Clinical trial results:
Multicenter, Open-Label Study to Evaluate the Efficacy and Safety of Perampanel as Monotherapy or First Adjunctive Therapy in Subjects With Partial Onset Seizures With or Without Secondarily Generalized Seizures or With Primary Generalized Tonic-Clonic Seizures

Summary

EudraCT number	2017-001180-20
Trial protocol	Outside EU/EEA
Global end of trial date	27 April 2021

Results information

Result version number	v1 (current)
This version publication date	13 November 2021
First version publication date	13 November 2021

Trial information

Trial identification

Sponsor protocol code	E2007-G000-410

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03288129
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Inc.
Sponsor organisation address	100 Tice Boulevard, Woodcliff Lake, New Jersey, United States, 07677
Public contact	Eisai Medical Information, Eisai Inc., 1 888-274-2378, esi_medinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., 1 888-274-2378, esi_medinfo@eisai.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	27 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 April 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the retention rate of perampanel when given as monotherapy or 1st adjunctive therapy in subjects with partial-onset seizures (POS) or primary generalized tonic clonic seizures (PGTCS).

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 - 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.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 August 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	United States: 54
Worldwide total number of subjects	54
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)	4
Adults (18-64 years)	44
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 14 investigative sites in the United States from 23 August 2017 to 27 April 2021.

Pre-assignment

Screening details:

A total of 68 subjects were screened, of which 55 were enrolled and 54 were treated with perampanel. The study consisted of 4 periods: Screening Period (to start no earlier than 6 weeks before the 1st dose of study drug), Titration Period (up to 13 weeks), Maintenance Period (39 weeks), and Follow up Period (4 weeks).

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Perampanel

Arm description:

The study treatment phase consisted of a Titration Period (up to 13 weeks) and a Maintenance Period (39 weeks) for up to a total of 52 weeks. Each subject received oral perampanel once daily at bedtime. During the Titration Period, the starting daily dose was 2 milligram (mg) for 2 weeks, then titrated to 4 mg for 2 weeks. Thereafter, further dose titrations in increments of 2 mg up to 12 mg were allowed based on the subject's response and tolerability and at the investigator's judgement. During the Maintenance Period, subjects continued to receive the perampanel dose level that was administered at the end of the Titration Period.

Arm type	Experimental
Investigational medicinal product name	Perampanel
Investigational medicinal product code	
Other name	Fycompa, E2007
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received oral perampanel once daily at bedtime. During the Titration Period, the starting daily dose was 2 mg for 2 weeks, then titrated to 4 mg for 2 weeks. Thereafter, further dose titrations in increments of 2 mg up to 12 mg were allowed based on the subject's response and tolerability and at the investigator's judgement. During the Maintenance Period, subjects continued to receive the perampanel dose level that was administered at the end of the Titration Period.

Number of subjects in period 1	Perampanel
Started	54
Completed	32
Not completed	22
Withdrawal of consent/assent	1
Adverse events leading to withdrawal	10
Unspecified	5

Lost to follow-up	3
Subject choice	3

Baseline characteristics

Reporting groups	
Reporting group title	Perampanel

Reporting group description:

The study treatment phase consisted of a Titration Period (up to 13 weeks) and a Maintenance Period (39 weeks) for up to a total of 52 weeks. Each subject received oral perampanel once daily at bedtime. During the Titration Period, the starting daily dose was 2 milligram (mg) for 2 weeks, then titrated to 4 mg for 2 weeks. Thereafter, further dose titrations in increments of 2 mg up to 12 mg were allowed based on the subject's response and tolerability and at the investigator's judgement. During the Maintenance Period, subjects continued to receive the perampanel dose level that was administered at the end of the Titration Period.

Reporting group values	Perampanel	Total	
Number of subjects	54	54	
Age Categorical Units: Subjects			
Adolescents (12-17 years)	4	4	
Adults (18-64 years)	44	44	
From 65-84 years	6	6	
Age Continuous Units: years			
arithmetic mean	38.5		
standard deviation	± 17.32	-	
Gender Categorical Units: subjects			
Female	27	27	
Male	27	27	
Ethnicity Units: Subjects			
Hispanic or Latino	7	7	
Not Hispanic or Latino	47	47	
Race (NIH/OMB) Units: Subjects			
White	42	42	
Black or African American	9	9	
Asian	1	1	
Other	2	2	

End points

End points reporting groups

Reporting group title	Perampanel

Reporting group description:

The study treatment phase consisted of a Titration Period (up to 13 weeks) and a Maintenance Period (39 weeks) for up to a total of 52 weeks. Each subject received oral perampanel once daily at bedtime. During the Titration Period, the starting daily dose was 2 milligram (mg) for 2 weeks, then titrated to 4 mg for 2 weeks. Thereafter, further dose titrations in increments of 2 mg up to 12 mg were allowed based on the subject's response and tolerability and at the investigator's judgement. During the Maintenance Period, subjects continued to receive the perampanel dose level that was administered at the end of the Titration Period.

Primary: Percentage of Subjects Remaining on Perampanel Treatment at 3 months After the Initiation of Treatment

End point title	Percentage of Subjects Remaining on Perampanel Treatment at 3 months After the Initiation of Treatment[1]

End point description:

The retention rate was defined as the percentage of subjects remaining on perampanel treatment at 3 months after the initiation of treatment. The Safety Analysis Set included 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:

Month 3

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: 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	54			
Units: percentage of subjects				
number (not applicable)	85.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Remaining on Perampanel Treatment at 6 months After the Initiation of Treatment

End point title	Percentage of Subjects Remaining on Perampanel Treatment at 6 months After the Initiation of Treatment[2]

End point description:

The retention rate was defined as the percentage of subjects remaining on perampanel treatment at 6 months after the initiation of treatment. The Safety Analysis Set included 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:

Month 6

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 statistics data was planned to be analyzed for this endpoint.

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percentage of subjects				
number (not applicable)	68.5			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Remaining on Perampanel Treatment at 12 months After the Initiation of Treatment

End point title	Percentage of Subjects Remaining on Perampanel Treatment at 12 months After the Initiation of Treatment[3]

End point description:

The retention rate was defined as the percentage of subjects remaining on perampanel treatment at 12 months after the initiation of treatment. The Safety Analysis Set included 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:

Month 12

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 statistics data was planned to be analyzed for this endpoint.

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percentage of subjects				
number (not applicable)	51.9			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects Remaining on Perampanel Treatment at 9 months After the Initiation of Treatment

End point title	Percentage of Subjects Remaining on Perampanel Treatment at 9 months After the Initiation of Treatment[4]

End point description:

The retention rate was defined as the percentage of subjects remaining on perampanel treatment at 9 months after the initiation of treatment. The Safety Analysis Set included 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:

Month 9

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 statistics data was planned to be analyzed for this endpoint.

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: percentage of subjects				
number (not applicable)	63.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved Seizure-free Status During the Maintenance Period

End point title	Percentage of Subjects who Achieved Seizure-free Status During the Maintenance Period

End point description:

Seizure-free status was defined as no incidence of seizure during the entire maintenance period. Partial seizures: when abnormal electrical activity begins in only one part of brain include (1) simple partial seizures: subject does not lose consciousness may experience muscle jerking or stiffening, (2) complex partial seizures: subject loses awareness. SGS: disturbances that spread to both sides of brain after partial seizure has already begun and happen when burst of electrical activity in limited area (the partial seizure) spreads throughout brain. PGTCS: disturbances in functioning of both sides of brain that caused by electrical signals spreading through brain inappropriately. The Full Analysis Set (FAS) included subjects who received at least 1 dose of study drug and had at least 1 postdose seizure measurement. Here "number analyzed" were subjects who were evaluable for the outcome measure at given time points.

End point type	Secondary

End point timeframe:

Up to 39 weeks in Maintenance Period

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of subjects				
number (not applicable)	19.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved 3-month Seizure-free Status

End point title	Percentage of Subjects who Achieved 3-month Seizure-free Status

End point description:

Seizure-free status was defined as no incidence of seizure at 3 months. Partial seizures: when abnormal electrical activity begins in only one part of brain include (1) simple partial seizures: subject does not lose consciousness may experience muscle jerking or stiffening, (2) complex partial seizures: subject loses awareness. SGS: disturbances that spread to both sides of brain after partial seizure has already begun and happen when burst of electrical activity in limited area (the partial seizure) spreads throughout brain. PGTCS: disturbances in functioning of both sides of brain that caused by electrical signals spreading through brain inappropriately. The FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose seizure measurement. Here "number analyzed" were subjects who were evaluable for the outcome measure at given time points.

End point type	Secondary

End point timeframe:

Up to Month 3 in Maintenance Period

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of subjects				
number (not applicable)	34.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Achieved 6-month Seizure-free Status

End point title	Percentage of Subjects who Achieved 6-month Seizure-free Status

End point description:

Seizure-free status was defined as no incidence of seizure at 6 months. Partial seizures: when abnormal electrical activity begins in only one part of brain include (1) simple partial seizures: subject does not lose consciousness may experience muscle jerking or stiffening, (2) complex partial seizures: subject loses awareness. SGS: disturbances that spread to both sides of brain after partial seizure has already begun and happen when burst of electrical activity in limited area (the partial seizure) spreads throughout brain. PGTCS: disturbances in functioning of both sides of brain that caused by electrical signals spreading through brain inappropriately. The FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose seizure measurement. Here "number analyzed" were subjects who were evaluable for the outcome measure at given time points.

End point type	Secondary

End point timeframe:

Up to Month 6 in Maintenance Period

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of subjects				
number (not applicable)	23.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects who Receive Perampanel as a First Adjunctive Therapy and Converted to Perampanel Monotherapy

End point title	Percentage of Subjects who Receive Perampanel as a First Adjunctive Therapy and Converted to Perampanel Monotherapy

End point description:

The number of subjects who receive perampanel as a first adjunctive therapy who were able to convert to perampanel monotherapy were reported. The FAS included subjects who received at least 1 dose of study drug and had at least 1 postdose seizure measurement. Here "number analyzed" were subjects who were evaluable for the outcome measure at given time points.

End point type	Secondary

End point timeframe:

Up to 39 weeks

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: percentage of subjects				
number (not applicable)	28.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAE)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAE)

End point description:

A treatment-emergent AE (TEAE) was defined as an AE that emerged during treatment, having been absent at pretreatment (Baseline) or reemerged during treatment, having been present at pretreatment (Baseline) but stopped before treatment, or worsened in severity during treatment relative to the pretreatment state, when the AE was continuous. The Safety Analysis Set included 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:

From date of first administration of study drug up to 28 days after last dose of study drug up to approximately 56 weeks

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: subjects	48			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment-emergent Serious Adverse Events (SAE)

End point title	Number of Subjects With Treatment-emergent Serious Adverse Events (SAE)

End point description:

A SAE was defined as any untoward medical occurrence that at any dose: resulted in death; was life-threatening; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; was a congenital anomaly/birth defect. A treatment-emergent AE was defined as an event that emerges during treatment having been absent pre-treatment, or worsens relative to the pre-treatment state. The Safety Analysis Set included 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:

From date of first administration of study drug up to 28 days after last dose of study drug up to approximately 56 weeks

End point values	Perampanel			
Subject group type	Reporting group			
Number of subjects analysed	54			
Units: subjects	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first administration of study drug up to 28 days after last dose of study drug up to approximately 56 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Perampanel

Reporting group description:

The study treatment phase consisted of a Titration Period (up to 13 weeks) and a Maintenance Period (39 weeks) for up to a total of 52 weeks. Each subject received oral perampanel once daily at bedtime. During the Titration Period, the starting daily dose was 2 mg for 2 weeks, then titrated to 4 mg for 2 weeks. Thereafter, further dose titrations in increments of 2 mg up to 12 mg were allowed based on the subject's response and tolerability and at the investigator's judgement. During the Maintenance Period, subjects continued to receive the perampanel dose level that was administered at the end of the Titration Period.

Serious adverse events	Perampanel		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 54 (7.41%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Transient ischaemic attack			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden unexplained death in epilepsy			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Suicidal ideation			

subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Depression			
subjects affected / exposed	1 / 54 (1.85%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Perampanel		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	47 / 54 (87.04%)		
Nervous system disorders			
Dizziness			
subjects affected / exposed	15 / 54 (27.78%)		
occurrences (all)	19		
Balance disorder			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	5 / 54 (9.26%)		
occurrences (all)	5		
Somnolence			
subjects affected / exposed	8 / 54 (14.81%)		
occurrences (all)	10		
Memory impairment			
subjects affected / exposed	3 / 54 (5.56%)		
occurrences (all)	3		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	9 / 54 (16.67%) 12		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 6 / 54 (11.11%) 6 4 / 54 (7.41%) 7		
Respiratory, thoracic and mediastinal disorders Oropharyngeal pain subjects affected / exposed occurrences (all)	 3 / 54 (5.56%) 3		
Psychiatric disorders Aggression subjects affected / exposed occurrences (all) Irritability subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	 3 / 54 (5.56%) 3 5 / 54 (9.26%) 6 3 / 54 (5.56%) 3		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Ear infection subjects affected / exposed occurrences (all)	 3 / 54 (5.56%) 4 5 / 54 (9.26%) 6 4 / 54 (7.41%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 April 2019	Amendment 01: Added number and location of study sites, and the number of subjects. Screening Period seizure requirements, the length of Titration Period were clarified. Updated minimum age for study inclusion. The requirements to support epilepsy diagnosis and analysis of efficacy endpoints were clarified. Updated exclusion criteria regarding concomitant therapies and procedures. Updated subject treatment during the follow-Up Period. Added fasting laboratory assessments at screening and last treatment visit. Updated Medical Monitor and Study Director information.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported