

# Clinical Trial Results



**Research Sponsor:** Eisai  
**Drug Studied:** Perampanel or E2007  
**National Clinical Trial #:** NCT01393743 (Part A)  
NCT02307578 (Part B)  
**EudraCT Number:** 2011-000265-12  
**Protocol #:** E2007-G000-332  
**Trial Period:** July 2011 to May 2014  
**Short Trial Title:** A trial to see if perampanel helps reduce  
the number of seizures in people with  
tonic-clonic seizures

## *Thank you!*

As a clinical trial participant, you belong to a large community of participants around the world who help researchers answer important health questions and discover new medical treatments.

Eisai, a Japanese pharmaceutical company and the sponsor of this trial, thanks you for your help. Eisai is committed to improving health through continuing research in areas of unmet need and sharing with you the results of the trial you participated in. Eisai prepared this summary with an independent non-profit organization called CISCRP and a medical and regulatory writing organization called Synchrogenix.

If you have questions about the results, please speak with the doctor, research nurse, or other team member at your trial site.

## What's happened since my trial ended?

You were in this trial for about 3 years, but the trial took about 4 years to complete. When the trial ended in May 2014, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

This trial was done in 2 parts. Part A included 164 participants from 78 sites. Part B included 138 participants from 69 sites. Trial sites were located in:

- 
- |                  |             |                     |
|------------------|-------------|---------------------|
| • Australia      | • Greece    | • Poland            |
| • Austria        | • India     | • Serbia            |
| • China          | • Israel    | • South Korea       |
| • Czech Republic | • Japan     | • The United States |
| • France         | • Latvia    |                     |
| • Germany        | • Lithuania |                     |
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## Why was the research needed?

Researchers were looking for a better way to treat people with epilepsy who experience “primary generalized tonic-clonic seizures”. When a person has a tonic-clonic seizure, all of the muscles in the body stiffen, and then the body begins to jerk uncontrollably. It is thought that over activity of glutamate, a chemical in the brain, may cause seizures.

Researchers in this trial wanted to know if a drug called perampanel could help people who do not respond to other anti-seizure medications. Perampanel reduces the activity of glutamate in the brain.

The main questions researchers asked in the trial were:

- Did perampanel reduce the number of tonic-clonic seizures participants had compared to their current or previous anti-seizure treatment?
- How safe was perampanel, and what were the adverse events? An adverse event is any sign or symptom that may or may not be caused by the trial drug.

To answer these questions, researchers asked for the help of adults and adolescents like you. The participants in this trial were 12 to 70 years old. All participants had tonic-clonic seizures that did not improve with other anti-epileptic treatment. Throughout the trial, participants continued taking their anti-epileptic treatment in addition to the trial drugs.

## What kind of trial was this?

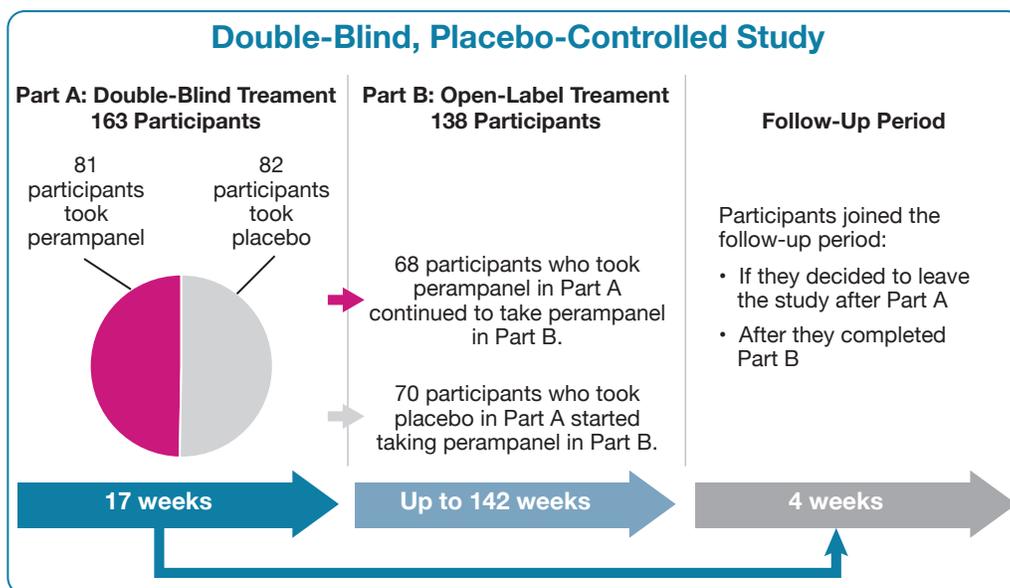
This trial had 2 parts: Part A and Part B.

**Part A was “double-blind”.** This means none of the participants, researchers and staff, or the sponsor knew what treatment each patient received. Participants in this trial took either perampanel or a placebo. A placebo looks like the trial drug but has no real medicine in it. Using a placebo helps researchers learn if the study drug is better than no treatment at all. When the trial ended, the sponsor found out which treatment participants took so they could create a report of the trial results.

**Part B was “open-label”.** This means that the participants, researchers and staff, and the sponsor knew what drugs the participants were getting. During Part B, all participants took perampanel, and researchers continued to look at the effects of perampanel over a longer period of time.

## What happened during the trial?

The figure below shows how the trial was done.



Before the trial started, researchers did a full check-up and physical exam of all participants to make sure they could join the trial. Researchers also took blood and urine samples, and checked participants’ heart health using an electrocardiogram (ECG). Participants were also given a diary to keep track of all seizures they had. If participants met the physical requirements and had 3 or more tonic-clonic seizures over 8 weeks, they were eligible to enter the trial.

**During Part A**, participants were randomly assigned to take either perampanel or a placebo for 17 weeks. For every 1 participant who received perampanel, 1 participant received a placebo. This means that participants had an equal chance of receiving perampanel or the placebo. In the first week, participants took 2 milligrams (mg) each day of their assigned trial drug. If participants had no bad adverse events, their dose was raised by 2 mg each week until Week 4. The highest dose a participant could take was 8 mg each day. Participants kept taking the same dose they received in Week 4 for 13 weeks. At the end of Part A, participants could choose to stop taking the trial drug and begin a 4-week follow-up period, or to enter Part B of the trial.

**During Part B**, every participant took perampanel for up to 142 weeks. If the participant had taken perampanel in Part A, they could continue with the same dose, or raise their dose up to 12 mg per day. If the participant had taken a placebo in Part A, they began with a dose of 2 mg each day, and their dose was raised by 2 mg each week up to a maximum of 12 mg each day.

At the end of Part B, all participants began a 4-week follow-up period.

Throughout the trial, participants continued taking their anti-epileptic treatment in addition to the trial drugs. Researchers also:

- Took blood and urine samples,
- Checked participants' blood pressure, weight, and heart rate,
- Asked participants to keep a diary about their seizures, and checked the diary at each visit, and
- Asked about their quality of life at each visit.

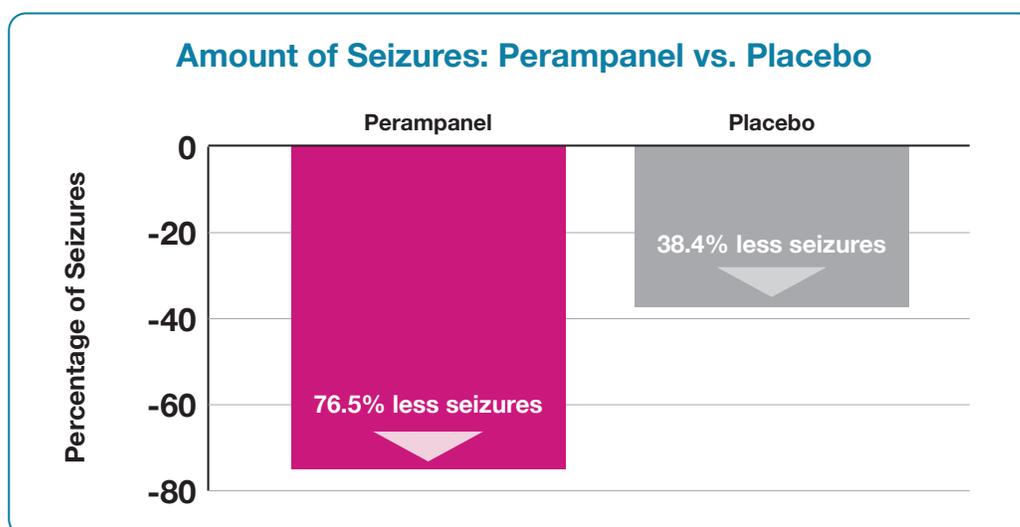
At the end of the follow-up period, participants were given another check-up and physical exam.

## What were the trial results?

This is a summary of the overall results of this trial, not your individual results. The results for each participant may have been different. Researchers look at results of many studies to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

### ***Did perampanel reduce the number of tonic-clonic seizures participants had compared to their current or previous anti-seizure treatment?***

Yes. During Part A, researchers looked at participants' trial diaries every 28 days to see how often participants had seizures since the trial started. Participants in the perampanel group had about 76.5% fewer seizures than before the trial started. Participants in the placebo group had about 38.4% fewer seizures than before the trial started (researchers did not have seizure data from one participant in the placebo group). The chart below shows the average decrease in seizures participants had compared to before treatment.



During Part B, researchers also continued to count how many seizures participants had. They found that after at least 2 years of treatment, participants had 100% fewer tonic-clonic seizures compared to before treatment with perampanel.

Researchers also wanted to know if perampanel could help with other types of seizures, including absence seizures and myoclonic seizures. Absence seizures cause a brief, sudden loss of attention that people describe as “blinking out”. Myoclonic seizures are similar to tonic-clonic seizures, but only happen in a single muscle or a smaller group of muscles.

The table below shows the overall percentage of absence and myoclonic seizures participants had compared to before treatment in Part A and after 2 years of treatment in Part B. Even though there were 82 participants in the placebo group for Part A, researchers only had this information for 81 of the participants.

**Percentage of Absence and Myoclonic Seizures Compared to Before Treatment**

Type of Seizure	Part A		Part B
	Perampanel (Out of 81 participants)	Placebo (Out of 81 participants)	Perampanel (Out of 138 participants)
Absence seizures	41.2% fewer seizures	7.6% fewer seizures	74.3% fewer seizures
Myoclonic seizures	24.5% fewer seizures	52.5% fewer seizures	48.8% fewer seizures

## What medical problems did participants have?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called “adverse events”.

### *How many participants had adverse events during the trial?*

The table below shows how many participants had adverse events in Part A of this trial.

**Adverse Events in This Trial**

	Part A		Part B
	Perampanel (Out of 81 participants)	Placebo (Out of 82 participants)	Perampanel (Out of 138 participants)
How many participants had adverse events?	67 participants (82.7%)	59 participants (72.0%)	120 participants (87.0%)
How many participants stopped taking the trial drug because of adverse events?	9 participants (11.1%)	5 participants (6.1%)	13 participants (9.4%)

**Did any participants have serious adverse events?**

An adverse event is called “serious” when it is life-threatening, causes lasting problems, or the participant needs to be admitted to a hospital.

In Part A of this trial, 6 participants (7.4%) in the perampanel group and 7 participants (8.5%) in the placebo group had serious adverse events. Some patients experienced more than one serious adverse event. The table below shows the serious adverse events in Part A of this trial.

**Serious Adverse Events in This Trial - Part A**

<b>Serious Adverse Event</b>	<b>Perampanel (Out of 81 participants)</b>	<b>Placebo (Out of 82 participants)</b>
<b>Constipation</b>	1 participant (1.2%)	0 participants (0.0%)
<b>Nausea</b>	0 participants (0.0%)	1 participant (1.2%)
<b>Drowning</b>	1 participant (1.2%)	0 participants (0.0%)
<b>Chronic cholecystitis (repeated inflammation of the gallbladder)</b>	1 participant (1.2%)	0 participants (0.0%)
<b>Fall</b>	0 participants (0.0%)	1 participant (1.2%)
<b>Thermal burn</b>	0 participants (0.0%)	1 participant (1.2%)
<b>Convulsion</b>	1 participant (1.2%)	2 participants (2.4%)
<b>Grand mal convulsion</b>	0 participants (0.0%)	1 participant (1.2%)
<b>Status epilepticus</b>	1 participant (1.2%)	1 participant (1.2%)
<b>Suicidal thoughts</b>	1 participant (1.2%)	0 participants (0.0%)
<b>Suicide attempt</b>	1 participant (1.2%)	0 participants (0.0%)

During Part B, the most frequently occurring serious adverse events were convulsion (3 participants, 2.2%) and suicide attempt (2 participants, 1.4%).

In this trial, there were 2 deaths during Part A: drowning in the perampanel group and convulsion in the placebo group. There was 1 death in Part B: acute pancreatitis, or inflammation of the pancreas. Trial doctors did not think any of the deaths were related to the trial drugs, though the trial doctor thought that the convulsion in Part A may have been related to the participant’s seizure disorder

**What were the most common non-serious adverse events?**

The table below shows the most common non-serious adverse events in Part A of this trial. A non-serious adverse event was considered “common” if it happened in at least 10% of participants.

**Most Common Non-Serious Adverse Events in This Trial - Part A**

<b>Adverse Event</b>	<b>Perampanel (Out of 81 participants)</b>	<b>Placebo (Out of 82 participants)</b>
<b>Dizziness</b>	26 participants (32.1%)	5 participants (6.1%)
<b>Tiredness</b>	12 participants (14.8%)	5 participants (6.1%)
<b>Headache</b>	10 participants (12.3%)	8 participants (9.8%)
<b>Drowsiness</b>	9 participants (11.1%)	3 participants (3.7%)
<b>Irritability</b>	9 participants (11.1%)	2 participants (2.7%)

The table below shows the most common non-serious adverse events in Part B.

**Most Common Non-Serious Adverse Events in This Trial - Part B**

<b>Adverse Event</b>	<b>Perampanel (Out of 138 participants)</b>
<b>Irritability</b>	19 participants (13.8%)
<b>Upper respiratory tract infection (common infection of the nose, throat, and airways)</b>	18 participants (13.0%)
<b>Drowsiness</b>	18 participants (13.0%)
<b>Headache</b>	17 participants (12.3%)
<b>Vertigo (dizziness that feels like spinning)</b>	15 participants (10.9%)
<b>Tiredness</b>	14 participants (10.1%)

## Where can I learn more about the study?

You can find more information about your trial online at:

- Part A: [www.clinicaltrials.gov/show/results/NCT01393743](http://www.clinicaltrials.gov/show/results/NCT01393743)
- Part B: [www.clinicaltrials.gov/show/results/NCT02307578](http://www.clinicaltrials.gov/show/results/NCT02307578)
- [www.clinicaltrialsregister.eu/ctr-search/trial/2011-000265-12/results](http://www.clinicaltrialsregister.eu/ctr-search/trial/2011-000265-12/results)

**Official trial title:** A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate the Efficacy and Safety of Adjunctive Perampanel in Primary Generalized Tonic Clonic Seizures.

**The results presented here are for a single trial. Other studies may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.**

Eisai, the sponsor of this trial, has its headquarters in Tokyo, Japan and regional headquarters in Woodcliff Lake, New Jersey, USA and Hatfield, Hertfordshire, UK. The phone number for general information is 44-845-676-1400.

## Thank you

Eisai would like to thank you for your time and interest in participating in this clinical trial. Your participation has provided a valuable contribution to research and improvement in health care.



Eisai Co., Ltd. is a global research and development-based pharmaceutical company headquartered in Japan. We define our corporate mission as “giving first thought to patients and their families and to increasing the benefits health care provides,” which we call our human health care (hhc) philosophy. With over 10,000 employees working across our global network of R&D facilities, manufacturing sites, and marketing subsidiaries, we strive to realize our hhc philosophy by delivering innovative products in multiple therapeutic areas with high unmet medical needs, including Oncology and Neurology. For more information, please visit <http://www.eisai.com>.



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