A DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, THREE-WAY CROSSOVER STUDY TO INVESTIGATE THE DRUG-DRUG INTERACTIONS OF BRIVARACETAM AND ETHANOL IN HEALTHY MALE SUBJECTS

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Primary objectiveTo evaluate if BRV influences the psychomotor and cognitive impairing effects of ethanolSecondary objectivesTo evaluate the potential PK interactions between BRV and ethanolTo evaluate the safety and tolerability of co-...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Seizures (incl subtypes)
Study type	Interventional

Summary

ID

NL-OMON37186

Source
ToetsingOnline

Brief title
Brivaracetam - ethanol interaction study

Condition

- Seizures (incl subtypes)

Synonym
epilepsy / seizures

Research involving

Human

Sponsors and support

Primary sponsor: UCB Pharma
Source(s) of monetary or material Support: UCB Pharma SA

Intervention

Keyword: Epilepsy, Ethanol, Interaction, Pharmacokinetetic

Outcome measures

Primary outcome

PD variables

• Saccadic eye movements to assess sedation

• Smooth pursuit eye movements to assess attention and eye movement coordination

• Adaptive tracking to assess visuo-motor control and attention

Secondary outcome

PK variables

BRV

The area under the plasma concentration-time curve, maximum concentration, and

the terminal half-life, amongst others

Ethanol

Serum ethanol concentrations, Breath ethanol concentrations (BrEC), Total

ethanol dose used, etc..

Safety variables

Incidence and severity of adverse events, Vital signs, and Clinical laboratory

test results

Study description

Background summary

Brivaracetam (BRV) is being investigated as an adjunctive treatment for refractory epilepsy. As part of its development, it is essential to investigate the possibility of pharmacokinetic (PK) and pharmacodynamic (PD) interaction between BRV and ethanol, one of the most widely used central nervous system (CNS) active substances in Western society.

Study objective

Primary objective
To evaluate if BRV influences the psychomotor and cognitive impairing effects of ethanol

Secondary objectives
To evaluate the potential PK interactions between BRV and ethanol
To evaluate the safety and tolerability of co-administration of BRV and ethanol

Study design

This is a single-center, double-blind, randomized, placebo-controlled, three-way crossover, Phase 1 study in 18 healthy male subjects.

Intervention

All eligible subjects will receive: ethanol+oral BRV 200mg, ethanol placebo+oral BRV 200mg, and ethanol+oral BRV placebo in sequence in a randomly assigned order.

Study burden and risks

During the screening, clinical significant abnormalities may be found.

The study days are intensive (CNS battery, ethanol infusion, blood sampling and the measurement of vital signs and ECG)

The effects of alcohol are well-known and include feeling drunk, sleepiness,

headache or dizziness. In addition, the intravenous ethanol infusion could give local pain or irritation in the beginning of the infusion.The most frequently noted side effects associated with brivaracetam in healthy volunteers are dizziness, sleepiness, fatigue, feeling drunk, euphoric mood, headache, feeling weak and nausea. The potential side-effects associated with the combination of alcohol and brivaracetam are increases in symptoms observed with either alcohol or brivaracetam alone.

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

1. Subject understands and has signed and dated an Independent Ethics Committee (IEC) approved written Informed Consent form.
2. Subject is able to communicate well with the Investigator in the local language, and to

understand and comply with the requirements of the study.
3. Subject is considered reliable and capable of adhering to the protocol according to the judgment of the Investigator.
4. Subject is male and between 18 to 55 years of age, inclusive, at Screening.
5. Subject has a body mass index (BMI) of 18 to 30kg/m2, inclusive, at Screening.
6. Subject has blood pressure and PR within normal range in a supine position after 5 minutes rest, measured on the dominant arm at Screening:
a. SBP: 100 mmHg to 145mmHg, inclusive
b. DBP: 50mmHg to 90mmHg, inclusive
c. PR: 45bpm to 90bpm, inclusive.
7. Subject*s 12-lead electrocardiogram (ECG) is free of any clinically relevant abnormal ECG findings according to the Investigator at Screening.
8. Subject is in good physical and mental health, in the opinion of the Investigator, determined on the basis of medical history and a general clinical examination at Screening.
9. Subject has normal renal and hepatic function as assessed by clinical laboratory test results (clinical chemistry, hematology, and urinalysis) within the reference ranges of the laboratory at Screening. Subjects with test results that are outside the specified ranges and that are
deemed as not clinically significant will be allowed at the discretion of the Investigator.
10. Subject has adequate venous access.
11. Subject agrees that, during the study period and for a period of 3 months after dosing with BRV, when having sexual intercourse (for males - with a woman of childbearing potential), a highly effective contraceptive barrier (condom+spermicide) will be used, AND that the respective partner will use an additional highly effective contraceptive method:
a. Diaphragm or cervical cap with spermicide, or
b. Intrauterine device, or
c. Stable oral, transdermal, injectable, or sustained-release vaginal hormonal contraceptive

Exclusion criteria

1. Subject has previously participated in this study or has previously been assigned to treatment in a study of the investigational medicinal product (IMP) under investigation in this study.
2. Subject has participated in another study of an IMP (or a medical device) within the previous 3 months prior to Screening or has participated in more than 4 IMP (or medical device) studies within 1 year prior to Screening.
3. Subject has received treatment with any prescribed or over-the-counter medications (including herbal medicines such as St John*s Wort) within 7 days or 5 half-lives (whichever is longer) prior to Screening. Note: Use of paracetamol within this period prior to Screening may be acceptable, subject to approval by the Investigator.
4. Subject has a known hypersensitivity to any components of the IMP as stated in this protocol.
5. Subject has a history or presence of drug or alcohol abuse.
6. Subject has history of an average alcohol consumption of more than 21 units of alcohol per week or an average daily intake of greater than 3 units, within 6 months of the study. One

unit is equivalent to a half-pint (220mL) of beer or 1 measure (25mL) of spirits or 1 glass (125mL) of wine.
7. Subject tests positive for alcohol (breath test) and/or drugs (urine test) at Screening.
8. Subject has ethanol intolerance.
9. Subject has an average caffeine consumption of more than 800mg of caffeine per day (1 cup of coffee contains approximately 100mg of caffeine, 1 cup of tea approximately 30mg, and 1 glass of cola approximately 20mg).
10. Subject has history of smoking within 3 months prior to Screening or is not able to refrain from smoking during the course of the study.
11. Subject has consumed any grapefruit, grapefruit juice, grapefruit-containing products, or star fruit within 14 days prior to dosing or is not able to refrain from these products during the course of the study.
12. Subject has not been vaccinated for hepatitis and tests positive for hepatitis at Screening.
13. Subject tests positive for Human Immunodeficiency Virus (HIV) at Screening.
14. Subject has had significant blood loss (500mL) within 3 months prior to Screening.
15. Subject has history or clinical evidence of any disease and/or existence of any surgical or medical condition that, in the opinion of the Investigator, might interfere with the absorption, distribution, metabolism, or excretion of BRV or ethanol.
16. Subject has a lifetime history of suicide attempt (including an actual attempt, interrupted attempt, or aborted attempt), or has suicidal ideation in the past 6 months as indicated by a positive response (*Yes*) to either Question 4 or 5 of the Columbia Suicide Severity Rating Scale (C-SSRS) at Screening.
17. Subject is an employee of the Investigator or study center, with direct involvement in the proposed study or other studies under the direction of that Investigator or study center, or subject is a first line family member of an employee working in the respective study center or of the Investigator.
18. Any circumstances or conditions of the subject, which, in the opinion of the Investigator, may affect full participation in the study or compliance with the study.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-09-2012
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	not applicable
Generic name:	Brivaracetam

Ethics review

Approved WMO Date:	13-09-2012
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-09-2012
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	EUCTR2012-002591-14-NL
CCMO	NL41930.056.12