Safety, tolerability, pharmacokinetics and pharmacodynamics of single rising subcutaneous doses of BI 3006337 in healthy male subjects (single-blind, partially randomised within dose groups, placebo-controlled, parallel (sequential) group design)

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Ethical review	Approved WMO
Status	Completed
Health condition type	Metabolism disorders NEC
Study type	Interventional

Summary

ID

NL-OMON51833

Source
ToetsingOnline

Brief title
A study to test how well men tolerate different doses of BI 3006337

Condition

- Metabolism disorders NEC

Synonym
Liver disease

Research involving
Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: Pharmaceutical Industry

Intervention

Keyword: BI3006337, Healthy Volunteers, non-alcoholic liver inflammation

Outcome measures

Primary outcome

To investigate safety, tolerability and pharmacokinetics of single doses of BI

3006337 in healthy male subjects

Secondary outcome

Not applicable.

Study description

Background summary

BI 3006337 is a new compound that may potentially be used for the treatment of non-alcoholic liver inflammation (NASH). NASH is a common liver disease that occurs when the liver becomes inflamed due to the build-up of fat in the liver. If the liver damage continues for a long time, scarring can develop in the liver. This is also known as 'cirrhosis'. People with NASH have an increased risk of developing liver cancer.

BI 3006337 combines the activity of 2 different hormone systems that are naturally present in the body, the so called glucagon-like peptide 1 (GLP-1) and fibroblast growth factor 21 (FGF21). GLP-1 is released in the intestines and plays an important role in regulating the glucose metabolism. The hormone FGF21 released by the liver plays a key role in the energy metabolism and stimulates the burning of fat in the liver. It is assumed that the combined effect of both hormones can have a positive impact on the above-mentioned NASH.

Study objective

In this study we investigate how safe the new drug BI 3006337 is and how well it is tolerated when used in healthy subjects.

We also investigate how quickly and to what extent BI 3006337 is absorbed, transported and excreted by the body. We also look at the effect of BI 3006337 on certain biomarkers in the blood.

We compare the effects of BI 3006337 with the effects of a placebo.

BI 3006337 has not been administered to humans before. It has been extensively tested in the laboratory and on animals. BI 3006337 is tested in different strengths.

Study design

The study lasts a maximum of 9 weeks from the inspection to the follow-up check.

In total, volunteers visit the research center 10 times:

Once for the inspection
Once for a stay at the research center. For the research it is necessary to stay in the research center for 1 period of 6 days (5 nights). We expect the volunteer 2 days prior to the administration of the study drug at the study center (Day -2).
Day 1 is the day on which the study drug is received.

One leaves the research center on Day 4 of the research.
After the stay in the research center there are 7 short visits to the research center.
They come one more time for the check-up.

They will be given BI 3006337 or placebo as a subcutaneous injection into a raised skin fold of your abdomen while lying down. After that, the volunteer must also remain in bed for at least 30 minutes.

Intervention

Group 1, Day 1, BI 3006337 0.2 mg (6 subjects) or placebo (2 subjects) once
Group 2, Day 1 BI 3006337 0.5 mg (6 subjects) or placebo (2 subjects) once
Group 3, Day 1 BI 3006337 1 mg (6 subjects) or placebo (2 subjects) once
Group 4, Day 1 BI 3006337 2 mg (6 subjects) or placebo (2 subjects) once
Group 5, Day 1 BI 3006337 4 mg (6 subjects) or placebo (2 subjects) once
Group 6, Day 1 BI 3006337 8 mg (6 subjects) or placebo (2 subjects) once
Group 7, Day 1 BI 3006337 15 mg (6 subjects) or placebo (2 subjects) once
Group 8, Day 1 BI 3006337 30 mg (6 subjects) or placebo (2 subjects) once
Group 9, Day 1 BI 3006337 50 mg (6 subjects) or placebo (2 subjects) once

Group 10, Day 1 BI 3006337 100 mg (6 subjects) or placebo (2 subjects) once
Group 11, Day 1 BI 3006337 150 mg (9 subjects) or placebo (3 subjects) once

Study burden and risks

Blood draw
Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment (bruising) of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, sweating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 500 milliliters (mL) of blood from you from screening to follow-up. This amount does not cause any problems in adults. If the investigator thinks it is necessary for the safety of a subject, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes will be placed on your arms, chest and legs. To monitor the electrical activity of your heart over a longer period, electrodes will be placed on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Fasting
If you have to fast for a prolonged time during the study, this may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
Samples for the coronavirus test will be taken from the back of your nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of your throat may cause you to gag. When the sample is taken from the back of your nose, you may experience a stinging sensation and your eyes may become watery.

Stomach emptying test
Drinking the paracetamol solution can lead to undesirable effects or discomforts. Undesirable side effects observed to date include:
- Rare (1 to 10 in 10,000 patients treated): Increase in liver enzymes, hypersensitivity reactions and bronchospasm (tightening of the airways) due to sodium metabifulsite as an ingredient of the paracetamol solution.
- Very rare (less than 1 in 10,000 patients treated): Changes in the blood count, such as thrombocytopenia (decrease in platelets) and agranulocytosis (deficiency of specific white blood cells); severe skin reactions, partly with blistering and peeling of the skin (drug-induced Stevens-Johnson syndrome, toxic epidermal necrolysis, acute generalised exanthematous pustulosis);

bronchospasm (tightening of the airways due to drug induced asthma); hypersensitivity reactions from simple reddening of the skin all the way to urticaria (hives), Quincke's oedema (swelling mainly in the face) and life-threatening anaphylactic shock (severe allergic reaction).

Sugar tolerance test
Drinking the sugar solution can lead to undesirable effects or discomforts. Undesirable side effects observed to date include:
- Common (1 to 10 in 100 patients treated): Symptoms of hypoglycemia (low blood sugar level) with an influence on wellbeing during the sugar tolerance test or at a later point. Symptoms of hypoglycemia may also impair the ability to react, thus limiting the ability to drive and use machines.
- Uncommon (1 to 10 in 1,000 patients treated): Gastric (stomach) pressure, nausea or vomiting.
- Rare (1 to 10 in 10,000 patients treated): Allergic reactions, such as reddening of the skin.

Contacts

Public
Boehringer Ingelheim

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Scientific
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DE

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Healthy male subjects according to the assessment of the investigator, as based on a complete medical history including a physical examination, vital signs (Temperature, BP, PR), 12-lead ECG, neurological examination, and clinical laboratory tests
2. Age of >=18 to <=55 years at SCR
3.BMI of >=20.0 to <32.0 kg/m2 at SCR
4. A minimum absolute BW of 70 kg at SCR

Exclusion criteria

1.Female gender
2. Any finding in the medical examination (including BP, PR or ECG) or neurological examination deviating from normal and assessed as clinically relevant by the investigator
3. 3 times repeated measurements of systolic BP outside the range of 90 to 150 mmHg, diastolic BP outside the range of 50 to 90 mmHg, or PR outside the range of 40 to 100 bpm. In case of documented white coat hypertension the decision for eligibility is left to the investigator.
4. Any laboratory value outside the reference range that the investigator considers to be of clinical relevance, in particular, hepatic parameters ALT (1.25xULN), AST
(1.25xULN) and T-BIL (1.5xULN) or renal parameters (creatinine 1.25xULN) exceeding the Upper Limit of Normal (ULN) as specified: after 2 times repeated measurements

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-11-2022
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	10-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	01-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	15-04-2023
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	EUCTR2020-002600-38-NL
CCMO	NL82623.056.22

Study results

Date completed: 02-03-2023

Results posted: 30-01-2024

First publication
16-01-2024