



Clinical trial results:

An Open-Label, Multicenter Study With an Extension Phase to Evaluate the Safety, Tolerability, and Exposure-Efficacy Relationship of Perampanel Oral Suspension When Administered as an Adjunctive Therapy in Pediatric Subjects (Age 4 to Less Than 12 Years) With Inadequately Controlled Partial-Onset Seizures or Primary Generalized Tonic-Clonic Seizures

Summary

| | |
|--------------------------|----------------------------------|
| EudraCT number | 2014-002167-16 |
| Trial protocol | HU LV ES PL BE IT Outside EU/EEA |
| Global end of trial date | 06 December 2021 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 17 June 2022 |
| First version publication date | 17 June 2022 |

Trial information

Trial identification

| | |
|-----------------------|----------------|
| Sponsor protocol code | E2007-G000-311 |
|-----------------------|----------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02849626 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Eisai Ltd |
| Sponsor organisation address | European Knowledge Centre Mosquito Way, Hatfield Hertfordshire, United Kingdom, AL10 9SN |
| Public contact | EMA Medical Information, Eisai Europe Ltd., +44 (0)208 600 1400, EUMedInfo@eisai.net |
| Scientific contact | EMA Medical Information, Eisai Europe Ltd., +44 (0)208 600 1400, EUMedInfo@eisai.net |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000467-PIP01-08 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 06 December 2021 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 06 December 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This is an open-label, multicenter study with an Extension Phase to evaluate the safety and tolerability of perampanel oral suspension when administered as an adjunctive therapy in children (ages 4 to less than [$<$] 12 years) with inadequately controlled partial onset seizures (POS) or primary generalized tonic clonic (PGTC) seizures.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008) - International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use - Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. - Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan's GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 November 2016 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 1 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Belgium: 5 |
| Country: Number of subjects enrolled | France: 10 |
| Country: Number of subjects enrolled | Hungary: 26 |
| Country: Number of subjects enrolled | Japan: 65 |
| Country: Number of subjects enrolled | Latvia: 6 |
| Country: Number of subjects enrolled | Poland: 16 |

| | |
|--------------------------------------|-----------------------|
| Country: Number of subjects enrolled | Korea, Republic of: 1 |
| Country: Number of subjects enrolled | Spain: 14 |
| Country: Number of subjects enrolled | United States: 37 |
| Worldwide total number of subjects | 180 |
| EEA total number of subjects | 77 |

Notes:

| Subjects enrolled per age group | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 180 |
| 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:

Subjects took part at 58 sites in the United States, European Union, Asia Pacific. 208 subjects were screened/enrolled. Of which 28 screen failures and 180 received treatment in Core Phase. Of 146 who completed Core Phase, 136 entered Extension Phase A. Of 122 who completed Extension Phase A, 42 entered Extension Phase B and 41 received treatment.

Pre-assignment

Screening details:

This study included a Core Phase and two Extension Phases (Extension Phase A and Extension Phase B).

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Core Phase (up to 23 weeks) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Perampanel 0.5 mg/mL: POS |

Arm description:

Core Phase: Subjects with partial onset-seizures (POS) received perampanel 0.5 milligrams per milliliter (mg/mL) oral suspension titrated beyond 8 milligram per day (mg/day) up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any enzyme-inducing antiepileptic drug [EIAED]), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Perampanel 0.5 mg/mL oral suspension

| | |
|------------------|-------------------------------------|
| Arm title | Perampanel 0.5 mg/mL: PGTC Seizures |
|------------------|-------------------------------------|

Arm description:

Core Phase: Subjects with primary generalized tonic clonic (PGTC) seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

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

| | |
|--|------------------------|
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Perampanel 0.5 mg/mL oral suspension

| Number of subjects in period 1 | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures |
|--------------------------------|---------------------------|-------------------------------------|
| | | |
| Started | 149 | 31 |
| Completed | 122 | 24 |
| Not completed | 27 | 7 |
| Inadequate Therapeutic Effect | 6 | 2 |
| Consent withdrawn by subject | 7 | 2 |
| Non-specified | 3 | - |
| Adverse event, non-fatal | 11 | 3 |

Period 2

| | |
|------------------------------|------------------------------------|
| Period 2 title | Extension Phase A (up to 29 weeks) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|---------------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Perampanel 0.5 mg/mL: POS |

Arm description:

Core Phase: Subjects with POS received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any [EIAED]), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Perampanel 0.5 mg/mL oral suspension

| | |
|---|-------------------------------------|
| Arm title | Perampanel 0.5 mg/mL: PGTC Seizures |
| Arm description: | |
| Core Phase: Subjects with PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks. | |
| Arm type | Experimental |
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Perampanel 0.5 mg/mL oral suspension | |

| Number of subjects in period 2^[1] | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures |
|---|---------------------------|-------------------------------------|
| Started | 116 | 20 |
| Completed | 105 | 17 |
| Not completed | 11 | 3 |
| Inadequate Therapeutic Effect | 3 | 1 |
| Consent withdrawn by subject | 4 | - |
| Non-specified | 1 | - |
| Adverse event, non-fatal | 3 | 2 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only eligible participants who completed Core Phase entered into Extension Phase A.

Period 3

| | |
|------------------------------|------------------------------------|
| Period 3 title | Extension Phase B (up to 89 weeks) |
| Is this the baseline period? | No |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--|
| Are arms mutually exclusive? | Yes |
| Arm title | Extension B: Perampanel 0.5 mg/mL: POS |

Arm description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

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

| | |
|--|--|
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |
| Dosage and administration details: Perampanel 0.5 mg/mL oral suspension | |
| Arm title | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures |

Arm description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

| | |
|--|------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Perampanel |
| Investigational medicinal product code | |
| Other name | E2007 |
| Pharmaceutical forms | Oral drops, suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Perampanel 0.5 mg/mL oral suspension

| Number of subjects in period 3 ^[2] | Extension B: Perampanel 0.5 mg/mL: POS | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures |
|--|--|---|
| | | |
| Started | 41 | 1 |
| Completed | 36 | 1 |
| Not completed | 5 | 0 |
| Inadequate Therapeutic Effect | 3 | - |
| Unspecified | 1 | - |
| Subject choice | 1 | - |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only eligible participants who completed Core Phase and Extension A entered into Extension Phase B.

Baseline characteristics

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: POS |
|-----------------------|---------------------------|

Reporting group description:

Core Phase: Subjects with partial onset-seizures (POS) received perampanel 0.5 milligrams per milliliter (mg/mL) oral suspension titrated beyond 8 milligram per day (mg/day) up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any enzyme-inducing antiepileptic drug [EIAED]), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|-------------------------------------|

Reporting group description:

Core Phase: Subjects with primary generalized tonic clonic (PGTC) seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| Reporting group values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | Total |
|--|---------------------------|-------------------------------------|-------|
| Number of subjects | 149 | 31 | 180 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 149 | 31 | 180 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 8.1 | 8.5 | - |
| standard deviation | ± 2.10 | ± 2.03 | - |
| Sex: Female, Male | | | |
| Units: subjects | | | |
| Female | 77 | 11 | 88 |
| Male | 72 | 20 | 92 |

| | | | |
|----------------------------------|-----|----|-----|
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 3 | 7 | 10 |
| Not Hispanic or Latino | 141 | 19 | 160 |
| Unknown or Not Reported | 5 | 5 | 10 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White | 70 | 23 | 93 |
| Black or African American | 2 | 1 | 3 |
| Japanese | 65 | 0 | 65 |
| Other Asian | 5 | 1 | 6 |
| American Indian or Alaska Native | 1 | 0 | 1 |
| Other | 2 | 1 | 3 |
| Missing | 4 | 5 | 9 |

End points

End points reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: POS |
|-----------------------|---------------------------|

Reporting group description:

Core Phase: Subjects with partial onset-seizures (POS) received perampanel 0.5 milligrams per milliliter (mg/mL) oral suspension titrated beyond 8 milligram per day (mg/day) up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any enzyme-inducing antiepileptic drug [EIAED]), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|-------------------------------------|

Reporting group description:

Core Phase: Subjects with primary generalized tonic clonic (PGTC) seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|---------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: POS |
|-----------------------|---------------------------|

Reporting group description:

Core Phase: Subjects with POS received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any [EIAED]), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|-------------------------------------|

Reporting group description:

Core Phase: Subjects with PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|--|
| Reporting group title | Extension B: Perampanel 0.5 mg/mL: POS |
|-----------------------|--|

Reporting group description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

| | |
|-----------------------|--|
| Reporting group title | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|--|

Reporting group description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|-----------------|
| Subject analysis set title | Perampanel: POS |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects with POS who received perampanel 0.5 mg/mL oral suspension (for subjects with age less than [$<$] 12 years) or tablets (for subjects with age \geq 12 years) titrated to a dose of up to 8 mg/day for up to 23 weeks in studies E2007-G000-304 (NCT00699972), E2007-G000-305 (NCT00699582), E2007-G000-306 (NCT00700310), E2007-J000-335 (NCT01618695) and this current study (E2007-G000-311).

| | |
|----------------------------|---------------------------|
| Subject analysis set title | Perampanel: PGTC Seizures |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects with PGTC seizures who received perampanel 0.5 mg/mL oral suspension (for subjects with age $<$ 12 years) or tablets (for subjects with age \geq 12 years) titrated to a dose of up to 8 mg/day for up to 23 weeks in studies E2007-G000-232 (NCT01527006) and E2007-G000-332 (NCT01393743) and this current study (E2007-G000-311).

| | |
|----------------------------|---|
| Subject analysis set title | Perampanel: Subjects aged ($<$ 12 years) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All non-Asian subjects with POS, received perampanel oral suspension (subjects with age $<$ 12 years) titrated to a dose of up to 8 mg/day or up to 12 mg/day for up to 23 weeks in this current study E2007-G000-311.

| | |
|----------------------------|--|
| Subject analysis set title | Perampanel: Subjects aged (\geq 12 years) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All non-Asian subjects with POS, received perampanel tablets (subjects with age \geq 12 years) titrated to

a dose of up to 8 mg/day or up to 12 mg/day for up to 23 weeks in studies E2007-G000-304 (NCT00699972), E2007-G000-305 (NCT00699582), E2007-G000-306 (NCT00700310), E2007-J000-335 (NCT01618695).

| | |
|--|------------------------------------|
| Subject analysis set title | Perampanel: Without Topiramate |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects with PGTC seizures received perampanel as oral suspension (aged <12 years) or as oral tablets (aged ≥12 years) titrated to a dose of up to 8 mg/day or up to 12 mg/day without topiramate for up to 23 weeks in studies E2007-G000-232 (NCT01527006) and E2007-G000-332 (NCT01393743) and this current study (E2007-G000-311). | |
| Subject analysis set title | Perampanel: With Topiramate |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects with PGTC seizures received perampanel as oral suspension (aged <12 years) or as oral tablets (aged ≥12 years) titrated to a dose of up to 8 mg/day or up to 12 mg/day along with topiramate for up to 23 weeks in studies E2007-G000-232 (NCT01527006) and E2007-G000-332 (NCT01393743) and this current study (E2007-G000-311). | |
| Subject analysis set title | Perampanel: POS |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All subjects with POS who received perampanel 0.5 mg/mL oral suspension (for subjects with age <12 years) or tablets (for subjects with age ≥12 years) titrated to a dose of up to 8 mg/day for up to 23 weeks in studies E2007-G000-304 (NCT00699972), E2007-G000-305 (NCT00699582), E2007-G000-306 (NCT00700310), E2007-J000-335 (NCT01618695) and this current study (E2007-G000-311). | |
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks. | |
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks. | |
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks. | |
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: All Subjects |
|----------------------------|------------------------------------|

| | |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Core Phase: Subjects with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|-------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: 4 to <7 Years |
|----------------------------|-------------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Core Phase: Subjects of age 4 to <7 years with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|----------------------------|--------------------------------------|
| Subject analysis set title | Perampanel 0.5 mg/mL: 7 to <12 Years |
|----------------------------|--------------------------------------|

| | |
|---------------------------|---------------|
| Subject analysis set type | Full analysis |
|---------------------------|---------------|

Subject analysis set description:

Core Phase: Subjects of age 7 to <12 years with POS or PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

Primary: Percentage of Subjects With Treatment Emergent Adverse Events (AEs) and Treatment Emergent Serious Adverse Events (SAEs) for Total Group of Subjects - Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Treatment Emergent Adverse Events (AEs) and Treatment Emergent Serious Adverse Events (SAEs) for Total Group of Subjects - Core Phase and Extension Phase A of This Study ^[1] |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline up to 4 weeks (follow up in Extension Phase A) after last dose of study drug in Extension Phase

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: Only descriptive data was planned to be analyzed for this endpoint.

| | | | | |
|-------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 180 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Treatment Emergent AEs | 90.0 | | | |
| Treatment Emergent SAEs | 20.0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Treatment Emergent Markedly Abnormal Laboratory Values for Total Group of Subjects - Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Treatment Emergent Markedly Abnormal Laboratory Values for Total Group of Subjects - Core Phase and Extension Phase A of This Study ^[2] |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline up to 52 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

| | | | | |
|---|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 180 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Potassium: Markedly Abnormal High (n=177) | 0.6 | | | |
| Sodium: Markedly Abnormal Low (n=177) | 1.1 | | | |
| Alanine Aminotransferase: Abnormal High (n=177) | 1.1 | | | |
| Calcium: Abnormal Low (n=177) | 0.6 | | | |
| Gamma Glutamyl Transferase: Abnormal High (n=177) | 2.8 | | | |
| Neutrophils: Abnormal Low (n=176) | 9.1 | | | |

| | | | | |
|----------------------------------|-----|--|--|--|
| Hemoglobin: Abnormal Low (n=176) | 1.7 | | | |
| Leukocytes: Abnormal Low (n=176) | 0.6 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Abnormal Vital Sign Values for Total Group of Subjects- Core Phase and Extension Phase A of This Study

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Abnormal Vital Sign Values for Total Group of Subjects- Core Phase and Extension Phase A of This Study ^[3] |
|-----------------|---|

End point description:

Pre-defined criteria of vital signs abnormalities: maximum (max.) increase or decrease from baseline in sitting/supine systolic blood pressure (SBP) of greater than or equal to (\geq) 20 or 40 millimeter of mercury (mmHg); maximum increase or decrease from baseline in sitting/supine diastolic blood pressure (DBP) \geq 10 or 20 mmHg; increase or decrease from baseline in pulse rate (number of heart beats per minute [bpm]) of \geq 15 or 30 bpm. Data for this outcome measure has been assessed and reported till Week 52. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subjects analyzed" signifies subjects who were evaluable for this outcome measure.

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

End point timeframe:

Baseline up to 52 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
|--|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 179 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Systolic Blood Pressure: Increment \geq 20 mmHg | 24.6 | | | |
| Systolic Blood Pressure: Increment \geq 40 mmHg | 2.2 | | | |
| Systolic Blood Pressure: Decrement \geq 20 mmHg | 20.1 | | | |
| Systolic Blood Pressure: Decrement \geq 40 mmHg | 0.6 | | | |
| Diastolic Blood Pressure: Increment \geq 10 mmHg | 48.0 | | | |
| Diastolic Blood Pressure: Increment \geq 20 mmHg | 26.8 | | | |
| Diastolic Blood Pressure: Decrement \geq 10 mmHg | 38.0 | | | |
| Diastolic Blood Pressure: Decrement \geq 20 mmHg | 16.8 | | | |
| Pulse: Increment \geq 15 bpm | 35.8 | | | |
| Pulse: Increment \geq 30 bpm | 11.7 | | | |

| | | | | |
|--------------------------------|------|--|--|--|
| Pulse: Decrement ≥ 15 bpm | 39.7 | | | |
| Pulse: Decrement ≥ 30 bpm | 13.4 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With Markedly Abnormal Electrocardiogram (ECG) Parameters for Total Group of Subjects - Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Markedly Abnormal Electrocardiogram (ECG) Parameters for Total Group of Subjects - Core Phase and Extension Phase A of This Study ^[4] |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subjects analyzed" signifies subjects who were evaluable for this outcome measure.

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

End point timeframe:

Baseline up to 52 weeks

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive data was planned to be analyzed for this endpoint.

| | | | | |
|--|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 174 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| QTc Bazett: Increase of >30 millisecond (msec) | 8.0 | | | |
| QTc Bazett: Increase of >60 msec | 0 | | | |
| QTc Bazett: >450 msec | 4.0 | | | |
| QTc Bazett: >480 msec | 0 | | | |
| QTc Bazett: >500 msec | 0 | | | |
| QTc Fridericia: Increase of >30 msec | 5.2 | | | |
| QTc Fridericia: Increase of >60 msec | 0 | | | |
| QTc Fridericia: >450 msec | 0 | | | |
| QTc Fridericia: >480 msec | 0 | | | |
| QTc Fridericia: >500 msec | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Percent Change in Average Seizure Frequency Over 28 Days During Maintenance Period in Core Phase of This Study From Baseline- Assessed as Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel (518 ng/mL)

| | |
|-----------------|---|
| End point title | Model Predicted Percent Change in Average Seizure Frequency Over 28 Days During Maintenance Period in Core Phase of This Study From Baseline- Assessed as Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel (518 ng/mL) |
|-----------------|---|

End point description:

Seizure frequency was derived from information recorded in subject diary. Seizure frequency per 28 days calculated as number of seizures divided by number of days in the interval and multiplied by 28. Due to sparse pharmacokinetic (PK) sampling, data of OM was analyzed by pooling data from other Phase II/III studies of perampanel along with data of current study, subjects with POS or PGTC. Only data for subjects taking perampanel 8 mg/day (Cav, ss of 518 ng/mL) were reported. Subjects taking perampanel 12 mg/day in the studies from which data were pooled, were not included in analysis. ng/mL refers to nanogram per milliliter. Data for this OM was calculated through model prediction. All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Population for this OM included subjects from other studies as well subjects from current study. Here "number of subject analyzed" signifies subjects evaluable for this measure.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 23 | |

| End point values | Perampanel: POS | Perampanel: PGTC Seizures | | |
|-----------------------------|----------------------|---------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1371 | 92 | | |
| Units: percent change | | | | |
| number (not applicable) | -43.1 | -63.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Responder Probability For Non-Asian Subjects With POS During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel

| | |
|-----------------|--|
| End point title | Overall Responder Probability For Non-Asian Subjects With POS During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel |
|-----------------|--|

End point description:

For this OM, responders were those who experienced a 50 percent (%) or greater reduction in seizure frequency per 28 days from baseline. Due to the sparse PK sampling in this study, the data of this OM were pooled with data from other Phase III studies of perampanel conducted in subjects with POS. "AEDs not affecting PK" refers to AEDs not affecting PK of perampanel. Data for this OM has been reported for only non-Asian subjects with POS per age groups. Responder probability has been reported for Cav,ss of perampanel when given along with different antiepileptic drugs (AEDs). All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Population for this OM included subjects from other studies as well subjects from this current study. Here "number of subjects analyzed" signifies subjects who were evaluable for this measure.

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

End point timeframe:
Baseline up to 23 weeks

| End point values | Perampanel: Subjects aged (<12 years) | Perampanel: Subjects aged (≥12 years) | | |
|---|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 123 | 1420 | | |
| Units: Responder probability | | | | |
| number (not applicable) | | | | |
| 8 mg/day+ AEDs not affecting PK:Cav ss 518 ng/mL | 0.605 | 0.466 | | |
| 12 mg/day+ AEDs not affecting PK:Cav ss 778 ng/mL | 0.669 | 0.535 | | |
| 8 mg/day+ Oxcarbazepine/Phenytoin:Cav ss 258 | 0.520 | 0.382 | | |
| 12 mg/day+ Oxcarbazepine/Phenytoin:Cav ss 263 | 0.565 | 0.426 | | |
| 8 mg/day+ Carbamazepine:Cav ss 175 ng/mL | 0.485 | 0.350 | | |
| 12 mg/day+ Carbamazepine:Cav ss 263 ng/mL | 0.522 | 0.384 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Responder Probability For Subjects With PGTC Seizures During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel

| | |
|-----------------|--|
| End point title | Overall Responder Probability For Subjects With PGTC Seizures During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel |
|-----------------|--|

End point description:

For this OM, responders were those who experienced a 50% or greater reduction in seizure frequency per 28 days from baseline. Due to the sparse PK sampling in this study, the data of this OM were analyzed by pooling the data from other Phase II and III studies of perampanel along with data of this current study, including subjects with PGTC seizures. In this outcome measure, responder probability at different concentration values of perampanel when given with or without topiramate (an antiepileptic) has been reported to compare the effect of topiramate on responder probability. All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Population for this measure included subjects from other studies as well subjects from this current study. Here "number of subjects analyzed" signifies subjects who were evaluable for this measure.

| | |
|-------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to 23 weeks | |

| End point values | Perampanel: Without Topiramate | Perampanel: With Topiramate | | |
|------------------------------|--------------------------------------|-----------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 138 | 31 | | |
| Units: Responder probability | | | | |
| number (not applicable) | | | | |
| 0 ng/mL | 0.46 | 0.26 | | |
| 100 ng/mL | 0.71 | 0.50 | | |
| 200 ng/mL | 0.74 | 0.54 | | |
| 300 ng/mL | 0.76 | 0.57 | | |
| 400 ng/mL | 0.77 | 0.58 | | |
| 500 ng/mL | 0.78 | 0.59 | | |
| 600 ng/mL | 0.79 | 0.60 | | |
| 700 ng/mL | 0.80 | 0.61 | | |
| 800 ng/mL | 0.80 | 0.62 | | |
| 900 ng/mL | 0.80 | 0.63 | | |
| 1000 ng/mL | 0.81 | 0.63 | | |
| 1200 ng/mL | 0.82 | 0.64 | | |
| 1400 ng/mL | 0.82 | 0.65 | | |
| 1600 ng/mL | 0.82 | 0.66 | | |
| 1800 ng/mL | 0.83 | 0.66 | | |
| 2000 ng/mL | 0.83 | 0.67 | | |
| 2200 ng/mL | 0.84 | 0.67 | | |
| 2400 ng/mL | 0.84 | 0.68 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Seizure Free Observations During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel

| | |
|-----------------|--|
| End point title | Number of Seizure Free Observations During Core Phase of This Study: Assessment Based on Relationship With Average Steady State Plasma Concentration (Cav, ss) of Perampanel |
|-----------------|--|

End point description:

Due to the sparse PK sampling in this study, the data of this OM were analyzed by pooling data from other Phase II and III studies of perampanel along with this current study, including subjects with POS or PGTC. Data for this OM have been reported in relationship with different ranges of Cav, ss of Perampanel as "number of observations" those were seizure free for up to 3 visits. The reason for using number of observations for analysis of this OM was because data were available as up to 3 visits per subjects and not necessarily that the subject was seizure-free on all three visits. All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Population for this measure included subjects from other studies as well subjects from this current study. Here "number of subjects analyzed" signifies subjects who were evaluable for this measure and SFO denotes Seizure free observations.

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

End point timeframe:

Baseline up to Week 23

| End point values | Perampanel: POS | Perampanel: PGTC Seizures | | |
|---|----------------------|------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1371 | 92 | | |
| Units: Seizure free observations | | | | |
| >0 - <500 ng/mL(3189,127:POS/PGTC SFO) | 275 | 57 | | |
| 500 - <1000 ng/mL(583,104:POS/PGTC SFO) | 103 | 67 | | |
| 1000 - <1500 ng/mL(159,15:POS/PGTC SFO) | 33 | 11 | | |
| 1500 - 2000 ng/mL(33,6:POS/PGTC SFO) | 7 | 4 | | |
| >2000 ng/mL(10,3:POS/PGTC SFO) | 0 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Change From Baseline in Total Aldenkamp-Baker Neuropsychological Assessment Schedule (ABNAS) Score During Core Phase of this Study: Assessment Based on Relationship With Plasma Levels of Perampanel

| | |
|-----------------|---|
| End point title | Model Predicted Change From Baseline in Total Aldenkamp-Baker Neuropsychological Assessment Schedule (ABNAS) Score During Core Phase of this Study: Assessment Based on Relationship With Plasma Levels of Perampanel |
|-----------------|---|

End point description:

The ABNAS assessment measured 5 aspects of cognitive function such as fatigue, memory, concentration, motor speed, and reading. The assessment was a measure of subject-perceived cognitive effects of AEDs. This instrument was aimed at assessing subject perceived drug-related cognitive impairment. Total score ranged from 0-72. Higher scores indicate a worsening of these cognitive functions. Analysis for this OM was planned to be performed via Pharmacokinetic/Pharmacodynamic (PK/PD) modelling only if a graphical relationship between perampanel exposure and change from baseline in ABNAS could be discerned. All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Here "number of subjects analyzed" signifies subjects who were evaluable for this outcome measure and 99999 signifies no discernible graphical relationship between plasma level of perampanel and change from baseline.

| | |
|------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline up to Week 23 | |

| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
|--------------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 148 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Change From Baseline in Total Child Behavior Check List (CBCL) Score (Subjects Aged 4 to 5 Years) During Core Phase of This Study: Assessment Based on Relationship With Plasma Levels of Perampanel

| | |
|-----------------|--|
| End point title | Model Predicted Change From Baseline in Total Child Behavior Check List (CBCL) Score (Subjects Aged 4 to 5 Years) During Core Phase of This Study: Assessment Based on Relationship With Plasma Levels of Perampanel |
|-----------------|--|

End point description:

CBCL for subjects with age 4-5 years is questionnaire to assess behavioral;emotional problems in children as reported by primary caregiver for following domains activities: emotionally reactive, anxious/depressed, withdrawn, somatic complaints, internalizing, attention problems, aggressive behavior, externalizing, sleep problems. CBCL total score ranged from 0 to 200,calculated by adding individual score of each domain. Higher scores greater problems in child behavior. Analysis for this OM was planned to be performed via PK/PD modelling only if graphical relationship between perampanel exposure; change from baseline in CBCL score (subjects aged 4 to 5 years) could be discerned. All subjects who received perampanel who have seizure frequency, cognition, or AE data with documented dosing history. Here "number of subjects analyzed": subjects who were evaluable for this OM and 99999 signifies no discernible graphical relationship between plasma level of perampanel; change from baseline.

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

End point timeframe:

Baseline up to Week 23

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 19 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Change From Baseline in Total Child Behavior Check List (CBCL) Score (Subjects Aged Greater Than [>] 5 to <12 Years) During Core Phase of This Study: Assessment Based on Relationship With Plasma Levels of Perampanel

| | |
|-----------------|--|
| End point title | Model Predicted Change From Baseline in Total Child Behavior Check List (CBCL) Score (Subjects Aged Greater Than [>] 5 to <12 Years) During Core Phase of This Study: Assessment |
|-----------------|--|

End point description:

CBCL for subjects >5 -<12 years questionnaire to assess behavioral;emotional problems in children reported by primary caregiver for following domain activities: activity, social, school, total competence, anxious/depressed, withdrawn/depressed, somatic complaints, internalizing, rule-breaking behavior, aggressive behavior, externalizing, social problems, thought problems, attention problems.Total score for subjects:>5 -<12 years ranged: 0-240, calculated by adding individual score of each domain.Higher scores greater problems in behavior.Analysis performed via PK/PD modelling only if graphical relationship between perampanel exposure;change from baseline in CBCL score(aged >5 -<12 years) could discerned.All subjects received perampanel with seizure frequency,cognition,or AE data with documented dosing history. "number of subjects analyzed": subjects evaluable for this OM; 99999 signifies no discernible graphical relationship between plasma level of perampanel; change from baseline.

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

End point timeframe:

Baseline up to Week 23

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 115 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Change From Baseline in Total Time to Complete LGPT Score for Dominant Hand in Core Phase of This Study for All Subjects Aged 4 to <12 Years: Assessment Based on Relationship With Plasma Levels of Perampanel

| | |
|-----------------|---|
| End point title | Model Predicted Change From Baseline in Total Time to Complete LGPT Score for Dominant Hand in Core Phase of This Study for All Subjects Aged 4 to <12 Years: Assessment Based on Relationship With Plasma Levels of Perampanel |
|-----------------|---|

End point description:

Lafayette Grooved Pegboard Test (LGPT) measures visuomotor skills. It is manipulative dexterity test consist of metal matrix of 25 holes; randomly positioned slots.Subjects require to insert 10 grooved pegs into holes.Task needs to complete once for each hand; firstly, dominant hand and by non-dominant hand.Task is timed; scores are time taken for subject to complete all 10 pegs for each hand. If cannot be completed within 300 secs, 300 secs recorded for time.Longer time worsening of visuomotor skills.Analysis was planned to be performed via PK/PD modelling only if graphical relationship between perampanel exposure;change from baseline in Total Time to Complete LGPT Score for Non-dominant Hand could be discerned.All subjects who received perampanel who have seizure frequency,cognition,or AE data documented dosing history."number of subjects analyzed": subjects evaluable for this OM; 99999: no discernible graphical relationship between plasma level of perampanel; change from baseline.

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

End point timeframe:

Baseline up to Week 23

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 117 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Model Predicted Change From Baseline in Total Time to Complete LGPT Score for Non-dominant Hand in Core Phase of This Study for All Subjects Aged 4 to <12 Years: Assessment Based on Relationship With Plasma Levels of Perampanel

| | |
|-----------------|---|
| End point title | Model Predicted Change From Baseline in Total Time to Complete LGPT Score for Non-dominant Hand in Core Phase of This Study for All Subjects Aged 4 to <12 Years: Assessment Based on Relationship With Plasma Levels of Perampanel |
|-----------------|---|

End point description:

Lafayette Grooved Pegboard Test (LGPT) measures visuomotor skills. It is manipulative dexterity test consist of metal matrix of 25 holes; randomly positioned slots. Subjects require to insert 10 grooved pegs into holes. Task needs to complete once for each hand; firstly, dominant hand and by non-dominant hand. Task is timed; scores are time taken for subject to complete all 10 pegs for each hand. If cannot be completed within 300 secs, 300 secs recorded for time. Longer time worsening of visuomotor skills. Analysis was planned to be performed via PK/PD modelling only if graphical relationship between perampanel exposure; change from baseline in Total Time to Complete LGPT Score for Non-dominant Hand could be discerned. All subjects who received perampanel who have seizure frequency, cognition, or AE data documented dosing history. "number of subjects analyzed": subjects evaluable for this OM; 99999: no discernible graphical relationship between plasma level of perampanel; change from baseline.

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

End point timeframe:

Baseline up to Week 23

| | | | | |
|--------------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 113 | | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | 99999 (± 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Most Frequent Treatment Emergent Adverse Events (AEs) for Total Group of Subjects That Were Considered Related to Perampanel- Core Phase of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Most Frequent Treatment Emergent Adverse Events (AEs) for Total Group of Subjects That Were Considered Related to Perampanel- Core Phase of This Study |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline up to 23 weeks

| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 180 | | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Irritability | 12.8 | | | |
| Nasopharyngitis | 14.7 | | | |
| Influenza | 6.4 | | | |
| Pyrexia | 9.0 | | | |
| Somnolence | 13.5 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Aldenkamp-Baker Neuropsychological Assessment Schedule (ABNAS) Score at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|---|
| End point title | Change From Baseline in Aldenkamp-Baker Neuropsychological Assessment Schedule (ABNAS) Score at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|---|

End point description:

The ABNAS assessment measured 5 aspects of cognitive function such as fatigue, memory, concentration, motor speed, and reading. The assessment was a measure of subject-perceived cognitive effects of AEDs. This instrument was aimed at assessing subject perceived drug-related cognitive impairment. Total score ranged from 0-72. Higher scores indicate a worsening of these cognitive functions. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline, Week 23, Week 52

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|---|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n =140,30) | 17.7 (± 18.96) | 28.6 (± 21.01) | | |
| Change from Baseline at Week 23 (n=107,19) | -1.2 (± 12.77) | 3.3 (± 12.42) | | |
| Change from Baseline at Week 52 (n=95,17) | -3.9 (± 16.91) | -0.2 (± 14.67) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Child Behavior Check List (CBCL) Score (Age Group 1.5 to 5 Years) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|--|
| End point title | Change From Baseline in Total Child Behavior Check List (CBCL) Score (Age Group 1.5 to 5 Years) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|--|

End point description:

The CBCL for subjects (age group 1.5 to 5 years) is a questionnaire to assess behavioral and emotional problems in children as reported by the primary caregiver for the following domains activities: emotionally reactive, anxious/depressed, withdrawn, somatic complaints, internalizing, attention problems, aggressive behavior, externalizing, sleep problems. CBCL total score for subjects (age group 1.5 to 5 years) ranged from 0 to 200, was calculated by adding individual score of each domain. Higher scores indicate greater problems in child behavior. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subjects analyzed" signifies subjects who were evaluable for this OM and '99999' indicates that standard deviation could not be estimated for single subject for the specified arm.

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

End point timeframe:

Baseline, Week 23, Week 52

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|---|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 24 | 2 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=24,2) | 35.0 (± 28.30) | 54.0 (± 21.21) | | |
| Change from Baseline at Week 23 (n=15,1) | -0.3 (± 14.71) | -13.0 (± 99999) | | |

| | | | | |
|---|---------------------|----------------------|--|--|
| Change from Baseline at Week 52 (n=16,1) | -5.7 (\pm 14.36) | -11.0 (\pm 99999) | | |
|---|---------------------|----------------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Total Child Behavior Check List (CBCL) Score (Age Group 6 to 18 Years) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|---|
| End point title | Change From Baseline in Total Child Behavior Check List (CBCL) Score (Age Group 6 to 18 Years) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|---|

End point description:

CBCL for subjects (age 6 to 18 years) questionnaire to assess behavioral and emotional problems in children as reported by primary caregiver for the following domains activities: activity, social, school, total competence, anxious/depressed, withdrawn/depressed, somatic complaints, internalizing, rule-breaking behavior, aggressive behavior, externalizing, social problems, thought problems, attention problems. Total score for subjects (age group 6 to 18 years) ranged from 0 to 240, calculated by adding individual score of each domain. Higher scores indicate greater problems in child behavior. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subjects analyzed" signifies subjects who were evaluable for this OM.

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

End point timeframe:

Baseline, Week 23, Week 52

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 123 | 28 | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=123,28) | 33.3 (\pm 22.66) | 44.6 (\pm 26.16) | | |
| Change from Baseline at Week 23 (n=96,18) | -0.6 (\pm 12.26) | -2.2 (\pm 22.84) | | |
| Change from Baseline at Week 52 (n=86,16) | -1.7 (\pm 14.51) | -0.7 (\pm 16.36) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Complete Lafayette Grooved Pegboard Test (LGPT) Scores for 8 Years and Under at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|---|
| End point title | Change From Baseline in Time to Complete Lafayette Grooved Pegboard Test (LGPT) Scores for 8 Years and Under at Week 23 |
|-----------------|---|

End point description:

LGPT test measured visuomotor skills. This test was a manipulative dexterity test that consisted of a metal matrix of 25 holes with randomly positioned slots. The subject was required to insert 10 grooved pegs into the holes. The task was completed once for each hand; firstly, using the dominant hand followed by the non-dominant hand. The task was timed and the scores were the time taken for the subject to complete all 10 pegs for each hand. If the test cannot be completed within 300 seconds, 300 seconds were recorded for the time. An increase in score (longer time) indicated worsening of visuomotor skills. The time to complete test is presented as mean seconds plus/minus (+/-) SD. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subject analyzed" signifies subject who were evaluable for this OM and CFB indicates change from baseline.

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

End point timeframe:

| |
|----------------------------|
| Baseline, Week 23, Week 52 |
|----------------------------|

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|---|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 51 | 10 | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dominant Hand: Baseline (n=51,10) | 196.4 (± 113.12) | 155.0 (± 108.10) | | |
| Dominant Hand: CFB :Week 23 (n=36,3) | 12.8 (± 49.37) | -4.3 (± 3.79) | | |
| Dominant Hand: CFB: Week 52 (n=28,5) | 3.9 (± 50.50) | 13.4 (± 33.72) | | |
| Non Dominant Hand: Baseline (n=50,9) | 224.3 (± 108.19) | 169.6 (± 106.49) | | |
| Non Dominant Hand: CFB Week 23 (n=36,3) | 3.3 (± 39.59) | -4.3 (± 14.98) | | |
| Non Dominant Hand: CFB Week 52 (n=29,5) | 2.6 (± 46.88) | 3.4 (± 29.35) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Time to Complete Lafayette Grooved Pegboard Test (LGPT) Scores Over 8 Years at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|--|
| End point title | Change From Baseline in Time to Complete Lafayette Grooved Pegboard Test (LGPT) Scores Over 8 Years at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|--|

End point description:

The LGPT test measured visuomotor skills. This test was a manipulative dexterity test that consisted of a metal matrix of 25 holes with randomly positioned slots. The subject was required to insert 25 grooved pegs into the holes. The task was completed once for each hand; firstly, using the dominant hand followed by the non-dominant hand. The task was timed and the scores were the time taken for the subject to complete all 25 pegs for each hand. If the test cannot be completed within 300 seconds, 300 seconds were recorded for the time. An increase in score (longer time) indicated worsening of

visuomotor skills. The time to complete test is presented as mean seconds +/- SD. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subjects analyzed" signifies subjects who were evaluable for this OM and CFB indicates change from baseline.

| | |
|----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 23, Week 52 | |

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 63 | 11 | | |
| Units: seconds | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dominant Hand: Baseline (n=63,11) | 189.8 (± 103.58) | 150.7 (± 99.68) | | |
| Dominant Hand: CFB at Week 23 (n=50,9) | 0.1 (± 21.77) | -11.8 (± 35.05) | | |
| Dominant Hand: CFB at Week 52 (n=44,7) | 3.0 (± 21.24) | -15.4 (± 30.43) | | |
| Non Dominant Hand: Baseline (n=61,10) | 197.4 (± 100.01) | 159.9 (± 84.66) | | |
| Non Dominant Hand: CFB at Week 23 (n=49,8) | 7.8 (± 36.03) | -7.0 (± 21.98) | | |
| Non Dominant Hand: CFB at Week 52 (n=42,6) | 2.7 (± 23.75) | -28.7 (± 36.15) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Height (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|--|
| End point title | Change From Baseline in Height (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

| | |
|----------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 23, Week 52 | |

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: centimeter (cm) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=149,29) | 126.65 (\pm 14.293) | 131.08 (\pm 13.311) | | |
| Change from Baseline Week 23 (n=114,18) | 2.57 (\pm 1.926) | 1.84 (\pm 1.111) | | |
| Change from Baseline Week 52 (n=104,17) | 5.97 (\pm 2.580) | 5.82 (\pm 2.544) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|-----------------|--|
| End point title | Change From Baseline in Weight (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline, Week 23, Week 52

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: kilogram (kg) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=149,31) | 28.09 (\pm 10.649) | 30.43 (\pm 11.299) | | |
| Change from Baseline Week 23 (n=117,21) | 1.86 (\pm 2.570) | 1.70 (\pm 3.149) | | |
| Change from Baseline Week 52 (n=104,18) | 3.75 (\pm 4.421) | 3.74 (\pm 4.204) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thyrotropin Value (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|--|---|
| End point title | Change From Baseline in Thyrotropin Value (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
| End point description: Thyrotropin level was measured in milli-international units per liter (mIU/L). SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 23, Week 52 | |

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: mIU/L | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=146,30) | 2.682 (± 1.5897) | 3.080 (± 2.2919) | | |
| Change from Baseline Week 23 (n=104,17) | 0.141 (± 1.0523) | -0.519 (± 1.4828) | | |
| Change from Baseline Week 52 (n=97,17) | 0.112 (± 1.2559) | -0.632 (± 1.5632) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Thyroxine, Free and Triiodothyronine, Free Values (Growth and Development Parameters) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|---|--|
| End point title | Change From Baseline in Thyroxine, Free and Triiodothyronine, Free Values (Growth and Development Parameters) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
| End point description: SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. | |
| End point type | Secondary |
| End point timeframe: Baseline, Week 23, Week 52 | |

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: picomoles per liter (pmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Thyroxine,free:Baseline (n=146,30) | 15.29 (± 3.993) | 15.37 (± 2.160) | | |
| Thyroxine,free:Change Week 23 (n=103,17) | -0.07 (± 4.107) | -0.38 (± 2.088) | | |
| Thyroxine,free:Change Week 52 (n=96,17) | 0.10 (± 3.868) | 0.08 (± 2.968) | | |
| Triiodothyronine,free:Baseline (n=146,30) | 5.96 (± 1.061) | 6.10 (± 0.812) | | |
| Triiodothyronine,free: Change Week 23 (n=105,18) | 0.06 (± 0.915) | -0.16 (± 0.699) | | |
| Triiodothyronine,free:Change Week 52 (n= 96,17) | 0.04 (± 0.987) | -0.04 (± 1.107) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Insulin-like Growth Factor-1 (IGF-1) Values (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study

| | |
|---|---|
| End point title | Change From Baseline in Insulin-like Growth Factor-1 (IGF-1) Values (a Growth and Development Parameter) at Week 23 (Core Phase) and at Week 52 (Extension Phase A) of This Study |
| End point description: | |
| SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Week 23, Week 52 | |

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|---|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: nanomoles per liter (nmol/L) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Baseline (n=144,31) | 24.2 (± 14.83) | 25.9 (± 13.91) | | |
| Change from Baseline Week 23 (n=107,18) | 1.6 (± 8.96) | 0.6 (± 7.25) | | |
| Change from Baseline Week 52 (n=96,16) | 6.5 (± 9.01) | 5.1 (± 8.02) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Change From Baseline in Markedly Abnormal Encephalogram (EEG) Parameter Values During Awake and Sleep State for Total Group of Subject: Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Change From Baseline in Markedly Abnormal Encephalogram (EEG) Parameter Values During Awake and Sleep State for Total Group of Subject: Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline up to 52 weeks

| | | | | |
|-------------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 180 | | | |
| Units: percentage of subjects | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Encephalogram (EEG) Abnormalities During Awake and Sleep State for Total Group of Subjects: Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Number of Encephalogram (EEG) Abnormalities During Awake and Sleep State for Total Group of Subjects: Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

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

End point timeframe:

Baseline up to 52 weeks

| | | | | |
|-----------------------------|--|--|--|--|
| End point values | Perampanel 0.5 mg/mL: All Subjects | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 180 | | | |
| Units: EEG abnormality | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Any Treatment-emergent Reports of Suicidal Ideation and Behavior Assessed Using the Columbia-Suicide Severity Rating Scale (C-SSRS)- Core Phase and Extension Phase A of This Study

| | |
|-----------------|---|
| End point title | Percentage of Subjects With Any Treatment-emergent Reports of Suicidal Ideation and Behavior Assessed Using the Columbia-Suicide Severity Rating Scale (C-SSRS)- Core Phase and Extension Phase A of This Study |
|-----------------|---|

End point description:

C-SSRS: interview-based instrument to systematically assess suicidal ideation (SI); suicidal behavior, whether: completed suicide, suicide attempt (response of "yes" on "actual attempt"), preparatory acts toward imminent suicidal behavior ("yes" on "preparatory acts or behavior", "aborted attempt" or "interrupted attempt"), suicidal ideation ("yes" on "wish to be dead", "non-specific active suicidal thoughts", "active SI with methods without intent to act or some intent to act, without specific plan or with specific plan and intent), any self-injurious behavior with no suicidal intent ("yes" on "has subject engaged in non-suicidal self-injurious behavior"). Percentage of subjects with ≥ 1 positive behavior/ideations, suicidality were reported. C-SSRS performed: ≥ 6 years at time of consent. SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment. "number of subjects analyzed" signifies subjects who were evaluable for this OM.

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

End point timeframe:

Up to 52 weeks

| | | | | |
|--|---------------------------------|---|--|--|
| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 122 | 27 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Subjects with ≥ 1 Positive Behavior | 0.8 | 0 | | |
| Subjects with \geq Positive Ideations | 1.6 | 7.4 | | |
| Suicidality | 1.6 | 7.4 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Shift From Baseline in Suicidal Ideation and Behaviors Assessed Using C-SSRS Scores to Extension Phase A (Week 52) of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Shift From Baseline in Suicidal Ideation and Behaviors Assessed Using C-SSRS Scores to Extension Phase A (Week 52) of This Study |
|-----------------|--|

End point description:

C-SSRS: interview-based instrument to systematically assess SI and suicidal behavior, to assess whether subject experienced any of the following: completed suicide, suicide attempt (response of "yes" on "actual attempt"), preparatory acts toward imminent suicidal behavior ("yes" on "preparatory acts or behavior", "aborted attempt" or "interrupted attempt"), suicidal ideation ("yes" on "wish to be dead", "non-specific active suicidal thoughts", "active SI with methods without intent to act or some intent to act, without specific plan or with specific plan and intent), any self-injurious behavior with no suicidal intent ("yes" on "has subject engaged in non-suicidal self-injurious behavior"). "w/" refers to "with", "W" refers to "Week" and "&" refers to "and". SAS included all subject who received at least 1 dose of study drug and had at least 1 postdose safety assessment. Here "number of subject analyzed" signifies subject who were evaluable for this measure.

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

End point timeframe:

Up to 52 weeks

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|--|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 122 | 27 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| No Ideation(Baseline) to No Ideation(Week 52) | 96.6 | 88.9 | | |
| Wish to be Dead(Baseline) to No ideation(Week 52) | 0.9 | 3.7 | | |
| Active w/ Method(Baseline) to No Ideation(Week 52) | 0.9 | 0 | | |
| No Ideation(Baseline)to Active Nonspecific(Week52) | 0 | 3.7 | | |
| No Ideation(Baseline) to Active w/ Method(Week 52 | 0.9 | 3.7 | | |
| No Ideation(Baseline)to Active w/ Intent&Plan(W52) | 0.9 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Median Percent Change in Seizure Frequency Per 28 Days During the Treatment Phase Relative to the Pretreatment Phase (Baseline)- Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Median Percent Change in Seizure Frequency Per 28 Days |
|-----------------|--|

End point description:

Seizure frequency was based on number of seizures per 28 days, calculated as number of seizures over entire time interval divided by number of days in interval and multiplied by 28. Total POS: sum of all POS including simple partial seizures without motor signs, simple partial seizures with motor signs, complex partial seizures, and complex partial seizures with secondary generalization (SG). Data for this measure has been reported for 13 week time periods as per age groups. Full Analysis Set (FAS) included subjects who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement.

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

End point timeframe:

Baseline, Weeks 1-13, Weeks 14-26, Weeks 27-39, Weeks 40-52

| End point values | Perampanel 0.5 mg/mL: 4 to <7 Years | Perampanel 0.5 mg/mL: 7 to <12 Years | | |
|------------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 134 | | |
| Units: percent change | | | | |
| median (full range (min-max)) | | | | |
| POS Seizures:Weeks 1-13 (n=40,108) | -47.99 (-100.0 to 79.1) | -40.97 (-100.0 to 549.0) | | |
| POS Seizures:Weeks 14-26 (n=38,91) | -38.93 (-100.0 to 175.0) | -50.77 (-100.0 to 360.5) | | |
| POS Seizures:Weeks 27-39 (n=32,82) | -52.53 (-100.0 to 344.2) | -67.30 (-100.0 to 387.9) | | |
| POS Seizures:Weeks 40-52 (n=31,77) | -58.92 (-100.0 to 482.7) | -70.33 (-100.0 to 436.3) | | |
| PGTC Seizures:Weeks 1-13 (n=3,19) | -100.00 (- 100.0 to 2115.9) | -70.33 (-100.0 to 6783.5) | | |
| PGTC Seizures:Weeks 14-26 (n=3,15) | -100.00 (- 100.0 to -7.7) | -70.70 (-100.0 to 879.1) | | |
| PGTC Seizures:Weeks 27-39 (n=2,13) | -80.77 (-100.0 to -61.5) | -65.43 (-100.0 to 315.4) | | |
| PGTC Seizures:Weeks 40-52 (n=2,11) | -100.00 (- 100.0 to - 100.0) | -96.54 (-100.0 to 658.4) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Based on 25% Responder Rate- Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects Based on 25% Responder Rate- Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

A 25% responder was a subject who experienced a 25% or greater reduction in seizure frequency per 28 days from baseline. Total POS: sum of all POS including simple partial seizures without motor signs, simple partial seizures with motor signs, complex partial seizures, and complex partial seizures with SG. Data for this OM has been reported for 13 week time periods as per age groups. FAS included subjects

who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1-13, Weeks 14-26, Weeks 27-39, Weeks 40-52 | |

| End point values | Perampanel 0.5 mg/mL: 4 to <7 Years | Perampanel 0.5 mg/mL: 7 to <12 Years | | |
|---------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 134 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Total POS Seizures: Weeks 1-13 | 67.5 | 61.1 | | |
| Total POS Seizures: Weeks 14-26 | 57.9 | 71.4 | | |
| Total POS Seizures: Weeks 27-39 | 71.9 | 78.0 | | |
| Total POS Seizures: Weeks 40-52 | 71.0 | 81.8 | | |
| PGTC Seizures: Weeks 1-13 | 66.7 | 73.7 | | |
| PGTC Seizures: Weeks 14-26 | 66.7 | 73.3 | | |
| PGTC Seizures: Weeks 27-39 | 100.0 | 69.2 | | |
| PGTC Seizures: Weeks 40-52 | 100.0 | 63.6 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Based on 50% Responder Rate- Core Phase and Extension Phase A of This Study

| | |
|---|--|
| End point title | Percentage of Subjects Based on 50% Responder Rate- Core Phase and Extension Phase A of This Study |
| End point description: | |
| A 50% responder was a subject who experienced a 50% or greater reduction in seizure frequency per 28 days from baseline. Total POS: sum of all POS including simple partial seizures without motor signs, simple partial seizures with motor signs, complex partial seizures, and complex partial seizures with SG. Data for this OM has been reported for 13 week time periods as per age groups. FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 1-13, Weeks 14-26, Weeks 27-39, Weeks 40-52 | |

| End point values | Perampanel 0.5 mg/mL: 4 to <7 Years | Perampanel 0.5 mg/mL: 7 to <12 Years | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 134 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |

| | | | | |
|---------------------------------|-------|------|--|--|
| Total POS Seizures: Weeks 1-13 | 47.5 | 45.4 | | |
| Total POS Seizures: Weeks 14-26 | 44.7 | 50.5 | | |
| Total POS Seizures: Weeks 27-39 | 53.1 | 65.9 | | |
| Total POS Seizures: Weeks 40-52 | 61.3 | 62.3 | | |
| PGTC Seizures: Weeks 1-13 | 66.7 | 57.9 | | |
| PGTC Seizures: Weeks 14-26 | 66.7 | 60.0 | | |
| PGTC Seizures: Weeks 27-39 | 100.0 | 61.5 | | |
| PGTC Seizures: Weeks 40-52 | 100.0 | 54.5 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects Based on 75% Responder Rate- Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects Based on 75% Responder Rate- Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

A 75% responder was a subject who experienced a 75% or greater reduction in seizure frequency per 28 days from baseline. Total POS: sum of all POS including simple partial seizures without motor signs, simple partial seizures with motor signs, complex partial seizures, and complex partial seizures with SG. Data for this OM has been reported for 13 week time periods as per age groups. FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement.

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

End point timeframe:

Baseline, Weeks 1-13, Weeks 14-26, Weeks 27-39, Weeks 40-52

| End point values | Perampanel 0.5 mg/mL: 4 to <7 Years | Perampanel 0.5 mg/mL: 7 to <12 Years | | |
|---------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 134 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Total POS Seizures: Weeks 1-13 | 17.5 | 25.0 | | |
| Total POS Seizures: Weeks 14-26 | 18.4 | 34.1 | | |
| Total POS Seizures: Weeks 27-39 | 31.3 | 46.3 | | |
| Total POS Seizures: Weeks 40-52 | 38.7 | 41.6 | | |
| PGTC Seizures: Weeks 1-13 | 66.7 | 47.4 | | |
| PGTC Seizures: Weeks 14-26 | 66.7 | 46.7 | | |
| PGTC Seizures: Weeks 27-39 | 50.0 | 46.2 | | |
| PGTC Seizures: Weeks 40-52 | 100.0 | 54.5 | | |

Statistical analyses

Secondary: Percentage of Subjects Who Were Seizure-free- Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects Who Were Seizure-free- Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

Subjects were considered seizure free if subjects completed a 13-week time period and were seizure-free for that entire time period. Total POS: sum of all POS including simple partial seizures without motor signs, simple partial seizures with motor signs, complex partial seizures, and complex partial seizures with SG. Data for this OM has been reported for 13 week time periods as per age groups. FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement.

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

End point timeframe:

Weeks 1-13, Weeks 14-26, Weeks 27-39, Weeks 40-52

| End point values | Perampanel 0.5 mg/mL: 4 to <7 Years | Perampanel 0.5 mg/mL: 7 to <12 Years | | |
|---------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 46 | 134 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Total POS Seizures: Weeks 1-13 | 7.9 | 9.9 | | |
| Total POS Seizures: Weeks 14-26 | 9.4 | 15.9 | | |
| Total POS Seizures: Weeks 27-39 | 12.9 | 24.7 | | |
| Total POS Seizures: Weeks 40-52 | 15.0 | 20.8 | | |
| PGTC Seizures: Weeks 1-13 | 66.7 | 40.0 | | |
| PGTC Seizures: Weeks 14-26 | 50.0 | 46.2 | | |
| PGTC Seizures: Weeks 27-39 | 50.0 | 45.5 | | |
| PGTC Seizures: Weeks 40-52 | 100.0 | 57.1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Clinical Global Impression of Change Scores (CGIC)- Core Phase and Extension Phase A of This Study

| | |
|-----------------|--|
| End point title | Percentage of Subjects With Clinical Global Impression of Change Scores (CGIC)- Core Phase and Extension Phase A of This Study |
|-----------------|--|

End point description:

Assessment of disease severity utilized the CGIC scale at end of treatment to evaluate subject's change in disease status from baseline. The CGIC is a 7-point scale that measures a physician's global impression of a subject's clinical condition. Scale ranged from 1 to 7 with lower score indicated improvement (1=very much improved, 2=much improved, 3=minimally improved), higher score indicated worsening (5=minimally worse, 6= much worse, 7=very much worse), and a score of 4 indicated no change. FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose primary efficacy measurement.

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

End point timeframe:

Baseline, Week 23, Week 52

| End point values | Perampanel 0.5 mg/mL: POS | Perampanel 0.5 mg/mL: PGTC Seizures | | |
|-------------------------------|---------------------------------|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 149 | 31 | | |
| Units: percentage of subjects | | | | |
| number (not applicable) | | | | |
| Week 23: Very much improved | 11.5 | 8.7 | | |
| Week 23: Much improved | 31.1 | 26.1 | | |
| Week 23: Minimally improved | 38.5 | 26.1 | | |
| Week 23: No change | 14.8 | 26.1 | | |
| Week 23: Minimally worse | 3.3 | 13.0 | | |
| Week 23: Much worse | 0.8 | 0 | | |
| Week 52: Very much improved | 14.4 | 5.9 | | |
| Week 52: Much improved | 39.4 | 41.2 | | |
| Week 52: Minimally improved | 35.6 | 29.4 | | |
| Week 52: No change | 7.7 | 17.6 | | |
| Week 52: Minimally worse | 1.9 | 5.9 | | |
| Week 52: Much worse | 1.0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to approximately 5 years

Adverse event reporting additional description:

SAS included all subjects who received at least 1 dose of study drug and had at least 1 postdose safety assessment.

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 21.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: POS |
|-----------------------|---------------------------|

Reporting group description:

Core Phase: Subjects with POS received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel once daily at optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed Core Phase, entered Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| | |
|-----------------------|--|
| Reporting group title | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|--|

Reporting group description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

| | |
|-----------------------|--|
| Reporting group title | Extension B: Perampanel 0.5 mg/mL: POS |
|-----------------------|--|

Reporting group description:

Subjects who completed Core Phase and Extension Phase A entered Extension Phase B, and continued with their optimal perampanel dose from Core Phase until a subject reached 12 years of age, switched to the commercial perampanel product, or discontinued for safety or administrative reasons.

| | |
|-----------------------|-------------------------------------|
| Reporting group title | Perampanel 0.5 mg/mL: PGTC Seizures |
|-----------------------|-------------------------------------|

Reporting group description:

Core Phase: Subjects with PGTC seizures received perampanel 0.5 mg/mL oral suspension titrated beyond 8 mg/day up to 12 mg/day, if 8 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are not taking any other EIAED), or titrated beyond 12 mg/day up to 16 mg/day, if 12 mg/day was tolerable and were deemed likely to be benefitted by higher dose (for subjects who are taking any EIAED). Dose titration- up to 11 weeks to identify each subject's optimum dose. Subjects then continued to take perampanel oral suspension once daily at the optimal dose level as a maintenance dose for up to 12 weeks. Extension Phase A: Subjects who completed the Core Phase, entered the Extension Phase A, and continued with their optimal perampanel dose from Core Phase for up to 29 weeks. Total duration of treatment for Core Phase and Extension Phase A was up to 52 weeks.

| Serious adverse events | Perampanel 0.5 mg/mL: POS | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures | Extension B: Perampanel 0.5 mg/mL: POS |
|---|---------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 29 / 149 (19.46%) | 0 / 1 (0.00%) | 8 / 41 (19.51%) |
| number of deaths (all causes) | 1 | 0 | 0 |
| number of deaths resulting from | 1 | 0 | 0 |

| | | | |
|---|-----------------|---------------|----------------|
| adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign neoplasm of testis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemangioma | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Subgaleal haematoma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Dysarthria | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ataxia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Epilepsy | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Generalised tonic-clonic seizure | | | |

| | | | |
|--|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rasmussen encephalitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Petit mal epilepsy | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure cluster | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Somnolence | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Gait disturbance | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperthermia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |

| | | | |
|---|-----------------|---------------|----------------|
| Dental caries | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis erosive | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory failure | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|---------------|----------------|
| Atelectasis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory distress | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Aggression | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disruptive mood dysregulation disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hallucination, visual | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Epiphysiolysis | | | |

| | | | |
|---|-----------------|---------------|-----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Encephalitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 5 / 41 (12.20%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 0 | 0 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhinovirus infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |

| | | | |
|---|-----------------|---------------|----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral myocarditis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Product issues | | | |
| Device malfunction | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|-----------------|---------------|----------------|
| Dehydration | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-------------------------------------|--|--|
| Serious adverse events | Perampanel 0.5 mg/mL: PGTC Seizures | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 31 (22.58%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Benign neoplasm of testis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haemangioma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Subgaleal haematoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Dysarthria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ataxia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Epilepsy | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Generalised tonic-clonic seizure | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rasmussen encephalitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Petit mal epilepsy | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Seizure cluster | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Gait disturbance | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis erosive | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | | |
|---|----------------|--|--|--|
| Acute respiratory failure | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthma | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Atelectasis | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract inflammation | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory distress | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia aspiration | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| Aggression | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Disruptive mood dysregulation disorder | | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|----------------|--|--|
| Hallucination, visual | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Epiphysiolysis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Encephalitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection pseudomonal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------|--|--|
| Rhinovirus infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral myocarditis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Product issues | | | |

| | | | |
|---|----------------|--|--|
| Device malfunction subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events | Perampanel 0.5 mg/mL: POS | Extension B: Perampanel 0.5 mg/mL: PGTC Seizures | Extension B: Perampanel 0.5 mg/mL: POS |
|---|---------------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 135 / 149 (90.60%) | 1 / 1 (100.00%) | 34 / 41 (82.93%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Vascular disorders | | | |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Subgaleal haematoma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Crying | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fatigue | | | |

| | | | |
|---|-------------------|---------------|----------------|
| subjects affected / exposed | 9 / 149 (6.04%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 11 | 0 | 0 |
| Gait disturbance | | | |
| subjects affected / exposed | 7 / 149 (4.70%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 25 / 149 (16.78%) | 0 / 1 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 39 | 0 | 4 |
| Medical device pain | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Screaming | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Immune system disorders | | | |
| Rubber sensitivity | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seasonal allergy | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 0 | 1 |
| Epistaxis | | | |

| | | | |
|--------------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Lower respiratory tract congestion | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 5 | 0 | 1 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 4 | 0 | 3 |
| Respiratory disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper airway obstruction | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Bronchitis chronic | | | |

| | | | |
|---|-------------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Increased bronchial secretion subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Pneumonia aspiration subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Psychiatric disorders | | | |
| Abnormal behaviour subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Adjustment disorder subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Affect lability subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Agitation subjects affected / exposed occurrences (all) | 7 / 149 (4.70%) 11 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Aggression subjects affected / exposed occurrences (all) | 15 / 149 (10.07%) 22 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Anger subjects affected / exposed occurrences (all) | 3 / 149 (2.01%) 3 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Anxiety subjects affected / exposed occurrences (all) | 3 / 149 (2.01%) 5 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all) | 4 / 149 (2.68%) 4 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Defiant behaviour | | | |

| | | | |
|-----------------------------|-------------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bradyphrenia | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Dysphemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysphoria | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Enuresis | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Euphoric mood | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypervigilance | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 5 | 0 | 2 |
| Irritability | | | |
| subjects affected / exposed | 19 / 149 (12.75%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 20 | 0 | 1 |
| Learning disability | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mood altered | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Middle insomnia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nightmare | | | |

| | | | |
|-------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oppositional defiant disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Negativism | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Personality change | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Restlessness | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 0 | 1 |
| Somnambulism | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sleep disorder | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Tic | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Distractibility | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Initial insomnia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Intentional self-injury | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Investigations | | | |

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|--|----------------------|--------------------|---------------------|
| Body temperature increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 2 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Urine output decreased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 2 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Weight decreased subjects affected / exposed occurrences (all) | 3 / 149 (2.01%) 3 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Weight increased subjects affected / exposed occurrences (all) | 6 / 149 (4.03%) 6 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Blood pressure systolic increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Crystal urine present subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Blood uric acid increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Eosinophil count increased subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Tri-iodothyronine free increased subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| White blood cells urine positive | | | |

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| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ammonia increased | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Blast cell count increased | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 0 | 3 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Animal bite | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Arthropod sting | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Contusion | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 6 | 0 | 1 |
| Eye contusion | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye injury | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fall | | | |

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| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Head injury | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 2 |
| Foot fracture | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Forearm fracture | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Laceration | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Joint injury | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 0 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mallet finger | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nail avulsion | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scar | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seroma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |

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|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 5 | 0 | 1 |
| Wound | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Wrist fracture | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Clavicle fracture | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint dislocation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Heat stroke | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stoma site hypergranulation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Traumatic haematoma | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Incision site erosion | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Lip injury | | | |

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|--|----------------------|--------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Nervous system disorders | | | |
| Amnesia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ataxia | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Atonic seizures | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Balance disorder | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Coordination abnormal | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Clumsiness | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 19 / 149 (12.75%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 24 | 0 | 0 |
| Disturbance in attention | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Droping | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |

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| Dysarthria | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dyslexia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysstasia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Headache | | | |
| subjects affected / exposed | 10 / 149 (6.71%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 18 | 0 | 1 |
| Hypotonia | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Motor dysfunction | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Nystagmus | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Persistent postural-perceptual dizziness | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Petit mal epilepsy | | | |

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| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Postictal state | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Psychomotor skills impaired | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sedation | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Somnolence | | | |
| subjects affected / exposed | 43 / 149 (28.86%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 49 | 0 | 1 |
| Status epilepticus | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hippocampal sclerosis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Migraine | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Poor quality sleep | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Seizure cluster | | | |

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|--------------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 2 |
| Simple partial seizures | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Fine motor skill dysfunction | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Increased tendency to bruise | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Macrocytosis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |

| | | | |
|-------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vertigo | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Eye disorders | | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 2 | 0 | 5 |
| Corneal disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diplopia | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Mydriasis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Keratitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 0 | 2 |
| Strabismus | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye discharge | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |

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| Eyelid oedema | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Lagophthalmos | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 5 | 0 | 3 |
| Anal incontinence | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 149 (6.04%) | 0 / 1 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 13 | 0 | 6 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 0 | 1 |
| Enteritis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erosive oesophagitis | | | |

| | | | |
|--------------------------------------|-------------------|---------------|-----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 4 | 0 | 1 |
| Odynophagia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 20 / 149 (13.42%) | 0 / 1 (0.00%) | 5 / 41 (12.20%) |
| occurrences (all) | 23 | 0 | 13 |
| Dental caries | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 0 | 2 |
| Functional gastrointestinal disorder | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ranula | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Enterocolitis | | | |

| | | | |
|--|-----------------|---------------|----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal motility disorder | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Gingival hypertrophy | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth discolouration | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Alopecia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 4 | 0 | 1 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 1 | 0 | 3 |
| Drug eruption | | | |

| | | | |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 2 | 0 | 2 |
| Mechanical urticaria | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 13 | 0 | 2 |
| Miliaria | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Rash erythematous | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash morbilliform | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angioedema | | | |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash generalised | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin erosion | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blister | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Yellow skin | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Nail dystrophy | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 1 / 1 (100.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Polyuria | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------------|--------------------|---------------------|
| Hypertonic bladder subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Pollakiuria subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Vesicoureteric reflux subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Precocious puberty subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Kyphosis subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Muscle spasms subjects affected / exposed occurrences (all) | 1 / 149 (0.67%) 1 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Muscle rigidity subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Pain in extremity subjects affected / exposed occurrences (all) | 0 / 149 (0.00%) 0 | 0 / 1 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Periosteal haematoma | | | |

| | | | |
|---|------------------|-----------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Beta haemolytic streptococcal infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 10 / 149 (6.71%) | 0 / 1 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 11 | 0 | 6 |
| Conjunctivitis | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 5 | 0 | 5 |
| Ear infection | | | |
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Enterocolitis viral | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 11 / 149 (7.38%) | 1 / 1 (100.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 14 | 1 | 1 |
| Hordeolum | | | |

| | | | |
|-----------------------------|-------------------|---------------|------------------|
| subjects affected / exposed | 3 / 149 (2.01%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 20 / 149 (13.42%) | 0 / 1 (0.00%) | 6 / 41 (14.63%) |
| occurrences (all) | 23 | 0 | 6 |
| Lymphangitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 40 / 149 (26.85%) | 0 / 1 (0.00%) | 14 / 41 (34.15%) |
| occurrences (all) | 73 | 0 | 25 |
| Oral herpes | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Otitis media | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 6 | 0 | 2 |
| Paronychia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 6 / 41 (14.63%) |
| occurrences (all) | 1 | 0 | 8 |
| Respiratory tract infection | | | |

| | | | |
|---|-------------------|---------------|----------------|
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Streptococcal infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 1 | 0 | 4 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 2 | 0 | 1 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 15 / 149 (10.07%) | 0 / 1 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 17 | 0 | 6 |
| Urinary tract infection | | | |
| subjects affected / exposed | 5 / 149 (3.36%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 4 / 149 (2.68%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 6 | 0 | 1 |
| Viral rash | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastroenteritis viral | | | |

| | | | |
|-----------------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Oral fungal infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Perianal streptococcal infection | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tinea pedis | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Varicella | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 1 | 0 | 2 |
| Corona virus infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema infectiosum | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Pneumonia mycoplasmal | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Pyelonephritis acute | | | |

| | | | |
|--|-----------------|---------------|----------------|
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory syncytial virus bronchitis | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 149 (1.34%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Increased appetite | | | |
| subjects affected / exposed | 6 / 149 (4.03%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Polydipsia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dehydration | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 149 (0.67%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 1 | 0 | 1 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 149 (0.00%) | 0 / 1 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|--|--|--|
| Non-serious adverse events | Perampanel 0.5 mg/mL: PGTC Seizures | | |
| Total subjects affected by non-serious adverse events subjects affected / exposed | 25 / 31 (80.65%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Vascular disorders Peripheral coldness subjects affected / exposed occurrences (all) Subgaleal haematoma subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 0 / 31 (0.00%) 0 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Crying subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Gait disturbance subjects affected / exposed occurrences (all) Influenza like illness subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all) Pyrexia | 1 / 31 (3.23%) 2 0 / 31 (0.00%) 0 2 / 31 (6.45%) 2 0 / 31 (0.00%) 0 1 / 31 (3.23%) 1 0 / 31 (0.00%) 0 | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 4 / 31 (12.90%) | | |
| occurrences (all) | 6 | | |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Screaming | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Immune system disorders | | | |
| Rubber sensitivity | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Seasonal allergy | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 7 | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Lower respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Increased upper airway secretion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasal congestion | | | |

| | | | |
|--------------------------------------|----------------|--|--|
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract inflammation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper airway obstruction | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis chronic | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Increased bronchial secretion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia aspiration | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychiatric disorders | | | |
| Abnormal behaviour | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |

| | | | |
|--|----------------|--|--|
| Adjustment disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Affect lability | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Agitation | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Aggression | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Anger | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Anxiety | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Defiant behaviour | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bradyphrenia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysphemia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Dysphoria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Enuresis | | | |

| | | | |
|-------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Euphoric mood | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Hypervigilance | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Irritability | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 5 | | |
| Learning disability | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Mood altered | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Middle insomnia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nightmare | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Oppositional defiant disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Negativism | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Personality change | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Restlessness | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Somnambulism | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 2 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tic | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Distractibility | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Initial insomnia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Intentional self-injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Investigations | | | |
| Body temperature increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urine output decreased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Weight increased | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |

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|--------------------------------------|----------------|--|--|
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blood pressure systolic increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Crystal urine present | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eosinophil count increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tri-iodothyronine free increased | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ammonia increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blast cell count increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gamma-glutamyltransferase increased | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Neutrophil count decreased | | | |

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|--|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthropod sting | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eye injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fall | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Forearm fracture | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Laceration | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Mallet finger | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nail avulsion | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Scar | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Seroma | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wound | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wrist fracture | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Clavicle fracture | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Joint dislocation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Heat stroke | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stoma site hypergranulation | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Traumatic haematoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Incision site erosion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lip injury | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Amnesia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Ataxia | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Atonic seizures | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |

| | | | |
|-----------------------------|-----------------|--|--|
| Balance disorder | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Cerebral haematoma | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Clumsiness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Dizziness | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 8 | | |
| Disturbance in attention | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Droling | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysarthria | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Dyslexia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Focal dyscognitive seizures | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysstasia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |

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|--|-----------------|--|--|
| Headache | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 7 | | |
| Hypotonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Memory impairment | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 3 | | |
| Motor dysfunction | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Nystagmus | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Persistent postural-perceptual dizziness | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Petit mal epilepsy | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Postictal state | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Psychomotor hyperactivity | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 3 | | |
| Psychomotor skills impaired | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sedation | | | |

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|------------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 3 | | |
| Seizure | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 4 | | |
| Somnolence | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 9 | | |
| Status epilepticus | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hippocampal sclerosis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Migraine | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Poor quality sleep | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Seizure cluster | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Simple partial seizures | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tremor | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Myoclonus | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fine motor skill dysfunction | | | |

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|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Increased tendency to bruise | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Macrocytosis | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Neutropenia | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Tympanic membrane perforation | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Vertigo | | | |
| subjects affected / exposed occurrences (all) | 3 / 31 (9.68%) 3 | | |
| Eye disorders | | | |
| Conjunctivitis allergic | | | |
| subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Corneal disorder | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Diplopia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 2 | | |
| Mydriasis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Conjunctival hyperaemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Keratitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Strabismus | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Eye discharge | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eyelid oedema | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lagophthalmos | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |

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|----------------------------------|----------------|--|--|
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 5 | | |
| Anal incontinence | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 5 | | |
| Dry mouth | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erosive oesophagitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Odynophagia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |

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|--------------------------------------|-----------------|--|--|
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Stomatitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 5 / 31 (16.13%) | | |
| occurrences (all) | 6 | | |
| Dental caries | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Functional gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ranula | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastrointestinal motility disorder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival hypertrophy | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |

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|--|---------------------|--|--|
| Tooth discolouration subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Hepatobiliary disorders Drug-induced liver injury subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Skin and subcutaneous tissue disorders Acne subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | | |
| Alopecia subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | | |
| Dermatitis contact subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Dermatitis subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Drug eruption subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Dermatitis diaper subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Eczema subjects affected / exposed occurrences (all) | 1 / 31 (3.23%) 1 | | |
| Mechanical urticaria subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Erythema subjects affected / exposed occurrences (all) | 0 / 31 (0.00%) 0 | | |
| Rash | | | |

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|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Miliaria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash erythematous | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Rash papular | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash morbilliform | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin hyperpigmentation | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Angioedema | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin erosion | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Blister | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Yellow skin | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nail dystrophy | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Renal and urinary disorders | | | |
| Urinary incontinence | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Polyuria | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypertonic bladder | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vesicoureteric reflux | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Endocrine disorders | | | |
| Hypothyroidism | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Precocious puberty | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Kyphosis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Muscle rigidity | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 2 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Periosteal haematoma | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Arthritis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Beta haemolytic streptococcal infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Bronchitis | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Ear infection | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Enterocolitis viral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fungal infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 31 (6.45%) | | |
| occurrences (all) | 2 | | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Influenza | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lymphangitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 4 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis externa | | | |

| | | | |
|-----------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Paronychia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 4 | | |
| Streptococcal infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tonsillitis | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 31 (9.68%) | | |
| occurrences (all) | 3 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral rash | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 2 | | |
| Croup infectious | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Impetigo | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Oral fungal infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Perianal streptococcal infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tinea pedis | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Varicella | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Corona virus infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Erythema infectiosum | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia mycoplasmal | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory syncytial virus bronchitis | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 4 / 31 (12.90%) | | |
| occurrences (all) | 4 | | |
| Increased appetite | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Polydipsia | | | |
| subjects affected / exposed | 1 / 31 (3.23%) | | |
| occurrences (all) | 1 | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 31 (0.00%) | | |
| occurrences (all) | 0 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 20 April 2017 | Amendment 01: Added that the Titration Period is a fixed duration of 11 weeks and subjects will remain on their optimum dose once it is achieved during this period. Separated the Titration Period dosing schedule into separate presentations for Global sites and Japan sites. Increased the time prior to Visit 2 that subjects must meet the prior seizure criterion from 4 to 12 weeks. Increased the number of approved antiepileptic drug (AEDs) subjects may currently be receiving from 2 to 3. Added exclusion criterion for cannabinoids. Added exclusion of subjects with hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. Added emphasis that efforts should be made to perform all clinical laboratory and screening tests on the scheduled day, or as close as possible to that day, within 4 week period prior Visit 2. Added emphasis that efforts should be made to perform all clinical laboratory and screening tests on the scheduled day, or as close as possible to that day, within 4 week period prior Visit 2. Added mandatory blood collection for pharmacokinetic (PK) assessment. Revised study visit window to ± 7 days of the scheduled visit. Grammatical, typographical, and formatting changes were also made. |
| 19 October 2017 | Amendment 02: Revised the Pretreatment Screening/Baseline Period (outside of Japan) to allow subjects to enrol sooner after a qualifying seizure, while maintaining the 4 weeks ± 3 days required in Japan. Added that the study period durations were "up to" the specified nominal times. Added that analyses for regional submissions may be performed during the course of the study. Revised the sample size to state "at least" 160 subjects "(with up to 40 subjects with PGTC and the balance with POS)". Added that each study visit is based on the actual prior visit (eg, Visit 3 is completed 2 weeks ± 3 days of Visit 2, Visit 4 is completed 3 weeks ± 3 days of Visit 3, etc). Revised study visit window during the Extension Phase back to ± 6 days of the scheduled visit for Visits 10 through 12 (as per the original protocol). Grammatical, typographical, and formatting changes were also made. |
| 19 January 2018 | Amendment 03: Clarified, in the text, that the Followup Visit would be conducted at 4 weeks ± 7 days after the last dose of study drug for all subjects, except for subjects entering into Extension A. Clarified, in the text, that the follow-up period of Extension A was only for subjects not entering into Extension B and that Extension B will occur in Japan only. Clarified, in the text, that a follow-up period of Extension B, would include a Follow-up visit at 4 weeks ± 7 days after the Discontinuation Visit, and would occur for subjects who discontinue or who choose not to switch to the commercial product. Clarified, in the text, that subjects in all countries can enroll in Extension A. Clarified that the study visit window during Extension B is ± 6 days of the scheduled visit. Clarified that the initial assessment of Extension B was performed at the final visit of Extension A Maintenance period (ie, Visit 12). Grammatical, typographical, and formatting changes were also made. |
| 13 July 2018 | Amendment 04: Clarified, in the text, that the Pretreatment Phase consists of a Screening/Baseline period. Clarified, in the text, the approximate total study duration. Clarified, in the text, that subjects in Japan and in countries where an extended access program (EAP) cannot be implemented can enroll in Extension B. Specified criteria for participation in Extension B for subjects in countries where an EAP cannot be implemented. Clarified the CGI objective (CGIS is the baseline assessment and CGIC is the postbaseline assessment of the CGI). Grammatical, typographical, and formatting changes were also made. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported