Clinical trial results:
A Multicenter, Open-Label Study to Evaluate the Pharmacokinetics, Safety, and Tolerability of Intravenous Brivaracetam in Subjects >= 1 Month to < 16 Years of Age With Epilepsy

Summary

EudraCT number	2016-002452-25
Trial protocol	ES HU CZ DE IT
Global end of trial date	04 November 2020

Results information

Result version number	v1 (current)
This version publication date	20 May 2021
First version publication date	20 May 2021

Trial information

Trial identification

Sponsor protocol code	EP0065

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03405714
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	20 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 November 2020
Global end of trial reached?	Yes
Global end of trial date	04 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the pharmacokinetics (PK), safety, and tolerability of Brivaracetam (BRV) administered intravenously (iv) in subjects greater than or equal to (>=) 1 month to less than (<) 16 years of age with epilepsy.

Protection of trial subjects:

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

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	01 June 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy, Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 1
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Hungary: 30
Country: Number of subjects enrolled	Italy: 4
Country: Number of subjects enrolled	Mexico: 2
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	50
EEA total number of subjects	44

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)	13
Children (2-11 years)	25
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in June 2018 and concluded in November 2020.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set-Intravenous (SS-iv).

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

Are arms mutually exclusive?	Yes
Arm title	Age Cohort: >=12 to <16 years

Arm description:

Screening Period (1-10 days): Participants receiving open-label BRV (OLB) or prescribed oral BRV (RxB) continued to receive oral BRV.
IOB Treatment Period (2-10 days): Participants who initiated Oral BRV (IOB) continued with oral BRV 2 milligram/kilogram/day (mg/kg/day).
IV PK (Intravenous Pharmacokinetic) Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv Brivaracetam (BRV) dose was equivalent to final dose of oral BRV and for Initiating iv BRV (IIB) participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam-Solution for iv injection
Investigational medicinal product code	BRV
Other name	UCB 34714
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Brivaracetam (BRV) was administered as a 15-minute infusion or bolus (up to 2- minute infusion) every 12 hours in IV PK Period (1-6 days).

Arm title	Age Cohort: >=6 to <12 years

Arm description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam-Solution for iv injection
Investigational medicinal product code	BRV
Other name	UCB 34714
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Brivaracetam (BRV) was administered as a 15-minute infusion or bolus (up to 2- minute infusion) every 12 hours in IV PK Period (1-6 days).

Arm title	Age Cohort: >=2 to <6 years

Arm description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam-Solution for iv injection
Investigational medicinal product code	BRV
Other name	UCB 34714
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Brivaracetam (BRV) was administered as a 15-minute infusion or bolus (up to 2- minute infusion) every 12 hours in IV PK Period (1-6 days).

Arm title	Age Cohort: >=1 month to <2 years

Arm description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Arm type	Experimental
Investigational medicinal product name	Brivaracetam-Solution for iv injection
Investigational medicinal product code	BRV
Other name	UCB 34714
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Brivaracetam (BRV) was administered as a 15-minute infusion or bolus (up to 2- minute infusion) every 12 hours in IV PK Period (1-6 days).

Number of subjects in period 1	Age Cohort: >=12 to <16 years	Age Cohort: >=6 to <12 years	Age Cohort: >=2 to <6 years
Started	12	12	13
Completed	12	12	13

Number of subjects in period 1	Age Cohort: >=1 month to <2 years
Started	13

Completed	13

Baseline characteristics

Reporting groups

Reporting group title	Age Cohort: >=12 to <16 years

Reporting group description:

Screening Period (1-10 days): Participants receiving open-label BRV (OLB) or prescribed oral BRV (RxB) continued to receive oral BRV.
IOB Treatment Period (2-10 days): Participants who initiated Oral BRV (IOB) continued with oral BRV 2 milligram/kilogram/day (mg/kg/day).
IV PK (Intravenous Pharmacokinetic) Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv Brivaracetam (BRV) dose was equivalent to final dose of oral BRV and for Initiating iv BRV (IIB) participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=6 to <12 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=2 to <6 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=1 month to <2 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group values	Age Cohort: >=12 to <16 years	Age Cohort: >=6 to <12 years	Age Cohort: >=2 to <6 years
Number of subjects	12	12	13
Age categorical Units: Subjects			
<=18 years	12	12	13
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age continuous Units: years			
arithmetic mean	13.08	8.33	3.85

standard deviation	± 1.16	± 1.61	± 0.99

Gender categorical Units: Subjects			
Female	6	8	5
Male	6	4	8

Reporting group values	Age Cohort: >=1 month to <2 years	Total	
Number of subjects	13	50	
Age categorical Units: Subjects			
<=18 years	13	50	
Between 18 and 65 years	0	0	
>=65 years	0	0	
Age continuous Units: years			
arithmetic mean	0.95		
standard deviation	± 0.59	-	
Gender categorical Units: Subjects			
Female	5	24	
Male	8	26	

End points

End points reporting groups

Reporting group title	Age Cohort: >=12 to <16 years

Reporting group description:

Screening Period (1-10 days): Participants receiving open-label BRV (OLB) or prescribed oral BRV (RxB) continued to receive oral BRV.
IOB Treatment Period (2-10 days): Participants who initiated Oral BRV (IOB) continued with oral BRV 2 milligram/kilogram/day (mg/kg/day).
IV PK (Intravenous Pharmacokinetic) Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv Brivaracetam (BRV) dose was equivalent to final dose of oral BRV and for Initiating iv BRV (IIB) participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=6 to <12 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=2 to <6 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Reporting group title	Age Cohort: >=1 month to <2 years

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.

Subject analysis set title	Age Cohort: >=12 to <16 years (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining as a bolus (up to 2-minute infusion).
Participants formed the Pharmacokinetic Per-protocol Set (PK-PPS).

Subject analysis set title	Age Cohort: >=6 to <12 years (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining as a bolus (up to 2-minute infusion).

Participants formed the PK-PPS.

Subject analysis set title	Age Cohort: >=2 to <6 years (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining as a bolus (up to 2-minute infusion).
Participants formed the PK-PPS.

Subject analysis set title	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining as a bolus (up to 2-minute infusion).
Participants formed the PK-PPS.

Subject analysis set title	15-minute Infusion (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6 days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion. Participants formed the PK-PPS.

Subject analysis set title	Bolus (PK-PPS)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants received iv administration of BRV every 12 hours during the IV PK Period (1-6days). For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort the second half received the bolus (up to 2-minute infusion).
Participants formed PK-PPS.

Subject analysis set title	Age Cohort: >=12 to <16 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the Safety Set-Intravenous (SS-iv).

Subject analysis set title	Age Cohort: >=6 to <12 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the SS-iv.

Subject analysis set title	Age Cohort: >=2 to <6 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.

IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the Safety SS-iv.

Subject analysis set title	Age Cohort: >=1 month to <2 years (SS-iv)
Subject analysis set type	Safety analysis

Subject analysis set description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the SS-iv.

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3[1]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment. 999 is used as a placeholder for Age Cohort >=6 to <12 years and >=2 to <6 years because Geometric mean and 95% CI were only calculated if at least two-thirds of the data were greater than the lower Limit of quantification (LOQ).

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 3

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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	10	12	11
Units: nanograms per milliliter (ng/mL)				
geometric mean (confidence interval 95%)	149.0 (27.6 to 805.1)	999 (999 to 999)	999 (999 to 999)	310.6 (92.5 to 1042.7)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit

3

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 3[2]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 3

Notes:

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

End point values	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	10	8	10
Units: ng/mL				
geometric mean (confidence interval 95%)	1844.6 (1110.4 to 3064.3)	2058.8 (1726.4 to 2455.2)	1774.9 (1087.4 to 2897.1)	1566.6 (973.1 to 2522.2)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3[3]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 3

Notes:

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

End point values	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	10	11	9
Units: ng/mL				
geometric mean (confidence interval 95%)	1260.6 (962.6 to 1650.8)	1189.5 (1005.5 to 1407.1)	1225.3 (676.8 to 2218.6)	1341.7 (657.9 to 2735.9)

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4[4]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 4

Notes:

[4] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[5]	3	0[6]	0[7]
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	290.5 (101.2 to 834.0)	(to)	(to)

Notes:

[5] - PK samples were not collected at Visit 4 in >=12 to <16 years patients.

[6] - PK samples were not collected at Visit 4 in >=2 to <6 years patients.

[7] - PK samples were not collected at Visit 4 in >=1 to <2 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4[8]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 4

Notes:

[8] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[9]	3	0[10]	0[11]
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	2084.3 (681.2 to 6377.0)	(to)	(to)

Notes:

[9] - PK samples were not collected at Visit 4 in >=12 to <16 years patients.

[10] - PK samples were not collected at Visit 4 in >=2 to <6 years patients.

[11] - PK samples were not collected at Visit 4 in >=1 to <2 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4[12]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 4

Notes:

[12] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[13]	3	0[14]	0[15]
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	1149.8 (613.1 to 2156.4)	(to)	(to)

Notes:

[13] - PK samples were not collected at Visit 4 in >=12 to <16 years patients.

[14] - PK samples were not collected at Visit 4 in >=2 to <6 years patients.

[15] - PK samples were not collected at Visit 4 in >=1 to <2 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5[16]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment. 99/999 is used as a placeholder for Age Cohort >=6 to <12 years because 95% CI could not be calculated for a single participant.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 5

Notes:

[16] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[17]	1	2	3
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	466.0 (99 to 999)	204.5 (0.1 to 383063.7)	482.9 (4.8 to 48506.1)

Notes:

[17] - PK samples were not collected at Visit 5 in >=12 to <16 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit

5

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 5[18]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment. 999/9999 is used as a placeholder for Age Cohort >=6 to <12 years because 95% CI could not be calculated for a single participant.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes and post-initiation of iv BRV infusion at Visit 5

Notes:

[18] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[19]	1	3	3
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	2890.0 (999 to 9999)	1948.8 (690.8 to 5497.7)	2072.4 (743.2 to 5778.8)

Notes:

[19] - PK samples were not collected at Visit 5 in >=12 to <16 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5[20]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment. 999/9999 is used as a placeholder for Age Cohort >=6 to <12 years because 95% CI could not be calculated for a single participant.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 5

Notes:

[20] - 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	Age Cohort: >=12 to <16 years (PK-PPS)	Age Cohort: >=6 to <12 years (PK-PPS)	Age Cohort: >=2 to <6 years (PK-PPS)	Age Cohort : >=1 month to <2 years (PK-PPS)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	0[21]	1	2	3
Units: ng/mL				
geometric mean (confidence interval 95%)	(to)	1820 (999 to 9999)	1203.5 (147.1 to 9847.1)	727.4 (144.9 to 3652.9)

Notes:

[21] - PK samples were not collected at Visit 5 in >=12 to <16 years patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3 by Infusion Duration - 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3 by Infusion Duration - 15 Minutes[22]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment. 999 is used as a placeholder because Geometric mean and 95% CI were only calculated if at least two-thirds of the data were greater than the lower Limit of quantification (LOQ).

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 3

Notes:

[22] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: ng/mL				
geometric mean (confidence interval 95%)	999 (999 to 999)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 3 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15

	minutes, Visit 3 by Infusion Duration- 15 Minutes[23]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 3

Notes:

[23] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: ng/mL				
geometric mean (confidence interval 95%)	1903.0 (1474.9 to 2455.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3 by Infusion Duration- 15 Minutes[24]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 3

Notes:

[24] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: ng/mL				
geometric mean (confidence interval 95%)	1130.3 (882.1 to 1448.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4 by Infusion Duration- 15 Minutes[25]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 4

Notes:

[25] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	290.5 (101.2 to 834.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4 by Infusion Duration- 15 Minutes[26]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma

concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 4

Notes:

[26] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	2084.3 (681.2 to 6377.0)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4 by Infusion Duration- 15 Minutes[27]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 4

Notes:

[27] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	1149.8 (613.1 to 2156.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5 by Infusion Duration- 15 Minutes[28]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 5

Notes:

[28] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	776.0 (51.9 to 11611.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 5 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 5 by Infusion Duration- 15 Minutes[29]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 5

Notes:

[29] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: ng/mL				
geometric mean (confidence interval 95%)	2697.8 (1911.1 to 3808.3)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5 by Infusion Duration- 15 Minutes

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5 by Infusion Duration- 15 Minutes[30]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 5

Notes:

[30] - 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	15-minute Infusion (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	4			
Units: ng/mL				
geometric mean (confidence interval 95%)	1030.0 (376.1 to 2820.9)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 3 by Infusion Duration- Bolus[31]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 3

Notes:

[31] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	22			
Units: ng/mL				
geometric mean (confidence interval 95%)	120.5 (44.7 to 325.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 3 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 3 by Infusion Duration- Bolus[32]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 3

Notes:

[32] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	19			
Units: ng/mL				
geometric mean (confidence interval 95%)	1704.8 (1237.5 to 2348.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 3 by Infusion Duration- Bolus[33]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 3

Notes:

[33] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	21			
Units: ng/mL				
geometric mean (confidence interval 95%)	1383.9 (989.3 to 1935.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 4 by Infusion Duration- Bolus[34]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling

time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses.

End point type	Primary

End point timeframe:

At <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 4

Notes:

[34] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[35]			
Units: ng/mL				
geometric mean (confidence interval 95%)				

Notes:

[35] - PK samples were not collected at Visit 4 in bolus patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 4 by Infusion Duration- Bolus[36]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses.

End point type	Primary

End point timeframe:

At 15 minutes post-initiation of iv BRV infusion at Visit 4

Notes:

[36] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[37]			
Units: ng/mL				
geometric mean (confidence interval 95%)				

Notes:

[37] - PK samples were not collected at Visit 4 in bolus patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 4 by Infusion Duration- Bolus[38]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses.

End point type	Primary

End point timeframe:

At 3 hours post-initiation of iv BRV infusion at Visit 4

Notes:

[38] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	0[39]			
Units: ng/mL				
geometric mean (confidence interval 95%)				

Notes:

[39] - PK samples were not collected at Visit 4 in bolus patients.

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Predose (<=1 hour), Visit 5 by Infusion Duration- Bolus[40]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at <= 1 hour pre-initiation of intravenous (iv) BRV infusion at Visit 5

Notes:

[40] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	167.5 (9.6 to 2932.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 5 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 15 minutes, Visit 5 by Infusion Duration- Bolus[41]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 15 minutes post-initiation of iv BRV infusion at Visit 5

Notes:

[41] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	3			
Units: ng/mL				
geometric mean (confidence interval 95%)	1531.8 (837.3 to 2802.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5 by Infusion Duration- Bolus

End point title	Plasma Concentration of Brivaracetam (BRV) at Postdose 3 hours, Visit 5 by Infusion Duration- Bolus[42]

End point description:

Blood samples were taken at indicated time points to determine brivaracetam (BRV) plasma concentration before, during, and after iv BRV administration. The PK-PPS included all study participants in the SS-iv having provided at least 1 measurable postdose plasma sample (with recorded sampling time) during the iv PK Period with documented iv BRV infusion times and without IPDs impacting the

interpretability of the PK analyses. Here, N (number of participants analyzed) were included who were evaluable for the assessment.

