Original research

Safety and efficacy of hydrothermal duodenal mucosal resurfacing in patients with type 2 diabetes: the randomised, double-blind, sham-controlled, multicentre REVITA-2 feasibility trial

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ABSTRACT

Objective Hydrothermal duodenal mucosal resurfacing (DMR) is a safe, outpatient endoscopic procedure. REVITA-2, a double-blind, superiority randomised controlled trial, investigates safety and efficacy of DMR using the single catheter Revita system (Revita DMR (catheter and system)), on glycaemic control and liver fat content in type 2 diabetes (T2D).

Design Eligible patients (haemoglobin A1c (HbA1c) 59–86 mmol/mol, body mass index ≥ 24 and ≤ 40 kg/m2, fasting insulin > 48.6 μmol/L, ≥ 1 oral antidiabetic medication) enrolled in Europe and Brazil. Primary endpoints were safety, change from baseline in HbA1c at 24 weeks, and liver MRI proton-density fat fraction (MRI-PDDF) at 12 weeks.

Results Overall mITT (DMR n=56; sham n=52), 24 weeks post DMR, median (IQR) HbA1c change was −10.4 (18.6) mmol/mol in DMR group versus −7.1 (16.4) mmol/mol in sham group (p=0.147). In patients with baseline liver MRI-PDDF > 5% (DMR n=48; sham n=43), 12-week post-DMR liver-fat change was −5.4 (5.6)% in DMR group versus −2.9 (6.2)% in sham group (p=0.096). Results from prespecified interaction testing and clinical parameter assessment showed heterogeneity between European (DMR n=39; sham n=37) and Brazilian (DMR n=17; sham n=16) populations (p=0.063); therefore, results were stratified by region. In European mITT, 24 weeks post DMR, median (IQR) HbA1c change was −6.6 (15.7) mmol/mol versus −3.3 (10.9) mmol/mol post-sham (p=0.033); 12-week post-DMR liver-fat change was −5.4% (6.1%) versus −2.2% (4.3%) post-sham (p=0.035). Brazilian mITT results trended towards DMR benefit in HbA1c, but not liver fat, in context of a large sham effect. In overall PP, patients with high baseline fasting plasma glucose (FPG) ≥ 10 mmol/L had significantly greater reductions in HbA1c post-DMR versus sham (p=0.002). Most adverse events were mild and transient.

Conclusions DMR is safe and exerts beneficial disease-modifying metabolic effects in T2D with or without non-alcoholic liver disease, particularly in patients with high FPG.

Trial registration number NCT02879383

Significance of this study

What is already known about this subject?
⇒ More than half of patients with type 2 diabetes mellitus are unable to sustain adequate glycaemic control with the current standard of care.
⇒ Current approaches do not adequately target underlying disease pathophysiology (ie, insulin resistance (IR) and hyperinsulinaemia).
⇒ Bariatric surgeries that bypass nutrient contact from the duodenum (eg, Roux-en-Y gastric bypass) improve glycaemic control and insulin sensitivity.
⇒ Duodenal mucosal resurfacing is a minimally invasive, outpatient endoscopic procedure that targets duodenal pathology to treat insulin-resistance–related metabolic disease, including type 2 diabetes mellitus. Published data from earlier open-label studies have shown statistically significant improvements in haemoglobin A1c (HbA1c), alanine transaminase, aspartate transaminase, weight and homeostatic model assessment of IR in otherwise stable patients with type 2 diabetes mellitus.

What are the new findings?
⇒ In this first prospective, double-blind, sham-controlled study of Revita duodenal mucosal resurfacing, a single duodenal mucosal resurfacing procedure was well tolerated, safe, and elicited clinically and statistically significant improvements in HbA1c levels and liver fat content in European patients with poorly controlled type 2 diabetes mellitus.
⇒ These results confirm that the duodenal mucosa is a therapeutic target for type 2 diabetes with or without non-alcoholic fatty liver disease/non-alcoholic steatohepatitis.
A data monitoring committee oversaw this study (see online supplemental methods for details).

Randomisation and masking
Patients (see online supplemental table 1 for complete eligibility criteria) were randomised (1:1) to undergo the DMR or sham procedure by using a central web-based random allocation system (see online supplemental methods for details). Endocrinologists and patients were unaware of the treatment assignment until the 24-week follow-up visit.

Procedures
DMR was performed with the single catheter Revitasystem (Revita DMR catheter and system), Fractyl Laboratories, Lexington, Massachusetts, USA) as previously described (online supplemental figure 2).16–18 A full DMR procedure was defined as five sequential ablutions of 2 axial centimetres each, starting within 3 centimetres distal to the Ampulla of Vater towards the Ligament of Treitz, totalling 10 axial centimetres of circumferentially ablated tissue in the duodenum during a single endoscopic session. The sham procedure consisted of placing the DMR catheter over the guidewire into the stomach and leaving it in place for 30 min prior to removing it from the patient.

Study endpoints and assessments
The two primary efficacy endpoints were the absolute change from baseline at 24 weeks in HbA1c in all patients and absolute change from baseline at 12 weeks in liver MRI proton density fat fraction (MRI-PDFF), specifically in those patients with NAFLD at baseline (liver MRI-PDFF >5%). The primary safety endpoints assessed were the incidence of device-related and procedure-related serious adverse events (SAEs), unanticipated adverse device events (UADEs), and AES of special interest (AESIs), including hypoglycaemic events, through 24 weeks. Adverse events were recorded from the time the informed consent document was signed. The prespecified safety analysis tabulated the difference in the proportion of patients who experienced ≥1 major complication (DMR vs sham).

Secondary endpoints assessed were the relative change in liver MRI-PDFF from baseline at week 12 in patients with baseline liver MRI-PDFF >5% and absolute change from baseline at 24 weeks in fasting plasma glucose (FPG) levels, weight, and homeostatic model assessment of IR (HOMA-IR).

Exploratory endpoints assessed were absolute change from baseline at 24 weeks in triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein, alanine transaminase (ALT), and aspartate transaminase levels, and change in oral antidiabetic medication from baseline at week 24. In addition, the percentage of patients achieving HbA1c levels <53 mmol/mol or liver fat content reduction >30% at the end of the study as well as the number of antihyperglycaemic drugs during the trial were assessed (see online supplemental table 2).

Rescue medications: persistent hyperglycaemia was a criterion to receive rescue medication, which was prescribed, per protocol (PP), with increasing doses of oral medications and/or insulin according to clinical practice guidelines (see online supplemental table 3).19 20

Patients continued in the trial after receiving rescue medication.

Statistical analysis
The primary efficacy endpoints were planned to be tested for superiority of DMR versus sham with adjustment for multiple endpoints using the Hochberg procedure.21 Under this procedure, DMR was considered beneficial over sham for both primary endpoints if the one-sided p value for each endpoint was <0.05; and/or, if the one-sided treatment comparison p value was <0.025 for one endpoint,
then DMR was considered beneficial over sham for that given endpoint.

Intention-to-treat and PP analyses
The primary analysis population for primary and secondary endpoints was the modified intention-to-treat (mITT) population, defined as all randomised patients in whom the study procedure was attempted and who had a baseline measurement for ≥1 primary endpoint. The PP population was defined as the subset of mITT patients who received the treatment to which they were randomised and strictly adhered to the protocol.

Safety analyses were completed in all patients in whom the treatment (DMR or sham) was initiated and included all AEs revealed during the follow-up, independent of duration. AEs and SAEs are presented as the number and percent of patients; overall counts were compared using the two-sided Clopper-Pearson 95%CI of the incidence rates.

The following additional analyses were conducted: (1) proportion of all patients who achieved an HbA1c level <5.3 mmol/mol at 24 weeks post procedure; (2) proportion of patients with baseline MRI-PDFF >5% who achieved a relative liver MRI-PDFF reduction >30% from baseline at week 12; (3) stratification of end-study HbA1c by baseline FPG levels. The change in oral antidiabetic medication from baseline at week 24 (increase, neutral, or decrease) was assessed in patients with 24 weeks of follow-up.

Statistical analyses were performed using Statistical Analysis Software V9.4 or later (SAS Institute) or R V3.3.2 or later. See supplemental material for additional analyses details and powering assumptions.

Analysis of normality and homogeneity in the study populations
Assessments of normality and homogeneity were performed as specified in the statistical analysis plan. The normality tests assessed whether each variable was normally distributed. Assessments of homogeneity evaluated consistency in treatment effect across geographic regions (Belgium, Brazil, Italy, Netherlands and UK) with a prespecified treatment-by-region interaction p value of <0.10 (see additional methods for details).

