Investigation of the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple doses of NNC0480-0389 in combination with semaglutide s.c.

Published: 08-01-2020
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The purpose of this study is to investigate how safe, and how well tolerated, the new study drug NNC0480-0389 is when it is given together with semaglutide. It will also be investigated how quickly and to what extent NNC0480-0389 and semaglutide are...

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

Summary

ID

NL-OMON55332

Source
ToetsingOnline

Brief title
SAD and MAD of NNC0480-0389 in combination with semaglutide

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Glucose metabolism disorders (incl diabetes mellitus)

Synonym
diabetes

Research involving
Human

Sponsors and support

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

Intervention

Keyword: NNC0480-0389, pharmacodynamics, pharmacokinetics, safety

Outcome measures

Primary outcome

SAD part

To investigate the safety and tolerability of single doses of NNC0480-0389

subcutaneously coadministered

with semaglutide in healthy male subjects.

MAD part

To investigate the safety and tolerability of multiple doses of NNC0480-0389

subcutaneously

co-administered with semaglutide in healthy subjects

Secondary outcome

SAD part

To investigate the pharmacokinetics of NNC0480-0389 upon subcutaneous

co-administration of single doses of NNC0480-0389 and semaglutide in healthy

male subjects

MAD part:

To investigate the pharmacokinetics of NNC0480-0389 upon subcutaneous

co-administration of multiple doses of NNC0480-0389 and semaglutide in healthy subjects

MAD/POC part

To investigate the safety and tolerability of multiple doses of NNC0480-0389 subcutaneously co-administered with semaglutide in subjects with type 2 diabetes

To investigate the pharmacokinetics of NNC0480-0389 upon subcutaneous co-administration of multiple doses of NNC0480-0389 and semaglutide in subjects with type 2 diabetes

Study description

Background summary

People with diabetes have too much sugar in their blood and need treatment to control their sugar level. The study drug (NNC0480-0389) acts like a hormone called glucose-dependent insulinotropic peptide (GIP), which occurs naturally in the human body. GIP is released by the intestines. Semaglutide is a newly approved antidiabetic medicine that helps to lower blood sugar levels in patients with type 2 diabetes. In addition to the treatment of type 2 diabetes, semaglutide is currently also being developed for weight loss treatment for obesity. NNC0480-0389 is being developed to be given together with semaglutide. NNC0480-0389 targets a different part of the system that regulates glucose levels in the body than semaglutide. Therefore, it is expected that together NNC0480-0389 and semaglutide will more effectively lower glucose levels in blood.

Study objective

The purpose of this study is to investigate how safe, and how well tolerated, the new study drug NNC0480-0389 is when it is given together with semaglutide. It will also be investigated how quickly and to what extent NNC0480-0389 and

semaglutide are taken up and eliminated from the body.

Study design

This first human dose trial is a two part, single-centre, placebo-controlled, double-blinded, randomised, single ascending dose (SAD) and multiple ascending dose (MAD) trial with a sequential trial design, and a proof-of-concept (PoC) cohort. The study will be performed in 3 parts in a total of 156 healthy participants, 60 healthy male participants (Part 1), 66 healthy male and female participants (Part 2) and 30 male and female patients with type 2 diabetes (Part 3).

Intervention

NNC0480-0389 (1.7, 8.6, 43 or 60 mg) and/or semaglutide (0.5 mg) and/or placebo will be given as injections subcutaneous.

Study burden and risks

NNC0480-0389 has not been tested in humans before. Side effects have therefore not been observed in humans and we do not know whether or how often these side effects may happen.

- Hypersensitivity reactions
Hypersensitivity reactions may occur upon injection of a medicine. Hypersensitivity reactions may show as local skin problems at the injection site or allergic reactions.
Signs at the injection site may include:
- bruising
- pain and discomfort
- redness
- swelling
- itching
The problems usually go away after a few days.

Allergic reactions
Signs of mild allergic reactions may include:
- rash
- redness
- hives
- itching.

Signs of a serious allergic reaction may include:
- swelling of your throat, tongue and/or face
- trouble breathing
- wheezing

- fast heartbeat
- pale and cold skin
- feeling dizzy or weak.

Allergic reactions may become severe and can lead to shock and/or death if not treated.

- Fast heartbeat
In animal studies a fast heartbeat has been seen for 1-2 days after receiving a treatment with NNC0480-0389.

- Reddening of skin and gums
In animal studies reddening of skin or gums during treatment with NNC0480-0389 has been seen. This might be related to dilatation of small blood vessels which has been reported as an effect of GIP.

- Low blood pressure
In animal studies a small lowering of blood pressure has been seen within 5-10 hours after treatment with NNC0480-0389.

Semaglutide
Semaglutide has been extensively studied in healthy volunteer. diabetic and obese patients. The following side effects are most frequently observed (may affect more than 1 out of 10 people):
Stomach and gut problems. Signs may include:
- feeling sick
- diarrhea

The stomach and gut problems are usually mild to moderate. These side effects most often happen at the start of the treatment.

Possible discomforts due to procedures
During this study, small amounts of blood will be taken. This allows the study doctor to see how the volunteer is doing and if the study medicine works.
- The volunteer may feel a little discomfort, bruising, bleeding or swelling where the needle goes in.
- There is also a very small risk of infection where the needle goes in.

In total, we will take about 250 milliliters of blood from the volunteer. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken each time.

When making a recording of the electrical activity of your heart by an electrocardiogram, the skin may react to the sticky electrode patches. Any skin irritation usually disappears when the patches are removed.

A sample for the coronavirus test will be taken from the back of the nose and

throat using a swab. Taking the sample only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Novo Nordisk

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DK
Scientific
Novo Nordisk

Novo Allé 1
Bagsvaerd 2880
DK

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

SAD part
- Male aged 18-45 years (both inclusive) at the time of signing informed consent.
- BMI between 20.0 kg/m2 and 29.9 kg/m2 (both inclusive).

MAD part (not applicable for PoC cohort)
- BMI between 20.0 kg/m2 and 29.9 kg/m2 (both inclusive).
- Female of non-childbearing potential or male aged 18-55 years (both inclusive) at the time of signing informed consent.

MAD part (only applicable for PoC cohort)
- BMI between 25.0 kg/m2 and 39.9 kg/m2 (both inclusive). Overweight or obesity should be due to excess adipose tissue, as judged by the investigator.
-Female of non-childbearing potential or male aged 18-64 years (both inclusive) at the time of signing informed consent.
-Subjects treated with diet and exercise as monotherapy or in combination with 1-2 of the following anti-diabetic drug(s) at a stable dose for at least 30 days prior to screening: metformin, sulfonylureas, meglitinides, DPP-4 inhibitors, alpha-glucosidase inhibitors,
thiazolidinediones, GLP-1 receptor agonists or SLGT-2 inhibitors. The metformin dose should be >= 1500 mg to <= 3000 mg or maximum tolerated or effective dose documented in subject's medical record.

Exclusion criteria

- Any disorder (except for conditions associated with T2D for the PoC cohort included in the MAD part) which in the investigator*s opinion might jeopardise subject*s safety or compliance with the protocol.
- HbA1c >= 6.5 % (48 mmol/mol) at screening (except for MAD part only applicable for PoC cohort).
- Use of prescription medicinal products or non-prescription drugs, except routine vitamins,
occasional use of acetaminophen, ibuprofen and acetylsalicylic acid, or topical medication not
reaching systemic circulation within 14 days prior to the day of screening (except for the MAD part only applicable for PoC cohort).

Study design

Design

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):	17-02-2020
Enrollment:	156
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	08-01-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-03-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-03-2020
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-09-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-10-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	05-03-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-04-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-05-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-07-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-08-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-04-2022
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	EUCTR2019-002857-44-NL
CCMO	NL72389.056.19

Study results

Date completed: 16-03-2022

Results posted: 03-05-2023

First publication
01-01-1900