End point type	Primary

End point timeframe:

Blood samples were collected at 3 hours post-initiation of iv BRV infusion at Visit 5

Notes:

[42] - 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	Bolus (PK-PPS)			
Subject group type	Subject analysis set			
Number of subjects analysed	2			
Units: ng/mL				
geometric mean (confidence interval 95%)	949.5 (2.8 to 316987.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Events (AEs)

End point title	Number of Participants With Adverse Events (AEs)[43]

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. The SS-iv included study participants who received at least 1 dose of iv BRV.

End point type	Primary

End point timeframe:

From Screening until last visit (up to Day 68)

Notes:

[43] - 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	Age Cohort: >=12 to <16 years (SS-iv)	Age Cohort: >=6 to <12 years (SS-iv)	Age Cohort: >=2 to <6 years (SS-iv)	Age Cohort: >=1 month to <2 years (SS-iv)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	13	13
Units: participants	3	4	7	2

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participant Withdrawals due to Adverse Events

End point title	Number of Participant Withdrawals due to Adverse Events[44]

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. The SS-iv included study participants who received at least 1 dose of iv BRV.

End point type	Primary

End point timeframe:

From Screening until last visit (up to Day 68)

Notes:

[44] - 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	Age Cohort: >=12 to <16 years (SS-iv)	Age Cohort: >=6 to <12 years (SS-iv)	Age Cohort: >=2 to <6 years (SS-iv)	Age Cohort: >=1 month to <2 years (SS-iv)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	13	13
Units: participants	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Screening until last visit (up to Day 68)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	Age Cohort: >=12 to <16 years (SS-iv)

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the Safety Set-Intravenous (SS-iv).

Reporting group title	Age Cohort: >=2 to <6 years (SS-iv)

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the Safety SS-iv.

Reporting group title	Age Cohort: >=1 month to <2 years (SS-iv)

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the SS-iv.

Reporting group title	Age Cohort: >=6 to <12 years (SS-iv)

Reporting group description:

Screening Period (1-10 days): Participants receiving OLB or RxB continued to receive oral BRV.
IOB Treatment Period (2-10 days): IOB Participants continued with oral BRV 2mg/kg/day.
IV PK Period (1-6 days): During iv PK Period, iv BRV was administered every 12 hours. For OLB, RxB, and IOB participants, first iv BRV dose was equivalent to final dose of oral BRV and for IIB participants, first iv BRV dose was 1mg/kg. For each cohort, the first half received the 15-minute infusion, the remaining half as a bolus (up to 2-minute infusion).
Down-Titration Period: Participants who discontinued treatment, had their BRV dose reduced every week for a maximum of 4 weeks down to a dose of 1mg/kg/day.
Participants formed the SS-iv.

Serious adverse events	Age Cohort: >=12 to <16 years (SS-iv)	Age Cohort: >=2 to <6 years (SS-iv)	Age Cohort: >=1 month to <2 years (SS-iv)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Age Cohort: >=6 to <12 years (SS-iv)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 12 (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	Age Cohort: >=12 to <16 years (SS-iv)	Age Cohort: >=2 to <6 years (SS-iv)	Age Cohort: >=1 month to <2 years (SS-iv)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 12 (25.00%)	7 / 13 (53.85%)	2 / 13 (15.38%)
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 12 (16.67%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	1 / 13 (7.69%)
occurrences (all)	0	2	1
General disorders and administration			

site conditions			
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	2 / 13 (15.38%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 13 (7.69%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Pharyngitis			
subjects affected / exposed	1 / 12 (8.33%)	0 / 13 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 13 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1

Non-serious adverse events	Age Cohort: >=6 to <12 years (SS-iv)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Vessel puncture site haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Pruritus			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Psychiatric disorders			
Aggression			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Infections and infestations			
Conjunctivitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported