



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 (\geq) 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.

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|--|--|
| 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.

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|--|--|
| 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

| | |
|-----------------|---|
| 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

| | |
|-----------------|--|
| 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 |
|-----------------|---|

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 occurrences (all) | 0 / 12 (0.00%) 0 | 1 / 13 (7.69%) 1 | 0 / 13 (0.00%) 0 |
| Pharyngitis subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | 0 / 13 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Upper respiratory tract infection subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | 0 / 13 (0.00%) 0 | 1 / 13 (7.69%) 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 occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Vessel puncture site haemorrhage subjects affected / exposed occurrences (all) | 0 / 12 (0.00%) 0 | | |
| Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) | 1 / 12 (8.33%) 1 | | |
| Skin and subcutaneous tissue disorders Pruritus | | | |

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