Evaluation of the Glucoregulatory Effects of GLP-1 Receptor Activation in Patients with Type 2 Diabetes Mellitus

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Primary:to assess the glycemic effects of a single dose of OXM on the ambient glucose levels during a GGI assessmentto assess the insulinotropic effects of a single dose of OXM measured as a change in "*" during a GGI assessmentSecondary:...

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

Summary

ID

NL-OMON35750

Source
ToetsingOnline

Brief title
Glucose-dependent insulin secretion in type II diabetes mellitus

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes, insulin secretion

Research involving
Human

Sponsors and support

Primary sponsor: PRA International EDS
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Diabetic, Insulin Secretion

Outcome measures

Primary outcome

Pharmacodynamics

Pharmacokinetics

Safety

Secondary outcome

N/A

Study description

Background summary

You will participate in a study in which new methods for the assessment of future drug research for Type 2 Diabetes Mellitus medication are developed. Insulin is a hormone produced by the human body naturally and is involved in the regulation of the metabolism of sugar and fat in the body. Insulin causes cells in the liver, muscle, and fat tissue to take up blood sugar (glucose) from the blood, storing it as a long-term energy depot in the liver and muscle. When the natural control of insulin production by the body fails, the complication diabetes mellitus will develop. The insulin that will be administered temporarily, is used on a large scale and is internationally registered (NovoRapid) and approved. In this study, you will receive a glucose solution and an Oxyntomodulin infusion. Oxyntomodulin is a hormone that is naturally produced in your body which suppresses appetite.

In this study, you will also receive a single subcutaneous injection of Liraglutide in the evening prior to the Oxyntomodulin and glucose infusion. Liraglutide is a GLP-1 like peptide (stimulates insulin release) and registered for the treatment of type 2 diabetes.

Study objective

Primary:
to assess the glycemic effects of a single dose of OXM on the ambient glucose

levels during a GGI assessment
to assess the insulinotropic effects of a single dose of OXM measured as a change in "*" during a GGI assessment

Secondary:
to assess the reproducibility of the measures of insulinotropic effects and glycemic excursion in the setting of a GGI in patients with T2DM
to assess the treatment effects and dose response of a SD of 0.6 and 1.2 mg of liraglutide on glycemic excursion and insulinotropic effects in the setting of a GGI in patients with T2DM
to compare the treatment effects of a SD of OXM and those of liraglutide 0.6 and 1.2 mg on insulinotropic effects and glycemic excursions in the setting of a GGI in patients with T2DM
to assess the operational characteristics and feasibility of evaluating glucoregulatory effects in the setting of a GGI in a T2DM population

Study design

Design:
a double blind, randomized, placebo-controlled, four-period cross-over, single dose study with one cohort of twelve obese T2DM subjects; subjects will be randomized to one of eight sequences, during each of the periods, each subject will receive both a continuous infusion and subcutaneous injection to maintain the blind, during the first three periods each subject will receive one treatment period each with continuously infused OXM or placebo or subcutaneous liraglutide or placebo or double-placebo; furthermore, in period four, six subjects will receive 1.2 mg of liraglutide and the remaining six subjects will receive double placebo

Procedures and assessments
Screening and follow-up:
clinical laboratory, physical examination, weight, 12-lead ECG, vital signs (including oral temperature); at eligibility screening: medical history, HbA1c, lipid panel, HBsAg, anti HCV, anti-HIV 1/2, urine drug screen; weight and vital signs to be repeated upon admission

Observation period:
four periods in clinic from 24 h before start of the GGI up to completion of the weaning procedure in the afternoon of Day 1

Blood sampling:
for pharmacokinetics of oxyntomodulin: 30 min before start of the GGI and 20, 40, 80, 120 an 160 min after start of the GGI
for pharmacokinetics of liraglutide archive: 9 h and 30 minutes before start of the GGI and 40, 80, 120 and 160 min after start of the GGI
for glucose * central laboratory: every 30 minutes during overnight insulin

infusion, at start of the GGI, and 20, 40, 60, 80, 100, 120, 140 and 160 min after start of GGI
for glucose * YSI: every 30 minutes during overnight insulin infusion, 10 minutes before start of the GGI, and 40, 80, 120 and 160 min after start of GGI
for C-peptide: at start of the GGI, and 20, 40, 60, 80, 100, 120, 140 and 160 min after start of GGI
for insulin: at start of the GGI, and 20, 40, 60, 80, 100, 120, 140 and 160 min after start of GGI
for GLP-1/glucagon: at the start of the GGI and 40, 80, 120 and 160 min after start of GGI
for archive: 30 min before start of GGI and 160 min after start of GGI
for genetic and other biomedical research: 12 h before start of the GG
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Urine sampling:
for glucose: interval from 15 min before start of GGI up to 160 min after start of GGI

Safety assessments:
adverse events: throughout the study; vital signs: 12 h and 60 min before GGI and prior to discharge; blood sample for glucometer: every 3 hour during overnight insulin infusion, at start of the GGI and 40, 80, 120 and 160 min after start of GGI and 10 times during the weaning procedure

Insulin Infusion Procedures:
IV catheter placement: ~60 min before start of the insulin infusion; overnight insulin infusion: 11 * 1 h before GGI, blood glucose concentration should be kept between 5 mmol/L and 7.2 mmol/L

GGI Procedure:
infusion of glucose: 0 - 160 min on Day 1, glucose (20% glucose) will be administered as a stepwise, graded infusion of 2, 4, 6, and 10 mg/kg/min (down-regulated to 8 mg/kg/min at last step if applicable), each infusion step should be maintained over exactly 40 minutes

Bionalysis:
analysis of oxyntomodulin samples using a validate method by Sponsor
analysis of liraglutide samples using a validate method by Sponsor
analysis of glucose samples using a clinical chemistry method by PRA
analysis of C-peptide samples using a clinical chemistry method by PRA
analysis of insulin samples using a clinical chemistry method by PRA
analysis of GLP-1/glucagon samples using a validated method by PRA

Intervention

Insulin infusion
Oxyntomodulin infusion

Liraglutide injection

Study burden and risks

Procedures: pain, light bleeding, heamatoma and possibly an infection.

Contacts

Public
PRA International EDS

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9471 GP Zuidlaren
NL
Scientific
PRA International EDS

Stationsweg 163
9471 GP Zuidlaren
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Male, 18-65 years, inclusive
BMI is less than or equal to 38.0 kg/m2
Type 2 Diabetes Mellitus Patient

Exclusion criteria

Suffering from: hepatitis B, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study or in case of donating more than 1.5 liter of blood in the 10 months prior the start of this study.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-05-2011
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Insulin Aspart
Generic name:	NovoRapid
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Liraglutide
Generic name:	Victoza

Registration:	Yes - NL intended use

Ethics review

Approved WMO Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	EUCTR2011-001984-37-NL
CCMO	NL36827.056.11