An exploratory analysis using partial least-squares-discriminant analysis (PLS-DA) was performed to further understand and assess the interaction by regions in the prespecified study populations. PLS-DA is a useful exploratory analysis showing patterns related to a treatment effect without testing a formal hypothesis; in other words, it provides a comparative and clear visual of different patterns in two samples (see online supplemental methods for details).

HOMA-IR and Matsuda Index Calculation
Fasting IR was measured based on the HOMA-IR calculated as (FPG fasting insulin)/135, where FPG level was measured in mmol/L and fasting insulin was measured in pmol/L.

The Matsuda Index was calculated as 10000/(G1,I1*Gn,In)0.5, where G1 and In are premeal values for glucose and insulin and Gn and In are mean post-meal values during the first 120 min of the liquid meal tolerance test with glucose and insulin values in mmol/L and mU/L, as validated for a meal test. Since the square root of the denominator takes into account the correction of nonlinear values distribution, these values are reported as mean±SD.

Role of the funding source
The funder of the study participated in study design, data collection, data analysis, data interpretation and writing of the report. The corresponding author (GM) had full access to all the data in the study and had final responsibility for the decision to submit the manuscript for publication.

Patient and public involvement
Patients were not directly involved in the design, recruitment or conduct of the study.

RESULTS
Patient baseline characteristics
Between 11 September 2017 and 15 December 2018, 359 patients were screened and 250 were excluded from the study (figure 1). 109 patients were randomised (although one did not receive treatment due to oesophageal varices) 1:1 either to DMR (n=56) or to sham procedure (n=52); 75 in Europe (39 DMR, 36 sham procedure) and 33 in Brazil (17 DMR, 16 sham procedure).

Overall, 71 patients (65.7%) were white, 7 (6.5%) were black, 2 (1.8%) were Asian, 3 (2.8%) belonged to other races and 25 (23.1%) preferred not to disclose their race.

Patient demographics and baseline characteristics were well balanced between the DMR and sham procedure groups (table 1). Men accounted for 69.4% of the patients. At baseline, the median body mass index was 31.5 (4.7) kg/m2 in the DMR group and 30.7 (5.7) kg/m2 in the sham group. The median baseline HbA1c levels were 65.6 (8.7) mmol/mol in the DMR group and 66.1 (10.4) mmol/mol in the sham group. The median duration of diabetes was 10.0 (6.0) years and 9.1 (8.8) years among patients who underwent DMR or sham procedure, respectively. Most patients (85.3% in the DMR group and 82.7% in the sham group) had more than 3% fat accumulation in the liver as detected at baseline by MRI-PDFF.

mITT analysis and post-hoc analyses
In the overall mITT population (DMR n=56; sham n=52), the median change in HbA1c from baseline at 24 weeks post procedure was −10.4 (18.6) mmol/mol in the DMR group compared with −7.1 (16.4) mmol/mol in the sham group (p=0.147; treatment difference −3.3 mmol/mol). In patients with baseline liver MRI-PDFF >5% (DMR n=48; sham n=43), the median absolute change in liver MRI-PDFF from baseline at 12 weeks was −5.4 (5.6)% in the DMR group compared with −2.9 (6.2)% in the sham group (p=0.096; treatment difference −2.5%).

A post-hoc analysis of pooled data from the overall PP population stratified by baseline FPG levels demonstrated that in patients with FPG ≥10 mmol/L, the median (IQR) reduction in HbA1c at week 24 post procedure was −14.2 (17.5) mmol/mol post DMR compared with −4.4 (15.3) mmol/mol in the sham group (p=0.002); whereas, in patients with FPG <10 mmol/L, the median reductions in HbA1c were similar between groups (p=0.148; figure 2A).

In patients with baseline liver MRI-PDFF >5% and FPG ≥10 mmol/L, the median absolute change in liver MRI-PDFF was significantly greater in the DMR group compared with patients who underwent the sham procedure (p=0.001; figure 2B). Similar results were observed in the European PP population for both HbA1c and liver fat content changes (figure 2C,D) and in the Brazilian PP population, but only for liver fat content (figure 2E,F).

PRIMARY AND SECONDARY ENDPOINTS BY REGION
Demographics and baseline characteristics were similar (table 1), but prespecified interaction testing by region showed heterogeneity between patients in Europe (DMR N=39; sham N=36) and patients in Brazil (DMR N=17; sham N=16) for the HbA1c outcome (p=0.063). As such, European and Brazilian regions were analysed separately for all clinical outcomes. A post-hoc PLS-DA confirmed these regions were separate groups with different
variance/covariance structures (online supplemental figure 3). The primary endpoints were found to be not normally distributed and are therefore presented as median (IQR).

PLS-DA is a linear classification model that is able to predict the class of new samples. We used PLS-DA as a post-hoc analysis that confirmed the European and Brazilian populations were separate groups with different variance/covariance structures (figure 3). This analysis including all patients, regardless of treatment group, showed that the first two components of PLS-DA explained 35% of the variance that contributed to the separation of the European and Brazilian populations. The general predictive performance of the PLS-DA model in correctly classifying the patients as belonging to the European or to the Brazilian groups was very good as shown by the area under the curve of 0.89. Therefore, due to heterogeneity demonstrated by multiple statistical methods and the unexpected differences seen between Europe and Brazil in the sham arms (table 2), analyses were stratified by region.

In the European mITT population, the median change in HbA1c from baseline at 24 weeks post procedure was –6.6 (17.3) mmol/mol in the DMR group compared with –3.3 (10.9) mmol/mol in the sham procedure group (p=0.033; treatment difference –3.3 mmol/mol; figure 3A). In patients with baseline liver MRI-PDFF >5%, the median absolute change in liver MRI-PDFF from baseline at 12 weeks revealed a reduction of liver fat content by 5.4 (6.1)% in the DMR group compared with 2.2 (4.3)% in the sham procedure group (p=0.035; treatment difference –3.2%); figure 3B). Similar results were observed in the European PP population and using a prespecified mixed-model repeated measures analysis (MMRM) (described within the online supplemental material).

In the Brazilian mITT population, change from baseline in HbA1c levels (figure 3C) was not significantly different in DMR compared with sham in the primary analysis, but was significantly lower in the prespecified sensitivity MMRM analysis (p=0.104 and p=0.034, respectively). In Brazil, there was no significant difference between treatment groups in liver MRI-PDFF (figure 3D).

In the European mITT population, the median reduction in weight 24 weeks post procedure was significantly greater in the DMR group (–2.4 (2.8) kg) than in the sham group (–1.4 (2.4) kg; p=0.012; treatment difference –1.0 kg; figure 4A). At 12 weeks post procedure, European patients with baseline liver MRI-PDFF >5% had a significantly greater reduction of the median relative liver MRI-PDFF from baseline in the DMR group compared with the sham group (–32.1% (20.6%) vs –17.9% (25.6%); p=0.020; treatment difference –14.2%; figure 4B). Median reduction in FPG levels from baseline at 24 weeks post procedure was numerically lower in the DMR group than in the sham procedure group (–1.5 mmol/L (4.6 mmol/L) vs –0.9 mmol/L (3.0 mmol/L); p=0.217; treatment difference –0.6 mmol/L; figure 4C), and median reduction in HOMA-IR was numerically lower in the DMR group compared with the sham group (–1.3 (2.5) vs –0.4 (1.5); p=0.060; treatment difference –0.9; figure 4D). Sensitivity analysis of HOMA-IR reached statistical significance in non-imputed complete case analysis for missing secondary endpoint data (p=0.028), indicating an insulin-sensitising mechanism of DMR. The mean (SD) increase in Matsuda Index, a post-hoc analysis of insulin sensitivity (higher numbers denoting better insulin sensitivity), was greater in the DMR group compared with the sham group (1.2±2.7 vs 0.2±1.5; p=0.035; treatment difference 1.0).

The mITT analysis of the relative changes in weight, liver fat content (MRI-PDFF), FPG and HOMA-IR in the Brazilian population did not show any significant difference between DMR and sham groups (figure 4E–H, respectively).
Table 1  Baseline characteristics and demographics and change from baseline (modified intention-to-treat population*)

<table>
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<th>Parameter</th>
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<th>P value</th>
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<th>Overall</th>
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<td>Sham N=36</td>
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<td>56.0 (13.0)</td>
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<td>93.0 (15.9)</td>
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<td>−1.5 (3.3)</td>
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<td>−1.8 (3.3)</td>
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<td>−2.6 (3.4)</td>
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<td>31.4 (4.5)</td>
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<td>29.9 (5.5)</td>
<td>0.563</td>
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<td>29.7 (6.3)</td>
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<tr>
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DMR, duodenal mucosal resurfacing; HbA1c, haemoglobin A1c.

Figure 2  Post-hoc analysis of change in haemoglobin A1c (HbA1c) levels and liver MRI proton density fat fraction (MRI-PDFF) stratified by baseline fasting plasma glucose (FPG) level status (per-protocol (PP) populations). Median HbA1c per cent change from baseline to 24 weeks (duodenal mucosal resurfacing (DMR) versus sham procedure) in the overall (A), European (C) and Brazilian (E) PP patients with baseline FPG ≥10 mmol/L compared with patients with baseline FPG <10 mmol/L. In patients with baseline liver MRI-PDFF >5%, median liver MRI-PDFF per cent change from baseline to 12 weeks (DMR vs sham procedure) in the overall (B), European (D), and Brazilian (F) PP patients with baseline FPG ≥10 mmol/L compared with FPG <10 mmol/L. Treatment comparison of one-sided p value based on analysis of covariance model with multiple imputation on the rank values (modified ridit scores). Via multiple imputation, analysis is based on all patients in the population of interest. The overall PP population includes patients from both European and Brazilian study sites. The European PP population consists of patients from Italy, UK, Belgium and Netherlands.
In the European mITT population, the DMR group had significantly more patients achieving HbA1c levels <53 mmol/mol at 24 weeks compared with the sham group (26.3% vs 9.1%; p=0.031; online supplemental figure 4A). Similarly, 53% of patients in the DMR group with baseline MRI-PDFF >5% achieved a relative liver MRI-PDFF reduction >30% from baseline at week 12, compared with 22% in the sham procedure group (p=0.008; online supplemental figure 4B).

Finally, most patients experienced no change or had an increased use in oral antidiabetic medication from baseline at week 24 in both the European and Brazilian mITT populations (online supplemental table 4).

**TIME OF PROCEDURE**

The median total catheter indwelling time in the entire sample was 56.0 min (26.0 min).

**SAFETY ANALYSIS**

All patients were included in the safety analysis, 76 in Europe (DMR n=39; sham n=37) and 33 in Brazil (DMR n=17; sham n=16). Most AEs were mild and transient; the most common were abdominal pain, diarrhoea, hyperglycaemia, hypoglycaemia, nasopharyngitis and headache. In the European population, no device-related or procedure-related SAEs or UADEs were reported through 24 weeks post procedure (table 3). Approximately 33% of patients in the DMR group (n=13) experienced a device-related or procedure-related AESI, compared with 27% of patients (n=10) in the sham procedure group. The most common (occurring in ≥5% of patients) device-related or procedure-related AESIs occurring ≤30 days post procedure were abdominal pain and hypoglycaemia. Similar number of events and percentage of patients with events of hypoglycaemia (related to procedure) were found in both groups (4 events; 7.7% (3/39) patients with event in DMR group and 8 events; 10.8% (4/37 patients with events in the sham group)). There was an absence of pancreatitis, infection and thermal injury. Follow-up endoscopy was performed (n=32); overall, the duodenum appeared normal with complete healing.

In the Brazilian population, 11.8% of patients (n=2) in the DMR group experienced SAEs related to the procedure (table 3). One
Gastroduodenal SAE was a precautionary hospitalisation for evaluation for a patient who noted mild haematochezia 8 days after a DMR procedure. The haematochezia was ascribed to a visible external haemorrhoid; however, the investigator adjudicated it as possibly related to procedure. The other SAE was a jejunal perforation caused by manipulation of the endoscope used in the procedure during the performance of an upper endoscopy, requiring surgical repair with no further sequelae. Hypoglycaemia (related to procedure) was reported in 47% (8/17) of patients in the DMR group and 56% (n=9/16) in the sham group with 64 and 74 events in each arm, DMR versus sham, respectively. Follow-up endoscopy was performed (n=17); overall, the duodenum appeared normal with complete healing.

Figure 4 Clinically meaningful reductions in weight, liver fat and homeostatic model assessment of insulin resistance (HOMA-IR) with duodenal mucosal resurfacing (DMR). Median weight (kg) change from baseline to 24 weeks (DMR vs sham procedure) in the European (A) and Brazilian (B) modified intention-to-treat (mITT) and per-protocol (PP) populations. Median relative liver MRI proton density fat fraction (MRI-PDFF) per cent change from baseline to 12 weeks in patients with baseline MRI-PDFF >5% (*) in the European (C) and Brazilian (D) mITT and PP populations. Median fasting plasma glucose (FPG; millimoles per litre) change from baseline to 24 weeks (DMR vs sham procedure) in the European (E) and Brazilian (F) mITT and PP populations. Median HOMA-IR change from baseline to 12 weeks (DMR vs sham procedure) in the European (G) and Brazilian (H) mITT and PP populations. Data for continuous variables are on non-imputed unadjusted descriptive statistics based on patients with non-missing values. Treatment comparison one-sided p value based on analysis of covariance model on ranks (modified ridit scores) where post rescue values are first set to missing. Last rank carried forward on ranks was used for missing data for FPG levels, weight and HOMA-IR endpoints. HOMA-IR was determined as (FPG * fasting insulin)/135, where FPG levels were measured in millimoles per litre and fasting insulin is measured in picomoles per litre.
DISCUSSION
In REVITA-2, a randomised, double-blind, sham-controlled, multicentre trial in patients with poorly controlled T2D with or without NAFLD, a single DMR procedure was well tolerated. Due to the regional heterogeneity revealed by interaction testing, the European and Brazilian populations were analysed separately. Though there was less power to detect a statistical difference between DMR and sham arms, in the European population DMR elicited a greater improvement than sham procedure in both primary endpoints (HbA1c and liver fat content via MRI-PDFF), as well as in secondary measures of insulin sensitivity and body weight. Significant differences in weight loss, HbA1c and HDL-c were observed between the two European and Brazilian populations after unblinding, including in the sham arms. The fact that HbA1c in the sham group was reduced by 3.3 mmol/mol in the European population (consistent with prestudy assumptions), but by 17.5 mmol/mol in the Brazilian population (much greater than prestudy assumptions or even the magnitude of benefit from more potent anti-diabetic drugs) suggest these patients had a more intensive approach in their treatment of diabetes on study enrolment than the European ones, which led to the clinical and statistical differences observed between these populations. This is also true for dieting, since the weight loss was almost double in the Brazilian population as compared with the European population, which may explain the differences in observed treatment effect on study enrolment than the European ones, which led to the clinical and statistical differences observed between these populations. This is also true for dieting, since the weight loss was almost double in the Brazilian population as compared with the European population, which may explain the differences in observed treatment effect on study enrolment.
understand the long-term results of this study concluded at 48 weeks. In this study, patients with high baseline FPG levels (≥10 mmol/L) post-prandially demonstrated lower levels of ambient glycaemia in the Brazilian population relative to the European patients and also raises important considerations for DMR, at least in a selected population, to favourably treat both T2D and number of baseline medications were found, and this may be contributing to differences in outcomes. Next, while full type-1 error was incorporated for the two primary endpoints, we acknowledge that there is a lack of control for false discovery rate in this study for our secondary and exploratory endpoints; therefore, those results should be interpreted with appropriate context. In relation to the differences in statistical and clinical results seen between the European and Brazilian populations, it is important to acknowledge that adherence to previously prescribed medications could not be objectively assessed in this study and race was not collected in the majority of the patient population in Europe. In a follow-up study, it will also be important to confirm the MRI-PDF results with additional non-invasive tests such as fibroscan to evaluate Revita DMR's potential to additionally improve liver fibrosis. Lastly, this short-term study concluded at 48 weeks. Follow-up data on the 48-week DMR results are forthcoming, as well as plans for a pivotal study (Revita T2D; NCT04419779) in T2D insulin-treated patients. This will be important research to confirm the metabolic benefits seen thus far in patients with T2D with or without NAFLD, provide long-term follow-up (including biopsies of the duodenal mucosa to further understand the long-term morphological changes), and provide the opportunity to understand the biological mechanisms likely behind the benefit of DMR on the treatment of these pathological conditions.

In conclusion, DMR is a safe procedure that significantly improved glycaemic control and reduced liver fat content in the European population compared with the sham procedure. In addition, a post-hoc analysis in the overall population showed that patients with high baseline FPG levels (≥10 mmol/L) had significantly greater reductions in HbA1c post-DMR, versus sham.

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