



## Clinical trial results:

### An Open-Lable, Single-Arm, Multicenter Study of Levetiracetam as Monotherapy or Adjunctive Treatment of Partial Seizures in Pediatric Epileptic Subjects Ranging From 1 Month to Less Than 4 Years of Age Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2021-003372-13 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 28 July 2023   |

#### Results information

|                                |  |
|--------------------------------|--|
| Result version number          | v2 (current)   |
| This version publication date  | 03 August 2024   |
| First version publication date | 19 January 2024  |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set Alignment with final posting on ClinicalTrials.gov after NIH review.</li></ul> |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | EP0100 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03340064 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UCB Japan Co. Ltd.  |
| Sponsor organisation address | Shinjuku Grand Tower, 8-17-1 Nishi-Shinjuku, Shinjuku-ku, Tokyo, Japan, 160-0023  |
| 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                       | 29 August 2023 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 01 June 2021   |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 28 July 2023   |
| Was the trial ended prematurely?                     | No             |

Notes:

## General information about the trial

Main objective of the trial:

To confirm the efficacy of Levetiracetam (LEV) in reducing seizure frequency in the First Period compared to historical control as adjunctive treatment in pediatric epilepsy subjects aged 1 month to <4 years with partial seizures.

Protection of trial subjects:

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

Background therapy:

Adjunctive therapy must be on a stable maximum of two AED regimens, and Monotherapy must not receive AED treatment.

Evidence for comparator:

Not applicable.

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 30 November 2017 |
| Long term follow-up planned                               | Yes              |
| Long term follow-up rationale                             | Efficacy         |
| Long term follow-up duration                              | 5 Years          |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

## Population of trial subjects

### Subjects enrolled per country

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Japan: 38 |
| Worldwide total number of subjects   | 38        |
| EEA total number of subjects         | 0         |

Notes:

### Subjects enrolled per age group

|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 29 |
| Children (2-11 years)                     | 9  |
| Adolescents (12-17 years)                 | 0  |
| 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 November 2017 and concluded in July 2023.

### Pre-assignment

Screening details:

Participant Flow refers to the Safety Set Adjunctive therapy (SS\_A) and Safety Set Monotherapy (SS\_M).

### Period 1

|                              |                |
|------------------------------|----------------|
| Period 1 title               | First Period   |
| Is this the baseline period? | Yes            |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

### Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Levetiracetam: Adjunctive Therapy |

Arm description:

Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to (≥) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator.

|  |                     |
|--|---------------------|
| Arm type                               | Experimental        |
| Investigational medicinal product name | Levetiracetam       |
| Investigational medicinal product code | LEV                 |
| Other name                             | Keppra and E-Keppra |
| Pharmaceutical forms                   | Syrup               |
| Routes of administration               | Oral use            |

Dosage and administration details:

Participants received LEV as prespecified.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Levetiracetam: Monotherapy |
|------------------|----------------------------|

Arm description:

Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged ≥ 6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |                     |
|--|---------------------|
| Investigational medicinal product name | Levetiracetam       |
| Investigational medicinal product code | LEV                 |
| Other name                             | Keppra and E-Keppra |
| Pharmaceutical forms                   | Syrup               |
| Routes of administration               | Oral use            |

Dosage and administration details:

Participants received LEV as prespecified.

| Number of subjects in period 1 | Levetiracetam:<br>Adjunctive Therapy | Levetiracetam:<br>Monotherapy |
|--------------------------------|--------------------------------------|-------------------------------|
| Started                        | 32                                   | 6                             |
| Completed                      | 27                                   | 6                             |
| Not completed                  | 5                                    | 0                             |
| Adverse Event, non-fatal       | 2                                    | -                             |
| Lack of efficacy               | 3                                    | -                             |

## Period 2

|                              |                |
|------------------------------|----------------|
| Period 2 title               | Second Period  |
| Is this the baseline period? | No             |
| Allocation method            | Not applicable |
| Blinding used                | Not blinded    |

## Arms

|                              |                                   |
|------------------------------|-----------------------------------|
| Are arms mutually exclusive? | Yes                               |
| <b>Arm title</b>             | Levetiracetam: Adjunctive Therapy |

Arm description:

Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to ( $\geq$ ) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Levetiracetam |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Syrup         |
| Routes of administration               | Oral use      |

Dosage and administration details:

Participants received LEV as prespecified.

|                  |                            |
|------------------|----------------------------|
| <b>Arm title</b> | Levetiracetam: Monotherapy |
|------------------|----------------------------|

Arm description:

Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week

0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged ≥ 6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.

|  |               |
|--|---------------|
| Arm type                               | Experimental  |
| Investigational medicinal product name | Levetiracetam |
| Investigational medicinal product code |               |
| Other name                             |               |
| Pharmaceutical forms                   | Syrup         |
| Routes of administration               | Oral use      |

Dosage and administration details:

Participants received LEV as prespecified.

| <b>Number of subjects in period 2</b>       | Levetiracetam:<br>Adjunctive Therapy | Levetiracetam:<br>Monotherapy |
|---|--------------------------------------|-------------------------------|
| Started                                     | 27                                   | 6                             |
| Completed                                   | 8                                    | 4                             |
| Not completed                               | 19                                   | 2                             |
| Physician decision                          | 3                                    | -                             |
| Consent withdrawn by subject                | 2                                    | 1                             |
| Adverse Event, non-fatal                    | 1                                    | 1                             |
| Approved Drug Available For Indication      | 1                                    | -                             |
| Protocol-Specified Withdrawal Criterion Met | 1                                    | -                             |
| Lack of efficacy                            | 11                                   | -                             |

## Baseline characteristics

### Reporting groups

|  |                                   |
|--|-----------------------------------|
| Reporting group title  | Levetiracetam: Adjunctive Therapy |
| Reporting group description:<br>Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to (≥) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator. |                                   |
| Reporting group title  | Levetiracetam: Monotherapy        |
| Reporting group description:<br>Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged ≥ 6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.            |                                   |

| Reporting group values                   | Levetiracetam:<br>Adjunctive Therapy | Levetiracetam:<br>Monotherapy | Total |
|--|--------------------------------------|-------------------------------|-------|
| Number of subjects                       | 32                                   | 6                             | 38    |
| Age Categorical<br>Units: Participants   |                                      |                               |       |
| 28 days - <24 months                     | 26                                   | 3                             | 29    |
| 24 months - <12 years                    | 6                                    | 3                             | 9     |
| Age Continuous<br>Units: Years           |                                      |                               |       |
| arithmetic mean                          | 14.7                                 | 32.4                          |       |
| standard deviation                       | ± 10.7                               | ± 13.2                        | -     |
| Sex: Female, Male<br>Units: Participants |                                      |                               |       |
| Female                                   | 15                                   | 5                             | 20    |
| Male                                     | 17                                   | 1                             | 18    |

## End points

### End points reporting groups

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Levetiracetam: Adjunctive Therapy |
|-----------------------|-----------------------------------|

#### Reporting group description:

Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to ( $\geq$ ) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Levetiracetam: Monotherapy |
|-----------------------|----------------------------|

#### Reporting group description:

Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged  $\geq$  6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Levetiracetam: Adjunctive Therapy |
|-----------------------|-----------------------------------|

#### Reporting group description:

Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to ( $\geq$ ) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator.

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Levetiracetam: Monotherapy |
|-----------------------|----------------------------|

#### Reporting group description:

Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged  $\geq$  6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.

### Primary: Percent change in partial seizure frequency per week from Baseline to Visit 6

|                 |   |
|-----------------|---|
| End point title | Percent change in partial seizure frequency per week from Baseline to Visit 6 <sup>[1][2]</sup> |
|-----------------|---|

#### End point description:

The percent difference in partial seizure frequency per week at Baseline and Study Visit 6 (Week 6) was computed as:  $\{[(\text{Number of partial seizures per week at Baseline}) \text{ minus } (\text{Number of partial seizures per week at Visit 6})] / (\text{Number of partial seizures per week at Baseline})\} \times 100$



week at Study Visit 6)] divided by (Number of partial seizures per week at Baseline)} multiplied by 100. A positive value in percent difference from Baseline indicates a reduction in partial seizure frequency from Baseline. The Full Analysis Set Adjunctive therapy (FAS\_A) consisted of all participants in the SS\_A who had at least 1 post-Baseline efficacy assessment. Number of participants analyzed included those participants who were evaluable for the assessment.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

From Baseline (Week 0) to Visit 6 (up to Week 6)

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: Results were summarized and reported as descriptive statistics only for the single arm.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Inferential statistics are reported as descriptive statistics because the study is a single arm study.

|                                  |   |  |  |  |
|----------------------------------|---|--|--|--|
| <b>End point values</b>          | Levetiracetam:<br>Adjunctive<br>Therapy |  |  |  |
| Subject group type               | Reporting group                         |  |  |  |
| Number of subjects analysed      | 28                                      |  |  |  |
| Units: percent change            |   |  |  |  |
| median (confidence interval 95%) | 24.24 (-25.48<br>to 51.85)              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change in partial seizure frequency per week from Baseline to Visit 4

|                 |  |
|-----------------|--|
| End point title | Percent change in partial seizure frequency per week from Baseline to Visit 4 <sup>[3]</sup> |
|-----------------|--|

End point description:

The percent difference in partial seizure frequency per week at Baseline and Study Visit 4 (Week 2) was computed as: {[ (Number of partial seizures per week at Baseline) minus (Number of partial seizures per week at Study Visit 4)] divided by (Number of partial seizures per week at Baseline)} multiplied by 100. A positive value in percent difference from Baseline indicates a reduction in partial seizure frequency from Baseline. The FAS\_A consisted of all participants in the SS\_A who had at least 1 post-Baseline efficacy assessment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0) to Visit 4 (up to Week 2)

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data of this outcome measure was analyzed and reported for participants on adjunctive therapy.

|                               |   |  |  |  |
|-------------------------------|---|--|--|--|
| <b>End point values</b>       | Levetiracetam:<br>Adjunctive<br>Therapy |  |  |  |
| Subject group type            | Reporting group                         |  |  |  |
| Number of subjects analysed   | 32                                      |  |  |  |
| Units: percent change         |   |  |  |  |
| median (full range (min-max)) | 8.62 (-343.1 to<br>100.0)               |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change in partial seizure frequency per week from Baseline to Visit 5

|                 |  |
|-----------------|--|
| End point title | Percent change in partial seizure frequency per week from Baseline to Visit 5 <sup>[4]</sup> |
|-----------------|--|

End point description:

The percent difference in partial seizure frequency per week at Baseline and Study Visit 5 (Week 4) was computed as:  $\{[(\text{Number of partial seizures per week at Baseline}) - (\text{Number of partial seizures per week at Study Visit 5})] \text{ divided by } (\text{Number of partial seizures per week at Baseline})\}$  multiplied by 100. A positive value in percent difference from Baseline indicates a reduction in partial seizure frequency from Baseline. The FAS\_A consisted of all participants in the SS\_A who had at least 1 post-Baseline efficacy assessment.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0) to Visit 5 (up to Week 4)

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Data of this outcome measure was analyzed and reported for participants on adjunctive therapy.

|                               |   |  |  |  |
|-------------------------------|---|--|--|--|
| <b>End point values</b>       | Levetiracetam:<br>Adjunctive<br>Therapy |  |  |  |
| Subject group type            | Reporting group                         |  |  |  |
| Number of subjects analysed   | 32                                      |  |  |  |
| Units: percent change         |   |  |  |  |
| median (full range (min-max)) | 16.79 (-414.3<br>to 100.0)              |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from baseline for each analysis visit in partial seizure frequency per week on adjunctive therapy

|                 |   |
|-----------------|---|
| End point title | Percent change from baseline for each analysis visit in partial seizure frequency per week on adjunctive therapy <sup>[5]</sup> |
|-----------------|---|

End point description:

Percent difference in partial seizure frequency (PSF) per week (Wk) at each Analysis Visit:  $\{[(\text{Number of$

partial seizures [PS] per week at Baseline [BL]) - (Number of partial seizures per week at analysis visit X))/(Number of partial seizures per week at BL))\*100. Positive value indicates reduction in PSF from BL. End of study (EOS)/early discontinuation visit (EDV) was based on last EDV and calculation of number of partial seizure per week were based on period from previous EDV visit. Mapping of seizure data to Analysis Visits was based on target dates of the visits. A seizure date after that of target date of an Analysis Visit n and up to that of target date of next Analysis Visit n+1 was mapped to next Analysis Visit (n+1). Data for one participant assessed within study duration was mapped to Analysis Visit 35/Week 300 based on statistical plan. Analysis set: FAS\_A. Here, N = participants evaluable for this outcome measure. 'n' = participants evaluable at specified time points.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0), Week 8, 10, 12, 15, 18, 21, 24, 27, 30, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, EOS/ED (up to Week 295), and Safety follow-up (up to Week 295)

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data of this outcome measure was analyzed and reported for participants on adjunctive therapy.

| End point values              | Levetiracetam:<br>Adjunctive<br>Therapy |  |  |  |
|-------------------------------|---|--|--|--|
| Subject group type            | Reporting group                         |  |  |  |
| Number of subjects analysed   | 25                                      |  |  |  |
| Units: percent change         |   |  |  |  |
| median (full range (min-max)) |   |  |  |  |
| Week 8 (n = 25)               | 35.53 (-137.9 to 100.0)                 |  |  |  |
| Week 10 (n = 24)              | 59.39 (-138.2 to 100.0)                 |  |  |  |
| Week 12 (n = 22)              | 50.90 (-167.8 to 100.0)                 |  |  |  |
| Week 15 (n = 22)              | 60.29 (-129.4 to 100.0)                 |  |  |  |
| Week 18 (n = 20)              | 82.74 (-22.3 to 100.0)                  |  |  |  |
| Week 21 (n = 20)              | 80.33 (-44.1 to 100.0)                  |  |  |  |
| Week 24 (n = 19)              | 88.44 (-97.8 to 100.0)                  |  |  |  |
| Week 27 (n = 18)              | 93.84 (-4.8 to 100.0)                   |  |  |  |
| Week 30 (n = 17)              | 98.05 (-4.8 to 100.0)                   |  |  |  |
| Week 36 (n = 16)              | 100.00 (-94.5 to 100.0)                 |  |  |  |
| Week 48 (n = 16)              | 98.70 (-28.4 to 100.0)                  |  |  |  |
| Week 60 (n = 13)              | 100.00 (44.7 to 100.0)                  |  |  |  |
| Week 72 (n = 13)              | 100.00 (32.0 to 100.0)                  |  |  |  |
| Week 84 (n = 13)              | 100.00 (62.9 to 100.0)                  |  |  |  |
| Week 96 (n = 12)              | 99.57 (78.2 to 100.0)                   |  |  |  |
| Week 108 (n = 11)             | 100.00 (-48.0 to 100.0)                 |  |  |  |
| Week 120 (n = 10)             | 100.00 (80.4 to 100.0)                  |  |  |  |

|                           |                         |  |  |  |
|---------------------------|-------------------------|--|--|--|
| Week 132 (n = 8)          | 100.00 (50.7 to 100.0)  |  |  |  |
| Week 144 (n = 7)          | 100.00 (93.4 to 100.0)  |  |  |  |
| Week 156 (n = 6)          | 99.76 (93.5 to 100.0)   |  |  |  |
| Week 168 (n = 6)          | 99.74 (90.7 to 100.0)   |  |  |  |
| Week 180 (n = 6)          | 99.02 (86.1 to 100.0)   |  |  |  |
| Week 192 (n = 6)          | 99.76 (85.5 to 100.0)   |  |  |  |
| Week 204 (n = 5)          | 97.94 (78.3 to 100.0)   |  |  |  |
| Week 216 (n = 5)          | 96.58 (81.4 to 100.0)   |  |  |  |
| Week 228 (n = 3)          | 97.12 (96.6 to 100.0)   |  |  |  |
| Week 240 (n = 3)          | 96.36 (86.8 to 100.0)   |  |  |  |
| Week 252 (n = 2)          | 91.12 (85.3 to 96.9)    |  |  |  |
| Week 264 (n = 2)          | 96.91 (95.8 to 98.0)    |  |  |  |
| Week 276 (n = 2)          | 96.40 (95.2 to 97.6)    |  |  |  |
| Week 288 (n = 2)          | 96.14 (94.2 to 98.0)    |  |  |  |
| Week 300 (n = 1)          | 89.7 (89.7 to 89.7)     |  |  |  |
| EOS/EDV (n = 10)          | 21.86 (-120.1 to 100.0) |  |  |  |
| Safety Follow Up (n = 24) | 39.82 (-267.8 to 100.0) |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with a percent change in partial seizure frequency per week of <0%, 0% to <25%, 25% to <50%, ≥50%, ≥75%, or 100% on adjunctive therapy

|                 |  |
|-----------------|--|
| End point title | Percentage of participants with a percent change in partial seizure frequency per week of <0%, 0% to <25%, 25% to <50%, ≥50%, ≥75%, or 100% on adjunctive therapy <sup>[6]</sup> |
|-----------------|--|

End point description:

Percent difference in PSF per Wk at BL and each analysis visit:  $\{[(\text{Number (No.) of PS per Wk at BL}) - (\text{No. of PS per Wk at analysis visit X})] / (\text{No. of PS per Wk at BL})\} * 100$ . Percent difference in PSF per Wk from BL for each participant and analysis visit were mapped into 6 categories: <0%, 0% - <25%, 25% - <50%, ≥50%, ≥75%, and 100%, then % of participants in these categories derived using no. of participants at risk at each previous analysis visit as denominator. Positive value=reduction in PSF from BL. Categories ≥50%, ≥75% and 100% are overlapping, so % of categories can add up to more than 100%. Mapping of seizure data to Analysis Visits was based on target dates of visits. Seizure date after target date of Analysis Visit n and up to that of target date of next Visit n+1 was mapped to next Visit (n+1). Data for 1 participant assessed within study duration mapped to Analysis Visit 35/ Wk 300 based on statistical plan. FAS\_M. n=participants at risk at each previous analysis visit (X-1).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0), Week 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 27, 30, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, 288, 300, EOS/EDV Week 2, EOS/EDV Week 4, and Safety follow-up (up to Week 295)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data of this outcome measure was analyzed and reported for participants on adjunctive therapy.

| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy |  |  |  |
|-----------------------------------|---|--|--|--|
| Subject group type                | Reporting group                         |  |  |  |
| Number of subjects analysed       | 32                                      |  |  |  |
| Units: percentage of participants |   |  |  |  |
| number (not applicable)           |   |  |  |  |
| Week 2: <0% (n = 32)              | 43.8                                    |  |  |  |
| Week 2: 0% - <25% (n = 32)        | 18.8                                    |  |  |  |
| Week 2: 25% - <50% (n = 32)       | 9.4                                     |  |  |  |
| Week 2: ≥ 50% (n = 32)            | 28.1                                    |  |  |  |
| Week 2: ≥ 75% (n = 32)            | 12.5                                    |  |  |  |
| Week 2: 100% (n = 32)             | 9.4                                     |  |  |  |
| Week 4: <0% (n = 32)              | 37.5                                    |  |  |  |
| Week 4: 0% - <25% (n = 32)        | 18.8                                    |  |  |  |
| Week 4: 25% - <50% (n = 32)       | 15.6                                    |  |  |  |
| Week 4: ≥ 50% (n = 32)            | 28.1                                    |  |  |  |
| Week 4: ≥ 75% (n = 32)            | 18.8                                    |  |  |  |
| Week 4: 100% (n = 32)             | 9.4                                     |  |  |  |
| Week 6: <0% (n = 32)              | 31.3                                    |  |  |  |
| Week 6: 0% - <25% (n = 32)        | 15.6                                    |  |  |  |
| Week 6: 25% - <50% (n = 32)       | 12.5                                    |  |  |  |
| Week 6: ≥ 50% (n = 32)            | 28.1                                    |  |  |  |
| Week 6: ≥ 75% (n = 32)            | 18.8                                    |  |  |  |
| Week 6: 100% (n = 32)             | 15.6                                    |  |  |  |
| Week 8: <0% (n = 28)              | 21.4                                    |  |  |  |
| Week 8: 0% - <25% (n = 28)        | 14.3                                    |  |  |  |
| Week 8: 25% - <50% (n = 28)       | 17.9                                    |  |  |  |
| Week 8: ≥ 50% (n = 28)            | 35.7                                    |  |  |  |
| Week 8: ≥ 75% (n = 28)            | 25.0                                    |  |  |  |
| Week 8: 100% (n = 28)             | 17.9                                    |  |  |  |
| Week 10: <0% (n = 25)             | 24.0                                    |  |  |  |
| Week 10: 0% - <25% (n = 25)       | 12.0                                    |  |  |  |
| Week 10: 25% - <50% (n = 25)      | 8.0                                     |  |  |  |
| Week 10: ≥ 50% (n = 25)           | 52.0                                    |  |  |  |
| Week 10: ≥ 75% (n = 25)           | 28.0                                    |  |  |  |
| Week 10: 100% (n = 25)            | 20.0                                    |  |  |  |
| Week 12: <0% (n = 24)             | 20.8                                    |  |  |  |
| Week 12: 0% - <25% (n = 24)       | 4.2                                     |  |  |  |
| Week 12: 25% - <50% (n = 24)      | 20.8                                    |  |  |  |
| Week 12: ≥ 50% (n = 24)           | 45.8                                    |  |  |  |
| Week 12: ≥ 75% (n = 24)           | 37.5                                    |  |  |  |
| Week 12: 100% (n = 24)            | 25.0                                    |  |  |  |
| Week 15: <0% (n = 22)             | 13.6                                    |  |  |  |

|                              |      |  |  |  |
|------------------------------|------|--|--|--|
| Week 15: 0% - <25% (n = 22)  | 9.1  |  |  |  |
| Week 15: 25% - <50% (n = 22) | 13.6 |  |  |  |
| Week 15: ≥ 50% (n = 22)      | 63.6 |  |  |  |
| Week 15: ≥ 75% (n = 22)      | 36.4 |  |  |  |
| Week 15: 100% (n = 22)       | 27.3 |  |  |  |
| Week 18: <0% (n = 22)        | 9.1  |  |  |  |
| Week 18: 0% - <25% (n = 22)  | 4.5  |  |  |  |
| Week 18: 25% - <50% (n = 22) | 9.1  |  |  |  |
| Week 18: ≥ 50% (n = 22)      | 68.2 |  |  |  |
| Week 18: ≥ 75% (n = 22)      | 54.5 |  |  |  |
| Week 18: 100% (n = 22)       | 31.8 |  |  |  |
| Week 21: <0% (n = 20)        | 10.0 |  |  |  |
| Week 21: 0% - <25% (n = 20)  | 5.0  |  |  |  |
| Week 21: 25% - <50% (n = 20) | 5.0  |  |  |  |
| Week 21: ≥ 50% (n = 20)      | 80.0 |  |  |  |
| Week 21: ≥ 75% (n = 20)      | 55.0 |  |  |  |
| Week 21: 100% (n = 20)       | 30.0 |  |  |  |
| Week 24: <0% (n = 20)        | 10.0 |  |  |  |
| Week 24: 0% - <25% (n = 20)  | 10.0 |  |  |  |
| Week 24: 25% - <50% (n = 20) | 5.0  |  |  |  |
| Week 24: ≥ 50% (n = 20)      | 70.0 |  |  |  |
| Week 24: ≥ 75% (n = 20)      | 55.0 |  |  |  |
| Week 24: 100% (n = 20)       | 40.0 |  |  |  |
| Week 27: <0% (n = 19)        | 5.3  |  |  |  |
| Week 27: 0% - <25% (n = 19)  | 5.3  |  |  |  |
| Week 27: 25% - <50% (n = 19) | 10.5 |  |  |  |
| Week 27: ≥ 50% (n = 19)      | 73.7 |  |  |  |
| Week 27: ≥ 75% (n = 19)      | 52.6 |  |  |  |
| Week 27: 100% (n = 19)       | 36.8 |  |  |  |
| Week 30: <0% (n = 18)        | 5.6  |  |  |  |
| Week 30: 0% - <25% (n = 18)  | 11.1 |  |  |  |
| Week 30: 25% - <50% (n = 18) | 5.6  |  |  |  |
| Week 30: ≥ 50% (n = 18)      | 72.2 |  |  |  |
| Week 30: ≥ 75% (n = 18)      | 55.6 |  |  |  |
| Week 30: 100% (n = 18)       | 44.4 |  |  |  |
| Week 36: <0% (n = 17)        | 11.8 |  |  |  |
| Week 36: 0% - <25% (n = 17)  | 5.9  |  |  |  |
| Week 36: 25% - <50% (n = 17) | 0    |  |  |  |
| Week 36: ≥ 50% (n = 17)      | 76.5 |  |  |  |
| Week 36: ≥ 75% (n = 17)      | 70.6 |  |  |  |
| Week 36: 100% (n = 17)       | 52.9 |  |  |  |
| Week 48: <0% (n = 16)        | 6.3  |  |  |  |
| Week 48: 0% - <25% (n = 16)  | 12.5 |  |  |  |
| Week 48: 25% - <50% (n = 16) | 6.3  |  |  |  |
| Week 48: ≥ 50% (n = 16)      | 75.0 |  |  |  |
| Week 48: ≥ 75% (n = 16)      | 75.0 |  |  |  |
| Week 48:100% (n = 16)        | 43.8 |  |  |  |
| Week 60: <0% (n = 16)        | 0    |  |  |  |
| Week 60: 0% - <25% (n = 16)  | 0    |  |  |  |
| Week 60: 25% - <50% (n = 16) | 6.3  |  |  |  |
| Week 60: ≥ 50% (n = 16)      | 75.0 |  |  |  |
| Week 60: ≥ 75% (n = 16)      | 68.8 |  |  |  |

|                               |      |  |  |  |
|-------------------------------|------|--|--|--|
| Week 60: 100% (n = 16)        | 43.8 |  |  |  |
| Week 72: <0% (n = 13)         | 0    |  |  |  |
| Week 72: 0% - <25% (n = 13)   | 0    |  |  |  |
| Week 72: 25% - <50% (n = 13)  | 7.7  |  |  |  |
| Week 72: ≥ 50% (n = 13)       | 92.3 |  |  |  |
| Week 72: ≥ 75% (n = 13)       | 76.9 |  |  |  |
| Week 72: 100% (n = 13)        | 53.8 |  |  |  |
| Week 84: <0% (n = 13)         | 0    |  |  |  |
| Week 84: 0% - <25% (n = 13)   | 0    |  |  |  |
| Week 84: 25% - <50% (n = 13)  | 0    |  |  |  |
| Week 84: ≥ 50% (n = 13)       | 100  |  |  |  |
| Week 84: ≥ 75% (n = 13)       | 84.6 |  |  |  |
| Week 84: 100% (n = 13)        | 53.8 |  |  |  |
| Week 96: <0% (n = 13)         | 0    |  |  |  |
| Week 96: 0% - <25% (n = 13)   | 0    |  |  |  |
| Week 96: 25% - <50% (n = 13)  | 0    |  |  |  |
| Week 96: ≥ 50% (n = 13)       | 92.3 |  |  |  |
| Week 96: ≥ 75% (n = 13)       | 92.3 |  |  |  |
| Week 96: 100% (n = 13)        | 46.2 |  |  |  |
| Week 108: <0% (n = 12)        | 8.3  |  |  |  |
| Week 108: 0% - <25% (n = 12)  | 0    |  |  |  |
| Week 108: 25% - <50% (n = 12) | 0    |  |  |  |
| Week 108: ≥ 50% (n = 12)      | 83.3 |  |  |  |
| Week 108: ≥ 75% (n = 12)      | 75.0 |  |  |  |
| Week 108: 100% (n = 12)       | 50.0 |  |  |  |
| Week 120: <0% (n = 11)        | 0    |  |  |  |
| Week 120: 0% - <25% (n = 11)  | 0    |  |  |  |
| Week 120: 25% - <50% (n = 11) | 0    |  |  |  |
| Week 120: ≥ 50% (n = 11)      | 90.9 |  |  |  |
| Week 120: ≥ 75% (n = 11)      | 90.9 |  |  |  |
| Week 120: 100% (n = 11)       | 63.6 |  |  |  |
| Week 132: <0% (n = 10)        | 0    |  |  |  |
| Week 132: 0% - <25% (n = 10)  | 0    |  |  |  |
| Week 132: 25% - <50% (n = 10) | 0    |  |  |  |
| Week 132: ≥ 50% (n = 10)      | 80.0 |  |  |  |
| Week 132: ≥ 75% (n = 10)      | 70.0 |  |  |  |
| Week 132: 100% (n = 10)       | 50.0 |  |  |  |
| Week 144: <0% (n = 8)         | 0    |  |  |  |
| Week 144: 0% - <25% (n = 8)   | 0    |  |  |  |
| Week 144: 25% - <50% (n = 8)  | 0    |  |  |  |
| Week 144: ≥ 50% (n = 8)       | 87.5 |  |  |  |
| Week 144: ≥ 75% (n = 8)       | 87.5 |  |  |  |
| Week 144: 100% (n = 8)        | 50.0 |  |  |  |
| Week 156: <0% (n = 7)         | 0    |  |  |  |
| Week 156: 0% - <25% (n = 7)   | 0    |  |  |  |
| Week 156: 25% - <50% (n = 7)  | 0    |  |  |  |
| Week 156: ≥ 50% (n = 7)       | 85.7 |  |  |  |
| Week 156: ≥ 75% (n = 7)       | 85.7 |  |  |  |
| Week 156: 100% (n = 7)        | 42.9 |  |  |  |
| Week 168: <0% (n = 6)         | 0    |  |  |  |
| Week 168: 0% - <25% (n = 6)   | 0    |  |  |  |
| Week 168: 25% - <50% (n = 6)  | 0    |  |  |  |

|                                 |      |  |  |  |
|---------------------------------|------|--|--|--|
| Week 168: $\geq 50\%$ (n = 6)   | 100  |  |  |  |
| Week 168: $\geq 75\%$ (n = 6)   | 100  |  |  |  |
| Week 168: 100% (n = 6)          | 50.0 |  |  |  |
| Week 180: $<0\%$ (n = 6)        | 0    |  |  |  |
| Week 180: 0% - $<25\%$ (n = 6)  | 0    |  |  |  |
| Week 180: 25% - $<50\%$ (n = 6) | 0    |  |  |  |
| Week 180: $\geq 50\%$ (n = 6)   | 100  |  |  |  |
| Week 180: $\geq 75\%$ (n = 6)   | 100  |  |  |  |
| Week 180: 100% (n = 6)          | 50.0 |  |  |  |
| Week 192: $<0\%$ (n = 6)        | 0    |  |  |  |
| Week 192: 0% - $<25\%$ (n = 6)  | 0    |  |  |  |
| Week 192: 25% - $<50\%$ (n = 6) | 0    |  |  |  |
| Week 192: $\geq 50\%$ (n = 6)   | 100  |  |  |  |
| Week 192: $\geq 75\%$ (n = 6)   | 100  |  |  |  |
| Week 192: 100% (n = 6)          | 50.0 |  |  |  |
| Week 204: $<0\%$ (n = 6)        | 0    |  |  |  |
| Week 204: 0% - $<25\%$ (n = 6)  | 0    |  |  |  |
| Week 204: 25% - $<50\%$ (n = 6) | 0    |  |  |  |
| Week 204: $\geq 50\%$ (n = 6)   | 83.3 |  |  |  |
| Week 204: $\geq 75\%$ (n = 6)   | 83.3 |  |  |  |
| Week 204: 100% (n = 6)          | 16.7 |  |  |  |
| Week 216: $<0\%$ (n = 5)        | 0    |  |  |  |
| Week 216: 0% - $<25\%$ (n = 5)  | 0    |  |  |  |
| Week 216: 25% - $<50\%$ (n = 5) | 0    |  |  |  |
| Week 216: $\geq 50\%$ (n = 5)   | 100  |  |  |  |
| Week 216: $\geq 75\%$ (n = 5)   | 100  |  |  |  |
| Week 216: 100% (n = 5)          | 20.0 |  |  |  |
| Week 228: $<0\%$ (n = 5)        | 0    |  |  |  |
| Week 228: 0% - $<25\%$ (n = 5)  | 0    |  |  |  |
| Week 228: 25% - $<50\%$ (n = 5) | 0    |  |  |  |
| Week 228: $\geq 50\%$ (n = 5)   | 60.0 |  |  |  |
| Week 228: $\geq 75\%$ (n = 5)   | 60.0 |  |  |  |
| Week 228: 100% (n = 5)          | 20.0 |  |  |  |
| Week 240: $<0\%$ (n = 3)        | 0    |  |  |  |
| Week 240: 0% - $<25\%$ (n = 3)  | 0    |  |  |  |
| Week 240: 25% - $<50\%$ (n = 3) | 0    |  |  |  |
| Week 240: $\geq 50\%$ (n = 3)   | 100  |  |  |  |
| Week 240: $\geq 75\%$ (n = 3)   | 100  |  |  |  |
| Week 240: 100% (n = 3)          | 33.3 |  |  |  |
| Week 252: $<0\%$ (n = 3)        | 0    |  |  |  |
| Week 252: 0% - $<25\%$ (n = 3)  | 0    |  |  |  |
| Week 252: 25% - $<50\%$ (n = 3) | 0    |  |  |  |
| Week 252: $\geq 50\%$ (n = 3)   | 66.7 |  |  |  |
| Week 252: $\geq 75\%$ (n = 3)   | 66.7 |  |  |  |
| Week 252: 100% (n = 3)          | 0    |  |  |  |
| Week 264: $<0\%$ (n = 2)        | 0    |  |  |  |
| Week 264: 0% - $<25\%$ (n = 2)  | 0    |  |  |  |
| Week 264: 25% - $<50\%$ (n = 2) | 0    |  |  |  |
| Week 264: $\geq 50\%$ (n = 2)   | 100  |  |  |  |
| Week 264: $\geq 75\%$ (n = 2)   | 100  |  |  |  |
| Week 264: 100% (n = 2)          | 0    |  |  |  |
| Week 276: $<0\%$ (n = 2)        | 0    |  |  |  |



|                                       |      |  |  |  |
|---------------------------------------|------|--|--|--|
| Week 276: 0% - <25% (n = 2)           | 0    |  |  |  |
| Week 276: 25% - <50% (n = 2)          | 0    |  |  |  |
| Week 276: ≥ 50% (n = 2)               | 100  |  |  |  |
| Week 276: ≥ 75% (n = 2)               | 100  |  |  |  |
| Week 276: 100% (n = 2)                | 0    |  |  |  |
| Week 288: <0% (n = 2)                 | 0    |  |  |  |
| Week 288: 0% - <25% (n = 2)           | 0    |  |  |  |
| Week 288: 25% - <50% (n = 2)          | 0    |  |  |  |
| Week 288: ≥ 50% (n = 2)               | 100  |  |  |  |
| Week 288: ≥ 75% (n = 2)               | 100  |  |  |  |
| Week 288: 100% (n = 2)                | 0    |  |  |  |
| Week 300: <0% (n = 2)                 | 0    |  |  |  |
| Week 300: 0% - <25% (n = 2)           | 0    |  |  |  |
| Week 300: 25% - <50% (n = 2)          | 0    |  |  |  |
| Week 300: ≥ 50% (n = 2)               | 50.0 |  |  |  |
| Week 300: ≥ 75% (n = 2)               | 50.0 |  |  |  |
| Week 300: 100% (n = 2)                | 0    |  |  |  |
| EOS/EDV, Week 2: <0% (n = 32)         | 3.1  |  |  |  |
| EOS/EDV, Week 2: 0% - <25% (n = 32)   | 3.1  |  |  |  |
| EOS/EDV, Week 2: 25% - <50% (n = 32)  | 0    |  |  |  |
| EOS/EDV, Week 2: ≥ 50% (n = 32)       | 3.1  |  |  |  |
| EOS/EDV, Week 2: ≥ 75% (n = 32)       | 3.1  |  |  |  |
| EOS/EDV, Week 2: 100% (n = 32)        | 3.1  |  |  |  |
| EOS/EDV, Week 4: <0% (n = 10)         | 20.0 |  |  |  |
| EOS/EDV, Week 4: 0% - <25% (n = 10)   | 10.0 |  |  |  |
| EOS/EDV, Week 4: 25% - <50% (n = 10)  | 20.0 |  |  |  |
| EOS/EDV, Week 4: ≥ 50% (n = 10)       | 20.0 |  |  |  |
| EOS/EDV, Week 4: ≥ 75% (n = 10)       | 10.0 |  |  |  |
| EOS/EDV, Week 4: 100% (n = 10)        | 0    |  |  |  |
| Safety Follow Up: <0% (n = 24)        | 37.5 |  |  |  |
| Safety Follow Up: 0% - <25% (n = 24)  | 4.2  |  |  |  |
| Safety Follow Up: 25% - <50% (n = 24) | 12.5 |  |  |  |
| Safety Follow Up: ≥ 50% (n = 24)      | 45.8 |  |  |  |
| Safety Follow Up: ≥ 75% (n = 24)      | 29.2 |  |  |  |
| Safety Follow Up: 100% (n = 24)       | 20.8 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent change from baseline for each analysis visit in partial seizure frequency per week on monotherapy

|                 |  |
|-----------------|--|
| End point title | Percent change from baseline for each analysis visit in partial seizure frequency per week on monotherapy <sup>[7]</sup> |
|-----------------|--|

End point description:

The percent difference in partial seizure frequency per week on monotherapy at Baseline and each analysis visit was computed as:  $\{[(\text{Number of partial seizures per week at Baseline}) \text{ minus } (\text{Number of}$

partial seizures per week at analysis visit X)] divided by (Number of partial seizures per week at Baseline)} multiplied by 100. A positive value in percent difference from Baseline indicates a reduction in partial seizure frequency from Baseline. The maximum duration of study participation in monotherapy participants was shorter than in adjunctive therapy. Therefore, data at Week 288 and 300 is not reported for Monotherapy. The FAS\_M consisted of all participants in the SS\_M who had at least 1 post-Baseline efficacy assessment. 'n' signifies participants who were evaluable at specified time points.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0), Week 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 27, 30, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, and Safety follow-up (up to Week 295)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data of this outcome measure was analyzed and reported for participants on monotherapy.

| End point values              | Levetiracetam: Monotherapy |  |  |  |
|-------------------------------|----------------------------|--|--|--|
| Subject group type            | Reporting group            |  |  |  |
| Number of subjects analysed   | 6                          |  |  |  |
| Units: percent change         |                            |  |  |  |
| median (full range (min-max)) |                            |  |  |  |
| Week 2 (n = 6)                | -51.87 (-731.6 to 100.0)   |  |  |  |
| Week 4 (n = 6)                | 4.88 (-115.9 to 100.0)     |  |  |  |
| Week 6 (n = 6)                | 51.10 (-325.0 to 100.0)    |  |  |  |
| Week 8 (n = 5)                | 100.00 (-1.1 to 100.0)     |  |  |  |
| Week 10 (n = 5)               | 100.00 (-277.1 to 100.0)   |  |  |  |
| Week 12 (n = 5)               | 76.92 (-10.0 to 100.0)     |  |  |  |
| Week 15 (n = 5)               | 100.00 (-78.1 to 100.0)    |  |  |  |
| Week 18 (n = 5)               | 91.58 (58.1 to 100.0)      |  |  |  |
| Week 21 (n = 5)               | 100.00 (76.9 to 100.0)     |  |  |  |
| Week 24 (n = 5)               | 100.00 (92.3 to 100.0)     |  |  |  |
| Week 27 (n = 5)               | 100.00 (26.7 to 100.0)     |  |  |  |
| Week 30 (n = 5)               | 100.00 (37.1 to 100.0)     |  |  |  |
| Week 36 (n = 5)               | 100.00 (16.2 to 100.0)     |  |  |  |
| Week 48 (n = 5)               | 98.08 (-138.3 to 100.0)    |  |  |  |
| Week 60 (n = 5)               | 94.23 (-41.4 to 100.0)     |  |  |  |
| Week 72 (n = 5)               | 92.31 (-36.2 to 100.0)     |  |  |  |
| Week 84 (n = 5)               | 95.79 (-86.0 to 100.0)     |  |  |  |
| Week 96 (n = 5)               | 98.08 (-65.0 to 100.0)     |  |  |  |
| Week 108 (n = 5)              | 96.15 (-44.0 to 100.0)     |  |  |  |

|                          |                          |  |  |  |
|--------------------------|--------------------------|--|--|--|
| Week 120 (n = 5)         | 93.68 (-46.7 to 100.0)   |  |  |  |
| Week 132 (n = 4)         | 92.63 (-138.3 to 100.0)  |  |  |  |
| Week 144 (n = 4)         | 92.63 (-106.9 to 100.0)  |  |  |  |
| Week 156 (n = 4)         | 94.73 (8.3 to 100.0)     |  |  |  |
| Week 168 (n = 4)         | 100.00 (-70.2 to 100.0)  |  |  |  |
| Week 180 (n = 3)         | 100.00 (-274.5 to 100.0) |  |  |  |
| Week 192 (n = 3)         | 100.00 (-223.0 to 100.0) |  |  |  |
| Week 204 (n = 2)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 216 (n = 2)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 228 (n = 1)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 240 (n = 1)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 252 (n = 1)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 264 (n = 1)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Week 276 (n = 1)         | 100.00 (100.0 to 100.0)  |  |  |  |
| Safety Follow Up (n = 2) | 100.00 (100.0 to 100.0)  |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of participants with a percent change in partial seizure frequency per week of <0%, 0% to <25%, 25% to <50%, ≥50%, ≥75%, or 100% on monotherapy

|                 |   |
|-----------------|---|
| End point title | Percentage of participants with a percent change in partial seizure frequency per week of <0%, 0% to <25%, 25% to <50%, ≥50%, ≥75%, or 100% on monotherapy <sup>[8]</sup> |
|-----------------|---|

End point description:

Percent difference in PSF per week on monotherapy at BL and each analysis visit:  $\{[(\text{Number of partial seizures per week at BL}) - (\text{Number of partial seizures per week at analysis visit X})] / (\text{Number of partial seizures per week at BL})\} * 100$ . Percent difference in PSF per week from BL for each participant and analysis visit were mapped into 6 categories: <0%, 0% to <25%, 25% to <50%, ≥50%, ≥75%, and 100%, then percentages of participants in these categories derived using the number of participants at risk at each previous analysis visit as denominator. Positive value indicates reduction in PSF from BL. Outcome categories "≥50%", "≥75%" and "100%" are overlapping, so that percentages of categories of this outcome measure can add up to more than 100%. Maximum duration of study participation in monotherapy participants was shorter than adjunctive therapy. Therefore, data at Week 288 and 300 is not reported for Monotherapy. FAS\_M. 'n' = participants at risk at each previous analysis visit(X-1).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0), Week 2, 4, 6, 8, 10, 12, 15, 18, 21, 24, 27, 30, 36, 48, 60, 72, 84, 96, 108, 120, 132, 144, 156, 168, 180, 192, 204, 216, 228, 240, 252, 264, 276, and Safety follow-up (up to Week 295)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.  
Justification: Data of this outcome measure was analyzed and reported for participants on monotherapy.

| End point values                  | Levetiracetam:<br>Monotherapy |  |  |  |
|-----------------------------------|-------------------------------|--|--|--|
| Subject group type                | Reporting group               |  |  |  |
| Number of subjects analysed       | 6                             |  |  |  |
| Units: percentage of participants |                               |  |  |  |
| number (not applicable)           |                               |  |  |  |
| Week 2: <0% (n = 5)               | 60.0                          |  |  |  |
| Week 2: 0% - <25% (n = 5)         | 0                             |  |  |  |
| Week 2: 25% - <50% (n = 5)        | 20.0                          |  |  |  |
| Week 2: ≥ 50% (n = 5)             | 40.0                          |  |  |  |
| Week 2: ≥ 75% (n = 5)             | 20.0                          |  |  |  |
| Week 2: 100% (n = 5)              | 20.0                          |  |  |  |
| Week 4: <0% (n = 6)               | 50.0                          |  |  |  |
| Week 4: 0% - <25% (n = 6)         | 0                             |  |  |  |
| Week 4: 25% - <50% (n = 6)        | 16.7                          |  |  |  |
| Week 4: ≥ 50% (n = 6)             | 33.3                          |  |  |  |
| Week 4: ≥ 75% (n = 6)             | 33.3                          |  |  |  |
| Week 4: 100% (n = 6)              | 33.3                          |  |  |  |
| Week 6: <0% (n = 6)               | 33.3                          |  |  |  |
| Week 6: 0% - <25% (n = 6)         | 0                             |  |  |  |
| Week 6: 25% - <50% (n = 6)        | 16.7                          |  |  |  |
| Week 6: ≥ 50% (n = 6)             | 50.0                          |  |  |  |
| Week 6: ≥ 75% (n = 6)             | 33.3                          |  |  |  |
| Week 6: 100% (n = 6)              | 16.7                          |  |  |  |
| Week 8: <0% (n = 6)               | 16.7                          |  |  |  |
| Week 8: 0% - <25% (n = 6)         | 16.7                          |  |  |  |
| Week 8: 25% - <50% (n = 6)        | 0                             |  |  |  |
| Week 8: ≥ 50% (n = 6)             | 50.0                          |  |  |  |
| Week 8: ≥ 75% (n = 6)             | 50.0                          |  |  |  |
| Week 8: 100% (n = 6)              | 50.0                          |  |  |  |
| Week 10: <0% (n = 5)              | 20.0                          |  |  |  |
| Week 10: 0% - <25% (n = 5)        | 0                             |  |  |  |
| Week 10: 25% - <50% (n = 5)       | 0                             |  |  |  |
| Week 10: ≥ 50% (n = 5)            | 80.0                          |  |  |  |
| Week 10: ≥ 75% (n = 5)            | 80.0                          |  |  |  |
| Week 10: 100% (n = 5)             | 60.0                          |  |  |  |
| Week 12: <0% (n = 5)              | 20.0                          |  |  |  |
| Week 12: 0% - <25% (n = 5)        | 0                             |  |  |  |
| Week 12: 25% - <50% (n = 5)       | 20.0                          |  |  |  |
| Week 12: ≥ 50% (n = 5)            | 60.0                          |  |  |  |
| Week 12: ≥ 75% (n = 5)            | 60.0                          |  |  |  |
| Week 12: 100% (n = 5)             | 40.0                          |  |  |  |
| Week 15: <0% (n = 5)              | 20.0                          |  |  |  |
| Week 15: 0% - <25% (n = 5)        | 0                             |  |  |  |
| Week 15: 25% - <50% (n = 5)       | 20.0                          |  |  |  |
| Week 15: ≥ 50% (n = 5)            | 60.0                          |  |  |  |
| Week 15: ≥ 75% (n = 5)            | 60.0                          |  |  |  |

|                             |      |  |  |  |
|-----------------------------|------|--|--|--|
| Week 15: 100% (n = 5)       | 60.0 |  |  |  |
| Week 18: <0% (n = 5)        | 0    |  |  |  |
| Week 18: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 18: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 18: ≥ 50% (n = 5)      | 100  |  |  |  |
| Week 18: ≥ 75% (n = 5)      | 80.0 |  |  |  |
| Week 18: 100% (n = 5)       | 40.0 |  |  |  |
| Week 21: <0% (n = 5)        | 0    |  |  |  |
| Week 21: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 21: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 21: ≥ 50% (n = 5)      | 100  |  |  |  |
| Week 21: ≥ 75% (n = 5)      | 100  |  |  |  |
| Week 21: 100% (n = 5)       | 60.0 |  |  |  |
| Week 24: <0% (n = 5)        | 0    |  |  |  |
| Week 24: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 24: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 24: ≥ 50% (n = 5)      | 100  |  |  |  |
| Week 24: ≥ 75% (n = 5)      | 100  |  |  |  |
| Week 24: 100% (n = 5)       | 80.0 |  |  |  |
| Week 27: <0% (n = 5)        | 0    |  |  |  |
| Week 27: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 27: 25% - <50% (n = 5) | 20.0 |  |  |  |
| Week 27: ≥ 50% (n = 5)      | 80.0 |  |  |  |
| Week 27: ≥ 75% (n = 5)      | 80.0 |  |  |  |
| Week 27: 100% (n = 5)       | 80.0 |  |  |  |
| Week 30: <0% (n = 5)        | 0    |  |  |  |
| Week 30: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 30: 25% - <50% (n = 5) | 20.0 |  |  |  |
| Week 30: ≥ 50% (n = 5)      | 80.0 |  |  |  |
| Week 30: ≥ 75% (n = 5)      | 60.0 |  |  |  |
| Week 30: 100% (n = 5)       | 60.0 |  |  |  |
| Week 36: <0% (n = 5)        | 0    |  |  |  |
| Week 36: 0% - <25% (n = 5)  | 20.0 |  |  |  |
| Week 36: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 36: ≥ 50% (n = 5)      | 80.0 |  |  |  |
| Week 36: ≥ 75% (n = 5)      | 80.0 |  |  |  |
| Week 36: 100% (n = 5)       | 60.0 |  |  |  |
| Week 48: <0% (n = 5)        | 20.0 |  |  |  |
| Week 48: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 48: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 48: ≥ 50% (n = 5)      | 80.0 |  |  |  |
| Week 48: ≥ 75% (n = 5)      | 80.0 |  |  |  |
| Week 48: 100% (n = 5)       | 40.0 |  |  |  |
| Week 60: <0% (n = 5)        | 20.0 |  |  |  |
| Week 60: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 60: 25% - <50% (n = 5) | 0    |  |  |  |
| Week 60: ≥ 50% (n = 5)      | 80.0 |  |  |  |
| Week 60: ≥ 75% (n = 5)      | 80.0 |  |  |  |
| Week 60: 100% (n = 5)       | 40.0 |  |  |  |
| Week 72: <0% (n = 5)        | 20.0 |  |  |  |
| Week 72: 0% - <25% (n = 5)  | 0    |  |  |  |
| Week 72: 25% - <50% (n = 5) | 0    |  |  |  |

|                                 |      |  |  |  |
|---------------------------------|------|--|--|--|
| Week 72: $\geq 50\%$ (n = 5)    | 80.0 |  |  |  |
| Week 72: $\geq 75\%$ (n = 5)    | 80.0 |  |  |  |
| Week 72: 100% (n = 5)           | 40.0 |  |  |  |
| Week 84: $<0\%$ (n = 5)         | 20.0 |  |  |  |
| Week 84: 0% - $<25\%$ (n = 5)   | 0    |  |  |  |
| Week 84: 25% - $<50\%$ (n = 5)  | 0    |  |  |  |
| Week 84: $\geq 50\%$ (n = 5)    | 80.0 |  |  |  |
| Week 84: $\geq 75\%$ (n = 5)    | 80.0 |  |  |  |
| Week 84: 100% (n = 5)           | 40.0 |  |  |  |
| Week 96: $<0\%$ (n = 5)         | 20.0 |  |  |  |
| Week 96: 0% - $<25\%$ (n = 5)   | 0    |  |  |  |
| Week 96: 25% - $<50\%$ (n = 5)  | 0    |  |  |  |
| Week 96: $\geq 50\%$ (n = 5)    | 80.0 |  |  |  |
| Week 96: $\geq 75\%$ (n = 5)    | 80.0 |  |  |  |
| Week 96: 100% (n = 5)           | 40.0 |  |  |  |
| Week 108: $<0\%$ (n = 5)        | 20.0 |  |  |  |
| Week 108: 0% - $<25\%$ (n = 5)  | 0    |  |  |  |
| Week 108: 25% - $<50\%$ (n = 5) | 0    |  |  |  |
| Week 108: $\geq 50\%$ (n = 5)   | 80.0 |  |  |  |
| Week 108: $\geq 75\%$ (n = 5)   | 80.0 |  |  |  |
| Week 108: 100% (n = 5)          | 40.0 |  |  |  |
| Week 120: $<0\%$ (n = 5)        | 20.0 |  |  |  |
| Week 120: 0% - $<25\%$ (n = 5)  | 0    |  |  |  |
| Week 120: 25% - $<50\%$ (n = 5) | 0    |  |  |  |
| Week 120: $\geq 50\%$ (n = 5)   | 80.0 |  |  |  |
| Week 120: $\geq 75\%$ (n = 5)   | 80.0 |  |  |  |
| Week 120: 100% (n = 5)          | 40.0 |  |  |  |
| Week 132: $<0\%$ (n = 5)        | 20.0 |  |  |  |
| Week 132: 0% - $<25\%$ (n = 5)  | 0    |  |  |  |
| Week 132: 25% - $<50\%$ (n = 5) | 0    |  |  |  |
| Week 132: $\geq 50\%$ (n = 5)   | 60.0 |  |  |  |
| Week 132: $\geq 75\%$ (n = 5)   | 60.0 |  |  |  |
| Week 132: 100% (n = 5)          | 40.0 |  |  |  |
| Week 144: $<0\%$ (n = 4)        | 25.0 |  |  |  |
| Week 144: 0% - $<25\%$ (n = 4)  | 0    |  |  |  |
| Week 144: 25% - $<50\%$ (n = 4) | 0    |  |  |  |
| Week 144: $\geq 50\%$ (n = 4)   | 75.0 |  |  |  |
| Week 144: $\geq 75\%$ (n = 4)   | 75.0 |  |  |  |
| Week 144: 100% (n = 4)          | 50.0 |  |  |  |
| Week 156: $<0\%$ (n = 4)        | 0    |  |  |  |
| Week 156: 0% - $<25\%$ (n = 4)  | 25.0 |  |  |  |
| Week 156: 25% - $<50\%$ (n = 4) | 0    |  |  |  |
| Week 156: $\geq 50\%$ (n = 4)   | 75.0 |  |  |  |
| Week 156: $\geq 75\%$ (n = 4)   | 75.0 |  |  |  |
| Week 156: 100% (n = 4)          | 50.0 |  |  |  |
| Week 168: $<0\%$ (n = 4)        | 25.0 |  |  |  |
| Week 168: 0% - $<25\%$ (n = 4)  | 0    |  |  |  |
| Week 168: 25% - $<50\%$ (n = 4) | 0    |  |  |  |
| Week 168: $\geq 50\%$ (n = 4)   | 75.0 |  |  |  |
| Week 168: $\geq 75\%$ (n = 4)   | 75.0 |  |  |  |
| Week 168: 100% (n = 4)          | 75.0 |  |  |  |
| Week 180: $<0\%$ (n = 4)        | 25.0 |  |  |  |

|                              |      |  |  |  |
|------------------------------|------|--|--|--|
| Week 180: 0% - <25% (n = 4)  | 0    |  |  |  |
| Week 180: 25% - <50% (n = 4) | 0    |  |  |  |
| Week 180: ≥ 50% (n = 4)      | 50.0 |  |  |  |
| Week 180: ≥ 75% (n = 4)      | 50.0 |  |  |  |
| Week 180: 100% (n = 4)       | 50.0 |  |  |  |
| Week 192: <0% (n = 3)        | 33.3 |  |  |  |
| Week 192: 0% - <25% (n = 3)  | 0    |  |  |  |
| Week 192: 25% - <50% (n = 3) | 0    |  |  |  |
| Week 192: ≥ 50% (n = 3)      | 66.7 |  |  |  |
| Week 192: ≥ 75% (n = 3)      | 66.7 |  |  |  |
| Week 192: 100% (n = 3)       | 66.7 |  |  |  |
| Week 204: <0% (n = 3)        | 0    |  |  |  |
| Week 204: 0% - <25% (n = 3)  | 0    |  |  |  |
| Week 204: 25% - <50% (n = 3) | 0    |  |  |  |
| Week 204: ≥ 50% (n = 3)      | 66.7 |  |  |  |
| Week 204: ≥ 75% (n = 3)      | 66.7 |  |  |  |
| Week 204: 100% (n = 3)       | 66.7 |  |  |  |
| Week 216: <0% (n = 2)        | 0    |  |  |  |
| Week 216: 0% - <25% (n = 2)  | 0    |  |  |  |
| Week 216: 25% - <50% (n = 2) | 0    |  |  |  |
| Week 216: ≥ 50% (n = 2)      | 100  |  |  |  |
| Week 216: ≥ 75% (n = 2)      | 100  |  |  |  |
| Week 216: 100% (n = 2)       | 100  |  |  |  |
| Week 228: <0% (n = 2)        | 0    |  |  |  |
| Week 228: 0% - <25% (n = 2)  | 0    |  |  |  |
| Week 228: 25% - <50% (n = 2) | 0    |  |  |  |
| Week 228: ≥ 50% (n = 2)      | 50.0 |  |  |  |
| Week 228: ≥ 75% (n = 2)      | 50.0 |  |  |  |
| Week 228: 100% (n = 2)       | 50.0 |  |  |  |
| Week 240: <0% (n = 1)        | 0    |  |  |  |
| Week 240: 0% - <25% (n = 1)  | 0    |  |  |  |
| Week 240: 25% - <50% (n = 1) | 0    |  |  |  |
| Week 240: ≥ 50% (n = 1)      | 100  |  |  |  |
| Week 240: ≥ 75% (n = 1)      | 100  |  |  |  |
| Week 240: 100% (n = 1)       | 100  |  |  |  |
| Week 252: <0% (n = 1)        | 0    |  |  |  |
| Week 252: 0% - <25% (n = 1)  | 0    |  |  |  |
| Week 252: 25% - <50% (n = 1) | 0    |  |  |  |
| Week 252: ≥ 50% (n = 1)      | 100  |  |  |  |
| Week 252: ≥ 75% (n = 1)      | 100  |  |  |  |
| Week 252: 100% (n = 1)       | 100  |  |  |  |
| Week 264: <0% (n = 1)        | 0    |  |  |  |
| Week 264: 0% - <25% (n = 1)  | 0    |  |  |  |
| Week 264: 25% - <50% (n = 1) | 0    |  |  |  |
| Week 264: ≥ 50% (n = 1)      | 100  |  |  |  |
| Week 264: ≥ 75% (n = 1)      | 100  |  |  |  |
| Week 264: 100% (n = 1)       | 100  |  |  |  |
| Week 276: <0% (n = 1)        | 0    |  |  |  |
| Week 276: 0% - <25% (n = 1)  | 0    |  |  |  |
| Week 276: 25% - <50% (n = 1) | 0    |  |  |  |
| Week 276: ≥ 50% (n = 1)      | 100  |  |  |  |
| Week 276: ≥ 75% (n = 1)      | 100  |  |  |  |

|                                      |     |  |  |  |
|--------------------------------------|-----|--|--|--|
| Week 276: 100% (n = 1)               | 100 |  |  |  |
| Safety Follow Up: <0% (n = 2)        | 0   |  |  |  |
| Safety Follow Up: 0% - <25% (n = 2)  | 0   |  |  |  |
| Safety Follow Up: 25% - <50% (n = 2) | 0   |  |  |  |
| Safety Follow Up: ≥ 50% (n = 2)      | 100 |  |  |  |
| Safety Follow Up: ≥ 75% (n = 2)      | 100 |  |  |  |
| Safety Follow Up: 100% (n = 2)       | 100 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with treatment-emergent adverse events (TEAEs) during the First Period

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with treatment-emergent adverse events (TEAEs) during the First Period |
|-----------------|---|

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation Participant administered a pharmaceutical product that does not necessarily have a causal relationship treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. The TEAEs were defined as those events that started on or after the date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after the date (and time) of first dose of study medication. The SS\_A consisted of all enrolled participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. The SS\_M consisted of all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0) to Visit 6 (up to Week 6)

| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 62.5                                    | 0                             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with treatment-emergent serious adverse events (SAEs) during the First Period

|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with treatment-emergent serious adverse events (SAEs) during the First Period |
|-----------------|--|



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**End point description:**

Serious adverse event (SAE) is defined any untoward medical occurrence at any dose results in: Death; Life-threatening; Significant or persistent disability/incapacity; Congenital anomaly/birth defect (including that occurring in fetus); Important medical event that, based upon appropriate medical judgment, may jeopardize patient or participant and may require medical or surgical intervention to prevent 1 of other outcomes listed in definition of serious; Initial inpatient hospitalization or prolongation of hospitalization. TEAEs were defined as those events that started on or after date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after date (and time) of first dose of study medication. SS\_A: all enrolled participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. SS\_M: all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

From Baseline (Week 0) to Visit 6 (up to Week 6)

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| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 9.4                                     | 0                             |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Percentage of Participants with TEAEs leading to discontinuation from study medication during the First Period**

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|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with TEAEs leading to discontinuation from study medication during the First Period |
|-----------------|--|

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**End point description:**

AE is any untoward medical occurrence in patient or clinical investigation participant administered pharmaceutical product that does not necessarily have causal relationship treatment. AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with use of medicinal (investigational) product, whether or not related to medicinal (investigational) product. TEAEs were defined as those events that started on or after the date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after date (and time) of first dose of study medication. TEAEs leading to discontinuation from study medication are reported. SS\_A: participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. SS\_M consisted of all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

From Baseline (Week 0) to Visit 6 (up to Week 6)

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| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 6.3                                     | 0                             |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with TEAEs during the Combined First and Second Period

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with TEAEs during the Combined First and Second Period |
|-----------------|---|

End point description:

An AE is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship treatment. An AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. The TEAEs were defined as those events that started on or after the date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after the date (and time) of first dose of study medication. The SS\_A consisted of all enrolled participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. The SS\_M consisted of all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From Baseline (Week 0) to the End of Safety Follow-up (up to Week 295)

| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 96.9                                    | 100                           |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Participants with treatment-emergent SAEs during the Combined First and Second Period

|                 |   |
|-----------------|---|
| End point title | Percentage of Participants with treatment-emergent SAEs during the Combined First and Second Period |
|-----------------|---|

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**End point description:**

A SAE is defined as any untoward medical occurrence at any dose results in: Death; Life-threatening; Significant or persistent disability/incapacity; Congenital anomaly/birth defect (including that occurring in fetus); Important medical event that, based upon appropriate medical judgment, may jeopardize patient or participant and may require medical or surgical intervention to prevent 1 of other outcomes listed in definition of serious; Initial inpatient hospitalization or prolongation of hospitalization. TEAEs were defined as those events that started on or after date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after date (and time) of first dose of study medication. SS\_A: all enrolled participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. SS\_M: all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

From Baseline (Week 0) to the End of Safety Follow-up (up to Week 295)

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| End point values                  | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 56.3                                    | 33.3                          |  |  |

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**Statistical analyses**

No statistical analyses for this end point

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**Secondary: Percentage of Participants with TEAEs leading to discontinuation from study medication during the Combined First and Second Period**

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|                 |  |
|-----------------|--|
| End point title | Percentage of Participants with TEAEs leading to discontinuation from study medication during the Combined First and Second Period |
|-----------------|--|

---

**End point description:**

AE is any untoward medical occurrence in patient or clinical investigation participant administered pharmaceutical product that does not necessarily have causal relationship treatment. AE could therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with use of medicinal (investigational) product, whether or not related to medicinal (investigational) product. TEAEs were defined as those events that started on or after the date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after date (and time) of first dose of study medication. TEAEs leading to discontinuation from study medication are reported. SS\_A: participants on adjunctive therapy who received at least 1 dose of study medication in the evaluation period. SS\_M consisted of all enrolled participants on monotherapy who received at least 1 dose of study medication in the evaluation period.

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|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

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**End point timeframe:**

From Baseline (Week 0) to the End of Safety Follow-up (up to Week 295)

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| <b>End point values</b>           | Levetiracetam:<br>Adjunctive<br>Therapy | Levetiracetam:<br>Monotherapy |  |  |
|-----------------------------------|---|-------------------------------|--|--|
| Subject group type                | Reporting group                         | Reporting group               |  |  |
| Number of subjects analysed       | 32                                      | 6                             |  |  |
| Units: percentage of participants |   |                               |  |  |
| number (not applicable)           | 9.4                                     | 16.7                          |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From Baseline (Week 0) to the End of Safety Follow-up (up to Week 295)

Adverse event reporting additional description:

The TEAEs were defined as those events that started on or after the date (and time) of first dose of study medication, or adverse events whose intensity worsened on or after the date (and time) of first dose of study medication. TEAEs were analyzed and reported for SS\_A and SS\_M.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 23.0 |
|--------------------|------|

### Reporting groups

|                       |                            |
|-----------------------|----------------------------|
| Reporting group title | Levetiracetam: Monotherapy |
|-----------------------|----------------------------|

Reporting group description:

Participants aged 1 month to < 6 months received LEV 14 mg/kg/day as monotherapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3 (Week 0) of first period and dose up titrated up to a maximum of 60 mg/kg/day up to 6 weeks. The dose was increased by 2 weeks interval as per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged  $\geq$  6 months <4 years at the discretion of the Investigator. Participants visited every 4 weeks for the first 6 months of administration and then every 12 weeks thereafter until approval or till the program discontinued. The dose down-titrated during 4 weeks Interval at the discretion of Investigator.

|                       |                                   |
|-----------------------|-----------------------------------|
| Reporting group title | Levetiracetam: Adjunctive Therapy |
|-----------------------|-----------------------------------|

Reporting group description:

Participants aged 1 month to less than (<) 6 months received LEV 14 milligram per kilogram per day (mg/kg/day) as adjunctive therapy at Visit 3 (Week 0) of First Period and dose up titrated up to 42 mg/kg/day. Participants aged 6 months to <4 years received LEV 20 mg/kg/day at Visit 3(Week 0) of first period and dose up titrated up to maximum of 60 mg/kg/day up to 6 weeks. Dose increased by 2 weeks interval per Investigator's discretion. At Visit 6 (Week 6), dose of participants either down-titrated during 4 weeks interval or they entered in second period and continued LEV 14 to 42 mg/kg/day in participants aged 1 month to <6 months or LEV 20 to 60 mg/kg/day for participants aged greater than or equal to ( $\geq$ ) 6 months <4 years. Participants visited every 4 weeks for first 6 months of administration and then every 12 weeks thereafter until approval or till program discontinued. Dose down-titrated during 4 weeks Interval at discretion of Investigator.

| Serious adverse events                            | Levetiracetam: Monotherapy | Levetiracetam: Adjunctive Therapy |  |
|---|----------------------------|-----------------------------------|--|
| Total subjects affected by serious adverse events |                            |                                   |  |
| subjects affected / exposed                       | 2 / 6 (33.33%)             | 18 / 32 (56.25%)                  |  |
| number of deaths (all causes)                     | 0                          | 0                                 |  |
| number of deaths resulting from adverse events    | 0                          | 0                                 |  |
| Investigations                                    |                            |                                   |  |
| Blood pressure increased                          |                            |                                   |  |
| subjects affected / exposed                       | 0 / 6 (0.00%)              | 1 / 32 (3.13%)                    |  |
| occurrences causally related to treatment / all   | 0 / 0                      | 0 / 1                             |  |
| deaths causally related to treatment / all        | 0 / 0                      | 0 / 0                             |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Injury, poisoning and procedural complications  |                |                |  |
| Post procedural fistula                         |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Congenital, familial and genetic disorders      |                |                |  |
| Cryptorchism                                    |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Surgical and medical procedures                 |                |                |  |
| Epilepsy surgery                                |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Nervous system disorders                        |                |                |  |
| Epilepsy  |                |                |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 1 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Infantile spasms                                |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 3 / 32 (9.38%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Status epilepticus                              |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 3 / 32 (9.38%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 7          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Somnolence                                      |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Seizure cluster                                 |                |                |  |

|  |                |                |  |
|--|----------------|----------------|--|
| subjects affected / exposed                          | 1 / 6 (16.67%) | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 2          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| General disorders and administration site conditions |                |                |  |
| Pyrexia  |                |                |  |
| subjects affected / exposed                          | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences causally related to treatment / all      | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastrointestinal disorders                           |                |                |  |
| Dysphagia  |                |                |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Respiratory, thoracic and mediastinal disorders      |                |                |  |
| Respiratory failure                                  |                |                |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Pneumonia aspiration                                 |                |                |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 2          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Psychiatric disorders                                |                |                |  |
| Selective eating disorder                            |                |                |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Infections and infestations                          |                |                |  |
| Respiratory syncytial virus bronchiolitis            |                |                |  |
| subjects affected / exposed                          | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all      | 0 / 0          | 0 / 1          |  |
| deaths causally related to treatment / all           | 0 / 0          | 0 / 0          |  |
| Gastroenteritis norovirus                            |                |                |  |

|   |               |                |  |
|---|---------------|----------------|--|
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Pneumonia viral                                 |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 3 / 32 (9.38%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 3          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Bronchitis                                      |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Respiratory syncytial virus bronchitis          |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Respiratory syncytial virus infection           |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 2 / 32 (6.25%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Bronchitis viral                                |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Coronavirus infection                           |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 2          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Cellulitis                                      |               |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%) | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0         | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0         | 0 / 0          |  |
| Gastroenteritis                                 |               |                |  |



|   |                |                |  |
|---|----------------|----------------|--|
| subjects affected / exposed                     | 1 / 6 (16.67%) | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Influenza                                       |                |                |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Pneumonia bacterial                             |                |                |  |
| subjects affected / exposed                     | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |
| Metabolism and nutrition disorders              |                |                |  |
| Dehydration                                     |                |                |  |
| subjects affected / exposed                     | 0 / 6 (0.00%)  | 1 / 32 (3.13%) |  |
| occurrences causally related to treatment / all | 0 / 0          | 1 / 1          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | Levetiracetam:<br>Monotherapy | Levetiracetam:<br>Adjunctive Therapy |  |
|---|-------------------------------|--------------------------------------|--|
| Total subjects affected by non-serious adverse events |                               |                                      |  |
| subjects affected / exposed                           | 6 / 6 (100.00%)               | 28 / 32 (87.50%)                     |  |
| General disorders and administration site conditions  |                               |                                      |  |
| Pyrexia   |                               |                                      |  |
| subjects affected / exposed                           | 2 / 6 (33.33%)                | 12 / 32 (37.50%)                     |  |
| occurrences (all)                                     | 3                             | 51                                   |  |
| Immune system disorders                               |                               |                                      |  |
| Food allergy  |                               |                                      |  |
| subjects affected / exposed                           | 0 / 6 (0.00%)                 | 2 / 32 (6.25%)                       |  |
| occurrences (all)                                     | 0                             | 2                                    |  |
| Reproductive system and breast disorders              |                               |                                      |  |
| Balanoposthitis                                       |                               |                                      |  |
| subjects affected / exposed                           | 0 / 6 (0.00%)                 | 2 / 32 (6.25%)                       |  |
| occurrences (all)                                     | 0                             | 2                                    |  |
| Respiratory, thoracic and mediastinal                 |                               |                                      |  |

|                                      |                |                |  |
|--------------------------------------|----------------|----------------|--|
| disorders                            |                |                |  |
| Upper respiratory tract inflammation |                |                |  |
| subjects affected / exposed          | 2 / 6 (33.33%) | 3 / 32 (9.38%) |  |
| occurrences (all)                    | 2              | 8              |  |
| Cough                                |                |                |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 3 / 32 (9.38%) |  |
| occurrences (all)                    | 0              | 7              |  |
| Rhinitis allergic                    |                |                |  |
| subjects affected / exposed          | 2 / 6 (33.33%) | 3 / 32 (9.38%) |  |
| occurrences (all)                    | 2              | 4              |  |
| Rhinorrhoea                          |                |                |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |  |
| occurrences (all)                    | 0              | 2              |  |
| Allergic bronchitis                  |                |                |  |
| subjects affected / exposed          | 1 / 6 (16.67%) | 1 / 32 (3.13%) |  |
| occurrences (all)                    | 1              | 1              |  |
| Epistaxis                            |                |                |  |
| subjects affected / exposed          | 3 / 6 (50.00%) | 1 / 32 (3.13%) |  |
| occurrences (all)                    | 4              | 1              |  |
| Psychiatric disorders                |                |                |  |
| Agitation                            |                |                |  |
| subjects affected / exposed          | 1 / 6 (16.67%) | 2 / 32 (6.25%) |  |
| occurrences (all)                    | 1              | 2              |  |
| Irritability                         |                |                |  |
| subjects affected / exposed          | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |  |
| occurrences (all)                    | 0              | 2              |  |
| Investigations                       |                |                |  |
| Alanine aminotransferase increased   |                |                |  |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Aspartate aminotransferase increased |                |                |  |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |
| Glucose urine present                |                |                |  |
| subjects affected / exposed          | 1 / 6 (16.67%) | 0 / 32 (0.00%) |  |
| occurrences (all)                    | 1              | 0              |  |

|  |                |                 |  |
|--|----------------|-----------------|--|
| Injury, poisoning and procedural complications |                |                 |  |
| Skin abrasion                                  |                |                 |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 3 / 32 (9.38%)  |  |
| occurrences (all)                              | 0              | 3               |  |
| Arthropod bite                                 |                |                 |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 2 / 32 (6.25%)  |  |
| occurrences (all)                              | 0              | 3               |  |
| Fall   |                |                 |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 2 / 32 (6.25%)  |  |
| occurrences (all)                              | 0              | 2               |  |
| Thermal burn                                   |                |                 |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 1 / 32 (3.13%)  |  |
| occurrences (all)                              | 1              | 1               |  |
| Contusion                                      |                |                 |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 32 (0.00%)  |  |
| occurrences (all)                              | 1              | 0               |  |
| Lip injury                                     |                |                 |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 32 (0.00%)  |  |
| occurrences (all)                              | 2              | 0               |  |
| Oral contusion                                 |                |                 |  |
| subjects affected / exposed                    | 1 / 6 (16.67%) | 0 / 32 (0.00%)  |  |
| occurrences (all)                              | 1              | 0               |  |
| Nervous system disorders                       |                |                 |  |
| Somnolence                                     |                |                 |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 6 / 32 (18.75%) |  |
| occurrences (all)                              | 0              | 7               |  |
| Eye disorders                                  |                |                 |  |
| Conjunctivitis allergic                        |                |                 |  |
| subjects affected / exposed                    | 2 / 6 (33.33%) | 3 / 32 (9.38%)  |  |
| occurrences (all)                              | 2              | 4               |  |
| Gastrointestinal disorders                     |                |                 |  |
| Nausea   |                |                 |  |
| subjects affected / exposed                    | 0 / 6 (0.00%)  | 3 / 32 (9.38%)  |  |
| occurrences (all)                              | 0              | 3               |  |
| Constipation                                   |                |                 |  |

|  |                |                 |  |
|--|----------------|-----------------|--|
| subjects affected / exposed            | 1 / 6 (16.67%) | 6 / 32 (18.75%) |  |
| occurrences (all)                      | 1              | 10              |  |
| Diarrhoea                              |                |                 |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 8 / 32 (25.00%) |  |
| occurrences (all)                      | 0              | 10              |  |
| Dental caries                          |                |                 |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 32 (6.25%)  |  |
| occurrences (all)                      | 0              | 2               |  |
| Abdominal pain                         |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 0 / 32 (0.00%)  |  |
| occurrences (all)                      | 1              | 0               |  |
| Vomiting                               |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 4 / 32 (12.50%) |  |
| occurrences (all)                      | 1              | 4               |  |
| Skin and subcutaneous tissue disorders |                |                 |  |
| Rash                                   |                |                 |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 32 (6.25%)  |  |
| occurrences (all)                      | 0              | 2               |  |
| Miliaria                               |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 2 / 32 (6.25%)  |  |
| occurrences (all)                      | 1              | 2               |  |
| Eczema                                 |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 9 / 32 (28.13%) |  |
| occurrences (all)                      | 1              | 16              |  |
| Dermatitis diaper                      |                |                 |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 4 / 32 (12.50%) |  |
| occurrences (all)                      | 0              | 9               |  |
| Dry skin                               |                |                 |  |
| subjects affected / exposed            | 0 / 6 (0.00%)  | 2 / 32 (6.25%)  |  |
| occurrences (all)                      | 0              | 3               |  |
| Dermatitis                             |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 1 / 32 (3.13%)  |  |
| occurrences (all)                      | 1              | 1               |  |
| Dermatitis atopic                      |                |                 |  |
| subjects affected / exposed            | 1 / 6 (16.67%) | 1 / 32 (3.13%)  |  |
| occurrences (all)                      | 1              | 1               |  |

|  |                      |                         |  |
|--|----------------------|-------------------------|--|
| Urticaria thermal<br>subjects affected / exposed<br>occurrences (all)                                    | 1 / 6 (16.67%)<br>1  | 0 / 32 (0.00%)<br>0     |  |
| Renal and urinary disorders<br>Pollakiuria<br>subjects affected / exposed<br>occurrences (all)           | 1 / 6 (16.67%)<br>1  | 0 / 32 (0.00%)<br>0     |  |
| Infections and infestations<br>Molluscum contagiosum<br>subjects affected / exposed<br>occurrences (all) | 1 / 6 (16.67%)<br>1  | 2 / 32 (6.25%)<br>2     |  |
| Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                                      | 5 / 6 (83.33%)<br>21 | 17 / 32 (53.13%)<br>108 |  |
| Gastroenteritis<br>subjects affected / exposed<br>occurrences (all)                                      | 2 / 6 (33.33%)<br>4  | 7 / 32 (21.88%)<br>11   |  |
| Conjunctivitis<br>subjects affected / exposed<br>occurrences (all)                                       | 0 / 6 (0.00%)<br>0   | 6 / 32 (18.75%)<br>16   |  |
| Influenza<br>subjects affected / exposed<br>occurrences (all)  | 1 / 6 (16.67%)<br>1  | 5 / 32 (15.63%)<br>6    |  |
| Exanthema subitum<br>subjects affected / exposed<br>occurrences (all)                                    | 0 / 6 (0.00%)<br>0   | 5 / 32 (15.63%)<br>5    |  |
| Respiratory syncytial virus infection<br>subjects affected / exposed<br>occurrences (all)                | 1 / 6 (16.67%)<br>1  | 4 / 32 (12.50%)<br>5    |  |
| Otitis media<br>subjects affected / exposed<br>occurrences (all)   | 0 / 6 (0.00%)<br>0   | 3 / 32 (9.38%)<br>5     |  |
| COVID-19<br>subjects affected / exposed<br>occurrences (all)   | 1 / 6 (16.67%)<br>1  | 3 / 32 (9.38%)<br>3     |  |
| Hand-foot-and-mouth disease  |                      |                         |  |

|                                   |                |                |
|-----------------------------------|----------------|----------------|
| subjects affected / exposed       | 3 / 6 (50.00%) | 3 / 32 (9.38%) |
| occurrences (all)                 | 3              | 3              |
| Hordeolum                         |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |
| occurrences (all)                 | 0              | 4              |
| Upper respiratory tract infection |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |
| occurrences (all)                 | 0              | 3              |
| Coronavirus infection             |                |                |
| subjects affected / exposed       | 0 / 6 (0.00%)  | 2 / 32 (6.25%) |
| occurrences (all)                 | 0              | 2              |
| Pharyngitis streptococcal         |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 32 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Cystitis                          |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 0 / 32 (0.00%) |
| occurrences (all)                 | 1              | 0              |
| Tonsillitis                       |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 1 / 32 (3.13%) |
| occurrences (all)                 | 1              | 1              |
| Pharyngitis                       |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 1 / 32 (3.13%) |
| occurrences (all)                 | 1              | 1              |
| Impetigo                          |                |                |
| subjects affected / exposed       | 1 / 6 (16.67%) | 1 / 32 (3.13%) |
| occurrences (all)                 | 1              | 1              |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment   |
|------------------|---|
| 28 June 2018     | Protocol Amendment 2, dated 28 Jun 2018, provided the following changes: • The long-term efficacy and safety assessments were updated so that they were more appropriate, taking into account 48h video-electroencephalogram (EEG) failures. – The secondary objectives to be evaluated during the Second Period were changed to be evaluated during the combined First and Second Periods. – Efficacy variables, safety variables, the schedule of assessments for study participants who were 48h video-EEG failures, the study schematic, and the planned analyses and analysis sets were updated. • Minor administrative edits, including typographical changes for formatting, were made.  |
| 29 June 2020     | Protocol Amendment 3, dated 29 Jan 2020, provided the following changes: • The primary efficacy variable was changed from daily partial seizure frequency monitored by 48h video-EEG to partial seizure frequency per week from Baseline to Visit 6 as agreed with Pharmaceuticals and Medical Devices Agency (PMDA). Text was revised throughout to reflect the change from 48h video-EEG to patient diary (ie, Daily Record Card [DRC]). • Study participants who were directly enrolled in the Second Period based on the protocol prior to Amendment 3 were to be included in the efficacy and safety analyses, with remapping of visit numbers to correspond to those for study participants who enrolled in the First Period. • Minor administrative edits were made.   |
| 22 February 2023 | Protocol Amendment 4, dated 22 Feb 2023, provided the following changes: • The summary was updated to comply with regulations in Japan for the conduct of postmarketing clinical studies: – EP0100 was to be conducted as a clinical study (Phase 3) until approval was obtained for the indication of levetiracetam (LEV) as monotherapy or adjunctive treatment in study participants aged 1 month to <4 years with partial seizures, and continued as a postmarketing clinical study (Phase 4) after the date of approval until the study participant was switched to commercial LEV as soon as possible, or until LEV was discontinued after a period of dose reduction. In Japan, the meaning and expressions related to "clinical study" shall automatically be read as "postmarketing clinical study" after the date of approval in Japan. • Minor administrative edits were made. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported