The efficacy and safety of liraglutide adjunct to insulin treatment in type 1 diabetes;
A 26-weeks randomised, insulin capped, placebo-controlled, double-blinded, parallelgroup, multinational, multi-centre trial

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To confirm superiority of liraglutide compared to placebo, both adjunct to insulin treatment, on glycaemic control, after 26 weeks of treatment in subjects with established type 1 diabetes in inadequate glycaemic control.

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

Summary

ID

NL-OMON40721

Source
ToetsingOnline

Brief title
ADJUNCT TWO*

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Novo Nordisk

Intervention

Keyword: GLP-1 analogue, liraglutide, type 1 diabetes

Outcome measures

Primary outcome

Change from baseline in glycosylated haemoglobin (HbA1c) after 26 weeks of

treatment.

Secondary outcome

Change from baseline in body weight after 26 weeks of treatment

Number of treatment-emergent symptomatic hypoglycaemic episodes during 26 weeks

of treatment

Study description

Background summary

Despite the knowledge of the benefits of improved glycaemic control, many patients with type 1 diabetes find it a challenge to reach glycaemic targets, not the least due to the associated potential increased risk of experiencing hypoglycaemic episodes and weight gain.
Small scale studies and case reports in subjects with type 1 diabetes indicate that treatment with a GLP-1 receptor agonist, such as liraglutide as adjunct to insulin, may result in:
a) improvement in glycaemic control through reduction in fasting and postprandial hyperglycaemia, in part due to inhibition of postprandial hyperglucagonaemia,
b) reduction in glucose excursions,
c) reduction in episodes of hypoglycaemia,

d) reduction in insulin requirements and
e) a body weight benefit
The clinical circumstances of insulin treatment not being optimal imply, that new efforts to improve treatment for type 1 diabetes subjects are needed.

Study objective

To confirm superiority of liraglutide compared to placebo, both adjunct to insulin treatment, on glycaemic control, after 26 weeks of treatment in subjects with established type 1 diabetes in inadequate glycaemic control.

Study design

The trial is a randomised, placebo-controlled, double-blinded, parallel group, multinational, multi-centre insulin capped trial designed for evaluation of the efficacy and safety of adding liraglutide (0.6 mg, 1.2 mg or 1.8 mg) versus placebo to insulin treatment in subjects with type 1 diabetes during 26 weeks of treatment. After a maximum of 2 weeks of screening, subjects will be randomised in a 3:3:3:1:1:1 manner to liraglutide treatment (0.6 mg, 1.2 mg or 1.8 mg), or corresponding volume of liraglutide placebo both adjunct to insulin treatment.

Intervention

Self-injection once daily with liraglutide or placebo 0.6 mg, 1.2 mg or 1.8 mg.

Study burden and risks

Subjects are requested to visit the trial site and attend telephone calls more often than during regular treatment and several assessments are part of standard diabetes care, but the frequency in the trial is higher. Hypoglycamia and adverse events could occur. Therefore the subject is closely followed at start of treatment and at dose increase, in order to adjust the insulin dose to the subjects individual needs. Subjects will be informed of the characteristic symptoms of acute pancreatitis and lipase, amylase and calcitonine will be monitored closely during the trial. Subjects are requested explicitly to take in plenty of fluids due to risk of gastrointestinal adverse events.
Liraglutide is registered for the use in diabetes type 2 and trial subjects may have therapeutic benefits.

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

-Informed consent obtained
-Male or female, aged *18 years
-Type 1 diabetes mellitus* 12 months
-Basal bolus or CSII (Continuous Subcutaneous Insulin Infusion, insulin pump) treatment * 6 months
- Stable insulin treatment for the last 3 month prior to Screening, as judged and documented by the investigator
- HbA1c 7.0-10% (53-86 mmol/mol) both inclusive

Exclusion criteria

- Prior use of glucagon-like peptide-1 (GLP-1) receptor agonist or dipeptidyl peptidase IV (DPP-4) inhibitors
- Use of any medication, which in the investigator*s opinion could interfere with the glycaemic control or affect the subject*s safety. Premix insulin is not allowed.
- Known proliferative retinopathy or maculopathy requiring acute treatment
- Severe neuropathy, in particular autonomic neuropathy, i.e. gastroparesis, as judged by the

investigator
- Uncontrolled/ untreated blood pressure at screening >160 mmHg for systolic or >100 mmHg for diastolic
- History of acute or chronic pancreatitis
- Screening calcitonin value * 50 ng/L
- Personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia type 2 (MEN2)
- Diagnosis of malignant neoplasm in the previous 5 years (except basal cell skin cancer or squamous cell skin cancer)

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-06-2014
Enrollment:	30
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Victoza
Generic name:	Liraglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	06-03-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-05-2014
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-05-2014
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2012-005778-74-NL
CCMO	NL47705.060.14