Clinical Trial Results

Research Sponsor:	Eisai Ltd.
Drug Studied:	Perampanel, also called Fycompa® or E2007
Short Trial Title:	A trial to learn how perampanel works and how safe it is when taken with other treatments by people with refractory partial-onset seizures caused by epilepsy

Thank you!

You and your caregiver took part in this clinical trial for the trial drug perampanel, also called E2007. You, your caregiver, and all of the participants helped researchers learn more about perampanel, which may help people with refractory partial onset seizures caused by epilepsy.

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 and your caregiver participated in.

Eisai prepared this summary with a medical and regulatory writing organization called Certara Synchrogenix.

If you and your caregiver participated in the trial and have questions about the results, please speak with the trial doctor or staff at your trial site.

What is this summary about?

This is a summary of the main results of this trial and shows the overall results. Individual results for each person who took part are not shown in this summary and might be different from the overall results.

A full list of the questions researchers wanted to answer in this trial can be found on the websites listed at the end of this summary. When a scientific report of this clinical trial is available, it can also be found on the websites listed at the end of this summary.

Researchers look at the results of many trials to decide which treatment options may work best and are well tolerated. Other trials may provide new information or different results. Always talk to a doctor before making any treatment decisions.

What is epilepsy?

Epilepsy is a condition that affects the brain, causing seizures. It is a nervous system disorder in which brain activity becomes abnormal. The brain contains billions of nerve cells that connect to each other, called neurons. In people with epilepsy, the neurons become disturbed, causing abnormal activity inside the brain. This abnormal activity can cause seizures and loss of awareness or consciousness. As the epilepsy gets worse, so can the symptoms.

A partial-onset seizure, sometimes called a focal-onset seizure, describes where the abnormal activity in the brain begins. Partial or focal means the abnormal activity starts in a specific part or on one side of the brain. Refractory means that the medicines currently available for a disease or condition do not work. For people with epilepsy, this means their seizures are uncontrolled.

What has happened since the trial started?

The trial included 940 participants from 119 trial sites in Australia, China, Korea, Japan, Malaysia, Taiwan, and Thailand. It started in May 2012 and ended in May 2020.

The sponsor of the trial reviewed the data collected and created a report of the results. This is a summary of that report.

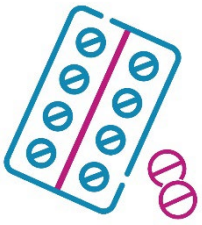
Why was the research needed?

Clinical trials answer many important questions. The main question for the researchers in this trial was:

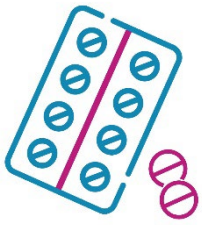
“Does perampanel improve seizure control in young people and adults with uncontrolled partial-onset seizures?”

To answer this, the researchers needed to find the answer to several questions. This summary only shows the questions and answers to the main question. A full list of questions and answers are available on the websites shown at the end of this summary.

This trial had 2 parts:



In **Part 1**, the researchers wanted to find out:
"Is **4 mg, 8 mg, or 12 mg** doses of perampanel effective at improving seizure control when taken once a day for **approximately 4 months**?”



In **Part 2**, the researchers wanted to find out:
“Is **12 mg** of perampanel effective at improving seizure control when taken once a day for **at least 1 year and 5 months**?”

To answer these questions, the researchers needed to see if perampanel reduced the number of seizures the participants had each month during both parts of the trial.

mg = milligrams
In this trial, 1 month = 28 days. Treatment length, numbers, and percentages shown in this summary have been rounded for simplicity.

What kind of trial was this?

To learn more about how perampanel works and how safe it is, the researchers asked for the help of people like you.

The participants in the trial were between 12 and 71 years of age.

All of the participants in this trial had:

- been diagnosed with epilepsy
- uncontrolled partial-onset seizures
- experienced 5 or more partial seizures over a 6-week period

The ideal way to test treatments in a trial is “randomized” and “placebo-controlled.”

Randomized means a computer program was used to determine which treatment each participant received. It helps make trials fair for everyone who takes part.

Placebos, or “dummy tablets,” do not have any medicine in them. They help researchers learn about the effects of the real medicine and if it is safe.

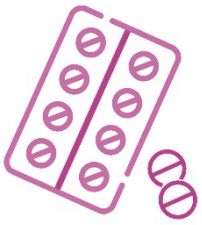
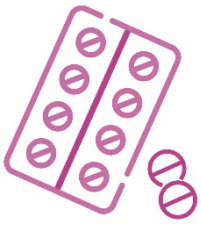
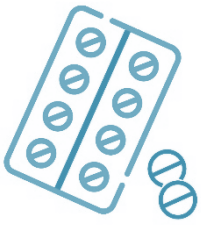
Part 1 of this trial was randomized and placebo controlled. This means some of the participants received 4 mg, 8 mg, or 12 mg doses of perampanel and some received placebo. Neither the participants nor the staff in the trial knew which tablets the participants received during Part 1 of the trial.

In Part 2 of this trial, all participants received up to 12 mg perampanel and no-one received placebo.

During both parts of the trial, the participants took the trial treatment in addition to their usual epilepsy medications. This is called “adjunctive” or add-on treatment.

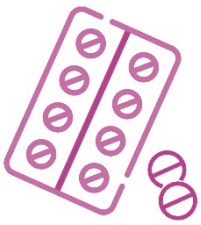
How did participants receive the treatment?

Part 1

4 mg perampanel	8mg perampanel	12 mg perampanel	placebo
			
176 participants	**175** participants	**180** participants	**176** participants

Participants took their assigned treatment once a day, by mouth, for approximately 4 months

Part 2

Up to 12 mg perampanel	placebo
	
596 participants	**0** participants

Participants took up to 12 mg perampanel once a day, by mouth,
for at least 1 year and 5 months

What happened during the trial?

Before the trial started, participants had a full check-up, completed questionnaires, and had tests and procedures to make sure they could take part.

During Part 1, participants, along with their caregivers, visited the trial site around 8 times. During these visits, the trial doctors continued to check the participants' health and perform tests and procedures, including:

- Heart health checks
- Blood and urine tests

All participants, with the support of their caregivers, were asked to complete questionnaires about their symptoms. Participants were also asked to keep a diary of how many seizures they had each day, called seizure count. The trial doctors completed questionnaires assessing the participants' seizure count and how severe the seizures were. The answers to the diaries and all questionnaires helped the researchers understand more about how severe the participants' epilepsy symptoms and seizures were.

At the end of Part 1, participants who had completed all trial visits could join Part 2. Participants had a full check-up again, completed questionnaires, and had tests and procedures to make sure they could take part.

- Participants who had taken 12 mg perampanel in Part 1 of the trial continued to take the same dose in Part 2.
- Participants who had taken 4 mg or 8 mg perampanel in Part 1 of the trial steadily increased their dose in Part 2 until they reached 12 mg.
- Participants who had taken placebo in Part 1 of the trial started taking 2 mg of perampanel and steadily increased this to 12 mg.

During Part 2, participants along with their caregivers regularly visited the trial site and completed the seizure diaries and questionnaires. The trial doctors also continued to complete questionnaires about the participants' seizure count. The trial doctors continued to check the participants' health and performed tests and procedures including heart health checks and blood and urine tests.

What were the results of Part 1 of the trial?

Is 4 mg, 8 mg, or 12 mg doses of perampanel effective at improving seizure control when taken once a day for approximately 4 months?

To answer this, the researchers needed to look at the results of the seizure diaries the participants completed during Part 1. They compared the number of seizures per month that participants had when they took perampanel or placebo.

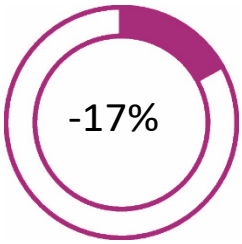
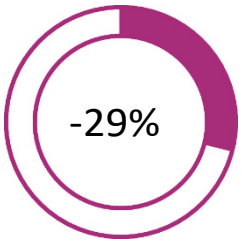
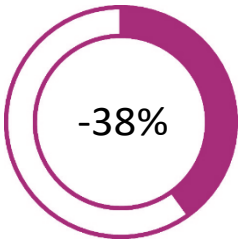
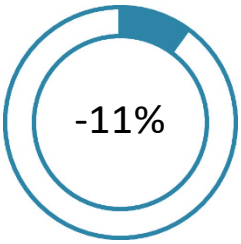
The diaries showed that, at the start of the trial:

- The average number of seizures per month for participants who took **4 mg** of perampanel was **10 seizures**.
- The average number of seizures per month for participants who took **8 mg** of perampanel was **9 seizures.**
- The average number of seizures per month for participants who took **12 mg** perampanel was **10 seizures.**
- The average number of seizures per month for participants who took **placebo** was **10 seizures.**

Using this information, the researchers were able to work out the average change in seizure count over time for each treatment group. This change is calculated as a percentage and is called the "median percent change".

