Clinical trial results:
A Double-Blind, Placebo-Controlled, Dose-Escalation, Parallel-Group Study to Evaluate the Efficacy and Safety of E2007 (Perampanel) Given as Adjunctive Therapy in Subjects With Refractory Partial Seizures

Summary

EudraCT number	2007-006191-11
Trial protocol	Outside EU/EEA
Global end of trial date	11 November 2010

Results information

Result version number	v1 (current)
This version publication date	30 May 2019
First version publication date	30 May 2019

Trial information

Trial identification

Sponsor protocol code	E2007-G000-304

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00699972
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Inc.
Sponsor organisation address	300 Tice Boulevard, Woodcliff Lake, United States, 07677
Public contact	Eisai Call Center, Eisai Inc., 888 422-4743,
Scientific contact	Eisai Call Center, Eisai Inc., 888 422-4743,

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	11 November 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 November 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of two doses of perampanel (8 and 12 mg) in comparison to placebo given as adjunctive therapy in subjects with refractory partial 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 Conference 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 Conference on Harmonisation 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).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 April 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 100
Country: Number of subjects enrolled	Canada: 25
Country: Number of subjects enrolled	Chile: 38
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	United States: 203
Worldwide total number of subjects	390
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)	40
Adults (18-64 years)	338
From 65 to 84 years	12
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 534 subjects were screened for entry into the study. Of 534 subjects, 147 were screen failures and 387 were eligible to continue in the study. A total of 390 subjects were randomized into the study; 387 who were eligible and 3 who failed screening but were inappropriately randomized (2 received study treatment and 1 did not).

Pre-assignment

Screening details:

This was a randomized, double-blind, placebo-controlled parallel-group study consisting of three phases: Prerandomization, Double-blind, and Follow-up. Subjects who experienced the required minimum number of seizures during the Prerandomization phase, entered the Double-blind Phase and were randomized to placebo or 8 or 12 mg perampanel groups.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Assessor

Blinding implementation details:

Placebo tablets were identical in appearance to active drug tablets. All study drugs were packaged and labeled so as to be indistinguishable between treatment groups. A master list of all treatments, and subject numbers associated with them, was maintained in a sealed envelope. If knowledge of a given treatment was required due to an emergency or for regulatory reporting of safety information, the blind would be broken via the code-break facility in the IVRS.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

6 placebo tablets received daily during both Titration and Maintenance Periods.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

6 placebo tablets received daily during both Titration and Maintenance Periods.

Arm title	Perampanel 8 mg

Arm description:

Perampanel 8 mg maximum daily dose (Titration from 2 mg to 8 mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks).

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

Dosage and administration details:

Treatment was administered orally once a day as 4 x 2-mg perampanel tablets plus 2 x placebo tablets before bedtime and with food.

Arm title	Perampanel 12 mg

Arm description:

Perampanel 12 mg maximum daily dose (Titration from 2 mg to 12 mg daily over 6-weeks; Maintenance at 12 mg daily over 13 weeks).

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

Dosage and administration details:

Treatment was administered orally once a day as 6 x 2-mg perampanel tablets plus 2 x placebo tablets before bedtime and with food.

Number of subjects in period 1[1]	Placebo	Perampanel 8 mg	Perampanel 12 mg
Started	121	133	134
Completed	106	114	100
Not completed	15	19	34
Adverse event, non-fatal	7	9	24
Administrative/Other	3	1	4
Inadequate therapeutic effect	2	-	2
Lost to follow-up	-	2	-
Subject choice	3	7	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: The number of subjects in the Baseline period are those who received the study treatment.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
6 placebo tablets received daily during both Titration and Maintenance Periods.	
Reporting group title	Perampanel 8 mg
Reporting group description:	
Perampanel 8 mg maximum daily dose (Titration from 2 mg to 8 mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks).	
Reporting group title	Perampanel 12 mg
Reporting group description:	
Perampanel 12 mg maximum daily dose (Titration from 2 mg to 12 mg daily over 6-weeks; Maintenance at 12 mg daily over 13 weeks).	

Reporting group values	Placebo	Perampanel 8 mg	Perampanel 12 mg
Number of subjects	121	133	134
Age categorical			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
<18 years	14	15	10
18-64 years	102	116	119
>64 years	5	2	5
Gender categorical			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
Female	67	68	65
Male	54	65	69
Race/Ethnicity, Customized			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
White	103	115	116
Black or African American	13	6	8
Asian	0	1	1
Chinese	0	1	1
American Indian or Alaska Native	0	4	2
Other	5	6	6

Reporting group values	Total		
Number of subjects	388		
Age categorical			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
<18 years	39		
18-64 years	337		
>64 years	12		

Gender categorical			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
Female	200		
Male	188		
Race/Ethnicity, Customized			
Safety Population used. One subject in Arm 1 and one subject in Arm 3 were randomized, but not treated.			
Units: Subjects			
White	334		
Black or African American	27		
Asian	2		
Chinese	2		
American Indian or Alaska Native	6		
Other	17		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
6 placebo tablets received daily during both Titration and Maintenance Periods.	
Reporting group title	Perampanel 8 mg
Reporting group description:	
Perampanel 8 mg maximum daily dose (Titration from 2 mg to 8 mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks).	
Reporting group title	Perampanel 12 mg
Reporting group description:	
Perampanel 12 mg maximum daily dose (Titration from 2 mg to 12 mg daily over 6-weeks; Maintenance at 12 mg daily over 13 weeks).	

Primary: 50 Percent (%) Responder Rate

End point title	50 Percent (%) Responder Rate[1]
End point description:	
A responder was a subject who had a 50 % or greater reduction in seizure frequency per 28 days from the Prerandomization phase. Analysis was carried out on the Full Intent-to-Treat (ITT) Analysis Set which included all randomized subjects who received study drug and had any seizure frequency data from the Double-blind Phase- Last Observation Carried Forward (LOCF).	
End point type	Primary
End point timeframe:	
Baseline (Pre-randomization) through Week 19	

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 in the end point.

End point values	Placebo	Perampanel 8 mg	Perampanel 12 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	121	133	133	
Units: percentage of subjects				
number (not applicable)				
Yes (Responder)	26.4	37.6	36.1	
No (Non-Responder)	73.6	62.4	63.9	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)

End point title	Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)

End point description:

Seizure frequency per 28 days was derived from the information recorded in the subject diaries. Analysis was carried out on the Full ITT Analysis Set.

End point type	Secondary

End point timeframe:

Baseline (Pre-randomization) through Week 19

End point values	Placebo	Perampanel 8 mg	Perampanel 12 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	121	133	133	
Units: Percent Change in seizure frequency				
median (full range (min-max))	-20.95 (-100 to 397.5)	-26.34 (-100 to 150.7)	-34.49 (-100 to 659.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change in the 28-day Complex Partial Plus Secondarily Generalized Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)

End point title	Percent Change in the 28-day Complex Partial Plus Secondarily Generalized Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)

End point description:

Percent Change in the Seizure frequency per 28 days was derived from the information recorded in the subject diaries. Analysis was carried out on the Full ITT Analysis Set.

End point type	Secondary

End point timeframe:

Baseline (Pre-randomization) through Week 19

End point values	Placebo	Perampanel 8 mg	Perampanel 12 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	120	120	
Units: Percent Change				
median (full range (min-max))	-17.88 (-100 to 653.5)	-33.03 (-100 to 150.7)	-33.06 (-100 to 1006.5)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time the subject signed the informed consent form to 30 days after the last dose of the study drug (approximately 2 years and 7 months)

Adverse event reporting additional description:

Adverse events (AE) were assessed at clinical visits based on the subject's diary, vitals, weight, physical exam, neurological exam, laboratory evaluations; and by telephone interviews/contact. Safety Population used which consists of subjects who were randomized to study drug, received study drug, and had at least one postdose safety assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	V. 13.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

6 placebo tablets received daily during both Titration and Maintenance Periods.

Reporting group title	Perampanel 12 mg

Reporting group description:

Perampanel 12 mg maximum daily dose (Titration from 2 mg to 12 mg daily over 6-weeks; Maintenance at
12 mg daily over 13-weeks).

Reporting group title	Perampanel 8 mg

Reporting group description:

Perampanel 8 mg maximum daily dose (Titration from 2 mg to 8 mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks).

Serious adverse events	Placebo	Perampanel 12 mg	Perampanel 8 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 121 (4.96%)	9 / 134 (6.72%)	8 / 133 (6.02%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Multiple drug overdose intentional			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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
Thermal burn			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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
Surgical and medical procedures			
Skin graft			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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
Nervous system disorders			
Grand mal convulsion			
subjects affected / exposed	1 / 121 (0.83%)	1 / 134 (0.75%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Presyncope			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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
Convulsion			
subjects affected / exposed	0 / 121 (0.00%)	2 / 134 (1.49%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	1 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Omental infarction			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aggression			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conversion disorder			

subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disorientation			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impulse-control disorder			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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
Psychotic disorder			
subjects affected / exposed	1 / 121 (0.83%)	0 / 134 (0.00%)	0 / 133 (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			
Osteoarthritis			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	1 / 133 (0.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Wound infection staphylococcal			
subjects affected / exposed	0 / 121 (0.00%)	0 / 134 (0.00%)	2 / 133 (1.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hyponatraemia			
subjects affected / exposed	0 / 121 (0.00%)	1 / 134 (0.75%)	0 / 133 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	Perampanel 12 mg	Perampanel 8 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	71 / 121 (58.68%)	98 / 134 (73.13%)	101 / 133 (75.94%)
Investigations			
Weight increased			
subjects affected / exposed	1 / 121 (0.83%)	4 / 134 (2.99%)	8 / 133 (6.02%)
occurrences (all)	1	5	8
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 121 (6.61%)	16 / 134 (11.94%)	13 / 133 (9.77%)
occurrences (all)	10	19	20
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 121 (0.00%)	16 / 134 (11.94%)	8 / 133 (6.02%)
occurrences (all)	0	18	9
Balance disorder			
subjects affected / exposed	1 / 121 (0.83%)	5 / 134 (3.73%)	10 / 133 (7.52%)
occurrences (all)	1	6	11
Dizziness			
subjects affected / exposed	12 / 121 (9.92%)	51 / 134 (38.06%)	50 / 133 (37.59%)
occurrences (all)	15	86	74
Headache			
subjects affected / exposed	16 / 121 (13.22%)	18 / 134 (13.43%)	20 / 133 (15.04%)
occurrences (all)	29	27	39

Somnolence			
subjects affected / exposed	16 / 121 (13.22%)	23 / 134 (17.16%)	24 / 133 (18.05%)
occurrences (all)	18	26	27
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 121 (4.13%)	11 / 134 (8.21%)	10 / 133 (7.52%)
occurrences (all)	5	11	22
Irritability			
subjects affected / exposed	6 / 121 (4.96%)	19 / 134 (14.18%)	10 / 133 (7.52%)
occurrences (all)	6	23	10
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 121 (0.00%)	7 / 134 (5.22%)	4 / 133 (3.01%)
occurrences (all)	0	14	5
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 121 (6.61%)	6 / 134 (4.48%)	9 / 133 (6.77%)
occurrences (all)	11	18	9
Nausea			
subjects affected / exposed	8 / 121 (6.61%)	8 / 134 (5.97%)	9 / 133 (6.77%)
occurrences (all)	9	8	12
Vomiting			
subjects affected / exposed	5 / 121 (4.13%)	7 / 134 (5.22%)	4 / 133 (3.01%)
occurrences (all)	5	7	4
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	3 / 121 (2.48%)	8 / 134 (5.97%)	6 / 133 (4.51%)
occurrences (all)	3	8	7
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 121 (2.48%)	7 / 134 (5.22%)	7 / 133 (5.26%)
occurrences (all)	3	9	7
Insomnia			
subjects affected / exposed	6 / 121 (4.96%)	8 / 134 (5.97%)	8 / 133 (6.02%)
occurrences (all)	7	8	9
Musculoskeletal and connective tissue disorders			

Myalgia			
subjects affected / exposed	3 / 121 (2.48%)	7 / 134 (5.22%)	2 / 133 (1.50%)
occurrences (all)	3	7	2
Infections and infestations			
Influenza			
subjects affected / exposed	8 / 121 (6.61%)	4 / 134 (2.99%)	6 / 133 (4.51%)
occurrences (all)	11	6	6
Nasopharyngitis			
subjects affected / exposed	6 / 121 (4.96%)	6 / 134 (4.48%)	10 / 133 (7.52%)
occurrences (all)	6	7	13

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 March 2009	In addition to minor administrative changes, the amendment made the following changes to the protocol: • Added evaluations of photosensitivity, withdrawal symptoms, pharmacogenomics tests as exploratory objectives, and added the photosensitivity and withdrawal questionnaires to the list of safety parameters to be evaluated • Clarified that QT interval was to be corrected (QTc) and specified that the QTc to be reported to the investigator by the central ECG laboratory would be QTcB • Defined the end of the study as the date of database lock to ensure that all data were collected, verified, and cleaned thoroughly following the last subject visit • Deleted text that advised subjects to minimize their exposure to sunlight and added text advising subjects who experienced light-related skin changes to discuss them with their doctor • Clarified how the urine drug screen results were to be used by the investigator • Specified that the investigator should review the subject diary with the subject at Visits 1 and 2 to ensure correct seizure classification • Included specific information about safety monitoring via the DMC • Clarified that urine microscopy was only to be performed as an unscheduled retest at the discretion of the investigator In addition, a letter sent on 8 Jan 2009 instructed all study sites to record all secondarily generalized seizures (simple or complex) under the "complex partial with secondarily generalized seizures" module in the CRFs, to comply with International League Against Epilepsy guidelines for data completeness.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported