Effect of semaglutide versus placebo on the progression of renal impairment in subjects with type 2 diabetes and chronic kidney disease

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

Summary

ID

NL-OMON54810

Source
ToetsingOnline

Brief title
FLOW

Condition

- Diabetic complications
- Nephropathies

Synonym
chronic kidney disease, kidney damage

Research involving
Human

Sponsors and support

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

Intervention

Keyword: chronic kidney disease, diabetes type 2, semaglutide

Outcome measures

Primary outcome

The primary endpoint is time to first occurrence of a composite endpoint consisting of: Onset of persistent >= 50% reduction in estimated glomerular filtration rate (eGFR) (CKD-EPI) compared with baseline, onset of persistent eGFR (CKD-EPI) < 15 mL/min/1.73 m2, initiation of chronic renal replacement therapy (dialysis or kidney transplantation), renal death, or cardiovascular death.

Secondary outcome

The key secondary endpoints are annual rate of change in eGFR (CKD-EPI) (total eGFR slope), time to first occurrence of a composite major adverse cardiovascular event (MACE) endpoint (consisting of: non-fatal myocardial infarction, non-fatal stroke, CV death) and all-cause death.

Study description

Background summary

Chronic kidney disease (CKD) and diabetes often co-exist and for the majority of cases, the kidney damage and/or reduced kidney function is caused directly by longstanding and poorly controlled diabetes. Improved glycaemic control has been suggested to reduce the progression of CKD in type 2 diabetes (T2D) and both glycaemic and blood pressure control are key recommendations in

international treatment guidelines for CKD in T2D. Yet there remains a major unmet medical need to improve the treatment of CKD in patients with T2D. The purpose of this trial is to demonstrate that semaglutide subcutaneously (s.c.) delays the progression of renal impairment and lowers the risk of renal and cardiovascular (CV) mortality in subjects with T2D and CKD.

Study objective

The primary objective is to demonstrate that semaglutide delays the progression of renal impairment and lowers the risk of renal and cardiovascular mortality compared to placebo, both added to standard-of-care, in subjects with type 2 diabetes and chronic kidney disease.
The key secondary objectives are to compare the effect of treatment with semaglutide versus placebo, both added to standard-of-care in subjects with type 2 diabetes and chronic kidney disease with regards to cardiovascular morbidity, peripheral artery disease, glycaemic control, body weight, blood pressure and safety.

Study design

This is a multi-centre, international, randomised, double-blind, parallel-group, placebo-controlled trial comparing semaglutide 1.0 mg versus placebo both administered s.c. once weekly and added to standard-of-care in subjects with T2D and pre-existing CKD. Subjects will be randomised 1:1 to receive either semaglutide or placebo. Randomisation will be stratified by use of sodium glucose cotransporter-2 (SGLT-2) inhibitors (yes versus no) at baseline. The number of subjects with inclusion eGFR >= 60 mL/min/1.73 m2 will be capped at 20%.

Intervention

Once weekly semaglutide/placebo as subcutaneous injection, 1.0 mg.

Study burden and risks

Data from the development programme for semaglutide has not revealed any safety issues that would outweigh the benefits of participation in this trial. The trial population will consist of T2D subjects with CKD. Assessment of diabetes and CKD and appropriate attention to the standard-of-care treatment will be provided throughout the trial. It is therefore concluded that the potential benefits from trial participation 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 18 years or older at the time of signing informed consent. Japan: 20 years;
- Diagnosed with type 2 diabetes mellitus;
- HbA1c (glycated haemoglobin) equal to or below 10% (equal to or below 86 mmol/mol);
- Renal impairment defined either by;
a) serum creatinine-based eGFR (estimated glomerular filtration rate) equal to or above 50 and equal to or below 75 mL/min/1.73 m^2 (chronic kidney disease - epidemiology collaboration, CKD-EPI) and UACR (urinary albumin-to-creatinine ratio) above 300 and below 5000 mg/g
or
b) serum creatinine-based eGFR equal to or above 25 and below 50 mL/min/1.73

m^2 (CKD-EPI) and UACR above 100 and below 5000 mg/g;
- Treatment with maximum labelled or tolerated dose of a renin-angiotensin-aldosterone;
system (RAAS) blocking agent including an angiotensin converting enzyme (ACE) inhibitor or an angiotensin II receptor blocker (ARB), unless such treatment is contraindicated or not tolerated. Treatment dose must be stable for at least 4 weeks prior to the date of the laboratory assessments used for determination of the inclusion criteria for renal impairment and kept stable until screening.

Exclusion criteria

- Congenital or hereditary kidney diseases including polycystic kidney disease, autoimmune kidney diseases including glomerulonephritis or congenital urinary tract malformations;
- Use of any glucagon-like peptide-1 (GLP-1) receptor agonist within 30 days prior to screening;
- Myocardial infarction, stroke, hospitalisation for unstable angina pectoris or transient ischaemic attack within 60 days prior to the day of screening;
- Presently classified as being in New York Heart Association (NYHA) Class IV heart failure;
- Planned coronary, carotid or peripheral artery revascularisation;
- Current (or within 90 days) chronic or intermittent haemodialysis or peritoneal dialysis;
- Uncontrolled and potentially unstable diabetic retinopathy or maculopathy. Verified by a fundus examination performed within the past 90 days prior to screening or in the period between screening and randomisation. Pharmacological pupil-dilation is a requirement unless using a digital fundus photography camera specified for non-dilated examination

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):	24-07-2019
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ozempic
Generic name:	Semaglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-02-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2019
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	09-09-2019
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-02-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	08-09-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	29-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-01-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-05-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-07-2023

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-09-2023
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	EUCTR2018-002878-50-NL
ClinicalTrials.gov	NCT03819153
CCMO	NL68794.056.19