Evaluating 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:
NCT00700310

First received: June 17, 2008
Last updated: December 17, 2015
Last verified: November 2015
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: 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	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)

Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)

Participant Flow: Overall Study

	Placebo	Perampanel 2mg	Perampanel 4mg	Perampanel 8 mg
STARTED	187	180	174	171
COMPLETED	166	154	158	145
NOT COMPLETED	21	26	16	26
Adverse Event	6	10	5	11
Lost to Follow-up	4	1	0	1
Withdrawal by Subject	8	9	8	8
Lack of Efficacy	0	3	0	1
Administrative/Other	1	3	1	3
Randomized, Not Treated	2	0	2	2

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	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)
Total	Total of all reporting groups

Baseline Measures

	Placebo	Perampanel 2mg	Perampanel 4mg	Perampanel 8 mg	Total
Overall Participants Analyzed [Units: Participants]	185	180	172	169	706
Age, Customized [Units: Participants]					
<18 Years	14	21	13	12	60
18-64 Years	169	156	158	153	636
>64 Years	2	3	1	4	10

Gender [1] [Units: Participants]					
Female	90	95	84	92	361
Male	95	85	88	77	345

[1] The number of participants started is not consistant with the number of Baseline Participants due to 6 participants who were randomized in the study, but not treated with study drug.

Race/Ethnicity, Customized [1] [Units: Participants]					
White	119	119	105	116	459
Asian	34	35	37	28	134
Chinese	31	25	29	25	110
Other	1	1	1	0	3

[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 Double-blind Phase.

Reporting Groups

	Description
Placebo	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)

Measured Values

	Placebo	Perampanel 2mg	Perampanel 4mg	Perampanel 8 mg

Participants Analyzed [Units: Participants]	**184**	**180**	**172**	**169**
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)	**-10.69 (-100.0 to 420.6)**	**-13.63 (-100.0 to 346.3)**	**-23.33 (-100.0 to 416.0)**	**-30.80 (-100.0 to 390.6)**

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.

Reporting Groups

	Description
Placebo	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)

Measured Values

	Placebo	**Perampanel 2mg**	**Perampanel 4mg**	**Perampanel 8 mg**
Participants Analyzed [Units: Participants]	**184**	**180**	**172**	**169**
Responder Rate [Units: Percentage of Participants]				
Responders (Yes)	**17.9**	**20.6**	**28.5**	**34.9**
Non-Responders (No)	**82.1**	**79.4**	**71.5**	**65.1**

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

Reporting Groups

	Description
Placebo	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)

Measured Values

	Placebo	**Perampanel 2mg**	**Perampanel 4mg**	**Perampanel 8 mg**
Participants Analyzed [Units: Participants]	**169**	**167**	**157**	**154**
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)	**-17.63 (-100.0 to 602.9)**	**-20.50 (-100.0 to 13744.2)**	**-31.18 (-100.0 to 416.0)**	**-38.69 (-100.0 to 583.3)**

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 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	Placebo over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 2mg	Perampanel 2mg daily over 19-weeks (during 6-week Titration phase and 13-week Maintenance phase)
Perampanel 4mg	Perampanel 4mg maximum daily dose (Titration from 2mg to 4mg daily over 6-weeks; Maintenance at 4 mg daily over 13-weeks)
Perampanel 8 mg	Perampanel 8mg maximum daily dose (Titration from 2mg to 8mg daily over 6-weeks; Maintenance at 8 mg daily over 13-weeks)

Serious Adverse Events

	Placebo	Perampanel 2mg	Perampanel 4mg	Perampanel 8 mg
Total, serious adverse events				
# participants affected / at risk	**9/185 (4.86%)**	**6/180 (3.33%)**	**6/172 (3.49%)**	**6/169 (3.55%)**
Endocrine disorders				
Goitre [1]				
# participants affected / at risk	**0/185 (0.00%)**	**1/180 (0.56%)**	**0/172 (0.00%)**	**0/169 (0.00%)**
Eye disorders				
Conjunctivitis allergic [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**1/172 (0.58%)**	**0/169 (0.00%)**
Iritis [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**1/172 (0.58%)**	**0/169 (0.00%)**
Hepatobiliary disorders				
Cholelithiasis [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**1/172 (0.58%)**	**0/169 (0.00%)**
Infections and infestations				
Appendicitis [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**
Wound infection [1]				
# participants affected / at risk	**1/185 (0.54%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**
Bronchitis [1]				
# participants affected / at risk	**1/185 (0.54%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**0/169 (0.00%)**
Orchitis [1]				
# participants affected / at risk	**1/185 (0.54%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**0/169 (0.00%)**
Injury, poisoning and procedural complications				
Ankle fracture [1]				
# participants affected / at risk	**0/185 (0.00%)**	**1/180 (0.56%)**	**0/172 (0.00%)**	**0/169 (0.00%)**
Contusion [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**
Head injury [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**
Post concussion syndrome [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**
Rib fracture [1]				
# participants affected / at risk	**0/185 (0.00%)**	**0/180 (0.00%)**	**0/172 (0.00%)**	**1/169 (0.59%)**

Road traffic accident [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Traumatic brain injury [1]				
# participants affected / at risk	1/185 (0.54%)	0/180 (0.00%)	0/172 (0.00%)	0/169 (0.00%)
Metabolism and nutrition disorders				
Diabetes mellitus [1]				
# participants affected / at risk	1/185 (0.54%)	0/180 (0.00%)	0/172 (0.00%)	0/169 (0.00%)
Musculoskeletal and connective tissue disorders				
Bone erosion [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Soft tissue necrosis [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Benign lung neoplasm [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Nervous system disorders				
Convulsion [1]				
# participants affected / at risk	3/185 (1.62%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Dizziness [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Epilepsy [1]				
# participants affected / at risk	1/185 (0.54%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Simple partial seizures [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Somnolence [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Tremor [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	1/172 (0.58%)	0/169 (0.00%)
Grand mal convulsion [1]				
# participants affected / at risk	1/185 (0.54%)	0/180 (0.00%)	0/172 (0.00%)	0/169 (0.00%)
Transient ischaemic attack [1]				
# participants affected / at risk	1/185 (0.54%)	0/180 (0.00%)	0/172 (0.00%)	0/169 (0.00%)
Psychiatric disorders				
Aggression [1]				
# participants affected / at risk	0/185 (0.00%)	1/180 (0.56%)	0/172 (0.00%)	0/169 (0.00%)
Confusional state [1]				
# participants affected / at risk	0/185 (0.00%)	1/180 (0.56%)	0/172 (0.00%)	0/169 (0.00%)
Delirium [1]				
# participants affected / at risk	0/185 (0.00%)	1/180 (0.56%)	0/172 (0.00%)	0/169 (0.00%)
Renal and urinary disorders				
Nephrolithiasis [1]				
# participants affected / at risk	0/185 (0.00%)	1/180 (0.56%)	0/172 (0.00%)	0/169 (0.00%)
Skin and subcutaneous tissue disorders				
[1]				

Ecchymosis				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Surgical and medical procedures				
Medical device removal [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)
Vascular disorders				
Aortic stenosis [1]				
# participants affected / at risk	0/185 (0.00%)	0/180 (0.00%)	0/172 (0.00%)	1/169 (0.59%)

1 Term from vocabulary, MedDRA V. 13.0

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

Other Adverse Events

	Placebo	Perampanel 2mg	Perampanel 4mg	Perampanel 8 mg
Total, other (not including serious) adverse events				
# participants affected / at risk	48/185 (25.95%)	61/180 (33.89%)	66/172 (38.37%)	79/169 (46.75%)
General disorders				
Fatigue [1]				
# participants affected / at risk	5/185 (2.70%)	8/180 (4.44%)	13/172 (7.56%)	9/169 (5.33%)
Gait disturbance [1]				
# participants affected / at risk	2/185 (1.08%)	1/180 (0.56%)	2/172 (1.16%)	9/169 (5.33%)
Infections and infestations				
Nasopharyngitis [1]				
# participants affected / at risk	3/185 (1.62%)	7/180 (3.89%)	9/172 (5.23%)	3/169 (1.78%)
Upper respiratory tract infection [1]				
# participants affected / at risk	5/185 (2.70%)	11/180 (6.11%)	6/172 (3.49%)	3/169 (1.78%)

Nervous system disorders				
Dizziness [1]				
# participants affected / at risk	**18/185 (9.73%)**	**18/180 (10.00%)**	**28/172 (16.28%)**	**45/169 (26.63%)**
Headache [1]				
# participants affected / at risk	**16/185 (8.65%)**	**16/180 (8.89%)**	**19/172 (11.05%)**	**18/169 (10.65%)**
Somnolence [1]				
# participants affected / at risk	**12/185 (6.49%)**	**22/180 (12.22%)**	**15/172 (8.72%)**	**27/169 (15.98%)**

1 Term from vocabulary, MedDRA V. 13.0

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.

Krauss GL, Serratosa JM, Villanueva V, Endziniene M, Hong Z, French J, Yang H, Squillacote D, Edwards HB, Zhu J, Laurenza A. Randomized phase III study 306: adjunctive perampanel for refractory partial-onset seizures. Neurology. 2012 May 1;78(18):1408-15. doi: 10.1212/WNL.0b013e318254473a.

Responsible Party:	Eisai Inc.
ClinicalTrials.gov Identifier:	NCT00700310 History of Changes
Other Study ID Numbers:	E2007-G000-306 2007-006169-33 (EudraCT Number)
Study First Received:	June 17, 2008
Results First Received:	October 23, 2012
Last Updated:	December 17, 2015

Health Authority:	European Union: European Medicines Agency United States: Food and Drug Administration

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