Clinical trial results:
A Multicenter, Uncontrolled, Open-label Study and Extension Study for Verification of Efficacy and Safety for Perampanel Monotherapy in Untreated Patients with Partial Onset Seizures (Including Secondarily Generalized Seizures)

Summary

EudraCT number	2019-003734-17
Trial protocol	Outside EU/EEA
Global end of trial date	27 July 2020

Results information

Result version number	v1 (current)
This version publication date	07 February 2021
First version publication date	07 February 2021

Trial information

Trial identification

Sponsor protocol code	E2007-J000-342

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03201900
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Co., Ltd.
Sponsor organisation address	4-6-10 Koishikawa, Bunkyo-Ku, Tokyo , Japan, 112-8088
Public contact	Inquiry Service., Eisai, Inc., eisai-chiken_hotline@hhc.eisai.co.jp
Scientific contact	Inquiry Service., Eisai, Inc., eisai-chiken_hotline@hhc.eisai.co.jp

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 July 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the seizure-free rate of the 26-week Maintenance Period in untreated subjects with partial onset seizures (POS).

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	28 June 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 43
Country: Number of subjects enrolled	Korea, Republic of: 46
Worldwide total number of subjects	89
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	7
Adults (18-64 years)	71
From 65 to 84 years	11
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 38 investigative sites in Japan and Korea from 28 Jun 2017 to 27 Jul 2020. A total of 98 subjects were screened, of which 07 were screen failures and 91 entered Treatment Phase. Of these, 89 subjects received the study treatment.

Pre-assignment

Screening details:

Study consisted of 2 main phases: Treatment Phase (consisted of a 4¬milligram [mg] Treatment Phase [Titration Period {6 weeks} and Maintenance Period {26 weeks}], and for those subjects who need a higher dose, the 8 mg Treatment Phase [Titration Period {4 weeks} and Maintenance Period {26 weeks}]) and Extension Phase.

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Perampanel

Arm description:

Subjects received 2 mg of perampanel tablets orally once daily (QD) for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional antiepileptic drug (AEDs).

Arm type	Experimental
Investigational medicinal product name	Perampanel
Investigational medicinal product code	E2007
Other name	Fycompa
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 2 mg of perampanel tablets orally QD for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional AEDs.

Number of subjects in period 1	Perampanel
Started	89
Completed	54
Not completed	35
Adverse event, non-fatal	9
Subject Choice	1
Other than specified	11
Withdrawal of consent	6
Inadequate therapeutic effect	6
Lost to follow-up	2

Period 2

Period 2 title	Extension Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Perampanel

Arm description:

Subjects received 2 mg of perampanel tablets orally QD for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional AEDs.

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Number of subjects in period 2[1]	Perampanel
Started	46
Completed	38
Not completed	8
Consent withdrawn by subject	3
Subject Choice	1
Pregnancy	1
Unspecified	1
Inadequate therapeutic effect	1
Lost to follow-up	1

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: Eligible subjects who completed Treatment Phase and agreed to continue in the Extension Phase.

Baseline characteristics

Reporting groups	
Reporting group title	Perampanel

Reporting group description:

Subjects received 2 mg of perampanel tablets orally once daily (QD) for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional antiepileptic drug (AEDs).

Reporting group values	Perampanel	Total	
Number of subjects	89	89	
Age categorical Units: Subjects			
Age continuous Units: years arithmetic mean standard deviation	 42.1 ± 18.19	 -	
Gender categorical Units: Subjects			
Female	44	44	
Male	45	45	
Race Units: Subjects			
Asian	89	89	
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	
Not Hispanic or Latino	89	89	
Unknown or Not	0	0	

End points

End points reporting groups

Reporting group title	Perampanel

Reporting group description:

Subjects received 2 mg of perampanel tablets orally once daily (QD) for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional antiepileptic drug (AEDs).

Reporting group title	Perampanel

Reporting group description:

Subjects received 2 mg of perampanel tablets orally QD for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional AEDs.

Primary: Percentage of Subjects With POS Who Achieved Seizure-free Status During the 26-week Maintenance Period of 4 mg Perampanel

End point title	Percentage of Subjects With POS Who Achieved Seizure-free Status During the 26-week Maintenance Period of 4 mg Perampanel[1]

End point description:

A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. POS was a seizure that starts in one area of the brain that may or may not associated with loss of awareness and consciousness. Seizure-free status was defined as no incidence of seizure during the 26-week Maintenance Period of 4 mg perampanel. Modified intent to treat (mITT) set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period.

End point type	Primary

End point timeframe:

26 weeks in Maintenance Period of 4 mg perampanel

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 statistics data was planned to be analyzed for this endpoint.

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: percentage of subjects				
number (not applicable)	63.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With POS Who Achieved Seizure-free Status During the 26-week Maintenance Period of 4 or 8 mg Perampanel

End point title	Percentage of Subjects With POS Who Achieved Seizure-free Status During the 26-week Maintenance Period of 4 or 8 mg Perampanel

End point description:

A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. POS was a seizure that starts in one area of the brain that may or may not associated with loss of awareness and consciousness. Seizure-free status was defined as no incidence of seizure during the 26-week Maintenance Period of last evaluated dose of 4 or 8 mg perampanel. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period.

End point type	Secondary

End point timeframe:

26 weeks in Maintenance Period of 4 or 8 mg perampanel

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: percentage of subjects				
number (not applicable)	74.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With POS Who Achieved Seizure-free Status During the 52-week Treatment Phase (26-week Maintenance Period Plus 26-week Extension Phase) of 4 mg of Perampanel

End point title	Percentage of Subjects With POS Who Achieved Seizure-free Status During the 52-week Treatment Phase (26-week Maintenance Period Plus 26-week Extension Phase) of 4 mg of Perampanel

End point description:

A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. POS was a seizure that started in one area of the brain that may or may not associated with loss of awareness and consciousness. Seizure-free status was defined as no incidence of seizure during the 52-week treatment phase of 4 mg perampanel. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance

Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period.

End point type	Secondary

End point timeframe:

52-week (Maintenance Period of 4 mg perampanel + Extension Phase of 4 mg perampanel)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: percentage of subjects				
number (not applicable)	32.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With POS Who Achieved Seizure-free Status During the 52-week of Treatment Phase (26-week Maintenance Period Plus 26-week Extension Phase) of Last Evaluated Dose of 4 or 8 mg Perampanel

End point title	Percentage of Subjects With POS Who Achieved Seizure-free Status During the 52-week of Treatment Phase (26-week Maintenance Period Plus 26-week Extension Phase) of Last Evaluated Dose of 4 or 8 mg Perampanel

End point description:

A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. POS was a seizure that starts in one area of the brain that may or may not associated with loss of awareness and consciousness. Seizure-free status was defined as no incidence of seizure during the 52-week treatment phase of last evaluated dose of 4 or 8 mg perampanel. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period.

End point type	Secondary

End point timeframe:

52-week (Maintenance Period of last evaluated dose of 4 or 8 mg perampanel + Extension Phase of 4 or 8 mg perampanel)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: percentage of subjects				
number (not applicable)	42.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Onset of First Seizure From the First dose of Study Drug in the Maintenance Period of 4 mg Perampanel

End point title	Time to Onset of First Seizure From the First dose of Study Drug in the Maintenance Period of 4 mg Perampanel

End point description:

Time to onset of first seizure was defined as the period from the first dose of study drug in the 4-mg Maintenance Period to the onset of first seizure. A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4 mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period. 99999 refers to data not reported as median time was not estimable because less than (<) 50 percent (%) of subjects experienced a POS seizure event.

End point type	Secondary

End point timeframe:

From the first dose of study drug in the Maintenance Period (Week 6) up to the first seizure onset (up to 150 weeks)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: hours				
median (full range (min-max))	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Onset of First Seizure From the First dose of Study Drug in the Maintenance Period of Last Evaluated Dose of 4 or 8 mg Perampanel

End point title	Time to Onset of First Seizure From the First dose of Study Drug in the Maintenance Period of Last Evaluated Dose of 4 or 8 mg Perampanel

End point description:

Time to onset of first seizure was defined as the period from the first dose of study drug in the 4 mg Maintenance Period to the onset of first seizure. A seizure was a brief episode of signs or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4 mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period. 99999 refers to data not reported as median time was not estimable because <50 % of subjects experienced a POS seizure event.

End point type	Secondary

End point timeframe:

From the first dose of study drug in the Maintenance Period (Week 6) up to the first seizure onset (up to 150 weeks)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: hours				
median (full range (min-max))	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Withdrawal From the First Dose of Study Drug in the Maintenance Period of 4 mg Perampanel

End point title	Time to Withdrawal From the First Dose of Study Drug in the Maintenance Period of 4 mg Perampanel

End point description:

Time to withdrawal from the study was defined as the period from the first dose of study drug in the 4-mg Maintenance Period to the date of withdrawal from study, regardless of reason. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week Maintenance Period. 99999 refers to median time was not estimable because <50% of subjects discontinued the study.

End point type	Secondary

End point timeframe:

From the first dose of study drug in the Maintenance Period (Week 6) up to the date of first withdrawal, regardless of reason (up to 150 weeks)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: hours				
median (full range (min-max))	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Withdrawal From the First Dose of Study Drug in the Maintenance Period of Last Evaluated Dose of 4 or 8 mg Perampanel

End point title	Time to Withdrawal From the First Dose of Study Drug in the Maintenance Period of Last Evaluated Dose of 4 or 8 mg Perampanel

End point description:

Time to withdrawal from the study was defined as the period from the first dose of study drug in the 4-mg Maintenance Period to the date of withdrawal from study, regardless of reason. mITT set: group of subjects who signed informed consent, received at least 1 dose of study drug, who entered the 4-mg Maintenance Period and had at least 1 postdose primary efficacy measurement in the 26-week

Maintenance Period. 99999 refers to median time was not estimable because <50% of subjects discontinued the study.

End point type	Secondary

End point timeframe:

From the first dose of study drug in the Maintenance Period (Week 6) up to the date of first withdrawal, regardless of reason (up to 150 weeks)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	73			
Units: hours				
median (full range (min-max))	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Any Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Event (TESAEs), and TEAEs Leading to Discontinuation of the Study Drug

End point title	Number of Subjects With Any Treatment-emergent Adverse Events (TEAEs), Treatment-emergent Serious Adverse Event (TESAEs), and TEAEs Leading to Discontinuation of the Study Drug

End point description:

The safety analysis set was the group of subjects who signed informed consent, received at least one dose of study drug and had at least one postdose safety assessment.

End point type	Secondary

End point timeframe:

From baseline up to 28 days after last dose of study drug (up to 160 weeks)

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	89			
Units: subjects				
TEAEs	74			
TESAEs	13			
TEAEs leading to discontinuation of study drug	9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From baseline up to 28 days after last dose of study drug (up to 160 weeks)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Perampanel

Reporting group description:

Subjects received 2 mg of perampanel tablets orally QD for up to 2 weeks, then dose was up-titrated to 4 mg QD for 4 weeks in 4-mg Titration Period (6 Weeks) followed by 4 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). If a subject experienced seizures during 4-mg Maintenance Period, the subject was transitioned to 8-mg Titration Period based on the subject's safety and tolerability. In 8-mg Titration Period (4 weeks), subjects received 6 mg of perampanel tablets orally QD for 2 weeks and up-titrated to 8 mg QD for 2 weeks followed by 8 mg of perampanel tablets orally QD in Maintenance Period (26 weeks). Subjects who completed Treatment Phase or who ended Maintenance Period of Treatment Phase due to insufficient efficacy or intolerability, and who agreed to continue perampanel monotherapy entered Extension Phase and received perampanel until insufficient seizure control or lack of tolerability, or initiation of additional AEDs.

Serious adverse events	Perampanel		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 89 (14.61%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Epilepsy			

subjects affected / exposed	2 / 89 (2.25%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial aneurysm				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Partial seizures with secondary generalisation				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postictal state				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Malaise				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary sarcoidosis				

subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media chronic			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Perampanel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	73 / 89 (82.02%)		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		

Feeling abnormal subjects affected / exposed occurrences (all)	4 / 89 (4.49%) 4		
Chest discomfort subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Gait disturbance subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Chest pain subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2		
Oedema peripheral subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Pyrexia subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Malaise subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	3 / 89 (3.37%) 3		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 2		
Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Menorrhagia subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Respiratory, thoracic and mediastinal disorders			

Nasal congestion subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Asthma subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Cough subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Dyspnoea subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Epistaxis subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 3		
Rhinitis allergic subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 2		
Respiratory symptom subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Psychiatric disorders Affect lability subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 1		
Anxiety subjects affected / exposed occurrences (all)	2 / 89 (2.25%) 2		
Insomnia subjects affected / exposed occurrences (all)	1 / 89 (1.12%) 2		
Depressed mood			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Irritability			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Emotional disorder			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Investigations			
Blood creatine phosphokinase increased			
subjects affected / exposed	4 / 89 (4.49%)		
occurrences (all)	4		
Blood cholesterol increased			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Liver function test increased			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Blood uric acid increased			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Weight increased			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Hepatic enzyme increased			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Thyroid function test abnormal			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Foot Fracture			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Ankle fracture			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Contusion			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Fall			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Procedural pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Laceration			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Ligament sprain			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Tooth fracture			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Cardiac disorders			
Myocardial ischaemia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Nervous system disorders			

Amnesia				
subjects affected / exposed	2 / 89 (2.25%)			
occurrences (all)	2			
Head discomfort				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Aphasia				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Headache				
subjects affected / exposed	12 / 89 (13.48%)			
occurrences (all)	15			
Disturbance in attention				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	2			
Hypersomnia				
subjects affected / exposed	2 / 89 (2.25%)			
occurrences (all)	2			
Memory impairment				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Dizziness				
subjects affected / exposed	34 / 89 (38.20%)			
occurrences (all)	40			
Dysarthria				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Nervous system disorder				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Epilepsy				
subjects affected / exposed	4 / 89 (4.49%)			
occurrences (all)	4			
Paraesthesia				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			

Postictal headache			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	4		
Somnolence			
subjects affected / exposed	12 / 89 (13.48%)		
occurrences (all)	13		
Syncope			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Tension headache			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
seizure			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hypoaesthesia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Ear and labyrinth disorders			
Auditory disorder			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Meniere’s disease			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hypoacusis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Vertigo			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Vestibular disorder			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Eye disorders			
Blepharitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Conjunctivitis allergic			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	2		
Asthenopia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Posterior capsule opacification			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Abdominal pain			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	3		
Constipation			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Dental caries			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Gastric ulcer			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	4 / 89 (4.49%)		
occurrences (all)	6		
Dyspepsia			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Stomatitis			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	4		
Gingival pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	7		
Aphthous ulcer			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Gastritis erosive			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Gingival atrophy			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	2		
Photosensitivity reaction			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Psoriasis			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Dry skin			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 89 (3.37%)		
occurrences (all)	3		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	2 / 89 (2.25%)		
occurrences (all)	2		
Spinal osteoarthritis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Tenosynovitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Infections and infestations			

Angular cheilitis				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Gingivitis				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Enterocolitis viral				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Helicobacter infection				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Gastroenteritis				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Hordeolum				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	19 / 89 (21.35%)			
occurrences (all)	42			
Influenza				
subjects affected / exposed	2 / 89 (2.25%)			
occurrences (all)	2			
Pharyngitis				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Otitis externa				
subjects affected / exposed	2 / 89 (2.25%)			
occurrences (all)	2			
Otitis media chronic				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			
Sinusitis				
subjects affected / exposed	1 / 89 (1.12%)			
occurrences (all)	1			

Skin infection			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Tinea versicolour			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Trichophytosis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Tonsillitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Urethritis gonococcal			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Pyelonephritis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Otitis media			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Periodontitis			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Paronychia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hyperkalaemia			

subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hyperlipidaemia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Hypercholesterolaemia			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 89 (1.12%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 December 2017	Amendment 02: The purpose of this amendment was to add exclusion of subject who was diagnosed with dementia to clarify that dementia patients were not eligible in this study, concomitant use of antidementia drugs was prohibited and expand prohibited concomitant therapy to neuromodulation therapy (including vagal nerve stimulation and transcranial magnetic stimulation).
05 July 2018	Amendment 04: The purpose of this amendment was to add "Analysis at primary endpoint achievement" to conduct analysis at if the primary endpoint is achieved.
22 February 2019	Amendment 05: The purpose of this amendment was to add the End of Study Visit to clarify how to switch to the commercial product promptly.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported