Clinical trial results:
An open-label, multicenter, single-arm study to evaluate the reduction in nonpsychotic behavioral side effects in subjects with epilepsy switching from Levetiracetam to Brivaracetam due to nonpsychotic behavioral side effects
phase 3b

Summary

EudraCT number	2011-005177-23
Trial protocol	GB DE ES IT
Global end of trial date	15 November 2013

Results information

Result version number	v1 (current)
This version publication date	28 June 2016
First version publication date	30 July 2015

Trial information

Trial identification

Sponsor protocol code	N01395

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01653262
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma SA
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, B-1070
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 2173 4815 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 2173 48 15 15, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 January 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to evaluate the reduction of nonpsychotic behavioral side effects in subjects with epilepsy who switched to Brivaracetam (BRV) 200 mg/day after discontinuing Levetiracetam (LEV) 1 g/day to 3 g/day due to these nonpsychotic behavioral side effects.

Protection of trial subjects:

In Phase 2/3 studies, a favorable safety and tolerability profile has been demonstrated for Brivaracetam (BRV). Therefore dose adjustments within the range of BRV 50 mg/day to 200 mg/day were permitted based on clinical response and tolerability in order to minimize distress.

Background therapy:

Patient receiving levetiracetam at the recommended therapeutic dose (dose ranging from 1 g/day to 3 g/day) for up to 16 weeks prior to study entry, and treated with not more than 2 other concomitant anti-epileptic drugs (AEDs).

Evidence for comparator:

Not applicable

Actual start date of recruitment	24 July 2012
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United States: 20
Worldwide total number of subjects	29
EEA total number of subjects	9

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)	0
Adults (18-64 years)	29
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study started to enroll subjects in July 2012. In Oct 2013, the Sponsor evaluated the study in light of the recruitment rate. Given the unanticipated lack of recruitment during the prior 8 weeks, a decision was made to stop recruitment as of 16 Oct 2013.

Pre-assignment

Screening details:

Participant Flow refers to the Enrolled Set.
In total, 32 subjects were screened and 29 subjects were enrolled instead of 30 subjects as per protocol amendment 2. This difference was considered as insignificant and not affecting the planned analysis.

Period 1

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

Arms

Arm title	Brivaracetam

Arm description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily. Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam
Investigational medicinal product code	ucb 34714
Other name	BRV
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

The study drug was oral film-coated tablets of BRV 10 mg and BRV 25 mg.
The subjects were treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks.

Number of subjects in period 1	Brivaracetam
Started	29
Completed	26
Not completed	3
AE, non-serious non-fatal	1
SAE, non-fatal	1
Lack of efficacy	1

Baseline characteristics

Reporting groups	
Reporting group title	Brivaracetam

Reporting group description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily. Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.

Reporting group values	Brivaracetam	Total	
Number of subjects	29	29	
Age Categorical Units: Subjects			
<=18 years	0	0	
Between 18 and 65 years	29	29	
>= 65 years	0	0	
Age Continuous Units: years			
arithmetic mean	35.8		
standard deviation	± 11.8	-	
Gender Categorical Units: Subjects			
Female	14	14	
Male	15	15	

End points

End points reporting groups

Reporting group title	Brivaracetam

Reporting group description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily. Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.

Subject analysis set title	Full Analysis Set (Brivaracetam treated subjects)
Subject analysis set type	Full analysis

Subject analysis set description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily.
Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.
At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.
The Full Analysis Set (FAS) consisted of all subjects who received at least 1 dose of Brivaracetam and had at least 1 post-Baseline evaluation of behavioral side effects.

Subject analysis set title	Safety Set (Brivaracetam treated subjects)
Subject analysis set type	Safety analysis

Subject analysis set description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily.
Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.
At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.
The Safety Set (SS) consisted of all subjects who received at least 1 dose of Brivaracetam.

Subject analysis set title	Efficacy Analysis Set (Brivaracetam treated subjects)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily.
Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.
At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.
The Efficacy Analysis Set (EAS) consisted of all subjects who received at least 1 dose of Brivaracetam and had at least 1 post-Baseline day of seizure daily record card (subject diary card).

Primary: Percentage of subjects who achieved a clinically meaningful reduction of nonpsychotic behavioral side effects based on the Investigator's overall assessment from Study Entry to the end of the Treatment Period

End point title	Percentage of subjects who achieved a clinically meaningful reduction of nonpsychotic behavioral side effects based on the Investigator's overall assessment from Study Entry to the end of the Treatment Period[1]

End point description:

Nonpsychotic behavioral side effects include (but are not limited to) such symptoms as aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, irritability, etc.
The Investigator completed the assessment by answering the following:
"Has there been a clinically meaningful reduction of nonpsychotic behavioral side effects since the start of BRV?"
- Yes/No

End point type	Primary

End point timeframe:

From Study Entry (Visit1, Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

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 in tables as descriptive statistics only.

End point values	Full Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: percentage of subjects				
number (not applicable)				
percentage of subjects	93.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Shift in the maximum intensity from Baseline to the end of the Treatment Period for side effects primarily associated with discontinuation of Levetiracetam (LEV) as determined by the Investigator

End point title	Shift in the maximum intensity from Baseline to the end of the Treatment Period for side effects primarily associated with discontinuation of Levetiracetam (LEV) as determined by the Investigator

End point description:

Nonpsychotic behavioral side effects include (but are not limited to) such symptoms as aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, irritability, etc.

End point type	Secondary

End point timeframe:

From Baseline (maximum of 12 weeks prior to Study Entry at Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Full Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: subjects				
Improvement	8			
Unchanged	2			
Worsening	0			
Resolved	19			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Study Entry in nonpsychotic behavioral side effects to the end of the Treatment Period/Early Discontinuation Visit, measured by means of the Investigator Global Evaluation of nonpsychotic Behavioral Side Effects (I-GEBSE) scale

End point title	Change from Study Entry in nonpsychotic behavioral side effects to the end of the Treatment Period/Early Discontinuation Visit, measured by means of the Investigator Global Evaluation of nonpsychotic Behavioral Side Effects (I-GEBSE) scale

End point description:

There are seven levels for the I-GEBSE:
- Marked improvement
- Moderate improvement
- Slight improvement
- No change
- Slight worsening
- Moderate worsening
- Marked worsening

End point type	Secondary

End point timeframe:

From Study Entry (Visit1, Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Full Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: subjects				
Marked improvement	10			
Moderate improvement	10			
Slight improvement	4			
No change	2			
Slight worsening	1			
Moderate worsening	0			
Marked worsening	1			
Missing	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who have a complete abatement of nonpsychotic behavioral side effects for the last assessment during the Treatment Period, based on the Investigator's overall assessment

End point title	Number of subjects who have a complete abatement of nonpsychotic behavioral side effects for the last assessment during the Treatment Period, based on the Investigator's overall assessment

End point description:

Nonpsychotic behavioral side effects include (but are not limited to) such symptoms as aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, irritability, etc.

End point type	Secondary

End point timeframe:

From Baseline (maximum of 12 weeks prior to Study Entry at Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Full Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: subjects				
Complete Abatement	18			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who are free from nonpsychotic behavioral side effects over the entire Treatment Period

End point title	Number of subjects who are free from nonpsychotic behavioral side effects over the entire Treatment Period

End point description:

Nonpsychotic behavioral side effects (NBSE) include (but are not limited to) such symptoms as aggression, agitation, anger, anxiety, apathy, depersonalization, depression, emotional lability, hostility, irritability, etc.

End point type	Secondary

End point timeframe:

From Visit 2 (Week 0) to Visit 6 (Week 12)

End point values	Full Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: subjects				
Freedom from NBSE	3			

Statistical analyses

No statistical analyses for this end point

Secondary: Incidence of Treatment Emergent Adverse Events during the Study Period

End point title	Incidence of Treatment Emergent Adverse Events during the Study Period

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. A treatment emergent AE is any event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state.

End point type	Secondary

End point timeframe:

From Study Entry (Visit1, Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Safety Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: events				
Treatment-Emergent Adverse Events	67			

Statistical analyses

No statistical analyses for this end point

Secondary: Withdrawal due to an Adverse Event (AE) during the Study Period

End point title	Withdrawal due to an Adverse Event (AE) during the Study Period

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment.

End point type	Secondary

End point timeframe:

From Study Entry (Visit1, Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Safety Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: subjects				
Subjects who withdrew due to AE	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of Serious Adverse Events during the Study Period

End point title	Occurrence of Serious Adverse Events during the Study Period

End point description:

A serious adverse event is any untoward medical occurrences in a subject administered study treatment, whether or not the event is related to treatment, with at least one of the follow outcomes: death, life-threatening, initial inpatient hospitalization or prolongation of hospitalization, significant or persistent disability/incapacity, congenital anomaly/birth defect, or an important medical event that may jeopardize the subject and require a medical/surgical intervention.

End point type	Secondary

End point timeframe:

From Study Entry (Visit1, Week -1) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Safety Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: events				
Serious Adverse Events	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Partial Onset Seizure (POS) frequency over the Treatment Period for subjects with focal Epilepsy

End point title	Partial Onset Seizure (POS) frequency over the Treatment Period for subjects with focal Epilepsy

End point description:

The POS frequency is standardized to a 28-day duration and changes in POS frequency are measured relative to the reported seizure counts for the 4 weeks prior to Visit 2 (Week 0).
Partial seizures can be classified into one of the following three groups:
- Simple partial seizures (IA)
- Complex partial seizures (IB)
- Partial seizures evolving to secondarily generalized seizures (IC)

End point type	Secondary

End point timeframe:

From 4 weeks prior to Visit 2 (Week 0) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Efficacy Analysis Set (Brivaracetam treated subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	15			
Units: POS frequency				
median (inter-quartile range (Q1-Q3))				
Median (Inter-Quartile Range)	6 (2.2 to 17.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Generalized seizure days over the Treatment Period for subjects with idiopathic generalized Epilepsy

End point title	Generalized seizure days over the Treatment Period for subjects with idiopathic generalized Epilepsy

End point description:

Generalized seizure days are standardized to a 28-day duration and changes in generalized seizure days are measured relative to the reported seizure counts for the 4 weeks prior to Visit 2 (Week 0).
Generalized seizures (Type II) include the following seizure types:
- Absence (IIA1)
- Atypical absence (IIA2)
- Myoclonic (IIB)
- Clonic (IIC)
- Tonic (IID)
- Tonic-clonic (IIE)
- Atonic (IIF)

A specific effect of BRV on the occurrence of generalized seizures was not assessed.

End point type	Secondary

End point timeframe:

From 4 weeks prior to Visit 2 (Week 0) to the end of the Treatment Period (Visit 6, Week 12) or Early Discontinuation Visit

End point values	Brivaracetam			
Subject group type	Reporting group			
Number of subjects analysed	0[2]			
Units: days				
median (inter-quartile range (Q1-Q3))				
Median (Inter-Quartile Range)	(to)			

Notes:

[2] - Please refer to End point description

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Screening Period (Week -1) over the 12-weeks Treatment Period until the Safety Visit (Week 15-18 + max 7 days).

Adverse event reporting additional description:

Adverse Events refer to the Safety Set (SS) consisting of all subjects who received at least 1 dose of Brivaracetam.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups

Reporting group title	Brivaracetam

Reporting group description:

The subjects will be treated with Brivaracetam (BRV) tablets 200 mg/day during 12 weeks: four 25 mg tablets, twice daily.
Based on the Investigator's judgement, at any time, the dose can be decreased to BRV 150 mg/day, 100 mg/day, or 50 mg/day. Flexible dosing, can be up- and down-titrated as needed.
At the end of the Treatment Period, the subject will either enter the N01372 long-term follow-up study or down-titrate during 4 weeks.

Serious adverse events	Brivaracetam		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 29 (3.45%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	1 / 29 (3.45%)		
occurrences causally related to treatment / all	0 / 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	13 / 29 (44.83%)		
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 29 (17.24%)		
occurrences (all)	7		
Tremor			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	3		
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Insomnia			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 29 (10.34%)		
occurrences (all)	4		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 29 (6.90%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2012	The protocol was amended for the following reasons: - To introduce a visit window of up to an additional 7 days maximum to the end of the Study Drug-Free Period to facilitate planning in compliance with the protocol. - To introduce a visit window of ±3 days for V2 to V7 in order to bring N01395 in line with the visit windows applied to other studies using BRV and to take into account practical considerations of requiring subjects to return to the clinic (in order to allow greater flexibility). - To clarify the timing of V7 throughout the protocol. - To update details of some of the team members as the Study Sponsor Physician, Clinical Project Manager (CPM), Clinical Program Director, and Clinical Trial Biostatistician had changed since the protocol was written. - To make some minor revisions to the schematic diagram for the study to show the plan for the visits at the end of the study more clearly and to clarify wording on a footnote pertaining to the inclusion/exclusion criteria.
28 September 2012	The protocol was amended for the following reasons: - To change the wording in the inclusion and exclusion criteria to make clear that subjects may have only been receiving LEV for up to 16 weeks prior to V1 at a dose of 1 g/day to 3 g/day. Previously, subjects who took LEV for more than 12 weeks prior to V1 were to be excluded; however, 12 weeks was considered by the Investigators to exclude a number of subjects who developed nonpsychotic behavioral side effects due to LEV, which were recognized at a time that it was too late to schedule and perform a Screening Visit no later than 12 weeks after the start date of LEV. This was partially due to the broad spectrum of nonpsychotic behavioral side effects and the different manifestations of nonpsychotic behavioral side effects that could have been expressed by the patient and/or a relative or close friend. It was necessary to state in the inclusion criteria that the maximum period of 16 weeks should have applied only for the recommended therapeutic dose ranging from 1 g/day to 3 g/day as doses below this range were not considered to be therapeutic. Changes were also made throughout the protocol to reflect the change from a 12-week period to a 16-week period and to specify that the Baseline for nonpsychotic behavioral side effects started when the first LEV dose at the therapeutic approved dose (1 g/day to 3 g/day) was started. - To include a clear definition of abstinence as an acceptable method of contraception, where abstinence was defined as “true abstinence” according to Medicines and Healthcare products Regulatory Agency guidance. - To update wording pertaining to suicide attempts and suicidal ideation captured by the Columbia-Suicide Severity Rating Scale (C-SSRS), in order to ensure the protocol was consistent with this global change for all UCB protocols.

28 September 2012	The protocol was amended for the following reasons: - To include further details on the permitted dose adjustments during the Treatment Period in the Treatment(s) to be administered section (Section 7.2) to be consistent with the text in Study description (Section 5.1) of the protocol. - To change the restriction for concomitant non-AEDs as the endpoints for the N01395 study did not require that strong hepatic inducers (which could have caused fluctuations in BRV concentrations) were to be restricted. - To clarify the documentation of the Patient Global Evaluation Scale (P-GES), Investigator Global Evaluation Scale (I-GES), and Investigator Global Evaluation of nonpsychotic Behavioral Side Effects (I-GEBSE) questionnaires during the study and to include the 7 items on the I-GEBSE to be consistent with the level of detail of presentation of the P-GES and I-GES. The numbering of the list of items in the P-GES and I-GES was removed in order to make the presentation consistent with the eCRF, which did not contain numbering in the lists. - To update the name of the Global Clinical Safety and Pharmacovigilance department to Drug Safety (DS) due to a change in the organizational structure at UCB, and to update the contact details for serious adverse event (SAE) reporting due to the formation of a new data processing team at UCB. - To correct a typographical error in the schedule of study assessments and to make some minor style and formatting changes throughout the protocol in order to ensure the document styles were consistent with the current template requirements.
29 April 2013	The protocol was amended for the following reason: - Based on review of the study objectives, the exploratory nature of the study design, and unanticipated recruitment challenges, the sample size was reassessed. The sample size for N01395 was reduced from the previous total of 100 subjects entering the BRV Treatment Period to a minimum of 32 subjects with the expectation that at least 30 subjects would receive at least 1 dose of BRV. This amendment was not due to any changes in the adverse event (AE), safety, or tolerability profile for BRV.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported