A Phase II, randomized, double blind, parallel group,46 weeks dose-finding study of BI 456906 administered once weekly subcutaneously compared with placebo in patients with obesity or overweight

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Appetite and general nutritional disorders
Study type	Interventional

Summary

ID

NL-OMON51000

Source
ToetsingOnline

Brief title
Combined PhIIa/b in Obesity

Condition

- Appetite and general nutritional disorders

Synonym
Obesity

Research involving

Human

Sponsors and support

Primary sponsor: Boehringer Ingelheim
Source(s) of monetary or material Support: De Opdrachtgever Boehringer Ingelheim

Intervention

Keyword: BI 456906, obesity, overweight

Outcome measures

Primary outcome

- Percentage change in body weight (%) from baseline to week 46

Secondary outcome

Secondary endpoints are:

- Weight loss of >= 5% of baseline weight at week 46

- Weight loss of >= 10% of baseline weight at week 46

- Weight loss of >= 15% of baseline weight at week 46

- Absolute change in body weight (kg) from baseline to week 46

- Absolute change in waist circumference (cm) from baseline to week 46

- Absolute change in systolic blood pressure (mmHg) from baseline to week 46

- Absolute change in diastolic blood pressure (mmHg) from baseline to week 46

Study description

Background summary

Obesity is a chronic, complex, heterogeneous disease caused by a disruption of homeostatic control of body weight and a failure to
maintain constant body fat mass.

To help patients with obesity targeting of multiple signaling pathways

(including CNS and peripheral organs) is probably necessary to achieve more significant improvements in weight management and might reverse the progression of these metabolic disorders and related comorbidities.

Currently, there are four major FDA-approved medications for chronic weight management, however those medications only provide modest reduction of body weight. BI 456906 is a dual agonist of GLP-1 and Glucagon receptors, targeting both GLP-1 and
Glucagon signalling pathways BI 456906 is expected to provide synergistic clinical benefit for chronic weight management and obesity.

Study objective

The overall purpose of this trial is to assess the efficacy on weight loss and maintenance, and tolerability of four different doses of BI 456906 compared to placebo in patients with obesity or overweight (BMI >= 27kg/m2), without type 1 or type 2 diabetes, in order to characterize the dose-response relationship within the therapeutic range, and to select the target dose(s) for phase III clinical development.

Study design

This is a 46 week randomised, double-blind, parallel-design, placebo-controlled, multinational and multi-centre study with 4 different maintenance doses (ranging from 0.6mg/week to 4.8mg/week) in patients with obesity or overweight (BMI >= 27kg/m2), and without diabetes.

All patients (including placebo) will receive counselling for a reduced-calorie diet with an energy deficit of approximately 500 kcal/day, as well as increased physical activity counselling (recommended minimum 150 minutes/week) on a monthly basis.

There will be a screening period of minimum one week (time needed to obtain all examination results), that could be extended up to 12 weeks. The treatment duration is 46 weeks in total including a dose escalation phase of 20 weeks to minimize GI side effects of BI 456906. This is followed by a 26-week maintenance phase, and a 3-week (4 weeks after last dose) follow-up period.

Intervention

Participants will be randomly assigned to one of the 4 active dose arms of BI 456906 or placebo at a 1:1:1:1:1 ratio.
The different treatment arms and the dose escalation scheme are presented in Table 4.1.4:1 of the protocol.

Study burden and risks

Burden for the subject:
- The subject will need to regularly visit the research center as part of the study (20 visits for approximately one year)
- The subject receive a diet and exercise program during the study
- Several questionnaires are to be completed:
* on suicidal thoughts (C-SSRC), depression/ psychiatric disorders (PHQ-9): 17x
* to assess eating behavior (TFEQ-R18v2, PGI and BI-eating behavior): 4x
* to assess daily activity (SF-36v2 (PF10) and PGI): 4x
- Complete a 3-day food diary: 3x
- Record on a paper diary the daily food intake and on an electronic diary: weekly injections, weight measurements and physical activity
- Other assessments include: blood sampling (18x), pregnancy test (14x), physical examination (15x), including heart rate and blood pressure meeting and ECG
- Females should use two forms of effective contraception

Risks:
- There is no identified risk for BI 456906, based on the toxicology programme or any clinical trials conducted for this product to date.
- The risk for patients caused by participation in the trial, including the study procedures and exposure to the study drug, are reasonably low
- The expected side effects are known to be temporary, dose dependent, easy to monitor and manageable in clinical trials.

Benefit:
Subjects treated with BI 456906 are expected to achieve improved weight management results compared to prior to their trial participation.

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

1. Adult >= 18 years and < 75 years of age at screening
2. Written informed consent
3. Obesity or Overweight defined as BMI >=27 kg/m2 at screening
4. A minimum absolute body weight of 70 kg for females and 80 kg for males at screening
5. Male or female participants. Women of childbearing potential must be willing and able to use two forms of effective contraception
6. Patients must have undergone at least one previous unsuccessful nonsurgical weight-loss attempt per investigator*s judgement

Exclusion criteria

1. Body weight change of over +/- 5% or more in the past 12 weeks prior to randomization. There must be documentation of weight in the past 12 weeks before randomization.
2. Obesity induced by an endocrinologic disorder (e.g. Cushing Syndrome)
3. A HbA1c >= 6.5% at screening or diagnosed with type 1 or type 2 diabetes mellitus
4. Exposure to GLP-1Ra based therapies within three months prior to screening

Further criteria apply.

Study design

Design

Study phase:	2
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):	20-05-2021
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BI 456906
Generic name:	BI 456906

Ethics review

Approved WMO Date:	28-12-2020
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	26-02-2021
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-10-2021

Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-10-2021
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Not approved Date:	08-04-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-10-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	30-11-2022
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2020-002479-37-NL
ClinicalTrials.gov	NCT04667377
CCMO	NL75490.100.20