Evaluation of the effect of Duodenal Mucosal Resurfacing (DMR) using the Revita System in the treatment of Type 2 diabetes (T2D)

Published: 17-10-2018
Last updated: 12-04-2024

Phase 1 (0 - 24 Weeks) Objective:To study the effect of DMR on glycemic and mechanistic endpoints24 weeks post-procedure in subjects with T2D.Phase 2 (24 - 48 Weeks) Objective:To study the effect of DMR on glycemic endpoints for assessment...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Diabetic complications
Study type	Interventional

Summary

ID

NL-OMON48696

Source
ToetsingOnline

Brief title
Revita-2 Study

Condition

- Diabetic complications

Synonym
Diabetes Type 2, T2D

Research involving
Human

Sponsors and support

Primary sponsor: Fractyl Laboratories Inc.

Source(s) of monetary or material Support: De sponsor van de studie

Intervention

Keyword: Diabetes, Medical Device, Revita, Type 2

Outcome measures

Primary outcome

Primary Efficacy Endpoint:

The primary efficacy endpoint is the change from baseline at 24 weeks in HbA1c, DMR vs Sham and the absolute change at 12 weeks in MR-PDFF In patients with baseline MR-PDFF > 5%, DMR vs Sham

Primary Safety Endpoint:

The primary safety endpoint is incidence rates of device or procedure related SAEs, UADEs and AESIs DMR vs Sham through 24 Weeks post procedure.

Secondary outcome

1. HbA1c change from baseline to Week 24(Visit 9) by visit over time, DMR vs. Sham

2. The relative MR-PDFF change from baseline to Week 12 in patients with baseline MR-PDFF > 5%, DMR vs. Sham

3. Proportion of randomized-DMR-treated subjects with an HbA1c improvement from baseline at 24 weeks (Visit 9) that maintain an HbA1c improvement at 48 weeks

4. Proportion of randomized-DMR-treated subjects with an MR-PDFF > 5% at baseline and MR-PDFF improvement from baseline at 24 weeks (Visit 9) that maintain an MR-PDFF improvement at 48 weeks

5. Fasting Plasma Glucose (FPG) change from baseline at 24 weeks DMR vs. Sham

6. FPG change from baseline to Week 24 by visit over time, DMR vs. Sham

7. Weight change from baseline at 24 weeks DMR vs. Sham

8. In randomized-DMR-treated subjects with an HbA1c improvement from baseline

at 24 weeks, average HbA1c improvement from baseline at 48 weeks

9. In randomized-DMR-treated subjects with an MR-PDFF > 5% at baseline and

MR-PDFF improvement from baseline at 12 weeks, average MR-PDFF improvement at

48 weeks

10. HOMA-IR change from baseline at 24 weeks DMR vs. Sham

Study description

Background summary

Type 2 is a condition that leads to high blood sugar. Good treatment is important because too high blood sugar leads to complications such as eye diseases, kidney disease, disease of nerve endings, myocardial infarction or stroke. Currently most people use tablets that lower blood sugar. Despite the use of tablets, in many people blood sugar is still too high in spite of these tablets, which means there is a greater chance of the above-mentioned complications occurring. A next step for these people could be that they are going to use additional medication, or that they will use insulin for example.

In the function of the mucosa of the duodenum, changes occur with type 2 diabetes. The endoscopic Revita DMR procedure has been developed to remove this mucous membrane by heating (ablation). After the procedure new mucous membrane grows back. The first studies show that the DMR treatment is safe. In people with type 2 diabetes who only took tablets, the HbA1C and fasting blood sugar dropped and they also dropped about 3 kg. In this study all subjects received DMR treatment and were not compared to a group that did not receive the treatment (SHAM).

In the REVITA-2 study we want to compare the effect of the DMR treatment with a SHAm treatment. There is a chance of 1 in 2 (50%) to get into the DMR group, and also a 1 in 2 (50%) chance of getting into the sham group.

The patiënt and treating physician do not know which treatment the patient will receive and will not be able to affect the draw in any way.

After 24 weeks, it will be announced in which group the patient is placed. If it turns out that the patient has undergone the SHAM treatment, the patient can then decide if he/she wants to crossover and receive the DMR procedure.

Study objective

Phase 1 (0 - 24 Weeks) Objective:
To study the effect of DMR on glycemic and mechanistic endpoints 24 weeks post-procedure in subjects with T2D.

Phase 2 (24 - 48 Weeks) Objective:
To study the effect of DMR on glycemic endpoints for assessment of durability.

Study design

Randomized double-blind sham-controlled prospective multicenter clinical investigation of subjects with type 2 diabetes sub-optimally controlled on 2 oral anti-diabetic medications.
• Up to 15 Investigational Sites in EU and global geographies
• Maximum of 50 training and up to 120 randomized subjects
• 1:1 randomized, double blind (subject and endocrinologist) trial comparing DMR treatment to sham procedure
• 4 week oral anti-diabetic medication run-in to assess stability of blood glucose control in conjunction with medication compliance and nutritional counseling
• Oral diabetic medications held constant from start of run in period through 24 Week endpoint with predefined rescue algorithm for hypo and hyper glycemia
• Unblinding to occur at 24 Weeks and:
o Sham treatment arm to cross over to receive DMR treatment at 24 Weeks with background medications held constant from 24 - 48 Weeks of follow up
o DMR treatment arm to be managed according to current diabetes standard of care for 24 - 48 Weeks of follow up

• Mechanism of action assessments, conducted in a subset of Study Sites, include: ambulatory blood pressure monitoring (ABPM) in training case only, Mixed Meal Tolerance Test (MMTT), Urine Micro Albumin, and Radiological Hepatic Status
• Subject follow-up visits will occur at 7 and 14 Days (by phone) and 4, 12, 18, 24, 36 and 48 Weeks (in clinic), and 15, 21, 30 and 42 weeks (by phone) post procedure*
* For cross-over patients that choose to undergo the active DMR treatment the following visits are not applicable: 30 and 42 weeks (per phone), and 36 and 48 weeks (in clinic) post procedure

Intervention

Every patient will undergo an endoscopic treatment where the medical device is placed into the duodenal. With the active patient, the device is activated and the ablation is performed. With the sham patient, the medical device will not be activated.

After 24 weeks, the sham patient can still be treated with an active endoscopic procedure as described above.

Study burden and risks

As per protocol paragraph 1.5, there are risks related to the endoscopic procedure in general, as well as, risks specific to the Fractyl Revita SystemTM procedural treatment for Type 2 Diabetes.

Specific risks associated with the endoscopic procedure include (in alphabetical order):

• abdominal tightness, cramping, pain
• diarrhea
• difficulty swallowing
• infection
• mucosal injury to GI tract
• pancreatitis
• perforation
• sore throat
• stricture
• transient bleeding
• worsening diabetic symptoms including hypoglycemia

Many of these risks and complications associated with the procedure would be similar to those associated with other commonly performed endoscopic procedures such as duodenal biopsies and endoscopic mucosal resection.

In addition to the risks listed above, the Fractyl Revita System may have unique risks associated with its catheter and console used to complete the procedure. This includes risks associated with the materials selected, its design and construction. These risks include:
• Allergic reaction to the device materials or endoscopic labeling dye or injectate
• Component degradation
• Control module delivers incorrect ablation time and temperature profile
• Device breakage
• Disarticulation of components from the device
• Device/Component lost in GI tract or wall

• Hole in hot fluid catheter balloon resulting in leakage of hot fluid
• Lost catheter component in the GI tract or wall
• Thermal damage to the duodenum wall or surrounding structures
• Unforeseen adverse events.

The benefit of the procedure is similar as when used commercially and could result in improved control of the blood glucose levels and secondary risks associated with this.

As the trial is performed under strict control and oversight by experienced physicians, the risk of the study related additional activities is minimized. The tests performed are standard tests.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. 28-75 years of age
2. Diagnosed with Type 2 Diabetes and evidence of preserved insulin secretion. Fasting insulin > 7.0 µU/ mL.
3. HbA1c of 7.5 - 10.0% (59-86 mmol/mol)
4. Body Mass Index (BMI) >= 24 and <= 40 kg/m2
5. Currently taking one or more oral glucose lowering medications, of which one must be Metformin, with no changes in dose or medication in the previous 12 Weeks prior to study entry.
6. Able to comply with study requirements and understand and sign the informed consent

Exclusion criteria

1. Diagnosed with Type 1 Diabetes or with a history of ketoacidosis
2. Current use of Insulin
3. Current use of GLP-1 analogues
4. Hypoglycemia unawareness or a history of severe hypoglycemia (more than 1 severe hypoglycemic event, as defined by need for third-party-assistance, in the last year)
5. Known autoimmune disease, as evidenced by a positive Anti-GAD test, including Celiac disease, or pre-existing symptoms of systemic lupus erythematosus, scleroderma or other autoimmune connective tissue disorder
6. Active H. pylori infection (Participants with active H. pylori may continue with the screening process if they are treated via medication.)
7. Previous GI surgery that could affect the ability to treat the duodenum such as subjects who have had a Bilroth 2, Rouxen-Y gastric bypass, or other similar procedures or conditions
8. History of chronic or acute pancreatitis
9. Known active hepatitis or active liver disease
10. Symptomatic gallstones or kidney stones, acute cholecystitis or history of duodenal inflammatory diseases including Crohn*s Disease and Celiac Disease
11. History of coagulopathy, upper gastro-intestinal bleeding conditions such as ulcers, gastric varices, strictures, congenital or acquired intestinal telangiectasia
12. Use of anticoagulation therapy (such as warfarin) which cannot be discontinued for 7 days before and 14 days after the procedure
13. Use of P2Y12 inhibitors (clopidogrel, pasugrel, ticagrelor)

which cannot be discontinued for 14 days before and 14 days after the procedure. Use of aspirin is allowed.
14. Unable to discontinue NSAIDs (non-steroidal antiinflammatory drugs) during treatment through 4 weeks post procedure phase
15. Taking corticosteroids or drugs known to affect GI motility (e.g. Metoclopramide)
16. Receiving weight loss medications such as Meridia, Xenical, or over the counter weight loss medications
17. Persistent Anemia, defined as Hgb<10 g/dl
18. eGFR or MDRD <30 ml/min/1.73m^2
19. Active systemic infection
20. Active malignancy within the last 5 years
21. Not potential candidates for surgery or general anesthesia
22. Active illicit substance abuse or alcoholism
23. Participating in another ongoing clinical trial of an investigational drug or device
24. Any other mental or physical condition which, in the opinion of the Investigator, makes the subject a poor candidate for clinical trial participation

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-10-2018
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	Fractyl Revita System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	17-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT02879383
CCMO	NL66981.018.18