A trial investigating the cardiovascular safety of oral semaglutide in subjects with type 2 diabetes

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

Summary

ID

NL-OMON43437

Source
ToetsingOnline

Brief title
PIONEER6 - Cardiovascular outcomes

Condition

- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
Diabetes, Diabetes Mellitus type 2

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cardiovascular endpoints, event-driven, oral once-daily GLP-1 receptor agonist, type 2 diabetes

Outcome measures

Primary outcome

The primary endpoint is time from randomisation to first occurrence of a MACE

composite endpoint consisting of: cardiovascular death, non-fatal myocardial

infarction or non-fatal stroke.

Secondary outcome

Key secondary endpoints:

* Time from randomisation to first occurrence of an expanded composite

cardiovascular

endpoint consisting of: cardiovascular death, non-fatal myocardial infarction,

non-fatal

stroke, unstable angina requiring hospitalisation or hospitalisation for heart

failure

* Time from randomisation to first occurrence of each of the individual

components in the

expanded composite cardiovascular endpoint

* Time from randomisation to first occurrence of a composite endpoint

consisting of: all-cause

death, non-fatal myocardial infarction or non-fatal stroke

Study description

Background summary

Semaglutide is in development for once-weekly subcutaneous injection and for oral once-daily treatment of T2D. This trial investigates the oral once-daily use (tablets). Semaglutide is a long-acting GLP-1 structurally similar to liraglutide (Victoza®), which is an once-daily GLP-1 receptor agonist developed by Novo Nordisk and approved worldwide for the treatment of T2D.
The purpose of this trial is to assess the cardiovascular safety of oral semaglutide in subjects with T2D at high risk of cardiovascular events. This trial has been designed to address the requirements contained in the US Food and Drug Administration (FDA) and European Medicines Agency (EMA) guidance documents which specify how to demonstrate that a new antidiabetic therapy is not associated with an unacceptable increase in cardiovascular risk.

Study objective

The primary objective is to confirm that treatment with oral semaglutide does not result in an unacceptable increase in cardiovascular risk compared to placebo (rule out 80% excess risk) in subjects with T2D at high risk of cardiovascular events.
The secondary objectives are to compare the efficacy and safety of oral semaglutide versus placebo in subjects with T2D at high risk of cardiovascular events.

Study design

This trial is a randomised, double-blind, placebo-controlled trial to assess the cardiovascular safety of oral semaglutide versus placebo when added to standard of care in subjects with type 2 diabetes at high risk of cardiovascular events. Subjects will be randomised 1:1 to receive either oral semaglutide or placebo. The trial will be event-driven and will be continued until at least 122 first major adverse cardiovascular events (MACEs) confirmed by adjudication have accrued. The treatment period for each subject is estimated to be between 12 and 19 months, depending on the time-point of recruitment and the accrual of first MACEs confirmed by adjudication.

Intervention

Daily administration of 3, 7 or 14 mg oral semaglutide/placebo tablets.

Study burden and risks

The safety profile for the investigational medicinal product generated from the

clinical and nonclinical development programme has not revealed any safety issues that would prohibit administration of oral semaglutide in accordance with the planned clinical trial.
Patients are requested to visit the trial site and to attend phone calls more often than during regular treatment. Several trial assessments are part of standard diabetes care, but the frequency in the trial is higher. Hypoglycaemia and (gastrointestinal) adverse events could occur. Therefor the subject is closely followed. As in the case with all protein based pharmaceuticals treatment with oral semaglutide may evoke allergic reactions. See section 18.1 of the protocol.

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

-Male or female diagnosed with type 2 diabetes (T2D)
-Age * 50 years at screening and presence of cardiovascular disease, or age * 60 years at screening and presence of at least one cardiovascular risk factor

Exclusion criteria

-Current or previous (within 90 days prior to screening) treatment with any GLP-1 receptor agonist, DPP-4 inhibitor or pramlintide
-Family or personal history of multiple endocrine neoplasia type 2 (MEN 2) or medullary thyroid carcinoma (MTC)
-History of pancreatitis (acute or chronic)
-History of major surgical procedures involving the stomach potentially affecting absorption of trial product (e.g. subtotal and total gastrectomy, sleeve gastrectomy, gastric bypass surgery)
-Subjects presently classified as being in New York Heart Association (NYHA) Class IV heart failure
-Planned coronary, carotid or peripheral artery revascularisation known on the day of screening
-Any of the following: myocardial infarction, stroke or hospitalisation for unstable angina or transient ischaemic attack within the past 60 days prior to screening
-Chronic or intermittent hemodialysis or peritoneal dialysis or severe renal impairment (corresponding to eGFR <30 mL/min/1.73 m2)
-History or presence of malignant neoplasms within the last 5 years (except basal and squamous cell skin cancer and carcinoma in situ)
-Proliferative retinopathy or maculopathy requiring acute treatment. Verified by fundus photography or dilated fundoscopy performed within 90 days prior to screening or within the period between screening and randomisation.

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):	17-01-2017
Enrollment:	75
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	oral semaglutide
Generic name:	oral semaglutide

Ethics review

Approved WMO Date:	15-03-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-05-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	02-06-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-08-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	12-08-2016

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-11-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-12-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-07-2017
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	04-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-04-2018
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	EUCTR2015-003563-10-NL
ClinicalTrials.gov	NCT02863419
CCMO	NL56580.091.16