To Evaluate The Efficacy and Safety of E2007 (Perampanel) Given as Adjunctive Therapy in Subjects With Refractory Partial Seizures

This study has been completed.

Sponsor:
Eisai Inc.

Information provided by (Responsible Party):
Eisai Inc.

ClinicalTrials.gov Identifier:
NCT00699582

First received: June 17, 2008
Last updated: June 26, 2014
Last verified: October 2012
History of Changes

Results First Received: October 23, 2012

Study Type:	Interventional
Study Design:	Allocation: Randomized; Endpoint Classification: Safety/Efficacy Study; Intervention Model: Parallel Assignment; Masking: Double Blind (Subject, Investigator); Primary Purpose: Treatment
Condition:	Refractory Partial Seizures
Interventions:	Drug: E2007 (perampanel) Drug: Placebo

Participant Flow

Hide Participant Flow

Recruitment Details

Key information relevant to the recruitment process for the overall study, such as dates of the recruitment period and locations
No text entered.

Pre-Assignment Details

Significant events and approaches for the overall study following participant enrollment, but prior to group assignment
No text entered.

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-

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

Participant Flow: Overall Study

	Placebo	Perampanel 8mg	Perampanel 12mg
STARTED	138	130	121
COMPLETED	120	108	93
NOT COMPLETED	18	22	28
Adverse Event	4	11	23
Withdrawal by Subject	6	7	4
Lack of Efficacy	1	0	1
Progressive Disease	1	0	0
Administrative/Other	4	3	0
Randomized, Not Treated	2	1	0

Baseline Characteristics

Hide Baseline Characteristics

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
No text entered.

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)
Total	Total of all reporting groups

Baseline Measures

	Placebo	Perampanel 8mg	Perampanel 12mg	Total
Overall Participants Analyzed [Units: Participants]	138	130	121	389
Age, Customized [Units: Participants]				
<18 years	17	17	10	44
18-64 years	120	110	109	339
>64 years	1	3	2	6
Gender [1] [Units: Participants]				

Female	**66**	**64**	**71**	**201**
Male	**72**	**66**	**50**	**188**

[1] For the placebo arm, there were 2 subjects who were randomized, but not treated. For the perampanel 8mg arm, there was 1 subject who was randomized, but not treated.

Race/Ethnicity, Customized [1] [Units: Participants]				
White	**117**	**108**	**100**	**325**
Black or African American	**1**	**2**	**1**	**4**
Asian	**12**	**14**	**16**	**42**
American Indian or Alaska Native	**1**	**0**	**0**	**1**
Other	**7**	**6**	**4**	**17**

[1] Race

Outcome Measures

Hide All Outcome Measures

1. Primary: Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases) [Time Frame: Baseline (Pre-randomization) through Week 19]

Measure Type	Primary
Measure Title	Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)
Measure Description	Seizure frequency per 28 days was derived from the information recorded in the subject diaries.
Time Frame	Baseline (Pre-randomization) through Week 19
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full Intent-to-Treat (ITT) Analysis Set - group of subjects who were randomized to study drug, received study drug, and had any seizure frequency data during the Doubleblind Phase. For Placebo arm, 2 subjects were randomized but not treated. For Perampanel 8mg arm, 1 subject was randomized but not treated.

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)

Measured Values

	Placebo	**Perampanel 8mg**	**Perampanel 12mg**
Participants Analyzed	**136**	**129**	**121**

[Units: Participants]			
Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases) [Units: Percent Change] Median (Full Range)	**-9.72** **(-91.8 to 404.3)**	**-30.52** **(-94.0 to 234.3)**	**-17.57** **(-100.0 to 858.3)**

No statistical analysis provided for Percent Change in the 28-day Seizure Frequency From Baseline to the End of the Double-blind Phase (Titration and Maintenance Phases)

2. Secondary: Responder Rate [Time Frame: Baseline (Pre-randomization) through Week 19]

Measure Type	Secondary
Measure Title	Responder Rate
Measure Description	The responder rate for the Full ITT Analysis Set from the maintenance LOCF (Last Observation Carried Forward). A responder was a subject who had a 50 percent or greater reduction in seizure frequency per 28 days from the Pre-randomization phase.
Time Frame	Baseline (Pre-randomization) through Week 19
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full ITT Analysis Set. For Placebo arm, 2 subjects were randomized but not treated. For Perampanel 8mg arm, 1 subject was randomized but not treated.

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)

Measured Values

	Placebo	**Perampanel 8mg**	**Perampanel 12mg**
Participants Analyzed [Units: Participants]	**136**	**129**	**121**
Responder Rate [Units: Percentage of Participants]			
Responders (Yes)	**14.7**	**33.3**	**33.9**
Non-Responders(No)	**85.3**	**66.7**	**66.1**

No statistical analysis provided for Responder Rate

3. 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) [Time Frame: Baseline (Pre-randomization) through Week 19]

Measure Type	Secondary
Measure 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)
Measure Description	Percent Change in the Seizure frequency per 28 days was derived from the information recorded in the subject diaries.
Time Frame	Baseline (Pre-randomization) through Week 19
Safety Issue	No

Population Description

Explanation of how the number of participants for analysis was determined. Includes whether analysis was per protocol, intention to treat, or another method. Also provides relevant details such as imputation technique, as appropriate.
Full ITT Analysis Set with Complex Partial plus Secondarily Generalized Seizures at Pre-randomization. For Placebo arm, 2 subjects were randomized but not treated. For Perampanel 8mg arm, 1 subject was randomized but not treated.

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)

Measured Values

	Placebo	**Perampanel 8mg**	**Perampanel 12mg**
Participants Analyzed [Units: Participants]	**126**	**119**	**113**
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) [Units: Percent Change] Median (Full Range)	**-8.05** **(-100.0 to 382.4)**	**-32.72** **(-100.0 to 1023.2)**	**-21.89** **(-100.0 to 733.3)**

No statistical analysis provided for 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)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	From the time the subject signed the informed consent form to 30 days after the last dose of the study drug.
Additional Description	Adverse events (AE) were assessed at clinical visits based on the subject's diary, vitals, weight, physical examination, neurological exam, and laboratory evaluations; and by telephone interviews/contact.

Reporting Groups

	Description

Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)

Serious Adverse Events

	Placebo	Perampanel 8mg	Perampanel 12mg
Total, serious adverse events			
# participants affected / at risk	**7/136 (5.15%)**	**10/129 (7.75%)**	**12/121 (9.92%)**
Blood and lymphatic system disorders			
Thrombocytopenia † 1			
# participants affected / at risk	**1/136 (0.74%)**	**0/129 (0.00%)**	**0/121 (0.00%)**
Gastrointestinal disorders			
Nausea † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**0/121 (0.00%)**
Haemorrhoids † 1			
# participants affected / at risk	**1/136 (0.74%)**	**0/129 (0.00%)**	**0/121 (0.00%)**
Infections and infestations			
Pneumonia † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**0/121 (0.00%)**
Injury, poisoning and procedural complications			
Facial bones fracture † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**1/121 (0.83%)**
Accidental overdose † 1			
# participants affected / at risk	**0/136 (0.00%)**	**0/129 (0.00%)**	**1/121 (0.83%)**
Head injury † 1			
# participants affected / at risk	**0/136 (0.00%)**	**0/129 (0.00%)**	**1/121 (0.83%)**
Radius fracture † 1			
# participants affected / at risk	**0/136 (0.00%)**	**0/129 (0.00%)**	**1/121 (0.83%)**
Skin laceration † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**0/121 (0.00%)**
Tibia fracture † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**0/121 (0.00%)**
Musculoskeletal and connective tissue disorders			
Periarthritis † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**0/121 (0.00%)**
Nervous system disorders			
Convulsion † 1			
# participants affected / at risk	**0/136 (0.00%)**	**2/129 (1.55%)**	**0/121 (0.00%)**
Dizziness † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**1/121 (0.83%)**
Somnolence † 1			
# participants affected / at risk	**0/136 (0.00%)**	**1/129 (0.78%)**	**1/121 (0.83%)**
† 1			

Headache			
# participants affected / at risk	1/136 (0.74%)	0/129 (0.00%)	1/121 (0.83%)
Ischaemic stroke † 1			
# participants affected / at risk	0/136 (0.00%)	1/129 (0.78%)	0/121 (0.00%)
Partial seizures with secondary generalisation † 1			
# participants affected / at risk	0/136 (0.00%)	1/129 (0.78%)	0/121 (0.00%)
Status epilepticus † 1			
# participants affected / at risk	1/136 (0.74%)	0/129 (0.00%)	1/121 (0.83%)
Epilepsy † 1			
# participants affected / at risk	1/136 (0.74%)	0/129 (0.00%)	0/121 (0.00%)
Psychiatric disorders			
Aggression † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Belligerence † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Psychotic disorder † 1			
# participants affected / at risk	0/136 (0.00%)	1/129 (0.78%)	0/121 (0.00%)
Conversion disorder † 1			
# participants affected / at risk	1/136 (0.74%)	0/129 (0.00%)	0/121 (0.00%)
Depression † 1			
# participants affected / at risk	1/136 (0.74%)	0/129 (0.00%)	0/121 (0.00%)
Renal and urinary disorders			
Cystitis haemorrhagic † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Urinary incontinence † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Reproductive system and breast disorders			
Ovarian mass † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Ovarian rupture † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)
Polycystic ovaries † 1			
# participants affected / at risk	0/136 (0.00%)	0/129 (0.00%)	1/121 (0.83%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA v13.1

Other Adverse Events

Hide Other Adverse Events

Time Frame	From the time the subject signed the informed consent form to 30 days after the last dose of the study drug.
Additional Description	Adverse events (AE) were assessed at clinical visits based on the subject's diary, vitals, weight, physical examination, neurological exam, and laboratory evaluations; and by telephone interviews/contact.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Placebo	No text entered.
Perampanel 8mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8mg daily over 13-weeks)
Perampanel 12mg	Perampanel 12mg maximum daily dose (Titration from 2mg to 12mg daily over 6-weeks; Maintenance at 12mg daily over 13-weeks)

Other Adverse Events

	Placebo	Perampanel 8mg	Perampanel 12mg
Total, other (not including serious) adverse events			
# participants affected / at risk	**55/136 (40.44%)**	**90/129 (69.77%)**	**90/121 (74.38%)**
Gastrointestinal disorders			
Constipation † 1			
# participants affected / at risk	**4/136 (2.94%)**	**4/129 (3.10%)**	**7/121 (5.79%)**
Nausea † 1			
# participants affected / at risk	**5/136 (3.68%)**	**11/129 (8.53%)**	**12/121 (9.92%)**
General disorders			
Fatigue † 1			
# participants affected / at risk	**11/136 (8.09%)**	**17/129 (13.18%)**	**20/121 (16.53%)**
Irritability † 1			
# participants affected / at risk	**5/136 (3.68%)**	**12/129 (9.30%)**	**11/121 (9.09%)**
Infections and infestations			
Nasopharyngitis † 1			
# participants affected / at risk	**9/136 (6.62%)**	**10/129 (7.75%)**	**5/121 (4.13%)**
Upper respiratory tract infection † 1			
# participants affected / at risk	**5/136 (3.68%)**	**9/129 (6.98%)**	**5/121 (4.13%)**
Injury, poisoning and procedural complications			
Fall † 1			
# participants affected / at risk	**4/136 (2.94%)**	**6/129 (4.65%)**	**9/121 (7.44%)**
Investigations			
Weight Increased † 1			
# participants affected / at risk	**3/136 (2.21%)**	**7/129 (5.43%)**	**7/121 (5.79%)**
Musculoskeletal and connective tissue disorders			
Back Pain † 1			
# participants affected / at risk	**2/136 (1.47%)**	**3/129 (2.33%)**	**7/121 (5.79%)**
Nervous system disorders			
Balance Disorder † 1			
# participants affected / at risk	**1/136 (0.74%)**	**7/129 (5.43%)**	**3/121 (2.48%)**
Convulsion † 1			
# participants affected / at risk	**7/136 (5.15%)**	**3/129 (2.33%)**	**5/121 (4.13%)**
Dizziness † 1			
# participants affected / at risk	**10/136 (7.35%)**	**41/129 (31.78%)**	**58/121 (47.93%)**

Headache † 1			
# participants affected / at risk	**17/136 (12.50%)**	**11/129 (8.53%)**	**15/121 (12.40%)**
Somnolence † 1			
# participants affected / at risk	**4/136 (2.94%)**	**16/129 (12.40%)**	**21/121 (17.36%)**

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA v13.1

Limitations and Caveats

Hide Limitations and Caveats

Limitations of the study, such as early termination leading to small numbers of participants analyzed and technical problems with measurement leading to unreliable or uninterpretable data

No text entered.

More Information

Hide More Information

Certain Agreements:

Principal Investigators are **NOT** employed by the organization sponsoring the study.

There is **NOT** an agreement between Principal Investigators and the Sponsor (or its agents) that restricts the PI's rights to discuss or publish trial results after the trial is completed.

Results Point of Contact:

Name/Title: Eisai Inc.
Organization: Eisai Call Center
phone: 888-422-4743

Publications automatically indexed to this study by ClinicalTrials.gov Identifier (NCT Number):

Rosenfeld W, Conry J, Lagae L, Rozentals G, Yang H, Fain R, Williams B, Kumar D, Zhu J, Laurenza A. Efficacy and safety of perampanel in adolescent patients with drug-resistant partial seizures in three double-blind, placebo-controlled, phase III randomized clinical studies and a combined extension study. Eur J Paediatr Neurol. 2015 Jul;19(4):435-45. doi: 10.1016/j.ejpn.2015.02.008.

Steinhoff BJ, Ben-Menachem E, Ryvlin P, Shorvon S, Kramer L, Satlin A, Squillacote D, Yang H, Zhu J, Laurenza A. Efficacy and safety of adjunctive perampanel for the treatment of refractory partial seizures: a pooled analysis of three phase III studies. Epilepsia. 2013 Aug;54(8):1481-9. doi: 10.1111/epi.12212.

French JA, Krauss GL, Steinhoff BJ, Squillacote D, Yang H, Kumar D, Laurenza A. Evaluation of adjunctive perampanel in patients with refractory partial-onset seizures: results of randomized global phase III study 305. Epilepsia. 2013 Jan;54(1):117-25. doi: 10.1111/j.1528-1167.2012.03638.x.

Responsible Party:	Eisai Inc.
ClinicalTrials.gov Identifier:	NCT00699582 History of Changes
Other Study ID Numbers:	E2007-G000-305 2007-006168-31 (EudraCT Number)
Study First Received:	June 17, 2008
Results First Received:	October 23, 2012
Last Updated:	June 26, 2014
Health Authority:	United States: Food and Drug Administration; European Union: European Medicines Agency