Clinical trial results:
An Open-Label, Multicenter, Follow-up Study to Evaluate the Long-Term Safety and Efficacy of Brivaracetam Used as Adjunctive Treatment in Subjects >=16 Years of Age With Partial Seizures With or Without Secondary Generalization

Summary

EudraCT number	2019-001205-25
Trial protocol	Outside EU/EEA
Global end of trial date	24 December 2024

Results information

Result version number	v2 (current)
This version publication date	24 July 2025
First version publication date	27 June 2025
Version creation reason	• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.

Trial information

Trial identification

Sponsor protocol code	EP0085

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03250377
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Biopharma SRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, 1070
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	06 February 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 December 2024
Global end of trial reached?	Yes
Global end of trial date	24 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Evaluate the long-term safety and tolerability of BRV in focal epilepsy subjects with partial seizures

Protection of trial subjects:

Invasive treatment is not planned in Protocol

Background therapy:

Background therapy as permitted in the protocol

Evidence for comparator:

Not Applicable

Actual start date of recruitment	05 August 2017
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	Japan: 132
Country: Number of subjects enrolled	China: 75
Worldwide total number of subjects	207
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)	7
Adults (18-64 years)	192
From 65 to 84 years	7
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in August 2017 and concluded in December 2024.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Set (SS). Study consisted of the Evaluation period (duration for rollover participants - 84 Months and for direct enrollers - 39 Months); Down-titration period (4 weeks); drug-free period (2 weeks).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	EP0083 Placebo

Arm description:

Participants who received Placebo in study EP0083 (NCT03083665) and completed the Treatment and Transition Period of study EP0083 are rolled over to this study and received brivaracetam (BRV) 50 milligram per day (mg/day) two times (bid) (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

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

Dosage and administration details:

Participants received Brivaracetam at prespecified time-points.

Arm title	EP0083 BRV All

Arm description:

Participants rolled over from study EP0083 received BRV 50 mg/day bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

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

Dosage and administration details:

Participants received Brivaracetam at prespecified time-points.

Arm title	N01379 BRV

Arm description:

Participants rolled over from study N01379 (NCT01339559) (core study N01358 [NCT01261325]) received BRV 200 mg/day during the evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

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

Dosage and administration details:

Participants received Brivaracetam at prespecified time-points.

Arm title	Direct Enrollers BRV

Arm description:

Participants directly enrolled in this study received BRV 50 mg bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. Up to 84 Month, however, were evaluated for 39 months only due to late enrollment). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

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

Dosage and administration details:

Participants received Brivaracetam at prespecified time-points.

Number of subjects in period 1	EP0083 Placebo	EP0083 BRV All	N01379 BRV
Started	54	112	7
Evaluation Period	54	112	7
Down-Titration Period	20 [1]	32 [2]	5
Study Drug-Free Period	39	76	5
Completed	37	74	4
Not completed	17	38	3

Epilepsy Surgery	-	1	2
Subjects underweight; intolerant to study drugs	-	1	-
Subjects felt no effect;want to discontinue study	-	1	-
Subject did not follow procedure or study drug	-	1	-
Subjects did not follow procedures or medication	-	1	-
Investigator's Judgment	1	-	-
Pregnancy Event	-	1	-
Subject moved to kanagawa (faraway from clinic)	-	1	-
PI’s opinion:Subject noncompliant with medication	-	1	-
Patient requested to change hospital	-	-	-
Admission To Geriatric Health Facility	-	-	-
Consent withdrawn by subject	7	7	-
Request From The Sponsor	-	1	-
Adverse event, non-fatal	2	4	-
She wanted to change other therapeutic medication	1	-	-
The Subject Go Abroad and Not Return	1	-	-
Subject stopped drug; did not wish to continue	-	1	-
Lost to follow-up	-	1	-
Lack of efficacy	5	14	1
Protocol deviation	-	2	-

Number of subjects in period 1	Direct Enrollers BRV
Started	34
Evaluation Period	34
Down-Titration Period	15 [3]
Study Drug-Free Period	17 [4]
Completed	20
Not completed	14
Epilepsy Surgery	-
Subjects underweight; intolerant to study drugs	-
Subjects felt no effect;want to discontinue study	-
Subject did not follow procedure or study drug	-
Subjects did not follow procedures or medication	-
Investigator's Judgment	-
Pregnancy Event	-
Subject moved to kanagawa (faraway from clinic)	-

PI’s opinion:Subject noncompliant with medication	-
Patient requested to change hospital	1
Admission To Geriatric Health Facility	1
Consent withdrawn by subject	4
Request From The Sponsor	-
Adverse event, non-fatal	4
She wanted to change other therapeutic medication	-
The Subject Go Abroad and Not Return	-
Subject stopped drug; did not wish to continue	-
Lost to follow-up	-
Lack of efficacy	3
Protocol deviation	1

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants who had an Early Discontinuation Visit (EDV) and had at least 1 dose of study drug after the date of EDV were considered to start Down-Titration Period.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants who had an Early Discontinuation Visit (EDV) and had at least 1 dose of study drug after the date of EDV were considered to start Down-Titration Period.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants who had at least one contact after the date of the last dose of BRV were considered to start study Drug-Free period.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: Participants who had an Early Discontinuation Visit (EDV) and had at least 1 dose of study drug after the date of EDV were considered to start Down-Titration Period.

Baseline characteristics

Reporting groups

Reporting group title	EP0083 Placebo

Reporting group description:

Participants who received Placebo in study EP0083 (NCT03083665) and completed the Treatment and Transition Period of study EP0083 are rolled over to this study and received brivaracetam (BRV) 50 milligram per day (mg/day) two times (bid) (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	EP0083 BRV All

Reporting group description:

Participants rolled over from study EP0083 received BRV 50 mg/day bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	N01379 BRV

Reporting group description:

Participants rolled over from study N01379 (NCT01339559) (core study N01358 [NCT01261325]) received BRV 200 mg/day during the evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	Direct Enrollers BRV

Reporting group description:

Participants directly enrolled in this study received BRV 50 mg bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. Up to 84 Month, however, were evaluated for 39 months only due to late enrollment). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group values	EP0083 Placebo	EP0083 BRV All	N01379 BRV
Number of subjects	54	112	7
Age Categorical Units: participants			
12 - <18 yrs	2	4	0
18 - <65 yrs	52	104	7
65 - <85 yrs	0	4	0
>=85 yrs	0	0	0
Age Continuous Units: years			
arithmetic mean	34.5	35.8	40.7

standard deviation	± 11.6	± 13.5	± 10.9

Sex: Female, Male Units: participants			
Female	32	53	3
Male	22	59	4

Reporting group values	Direct Enrollers BRV	Total	
Number of subjects	34	207	
Age Categorical Units: participants			
12 - <18 yrs	1	7	
18 - <65 yrs	29	192	
65 - <85 yrs	3	7	
>=85 yrs	1	1	
Age Continuous Units: years			
arithmetic mean	42.2		
standard deviation	± 18.6	-	
Sex: Female, Male Units: participants			
Female	19	107	
Male	15	100	

End points

End points reporting groups

Reporting group title	EP0083 Placebo

Reporting group description:

Participants who received Placebo in study EP0083 (NCT03083665) and completed the Treatment and Transition Period of study EP0083 are rolled over to this study and received brivaracetam (BRV) 50 milligram per day (mg/day) two times (bid) (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	EP0083 BRV All

Reporting group description:

Participants rolled over from study EP0083 received BRV 50 mg/day bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	N01379 BRV

Reporting group description:

Participants rolled over from study N01379 (NCT01339559) (core study N01358 [NCT01261325]) received BRV 200 mg/day during the evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	Direct Enrollers BRV

Reporting group description:

Participants directly enrolled in this study received BRV 50 mg bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. Up to 84 Month, however, were evaluated for 39 months only due to late enrollment). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Primary: Percentage of participants with Treatment-Emergent Adverse Events (TEAEs)

End point title	Percentage of participants with Treatment-Emergent Adverse Events (TEAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. Treatment-emergent AEs (TEAEs) were defined as AEs that had onset on or after the day of first BRV dose in EP0085 study. The Safety Set consisted of all participants who took at least 1 dose of study medication.

End point type	Primary

End point timeframe:

From Baseline until end of the safety follow up (up to 88.5 months)

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	EP0083 Placebo	EP0083 BRV All	N01379 BRV	Direct Enrollers BRV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	54	112	7	34
Units: percentage of participants				
number (not applicable)	88.9	95.5	100	94.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in partial seizure frequency (PSF) per 28 days from Baseline of EP0083 or N01358 to the Evaluation Period for rollover study participants

End point title	Percent change in partial seizure frequency (PSF) per 28 days from Baseline of EP0083 or N01358 to the Evaluation Period for rollover study participants[2]

End point description:

The seizure frequency was calculated as number of seizures per 28 days. Percent change of 28 day PSF from Baseline was defined as the percentage reduction of 28 day PSF for a designated post-baseline period in EP0085 compared with the Baseline 28 day PSF in the core study. Change in seizure frequency from Baseline was calculated: percent change = ([Baseline 28 day PSF − Post Baseline 28 day PSF]/[Baseline 28 day PSF]) × 100. For rollovers, the Baseline period was obtained from the core studies of EP0083 and N01358 directly. A negative value in percent change from Baseline indicates a decrease in PSF from Baseline. The Full Analysis Set (FAS) consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on Daily Record Card (DRC) during the Evaluation Period. Evaluation Period values for seizure frequency were calculated from the seizure diary data collected during the Evaluation Period on/after the first BRV administration.

End point type	Secondary

End point timeframe:

Baseline of EP0083 or N01358 and up to 84 months of Evaluation Period

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Percent change in partial seizure frequency (PSF) per 28 days for arm Direct Enrollers is reported in a separate endpoint. Therefore, no data was reported for this arm in this endpoint.

End point values	EP0083 Placebo	EP0083 BRV All	N01379 BRV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	112	7	
Units: percent change				
median (full range (min-max))	60.6 (-87 to 100)	43.2 (-497 to 100)	67.0 (-72 to 100)	

Statistical analyses

No statistical analyses for this end point

Secondary: 50 percent (%) Responder rate in partial seizure frequency per 28 days from Baseline of EP0083 or N01358 to the Evaluation Period for rollover study participants

End point title	50 percent (%) Responder rate in partial seizure frequency per 28 days from Baseline of EP0083 or N01358 to the Evaluation Period for rollover study participants[3]

End point description:

The seizure frequency was calculated as number of seizures per 28 days. 50% responders were defined as a participant with a >= 50% reduction in seizure frequency from the baseline period over the post-baseline period. Percentages are based on the number of participants who performed the seizure assessment at each time point. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Evaluation Period values for seizure frequency were calculated from the seizure diary data collected during the Evaluation Period on/after the first BRV administration.

End point type	Secondary

End point timeframe:

Baseline of EP0083 or N01358 and up to 84 months of Evaluation Period

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: 50 % Responder rate in partial seizure frequency per 28 days for arm Direct Enrollers is reported in a separate endpoint. Therefore, no data was reported for this arm in this endpoint

End point values	EP0083 Placebo	EP0083 BRV All	N01379 BRV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	112	7	
Units: percentage of responders				
number (not applicable)	66.7	47.3	57.1	

Statistical analyses

No statistical analyses for this end point

Secondary: 50 % responder rate in partial seizure frequency per 28 days over the Evaluation Period for directly enrolled study participants

End point title	50 % responder rate in partial seizure frequency per 28 days over the Evaluation Period for directly enrolled study participants[4]

End point description:

The seizure frequency for directly enrolled participants was calculated as number of seizures per 28 days from 8 weeks prior to BRV administration. 50% responders were defined as a participant with a >= 50% reduction in seizure frequency from the Baseline Period over the post-baseline period. Percentages are based on the number of participants who performed the seizure assessment at each time point. For direct enrollers, the Baseline Period was defined as seizure counts collected from 8 weeks prior to the first BRV administration in EP0085. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Evaluation Period values for seizure frequency were calculated from the seizure diary data collected during the Evaluation Period on/after the first BRV administration.

End point type	Secondary

End point timeframe:

Baseline (8 weeks prior to BRV administration), up to 39 months of Evaluation Period

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: 50 % Responder rate in partial seizure frequency per 28 days for the arms of rollover study participants is reported in a separate endpoint. Therefore, no data was reported for these arms in this endpoint.

End point values	Direct Enrollers BRV			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of responders				
number (not applicable)	26.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 6 months during the Evaluation Period for rollover study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 6 months during the Evaluation Period for rollover study participants[5]

End point description:

A study participant was considered seizure free, if no seizure occurred during 6 consecutive months in the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Here, number of participants analyzed signifies participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 84 months)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types for at least 6 months for arm Direct Enrollers is reported in a separate endpoint. Therefore, no data was reported for this arm in this endpoint.

End point values	EP0083 Placebo	EP0083 BRV All	N01379 BRV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	52	101	7	
Units: percentage of participants				
number (not applicable)	15.4	19.8	28.6	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in partial seizure frequency per 28 days from Baseline of directly enrolled study participants to the Evaluation Period

End point title	Percent change in partial seizure frequency per 28 days from Baseline of directly enrolled study participants to the Evaluation Period[6]

End point description:

The seizure frequency was calculated as number of seizures per 28 days. For direct enrollers, the Baseline Period was defined as seizure counts collected from 8 weeks prior to the first BRV administration in EP0085. Change in seizure frequency is calculated as the seizure frequency at the evaluation time point minus the seizure frequency at Baseline of directly enrolled participants. A negative value in percent change from Baseline indicates a decrease in PSF from Baseline. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Evaluation Period values for seizure frequency were calculated from the seizure diary data collected during the Evaluation Period on/after the first BRV administration.

End point type	Secondary

End point timeframe:

Baseline (8 weeks prior to BRV administration), up to 39 months of Evaluation Period

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Percent change in partial seizure frequency per 28 days for the arms of rollover study participants is reported in a separate endpoint. Therefore, no data was reported for these arms in this endpoint.

End point values	Direct Enrollers BRV			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percent change				
median (full range (min-max))	-32.6 (-3691 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 6 months during the Evaluation Period for directly enrolled study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 6 months during the Evaluation Period for directly enrolled study participants[7]

End point description:

A study participant was considered seizure free, if no seizure occurred during 6 consecutive months in the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Here, number of participants analyzed signifies participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 39 months)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types for at least 6 months for arms of rollover study participants is reported in a separate endpoint. Therefore, no data was reported for these arms in this endpoint.

End point values	Direct Enrollers BRV			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: percentage of participants				
number (not applicable)	24.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 12 months during the Evaluation Period for rollover study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 12 months during the Evaluation Period for rollover study participants[8]

End point description:

A study participant was considered seizure free, if no seizure occurred during 12 consecutive months in the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Here, number of participants analyzed signifies participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 84 months)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types for at least 12 months for the arm Direct Enrollers is reported in a separate endpoint. Therefore, no data was reported for this arm in this endpoint.

End point values	EP0083 Placebo	EP0083 BRV All	N01379 BRV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48	93	6	
Units: percentage of participants				
number (not applicable)	8.3	14.0	33.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period for rollover study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period for rollover study participants[9]

End point description:

A study participant was considered seizure free (partial, all epileptic seizure), if no seizure occurred during the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 84 months)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period is reported under a separate endpoint for the Direct Enrollers arm. Therefore, no data was reported for this arm in this endpoint.

End point values	EP0083 Placebo	EP0083 BRV All	N01379 BRV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	54	112	7	
Units: percentage of participants				
number (not applicable)				
Participants with partial seizure-freedom	1.9	7.1	14.3	
Participants with all-type seizure-freedom	1.9	7.1	14.3	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 12 months during the Evaluation Period for directly enrolled study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types (partial, generalized, and unclassified epileptic seizure) for at least 12 months during the Evaluation Period for directly enrolled study participants[10]

End point description:

A study participant was considered seizure free, if no seizure occurred during 12 consecutive months in the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period. Here, number of participants analyzed signifies participants who were evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 39 months)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types for at least 12 months for the arms of rollover study participants is reported in a separate endpoint. Therefore, no data was reported for these arms in this endpoint.

End point values	Direct Enrollers BRV			
Subject group type	Reporting group			
Number of subjects analysed	26			
Units: percentage of participants				
number (not applicable)	15.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period for directly enrolled study participants

End point title	Percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period for directly enrolled study participants[11]

End point description:

A study participant was considered seizure free (partial, all epileptic seizure), if no seizure occurred during the Evaluation Period and if met all of the following criteria: - the participant completed the designated period during the Evaluation Period - the participant has at least 90% non-missing diary days during the period of time - the participant did not report any seizures during the period. The FAS consisted of all participants who took at least 1 dose of study medication and have at least 1 seizure record on DRC during the Evaluation Period.

End point type	Secondary

End point timeframe:

During the Evaluation Period (up to 39 months)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The percentage of participants continuously seizure-free for partial seizure and all seizure types during the Evaluation Period for arms of rollover study participants is reported in a separate endpoint. Therefore, no data was reported for these arms in this endpoint.

End point values	Direct Enrollers BRV			
Subject group type	Reporting group			
Number of subjects analysed	34			
Units: percentage of participants				
number (not applicable)				
Participants with partial seizure-freedom	5.9			
Participants with all-type seizure-freedom	5.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Baseline until end of the safety follow up (up to 88.5 months)

Adverse event reporting additional description:

Treatment-emergent AEs (TEAEs) were defined as AEs that had onset on or after the day of first BRV dose in EP0085 study. The Safety Set consisted of all participants who took at least 1 dose of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	EP0083 Placebo

Reporting group description:

Participants who received Placebo in study EP0083 (NCT03083665) and completed the Treatment and Transition Period of study EP0083 are rolled over to this study and received brivaracetam (BRV) 50 milligram per day (mg/day) two times (bid) (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	EP0083 BRV All

Reporting group description:

Participants rolled over from study EP0083 received BRV 50 mg/day bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	N01379 BRV

Reporting group description:

Participants rolled over from study N01379 (NCT01339559) (core study N01358 [NCT01261325]) received BRV 200 mg/day during the evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. up to 84 months). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Reporting group title	Direct Enrollers BRV

Reporting group description:

Participants directly enrolled in this study received BRV 50mg bid (in total 100 mg/day) at Visit 1 (study entry) and were maintained at this dose for at least 2 weeks unless the participant was unable to tolerate treatment during evaluation period (from Visit 1 to end of study visit or early discontinuation visit i.e. Up to 84 Month, however, were evaluated for 39 months only due to late enrollment). Upon completion or early discontinuation from EP0085, there was a Down-Titration Period of 4 weeks to decrease in dose in steps on a weekly basis, up to 25 mg/day, followed by a 2-week Study Drug-Free Period during which the participant did not receive study drug. The BRV dose was adjusted (based on the individual participants' s seizure control and tolerability) between 50 mg/day and 200 mg/day during the study.

Serious adverse events	EP0083 Placebo	EP0083 BRV All	N01379 BRV
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 54 (11.11%)	23 / 112 (20.54%)	5 / 7 (71.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian clear cell carcinoma			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Brain operation			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abortion induced			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cranioplasty			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vagal nerve stimulator implantation			

subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Ovarian haemorrhage			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cyst ruptured			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometriosis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 54 (0.00%)	2 / 112 (1.79%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental disorder due to a general medical condition			

subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Self injurious behaviour			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Lumbar vertebral fracture			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Scapula fracture			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain contusion			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental overdose			

subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Sinus node dysfunction			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 54 (1.85%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinsonism			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			

subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ataxia			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure cluster			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 54 (1.85%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Large intestine polyp			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Gallbladder polyp			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Bone cyst			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovial cyst			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Peritonitis			
subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericoronitis			
subjects affected / exposed	1 / 54 (1.85%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Corona virus infection			

subjects affected / exposed	0 / 54 (0.00%)	0 / 112 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pilonidal cyst			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis bacterial			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 54 (0.00%)	1 / 112 (0.89%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Direct Enrollers BRV		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 34 (17.65%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			

subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian clear cell carcinoma			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung adenocarcinoma			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Brain operation			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abortion induced			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cranioplasty			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vagal nerve stimulator implantation			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian haemorrhage			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ovarian cyst ruptured				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometriosis				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pneumonia aspiration				
subjects affected / exposed	2 / 34 (5.88%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Suicidal ideation				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mental disorder due to a general medical condition				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Self injurious behaviour				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Lumbar vertebral fracture				

subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Scapula fracture				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foreign body				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contusion				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Concussion				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Brain contusion				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Sinus node dysfunction				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parkinsonism			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Loss of consciousness			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ataxia			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			

subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure cluster			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Eyelid ptosis			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cataract			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Gallbladder polyp				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Bone cyst				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Synovial cyst				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Peritonitis				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericoronitis				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Corona virus infection				
subjects affected / exposed	1 / 34 (2.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pilonidal cyst				
subjects affected / exposed	0 / 34 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pneumonia			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis bacterial			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 34 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	EP0083 Placebo	EP0083 BRV All	N01379 BRV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 54 (75.93%)	87 / 112 (77.68%)	6 / 7 (85.71%)
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	7 / 54 (12.96%)	11 / 112 (9.82%)	2 / 7 (28.57%)
occurrences (all)	8	19	10
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 54 (18.52%)	21 / 112 (18.75%)	0 / 7 (0.00%)
occurrences (all)	17	30	0
Dizziness			
subjects affected / exposed	12 / 54 (22.22%)	17 / 112 (15.18%)	3 / 7 (42.86%)
occurrences (all)	13	21	4
Somnolence			
subjects affected / exposed	14 / 54 (25.93%)	8 / 112 (7.14%)	2 / 7 (28.57%)
occurrences (all)	17	13	2
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	9 / 54 (16.67%)	21 / 112 (18.75%)	1 / 7 (14.29%)
occurrences (all)	14	43	2
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	3 / 54 (5.56%)	14 / 112 (12.50%)	0 / 7 (0.00%)
occurrences (all)	4	20	0
Nausea			
subjects affected / exposed	5 / 54 (9.26%)	11 / 112 (9.82%)	0 / 7 (0.00%)
occurrences (all)	7	13	0
Vomiting			
subjects affected / exposed	3 / 54 (5.56%)	6 / 112 (5.36%)	0 / 7 (0.00%)
occurrences (all)	6	6	0
Abdominal pain			
subjects affected / exposed	3 / 54 (5.56%)	6 / 112 (5.36%)	1 / 7 (14.29%)
occurrences (all)	5	8	2
Abdominal pain upper			
subjects affected / exposed	2 / 54 (3.70%)	6 / 112 (5.36%)	2 / 7 (28.57%)
occurrences (all)	3	9	2
Constipation			
subjects affected / exposed	5 / 54 (9.26%)	5 / 112 (4.46%)	0 / 7 (0.00%)
occurrences (all)	6	5	0
Stomatitis			
subjects affected / exposed	4 / 54 (7.41%)	4 / 112 (3.57%)	0 / 7 (0.00%)
occurrences (all)	11	4	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 54 (9.26%)	13 / 112 (11.61%)	0 / 7 (0.00%)
occurrences (all)	6	17	0
Oropharyngeal pain			
subjects affected / exposed	5 / 54 (9.26%)	11 / 112 (9.82%)	1 / 7 (14.29%)
occurrences (all)	12	19	1
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	4 / 54 (7.41%)	7 / 112 (6.25%)	0 / 7 (0.00%)
occurrences (all)	10	11	0

Psychiatric disorders			
Insomnia			
subjects affected / exposed	5 / 54 (9.26%)	7 / 112 (6.25%)	1 / 7 (14.29%)
occurrences (all)	6	7	1
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 54 (3.70%)	8 / 112 (7.14%)	0 / 7 (0.00%)
occurrences (all)	2	12	0
Back pain			
subjects affected / exposed	3 / 54 (5.56%)	7 / 112 (6.25%)	0 / 7 (0.00%)
occurrences (all)	3	9	0
Infections and infestations			
Corona virus infection			
subjects affected / exposed	13 / 54 (24.07%)	32 / 112 (28.57%)	0 / 7 (0.00%)
occurrences (all)	13	34	0
Nasopharyngitis			
subjects affected / exposed	20 / 54 (37.04%)	18 / 112 (16.07%)	3 / 7 (42.86%)
occurrences (all)	88	68	6
Upper respiratory tract infection			
subjects affected / exposed	5 / 54 (9.26%)	23 / 112 (20.54%)	0 / 7 (0.00%)
occurrences (all)	11	36	0
Cystitis			
subjects affected / exposed	3 / 54 (5.56%)	5 / 112 (4.46%)	0 / 7 (0.00%)
occurrences (all)	3	7	0

Non-serious adverse events	Direct Enrollers BRV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 34 (79.41%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	8		
Nervous system disorders			
Headache			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	8		
Dizziness			

subjects affected / exposed	5 / 34 (14.71%)		
occurrences (all)	5		
Somnolence			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	8		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 34 (17.65%)		
occurrences (all)	7		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 34 (11.76%)		
occurrences (all)	4		
Nausea			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	6		
Abdominal pain			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	1 / 34 (2.94%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	3 / 34 (8.82%)		
occurrences (all)	5		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 34 (5.88%)		
occurrences (all)	2		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	5 / 34 (14.71%) 5		
Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	 1 / 34 (2.94%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	 2 / 34 (5.88%) 2		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 2 / 34 (5.88%) 2 2 / 34 (5.88%) 2		
Infections and infestations Corona virus infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all) Cystitis subjects affected / exposed occurrences (all)	 11 / 34 (32.35%) 11 9 / 34 (26.47%) 19 1 / 34 (2.94%) 1 3 / 34 (8.82%) 13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 January 2019	Protocol amendment 2 (dated 28 Jan 2019): A total of 32 participants were enrolled at the time of this amendment. The following changes were made: • Updated the number of participants based on randomization of EP0083 and N01379 sites in Japan. • Updated safety variables. • Updated participating countries. • Included IEC. In addition, minor administrative edits, including typographical changes for formatting, were made.
20 November 2019	Protocol amendment 3 (dated 20 Nov 2019): A total of 56 participants were enrolled at the time of this amendment. The following changes were made: • Updated the Sponsor/Local Legal Representatives. • Added China as a participating country. • Included serious adverse event (SAE) reporting information for China. • Updated the number of participants expected to enter the study. • Changed exploratory safety variable to other safety variable. In addition, minor administrative edits, including typographical changes for formatting, were made.
15 March 2023	Protocol amendment 4 (dated 15 Mar 2023): A total of 207 participants were enrolled at the time of this amendment. The following changes were made: • Updated the Study Contact Information. • Changed the primary safety variable from adverse events (AEs) to treatment-emergent adverse events (TEAEs), in alignment with other studies across the brivaracetam development program. • Deleted mental status/psychiatric status from the list of other safety variables to be collected; abnormal findings upon physical or neurological examination were to be recorded as AEs. • Changed the planned duration of EP0085 to allow participants to continue in the study until market approval in countries where market approval will be requested and for 2 years in countries where market approval will not be requested or obtained. • Added details regarding EP0085 study participants' participation in EP0118 for clarification purposes. • Added to the study withdrawal criteria that a suicide attempt will necessitate a participant's withdrawal from the study. - This will eliminate the risk of another suicide attempt or completed suicide during the study in cases where the participant's recent suicidal ideation was not accurately reflected by the Columbia Suicide Severity Rating Scale (C SSRS). • Added information regarding numbering of directly enrolled participants entering the study. • Added a statement for TEAE and SAE disclosure on public registries per the current UCB protocol template. • Removed 2 efficacy analyses from the previous list of analyses planned for all participants per SAP amendments implemented following EP0085 protocol approval. • Corrected the handling of protocol deviations text as there was no pooling of stratification levels for statistical analysis and there were no statistical assumptions for the primary analysis for this study. In addition, minor clarifications and administrative edits including typographical changes for formatting were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported