Evaluation of Duodenal Mucosal Resurfacing for the Treatment of Type 2 Diabetes

Published: 11-06-2015
Last updated: 16-04-2024

To evaluate the feasibility, safety and efficacy related endpoints for the Fractyl Revita System for the treatment of uncontrolled type 2 diabetes.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Interventional

Summary

ID

NL-OMON44146

Source
ToetsingOnline

Brief title
REVITA-1

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Treatment diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Fractyl Laboratories, Inc.
Source(s) of monetary or material Support: Fractyl Laboratories

Intervention

Keyword: Diabetes, Evaluation, Magnitude, Safety

Outcome measures

Primary outcome

Study endpoints

Feasibility endpoints:

The feasibility endpoints (device performance) are assessed using the following criteria:

1. Successful Completion of Submucosal Expansion

2. Successful Completion of Ablation

Safety Endpoint:

The safety endpoint is the incidence rate of the following events at 24 weeks and at 36 months post-procedure:

1. All Serious Adverse Events (SAEs) and Unanticipated Adverse Device Effects (UADEs)

2. All Procedure and device-related Serious Adverse Events (SAEs) and Unanticipated Adverse Device Effects (UADEs)

3. Number of hypo-glycemic events (blood glucose level of < 56 mg/dL (3.1 mmol/L) or requiring 3rd party assistance)

Endpoints related to the efficacy:

The following outcomes related to the efficacy are assessed at 24 weeks and 36

months:

* Mean reduction in HbA1c from baseline

* Achievement of *1% reduction in HbA1c

* Reduction in Fasting Blood Glucose levels

* Reaching a target HbA1c * 7%

* Overall reduction in HbA1c

* Treatment responder rate

* DTSQ (s and c)

* Oral anti-diabetic Medication Use

* Weight loss (Kg and % EW)

* Measures of beta cell function involving plasma glucose, insulin, c-peptide

Secondary outcome

-

Study description

Background summary

Type 2 Diabetes is an endocrine disorder linked to the obesity epidemic. It is characterized by chronically elevated blood glucose and subsequent vascular complications. There are approximately 382 million subjects with type 2 diabetes throughout the world. The disease has spread rapidly in rich and poor nations and has been associated with increasing age, decreased physical activity and the explosion of Western dietary habits around the globe. In Europe alone, there are 56 million patients with type 2 diabetes * and this number is expected to triple by 2050. The UK National Health Service (NHS) apportions 10% of its budget to the disease and its complications. Type 2 diabetes is the most prevalent and costly pandemic of our time.

Type 2 Diabetes is also an imperfectly understood chronic and progressive condition. Early in the disease, patients display intolerance to ingested glucose and resistance to insulin. Insulin secretion from the pancreatic beta

cells initially increases to compensate for the body*s own acquired resistance. This maintains euglycemia through the early course of the illness. Physiologic studies during this time reveal insulin resistance in peripheral tissues and impaired capacity for insulin to suppress glucose production in the liver. However, as the disease progresses, beta cells eventually can no longer compensate for the body*s resistance to insulin and the body*s endogenous insulin secretion proves inadequate to maintain effective glucose homeostasis.

The hyperglycemia that results from this complex metabolic disturbance exerts its pathologic effect in small and large blood vessels. The impairment of small blood vessels can lead to nephropathy, retinopathy, and peripheral neuropathy. As a consequence, diabetes is a leading cause of renal failure, blindness, and non-traumatic amputations in developed nations. In addition, type 2 diabetes contributes significantly to large vessel atherosclerotic diseases, increasing the risk of myocardial infarctions, stroke, and peripheral vascular disease.

Study objective

To evaluate the feasibility, safety and efficacy related endpoints for the Fractyl Revita System for the treatment of uncontrolled type 2 diabetes.

Study design

* Up to 5 investigational sites
* Maximum of 25 cases in total
* 4 week oral anti-diabetic medication run-in period to confirm lack of blood glucose control in conjunction with medication compliance and nutritional counseling
* Interim analysis after 25 cases complete 24 week follow up
* Subject follow up at 14 days, 4, 12, 18, 24, 36 weeks and 12, 18, 24, 30 and 36 months post procedure

Intervention

DMR procedure

Study burden and risks

Risks: possible side effects of the study procedure

Burden: 14 visits

See question E4 for a further description of the procedures the patient has to undergo.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Screening Visit (Pre-Medication Run-In, Visit 1)
1. 28 -75 years of age
2. Diagnosed with Type 2 Diabetes for less than 10 years
3. HbA1c of 7.5 - 10.0% (59-86 mmol/mol)
4. BMI * 24 and * 40 kg/m2
5. On a minimum of 1 stable oral anti-diabetic medication with no changes in medication in the previous 3 months prior to study entry
6. Willing to comply with study requirements and able to understand and comply with informed consent
7. Sign an informed consent form

Exclusion criteria

Screening Visit (Pre-Medication Run-In, Visit 1)
1. Diagnosed with Type 1 Diabetes or with a history of ketoacidosis
2. Probable insulin production failure, defined as fasting C Peptide serum <1 ng/mL (333pmol/l)
3. Current use of Insulin
4. Use of GLP-1 analogues
5. 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)
6. 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
7. Previous GI surgery that could affect the ability to treat the duodenum such as subjects who have had a Bilroth 2, Roux-en-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 (clopidrogel, 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 anti-inflammatory 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 mg/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. Those who are pregnant, nursing or expect to become pregnant over the course of the study
24. Participating in another ongoing investigational clinical trial
25. Any other mental or physical condition which, in the opinion of the Investigator, makes the subject a poor candidate for clinical trial participation;Baseline Visit (Post Medication Run-In, Visit 2)
1. HbA1c post run-in phase < 7.5% (59 mmol/mol) or > 10.0% (86 mmol/mol)
2. Hypoglycemic event defined as a plasma glucose level of < 56 mg/dL (3.1 mmol/L) with symptoms, or at least 2 self-monitored finger sticks < 56mg/dL without symptoms or a severe hypoglycemic event, as defined by third-party-assistance, since the screening visit

(Visit 1)
3. Hyperglycemic event defined as three self-monitored finger sticks in 1 day during the run-in period with fasting blood glucose measurements >15 mmol/L (270 mg/dL) or non-fasting blood glucose measurements >20 mmol/L (360 mg/dL) or any combination of the two. Fasting glucose hyperglycemia is not an exclusion if measured at the actual baseline visit (Visit 2) blood analysis test.;Procedure (Visit 3)
1. Active and uncontrolled GERD defined as grade III esophagitis or greater
2. Abnormalities of the GI tract preventing endoscopic access to the duodenum
3. Anatomic abnormalities in the duodenum that would preclude the completion of the DMR procedure, including tortuous anatomy
4. Malignancy newly diagnosed by endoscopy
5. Upper gastro-intestinal conditions such as ulcers, gastric varices, strictures, congenital or acquired intestinal telangiectasia

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-07-2015
Enrollment:	20
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO

Date:	11-06-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Not approved	
Date:	10-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	17-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	29-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	02-06-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	
Date:	17-09-2018
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
CCMO	NL52396.018.15

Study results

Date completed:	01-01-1900
Results posted:	16-11-2020
Actual enrolment:	11

First publication
05-10-2020