The effect of semaglutide in non-cirrhotic non-alcoholic steatohepatitis

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This study has been transitioned to CTIS with ID 2023-506962-30-00 check the CTIS register for the current data. Primary objectivesThe trial has two parts, a part 1 and a part 2, with distinctive objectives and endpoints.Part 1 of the trial: To...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON54111

Source
ToetsingOnline

Brief title
ESSENCE

Condition

- Hepatic and hepatobiliary disorders

Synonym
non-alcoholic liver inflammation, non-alcoholic steatohepatitis

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Fibrose F2-F3, non-alcoholic steatohepatitis (NASH), once weekly, Semaglutide

Outcome measures

Primary outcome

Primary endpoint

Part 1 (two separate endpoints):

Resolution of steatohepatitis and no worsening of liver fibrosis - From randomisation (week 0) to week 72

Improvement in liver fibrosis and no worsening of steatohepatitis - From randomisation (week 0) to week 72

Part 2:

Time to first liver-related clinical event (composite endpoint) - From randomisation (week 0) to week 240

Secondary outcome

Secondary confirmatory endpoint

Progression of liver fibrosis - From randomisation (week 0) to week 72

Change in body weight - From randomisation (week 0) to week 72

Change in SF-36 Bodily Pain - From randomisation (week 0) to week 72

Change in body weight - From randomisation (week 0) to week 240

Study description

Background summary

Non-alcoholic steatohepatitis (NASH) is associated with increased risk of morbidity and mortality. Currently, treatment options are few and insufficient. There is therefore an unmet medical need for effective and safe pharmacological treatments options. Semaglutide, a glucagon-like peptide-1 receptor agonist (GLP-1 RA), has the potential to address metabolic and histological aspects of NASH and is therefore considered a strong candidate for the treatment of NASH.

Study objective

This study has been transitioned to CTIS with ID 2023-506962-30-00 check the CTIS register for the current data.

Primary objectives
The trial has two parts, a part 1 and a part 2, with distinctive objectives and endpoints.
Part 1 of the trial: To demonstrate that treatment with semaglutide s.c. improves liver histology compared to placebo in subjects with NASH and fibrosis stage 2 or 3.
Part 2 of the trial: To demonstrate that treatment with semaglutide s.c. lowers the risk of liverrelated clinical events compared to placebo in subjects with NASH and fibrosis stage 2 or 3.

Secondary objectives
To demonstrate that treatment with semaglutide s.c. lowers body weight compared to placebo in subjects with NASH and fibrosis stages 2 or 3.
To demonstrate that treatment with semaglutide s.c. 2.4 mg improves patient-reported outcomes compared to placebo in subjects with NASH and fibrosis stages 2 or 3.
To compare the effects of semaglutide s.c. 2.4 mg versus placebo on cardiovascular disease and cardio-metabolic factors in subjects with NASH and fibrosis stages 2 or 3
To compare the effect of semaglutide s.c. versus placebo on biomarkers related to fibrosis in subjects with NASH and fibrosis stages 2 or 3.

Study design

This is a randomised, multicentre, double-blinded, parallel-group trial comparing semaglutide s.c. once-weekly versus placebo in subjects with NASH and fibrosis stage 2 or 3.

The total trial duration for each subject is approximately 257 weeks (~4 years and 11 months). This includes a screening period of approximately 10 weeks followed by randomisation and a 240-week treatment period. The follow-up period is 7 weeks.
Subjects will be randomised 2:1 to receive treatment with semaglutide s.c. or placebo. The randomisation will be stratified based on the presence of type 2

diabetes (T2D) at screening, fibrosis stage and region. For both semaglutide s.c. and placebo there will be a period of dose escalation before reaching the target dose administrated subcutaneously once-weekly. All subjects must aim at reaching the recommended target dose of semaglutide.

Intervention

Once weekly subcutaneous semaglutide injection 2.4mg.

Study burden and risks

Necessary precautions have been implemented in the design and planned conduct of the trial to minimise the risks and inconveniences of participation. The safety profile for semaglutide has not revealed any safety issue that would prohibit administration of semaglutide in patients with NASH. On the contrary, previous studies suggest that semaglutide could provide clinically meaningful treatment effects for patients with NASH. Assessment of NASH and appropriate attention to the standard-of care treatment will be provided throughout the trial. Therefore, although there is a small risk associated with performing a liver biopsy, it is concluded that the potential benefits of trial participation will outweigh the potential risks for both semaglutide- and 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

- Age above or equal to 18 years at the time of signing informed consent.
- Histological evidence of NASH based on a central pathologist evaluation of the baseline liver biopsy. The baseline liver biopsy can be a historical biopsy obtained within 180 days prior to screening visit (V1).
- Histological evidence of fibrosis stage 2 or stage 3 according to the NASH CRN classification based on a central pathologist evaluation of the baseline liver biopsy.
- A histological NAS >= 4 with a score of 1 or more in both steatosis, lobular inflammation and hepatocyte ballooning based on a central pathologist evaluation of the baseline liver biopsy.

Exclusion criteria

- Positive HBsAg, positive anti-HIV, positive HCV-RNA at screening or any known presence of HCV RNA or HBsAg within 2 years of screening (V2A).
- Documented causes of chronic liver disease other than Non-Alcoholic Fatty Liver Disease NAFLD.
- Presence or history of ascites, variceal bleeding, hepatic encephalopathy, spontaneous bacterial peritonitis or liver transplantation at randomisation.
- Known or suspected excessive consumption of alcohol (>20 g/day for women or >30 g/day for men) or alcohol dependence (assessed by the Alcohol Use Disorders Identification Test (AUDIT questionnaire).
- Treatment with vitamin E (at doses >=800 IU/day) or pioglitazone or medications approved for treatment of NASH which has not been at a stable dose in the opinion of the investigator in the period from 90 days prior to the screening visit (V2A). In addition, for subjects with historical liver biopsies taken more than 90 days prior to screening, treatment should be at a stable dose in the opinion of the investigator from time of biopsy until screening.
- Treatment with GLP-1 RAs in the period from 90 days prior to the screening visit (V2A). In addition, for subjects with historical liver biopsies taken more than 90 days prior to screening, any treatment with GLP-1 RAs from time of

biopsy until screening.
- Treatment with glucose lowering agent(s) (other than GLP-1 RAs), lipid lowering medication or weight loss medication not stable in the opinion of the investigator in the period from 90 days prior to the screening visit (V2A). In addition, for subjects with historical liver biopsies taken more than 90 days prior to screening, treatment should be at a stable dose in the opinion of the investigator from time of biopsy until 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:	Recruiting
Start date (anticipated):	01-04-2021
Enrollment:	10
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	24-12-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-02-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-08-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-04-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO	

Date:	09-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	13-01-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	23-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Approved WMO

Date:	31-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam

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Approved WMO
Date: 21-04-2023

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 05-07-2023

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 18-08-2023

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 08-12-2023

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 19-01-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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Approved WMO
Date: 01-03-2024

Application type: Amendment

Review commission: MEC Academisch Medisch Centrum (Amsterdam)

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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	CTIS2023-506962-30-00
EudraCT	EUCTR2019-004594-44-NL
CCMO	NL75689.018.20