Clinical trial results:
An open-label, multi-center, follow-up trial to evaluate long term safety and efficacy of brivaracetam used as adjunctive treatment at a flexible dose up to a maximum of 200 mg/day in subjects aged 16 years or older suffering from epilepsy

Summary

EudraCT number	2014-004397-42
Trial protocol	Outside EU/EEA
Global end of trial date	18 September 2017

Results information

Result version number	v2 (current)
This version publication date	25 November 2018
First version publication date	05 April 2018
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	N01199

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00150800
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma Inc.
Sponsor organisation address	1950 Lake Park Drive, Smyrna, United States, 30080
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 November 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 September 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the long-term safety and tolerability of brivaracetam (BRV) at individualized doses with a maximum of 200 mg/day in subjects suffering from epilepsy.

Protection of trial subjects:

During the conduct of the study all subjects were closely monitored.

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	23 January 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 30
Country: Number of subjects enrolled	Brazil: 115
Country: Number of subjects enrolled	Canada: 13
Country: Number of subjects enrolled	India: 202
Country: Number of subjects enrolled	Mexico: 96
Country: Number of subjects enrolled	United States: 211
Worldwide total number of subjects	667
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0

Adolescents (12-17 years)	30
Adults (18-64 years)	632
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll patients in January 2006 and concluded in September 2017. 668 subjects were included in the Enrolled Set but 1 subject from India lost to follow up and was excluded from the Safety Analysis Set due to lack of medical data.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Analysis Set which included all subjects who took at least 1 dose of study drug.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Brivaracetam

Arm description:

Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam
Investigational medicinal product code	BRV
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Active investigational product (tablets containing 10 or 25 mg BRV) used as adjunctive treatment, flexible dosing up to 200 mg/day in b.i.d (twice daily) administration. Dose increase or decrease could be made in increments of maximum 50 mg/day on a weekly basis.

Number of subjects in period 1	Brivaracetam
Started	667
Completed	171
Not completed	496
Adverse event, serious fatal	18
Neurosurgery	2
Nobody to accompany patient	1
Surgical intervention	4
Distance too long for patient	1
PI discontinuation request	1
Subject's choice	90

No compliance	18
Site closure	24
Pregnancy planned	1
Patient insurance	1
BRV monotherapy	1
Sponsor's request	2
Adverse event, non-fatal	89
PI retiring	2
PI leaving site	2
IP misshandling	1
Generalized Epilepsy	1
Lost to follow-up	58
Moved from area/country	8
Protocol non-adherence	2
Lack of efficacy	166
Visit refusal	3

Baseline characteristics

Reporting groups	
Reporting group title	Brivaracetam
Reporting group description:	
Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.	

Reporting group values	Brivaracetam	Total	
Number of subjects	667	667	
Age categorical Units: Subjects			
<=18 years	30	30	
Between 18 and 65 years	632	632	
>=65 years	5	5	
Age continuous Units: years			
arithmetic mean	34.3		
standard deviation	± 12.2	-	
Gender categorical Units: Subjects			
Female	303	303	
Male	364	364	

End points

End points reporting groups

Reporting group title	Brivaracetam

Reporting group description:

Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.

Subject analysis set title	Brivaracetam (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.

Subject analysis set title	Brivaracetam (POS-ES)
Subject analysis set type	Full analysis

Subject analysis set description:

Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.

Primary: Percentage of participants with at least one Treatment-Emergent Adverse Event (TEAE) during the Study Period

End point title	Percentage of participants with at least one Treatment-Emergent Adverse Event (TEAE) during the Study Period[1]

End point description:

Treatment-Emergent Adverse Events (TEAEs) are any untoward medical incidence in a subject during administered study treatment, whether or not these events are related to study treatment.

End point type	Primary

End point timeframe:

Visit 1 through last Evaluation Period, Down-Titration, or Post-Treatment Periods (up to 11 years)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Brivaracetam (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	667			
Units: percentage of participants				
number (not applicable)	91.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants who withdrew due to an Adverse Event (AE) during the Study Period

End point title	Percentage of participants who withdrew due to an Adverse Event (AE) during the Study Period[2]

End point description:

Adverse Events (AE) are any untoward medical incidence in a subject during administered study treatment, whether or not these events are related to study treatment.

