

Endoscopic duodenal mucosal resurfacing (DMR) improves metabolic measures including hepatic transaminase levels in patients with type 2 diabetes (T2D): Data from a first-in-human study

Manoel Galvao Neto, MD¹, <u>Harith Rajagopalan, MD, PhD²</u>, Pablo Becerra, MD³, Patricia Rodriguez³, Paulina Vignolo, MD³, Jay Caplan, MBA², Leonardo Rodriguez, MD³ ¹Gastro Obeso Center, São Paulo, Brazil & Florida International University, Miami, Florida, USA, ²Fractyl Laboratories, Inc., Waltham, MA, USA, ³CCO Clinical Center for Diabetes, Obesity and Reflux, Santiago, Chile

BACKGROUND

- Bariatric surgeries that prevent nutrient contact with the duodenum improve measures of metabolism in type 2 diabetes (T2D), including indicators of fatty liver disease
- Duodenal mucosal resurfacing (DMR), a minimally invasive investigational endoscopic procedure involving thermal ablation of the duodenal mucosa, may offer similar metabolic benefit

AIM

• To evaluate the effect of DMR on metabolic parameters and assess procedural safety in patients with suboptimally controlled T2D (HbA1c > 7.5% on \geq 1 anti-diabetic agent)

METHODS

- Using novel balloon catheters (Revita[™] DMR System, Fractyl Laboratories, Waltham, MA, USA), we performed thermal ablation on varying lengths of duodenum in anesthetized patients with suboptimally controlled T2D
- Procedures were performed by trained endoscopists at a single medical center (Santiago, Chile)
- Procedural steps: Duodenal sizing \rightarrow Lifting of mucosa using saline \rightarrow Circumferential hydrothermal ablation of superficial mucosa to stimulate regeneration
- 2-week, low calorie, graduated diet for all patients postprocedure (liquids \rightarrow soft \rightarrow puree)
- No specific recommendation on post-procedure management of anti-diabetic medication

- mean BMI: $30.9 \pm 3.5 \text{ kg/m}^2$)

Efficacy

- 1-3)
- Safety & Tolerability

- hypoglycemia

segment DMR cohort

	Screening
HbA1c - %	9.6±1.4
Weight - kg	86±11
ALT – IU/L	40±23
AST – IU/L	32±17

Abbreviations: HbA1c=glycated hemoglobin; ALT=alanine transaminase; AST=aspartate transaminase. *Normal range based on ranges reported by the laboratory that processed the samples.

82±11

32±17

27±11

83±12

27±14

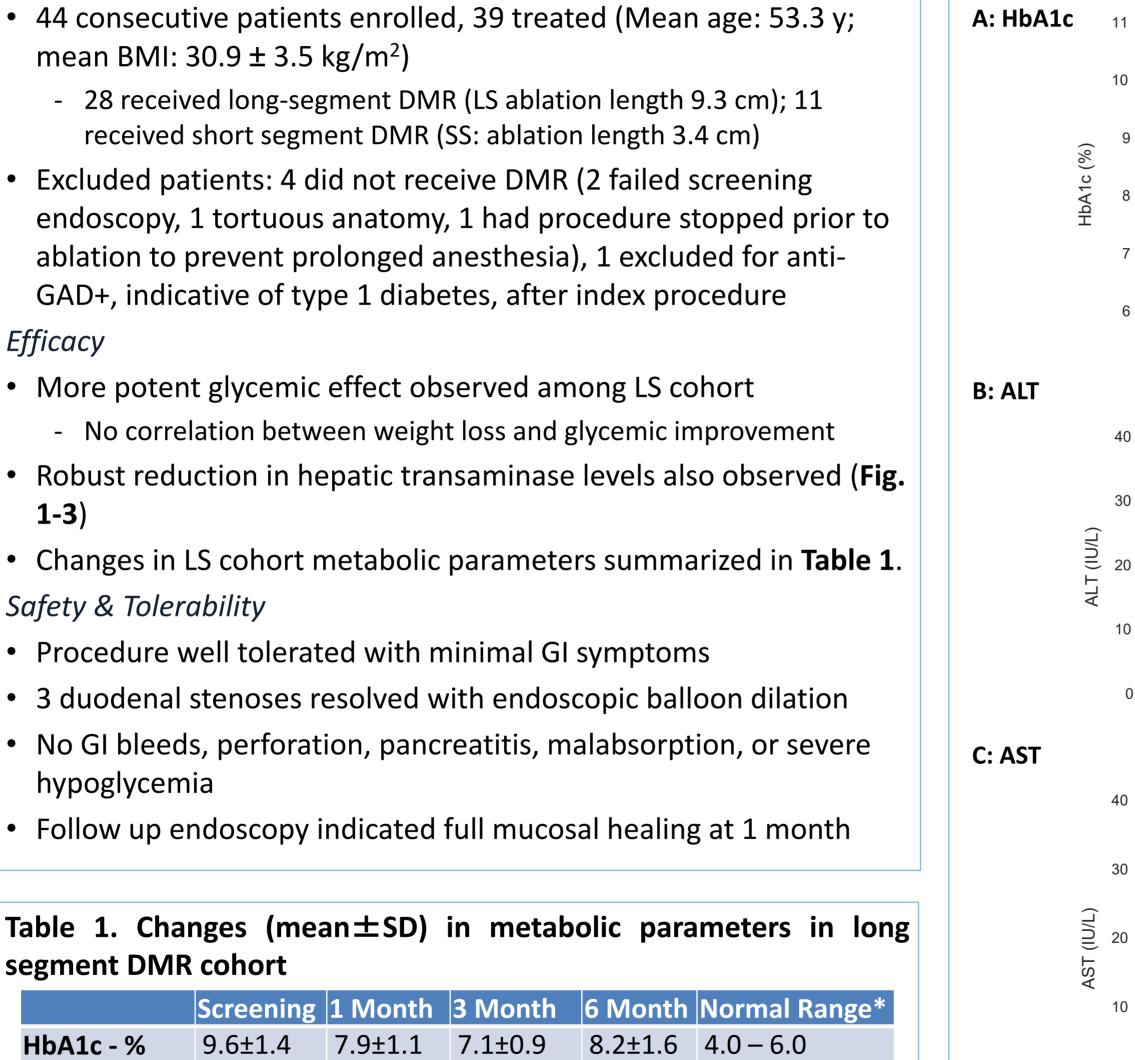
23±8

RESULTS

Months

Months

Months

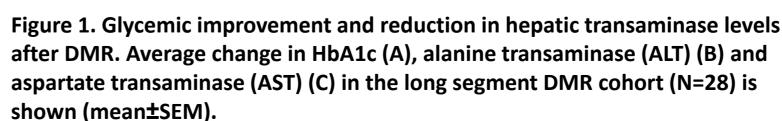


85±11 --

22±6

27±12 ≤38

≤40

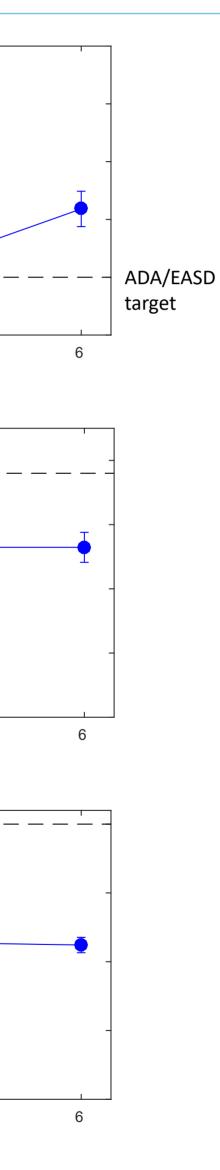


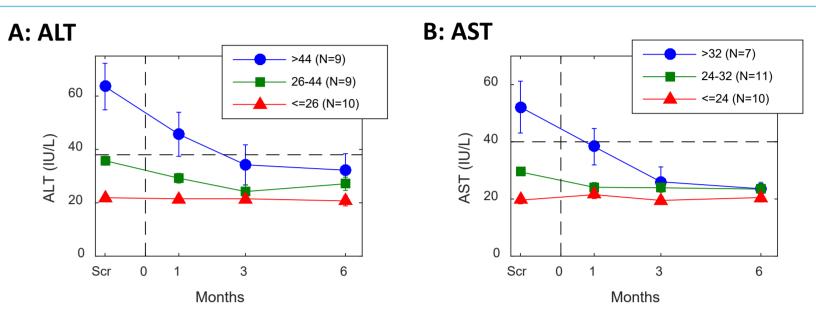
Scr

Scr

0









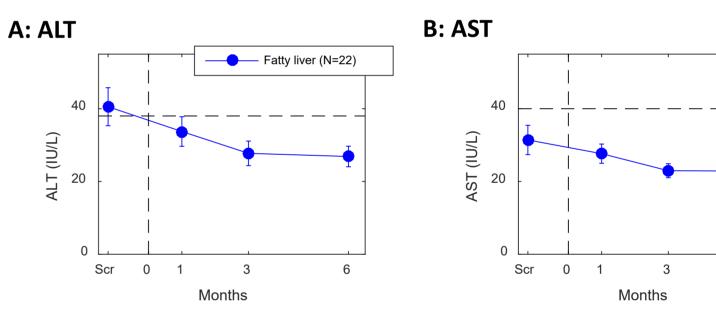


Figure 3. Changes in ALT (A) and AST (B) among long segment DMR patients with incidental finding of fatty liver on ultrasound.

CONCLUSIONS

- DMR improves metabolic control in T2D patients, including a robust and sustained lowering of hepatic transaminase levels, suggesting favorable end-organ hepatic effect
- DMR offers the potential for a single-point intervention that improves both glycemia and fatty liver
- Further study in patients with fatty liver disease is warranted

Study funding: Fractyl Laboratories, Inc. Disclosures: MGN: Scientific advisor to and received research funding from Fractyl Laboratories, Inc. and GI Dynamics. Inc. HR, JC: employees of Fractyl and own shares in the company; LR, PB, PR, PV: Research support from Fractyl. Contact: harith@fractyl.com