Clinical Trial Results

Research Sponsor: Eisai Inc.
Drug Studied: E2027, also called irsenontrine
Short Trial Title: A trial to learn about how E2027 works and its safety in patients with dementia with Lewy bodies

Thank you!

You and your study partner took part in this clinical trial for the trial drug, E2027. You, your study partner, and all of the participants helped researchers learn more about whether E2027 can help patient with dementia with Lewy bodies, also called DLB. Lewy bodies are tiny clumps of proteins that develop inside the nerve cells of the brain. They prevent the cells from communicating properly, eventually causing the cells to die. DLB can affect any part of the brain, leading to difficulties in memory and thinking, movement, concentration, alertness, and hallucination. Hallucination is seeing things that are not there. The symptoms of DLB get worse over time.

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 a medical and regulatory writing organization called Certara Synchrogenix.

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

What has happened since the trial started?

The trial started in May 2018 and ended in April 2020.

The trial included 200 participants from 61 study centers in the United States, Japan, United Kingdom, France, Spain, Germany, and Italy.

Of the 200 participants in this trial, 196 received trial treatment at least once.

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?

Researchers were looking for a different way to treat patients who have DLB. At the time of the trial and writing of this summary, there were no medications approved to treat DLB in the United States and the European Union. Researchers thought E2027 could help improve the symptoms of DLB.

The researchers in this trial wanted to find out if E2027 works in people with DLB. They also wanted to find out if people had any medical problems during the trial.

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

- Did E2027 improve participants' memory and thinking compared with placebo after 12 weeks of treatment when it was measured using the Montreal Cognitive Assessment scale also known as MoCA scale?
- Did E2027 improve participants' DLB symptoms compared with placebo after 12 weeks of treatment when it was measured using the Clinician's Interview Based Impression of Changes Plus Caregiver Input also known as CIBIC-Plus?
- What adverse reactions did participants receiving E2027 have? An adverse reaction is a medical problem that may be caused by the trial drug.

It is important to know that this trial was designed to get the most accurate answers to the questions listed above. There were other questions the researchers wanted to answer to learn more about how E2027 works. But, these were not the main questions the trial was designed to answer.

What kind of trial was this?

To answer these questions, researchers asked for the help of men and women like you. The participants in the trial were 56 to 86 years old. Of these participants, 62% were male, and 38% were female.

All of the participants in this trial had DLB and experienced hallucinations. They also either had mild or moderate cognitive impairment. Cognitive impairment means that a person has trouble remembering, learning, or making decisions that affect their everyday life.

In this trial, each participant needed to have a study partner to complete questionnaires and talk with study staff. A study partner is a person who was able to support the participant during the trial and spent at least 20 hours per week with the participant.

This trial was "double-blind". This means that the participants, their study partners, the trial doctors and staff, and the sponsor did not know which trial treatment the participants received.

Participants took either 50 milligrams, also called mg, of E2027 or placebo capsules by mouth once daily for up to 12 weeks. A placebo is a pill that looks like the trial drug but does not have any medicine in it.

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

What happened during the trial?

During the Screening period, the trial doctors did a full check-up to make sure each participant could join the trial.

The trial doctors or staff also:

- Confirmed that the participant had DLB
- Asked what medications each participant was taking
- Gave surveys to check participants' memory and thinking
- Took blood and urine samples
- Took pictures of the brain using a magnetic resonance imaging scan, also called an MRI scan
- Asked participants and their study partners to complete questionnaires

During the Treatment period, the participants were randomly assigned to take either 50 mg of E2027 or placebo once daily for up to 12 weeks.

Throughout the trial, the trial doctors or staff also:

- Asked participants to complete tests of memory and thinking
- Interviewed participants and their study partners about DLB symptoms
- Continued to check the participants' health, asked what medications they were taking, and took blood and urine samples
- Asked participants how they were feeling and if they had any medical problems

Four weeks after their last dose, all participants and their study partners returned to the study center.

The participants:

- Had their blood and urine samples taken
- Were asked if they had any medical problems
- Continued to complete tests of memory and thinking and interviews about DLB symptoms with their study partners.

Participants who did not complete all the trial treatments before the trial ended were urged to return to the study center 7 days after their last dose.

The figure below shows how the trial was done.

How did this trial work?

Screening period

The trial doctors or staff:

- Confirmed that the participant had DLB
- Checked participants' health if they can join the trial
- Gave surveys and questionnaires about participants' memory and thinking
- Took picture of participants' brain using MRI scan

Treatment period

All participants who could join the trial received an assigned treatment for up to 12 weeks.

The trial doctors or staff:

- Continued to check participants' health
- Asked if they had medical problems
- Gave tests to participants about their memory and thinking

After their last dose

All participants returned to study center about 4 weeks after receiving their last dose of trial treatment.

The trial doctors or staff took blood and urine samples.

All participants continued to complete tests about their memory and thinking.

What were the results of the trial?

The results each person had might be different and are not in this summary. But the results each person 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 trial results is available, it can also be found on those websites.

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.

Did E2027 improve participants' memory and thinking compared with placebo after 12 weeks of treatment when it was measured using the MoCA scale?

To answer this question, researchers asked participants to complete a test called the MoCA scale. This test is used to look at a participant's memory and thinking. Each participant was scored depending on how they complete the test. A score of 26 or above out of 30 means the participant's memory and thinking are normal. A decrease in MoCA scale score means that the participant's memory and thinking are getting worse.

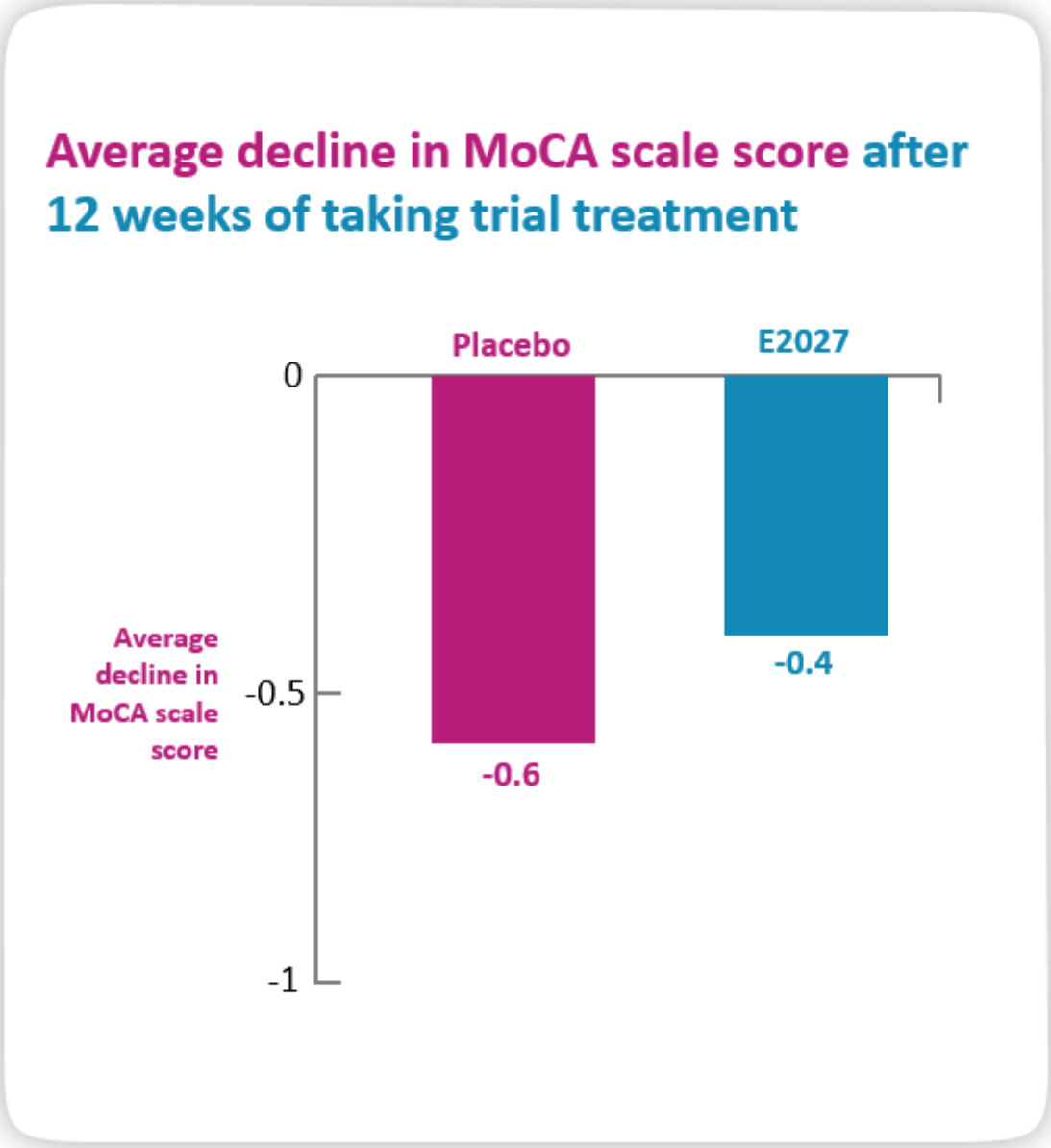
The researchers recorded the participants' MoCA scale score before they received their first trial treatment and then recorded the change in their MoCA scale score after 12 weeks of receiving trial treatment.

The researchers found that the average decline in MoCA scale score after 12 weeks of taking trial treatment was similar in participants who took placebo compared to participants who took E2027.

From before taking their first trial treatment to after 12 weeks of taking trial treatment, the average decline in MoCA scale score was:

- 0.6 for participants who took placebo
- 0.4 for participants who took E2027

The chart below shows the average decline in MoCA scale score.



Did E2027 improve participants' DLB symptoms compared with placebo after 12 weeks of treatment when it was measured using CIBIC-Plus?

To answer this question, researchers interviewed participants and their study partners using a test called CIBIC-Plus. This test is used to find out how serious the participant's DLB symptoms are.

The researchers used the CIBIC-Plus to compare symptoms before they start receiving their first trial treatment and after 12 weeks of receiving trial treatment. Then the researchers checked if the participants' DLB symptoms improved, got worse, or remained the same.

The researchers found that the percentage of participants who had small or moderate improvement in their DLB symptoms was similar in participants who took E2027 compared to participants who took placebo.

From before taking their first trial treatment to after 12 weeks of taking trial treatment, the percentage of participants who had small or moderate improvement was:

- 20.9% for participants who took placebo
- 23.6% for participants who took E2027

The table below shows how many participants had small or moderate improvement in their DLB symptoms after 12 weeks of taking trial treatment.

Small or Moderate Improvement in DLB Symptoms

	Out of 93 participants who received placebo	Out of 96 participants who received E2027
How many participants had small improvement after 12 weeks of taking trial treatment?	13 (15.1%)	18 (20.2%)
How many participants had moderate improvement after 12 weeks of taking trial treatment?	5 (5.8%)	3 (3.4%)

What medical problems did participants have?

Medical problems that happen in clinical trials are called “adverse events”. An adverse event that the trial doctors thought was caused by the trial 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 trial.

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

How many participants had adverse reactions?

In this trial,

- 27 out of 97 participants (28%) who received the placebo had adverse reactions.
- 24 out of 99 participants (24%) who received the E2027 had adverse reactions.

The table below shows how many participants had adverse reactions.

Adverse Reactions in this Trial

	Out of 97 participants who received placebo	Out of 99 participants who received E2027
How many participants had adverse reactions?	27 (28%)	24 (24%)
How many participants had serious adverse reactions?	2 (2%)	4 (4%)
How many participants stopped receiving the trial drug because of adverse reactions?	5 (5%)	8 (8%)

What were the most common serious adverse reactions?

In this trial,

- 2 out of 97 participants (2%) who received the placebo had serious adverse reactions.
- 4 out of 99 participants (4%) who received the E2027 had serious adverse reactions.

Most serious adverse reactions in this trial were experienced by 1 participant each.

No participant in this trial died due to a serious adverse reaction.

What were the most common adverse reactions?

In this trial, 51 out of 196 participants (26%) had an adverse reaction. The most common adverse reactions were hallucination, worsening DLB, and diarrhea.

The table below shows the adverse reactions that happened in at least 2% of participants in either group while on treatment. There were other adverse reactions, but these happened in fewer participants.

Most Common Adverse Reactions in This Trial

	Out of 97 participants who received placebo	Out of 99 participants who received E2027
Hallucination	6 (6%)	6 (6%)
Worsening DLB	1 (1%)	5 (5%)
Diarrhea	3 (3%)	2 (2%)
Aggression	0	2 (2%)
Dizziness	1 (1%)	2 (2%)
Sleepiness	0	2 (2%)
Constipation	2 (2%)	1 (1%)
Heart's electrical system takes longer than usual	2 (2%)	1 (1%)
Shakiness	2 (2%)	1 (1%)
Tiredness	2 (2%)	0
Irritability	2 (2%)	0
Slow movement with stiffness	2 (2%)	0

How has this trial helped patients and researchers?

In this trial, researchers learned more about how E2027 may have helped people with DLB.

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 E2027 are not planned.

There is 1 clinical trial with E2027 that is focused on learning about how E2027 affects the spinal fluid, how it works on the body, and its safety in patients with DLB or Parkinson's disease dementia. Details about this clinical trial are:

Full Title	An Open-Label Study To Evaluate the Pharmacodynamic Effects, Efficacy, Safety, and Tolerability of E2027 in Subjects With Dementia With Lewy Bodies or Parkinson's Disease Dementia With or Without Amyloid Copathology
Protocol number	E2027-A001-203
US Study number	NCT04764669
https://clinicaltrials.gov/ct2/show/NCT04764669	

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 websites listed below:

- http://www.clinicaltrialsregister.eu - Once you are on the website, click "**Home and Search**", then type **2017-003728-64** in the search box and click "**Search**".
- http://www.clinicaltrials.gov - Once you are on the website, type **NCT03467152** into the search box and click "**Search**".

Full trial title: A Placebo-Controlled, Double-Blind, Parallel-Group, Randomized Study to Evaluate the Efficacy, Safety, and Tolerability of E2027 in Subjects With Dementia With Lewy Bodies

Protocol number: E2027-G000-201

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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