End point type	Primary

End point timeframe:

Visit 1 through last Evaluation Period, Down-Titration, or Post-Treatment Periods (up to 11 years)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Brivaracetam (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	667			
Units: percentage of participants				
number (not applicable)	14.8			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with a Serious Adverse Event (SAE) during the Study Period

End point title	Percentage of participants with a Serious Adverse Event (SAE) during the Study Period[3]

End point description:

A Serious Adverse Event (SAE) is any untoward medical incidence that occurs at any dose.

End point type	Primary

End point timeframe:

Visit 1 through last Evaluation Period, Down-Titration, or Post-Treatment Periods (up to 11 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

End point values	Brivaracetam (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	667			
Units: percentage of participants				
number (not applicable)	22.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Partial Onset Seizure (POS) (type I) frequency per 28 days during the

Evaluation Period

End point title	Partial Onset Seizure (POS) (type I) frequency per 28 days during the Evaluation Period

End point description:

Baseline is the Baseline from subject's previous study of enrollment period.
N01193 [NCT00175825], N01252 [NCT00490035], N01253 [NCT00464269], N01254 [NCT00504881].
A 28 day Type 1 seizure frequency is the total number of Type 1 seizures divided by the total number of days evaluated multiplied by 28.

End point type	Secondary

End point timeframe:

From Baseline of the previous study to the Evaluation Period (up to 11 years)

End point values	Brivaracetam (POS-ES)			
Subject group type	Subject analysis set			
Number of subjects analysed	648			
Units: Seizures per 28 days				
median (inter-quartile range (Q1-Q3))				
baseline	9.2 (5.5 to 20.2)			
on treatment	4.2 (1.6 to 11.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Partial Onset Seizure (POS) (type I) frequency per 28 days from Baseline of the previous study to the Evaluation Period

End point title	Percent change in Partial Onset Seizure (POS) (type I) frequency per 28 days from Baseline of the previous study to the Evaluation Period

End point description:

The percent change from the previous study baselines, in Partial Onset Seizure (POS) (Type I) frequency per 28 days is defined as:
(the value at the previous study baselines) minus (the value at each time-points during the evaluation period) divided by the value at the previous study baselines.

End point type	Secondary

End point timeframe:

From Baseline of the previous study to the Evaluation Period (up to 11 years)

End point values	Brivaracetam (POS-ES)			
Subject group type	Subject analysis set			
Number of subjects analysed	648			
Units: percent change				
median (inter-quartile range (Q1-Q3))	57.3 (18.6 to 82.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with response for Partial Onset Seizure (POS) (type I) frequency over the Evaluation Period

End point title	Percentage of participants with response for Partial Onset Seizure (POS) (type I) frequency over the Evaluation Period

End point description:

A responder is defined as a subject with a higher than or equal to (>=) 50 % change in seizure frequency from Baseline period of the previous study.

End point type	Secondary

End point timeframe:

From Baseline of the previous study to the Evaluation Period (up to 11 years)

End point values	Brivaracetam (POS-ES)			
Subject group type	Subject analysis set			
Number of subjects analysed	648			
Units: percentage of participants				
number (not applicable)	55.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Visit 1 through last Evaluation Period, Down-Titration, or Post-Treatment Periods (up to 11 years)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Brivaracetam

Reporting group description:

Brivaracetam (BRV) used as adjunctive treatment, flexible dosing up to 200 mg /day in b.i.d (twice daily) administration. Dose increase or decrease can be made in increments of maximum 50 mg /day on a weekly basis.

Serious adverse events	Brivaracetam		
Total subjects affected by serious adverse events			
subjects affected / exposed	152 / 667 (22.79%)		
number of deaths (all causes)	18		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain cancer metastatic			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain neoplasm			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colon cancer metastatic			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal tract adenoma			

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lipoma				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma metastatic				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Malignant pleural effusion				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastatic bronchial carcinoma				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Non-small cell lung cancer				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ocular neoplasm				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oesophageal cancer metastatic				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ovarian epithelial cancer				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Ovarian germ cell teratoma benign				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal cell carcinoma				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer stage unspecified				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestine carcinoma metastatic				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Thyroid cancer				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Uterine leiomyoma				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypertension				

subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Surgical and medical procedures			
Abortion induced			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Abortion spontaneous			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Foetal death			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy			
subjects affected / exposed	5 / 667 (0.75%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Pregnancy on oral contraceptive			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy on contraceptive			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Unintended pregnancy				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Chest pain				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Drug ineffective				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Non-cardiac chest pain				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Sudden unexplained death in epilepsy				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	1 / 2			
Unevaluable event				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysfunctional uterine bleeding			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Menorrhagia			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Ovarian cyst			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Scrotal disorder			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Dyspnoea			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Asthma			

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Lung infiltration				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary congestion				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Respiratory failure				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				

subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Aggression			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 2		
Depression			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Paranoia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Major depression			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Self-injurious ideation				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Schizophrenia				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	7 / 667 (1.05%)			
occurrences causally related to treatment / all	5 / 8			
deaths causally related to treatment / all	0 / 0			
Investigations				
Anticonvulsant drug level increased				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Weight increased				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				

Abdominal injury			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Accident			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Anastomotic ulcer			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Animal bite			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	3 / 667 (0.45%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Brain contusion			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burns third degree			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Comminuted fracture			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			

subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Femur fracture				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ligament sprain				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post procedural haematoma				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Procedural hypotension				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haemorrhage				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tendon rupture				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	4 / 667 (0.60%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				

subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Wrist fracture			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina unstable			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	3 / 667 (0.45%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 2		
Myocardial ischaemia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Supraventricular tachycardia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Central nervous system lesion			

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cerebral infarction				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Complicated migraine				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	15 / 667 (2.25%)			
occurrences causally related to treatment / all	4 / 20			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Grand mal convulsion				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Partial seizures				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Postictal state				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Seizure cluster				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	6 / 667 (0.90%)			
occurrences causally related to treatment / all	4 / 7			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				

subjects affected / exposed	4 / 667 (0.60%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lymphadenopathy			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain upper			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Constipation			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastric fistula			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic artery aneurysm				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis acute				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Calculus ureteric				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Calculus urinary				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure acute				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc degeneration				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Joint instability				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Cellulitis staphylococcal				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coccidioidomycosis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dengue fever				
subjects affected / exposed	2 / 667 (0.30%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Disseminated tuberculosis				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Encephalitis herpes				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia sepsis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malaria				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mastoiditis				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Meningitis tuberculous				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Neurocysticercosis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic inflammatory disease				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	7 / 667 (1.05%)			
occurrences causally related to treatment / all	0 / 9			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rickettsiosis				

subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tooth abscess				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	3 / 667 (0.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyperammonaemia				
subjects affected / exposed	1 / 667 (0.15%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				

subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	2 / 667 (0.30%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hypoproteinaemia			
subjects affected / exposed	1 / 667 (0.15%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Brivaracetam		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	521 / 667 (78.11%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	40 / 667 (6.00%)		
occurrences (all)	72		
Contusion			
subjects affected / exposed	34 / 667 (5.10%)		
occurrences (all)	68		
Laceration			
subjects affected / exposed	34 / 667 (5.10%)		
occurrences (all)	65		
Vascular disorders			
Hypertension			
subjects affected / exposed	46 / 667 (6.90%)		
occurrences (all)	55		
Nervous system disorders			
Headache			
subjects affected / exposed	165 / 667 (24.74%)		
occurrences (all)	420		

Dizziness			
subjects affected / exposed	142 / 667 (21.29%)		
occurrences (all)	254		
Somnolence			
subjects affected / exposed	91 / 667 (13.64%)		
occurrences (all)	116		
Convulsion			
subjects affected / exposed	70 / 667 (10.49%)		
occurrences (all)	99		
Tremor			
subjects affected / exposed	38 / 667 (5.70%)		
occurrences (all)	48		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	69 / 667 (10.34%)		
occurrences (all)	132		
Fatigue			
subjects affected / exposed	51 / 667 (7.65%)		
occurrences (all)	63		
Irritability			
subjects affected / exposed	42 / 667 (6.30%)		
occurrences (all)	50		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	67 / 667 (10.04%)		
occurrences (all)	93		
Diarrhoea			
subjects affected / exposed	65 / 667 (9.75%)		
occurrences (all)	86		
Vomiting			
subjects affected / exposed	58 / 667 (8.70%)		
occurrences (all)	109		
Abdominal pain			
subjects affected / exposed	39 / 667 (5.85%)		
occurrences (all)	55		
Toothache			

subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	42 / 667 (6.30%) 66 38 / 667 (5.70%) 48		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 46 / 667 (6.90%) 69		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	 34 / 667 (5.10%) 56		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	 70 / 667 (10.49%) 85 49 / 667 (7.35%) 65 45 / 667 (6.75%) 65		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity alternative assessment type: Systematic subjects affected / exposed occurrences (all)	 64 / 667 (9.60%) 88 52 / 667 (7.80%) 66 44 / 667 (6.60%) 63		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Influenza subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	94 / 667 (14.09%) 154 76 / 667 (11.39%) 137 84 / 667 (12.59%) 177 64 / 667 (9.60%) 150		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	36 / 667 (5.40%) 41		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 June 2006	Clarified several sections of the protocol, including study title, study drug packaging, flow chart, study procedures and visit description, and Sponsor contact information.
02 March 2007	Permitted participation of subjects from the brivaracetam (BRV) Phase 3 studies (N01253, N01253, and N01254) and updates of several sections including study title, background information, exclusion criteria, objectives, variables, and the study schematic. Maximum dose of study drug was increased to 150 mg/day.
01 June 2007	Issued as a follow-up to the Food and Drug Administration (FDA) feedback received on study N01253 where FDA specifically requested to add an additional down-titration step for subjects taking 50 mg/day or more. The use of the 2.5 mg tablets was restricted to subjects taking less than BRV 40 mg/day. Additional clarifications were made to allow for a new Clinical Trial Manager, clarify additional information from Amendment 2, and update some minor typographical errors.
20 May 2008	Clarified that subjects rolling over from the Phase 2 brivaracetam (BRV) study, N01193, who were on placebo would have access to BRV, updated the inclusion criterion regarding contraceptive methods, and stipulated that dose increments were to be made using only 10 mg or 25 mg tablets beyond the dose of 40 mg/day.
26 June 2011	Introduced the increased maximum dose of brivaracetam (BRV) of 200 mg/day; provided that conversion to monotherapy would no longer be at the Investigator's discretion; updated procedures for reporting serious adverse events (SAEs) to implement Food and Drug Administration (FDA) Final Rule requirements; updated laboratory assessments (BRV and antiepileptic drug (AED) plasma levels were no longer obtained), statistical analyses, and contact information; reduced the number of study assessments; limited the assessments of exploratory variables (Patient Weighted Quality of Life in Epilepsy Questionnaire [QOLIE-31-P], Hospital Anxiety and Depression Scale [HADS], EuroQoL 5 Dimensions Questionnaire [EQ-5D], hospital stays, healthcare provider consultations not foreseen, school and work days lost, and socioprofessional data) to the first 2 years after study entry; added the Columbia Suicide Severity Rating Scale (C-SSRS) and respective withdrawal criteria; introduced a Partner Pregnancy Consent form; removal of 2.5 mg tablets; removal of references to subjects coming from N01258, since these subjects were no longer to be included in N01199; and made further minor changes for consistency between BRV studies.
15 October 2015	Aligned efficacy variables in statistics section with current N01199 statistical analysis plan (SAP); the study duration language was revised to include the possibility of a named patient or compassionate use program (or similar) as a reason for ending the study duration; language regarding Investigator deviation from the protocol in the event of a medical emergency was revised to align with current UCB standard language.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported