A 4-Year Open-Label Extension (OLE) Phase of the Double-Blind, Placebo-Controlled, Dose-Escalation, Parallel-Group Study of E2007 as an Adjunctive Therapy in Patients With Refractory Partial Seizures

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To evaluate the safety of E2007 given as adjunctive, long-term treatment in patients with refractory partial onset seizures with or without secondary generalization that completed the E2007-A001-206 or the E2007-G000-208 studies (revised per...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Movement disorders (incl parkinsonism)
Study type	Interventional

Summary

ID

NL-OMON38093

Source
ToetsingOnline

Brief title
OLE 207

Condition

- Movement disorders (incl parkinsonism)

Synonym
Epilepsy, uncontrolled seizures

Research involving

Human

Sponsors and support

Primary sponsor: Eisai
Source(s) of monetary or material Support: Farmaceutisch bedrijf: Eisai

Intervention

Keyword: OLE, Refractory, Seizures

Outcome measures

Primary outcome

Safety will be assessed by the nature, frequency, and intensity of adverse

events, vital signs, clinical laboratory tests, physical and neurological

examinations, and 12-lead ECGs.

Secondary outcome

Efficacy will be assessed by the change in partial seizure frequency from

Baseline in the E2007-A001-206 or the E2007-G000-208 studies to the OLE

Maintenance Phase.

Study description

Background summary

See page 24 of the protocol.
Refractory epilepsy with uncontrolled seizures often leads to significant life-style limitations and social handicaps. The required long-term pharmacological management also affects the patients' quality of life.
Over the past 15 years, several new AEDs have been developed to improve the treatment of these patients, compared to the classical AEDs. However, based on current date, clinicians feel that ther are still unmet needs in the pharmacological treatment need.As a consequence, the need for newer drugs with improved efficacy and tolerability profiles remains.
E2007 is a potent, orally active, non-competetive, and highly selective AMPA receptor antagonist. It is currently under development for the treatment of

Parkinson's disease, epilepsy, mutiple sclerosis, and migraine.

Study objective

To evaluate the safety of E2007 given as adjunctive, long-term treatment in patients with refractory partial onset seizures with or without secondary generalization that completed the E2007-A001-206 or the E2007-G000-208 studies (revised per Amendment 04).

Study design

For those patients who have completed E2007-G000-208 study, the 207 study will consist of the following phases during the OLE:
•OLE Titration Phase (12 weeks): Scheduled visits will be conducted every two weeks for 12 weeks. Titration will be made in 2 weeks intervals, on the basis of individual tolerance and in 2 mg incremental steps (ie, the patients will titrate from 2 mg to 4 mg to 6 mg to 8 mg to 10 mg to 12 mg).
•OLE Maintenance Phase (208 weeks): Scheduled visits will be conducted one month following the completion of OLE titration phase and every 3 months thereafter for a total of 208 weeks. During this phase, patients will continue the highest tolerated dose of E2007 that was established during the OLE Titration Phase.
•OLE Follow-up Phase (one visit): The purpose of this visit (Week 224) is a four-week follow up after the last dose of study drug was administered.

The amended text on the study design conform protocol Amendment 8 dd 26 Juni 12 is stated below:
•At the end of the study (after EU Marketing Authorisation Approval in the EU countries and after launch in the US), study personnel will schedule an EOT visit for patients to occur within 4 weeks.

Intervention

For patients who have completed E2007-G000-208 study:

The E2007 dose will be titrated up from 2 mg once daily for 2 weeks, then 4 mg once daily for 2 weeks, then 6mg once daily for 2 weeks, then 8 mg once daily for 2 weeks, then 10 mg once daily for 2 weeks, then 12 mg once daily for 2 weeks, on the basis of individual tolerance. The patients will then continue the highest tolerated dose achieved for a total of 208 weeks during the OLE maintenance phase.

Study burden and risks

Conform the patient information and consent form 'Master 8.0 (09JUL12)] NL V 8.0 (02AUG2012)' below the known side effects and risks that could occur

during treatment of perampanel are mentioned. This text is literally taken from the aforementioned patient information and consent form and therefore written in third person.

Very common side effects which may affect more than 1 user in 10 are:

• Feeling dizzy (dizziness)
• Feeling sleepy (somnolence)

Common side effects which may affect more than 1 user in 100 are:

• Spinning sensation (vertigo)
• Blurred vision
• Feeling sick (nausea)
• Feeling very tired (fatigue)
• Irritability
• Weight gain
• Decreased appetite
• Back pain
• Difficulty with walking (ataxia)
• Unsteady gait (gait disturbance)
• Balance problems (balance disorder)
• Falling down (fall)
• Slow speech (dysarthria)
• Anxiety
• Double vision (diplopia)
• Increased appetite
• Aggression
• Anger

Side effects and risks.
Antiepileptics, including perampanel, may increase the risk of suicidal thinking and behaviour. Patients, their caregivers, and families should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behaviour, or the emergence of suicidal thoughts, behaviour, or thoughts about self-harm. Behaviours of concern should be reported immediately to the study doctor.

As with many drugs that affect the brain, perampanel may cause dizziness and sleepiness and therefore may influence the ability to drive or use machines. Subjects are advised not to drive, operate complex machinery or engage in other potentially hazardous activities until it is known whether perampanel affects their ability to perform these tasks.

Using alcohol or other medications that cause sleepiness while taking perampanel can make you less alert and impair your ability to drive or use machinery. They can also worsen your feelings of anger, confusion and sadness.

Speak to your doctor before using alcohol or other medications

There is no information about the safety of perampanel in pregnant women. Pregnant woman must therefore not take part in this study, neither should women who plan to become pregnant during the study. Women who are at risk of pregnancy will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. If you are a female and capable of becoming pregnant, you must continue to use a reliable form of contraception for the duration of the study (i.e. abstinence, intrauterine device (IUD), condom and spermicide) and for 60 days after your last dose of study drug. If you become pregnant while taking part in the study, please inform your study doctor immediately.

Perampanel may make certain hormonal contraceptives containing levonorgestrel less effective. Under this circumstance, an additional form of safe and effective contraception (such as a condom or coil) is recommended when taking perampanel and should continue for one month after stopping treatment. The study doctor will be able to advise on the best contraception method.

It is not known whether perampanel can pass into breast milk. Females that are breasfeeding must therefore not take part in this study.

There may also be a risk of an allergic reaction to perampanel or its inactive ingredients. You should notify the study doctor immediately if you experience allergy symptoms such as a rash, hives, swelling, difficulty breathing, wheezing, sudden drop in blood pressure, fast pulse, sweating, or itching. Untreated allergic symptoms may lead to a life-threatening medical emergency.

Drawing Blood: May cause local pain, bruising, bleeding, blood clot formation, and, in rare instances, an infection might occur at the site where blood is drawn. There is also the possibility of dizziness or fainting while your blood is being drawn. The decision to use a catheter (narrow tube) for blood collecting may be made by the study staff. They will explain the catheter to you if its use is necessary.

Making an ECG: The ECG (electrocardiogram) is a procedure that requires you to lie still for a few minutes, while electrodes are attached to your chest to record the activity of your heart. The ECG leads placed on your skin may cause slight discomfort during their placement and removal.

As perampanel is an investigational drug, there is no guarantee that the study drug will improve your seizure control. You may also experience symptoms because of your participation in this study that you would not have otherwise experienced.

If any new information about perampanel that may impact your safety or willingness to participate in the study is discovered during the course of the

trial, you will be notified in a timely manner. If you experience any side effects described here, or if you have any other new symptoms during your participation in the study, please contact your study doctor immediately. Please be sure to mention any concerns or questions that you have regarding your health during your study visits or study phone calls and remember that you are free to call the study site at anytime should you be concerned.

Contacts

Public
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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Provide written informed consent signed by the patient or legal guardian prior to entering the OLE study or undergoing any study procedures.
2. Have completed all scheduled visits up to and including Visit 8 in the E2007-A001-206 study or Visit 9 of the E2007-G000-208 study.

3. Are reliable and willing to make themslves available for the study period ans are able to record seizures and report adverse events themselves or have a caregiver who can record and report the events.
4. Male and female patients will be eligible for enrollment. Females of childbearing potential must continue practicing a medically acceptable method of contraception (eg. a barrier method plus spermicide, or IUD) and for two months after the end of the OLE study. tThose women using hormonal contraceptive must also continue using an additional approved method of contraception (eg. a barrier method plus spermicide, or IUD) starting with the Titration Phase and continuing throughout the entire study period (revised per Amendment 2)
5. Are between the ages of 18 and 70 years of age, inclusive.
6. Are at least 40 kg (88lb) of weight.
7. Are currently being treated with a stable dose of one, or a maximum of three, marketed and approved AEDs and are known to take their medication(s) as directed (revised per Amendment 4).

Exclusion criteria

1. Show evidence of clinically significant disease (cardiac, respiratory, gastrointestinal, renal disease, etc.) that in the opinion of the Investigator(s) could affect the patient's safety or trial conduct.
2. Show evidence of significant active hepatic disease and/or bilirubin > 1.5 mg/dL. Stable elevations of liver enzymes, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) due to concomitant medication(s) will be allowed if they are less then two times the upper limit of normal (ULN).
3. Show evidence of significant active hematological disease. White blood cell (WBC) count cannot be (<=2500/microliter (2.50 1E+09/L) or an absolute neutrophil count <=1000/microliter (1.00 1E+09/L) (revised per Amendment 3)
4. Clinically significant ECG abnormality, including prolonged QTc (defined as>=450 msec) (revised per Amendments 03 and 04)
5. Presence of major active psychiatric disease. Patients taking a stable dose of selective serotonin reuptake inhibitor (SSRI) antidepressant will be allowed (revised per Amendment 03)

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2007
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	na
Generic name:	MARS

Ethics review

Approved WMO Date:	14-12-2007
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	04-07-2008
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-04-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	13-07-2009
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-10-2009
Application type:	Amendment

Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	16-02-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	09-09-2010
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	29-03-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	22-03-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-08-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	28-08-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2005-004293-24-NL
ClinicalTrials.gov	NCT00368472
CCMO	NL20052.058.07