Effect of INtervention with DMR, GLP-1 and lifestyle intensification -in Subjects with insulin dePendent type 2 diabetes- on Insulin Requirement and mEtabolic parameters

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The main objective of this pilot study is to evaluate the efficacy of the Duodenal Mucosal Resurfacing procedure combined with GLP-1 administration and lifestyle intervention in subjects with insulindependent type 2 diabetes. Study success is...

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

Summary

ID

NL-OMON50038

Source
ToetsingOnline

Brief title
INSPIRE study

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Type 2 diabetes

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Diabetes, Efficacy, Endoscopic, Treatment

Outcome measures

Primary outcome

Protocol driven free of insulin at 6 months including and an HbA1c * 7.5%.

Secondary outcome

Secondary efficacy endpoints at 3 (if applicable) and 6 months to identify

improvement in cardiovascular, metabolic and hepatic parameters:

a. HbA1c

b. Change in HbA1c

c. Achieving target HbA1c of 7%

d. FPG

e. Change in FPG

f. Peak and AUC glucose in MMTT

g. Gut hormones in MMTT

h. Pancreatic hormones in MMTT

i. Metabolic profile from MMTT

j. HOMA IR

k. Insulin sensitivity

l. Beta cell function

m. Liver fat fraction

n. Cardiac function

o. ALT and AST

p. Change in AST and ALT

q. Fibrosis-4 (FIB-4) score

r. Change in FIB-4 score

s. Urine microalbumin

t. Blood pressure

u. DEXA body scan

The safety endpoint is the incidence rate of the following events at 6 months

and 12 months post-procedure:

a. All Procedure and device-related Serious Adverse Events (SAEs) and

Unanticipated Adverse Device Effects (UADEs)

b. All SAEs and UADEs

c. Number of hypo-glycemic events (blood glucose level of < 56 mg/dL (3.1

mmol/L) or requiring 3rd party assistance)

Feasibility endpoints:

a. DMR procedure time

b. Percentage of subjects adequately using and tolerating GLP-1

Study description

Background summary

It is currently unknown whether the DMR procedure can be effective in terms of restoring euglycemia in already insulin dependent subjects with T2D. However, it is shown that DMR increases the insulin sensitivity in T2D subjects who use only oral glucose lowering medication. It is reasonably thinkable that in insulin dependent T2D subjects with a preserved beta-cell function (as indicated by a plasma C-peptide value of * 500 pmol/l), euglycemia and insulin independence can be achieved after the DMR procedure when treatment with insulin is replaced by Liraglutide to improve and preserve beta-cell function after DMR and is additionally supported by lifestyle intervention. Each of these 3 therapy modalities alone are not able to discontinue insulin therapy in a large subgroup of subjects. A combined approach however, may very well be beneficial.

The results of this pilot study will be used to estimate the effect size of the DMR procedure combined with liraglutide administration and lifestyle intervention. This effect size will then be used for a sample size calculation for a subsequent randomized controlled trial.

It is hypothesized that a combined treatment with DMR, GLP-1 and lifestyle intervention have an additional beneficial effect on cardiovascular, hepatic and metabolic state compared to similar glucose regulation with insulin treatment. The measures applied in this pilot will inform whether insulin withdrawal combined with a single DMR procedure, initiation of liraglutide administration and lifestyle intervention may improve metabolic, microbiome, hepatic and cardiac states. Favorable indicators will warrant further investigation of these effects. In a subsequent randomized controlled study, the assessments with notable results in this pilot study will be repeated in the different treatment arms.

Study objective

The main objective of this pilot study is to evaluate the efficacy of the Duodenal Mucosal Resurfacing procedure combined with GLP-1 administration and lifestyle intervention in subjects with insulindependent type 2 diabetes. Study success is defined as insulin independence at 6 months after DMR with an HbA1c level of * 7.5%. The second objective of this pilot study is to identify cardiovascular, metabolic and hepatic health benefits accompanied by this changed treatment strategy. The results of this pilot study will be used to estimate an effect size of this combined treatment in previously insulin dependent subjects. This effect size will be used for an adequate sample size calculation for a subsequent randomized controlled trial.

Study design

- Single site (Academic Medical Center: AMC), open label study
- 24 cases with complete DMR procedure
- No randomization
- Screening visit to assess subject eligibility, followed by baseline visit and DMR-procedure visit
- Endoscopic follow-up at 3 months.
- Follow-up of glucose parameters at 3, 6, 9, 12, 15, 18 and 24 months post-DMR

Intervention

Endoscopic Duodenal Mucosal Resurfacing (DMR) procedure, substitution of insulin by a GLP-1 analogue (Liraglutide) with the additional support of lifestyle counseling.

Study burden and risks

Risks: Possible side effects of study procedure (see E9)

Burden: 12 visits (see E2 - E6)

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

1. 28 -75 years of age
2. Treatment with long acting insulin * 5 years
3. On daily long acting insulin dose * 1 U/kg
4. BMI * 24 and * 40 kg/m2
5. HbA1c * 8.0% (64 mmol/mol)
6. Fasting C-peptide * 500 pmol/L (1.5 ng/ml)
7. Willing to comply with study requirements and able to understand and comply with informed consent
8. Signed informed consent form

Exclusion criteria

1. Diagnosed with Type 1 Diabetes or with a history of ketoacidosis
2. Fasting C-peptide < 500 pmol/L (1.5 ng/ml)
3. Current use of multiple daily doses insulin or insulin pump
4. Current use of a sulfonylurea derivate or meglitinide
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. 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
7. History of chronic or acute pancreatitis
8. Known active hepatitis or active liver disease
9. Symptomatic gallstones or kidney stones, acute cholecystitis or history of duodenal inflammatory diseases including Crohn*s Disease and Celiac Disease
10. History of coagulopathy, upper gastro-intestinal bleeding conditions such as ulcers, gastric varices, strictures, congenital or acquired intestinal telangiectasia
11. Use of anticoagulation therapy (such as phenprocoumon and acenocoumarol) and novel oral anticoagulants (such as rivaroxaban, apixaban, edoxaban and dabigatran) which cannot be discontinued for 7 days before and 14 days after the procedure
12. 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.
13. Unable to discontinue NSAIDs (non-steroidal anti-inflammatory drugs) during treatment through 4 weeks post procedure phase
14. Taking corticosteroids or drugs known to affect GI motility (e.g. Metoclopramide)

15. Receiving weight loss medications such as Meridia, Xenical, or over the counter weight loss medications
16. Persistent Anemia, defined as Hgb<10 g/dl
17. eGFR or MDRD <30 ml/min/1.73m^2
18. Active systemic infection
19. Active malignancy within the last 5 years
20. Not potential candidates for surgery or general anesthesia
21. Active illicit substance abuse or alcoholism
22. Participating in another ongoing clinical trial of an investigational drug or device
23. 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

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-10-2017
Enrollment:	16
Type:	Actual

Medical products/devices used

Generic name:	Fractyl Revita System
Registration:	Yes - CE intended use
Product type:	Medicine
Brand name:	Victoza
Generic name:	Liraglutide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	27-06-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-08-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-03-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-10-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-12-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-03-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-07-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-10-2019
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
EudraCT	EUCTR2017-000349-30-NL
CCMO	NL60669.018.17

Study results

Results posted: 13-07-2021

First publication
01-01-1900

URL result
Type
ext
Naam
pubmed.ncbi.nlm.nih.gov
URL