Introduction

- Insulin resistance (IR) and progressive failure of insulin production underlie type 2 diabetes (T2D), which has reached pandemic proportions in Westernized countries.\(^{1,2}\)
- Current pharmacotherapies for T2D require continuous administration, and even with optimal compliance, eventually become insufficient because they do not adequately address pathophysiological defects underlying IR.\(^{2,3}\)
- High-fat diets cause hyperlipidemia of the duodenal lining, altering both hormonal signaling and nutrient absorption from the duodenum, which can lead to abnormal digestion, IR, impaired glucose metabolism, and ultimately insulin resistance.\(^{4,5}\)
- Duodenal mucosal resurfacing (DMR) is a novel, minimally invasive, endoscopic procedure that submucosally lifts and hydrothermally ablates the hyperplastic duodenal mucosa to promote epithelial regrowth and restore insulin sensitivity in patients with T2D.\(^{4,6}\)
- Primary results from the multicenter, multinational, open-label, prospective REVITA-1 study demonstrated that a single DMR procedure safely and glycaemically improved over 12 months in patients with suboptimally controlled T2D.\(^{7,8}\)

Objective

To study the durability of response through 24 months in patients with T2D who underwent a single DMR procedure in the REVITA-1 study.

Methods

Patients

- Aged 38-75 years with T2D, body mass index (BMI) 24-40 kg/m\(^2\), hemoglobin A1c (HbA1c) levels of 8.0-10.0%, and on stable diabetes treatment with 1 or oral antidiabetic medication for 3 months at enrollment.
- Exclusion criteria included: clinical diagnosis and/or positive glutamic acid decarboxylase (GAD) antibodies for type 1 diabetes, history of ketosis, low-endogenous insulin production (fasting C-peptide levels < 0.333 nmol/L), use of injectable glucose-lowering medication, severe hypoglycemia, autoimmune disease, gastrointestinal (GI) surgery that could impact treatment of duodenal, chronic or auto-paracrine, active hepatitis or liver disease, upper GI bleeding conditions, or illicit substance use.
- Excluding anticoagulation therapy, P2Y12 inhibitors and/or nonsteroidal anti-inflammatory drugs, corticosteroids, or drugs known to affect GI motility, or taking weight-reducing medications.
- Estimated glomerular filtration rate (> 60 mL/min/1.73 m\(^2\)).

Statistical Analysis

- A 2-sided 0.05 level test was used to assess significance between baseline and 24 months for HbA1c and ALT levels at the 0.05 level.
- Mean (standard deviation [SD]) was calculated for continuous variables, and n (%) was calculated for categorical variables.
- Per-protocol (PP) population, defined as a complete circumferential lift of the mucosa (Step 2). The ablation cycle was started, and hot water was then circulated into the balloon submucosa through the needles within the lumens of the catheter to create a complete circumferential lift that drew the intestinal mucosal tissue onto the ports on the balloon, and the console delivered saline into the mucosal ablation (Figure 1). The ablation cycle was started, and hot water was then circulated into the balloon submucosa through the needles within the lumens of the catheter to create a complete circumferential lift that drew the intestinal mucosal tissue onto the ports on the balloon, and the console delivered saline into the mucosal ablation (Figure 1).

RESULTS

Analysis of the data showed that the HbA1c reduction after a single DMR procedure, approximately 80% of patients experienced an improvement in HbA1c level by month 6, which persisted through 12 months (Figure 2). The primary results at 6 months and durability through 24 months suggested that DMR is a potentially favorable and durable treatment for T2D. In summary, DMR is a potentially favorable and durable treatment for T2D.

Conclusions

- Disease modification in patients with T2D can be achieved with a single DMR procedure, as demonstrated by durable glycemic and hepatic improvements that persisted through 24 months.
- >80% of patients who experienced an improvement in glycemic and hepatic parameters at 12 months after a single DMR procedure maintained improvements through 24 months post-procedure.
- HbA1c improvements are clinically relevant, with 1%-15% reductions through 24 months.
- ALT reductions over 24 months support additional benefit of DMR on biomarkers of nonalcoholic fatty liver disease.
- In summary, DMR is a potentially favorable and durable treatment option for patients with T2D and/or nonalcoholic fatty liver disease.