A 2-part randomized, three-period cross-over, placebo controlled, proof of mechanism study to investigate the effect of RO5285119 on vasopressin (AVP) pathway activation in healthy male subjects

Published: 08-05-2014
Last updated: 21-04-2024

Primary Objectives- To replicate AVP-induced inhibition of anterior cingulate cortex (ACC) activity and functional connectivity as measured by BOLD fMRI during a face matching task. - To assess the effect of RO5285119 in the modulation of AVP...

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

Summary

ID

NL-OMON42183

Source
ToetsingOnline

Brief title
Effect of RO5285119 on vasopressin effects

Condition

- Other condition
- Developmental disorders NEC

Synonym
effect on brain, proof-of-mechanism

Health condition

Onderzoek naar werkingsmechanisme

Research involving
Human

Sponsors and support

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

Intervention

Keyword: fMRI, RO5285119, vasopressin

Outcome measures

Primary outcome

Blood oxygenation level dependent (BOLD) changes during 3 functional MRI tasks:

face matching task; emotional face processing task (Part A only); Theory of

Mind Task.

Secondary outcome

- Safety and tolerability

- Resting state BOLD fMRI

- Arterial spin labelling fMRI

- Pharmacokinetic

- Cortisol (Part A only)

- Genotyping

Study description

Background summary

RO5285119 is a vasopressin 1 receptor antagonist under development as an anxiolytic. One potential future indication is as a treatment to help people with autism spectrum disorder to navigate the social world. In order to gain more insight into the mechanism of action in relevant brain areas, however, this study will use functional MRI to investigate the combination of vasopressin and its antagonist RO5285119 in a pharmacological challenge model in healthy volunteers.

Study objective

Primary Objectives
- To replicate AVP-induced inhibition of anterior cingulate cortex (ACC) activity and functional connectivity as measured by BOLD fMRI during a face matching task.
- To assess the effect of RO5285119 in the modulation of AVP effects on ACC activity as measured by BOLD fMRI during a face matching task in healthy male subjects.

Secondary Objectives
- To assess the effects of RO5285119 on brain activity modulated by AVP during a Theory of Mind (ToM) task as evaluated by BOLD fMRI.
- To evaluate the effects of RO5285119 on brain activity modulated by AVP during an implicit and explicit emotional face processing task as evaluated by BOLD fMRI. (Part A only)
- To assess the relationship between RO5285119 plasma concentrations and the modulation of AVP effects on brain activity as measured by BOLD fMRI in healthy male subjects.
- To collect further data on safety and tolerability of RO5285119 in healthy male subjects.
-To evaluate the effects of RO5285119 on brain activity during ASL MRI and BOLD fMRI assessments (Resting state, Face matching and ToM tasks) (Part B only).

Study design

A 2-part randomized, three-period cross-over, placebo controlled, proof of mechanism study to investigate the effect of RO5285119 on vasopressin (AVP) pathway activation in healthy male subjects

Intervention

RO5285119 and vasopressin in a placebo controlled, randomized fashion. In part A the study is double-blind and placebo controlled for both RO5285119 and vasopressin. In part B the study is only placebo controlled for RO5285119, and only double-blind until day 6 of period 3. After this it is an open design in

which half of the subjects will receive active RO5285119.

Study burden and risks

There is no health benefit for participants. Risk is considered minimal. Burden consists of time investment and life style restricitions.

Contacts

Public
Hoffmann-La Roche

Falcon Way, Shire Park 6
Welwyn Garden City AL7 1TW
GB
Scientific
Hoffmann-La Roche

Falcon Way, Shire Park 6
Welwyn Garden City AL7 1TW
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Right-handed (Righthandedness as confirmed on the Edinburgh Handedness inventory), healthy non smoking male adults (18 - 45 years of age)
2. BMI between 18 to 32 kg/m2 (inclusive), total weight in the range of 50-100 kg.

3. Subjects and their partners of childbearing potential must use 2 methods of contraception, one of which must be a barrier method for the duration of the study and for 90 days after the last dose.
4. Able to participate and willing to give written informed consent and to comply with the study restrictions.
5. In the investigator*s opinion, the subject is deemed appropriate for participation in the study, capable of following the study schedule of assessments and complying with the study restrictions and discontinuation of prohibited medication will not pose undue risks to the subject.
6. Minimally completed secondary education or equivalent

Exclusion criteria

1. No alcohol and substance abuse/dependance
2. History of relapsing or current psychiatric or neurological disorders, including epilepsy and migraine.
3. Subjects who, in the Investigator's judgment, pose a suicidal risk, or any subject with a history of suicidal attempts or behavior
4. Positive results for serology test for HIV, Hepatitis B, hepatitis C viruses
5. Systolic blood pressure (SBP) greater than 140 or less than 90 mm Hg, and diastolic blood pressure (DBP) greater than 90 or less than 50 mm Hg.
6. Pulse below 40 BMP or above 90 BPM
7. Clinically significant abnormality on electrocardiogram (ECG), including QTcF > 450 ms.
8. Clinically significant abnormality in parameters of clinical chemistry and urinalysis.
9. Active stomach ulcer disease or active GI bleeding.
10. Personal or family history (first or second degree relatives) of cerebral aneurysm.
11. Personal history of stroke or traumatic head injury.
12. Clinically significant abnormality in parameters of hematology or coagulation.
13. History of coagulopathies, bleeding disorders or blood dyscrasias.
14. History of hematological malignancy or myelosuppression (including iatrogenic).
15. Contraindications to have MRI scans (e.g. no metallic implants)
16. Use of prohibited medications within 2 weeks prior to randomization, or 5 half-lives (whichever is longer).
17. No participation in other trials within 90 days prior to enrollment or prior participation in part
A of study BP29412.
18. Donation or loss of blood over 500mL within three months prior to randomization
19. Chronic rhinitis, allergic rhinitis, nasal polyps or any other nasal pathology that may affect the absorption of intranasal AVP.
20. Concomitant disease, condition or treatment which might interfere with the conduct of the study, or what would, in the opinion of the investigator, pose an unacceptable risk to the subject in this study such as asthma or ischemic events like Raynaud syndrome, angina pectoris or stroke.
21. unwilling to comply with lifestyles
22. Known allergic reaction to vasopressin or excipients present in the

formulation used in this study.
23. For Part B only: Contraindications for lumbar puncture:
- Any history of raised intra-cerebral pressure or clinically significant vertebral joint pathology.
- Clinically significant abnormalities in lumbar spine.
- Any major illness within one month prior to the screening examination, or febrile illness or any
- clinically significant infections within 21 days prior to CSF sampling.
- Thrombocytopenia or other bleeding diathesis (including ongoing anticoagulant therapy).
- Allergy to lidocaine.
- Any other spine abnormality that will not allow a lumbar puncture or other pathology that according
to the investigator*s judgment may interfere with the LP or may pose unacceptable risk for LP.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-08-2014
Enrollment:	60
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RO5285119
Generic name:	RO5285119

Product type:	Medicine
Brand name:	Vasostrict
Generic name:	vasopressin

Ethics review

Approved WMO Date:	08-05-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-05-2014
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-06-2014
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2015
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-05-2015
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	EUCTR2014-000867-42-NL
CCMO	NL49141.056.14