A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, SINGLE ASCENDING DOSE STUDY TO EVALUATE SAFETY, TOLERABILITY, PHARMACOKINETIC AND FOOD EFFECT OF BCI 838 AND AN OPEN-LABEL MINIDOSE BIOAVAILABILITY STUDY TO COMPARE SEVERAL BCI-632 PRO-DRUG CANDIDATES IN HEALTHY MALE SUBJECTS

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- to evaluate the safety and tolerability of BCI-838 following oral administration of single doses of BCI-838 in healthy male subjects- to determine the pharmacokinetics of BCI-838 and metabolite BCI-632 following oral administration of single…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON35311

Source
ToetsingOnline

Brief title
BCI-838 SAD and minidose bioavailability study

Condition

- Mood disorders and disturbances NEC

Synonym
depression, mood disorders

Research involving
Human

Sponsors and support

Primary sponsor: BrainCells Inc.
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: BCI-838, metabotropic glutamate receptors 2 and 3 antagonist, mood disorders

Outcome measures

Primary outcome

Criteria for evaluation

Safety: AEs, vital signs, 12-lead ECG, clinical laboratory and physical

examination

PK: plasma concentrations of BCI-838 and metabolite BCI-632; PK parameters in

plasma

Secondary outcome

NA

Study description

Background summary

The drugs to be given, BCI-838, BCI-1038, BCI-1206 and BCI-1283 are new, investigational compounds that may eventually be used for the treatment of mood disorders. Mood disorders are mental disorders in which the mood or emotion of

a person is seriously disturbed (for example depression).
BCI-632, the active form of BCI-838, BCI-1038, BCI-1206 and BCI-1283, is a specific and potent antagonist of the metabotropic glutamate receptors 2 and 3. BCI-632 could potentially produce new brain tissue, including neurons, which are responsible for transmitting signals in the brain.
It is expected that BCI-838, BCI-1038, BCI-1206 and BCI-1283 could have a positive effect on mood disorders.
These new compounds are not registered as a drug. BCI-838 has been given to humans before. BCI-1038, BCI-1206 and BCI-1283 are given to humans for the first time.

Study objective

- to evaluate the safety and tolerability of BCI-838 following oral administration of single doses of BCI-838 in healthy male subjects
- to determine the pharmacokinetics of BCI-838 and metabolite BCI-632 following oral administration of single ascending doses of BCI-838 in healthy male subjects
- to determine the effect of food on the pharmacokinetics of BCI-838 and metabolite BCI 632 following a single oral administration of BCI-838 in healthy male subjects
- to evaluate and compare the relative bioavailability and pharmacokinetics of metabolite BCI-632 following oral administration of several pro-drug candidates

Study design

Design:
This is a single-center study in healthy male subjects consisting of a single ascending dose (SAD) part with an integrated food effect (FE) part with a randomized, double-blind, placebo-controlled study design, and a minidose bioavailability part with an open-label study design to compare several BCI-632 pro-drug candidates in healthy male subjects.
The SAD part will consist of 3 groups of 8 healthy male subjects each (Groups 1 and 2), each participating in 2 periods. Group 4 consists of 1 period. In each group, 6 subjects will receive a single dose of BCI-838 and 2 subjects will receive a single dose of placebo.
The FE part is integrated in the SAD part and will consist of 1 group of 8 healthy male subjects participating in 2 periods (Group 1) with a fixed sequence. In the first period, 6 subjects will receive a single oral dose of BCI 838 in the fasted state and 2 subjects will receive a single dose of placebo in the fasted state. In the second period, 6 subjects will receive a single oral dose of BCI 838 in the fed state and 2 subjects will receive a single dose of placebo in the fed state. Subjects will receive the same study treatment (BCI-838 or placebo) in both the fasted and fed periods.
The minidose bioavailability part consist of 1 group of 6 subjects a single dose of 3 different BCI-632 pro-drugs (BCI-1038, BCI-1206 and BCI-1283) in 3

periods with a fixed sequence.

Procedures and assessments
Screening: demographics, body weight and height (including Body Mass Index (BMI) calculation), medical history, drug and alcohol screen, HBsAg, anti HCV and anti-HIV 1/2, clinical laboratory (including clinical chemistry, hematology and urinalysis), physical examination, vital signs (including supine systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature), 12 lead electrocardiogram (ECG) (in triplicate), adverse events (AEs) and previous medication
Each admission: clinical laboratory (including clinical chemistry, hematology and urinalysis), drug and alcohol screen, AEs, and previous and concomitant medication
Follow-up: clinical laboratory (including clinical chemistry, hematology and urinalysis), physical examination, vital signs (including supine systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature), 12 lead ECG (in triplicate), AEs and concomitant medication

Observation period: Groups 1 and 2: two periods in the clinic, each being from Day -1 until 48 h (Day 3) after drug administration
Group 3: three periods in the clinic from Day -1 until 48 h (Day 3) after drug administration. For Group 2 Period 2 and group 4 up to 72 h (Day 4) after drug administration.

Blood sampling: for pharmacokinetics (PK) of BCI-838 (only for Groups 1 and 2) and metabolite BCI-632 in plasma: pre-dose and 0.5, 1, 1.5, 2, 3, 4, 6, 8, 12, 16, 24, 36 and 48 hours post-dose. At 72 h post-dose an extra PK blood sample will be collected for Period 2 of Group 2 and group 4 only. Safety assessments: AEs: recorded from the time the Informed Consent Form is signed until completion of the follow up visit; clinical laboratory (including clinical chemistry, hematology and urinalysis): pre-dose and 12 and 48 hours post-dose; vital signs (including supine systolic and diastolic blood pressure, pulse rate, respiratory rate and body temperature) and 12-lead ECG (in triplicate): pre-dose and 1, 2.5, 3.5, 4.5, 7, 12.5, 23, 35 and 47 hours post-dose
Bioanalysis: Analysis of plasma PK samples for BCI-838 and metabolite BCI-632 by the bioanalytical laboratory at PRA International using a validated liquid chromatography-mass spectrometry/mass spectrometry method

Intervention

Study Medication
Active medication:
Active substance: BCI-838
Activity: antagonism of metabotropic glutamate receptors 2 and 3
Indication: mood disorders or cognitive impairment
Dosage form: oral capsule

Active medication:
Active substance: BCI-1038
Activity: antagonism of metabotropic glutamate receptors 2 and 3
Indication: mood disorders or cognitive impairment
Dosage form: oral capsule

Active medication:
Active substance: BCI-1206
Activity: antagonism of metabotropic glutamate receptors 2 and 3
Indication: mood disorders or cognitive impairment
Dosage form: oral capsule

Active medication:
Active substance: BCI-1283
Activity: antagonism of metabotropic glutamate receptors 2 and 3
Indication: mood disorders or cognitive impairment
Dosage form: oral capsule

Placebo:
Substance: microcrystalline cellulose
Activity: none
Indication: not applicable
Dosage form: oral capsule

Criteria for evaluation
Safety: AEs, vital signs, 12-lead ECG, clinical laboratory and physical examination
PK: plasma concentrations of BCI-838 and metabolite BCI-632; PK parameters in plasma

Treatments
SAD part
Group 1(integrated FE part):
Period 1: a single oral dose of 30 mg BCI-838 (n=6) or placebo (n=2) on Day 1 in the fasted state
Period 2: a single oral dose of 30 mg BCI-838 (n=6) or placebo (n=2) on Day 1 in the fed state

Group 2:
Period 1: a single oral dose of 100 mg BCI-838 (n=6) or placebo (n=2) on Day 1 in the fasted state
Period 2: a single oral dose of 300 mg BCI-838 (n=6) or placebo (n=2) on Day 1 in the fasted state

Minidose bioavailability part
Group 3:

Period 1: a single oral dose of 1 mg BCI-1038 (n=6) on Day 1 in the fasted state
Period 2: a single oral dose of 1 mg BCI-1206 (n=6) on Day 1 in the fasted state
Period 3: a single oral dose of 1 mg BCI-1283 (n=6) on Day 1 in the fasted state

For each individual subject, there will be a washout of at least 5 days between dosing in each period.

Study burden and risks

In a previous study in healthy volunteers, with single doses up to 3 mg, BCI-838 was considered safe and well tolerated. The adverse events that were reported were mild, transient and were considered not related to study drug. As BCI-1038, BCI-1206 and BCI-1283 will be administered to man for the first time in this study, to date adverse effects in man has not been reported. The insertion of the indwelling canula and the venepuncture may cause some pain, and sometimes lead to a bruise, but the actual collection of blood will not be painful. Light bleeding and possibly an infection may occur. However, chances these complications will occur are limited.

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

- Healthy male
- 18-55 years of age, inclusive
- BMI 18-30 kg/m2, inclusive
- non-smoker or moderate smoker (* 5 cigarettes per day)

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. In case of participation in another drug study within 60 days before the start of this study or being a blood donor within 60 days from the start of the study. In case of donating more than 1.5 liters of blood in the 10 months prior the start of the study.

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:	Recruitment stopped
Start date (anticipated):	12-10-2011
Enrollment:	30

Type:	Actual

Ethics review

Approved WMO Date:	26-09-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-10-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-11-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-12-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-12-2011
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	EUCTR2011-004409-26-NL
CCMO	NL38190.056.11