Endoscopic Duodenal Mucosal Resurfacing (DMR) Improves Metabolic Measures in Type 2 Diabetes: First-in-Human Study 6-Month Data

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Speaker Disclosures

Alan D. Cherrington, PhD, Vanderbilt University, reports the following financial relationships:	
Scientific Advisor/Consultant	Biocon, Eli Lilly & Co, Fractyl Laboratories*, Hanmi, Islet Sciences, Merck & Co., Metavention, Novo Nordisk, NuSirt Biopharma, Profil Institute for Clinical Research, Sensulin, Silver Lake, Thermalin Diabetes, Thetis Pharmaceuticals, vTv Therapeutics, ViaCyte, Viking, Zafgen
Research Support	Eli Lilly & Co, Merck & Co, Metavention, Novo Nordisk, Silver Lake, Thermalin Diabetes
Equity/Stock Options	Fractyl Laboratories, Metavention, Sensulin, Thetis Pharmaceuticals, Zafgen

*Fractyl provided funding for the current study

Background

- Bariatric surgeries that prevent nutrient contact with the duodenum improve metabolic measures in type 2 diabetes (T2D)

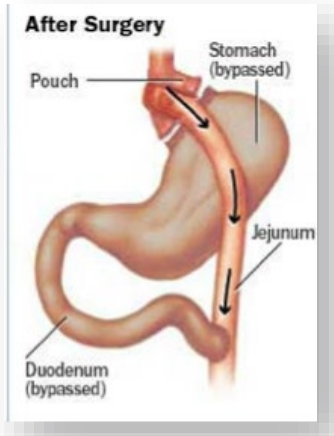
- Revita™ duodenal mucosal resurfacing (DMR) may offer similar metabolic benefit

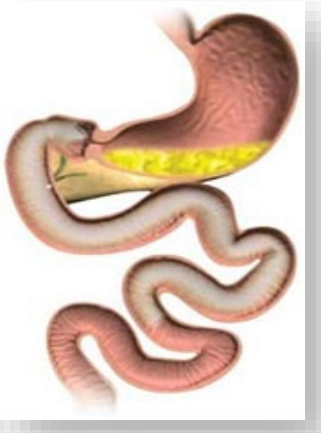
Aim

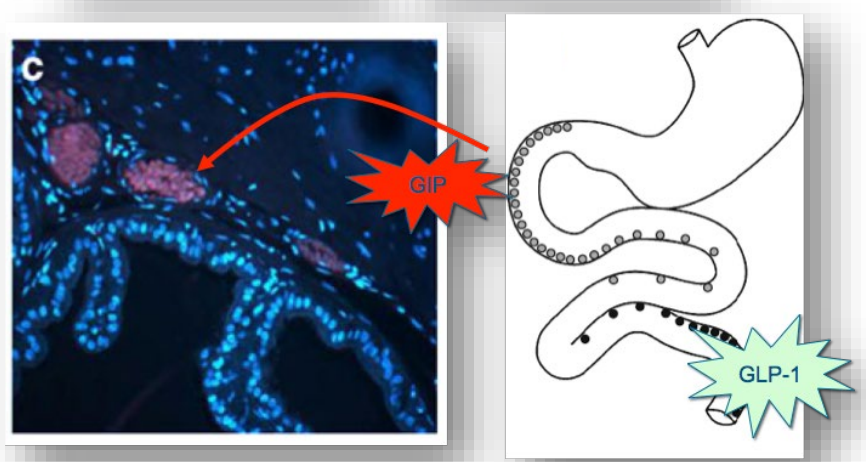
- To study the safety and efficacy of Revita DMR in patients with suboptimally controlled T2D
  - HbA1c > 7.5% on ≥ 1 anti-diabetic agent

Revita DMR: Pathophysiologic Principle

- Bypass of upper GI tract (surgery, sleeve) exerts potent effects on metabolism through insulin sensitizing pathways
- Nutrient re-exposure to the 'Roux' elicits return to hyperglycemia
- Abnormal hypertrophy of mucosa noted in diabetics' upper GI tract
- Abnormal entero-endocrine cell sub-population in upper GI mucosa of diabetic patients



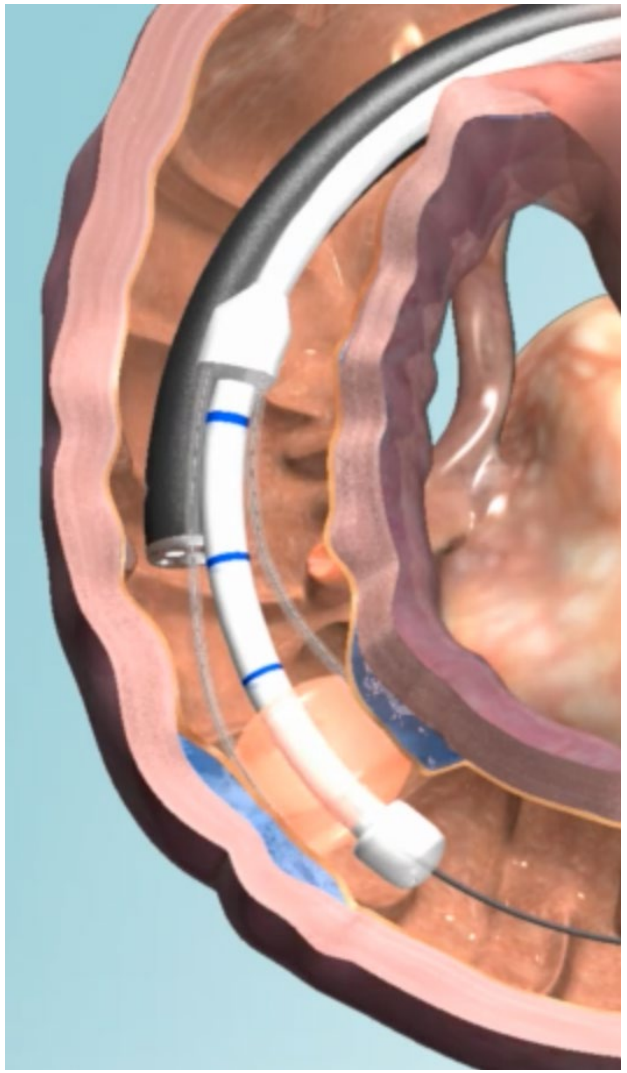




Pories et al. Ann Surg. 222 (3): 339–50, 1995; Rohde et al. BMJ. 3(9), 2013; Dirksen et al. Diabetes Care. 33(2):0–2, 2010; Verdam et al. JCEM. 96(2):E379–83, 2011; Theodorakis et al. AJP. 290(3):E550–9, 2006; Gniuli et al. Diabetologia. 53(10):2233–40, 2010

Revita DMR Procedure

- Minimally invasive upper endoscopic therapy using an innovative balloon catheter
- Targets duodenal mucosa between Ampulla of Vater and Ligament of Treitz
- Procedural Steps
  - Size duodenum and lift sub-mucosal space with saline injection to create protective barrier
  - Circumferentially ablate superficial mucosa using a hydrothermal approach to stimulate regeneration
  - Procedure duration ~60 minutes
- No implant, sutures or surgery



AC - would like someone to explain more about what the figure is depicting technically

First-in-Human Study: Methods

- Single center, single arm study performed in Santiago, Chile, in patients with suboptimally controlled T2D
- Thermal ablation performed on either a **short** (n=11; mean 3.4 cm) or **long** (n=28; mean: 9.3 cm) segment of duodenum
- Procedure performed by trained endoscopists with patients under anesthesia

  AC – remind me again what anesthesia
- 2-week, low calorie, graduated diet for all patients post-procedure (liquids→soft→puree)

  AC – remind me again what diet, what calories
- No specific recommendation on post-procedure management of anti-diabetic medication
- Post-procedure endoscopies performed at 1 and 3 months

Study Details

- **Inclusion criteria**
  - Age 28-75
  - BMI 24-40
  - HbA1c 7.5-12%
  - Disease diagnosed <10 years
  - Fasting c-peptide >1 ng/ml
  - ≥ 1 oral anti-diabetes medicine (Rx)

- **Exclusion criteria**
  - Prior GI surgery that would preclude procedure
  - Anatomical abnormalities
  - Anti-GAD Ab+
  - Injectable anti-diabetes Rx

Patient characteristics	Value (N=44)
Age, yrs (range)	53.4 ± 7.5 (38-65)
Sex, n (%)	
Female	16 (36)
Male	28 (64)
Weight, kg	84.4 ± 11.9
Height, cm	165.3 ± 8.4
BMI, kg/m^2	30.8 ± 3.5
Systolic BP, mmHg	122.0 ± 14.2
Diastolic BP, mmHg	77.0 ± 8.1
Duration T2D, yrs (range)	5.7 ± 2.2 (0.2-9.7)
HbA1c, %	9.6 ± 1.4
FPG, mg/dL %	187 ± 58
Oral anti-diabetic Rx	
Metformin, n (%)	42 (98)
Sulfonylurea, n(%)	16 (37)

Data are mean ± SD or n (%), unless otherwise indicated.

Safety & Tolerability

- Procedure well tolerated with minimal GI symptoms
- No difficulty tolerating oral diet in the days after the procedure
- AEs generally mild in severity & tended to occur in immediate post-procedure period
- Most common AE was transient abdominal pain due to air insufflation/ endotracheal intubation (8/40 patients)
- Most significant AE was duodenal stenosis (3/40 patients)
  - All cases occurred within the first 6 weeks post-procedure
  - Non-emergent and resolved with endoscopic balloon dilation
  - No new cases after procedure and device improvements
- No GI bleeds, perforation, pancreatitis, malabsorption
- No severe hypoglycemia

AC – need to reconcile 39 vs 40 patients
DM and DB discuss

Efficacy: DMR Ablation exhibits Dose-dependency

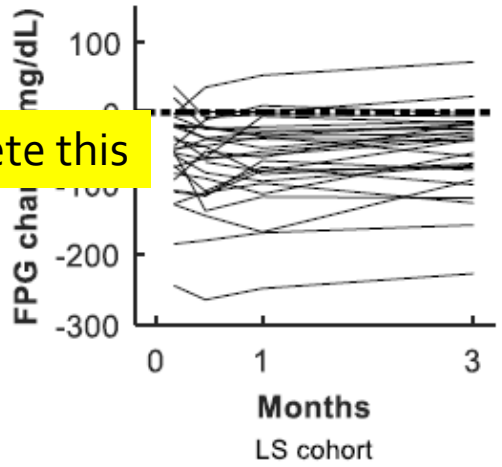
DM and DB discuss: SS vs LS data

DMR Impact on Glycemic Indices

- ADD COMMENTS HERE

A

FPG
LS Cohort (n=28)



LS cohort

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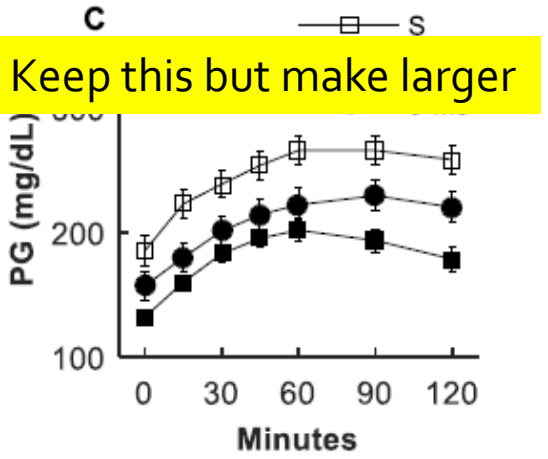
B

MMTT - PG
LS Cohort (n=28)



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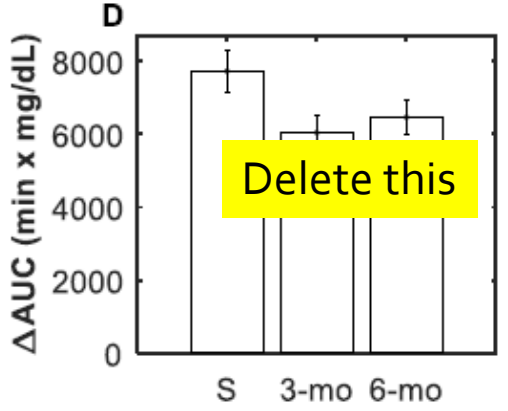
LS cohort, change from screening;
For PG(t=0): p<0.001 at 3-mo, p=0.07 at 6-mo
For PG AUC: p<0.001 at 3-mo, p<0.05 at 6-mo

C

ΔAUC
LS Cohort (n=28)



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LS cohort, change from screening
p<0.01 at 3-mo, p<0.05 at 6-mo

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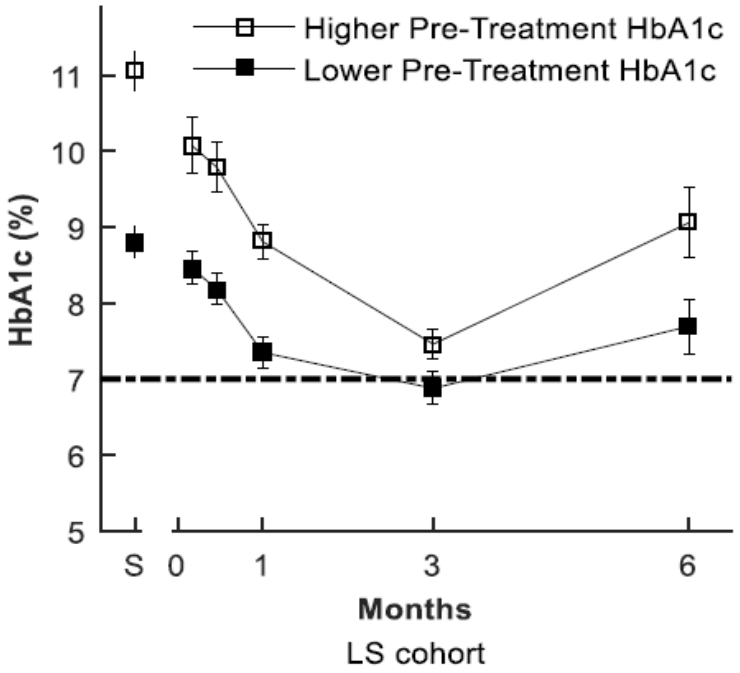
DMR Effect on HbA1c

by Screening HbA1c and Post-Procedure Medication Use

Keep this but clean up text and figures

A

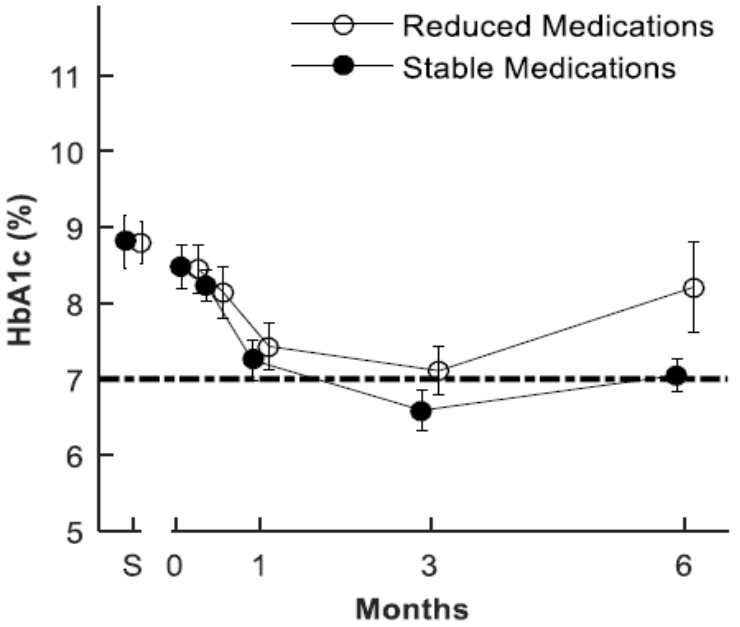
Higher vs Lower Screening HbA1c LS Cohort (n=28)



LS cohort

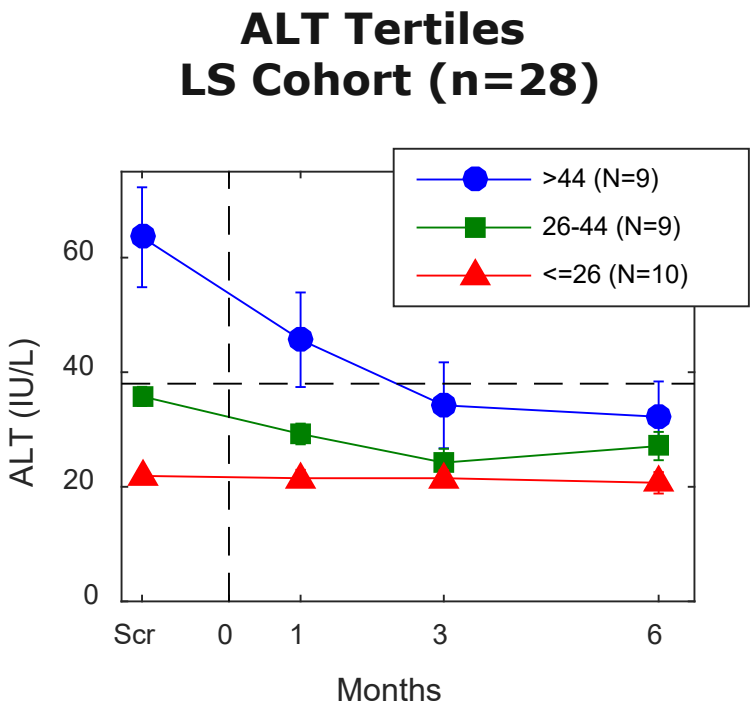
B

Reduced vs Stable Medications LS Cohort with HbA1c ≤10% at Screening (n=18)



LS cohort with lower pre-treatment HbA1c; p=0.11 for stable vs. reduced medications at 6 months

DMR Impact on Broader Metabolic Indices



DMR in LS cohort exhibited the following changes:

- **Minimal change in body weight**
- **Lowering of HOMA-IR**

Metabolomic analysis also observed:

- **Lowering of XX**
- **YY**
- **ZZ**

Conclusions

- DMR improves metabolic control in T2D patients, including improvements in glycemic and broader metabolic indices indicative of likely insulin sensitizing mechanism
- Low rate and severity of adverse events during 6 months of follow-up
- DMR offers the potential for a single-point, endoscopic, duodenum-directed treatment for T2D
- Further examination of DMR efficacy, safety and clinical utility is needed