A multi-center, double-blind, parallel-group, placebo-controlled, randomized study: evaluation of the efficacy and safety of brivaracetam in subjects (16 to 70 years old) with Partial Onset Seizures.

Published: 17-04-2007
Last updated: 08-05-2024

To evaluate the efficacy of BRV at the doses of 20, 50 and 100 mg/day in b.i.d. administration in reducing seizure frequency in subjects with partial onset seizures not fully controlled despite optimal treatment with 1 to 2 concomitant AED(s),...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Neurological disorders NEC
Study type	Interventional

Summary

ID

NL-OMON31126

Source
ToetsingOnline

Brief title
Protocol N01252

Condition

- Neurological disorders NEC

Synonym
epilepsy

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 2-pyrrolidone derivative, Anti Epileptic Drug, Brivaracetam, Partial Onset Seizures

Outcome measures

Primary outcome

The primary efficacy variable is the partial onset seizure (Type I) frequency

per week over the Treatment Period.

Secondary outcome

• Seizure Worry QOLIE-31-P score.

• Daily Activities QOLIE-31-P score.

• Total QOLIE-31-P score.

• Remaining QOLIE-31-P domain scores (Energy/Fatigue, Emotional Well-being,

Mental Activity/Cognitive Functioning, Overall Quality of Life and Medication

effects).

• Hospital Anxiety and Depression Scale (HADS) scores (Anxiety, Depression).

• Patient*s Global Evaluation Scale (GES).

• Investigator*s GES.

• All seizure frequency (Type I + II + III) per week over the Treatment Period.

• Seizure freedom rate (all seizure types).

• Percent reduction for partial onset seizure (Type I) frequency per week from

baseline to the Treatment Period.

• Responder rate (the proportion of subjects who have a >= 50% reduction in

seizure frequency per week from baseline) for partial onset seizures (Type I)

over the Treatment Period.

• Categorized percentage reduction from baseline in seizure frequency for

partial onset seizures (type I) over the Treatment Period. The categories

include: <-25%, -25% to < 25%, 25% to < 50%, 50% to < 75%, 75% to < 100%, and

100%.

• Reduction of Type IC/Type I seizure frequency ratio from baseline to the

Treatment Period.

Study description

Background summary

This adequate and well-controlled study will be performed to provide data confirming the efficacy and safety of brivaracetam (BRV) as an antiepileptic drug (AED) and to support the marketing authorization application / new drug application for BRV in the indication of adjunctive treatment in adults (18 years - 70 years) with refractory partial onset seizures (POS) with or without secondary generalization.
Studies using BRV as adjunctive therapy in POS in adults have shown promising results in terms of both efficacy (53.05% reduction in seizure frequency per week from baseline and 55.77% responder rate in Type I seizures) and safety.
The dosages of 20 mg/day, 50 mg/day and 100 mg/day have been chosen based upon a dose-response analysis performed on the data collected during the phase II program.

Study objective

To evaluate the efficacy of BRV at the doses of 20, 50 and 100 mg/day in b.i.d. administration in reducing seizure frequency in subjects with partial onset seizures not fully controlled despite optimal treatment with 1 to 2 concomitant AED(s), compared to placebo.

Study design

This is a multicenter, therapeutic confirmatory, parallel-group, double-blind, randomized, placebo-controlled study with 3 active doses of BRV and possible

conversion to a Long-Term Follow-Up (LTFU) study.
A 1:1:1:1 central randomization (random permuted blocks) stratified for the study region (Eastern Europe / Western Europe / ROW) and for the use of LEV (use / no use at study entry) will be used to ensure the balance between the different treatment groups (PBO, 20 mg BRV, 50 mg BRV and 100 mg BRV). The number of subjects using LEV as concomitant AED will be limited to 20% of the total study population.

Intervention

All subjects will be either randomised to brivaracetam:
- 20 mg/day,
- 50 mg/day,
- 100 mg/day or
- matching placebo.

All subjects will be asked to take 3 tablets in the morning and 3 tablets in the evening.

Study burden and risks

Physical examnination including neurologic examination and mental status 4x
ECG 4x
EEG 1x (unless performed within 5 years before start of study)
MRI/CT scan 1x (unless performed within 2 years before start of study)
3 health questionnaires 4x
lab testing 6x
DNA test 1x
pregnancy test 6x
vital sign's 7x

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

• Subjects from 16 to 70 years, both inclusive. Subjects under 18 years may only be included where legally permitted and ethically accepted.
• Well-characterized focal epilepsy or epileptic syndrome according to the ILAE classification (1).
• Subjects with a history of partial onset seizures whether or not secondarily generalized (Type I seizures according to the ILAE classification (2)).
• Subjects having at least two partial onset seizures whether or not secondarily generalized per month during the three months preceding Visit 1 (V1).
• Subjects having at least eight partial onset seizures whether or not secondarily generalized during the 8-week Baseline Period.
• Subjects being uncontrolled while treated by one to two permitted concomitant AED(s).

Exclusion criteria

• History or presence of seizures occurring only in clusters (too frequently or indistinctly separated to be reliably counted) before V3.
• History or presence of status epilepticus during the year preceding V1 or during baseline.
• Subject taking any drug with possible relevant CNS effects except if stable from at least 1 month before Visit 1 and expected to be kept stable during the Treatment Period.
• Subjects taking any drug that may significantly influence the metabolism of BRV (CYP2C or CYP3A potent inducers/inhibitors) except if the dose has been kept stable at least one month before V1, and is expected to be kept stable during the Treatment Period.
• History of cerebrovascular accident (CVA), including transient ischemic attack (TIA), in the last six months.
• Presence of any sign (clinical or imaging techniques) suggesting rapidly progressing (i.e.

not expected to stay stable during trial participation) brain disorder or brain tumor. Stable arteriovenous malformations, meningiomas or other benign tumors may be acceptable.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-02-2008
Enrollment:	24
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	Brivaracetam

Ethics review

Approved WMO

Date:	17-04-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO Date:	24-07-2007
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	16-08-2007
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-10-2007
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	08-08-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	18-08-2008
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	EUCTR2006-06344-59-NL
CCMO	NL17187.068.07