Semaglutide effects on cardiovascular outcomes in people with overweight or obesity

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON55704

Source
ToetsingOnline

Brief title
SELECT

Condition

- Other condition
- Cardiac disorders, signs and symptoms NEC

Synonym
cardiovascular disease, obesity

Health condition

obesitas en overgewicht, vaataandoening zoals beroerte en perifeer arterieel vaatlijden

Research involving
Human

Sponsors and support

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

Intervention

Keyword: cardiovascular disease, overweight/obesity, semaglutide 2.4 mg, subcutaneous once weekly

Outcome measures

Primary outcome

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

composite endpoint consisting of: CV death, non-fatal myocardial infarction, or

non-fatal stroke.

Secondary outcome

Confirmatory secondary endpoints

Time from randomisation to:

• CV death

• All-cause death

Study description

Background summary

Glucagon-like peptide-1 (GLP-1) is a physiological regulator of appetite and pharmacological levels of GLP-1 receptor agonists (RAs) have been shown to induce weight loss. Semaglutide is a next generation long-acting GLP-1 RA currently under development by Novo Nordisk.

Besides effects on appetite, GLP-1 regulates blood glucose by a glucose-dependent stimulatory effect on insulin- and inhibitory effect on glucagon secretion (i.e. when plasma glucose levels are above normal). GLP-1 has also several effects in the CV system. In the T2D development programme, the CV safety of semaglutide s.c. 0.5 mg and 1.0 mg once-weekly was assessed in

a pre-approval CV outcomes trial (SUSTAIN 6; NN9535-3744) in subjects with T2D and high CV risk. Semaglutide-treated subjects (0.5 and 1.0 mg dose groups combined) had a significant 26%
lower risk of the primary composite outcome of death from CV causes, nonfatal myocardialinfarction (MI), or nonfatal stroke than did those receiving placebo (hazard ratio (HR): 0.74 [0.58; 0.95] 95%CI). The exact mechanism behind the CV effect of semaglutide is not known. However, both pre-clinical and clinical studies suggest that GLP-1 RAs, including semaglutide1, have direct and beneficial effects on the CV system (including reductions in lipid levels and blood pressure as well as anti-inflammatory effects) resulting in attenuation of atherosclerosis. Weight loss of the magnitude seen in the recent phase 2 dose-finding trial in subjects with obesity (BMI >= 30 kg/m2) (trial NN9536-4153) might also lower CV risk independently. Specifically, semaglutide s.c. in doses of 0.05 to 0.4 mg once-daily was accompanied by an improvement in CV risk factors. Semaglutide s.c. 2.4 mg once-weekly is currently also in phase 3a development for weightmanagement.

In summary, these data indicate that semaglutide s.c. has beneficial effects on the CV system. Accordingly, semaglutide s.c. may target an unmet medical need in subjects with established CV disease and overweight or obesity.

Study objective

The primary objective
-To demonstrate that semaglutide 2.4 mg once weekly lowers the incidence risk of major adverse cardiovascular events (MACE) versus semaglutide placebo, both added to standard of care in patients with established CV disease and overweight or obesity.
Key secondary objective
To compare the effect of semaglutide 2.4 mg once weekly versus semaglutide placebo, both added to standard of care in patients with established CV disease and overweight or obesity with regards to:
• Mortality

Study design

This is a randomised, double-blind, parallel group, placebo-controlled trial comparing semaglutide 2.4 mg with semaglutide placebo both administered s.c. once weekly in patients with established CV disease and overweight or obesity. Subjets will be randomised in a 1:1 ratio to receive either semaglutide 2.4 mg or semaglutide placebo as an adjunct to standard-of-care.
The trial is event driven; therefore, end of trial will be scheduled according to projected trial closure. Trial duration is expected to be up to 59 months following randomisation.

Intervention

Once weekly semaglutide/placebo subcuteneous injection, dose 2.4 mg.

Study burden and risks

Data from the development programme for semaglutide for the T2D indication has not revealed any safety issues that would outweigh the benefits. The recently completed phase 2 programme with semaglutide s.c. in obesity did not reveal any new safety issues either. The trial population will consist of subjects with established CV disease and overweight or obesity. Assessment and treatment of the subjects* CV risk factors, including overweight or obesity, and with appropriate attention to the standard of care treatment will be provided throughout the trial. It is therefore concluded that the potential benefits from the trial will outweigh the potential risks for the semaglutide as well as the placebo treated subjects.

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, age >= 45 years at the time of signing informed consent
* Body mass index (BMI) >= 27 kg/m2
* Have established CV disease as evidenced by at least one of the following: prior myocardial infarction, prior stroke (ischemic and hemorrhagic stroke) or symptomatic peripheral arterial disease (PAD, as evidenced by intermittent claudication with ankle-brachial index (ABI) < 0.85 (at rest), or peripheral arterial revascularization procedure, or amputation due to atherosclerotic 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
* HbA1c >= 48 mmol/mol (6.5%) as measured by the central laboratory at screening
* History of type 1 or type 2 diabetes (history of gestational diabetes is allowed).

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):	19-02-2019
Enrollment:	250
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not yet known
Generic name:	semaglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-12-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	30-01-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	26-11-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-12-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-10-2020
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-02-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-05-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-07-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	18-08-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-12-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	07-06-2022
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-06-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-08-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-10-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-01-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2017-003380-35-NL
CCMO	NL65655.042.18