LEADER: Liraglutide Effect and Action in Diabetes Evaluation of cardiovascular outcome Results;A Long-term, Multi-centre, International, Randomised Double-blind, Placebo-controlled Trial to Determine Liraglutide Effects on Cardiovascular Events.

Published: 21-06-2010
Last updated: 30-04-2024

Primary objective:To assess the effect of treatment with liraglutide compared to placebo for at least 3.5 yearand up to 5 years on the incidence of cardiovascular events, as defined by the belowprimary and secondary endpoints, in adults with type 2...

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

Summary

ID

NL-OMON34550

Source
ToetsingOnline

Brief title
LEADER

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes Mellitus type 2, non insulin dependent diabetes

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Cardiovascular, GLP-1, Outcome, Type 2 diabetes

Outcome measures

Primary outcome

Primary Endpoint:

The primary objective will be addressed using the following primary endpoint:

Time from randomisation to first occurrence of cardiovascular death, non-fatal

myocardial

infarction, or non-fatal stroke (a composite cardiovascular outcome)

Secondary outcome

The following secondary endpoints will be used as supportive endpoints for the

primary objective:

• Time from randomisation to first occurrence of an expanded composite

cardiovascular

outcome, defined as either cardiovascular death, non-fatal myocardial

infarction, non-fatal

stroke, revascularisation, unstable angina or hospitalisation for chronic heart

failure

• Time from randomisation to all cause death

• Time from randomisation to each individual component of the expanded composite

cardiovascular outcome

The following secondary endpoints will be used as supportive endpoints for the

secondary

objective:

• Time from randomisation to first occurrence of a composite microvascular

outcome, defined

as either a need for retinal photocoagulation or vitreous haemorrhage or

diabetes-related

blindness or new or worsening nephropathy (defined as new onset of

macroalbuminuria, or

doubling of serum creatinine level and creatinine clearance per modification of

diet in renal

disease (MDRD) <= 45 mL/min/1.73m2, or the need for continuous renal-replacement

therapy

(in the absence of an acute reversible cause), or death due to renal disease)

• Time from randomisation to each individual component of the composite

microvascular

outcome

• Diabetic foot ulcer

• Change from baseline to the last assessment during the treatment period in:

* Weight and waist circumference

* HbA1c

* Blood lipids: total cholesterol, HDL-cholesterol, LDL-cholesterol and

triglycerides

* Blood pressure and pulse rate

* Selected aboratory parameters:

• Incidence of hypoglycaemic episodes

• Incidence of serious adverse events (SAE) and the following medical events of special interest (MESI): Neoplasm, Pancreatitis or acute, severe and persistent abdominal pain leading to a suspicion of pancreatitis, Acute gallstone disease (biliary colic or acute cholecystitis), First confirmed episode of calcitonin concentration increase >= 20 ng/L, Thyroid disease, Severe hypoglycaemic event, Immunogenicity event (antibody formation, allergic reactions, immunecomplex disease and injection site disorders), Adverse events leading to treatment discontinuation (if not any of the mentioned MESIs)

Study description

Background summary

The primary purpose of this trial is to determine the long-term effect of liraglutide on cardiovascular outcomes and other clinically important events.
The number of patients exposed to treatment and treatment duration will be substantially larger compared to the already completed phase 3 programme, which will enable the evaluation of liraglutide*s effects on clinically important outcomes: cardiovascular, microvascular and additional safety outcomes selected based on the information

derived
from the pre-registration programme.
The trial has been designed in order to accommodate the requirements contained in the
FDA guidance document *Evaluating Cardiovascular Risk in New Anti-diabetic Therapies
to Treat Type 2 Diabetes*
The trial will also determine the long-term effects of liraglutide on treatment surrogates,
namely glycaemic control, weight, waist circumference, lipid profile and blood pressure.

Study objective

Primary objective:
To assess the effect of treatment with liraglutide compared to placebo for at least 3.5 year
and up to 5 years on the incidence of cardiovascular events, as defined by the below
primary and secondary endpoints, in adults with type 2 diabetes that are at high risk for
cardiovascular events

Secondary objectives:
To assess the efficacy and safety with regard to clinically important events or other
surrogate parameters of treatment with liraglutide compared to placebo in adults with type
2 diabetes that are at high risk for cardiovascular events

Study design

The trial consist of a screening visit followed by a open label run-in period of two weeks. After the run-in period patients will be randomised to either treatment with liraglutide once daily injections or once daily placebo injections. The dosing of liraglutide or placebo will be increased per week (during a period of 3 weeks) from 0,6mg, 1,2mg up to a maximum 1,8mg. The treatment of liraglutide or placebo is in addition to the standard of care.

Intervention

Once daily injections with either liraglutide or once daily injections with placebo.

Study burden and risks

It's possible that bloodwithdrawals or self measurements of blood glucose values can cause haemorrhages or discomfort. If instructions of the pen injector are not followed or misused it's possible that patients administer the wrong dose of liraglutide or placebo. despite the fact that liraglutide's mode of action is glucose dependent there is a minor chance of experiencing low blood glucose values (hypo's). Local allergic reactions are possible or pain at the injection side is possible. The patient could experience side effects from liraglutide

Contacts

Public
Novo Nordisk

Flemingweg 18
2408 AV Alphen a/d Rijn
NL
Scientific
Novo Nordisk

Flemingweg 18
2408 AV Alphen a/d Rijn
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Men or women with type 2 diabetes
• Age >= 50 years at screening and concomitant cardiovascular, cerebrovascular or

peripheral
vascular disease or chronic renal failure or chronic heart failure OR age >= 60 years at screening and other specified risk factors of vascular disease
• HbA1c >= 7.0% at screening

Exclusion criteria

1.Type 1 diabetes
2. Use of a GLP-1 receptor agonist (exenatide, liraglutide or other) or pramlintide or any (dipeptidyl peptidase 4 (DPP-4) inhibitor within the 3 months prior to screening
3.Use of insulin other than human neutral protamine hagedorn (NPH) insulin or long-acting insulin analogue within 3 months prior to screening. Short-term use of other insulin during this
period in connection with intercurrent illness is allowed at Investigator*s discretion
4.Acute decompensation of glycaemic control requiring immediate intensification of treatment to
prevent acute complications of diabetes (e.g., diabetic ketoacidosis) in the previous 3 months
5.An acute coronary or cerebrovascular event in the previous 14 days
6. Current continuous renal replacement therapy
7.End-stage liver disease
8.Chronic heart failure NYHA IV
9.A prior solid organ transplant or awaiting solid organ transplant
10.Family or personal history of multiple endocrine neoplasia type 2 (MEN2) or familial medullary thyroid carcinoma (FMTC)
11.Personal history of non-familial medullary thyroid carcinoma
12. Malignant neoplasm requiring chemotherapy, surgery, radiation or palliative therapy in the
previous 5 years. Subjects with intraepithelial squamous cell carcinoma of the skin (Bowen*s disease) treated with topical 5-fluorouracil (5FU) and subjects with basal cell skin cancer are allowed to enter the trial

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):	07-02-2011
Enrollment:	175
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	21-06-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-12-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-01-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-02-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO	

Date:	19-07-2011
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	22-05-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-04-2013
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-06-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2009-012201-19-NL
CCMO	NL32383.091.10