A single-center, non-randomized, open-label, one-sequence, two-period within-subject study to investigate the effect of Rifampicin on the pharmacokinetics of multiple doses of Balovaptan in healthy volunteers

Published: 21-06-2018
Last updated: 11-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46088

Source
ToetsingOnline

Brief title
Balovaptan - Rifampicin DDI study

Condition

- Other condition

Synonym
Autism Spectrum Disorders (ASD)

Health condition

Autisme spectrum stoornissen (ASS)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Balovaptan, Drug-drug-interaction, Pharmacokinetic, Rifampicin

Outcome measures

Primary outcome

To investigate the effect of multiple doses of rifampicin on the

pharmacokinetics of balovaptan and its major metabolites at steady state in

healthy subjects

Secondary outcome

To evaluate the safety and tolerability of balovaptan administered alone and in

combination with rifampicin in healthy subjects.

To investigate the effect of multiple doses of rifampicin on secondary PK

parameters of multiple doses of balovaptan and its major metabolites at steady

state in healthy subjects

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), a diverse neurodevelopmental disorder. This disorder is typically characterized by social deficits, communication difficulties, repetitive behaviors, and in

some cases, learning disabilities. Vasopressin is a hormone that regulates blood pressure and the retention of water in the kidneys. Vasopressin is also present in the brain and may play a role in autism. 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.

Rifampicin, an approved drug for the treatment of tuberculosis, is known to interfere with the activity of the liver enzyme CYP3A4. This enzyme is involved in the breakdown of balovaptan in the body and may therefore interfere with the presence of balovaptan in the body. Rifampicin induces the enzyme CYP3A4, thereby increasing the activity of this enzyme. It will be investigated if increasing the activity of the CYP3A4 will affect the concentration of balovaptan in the blood. If so, rifampicin will be expected to decrease your blood levels of balovaptan during this study, though may increase the levels of its breakdown products (metabolites).

Study objective

The objective of the study is to investigate how quickly and to what extent balovaptan is absorbed and eliminated from the body (pharmacokinetics) when it is administered in combination with rifampicin. It will also be investigated to what extent balovaptan is tolerated by volunteer if administered alone or in combination with rifampicin.

Study design

In Period 1 you will stay in the research center for 12 days (11 nights). Day 1 is the first day of administration of the study compound. You are expected at the research center at 14:00 hr in the afternoon prior to the day of first administration of the study compound (Day -1). You will leave the research center on Day 11.

There will be a period of at least 14 days (and a maximum of 21 days) between the last administration of study compound in Period 1 and the first administration of study compound in Period 2. This is the so-called washout period.

You are expected to return to the research center at 14:00 hr in the afternoon on Day -1 of Period 2. In Period 2 you will stay in the research center for 18 days (17 nights). Then you will leave the research center on Day 17 of Period 2.

Intervention

In Period 1, balovaptan will be given once daily for 10 consecutive days, at a dose of 10 mg. Balovaptan will be given as an oral tablet with 240 milliliters (mL) of water after consumption of a standardized breakfast.

In Period 2, rifampicin will be given once daily at a dose of 600 mg for 6 consecutive days. Thereafter, rifampicin will be administered together with balovaptan for 10 consecutive days. When balovaptan and rifampicin are given on the same day, they will be given at the same time. Rifampicin will be given as 2 capsules of 300 mg with 240 mL of water.

The study compounds will be administered after an overnight fast (no eating and drinking for at least 8 hours). A breakfast will be administered 30 minutes after study compound administration. On Day 10 of Period 1 and Days 6 and 16 of Period 2, you will receive a standardized breakfast 30 minutes after administration of study compound, which has to be completed. A standardized lunch and standardized dinner will be provided 4 and 8 hours after administration of the study compounds.

One of the investigators will inspect your hands and mouth after each intake of study compound.

Study burden and risks

The study compound may cause side effects. Balovaptan has had limited testing in humans. Side effects that were observed in clinical trials with balovaptan are listed below. However, it is not clear whether balovaptan has been the cause of these side effects. On the other hand, there may be side effects that are not known at this time.

The most common side effect reported by healthy subjects was headache. The most common side effects reported by patients with ASD are listed below. The majority of the side effects were of mild or moderate intensity.

Side Effects Reported in Previous Clinical Trials with Balovaptan
Aggression
Anxiety, nightmares, and insomnia
Arthralgia (joint pain)
Back pain
Bronchitis
Diarrhea
Digestion troubles
Dizziness
Dysgeusia (affecting sense of taste)
Dyspepsia (indigestion)
Fatigue Headache
Irritability
Muscle pain

Nasopharyngitis (runny nose and sore throat)
Nausea
Runny nose
Skin lesion
Syncope (fainting) after standing up quickly
Taste alteration
Upper respiratory tract infection

Also, if the subject should experience lightheadedness or dizziness when standing up or even fainting, or should the subject experience muscle ache or cardiovascular symptoms, such as chest pain, palpitations, or breathlessness, the subject should inform the study doctor as soon as possible.

Rifampicin
The most common side effects for rifampicin reported are listed below.
• Thrombocytopenia (decrease in platelets) with or without purple-colored spots that are most recognizable on the skin
• Dizziness
• Headache
• Nausea
• Vomiting
• Increase in liver function enzymes
As rifampicin has a bright red color by itself, rifampicin may produce a reddish discoloration of the urine, sweat, sputum and tears. Please be aware that soft contact lenses (but also white clothes) may be permanently stained.

Tests
Drawing blood and/or insertion of the indwelling cannula may be painful or cause some bruising.

To monitor your heart rate, electrodes (small, plastic patches) will be pasted at specific locations on the chest and abdomen. Prolonged use of these electrodes can cause skin irritation (rash and itching).

Contacts

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Scientific

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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. Healthy male and female subjects, aged 18-65, inclusive at screening.
2. BMI of 18-30Kg/m2, inclusive at screening
3. Women of childbearing potential must agree to use one highly effective non-hormonal contraceptive method combined with a barrier method from screening until 90 days after the last drug dose.
4. Men must agree to use contraceptive measures and refrain from donating sperm.
5. Able to participate and willing to give written informed consent and to comply with the study restrictions.

Exclusion criteria

1. Female subjects who are pregnant or lactating.
2. If female of childbearing potential, a positive serum pregnancy test at Screening or at admission (Day 1 of either period).
3. 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.
4. 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.

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):	03-07-2018
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Balovaptan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	21-06-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	02-07-2018
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO

Date:	27-08-2018
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	EUCTR2018-001783-40-NL
CCMO	NL66326.056.18