Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: Perampanel, also called E2007
Short Study Title: A study to learn about the safety of perampanel and how it works in the bodies of children with epilepsy

Thank you!

Your child took part in this clinical study for the study drug E2007, also called perampanel. Your child and all of the other participating children helped researchers learn more about the safety of perampanel and how it works in the bodies of children with 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 activities in the brain. These abnormal activities can cause seizures and loss of awareness or consciousness.

Eisai, a Japanese pharmaceutical company and the sponsor of this study, thanks all participants and their families/caregivers, for their contribution. Eisai is committed to improving health through continuing research in areas of unmet need and sharing with you the results of the study your child participated in.

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

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

What has happened since the study started?

The study started in February 2017 and ended in April 2023.

The study included 26 participants from 8 study sites in Latvia and the United States. Out of 26 participants, 21 took at least 1 dose of study treatment. The study was designed to allow participation by children aged 1 month to less than 4 years old. The children who actually participated in the study were aged 5 months to 3 years old. Of these participants, 38% were male, and 62% were female.

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

Why was the research needed?

Researchers were looking for a different way to treat people who have epilepsy.

The standard treatments for people with epilepsy include medicines that help control their seizures, but these medicines may not help all people with epilepsy. Some of these medicines may not have been well studied in children less than 4 years old.

Perampanel has been approved in the European Union, the United States, and other countries as a single treatment and/or in combination with other treatments for people with certain kinds of seizures aged from 4 years and older, depending on the kind of seizure and the country where it is approved.

In this study, researchers wanted to find out how much and how long perampanel stayed in the bodies of participants with epilepsy aged from 1 month to 4 years when given as an oral (by mouth) suspension (a liquid with solid particles in it). The researchers also wanted to find out if participants had any medical problems during the study.

The main questions the researchers wanted to answer in this study were:

- What were the highest and average amounts of perampanel in the bodies of participants with epilepsy?
- What were the adverse reactions experienced by participants after receiving perampanel? An adverse reaction is a medical problem that may be caused by the study treatment.

It is important to know that this study was designed to get accurate answers to the questions listed above. There were other questions the researchers wanted to answer to learn more about how perampanel works, but these were not the main questions the study was designed to answer.

What kind of study was this?

This study was "open-label". This means that the participants, caregivers, the study doctors and staff, and the sponsor, knew what dose of perampanel the participants took. Children could not participate in the study if they needed to be admitted to a hospital because of their seizures, had seizures that were caused by treatable medical conditions, or if they had surgery or planned to have surgery because of epilepsy.

Perampanel was given as an oral suspension once a day before bedtime. Participants took perampanel measured in milligrams per day (or mg/day) for up to 20 weeks in the Core Study and for up to 36 weeks in the Extension phase.

To answer the main questions described in the previous section, researchers asked for the help of parents and caregivers like you.

The study had 2 parts:

- **Core Study**: This part was split into 2 periods:
  - In the first period, researchers wanted to learn the highest dose of perampanel that each participant could take with manageable side effects.
  - In the second period, researchers measured how much perampanel was in the body of each participant while they were taking their highest manageable dose.
- **Extension Phase**: Researchers wanted to learn about the safety of perampanel when taken for a long time (total of up to 52 weeks).

Participants in the study were divided into groups depending on their age as follows:

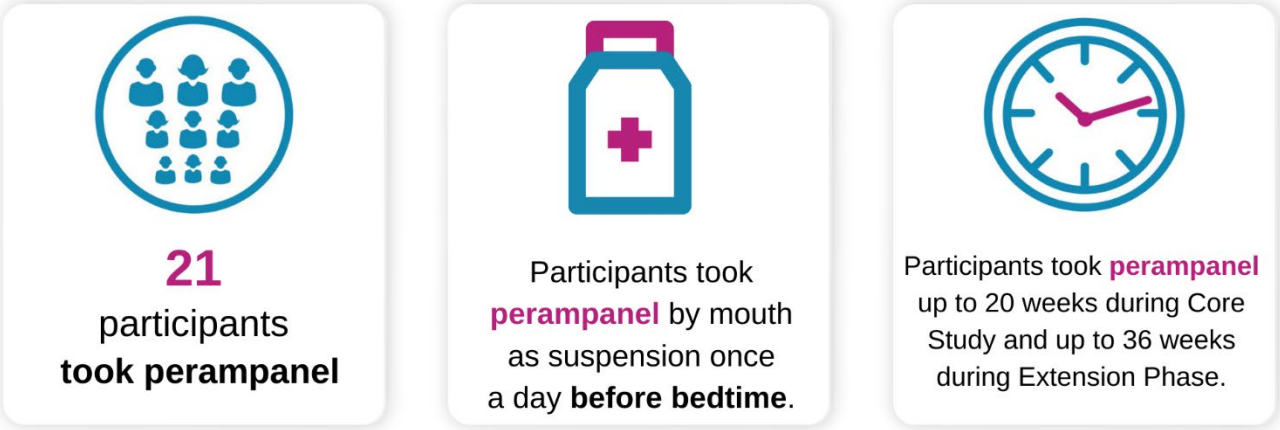
- 1 month to 6 months
- Greater than 6 months to 12 months
- Greater than 12 months to less than 24 months
- 24 months to less than 48 months

Participants were also divided into groups depending on if they were taking medicines for epilepsy that are enzyme inducers. Enzyme inducers increase the breakdown of perampanel. Participants were grouped as follows:

- Enzyme-inducing anti-epileptic drug (or EIAED)
- Non-enzyme-inducing anti-epileptic drug (or non-EIAED)

All the participants in this study had epilepsy with any type of seizure and had experienced 1 or more seizures before the start of the study.

The figure below shows how treatment was given in this study.



What happened during the study?

Before the study treatment was given, the study doctors did a full check-up to make sure each participant could join the study.

The study doctors or staff also:

- Checked each participant's heart health
- Took blood samples for analyses from each participant
- Reviewed each participant's seizure diary
- Checked the medicines each participant had been taking before they joined the study

During treatment the Core Study and Extension Phase, the participants took perampanel oral suspension once a day before bedtime.

Throughout the treatment, the study doctors or staff:

- Took blood samples for analyses from each participant
- Reviewed each participant's seizure diary
- Checked what other medicines each participant was taking
- Checked what medical problems each participant was experiencing

Within 28 days after the last dose, the participants' parents or caregivers brought them to their study site for a final visit, where they were examined and asked about any medical problems their children had experienced and what medicines they were taking.

For participants who continued to take perampanel outside of the study, their parents or caregivers received a final phone call from the study doctors or staff and were asked the same questions as above.

The figure below shows how the study was done.

How did this study work?

Before study treatment was given

The study doctors or staff:

- Checked each participant's health to see if they could join the study
- Took blood samples for analyses
- Reviewed participants' diary for seizures
- Checked the medicines participants were taking

During treatment period

All participants who could join the study took **perampanel** oral suspension once a day.

The study doctors or staff:

- Took blood samples for analyses
- Reviewed participants' diary for seizure
- Asked if participants had medical problems and what medicines participants were taking

After the last dose

All participants received a phone call within **28 days** after taking their last dose of study treatment.

The study doctors or staff asked if participants had medical problems and medicines participants were taking.

What were the results of the study?

This is a summary of the main results. The results each participant had might be different and are not in this summary, but the results each participant had are part of the summary of results. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. If a full report of the study results is available, it can also be found on these websites.

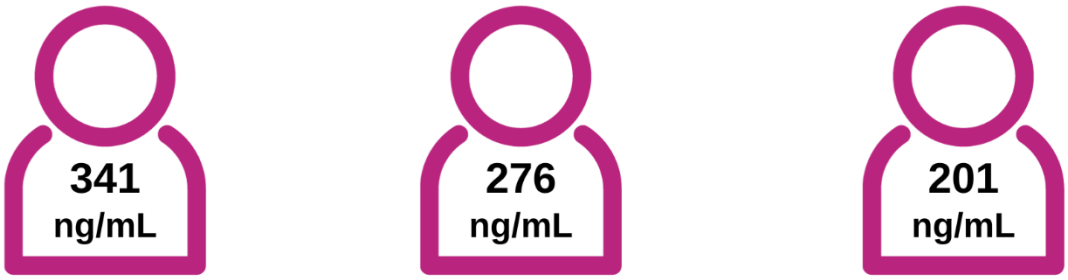
What were the highest and average amounts of perampanel in the bodies of participants with epilepsy when given as an oral suspension?

To answer this question, researchers used the blood samples taken from the participants during Part 2 of the Core Study and calculated the highest and average amounts of perampanel in each participant's body. The amount of perampanel in the body was measured in nanograms per milliliter (ng/mL).

The values displayed in the charts below show the calculated amount of perampanel present, on average, in the bodies of participants as if they were all taking 8 mg/day of perampanel. This is done to calculate an average value since participants took different doses of perampanel in the study.

The charts below show the highest amount of perampanel on average in the bodies of participants in the EIAED and non-EIAED groups during Part 2 of the Core Study. There were no participants in the study aged 1 month to 6 months who were taking EIADs.

Highest amount of perampanel on average in the bodies of participants in the EIAED group during Part 2 of the Core Study.



Participants aged greater than 6 months to 12 months

Participants aged greater than 12 months to less than 24 months

Participants aged 24 months to less than 48 months

Highest amount of perampanel on average in the bodies of participants in the non-EIAED group during Part 2 of the Core Study.

Participants aged 1 month to 6 months

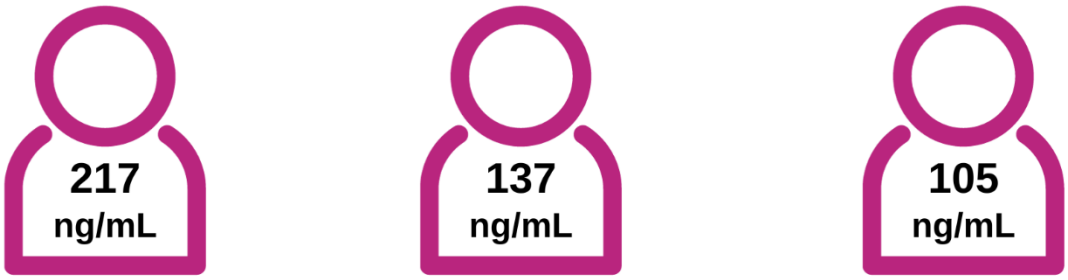
Participants aged greater than 6 months to 12 months

Participants aged greater than 12 months to less than 24 months

Participants aged 24 months to less than 48 months

The charts below show the overall average amount of perampanel in the bodies of participants in the EIAED and non-EIAED groups during Part 2 of the Core Study. There were no participants in the study aged 1 month to 6 months who were taking EIADs.

Overall average amount of perampanel in the bodies of participants in the EIAED group during Part 2 of the Core Study.



Participants aged greater than 6 months to 12 months

Participants aged greater than 12 months to less than 24 months

Participants aged 24 months to less than 48 months

Overall average amount of perampanel in the bodies of participants in the non-EIAED group during Part 2 of the Core Study.

Participants aged 1 month to 6 months

Participants aged greater than 6 months to 12 months

Participants aged greater than 12 months to less than 24 months

Participants aged 24 months to less than 48 months

What medical problems did participants have?

Medical problems that happen in clinical studies are called “adverse events” – these may or may not be caused by the study treatment. An adverse event that the study doctors thought was caused by the study drug is called an “adverse reaction”. An adverse reaction is called “serious” when it is life-threatening, causes lasting problems, or the participant needs to be admitted to a hospital.

This section is a summary of the adverse reactions that happened during this study. The websites listed at the end of this summary may have more information about the medical problems that happened in this study. A lot of research is needed to know whether a study drug causes a medical problem.

How many participants had adverse reactions?

In this study,

- 14 participants (67%) had adverse reactions during the Core Study.
- 13 participants (72%) had adverse reactions during the Entire Study (Core Study and Extension Phase).

The table below shows how many participants had adverse reactions in this study.

Adverse Reactions in the Study

	Core Study (21 participants)	Entire Study (18 participants who were in both Core and Extension)
How many participants had adverse reactions?	14 (67%)	13 (72%)
How many participants had serious adverse reactions?	1 (5%)	0 (0%)
How many participants stopped receiving perampanel because of adverse reactions?	0 (0%)	0 (0%)

What were the most common serious adverse reactions?

During the Core Study, a serious adverse reaction of altered mental status was experienced by 1 participant (5%). No other participants in the Core Study reported a serious adverse reaction.

No participant reported a serious adverse reaction during the Extension Study.

No participant died due to a serious adverse reaction in the study.

What were the most common adverse reactions?

During the study, the most common adverse reaction was sleepiness.

The table below shows the adverse reactions that happened in more than 1 participant in any stage of the study. There were other adverse reactions, but these happened in fewer participants.

Most Common Adverse Reactions in the Study

	Core Study (21 participants)	Entire Study (18 participants who entered Extension Study)
Sleepiness	4 (19%)	4 (22%)
Loss of muscle coordination	2 (10%)	2 (11%)
Balance disorder	2 (10%)	1 (6%)
Vomiting	2 (10%)	2 (11%)
Difficulty sleeping	1 (5%)	2 (11%)

How has this study helped patients and researchers?

In this study, researchers learned more about how perampanel may have helped children aged from 1 month to 4 years with epilepsy.

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

Further clinical studies with perampanel are ongoing at the time of this report.

Where can I learn more about the study?

You can find more information about this study on the websites listed below. If a full report of the study 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 **2013-005391-17** in the search box and click "**Search**".
- https://www.clinicaltrials.gov - Once you are on the website, type **NCT02914314** into the search box and click "**Search**".

Full study title: An Open-Label Study With an Extension Phase to Evaluate the Pharmacokinetics of Perampanel (E2007) Oral Suspension When Given as an Adjunctive Therapy in Subjects From 1 Month to Less Than 4 Years of Age With Epilepsy

Protocol number: E2007-G000-238

Eisai, the sponsor of this study, has headquarters in Tokyo, Japan, and regional headquarters in Nutley, New Jersey, USA and Hatfield, Hertfordshire, UK. The phone number for general information is 44-845-676-1400 (UK) and 1-888-274-2378 (USA).

Thank you

Eisai would like to thank you for your time and interest in participating in this clinical study. 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 https://www.eisai.com.

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