A single-center, non-randomized, open-label, parallel group, two-treatment study investigating the absolute oral bioavailability of balovaptan after single and multiple daily oral doses of balovaptan in healthy volunteers*

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cognitive and attention disorders and disturbances
Study type	Interventional

Summary

ID

NL-OMON46329

Source
ToetsingOnline

Brief title
Study to investigate the absolute oral bioavailability of balovaptan

Condition

- Cognitive and attention disorders and disturbances

Synonym
ASD, Autism spectrum disorder

Research involving

Human

Sponsors and support

Primary sponsor: F. Hoffmann-La Roche Ltd
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Balovaptan, Bioavailability, Open label, Parallel

Outcome measures

Primary outcome

To determine the absolute oral bioavailability of a single dose of 10 mg balovaptan.

Secondary outcome

To determine the absolute oral bioavailability of a single dose of 50 mg balovaptan.

To determine the absolute oral bioavailability of balovaptan after once daily doses of 10 mg or 50 mg for 14 days.

To characterize the dose- and time-dependency of the PK of oral balovaptan.

To determine plasma concentrations of [13C]-labeled balovaptan, balovaptan, and its metabolites M2, and M3, following a single oral dose of balovaptan 10 mg or 50 mg together with a slow IV infusion of a microdose of [13C]-labeled balovaptan.

To determine plasma concentrations of [13C]-labeled balovaptan, balovaptan, and its metabolites M2, and M3, following once daily oral dosing of 10 mg or 50 mg QD for 14 days together with a slow IV infusion of a microdose of [13C]-labeled balovaptan after the last oral dose.

To evaluate the safety and tolerability of balovaptan 10 mg QD and 50 mg QD

Study description

Background summary

Balovaptan (also known as RO5285119) is a new investigational compound that may eventually be used for the treatment of Autism Spectrum Disorder (ASD). Vasopressin is also present in the brain and may play a role in autism. Vasopressin is a hormone that regulates blood pressure and the retention of water in the kidneys. Balovaptan reduces signaling via vasopressin and is in development for treatment of ASD. Balovaptan is not yet registered as a drug but has been given to adults with ASD before at doses of up to 10 mg for a period of 12 weeks and to healthy volunteers at doses of up to 52 mg for a period of two weeks.

Study objective

The purpose of the study is to investigate how quickly and to what extent balovaptan is absorbed and eliminated from the body when it is administered to healthy volunteers. The pharmacokinetics of balovaptan given by mouth (oral) will be compared with the pharmacokinetics of a very low dose of balovaptan labeled with 13-Carbon (13C) given by an intravenous infusion.

Study design

The actual study will consist of two periods, Period 1 and Period 2. In each period, Day 1 is the day of (first) study compound administration.

In Period 1, balovaptan will be given once as (an) oral tablet(s) with 240 milliliters (mL) of water followed 1.25 hours later by a 15-minute intravenous infusion of 0.1 mg 13C-labeled balovaptan.

In Period 2, balovaptan will be given once daily for 14 consecutive days as

(an) oral tablet(s) with 240 mL of water. On Day 14, the final dose of balovaptan will be followed 1.25 hours later by a 15-minute intravenous infusion of 0.1 mg 13C-labeled balovaptan.

In a subset of the volunteers, cerebrospinal fluid will be collected.

Intervention

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In Period 2, balovaptan will be given once daily for 14 consecutive days as (an) oral tablet(s) with 240 mL of water. On Day 14, the final dose of balovaptan will be followed 1.25 hours later by a 15-minute intravenous infusion of 0.1 mg 13C-labeled balovaptan.

On Day 1 of Period 1, and Days 7 and 14 of Period 2, the study compound will be administered after an overnight fast (no food or beverages for at least 10 hours). No food is allowed for at least 4 hours after administration of the study compound. A standardized lunch will be provided 4 hours and a standardized dinner 10 hours after administration of the study compound. On the other days, a regular breakfast (30 minutes after administration of the study compound), lunch or dinner will be provided.

In a subset of the volunteers, cerebrospinal fluid will be collected. After the procedure the volunteer has to lie down on his back for another 1.5 - 2 hours, this is to decrease the risk on leakage of cerebrospinal fluid.

Study burden and risks

Disadvantages of participation in the study may be:
possible side effects
possible adverse effects or discomforts of the evaluations in the study
possible distressing questionnaires
Participation in the study also means:
that the subject will spend time on the study
that the subject will undergo tests
that the subject will need to follow instructions
All these aspects have been described above under Sections 4, 5 and 6 of the ICF.

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 or female subject, aged 18 to 65 years
- Body Mass Index (BMI) of 18 to 30 kg/m2
- For women of childbearing potential: agreement to use at least 2 acceptable contraceptive methods during the treatment period and for 90 days after the last dose of study drug. Also, total abstinence, in accordance with the lifestyle of the subject, is acceptable
- For men: agreement to use contraceptive measures, and agreement to refrain from donating sperm, with female partners of childbearing potential or pregnant female partners, men must remain abstinent or use a condom during the treatment period and for 90 days after the last dose of study drug to avoid exposing the embryo. Men must refrain from donating sperm during this same period
- Able to participate and willing to give written informed consent and to comply with the study restrictions
- Fluent in English or Dutch

Exclusion criteria

- If female of childbearing potential, a positive serum pregnancy test at screening or at admission to the clinical research unit
- Any condition or disease detected during the medical interview/physical examination that would render the subject unsuitable for the study, place the subject at undue risk or interfere with the ability of the subject to complete the study in the opinion of the Investigator
- In the opinion of the Investigator, any major illness within one month before the screening examination or any febrile illness within one week prior to screening and up to first study drug administration
- History of any clinically significant gastrointestinal, renal, hepatic, broncho-pulmonary, neurological, psychiatric, cardiovascular, endocrinological, hematological, lymphatic, musculoskeletal, genitourinary, immunological, dermatological, connective tissue or allergic disease, metabolic disorder, or cancer
- Signs and symptoms potentially indicative of peripheral neuropathy
- A history of clinically significant hypersensitivity or allergic reactions
- Known personal or family history of congenital long QT syndrome or sudden death
- History or presence of clinically significant ECG abnormalities before study drug administration.
- Subjects with screening or predose baseline mean QT interval corrected using Fridericia*s formula >450 milliseconds [msec] or <300 msec
- Notable resting bradycardia on screening or predose baseline ECG. Notable resting tachycardia on screening (mean heart rate [HR] > 90 bpm) or predose (mean HR > 100 bpm) baseline ECG
- Screening or baseline ECGs with QRS and/or T-wave judged to be unfavorable for a consistently accurate QT measurement and with evidence of clinically relevant abnormalities
- Systolic blood pressure greater than 139 or less than 90 mmHg, or diastolic blood pressure greater than 89 or less than 45 mmHg, based on the average of >= 3 consecutive measurements.
- Clinically significant abnormalities in laboratory test results. In the case of uncertain or questionable results, tests performed during screening may be repeated on Day -1 of Period 1 to confirm eligibility
- History of coagulopathies, bleeding disorders, or blood dyscrasias
- Subjects who have smoked within 3 months prior to first dose administration
- Any clinically relevant history or any suspicion of alcohol and/or other substance abuse or addiction. Past alcohol and/or other substance abuse or addiction is also not allowed
- Alcohol consumption of >24 units per week for males and females
- Positive urine alcohol test or urine drug screen at screening or each admission
- Positive result on human immunodeficiency virus (HIV)-1, HIV-2 antibodies, hepatitis C virus antibody, hepatitis B virus surface antigen, or hepatitis B core antibody screen
- Participation in an investigational drug or device study within 90 days prior to first dosing, or within 5 months prior to first dosing in case of a study with a biological, as calculated from the day of follow-up from the previous study
- Any donation of blood or plasma or significant blood loss within 3 months prior to screening
- Dietary restrictions that would prohibit the consumption of standardized meals
- Use of any prohibited medications or food before study start or subjects who do not agree to

refrain from consuming prohibited medications or food during the study
- Subjects likely to need concomitant medication during the study
- Subjects who have received any prescribed systemic or topical medication within 4 weeks of the first dose administration, unless in the opinion of the Investigator the medication will not interfere with the study procedures or compromise safety, and subjects who have received slow release medicinal formulations considered to still be active within 4 weeks of the first dose administration will also be excluded unless in the opinion of the Investigator the medication will not interfere with the study procedures or compromise safety
- Used the following within 7 days before the first study drug administration, unless in the opinion of the Investigator the medication will not interfere with the study procedures or compromise safety:
• Any non-prescribed systemic or topical medication
• Herbal remedies
- Subjects under judicial supervision, guardianship or curatorship
- Poor venous access for blood sampling
- Subjects who have previously taken part in or withdrawn from this study and unwilling to practice safe sex for the duration of the study
- For subjects with planned lumbar punctures
- Significant risk for suicidal behavior, in the opinion of the Investigator

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-12-2018
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[13C]-labeled balovaptan

Generic name:	N/A
Product type:	Medicine
Brand name:	Balovaptan
Generic name:	N/A

Ethics review

Approved WMO Date:	20-11-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-11-2018
Application type:	First submission
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	EUCTR2018-003634-32-NL
CCMO	NL68133.056.18