SOUL: Semaglutide cardiovascular outcomes trial in patients with type 2 diabetes

Published: 08-05-2019
Last updated: 16-11-2024

The primary objective is to demonstrate that oral semaglutide lowers the risk of major adverse cardiovascular events compared to placebo, both added to standard of care in patients with type 2 diabetes and at high risk of cardiovascular events.The...

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

Summary

ID

NL-OMON55698

Source
ToetsingOnline

Brief title
SOUL

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

Intervention

Keyword: cardiovascular endpoints, Oral Semaglutide, Type 2 diabetes

Outcome measures

Primary outcome

The primary endpoint is time from randomisation to first occurrence of a major adverse cardiovascular event, a composite endpoint consisting of: cardiovascular death, non-fatal myocardial infarction or non-fatal stroke.

Secondary outcome

Time from randomisation to first occurrence of:

• A composite chronic kidney disease endpoint consisting of: cardiovascular death, renal death, onset of persistent >= 50% reduction in estimated glomerular filtration rate (CKD-EPI) compared with baseline, onset of persistent eGFR (CKD-EPI) < 15 mL/min/1.73 m2 or initiation of chronic renal replacement therapy (dialysis or kidney transplantation)

• cardiovascular death

• Major adverse limb events, a composite endpoint consisting of: acute limb ischemia hospitalisation or chronic limb ischemia hospitalisation

Study description

Background summary

The cardiovascular (CV) effect of oral semaglutide 14 mg once daily (OD) and s.c. semaglutide 0.5 and 1 mg once weekly were assessed in 2 CV outcomes trials (NN9924-4221, PIONEER 6 and NN9535-3744, SUSTAIN 6), each designed to rule out an 80% increased CV risk in patients with type 2 diabetes (T2D) at high risk for CV disease (CVD) in accordance with FDA guidance. PIONEER 6 demonstrated CV safety with a favourable point estimate. SUSTAIN 6 however demonstrated a

statistically significant 26% risk reduction with s.c. semaglutide compared with placebo for the primary endpoint (time from randomisation to first occurrence of a major adverse cardiovascular event (MACE) consisting of: CV death, non-fatal myocardial infarction (MI) or non-fatal stroke). Clinical pharmacology and clinical efficacy data indicate that the action of semaglutide is the same whether administrated via a subcutaneous injection or orally in a tablet. Hence, once semaglutide has entered systemic circulation, the properties and actions of the molecule are similar and independent of the route of administration. Accordingly it is hypothesised that oral semaglutide in the dose of 14 mg OD can reduce CV risk.
The current trial serves the purpose of confirming that oral semaglutide reduces the risk of MACE in patients with T2D and established CVD and/or chronic kidney disease (CKD).

Study objective

The primary objective is to demonstrate that oral semaglutide lowers the risk of major adverse cardiovascular events compared to placebo, both added to standard of care in patients with type 2 diabetes and at high risk of cardiovascular events.

The key secondary objectives are to compare the effects of oral semaglutide versus placebo, both added to standard of care in patients with type 2 diabetes and at high risk of cardiovascular events with regards to chronic kidney disease, cardiovascular events, peripheral artery disease, glycaemic control and body weight, and safety

Study design

This is a randomised, double-blind, parallel-group, placebo-controlled trial comparing oral semaglutide versus placebo both administered once daily and added to standard of care in patients with type 2 diabetes at high risk of cardiovascular events. Patients will be randomised 1:1 to receive either oral semaglutide or placebo

Intervention

Oral semaglutide 3 mg, 7 mg and 14 mg tablets or placebo tablets

Study burden and risks

Data from the clinical development programme for semaglutide has not revealed any safety issues that would outweigh the benefits. The trial population will consist of T2D patients with high risk of CV events. Assessment of diabetes and CV risk factors and appropriate attention to the standard of care treatment will be ensured throughout the trial. It is therefore concluded that the

potential benefits from the trial will outweigh the potential risks for the oral semaglutide as well as the placebo treated patients.

Contacts

Public
Novo Nordisk

Flemingweg 8
Alphen a/d Rijn 2408 AV
NL
Scientific
Novo Nordisk

Flemingweg 8
Alphen a/d Rijn 2408 AV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

-Male or female, age >=50 years at the time of signing informed consent
-Diagnosed with type 2 diabetes mellitus
-HbA1c 6.5% - 10.0% (47 - 86 mmol/mol) (both inclusive)
-At least one of the below conditions (a-d):
a) Coronary heart disease
b) Cerebrovascular disease
c) Symptomatic peripheral artery disease (PAD)

d) Chronic kidney disease

Exclusion criteria

-Any of the following: myocardial infarction, stroke, hospitalisation for unstable angina pectoris or transient ischaemic attack within the past 60 days prior to the day of screening
-Planned coronary, carotid or peripheral artery revascularisation known on the day of screening
-Heart failure presently classified as being in New York Heart Association Class IV
-Treatment with any glucagon-like peptide-1 receptor agonist within 30 days before screening

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:	Completed
Start date (anticipated):	29-08-2019
Enrollment:	200
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend

Generic name:	oral semaglutide

Ethics review

Approved WMO Date:	08-05-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-07-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-07-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-01-2021
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-06-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2024
Application type:	Amendment
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	EUCTR2018-003141-42-NL
ClinicalTrials.gov	NCT03914326
CCMO	NL69133.056.19