The diagram below shows "median percent change" from the beginning of the trial to the end of Part 1.

The minus symbol means the seizure counts decreased over time.

4 mg perampanel	8 mg perampanel	12 mg perampanel	placebo
			
174 out of 176 participants had complete diary entries	175 out of 175 participants had complete diary entries	180 out of 180 participants had complete diary entries	175 out of 176 participants had complete diary entries

Overall, the results in Part 1 showed that:

- Add-on treatment with 8 mg or 12 mg of perampanel once per day was effective in improving seizure control in participants with uncontrolled partial-onset seizures
- Add-on treatment with 4 mg perampanel once per day showed some improvement in seizure control but there was not a large difference compared with placebo treatment.

What medical problems did participants have in Part 1?

Medical problems that happen in clinical trials are called “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. Adverse events may or may not be caused by the trial treatments.

The websites listed at the end of this summary may have more information about the medical problems that happened in this trial. It takes a lot of research to know whether a treatment causes a medical problem.

How many participants had adverse events?

The table below gives a summary of the adverse events the participants had.

Type of Adverse Events in Part 1

	4 mg perampanel 176 participants	8 mg perampanel 175 participants	12 mg perampanel 180 participants	Placebo 176 participants
How many participants had adverse events?	121 (69%)	129 (74%)	156 (87%)	117 (67%)
How many participants had serious adverse events?	6 (3%)	7 (4%)	12 (7%)	10 (6%)
How many participants stopped receiving the trial treatment because of adverse events?	8 (5%)	20 (11%)	25 (14%)	6 (3%)

What were the most common serious adverse events?

During Part 1 of the trial, 35 out of 707 participants (5%) had serious adverse events.

- 25 out of 531 participants (5%) took perampanel
- 10 out of 176 participants (6%) took placebo

The table below shows the serious adverse events that happened during Part 1 of the trial.

To protect the privacy of the participants, the information shows the number of serious adverse events that happened in 2 or more people in any of the treatment groups.

Most Common Serious Adverse Events in Part 1

	4 mg perampanel 176 participants	8 mg perampanel 175 participants	12 mg perampanel 180 participants	Placebo 176 participants
Lung infection	0	1 (1%)	0	2 (1%)
Spongy part of a disc in the spine pushed out from its normal space	2 (1%)	0	0	0
Seizure lasting longer than 5 minutes, or one seizure that follows another	0	0	2 (1%)	1 (1%)
Feeling aggressive	0	0	2 (1%)	0
Ending of pregnancy with medication or a medical procedure	0	0	0	2 (1%)

3 out of 707 participants (less than 1%) died due to a serious adverse event. Of these, 1 participant had not taken any treatment. The trial doctors did not think that any of the deaths were related to the trial treatments.

What were the most common adverse events?

During Part 1 of the trial, 523 out of 707 participants (74%) had adverse events.

- 406 out of 531 participants (77%) took perampanel
- 117 out of 176 participants (67%) took placebo

The table below shows the adverse events that happened in 5% or more of participants during Part 1.

There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in Part 1

	4 mg perampanel 176 participants	8 mg perampanel 175 participants	12 mg perampanel 180 participants	Placebo 176 participants
Dizziness	40 (23%)	50 (29%)	76 (42%)	10 (6%)
Feeling sleepy	28 (16%)	31 (18%)	32 (18%)	23 (13%)
Common cold	23 (13%)	24 (14%)	23 (13%)	26 (15%)
Headache	12 (7%)	13 (7%)	10 (6%)	13 (7%)
Nose/throat infection	8 (5%)	14 (8%)	11 (6%)	8 (5%)
Feeling irritable	8 (5%)	10 (6%)	9 (5%)	1 (1%)
Nausea	4 (2%)	4 (2%)	10 (6%)	6 (3%)
Feeling tired	4 (2%)	6 (3%)	9 (5%)	5 (3%)
Problems walking	2 (1%)	4 (2%)	9 (5%)	3 (2%)
Rash	2 (1%)	2 (1%)	9 (5%)	2 (1%)

What were the results of Part 2 of the trial?

Is 12 mg of perampanel effective at improving seizure control when taken once a day for at least 1 year and 5 months?

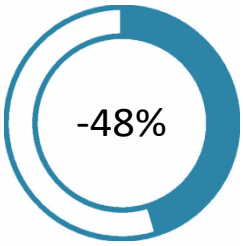
To answer this, the researchers looked at the results of the seizure diaries the participants completed during the trial.

The diaries showed that, at the start of the trial:

- The average number of seizures per month for participants who took perampanel in Part 1 and Part 2 was **9.6 seizures**.
- The average number of seizures per month for participants who took placebo in Part 1 and perampanel in Part 2 was **10 seizures.**

The diagram below shows “median percent change” from the beginning of the trial to the end of 1 year and 5 months of treatment.

The minus symbol means the seizure counts decreased over time.

Participants who took perampanel in Part 1 and Part 2	Participants who took placebo in Part 1 and perampanel in Part 2
	
304 out of 445 participants had complete diary entries. The remaining participants had diary entries missing, so their data has not been included	103 out of 151 participants had complete diary entries. The remaining participants had diary entries missing, so their data has not been included

Overall, the results in Part 2 showed that:

- Add-on treatment with 12 mg of perampanel once per day continued to be effective at helping participants control their partial-onset seizures
- Participants who took placebo in Part 1 and switched to perampanel in Part 2 had a similar reduction in seizure count per month to those participants who took perampanel in Part 1 and Part 2.

What medical problems did participants have in Part 2?

How many participants had adverse events?

The table below gives a summary of the adverse events the participants had. It shows the data from 679 participants from Part 1 and Part 2 who had complete information about adverse events after taking perampanel.

Type of Adverse Events in Part 2

	Total perampanel 679 participants
How many participants had adverse events?	624 (92%)
How many participants had serious adverse events?	113 (17%)
How many participants stopped receiving the trial treatment because of adverse events?	141 (21%)

What were the most common serious adverse events?

A total of 113 out of 679 participants (17%) had serious adverse events. The most common serious adverse events were related to having epilepsy. Other serious adverse events included a lung infection in 5 participants and bruises, skin wounds, clouding of the lens in the eye, or terminated a pregnancy (4 participants per event).

7 out of 679 participants (less than 1%) died due to serious adverse events. One participant's death, due to sudden unexplained death in epilepsy, was thought by the trial doctors as "possibly related" to the trial treatment.

What were the most common adverse events?

A total of 624 out of 679 participants (92%) had adverse events.

The table below shows the adverse events that happened in 5% or more participants. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in Part 2

	Total perampanel 679 participants
Dizziness	318 (47%)
Common cold	171 (25%)
Feeling sleepy	165 (24%)
Headache	94 (14%)
Nose/throat infection	70 (10%)
Feeling irritable	62 (9%)
Bruises	53 (8%)
Weight increased	40 (6%)
Fever	39 (6%)
Nausea	35 (5%)
Diarrhea	34 (5%)
Feeling tired	34 (5%)

How has this trial helped patients and researchers?

In this trial, researchers learned more about how well perampanel works at improving seizure control in young people and adults with uncontrolled partial-onset seizures. They also learned more about the adverse events participants have when they take up to 12 mg of perampanel once a day.

Researchers look at the results of many trials to decide which treatment options may work best and are well tolerated. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Further clinical trials with perampanel are not planned.

Where can I learn more about the trial?

You can find more information about this trial on the websites listed below. If a full report of the trial results is available, it can also be found here:

- https://www.clinicaltrialsregister.eu- Once you are on the website, click "**Home and Search**", then type **2020-002109-24** in the search box and click "**Search**".
- https://www.clinicaltrials.gov- Once you are on the website, type **NCT01618695** into the search box and click "**Search**".

Full trial title: A Double-blind, Placebo-controlled, Parallel-group Study with an Open-label Extension Phase to Evaluate the Efficacy and Safety of Perampanel (E2007) Administered as an Adjunctive Therapy in Subjects with Refractory Partial-onset Seizures

Protocol number: E2007-J000-335

Eisai, the sponsor of this trial, has 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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