMI of ≤45 kg/m^2
HbA1c of ≥7.0 and ≤10.0%
On oral and/or injectable GLAs and/or long-acting insulin
Key Exclusion Criteria
Type 1 diabetes
C-peptide <0.2 nmol/L
Severe hypoglycaemia 12 months prior to screening

1. Kempf et al. Diabetes Care 2017;40:863–871. BMI=body mass index; DMR=duodenal mucosal resurfacing; FBG=fasting blood glucose; GLAs=glucose-lowering agents; PROs=patient-reported outcomes; TeLiPro=telemedical lifestyle intervention program

Assessing Real-World Effectiveness of Revita DMR

Baseline characteristics: participants with inadequately controlled T2D

Most participants have obesity and longstanding T2D despite treatment with multiple GLAs in the majority of cases

Demographic	N = 31
Sex, % male	58
Age, years, mean (SD)	61 (7)
Baseline Characteristic	
HbA1c, %, mean (SD)	8.8 (1.4)
FBG, mg/dL, mean (SD)	168.6 (62.4)
Body Mass Index, mean (SD)	33.1 (5.6)
Body weight, kg, mean (SD)	102.0 (19.4)
Diabetes duration, years, mean (SD)	13.6 (9.2)
GLAs, % on ≥2	64.5%

DMR=duodenal mucosal resurfacing; FBG=fasting blood glucose; GLAs=glucose-lowering agents; T2D=type 2 diabetes

Assessing Real-World Effectiveness of Revita DMR

Safety: Revita DMR was well tolerated with no serious adverse events

Revita DMR was well tolerated with no serious procedural and/or device-related adverse events (SAEs), or unanticipated adverse device effects (UADEs) reported

One participant experienced an oxygen saturation decrease deemed "possibly related" to the Revita DMR procedure and/or device

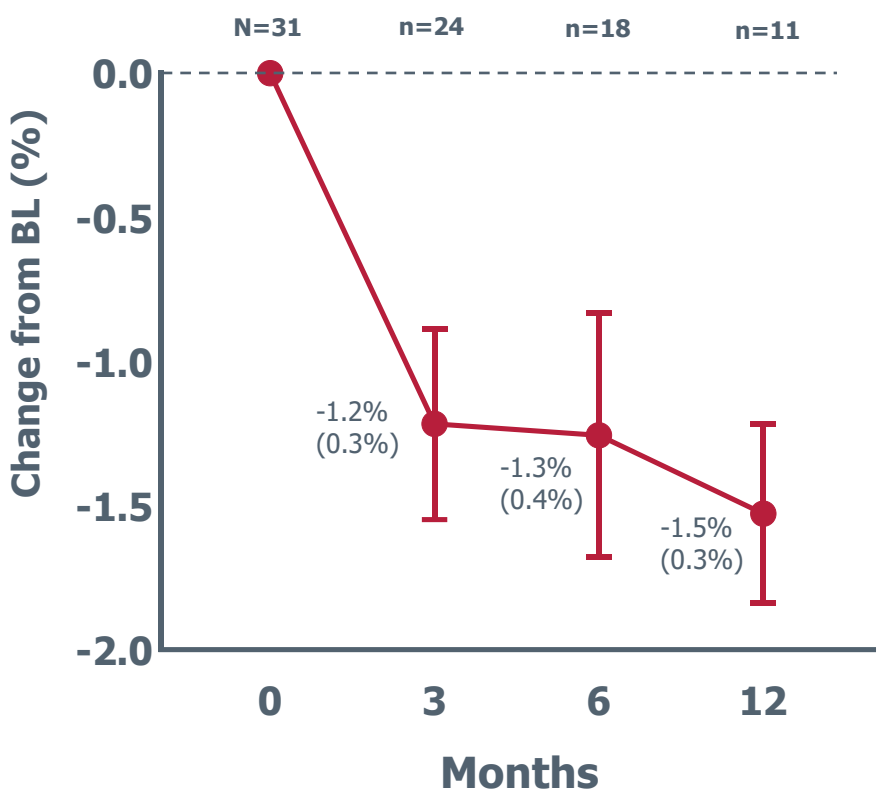
Procedural and/or Device Related Adverse Events	N = 31
SAE	0
Adverse Event	1

DMR=duodenal mucosal resurfacing; SAEs=serious adverse events, UADEs=unanticipated adverse device effects

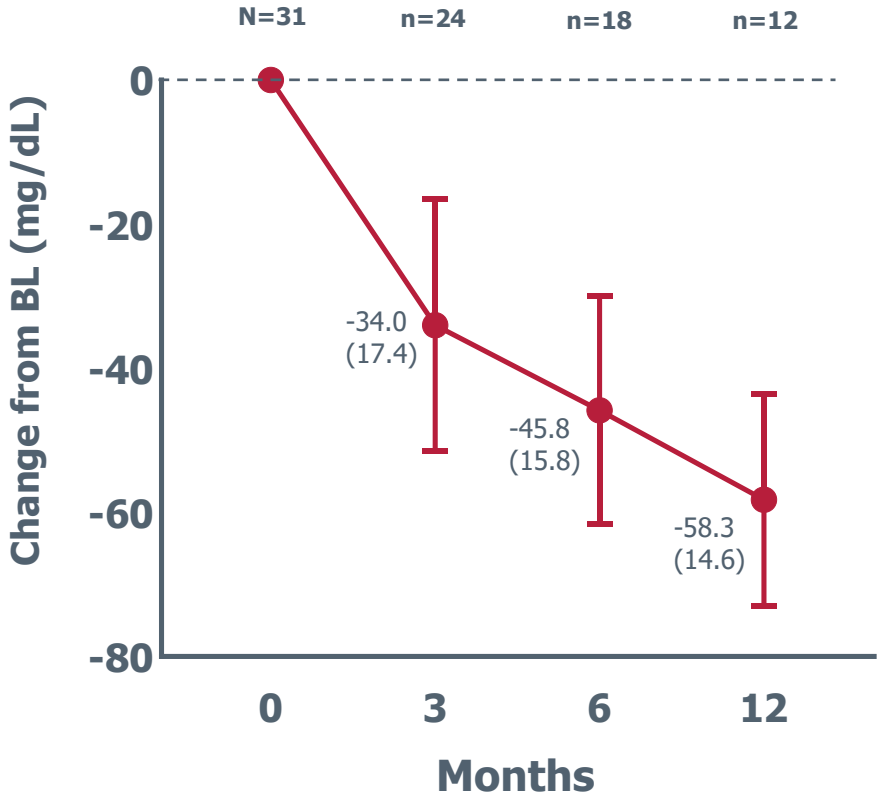
Assessing Real-World Effectiveness of Revita DMR

Glycaemia: improvements in HbA1c and FBG were maintained through follow-up

A) HbA1c (Mean ± SEM)



B) FBG (Mean ± SEM)

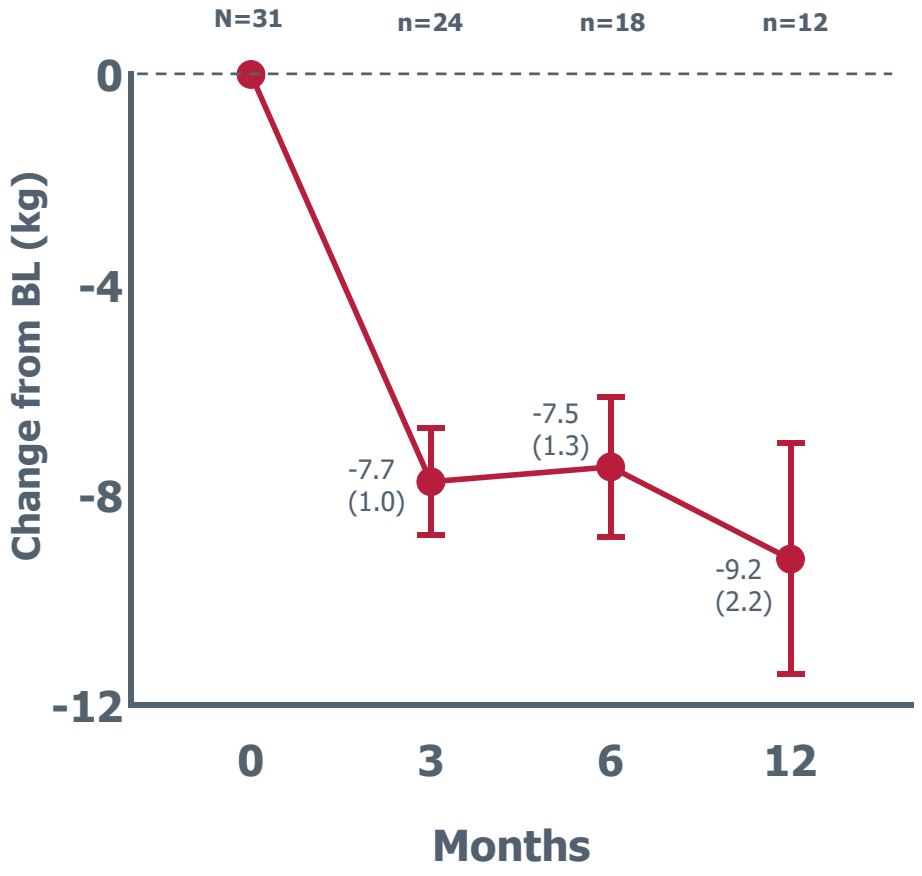


Of N=31 participants with baseline characteristics, 2 were lost to follow-up. BL=baseline; DMR=duodenal mucosal resurfacing; FBG= fasting blood glucose; SEM=standard error of the mean

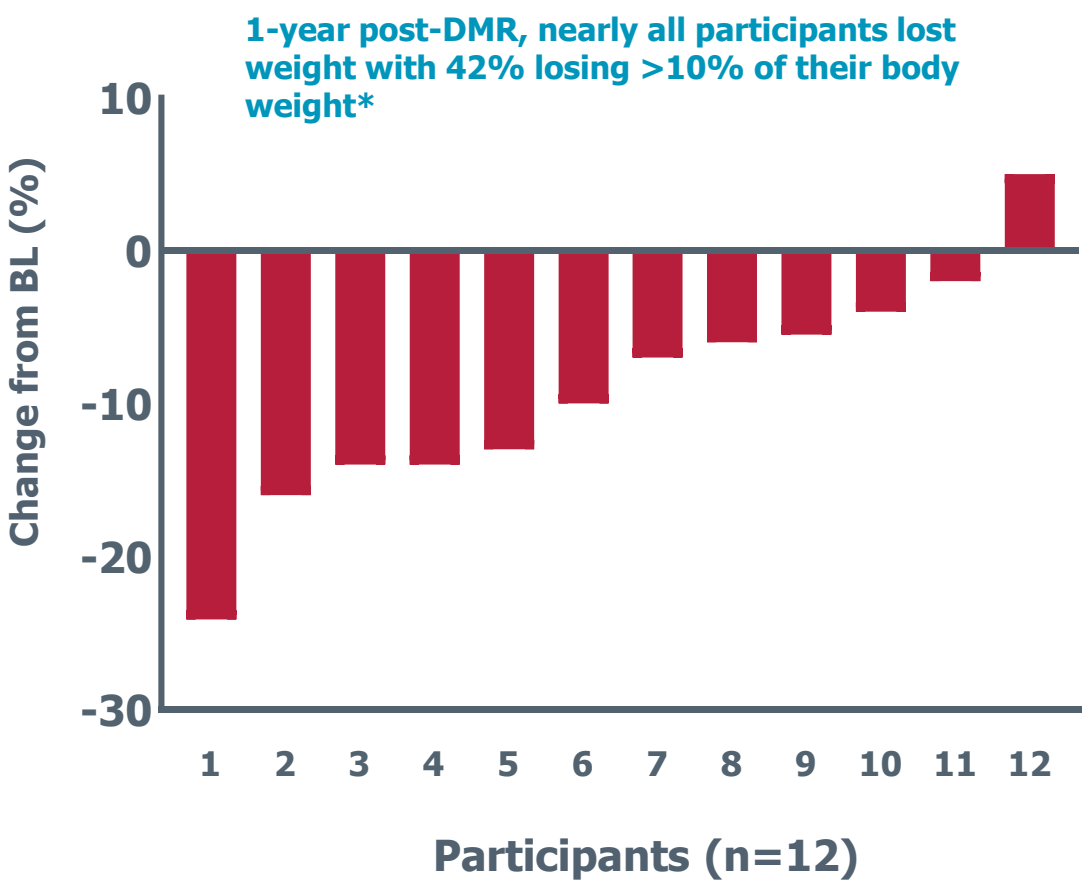
Assessing Real-World Effectiveness of Revita DMR

Weight: weight loss was maintained through follow-up

A) Body Weight (Mean ± SEM)



B) Individual 1-Year Body Weight



Of N=31 participants with baseline characteristics, 2 were lost to follow-up. BL=baseline; DMR=duodenal mucosal resurfacing; SEM=standard error of the mean

*One participant was administered cortisone therapy due to lumbar spine prolapse

Assessing Real-World Effectiveness of Revita DMR

Medication: majority of participants reduced or stabilized GLA usage

At 1 year, 83% of participants had stabilized or reduced GLA usage in addition to improvements in glycemia and weight

	Change in GLA Number (n [%])		
Time Period (n)	**Increased**	**Decreased**	**Stayed Same**
Baseline to 3 months (n=24)	0 (0%)	11 (46%)	13 (54%)
Baseline to 6 months (n=18)	0 (0%)	6 (33%)	12 (67%)
Baseline to 12 months (n=12)	2 (17%)	2 (17%)	8 (67%)

Glucose-lowering agents were assessed at baseline, 3, 6, and 12 months post-DMR. Of N=31 participants with baseline characteristics, 2 were lost to follow-up. Of the 2 participants who increased medications, both added tirzepatide, 1 at 6 weeks and 1 at 18 weeks prior to 12-month follow-up. DMR=duodenal mucosal resurfacing; GLA=glucose-lowering agent

Assessing Real-World Effectiveness of Revita DMR

PROs: Revita DMR was valued by participants and improved T2D management

Patient Reported Outcomes (PROs)	3 months (n=24)	6 months (n=18)	12 months (n=12)
Undergo Revita again? (% yes)	92%	89%	100%
Recommend Revita to friend/relative with T2D? (% yes)	96%	94%	100%
Revita Success in T2D management? (1-10, 10 highest) (mean [SD])	9.7 (0.8)	9.8 (0.7)	9.8 (0.9)
Quality of life improved? (1-10, 10 highest) (mean [SD])	9.2 (2.0)	9.5 (1.5)	9.3 (1.9)

Of N=31 participants with baseline characteristics, 2 were lost to follow-up. DMR=duodenal mucosal resurfacing; PROs=patient-reported outcomes; SD=standard deviation; T2D=type 2 diabetes

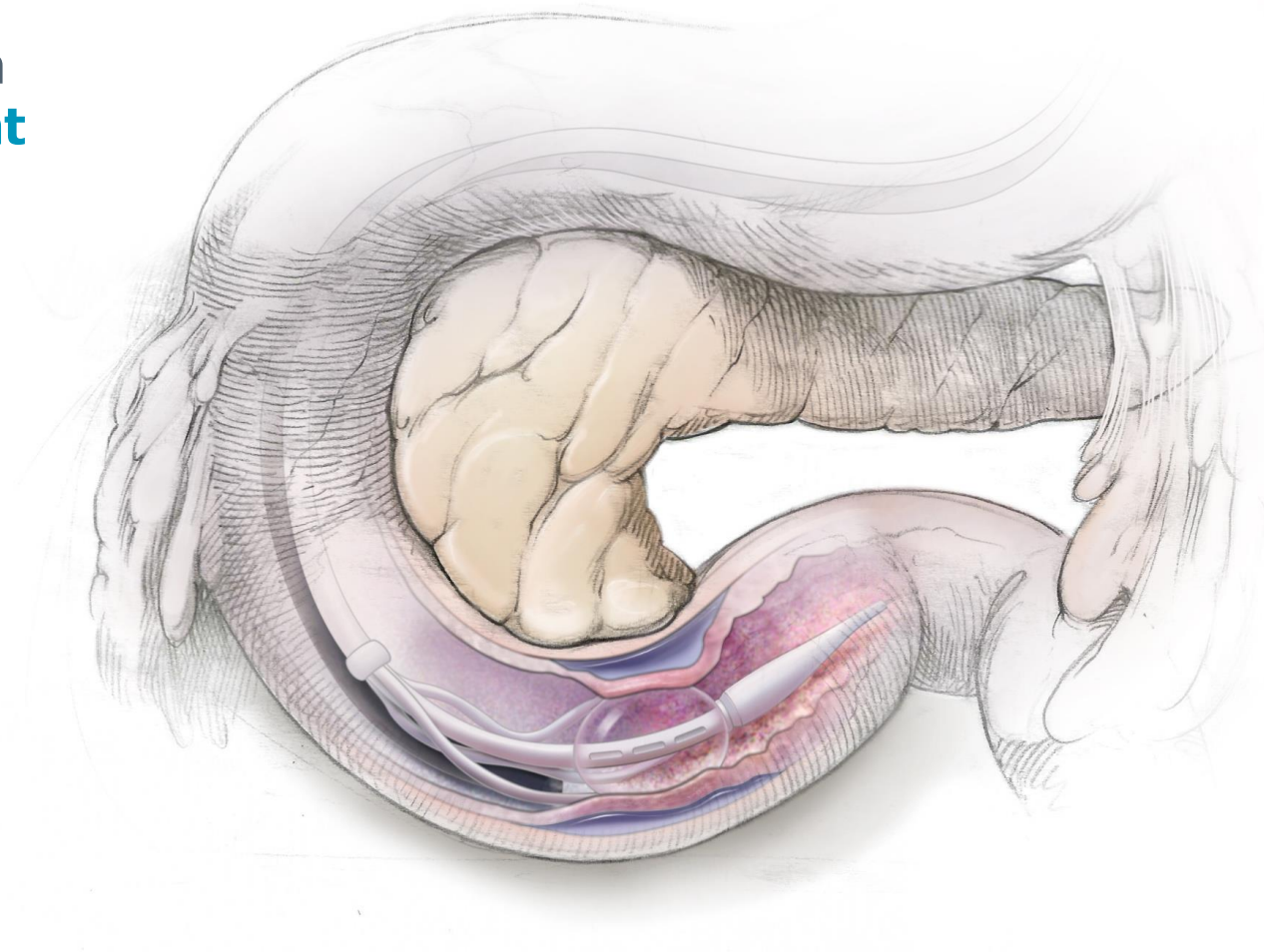
Assessing Real-World Effectiveness of Revita DMR

Summary and conclusions

Revita DMR in combination with lifestyle intervention **durably improved glycemia, maintained weight loss, improved PROs, and reduced/stabilized GLA usage** in inadequately controlled T2D patients

Revita DMR was **well tolerated with no serious procedural and/or device-related adverse events** reported to date

These results suggest that Revita DMR and lifestyle intervention can provide **durable metabolic benefits while improving patients' QOL in the real-world setting**



DMR=duodenal mucosal resurfacing; GLA=glucose-lowering agent; PROs=patient reported outcomes; QOL=quality of life; T2D=type 2 diabetes

Thank You

Acknowledgments

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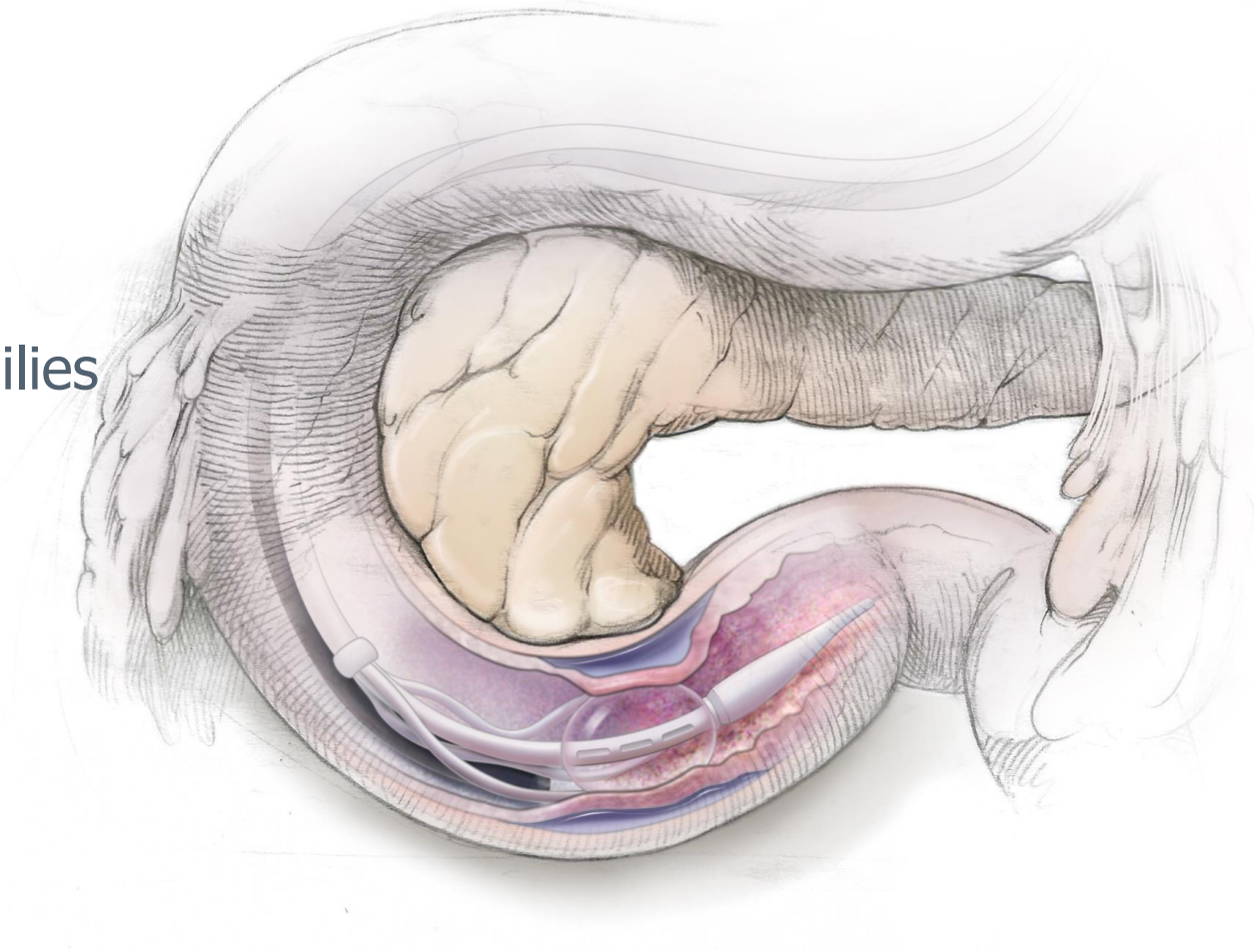
Ina Grafflage & Bettina Prete

Post-market Registry participants and their families



Supplementary Data

Assessing Real-World Effectiveness of Revita DMR

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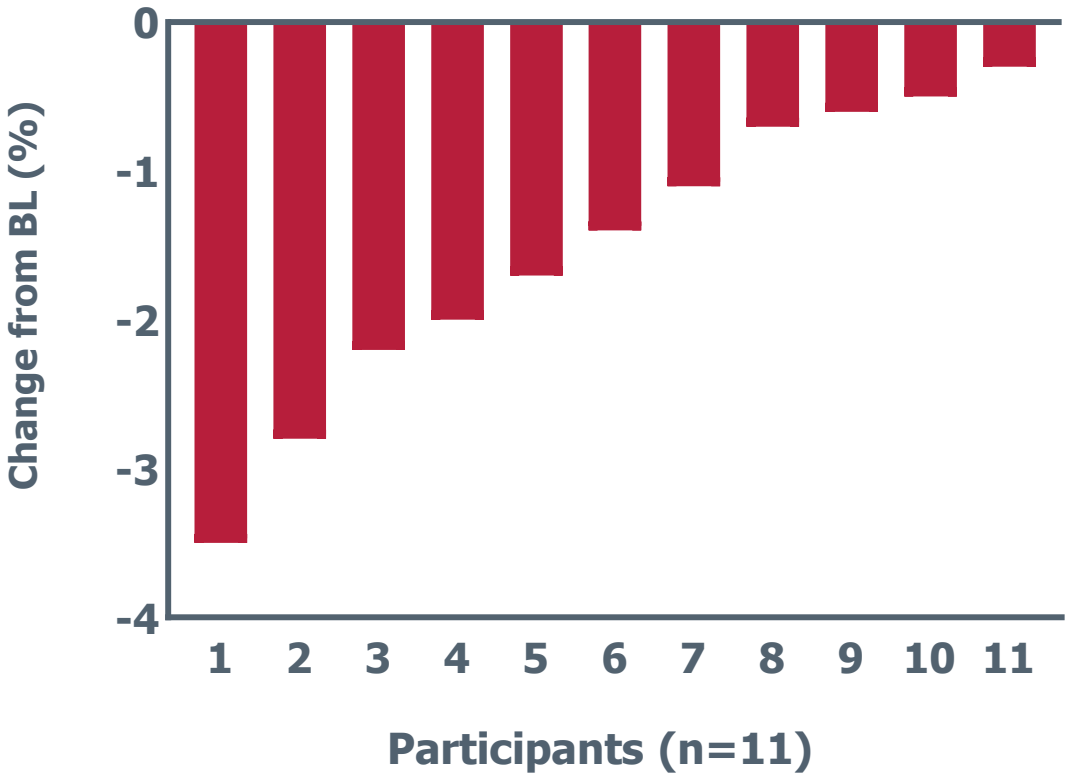
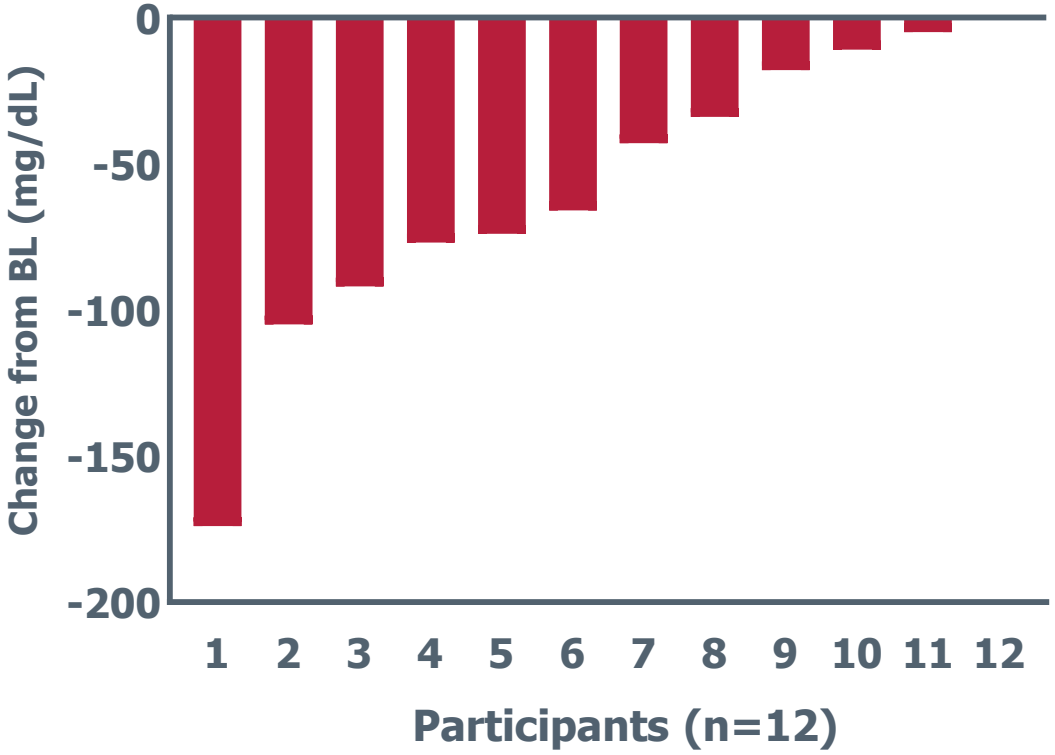
Glycaemia: HbA1c and FBG were maintained through follow-up

A) Individual 1-Year HbA1c



B) Individual 1-Year FBG



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