The cardiovascular safety of efficacy cagrilintide 2.4 mg s.c. in combination with semaglutide 2.4 mg s.c. (CagriSema 2.4 mg/2.4 mg s.c.) once-weekly in participants established cardiovascular disease

Published: 18-01-2023
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This study has been transitioned to CTIS with ID 2023-506924-94-00 check the CTIS register for the current data. Primary: to confirm non-inferiority of CagriSema 2.4 mg/2.4 mg versus placebo with respect to time to first major adverse cardiovascular...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac disorders, signs and symptoms NEC
Study type	Interventional

Summary

ID

NL-OMON55925

Source
ToetsingOnline

Brief title
Redefine 3

Condition

- Cardiac disorders, signs and symptoms NEC

Synonym
cardiovascular disease

Research involving

Human

Sponsors and support

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

Intervention

Keyword: cagrilintide, cardiovascular safety, once-weekly, semaglutide

Outcome measures

Primary outcome

Time to first occurrence of MACE (a composite endpoint consisting of CV death, non-fatal myocardial infarction and non-fatal stroke) from baseline (week 0) to end of study (up to 242 weeks or more).

Secondary outcome

Time to first occurrence of MACE (a composite endpoint consisting of CV death, non-fatal myocardial infarction and non-fatal stroke) from baseline (week 0) to end of study (up to 242 weeks or more).

Study description

Background summary

Cagrilintide is a new active substance and considered a *first in class* medicinal product in the EU, therefore, a dedicated CV outcome study to evaluate the CV safety profile is required by the EMA. The study has been designed to address requirements contained in the EMA reflection paper for evaluation of the CV safety profile of new medicinal products that are intended for long-term treatment of certain CV and metabolic diseases.
The primary purpose of this study is to investigate the long-term CV safety of CagriSema as fixed dose combination of cagrilintide and semaglutide in participants with established CVD. Secondly, the study will investigate the efficacy of CagriSema on CV risk reduction.

Study objective

This study has been transitioned to CTIS with ID 2023-506924-94-00 check the CTIS register for the current data.

Primary: to confirm non-inferiority of CagriSema 2.4 mg/2.4 mg versus placebo with respect to time to first major adverse cardiovascular event (MACE).

Secondary: to confirm superiority of CagriSema 2.4 mg/2.4 mg versus placebo with respect to time to first MACE.

Study design

The study consists of a screening period to assess the participant*s eligibility, an up to 235-week treatment period (including a 16-week dose escalation period) and a 7-week follow-up period. The total study duration for each participant will be up to approximately 245 weeks (up to 3 weeks screening, up to 235 weeks treatment and 7 weeks follow-up). The study is event driven; therefore, end of study will be scheduled according to projected study closure. Study duration is expected to be up to approximately 4.5 years following randomisation of the first participant.

Intervention

Participants will be randomised 1:1 to once weekly subcutaneous injection of CagriSema 2.4 mg/2.4 mg, or placebo.
The DV3384 pen-injector is a dual chamber single-dose device. The DV3384 pen-injector administers the two products as a single dose.

Study burden and risks

The study population will consist of participants with established CVD, BMI >=25 kg/m2, with or without T2D and/or CKD. Assessment and treatment of the participants' CV risk factors and appropriate attention to the standard of care treatment will be provided throughout the study. Taking into account the measures taken to minimise risk and burden to participants in this study, the potential risks identified in association with CagriSema are justified by the anticipated benefits that may be afforded to participants with established CVD with or without comorbidities such as obesity, overweight, T2D and CKD.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Male or female
- Age above or equal to 55 years at the time of signing informed consent.
- Body mass index (BMI) above or equal 25.0 kg/m2
- Established CVD as evidenced by at least one of the following:
Prior myocardial infarction
Prior stroke (ischemic or haemorrhagic stroke)
- Symptomatic peripheral arterial disease (PAD) defined as at least one of the following:
a. Intermittent claudication with an Ankle-brachial index (ABI) below 0.85 at rest
b. Intermittent claudication with a above or equal 50% stenosis in a lower extremity peripheral artery documented by X-ray angiography, MR angiography, CT angiography or Doppler ultrasound
c. Prior revascularization procedure of a lower extremity peripheral artery
d. Lower extremity amputation at or above ankle due to atherosclerotic disease (excluding e.g., trauma or osteomyelitis)

For participants with T2D at screening the following inclusion criteria also apply:

- Diagnosed with type 2 diabetes mellitus (T2D) above or equal to 180 days before screening
- HbA1c 6.5%-10% (48-86 mmol/mol) (both inclusive), as measured by central laboratory at screening.
- Treatment with either:
a. Lifestyle intervention alone
b. 1-3 marketed oral antidiabetic drugs (OAD)s (metformin, α-glucosidase inhibitors (AGI), glinides, sodium-glucose co-transporter 2 inhibitor (SGLT2i), DPP4-inhibitors, thiazolidinediones, or sulphonylureas (SU) as a single agent or in combination) according to local label
c. Basal insulin alone or in combination with up to two marketed OADs (refer to b. above), all according to local label

Exclusion criteria

- Myocardial infarction, stroke, hospitalization for unstable angina pectoris or transient ischaemic attack within 60 days before screening
- Planned coronary, carotid or peripheral artery revascularisation known on the day of screening
- Heart failure classified as being in New York Heart Association (NYHA) Class IV at screening
- Treatment with any GLP-1 RA or a medication with GLP-1 activity within 90 days before screening
- End stage renal disease defined as eGFR below 15 mL/min/1.73 m^2, as measured by the central laboratory at screening
- Chronic or intermittent haemodialysis or peritoneal dialysis

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:	Recruiting
Start date (anticipated):	25-04-2023
Enrollment:	160
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet bekend
Generic name:	cagrilintide
Product type:	Medicine
Brand name:	Wegovy
Generic name:	semaglutide
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	18-01-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-04-2023
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2023

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	24-10-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-11-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-12-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2024
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
EU-CTR	CTIS2023-506924-94-00
EudraCT	EUCTR2021-005855-35-NL
CCMO	NL82617.056.22
Other	UTN: U1111-1270-0943