A single-center, randomized, open-label, four-period, four-treatment, cross-over study to investigate the comparative bioavailability of dispersible tablet and capsule formulations of RO5285119 in healthy volunteers

Published: 14-08-2017
Last updated: 12-04-2024

The purpose of the study is to investigate how quickly and to what extent RO5285119 is absorbed from the gut and then eliminated from the body (this is called pharmacokinetics).It will also be investigated to what extent RO5285119 is tolerated.

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

Summary

ID

NL-OMON44542

Source
ToetsingOnline

Brief title
RO5285119 comparative bioavailability study

Condition

- Cognitive and attention disorders and disturbances

Synonym
Autism Spectrum Disorder

Research involving

Human

Sponsors and support

Primary sponsor: F. HoffmannLa Roche Ltd
Source(s) of monetary or material Support: Farmaceutische industrie

Intervention

Keyword: ASD, RO5285119

Outcome measures

Primary outcome

To investigate the relative bioavailability of the Phase 3 optimized dispersible tablet formulation versus the capsule formulation used in Phase 2 adult study

Secondary outcome

• To investigate the relative bioavailability of the Phase 3 optimized dispersible tablet formulation versus the dispersible tablet formulation used in Phase 2 pediatric study

• To investigate the relative bioavailability of the Phase 3 optimized dispersible tablet formulation versus the Phase 3 dispersible tablet formulation with a coarser drug substance particle size

• To investigate the relative bioavailability of the pediatric Phase 2 dispersible tablet formulation versus the capsule formulation used in Phase 2 adult study

• To investigate the safety and tolerability of a single 10 mg oral dose of RO5285119 inhealthy subjects

Study description

Background summary

RO5285119 is a new investigational compound that may eventually be used for the treatment of Autism Spectrum Disorders (ASD), a group of neurodevelopmental disorders including Autism Disorder, Asperger*s syndrome, and pervasive developmental disorder - not otherwise specified (PDD-NOS). These disorders are typically characterized by social deficits, communication difficulties, stereotyped or repetitive behaviors and interests, and in some cases, cognitive delays. 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. RO5285119 blocks activation of the vasopressin receptor and is in development for treatment of the core deficits in ASD.

RO5285119 is not registered as a drug but has been given to humans before.

Study objective

The purpose of the study is to investigate how quickly and to what extent RO5285119 is absorbed from the gut and then eliminated from the body (this is called pharmacokinetics).

It will also be investigated to what extent RO5285119 is tolerated.

Study design

The actual study will consist of 4 periods during which the volunteer will stay in the clinical research center in Groningen (location University Medical Center Groningen) for 3 days (2 nights), followed by 4 days during which the volunteer will visit the Medical Screening Center (location Martini Hospital) in Groningen for short visits. The time interval between the start of the different periods is at least 14 days and not more than 21 days.

During the study the volunteer will receive RO5285119 after an overnight fast (at least 10 hours no eating and drinking) as a tablet or capsule with 240 milliliters of (tap) water.

In each period, fasting will continue until 4 hours after administration of the study compound. Then the volunteer will receive a lunch. During fasting the volunteer is allowed to drink water with the exception of 1 hour prior to until 1 hour after administration of the study compound.

Intervention

The study will consist of 4 periods during which the volunteer will receive RO5285119 once in each period. During 3 periods, RO5285119 will be given as oral tablets and during one period as capsules. The oral tablets will be different with respect to the composition (formulation).

The order in which the volunteer will receive the different tablets and capsule will be determined by chance. The following orders are possible (see table for explanation of the code): ABCD, BDAC, CADB, DCBA.

The planning of the study is as follows:

Treatment code* Dose Formulation Number of capsules/ tablets How often
A 10 mg RO5285119 tablet 1 once in 1 of the 4 periods
B 10 mg RO5285119 capsule 2 once in 1 of the 4 periods
C 10 mg RO5285119 tablet 2 once in 1 of the 4 periods
D 10 mg RO5285119 tablet 1 once in 1 of the 4 periods

Study burden and risks

Sometimes, people participating in studies get headaches. The cause of this may be that the volunteer is not allowed to eat or drink for some time. In order to collect blood, a cannula is inserted in a vein of the arm. The insertion may be painful and sometimes lead to a bruise.

All potential drugs cause adverse effects; the extent to which this occurs differs. In the previous studies conducted in healthy volunteers, the study compound was safe and generally well tolerated. The most common side effects reported were headache, back pain, and muscle ache. In general side effects were mild in nature and all resolved.

The muscle enzyme values in the blood as well as blood cell counts will be regularly monitored in this study because toxicities of skeletal muscle and decreases in white blood cells were observed in animals. Specifically, in dogs, a severe decrease in white blood cells was noted at drug blood levels higher than expected in this study. In rats, again at drug blood levels higher than expected in this study, skeletal muscular toxicity was observed.

The volunteer needs to abstain from unusual physical exercise whilst being in this study.

Hypothetically, this study compound may lower the blood pressure and may impact the blood pressure regulation. In particular when standing up quickly which may result in symptoms like light-headedness and dizziness, and, if severe, even in syncope. While in clinical trials such adverse events did not appear to occur more often in drug treated than in placebo treated subjects, the volunteer needs to move carefully from supine / or seated position into standing position and watch him- or herself for symptoms like light-headedness and dizziness to

go back to lower body position.

In rats, at treatment duration for several weeks and at drug blood levels higher than expected in this study tissue changes around nerves and around small vessels in the brain were noted. Because the duration of treatment is short in this study, no particular safety precaution in this regard is included in this study.

Hypothetically, the mode of action of the study compound may interfere with platelet function and hence exaggerate bleeding events. However, as of now no such safety alert has emerged from animal studies or clinical trials in human beings. In case of bleeding abnormalities in the medical history the volunteer will not be eligible to participate in this study.

The study compound is interfering with the functionality of brain circuits and as such may hypothetically have the potential to cause side effects of the nervous system. No neurological or behavioural side effects considered causally associated with the intake of the study compound have been identified to date. However, the study compound is in early phase of development and the number of volunteers who have taken the study compound is rather small.

The volunteer should be aware that the aforementioned adverse effects and possibly other, still unknown adverse effects, may occur during the study. However, with the dose used in this study no serious adverse effects are expected.

Should, in the opinion of the investigators, unacceptable adverse effects appear, the study will be discontinued.

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 volunteers
- age 18-65 yrs, inclusive
- BMI between 18.0 to 30 kg/m2

Exclusion criteria

Suffering from hepatitis B, hepatitis C, cancer or HIV/AIDS. 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 over 500 mL or significant blood loss within 3 months prior to screening.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-08-2017
Enrollment:	14
Type:	Actual

Ethics review

Approved WMO Date:	14-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-08-2017
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-09-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-09-2017
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-10-2017
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	EUCTR2017-002578-37-NL
CCMO	NL62829.056.17