Efficacy, Safety and Tolerability of E2007 in Levodopa Treated Parkinson's Disease Patients With Motor Fluctuations

This study has been terminated.

(Study stopped due to lack of efficacy.)

Sponsor:
Eisai Limited

Information provided by (Responsible Party):
Eisai Inc. (Eisai Limited)

ClinicalTrials.gov Identifier:
NCT00360308

First received: August 2, 2006
Last updated: June 26, 2014
Last verified: August 2013
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:	Parkinson's Disease
Interventions:	Drug: Placebo Drug: E2007

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 identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Participant Flow: Overall Study

	Placebo	Entacapone	Perampanel
STARTED	**247**	**234**	**242**
COMPLETED	**171**	**155**	**154**
NOT COMPLETED	**76**	**79**	**88**
Adverse Event	**15**	**14**	**25**
Abnormal Laboratory Value(s)	**0**	**1**	**0**
Protocol Violation	**2**	**1**	**2**
Withdrawal by Subject	**11**	**7**	**14**
Lack of Efficacy	**3**	**0**	**2**
Not Specified	**2**	**1**	**1**
Study termination by sponsor	**43**	**55**	**44**

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 identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Total	Total of all reporting groups

Baseline Measures

	Placebo	Entacapone	Perampanel	Total
Overall Participants Analyzed [Units: Participants]	**247**	**234**	**242**	**723**
Age, Customized [Units: Participants]				
<65 years	**131**	**114**	**123**	**368**
≥65 years	**116**	**120**	**119**	**355**

Gender [1] [Units: Participants]				
Female	98	98	94	290
Male	149	136	148	433

[1] Safety Population was used. The safety population includes the same number of subjects as the Randomized Population except 1 additional subject in the placebo group who was not randomized, but completed the study.

Race/Ethnicity, Customized [1] [Units: Participants]				
White	191	176	185	552
Asian	55	57	57	169
Other	1	1	0	2

[1] Race.

Outcome Measures

Hide All Outcome Measures

1. Primary: Mean Change From Baseline in Total Daily OFF Time (Hours) to Week 18 (Including LOCF Data) [Time Frame: Baseline and Week 18]

Measure Type	Primary
Measure Title	Mean Change From Baseline in Total Daily OFF Time (Hours) to Week 18 (Including LOCF Data)
Measure Description	Efficacy assessments were recorded by subjects using a home diary card. ON state is when medication is providing benefits to mobility, slowness, and stiffness. OFF state is when medication has worn off and is no longer providing benefits with regard to stiffness, slowness, and tremor.
Time Frame	Baseline and Week 18
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.
The Intent-to-Treat (ITT) Population comprised all randomised patients who took at least one dose of study medication or placebo and who had a valid baseline efficacy measure and at least one post-baseline efficacy measure.

Reporting Groups

	Description
Placebo	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Measured Values

	Placebo	Entacapone	Perampanel
Participants Analyzed			

[Units: Participants]	228	221	213
Mean Change From Baseline in Total Daily OFF Time (Hours) to Week 18 (Including LOCF Data) [Units: Hours] Least Squares Mean (95% Confidence Interval)	**-0.82 (-1.16 to -0.48)**	**-1.29 (-1.63 to -0.96)**	**-0.92 (-1.27 to -0.57)**

No statistical analysis provided for Mean Change From Baseline in Total Daily OFF Time (Hours) to Week 18 (Including LOCF Data)

2. Secondary: Mean Change From Baseline in UPDRS Part II (ADL) Score in Total Daily OFF Time to Week 18 (Including LOCF Data) [Time Frame: Baseline and Week 18]

Measure Type	Secondary
Measure Title	Mean Change From Baseline in UPDRS Part II (ADL) Score in Total Daily OFF Time to Week 18 (Including LOCF Data)
Measure Description	Efficacy assessments were recorded by subjects using a home diary card. Unified Parkinson's Disease (PD) Rating Scale (UPDRS) is a standardized assessment of the symptoms and signs of PD. Part II assesses Activities of Daily Living (ADL) based on 13 items, such as speech, hygiene, and falling. Participants receive a score of 0-4 points per item, with a higher score indicating more severe symptoms. OFF state is when medication has worn off and is no longer providing benefits with regard to stiffness, slowness, and tremor.
Time Frame	Baseline and Week 18
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.
ITT Population

Reporting Groups

	Description
Placebo	The total number of subjects reflects 3 fewer subjects due to inavailability of the data
Entacapone	The total number of subjects reflects 5 fewer subjects due to inavailability of the data
Perampanel	The total number of subjects reflects 3 fewer subjects due to inavailability of the data

Measured Values

	Placebo	**Entacapone**	**Perampanel**
Participants Analyzed [Units: Participants]	**215**	**210**	**199**
Mean Change From Baseline in UPDRS Part II (ADL) Score in Total Daily OFF Time to Week 18 (Including LOCF Data) [Units: Scores on a scale] Least Squares Mean (95% Confidence Interval)	**-1.42 (-2.04 to -0.80)**	**-2.50 (-3.11 to -1.90)**	**-1.06 (-1.70 to -0.42)**

No statistical analysis provided for Mean Change From Baseline in UPDRS Part II (ADL) Score in Total Daily OFF Time to Week 18 (Including LOCF Data)

3. Secondary: Mean Change From Baseline in UPDRS Part III (Motor) Score in ON State (Hours) to Week 18 (Including LOCF Data) [Time

Frame: Baseline and Week 18]

Measure Type	Secondary
Measure Title	Mean Change From Baseline in UPDRS Part III (Motor) Score in ON State (Hours) to Week 18 (Including LOCF Data)
Measure Description	Efficacy assessments were recorded by subjects using a home diary card. UPDRS is a standardized assessment of the symptoms and signs of PD. Part III assesses motor activity, based on 14 items, such as gait, facial expression, and rigidity. Participants receive a score of 0-4 points per item, with a higher score indicating more severe symptoms. ON state is when medication is providing benefits to stiffness, slowness, and tremor.
Time Frame	Baseline and Week 18
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.
ITT Population

Reporting Groups

	Description
Placebo	The total number of subjects reflects 1 fewer subject due to inavailability of the data
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Measured Values

	Placebo	**Entacapone**	**Perampanel**
Participants Analyzed [Units: Participants]	**217**	**215**	**202**
Mean Change From Baseline in UPDRS Part III (Motor) Score in ON State (Hours) to Week 18 (Including LOCF Data) [Units: Scores on a scale] Least Squares Mean (95% Confidence Interval)	**-1.20** **(-2.12 to -0.29)**	**-3.08** **(-3.97 to -2.19)**	**-1.67** **(-2.61 to -0.73)**

No statistical analysis provided for Mean Change From Baseline in UPDRS Part III (Motor) Score in ON State (Hours) to Week 18 (Including LOCF Data)

4. Secondary: Mean Change From Baseline in Total Daily ON Time (Without Dyskinesias or With Non-troublesome Dyskinesias) (Hours) to Week 18 (Including LOCF Data) [Time Frame: Baseline and Week 18]

Measure Type	Secondary
Measure Title	Mean Change From Baseline in Total Daily ON Time (Without Dyskinesias or With Non-troublesome Dyskinesias) (Hours) to Week 18 (Including LOCF Data)
Measure Description	Efficacy assessments were recorded by subjects using a home diary card. ON state is when medication is providing benefits to stiffness, slowness, and tremor.
Time Frame	Baseline and Week 18
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.
ITT Population

Reporting Groups

	Description
Placebo	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Measured Values

	Placebo	Entacapone	Perampanel
Participants Analyzed [Units: Participants]	**228**	**221**	**213**
Mean Change From Baseline in Total Daily ON Time (Without Dyskinesias or With Non-troublesome Dyskinesias) (Hours) to Week 18 (Including LOCF Data) [Units: Hours] Least Squares Mean (95% Confidence Interval)	**0.88** **(0.52 to 1.24)**	**1.10** **(0.74 to 1.46)**	**0.47** **(0.10 to 0.84)**

No statistical analysis provided for Mean Change From Baseline in Total Daily ON Time (Without Dyskinesias or With Non-troublesome Dyskinesias) (Hours) to Week 18 (Including LOCF Data)

Serious Adverse Events

Hide Serious Adverse Events

Time Frame	Adverse events (AEs) were recorded from the time that the participant signed the informed consent form until 30 days after study drug discontinuation and through the termination visit, whichever is longer.
Additional Description	All AEs were reported on a case report form (CRF). AEs were recorded on subject diaries and by investigators during clinical visits.

Reporting Groups

	Description
Placebo	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Serious Adverse Events

	Placebo	Entacapone	Perampanel

Total, serious adverse events			
# participants affected / at risk	6/247 (2.43%)	8/234 (3.42%)	11/242 (4.55%)
Cardiac disorders			
Coronary Artery Disease † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	1/242 (0.41%)
Angina Unstable † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Cardiopulmonary Failure † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Gastrointestinal disorders			
Dyspepsia † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Infections and infestations			
Cellulitis † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	1/242 (0.41%)
Otitis Media † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Pneumonia † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Urinary Tract Infection † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	0/242 (0.00%)
Injury, poisoning and procedural complications			
Femoral Neck Fracture † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	1/242 (0.41%)
Hip Fracture † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	1/242 (0.41%)
Humerus Fracture † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Back Injury † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Head Injury † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Rib Fracture † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	0/242 (0.00%)
Metabolism and nutrition disorders			
Dehydration † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	0/242 (0.00%)
Musculoskeletal and connective tissue disorders			
Back Pain † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Uterine Leiomyoma † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Nervous system disorders			

Cerebrovascular Accident † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Dyskinesia † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
On and Off Phenomenon † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Transient Ischaemic Attack † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Psychiatric disorders			
Confusional State † 1			
# participants affected / at risk	0/247 (0.00%)	0/234 (0.00%)	1/242 (0.41%)
Psychotic Disorder † 1			
# participants affected / at risk	0/247 (0.00%)	1/234 (0.43%)	0/242 (0.00%)
Renal and urinary disorders			
Renal Colic † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	0/242 (0.00%)
Vascular disorders			
Hypertensive Crisis † 1			
# participants affected / at risk	1/247 (0.40%)	0/234 (0.00%)	0/242 (0.00%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA V. 10.0

Other Adverse Events

Hide Other Adverse Events

Time Frame	Adverse events (AEs) were recorded from the time that the participant signed the informed consent form until 30 days after study drug discontinuation and through the termination visit, whichever is longer.
Additional Description	All AEs were reported on a case report form (CRF). AEs were recorded on subject diaries and by investigators during clinical visits.

Frequency Threshold

Threshold above which other adverse events are reported	5

Reporting Groups

	Description
Placebo	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.
Entacapone	Placebo identical to perampanel (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as one entacapone 200 mg dose with each dose of levodopa.
Perampanel	Perampanel 2 mg (Weeks 0 to 2 one dose per day, Weeks 2 to 18 two doses per day); as well as a placebo identical to entacapone with each dose of levodopa.

Other Adverse Events

	Placebo	Entacapone	Perampanel
Total, other (not including serious) adverse events			

# participants affected / at risk	39/247 (15.79%)	63/234 (26.92%)	66/242 (27.27%)
Gastrointestinal disorders			
Nausea † 1			
# participants affected / at risk	9/247 (3.64%)	16/234 (6.84%)	9/242 (3.72%)
Nervous system disorders			
Dizziness † 1			
# participants affected / at risk	7/247 (2.83%)	9/234 (3.85%)	21/242 (8.68%)
Dyskinesia † 1			
# participants affected / at risk	8/247 (3.24%)	27/234 (11.54%)	17/242 (7.02%)
On and Off phenomenon † 1			
# participants affected / at risk	16/247 (6.48%)	19/234 (8.12%)	19/242 (7.85%)
Somnolence † 1			
# participants affected / at risk	4/247 (1.62%)	8/234 (3.42%)	17/242 (7.02%)

† Events were collected by systematic assessment
1 Term from vocabulary, MedDRA V. 10.0

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

Responsible Party: Eisai Inc. (Eisai Limited)
ClinicalTrials.gov Identifier: NCT00360308 History of Changes
Other Study ID Numbers: E2007-G000-309
2006-002937-20 (EudraCT Number)
Study First Received: August 2, 2006
Results First Received: October 23, 2012
Last Updated: June 26, 2014
Health Authority: European Union: European Medicines Agency

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