Clinical Trial Results

Research Sponsor: Eisai Ltd.

Drug Studied: Elenbecestat, also called E2609

Short Trial Title: A trial to learn how elenbecestat works and how safe it is in adults with early Alzheimer's disease or dementia due to Alzheimer's disease

Thank you!

You and your caregiver or study partner took part in this clinical trial for the trial drug elenbecestat, also called E2609. You, your caregiver/study partner, and all of the participants in this study helped researchers learn more about elenbecestat, which may help people with early signs of Alzheimer's disease or dementia due to Alzheimer's disease.

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/study partner participated in.

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

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

What is this summary about?

This is a summary of the main results of this trial. It shows the overall results of the study. 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 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 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 Alzheimer's disease?

Alzheimer's disease affects the brain. The brain has billions of nerve cells that connect to each other. Alzheimer's disease causes the connections between the nerve cells to die.

For people with early Alzheimer's disease, the loss of the nerve connections is small to start with. They may have trouble remembering and making decisions, but they can carry on with their daily lives. As their Alzheimer's disease gets worse, so will their symptoms.

What is dementia?

Dementia is a word used to describe the symptoms a person has when the nerve cell connections in the brain die. These symptoms include problems with memory, thinking, and behavior. They can be mild, moderate, or severe.

Over time, dementia symptoms will get worse and become severe enough to affect a person's daily life. Trials about early Alzheimer's disease and dementia are important because they look at ways to slow down or prevent the disease from getting worse.

What has happened since the trial started?

The trial included 70 participants from 30 sites in the United States. It started in November 2014 and ended in December 2019.

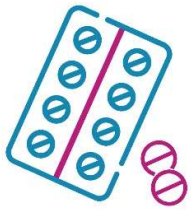
The trial was stopped on the recommendation of an independent monitoring group that reviewed the results of two other elenbecestat clinical trials (E2609-G000-301 & E2609-G000-302). This group found that there appeared to be no benefit with treatment, and an increase in some types of adverse events with treatment.

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

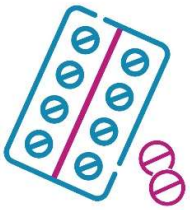
Why was the research needed?

Clinical trials answer many important questions. The main question for the researchers in this study was "is elenbecestat safe?" The researchers had other questions and they got many answers from the trial. This summary only shows the answer to the main question. A full list of questions and answers are available on the websites shown at the end of this summary.

This study had 2 parts:



In Part 1, the main question the researchers had was to find out about any medical problems participants had when they took **up to 50 mg* of elenbecestat** once a day.



In Part 2, the main question the researchers had was to find out about any medical problems participants had when they took **50 mg of elenbecestat** once a day.

* mg = milligrams

What kind of trial was this?

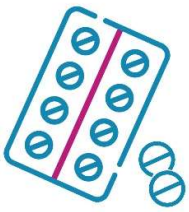
To learn more about how safe different doses of elenbecestat were, the researchers asked for the help of men and women like you. The participants in the trial were between 58 and 85 years old.

All of the participants in this trial had either mild cognitive impairment due to Alzheimer's disease or mild to moderate dementia due to Alzheimer's disease. Cognitive impairment means that a person has trouble remembering, learning, or making decisions that affect their everyday life.

In this trial, the participants needed to have a study partner to complete the questionnaires and talk with the study staff. A study partner is a person who was able to support the participant during the trial and spent at least 8 hours per week with the participant.

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.

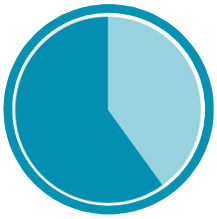
Part 1 of this trial was randomized and placebo-controlled. This means some of the participants received elenbecestat tablets and some received placebo tablets. No one knew which tablets the participants received until the end of Part 1.

In Part 2 of this trial, all participants received elenbecestat tablets and no one received placebo tablets.

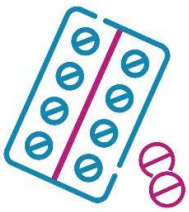
How did participants receive the treatment?

Part 1

70
participants
took part



40%
men
60%
women



53
participants
received
up to 50 mg elenbecestat

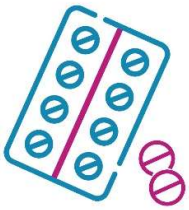
17 participants
received placebo

Tablets were taken
once a day
with food for
approximately 1.5 years

Part 2

41
participants
took part

44%
men
56%
women



All
participants
received
50 mg elenbecestat

Tablets were taken
once a day for
up to 2.5 years

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 or study partners, visited the trial site around 20 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
- Skin exams
- Brain scans

All participants had neurological exams. The answers helped the researchers understand more about how the participants' Alzheimer's disease and dementia symptoms were affecting their daily lives. All participants also completed questionnaires. The answers helped the researchers understand more about how severe the participants' Alzheimer's disease and dementia symptoms were.

At the end of Part 1, participants who had completed all of the 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.

During Part 2, participants along with their caregivers or study partners regularly visited the trial site and completed questionnaires. During their visits, the trial doctors continued to check the participants' health. They performed tests and procedures including heart health checks, blood and urine tests, brain scans, and neurological exams.

Part 2 ended earlier than planned. This was because the results of other elenbecestat trials found it did not work as well as it was hoped.

What were the results of Part 1 of the trial?

The main question for the researchers in Part 1 of this trial was "is elenbecestat safe?" To answer this, the researchers needed to compare any medical problems participants had when they took elenbecestat or placebo.

What are medical problems?

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.

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?

During Part 1 of the trial, 63 out of 70 participants (90%) had adverse events. The table below gives a summary of the adverse events the participants had.

Type of Adverse Events in Part 1

	Up to 50 mg elenbecestat (53 participants)	Placebo tablets (17 participants)
How many participants had adverse events?	48 out of 53 (91%)	15 out of 17 (88%)
How many participants had serious adverse events?	8 out of 53 (15%)	2 out of 17 (12%)
How many participants stopped receiving the trial drug because of adverse events?	12 out of 53 (23%)	2 out of 17 (12%)

What were the most common serious adverse events?

During Part 1 of the trial, 9 out of 70 participants (13%) had serious adverse events. The participants needed to go to hospital, but none of the events were life threatening or fatal. 8 out of 53 participants (15%) were taking elenbecestat. 2 out of 17 participants (12%) were taking 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.

Most Common Serious Adverse Events in Part 1

	Up to 50 mg elenbecestat (53 participants)	Placebo tablets (17 participants)
Fainting	2 out of 53 (4%)	0 out of 17 (0%)
Depression	2 out of 53 (4%)	0 out of 17 (0%)

What were the most common adverse events?

During Part 1 of the trial, 63 out of 70 participants (90%) had adverse events.

- 48 out of 53 participants (91%) were taking elenbecestat
- 15 out of 17 participants (88%) were taking placebo

The most common adverse events were:

- Infection of nose, throat, or voice box
- Skin reaction
- Headache

The table below shows the adverse events that happened in 10% 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

	Up to 50 mg elenbecestat (53 participants)	Placebo tablets (17 participants)
Infection of nose, throat, or voice box	8 out of 53 (15%)	4 out of 17 (24%)
Skin reaction	7 out of 53 (13%)	1 out of 17 (6%)
Headache	7 out of 53 (13%)	1 out of 17 (6%)
Fall	6 out of 53 (11%)	1 out of 17 (6%)
Diarrhea	6 out of 53 (11%)	0 out of 17 (0%)
Abnormal dreams	6 out of 53 (11%)	0 out of 17 (0%)

Did the treatments cause any of the adverse events?

During Part 1 of the trial, 30 out of 70 participants (43%) had adverse events that the trial doctors thought the treatments had caused. These events are called adverse reactions.

- 25 out of 53 participants (47%) were taking elenbecestat
- 5 out of 17 participants (29%) were taking placebo

2 participants taking elenbecestat had serious adverse reactions.

What were the results of Part 2 of the trial?

What medical problems did participants have when they took 50 mg elenbecestat?

In Part 2**,** the researchers wanted to find out about any medical problems participants had when they took 50 mg of elenbecestat once a day.

How many participants had adverse events?

During Part 2 of the trial, 30 out of 41 participants (73%) had adverse events. The table below gives a summary of the adverse events the participants had.

Type of Adverse Events in Part 2

	50 mg elenbecestat (41 participants)
How many participants had adverse events?	30 out of 41 (73%)
How many participants had serious adverse events?	6 out of 41 (15%)
How many participants stopped receiving the trial drug because of adverse events?	3 out of 41 (7%)

What were the most common serious adverse events?

During part 2 of the trial, 6 out of 41 participants (15%) had serious adverse events. Of these participants, 1 died due to worsening of dementia. The trial doctor did not think elenbecestat caused the participant's death.

What were the most common adverse events?

During part 2 of the trial, 30 out of 41 participants (73%) had adverse events.

The table on the next page shows the adverse events that happened in 10% or more of participants during Part 2. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in Part 2

	50 mg elenbecestat (41 participants)
Agitation	5 out of 41 (12%)
Fall	5 out of 41 (12%)
Difficulty falling asleep	4 out of 41 (10%)

Did the treatments cause any of the adverse events?

During Part 2 of the trial, 2 out of 41 participants (5%) had adverse reactions. This means the trial doctors thought the treatment had caused the reaction.

None of the participants had serious adverse reactions.

How has this trial helped patients and researchers?

In this trial, the researchers learned about the medical problems people with mild cognitive impairment due to Alzheimer's disease or mild to moderate dementia due to Alzheimer's disease have when they take up to 50 mg of elenbecestat 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 elenbecestat are not planned.

Where can I learn more about the trial?

You can find more information about this trial on the websites listed below. When a scientific report of this clinical trial is available, it can be found on the website listed below:

- www.clinicaltrials.gov - Once you are on the website, type **NCT02322021** into the search box and click "**Search**."

Full trial title: A Placebo-Controlled, Double-Blind, Parallel-Group, Randomized, Dose-Finding Study To Evaluate the Safety and Tolerability of E2609 in Subjects With Mild Cognitive Impairment Due to Alzheimer's Disease (Prodromal Alzheimer's Disease) and Mild to Moderate Dementia Due to Alzheimer's Disease

Protocol number: E2609-G000-202

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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