Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: E2814
Short Study Title: A study to learn about the safety and risks of E2814 and whether it reaches the brains of people with dominantly inherited Alzheimer's disease

Thank you

You and your caregiver took part in this clinical study for the study drug E2814. Everyone who participated helped researchers learn more about E2814 and how it may help people who have thinking, learning, and memory problems because of dominantly inherited Alzheimer's disease (DIAD). DIAD is a rare, inherited form of Alzheimer's disease caused by a change in a person's genes.

Eisai, a Japanese pharmaceutical company that was the sponsor of this study, thanks you for your help. Eisai is committed to improving health through continuing research in areas of unmet need and sharing study results with participants.

Eisai has prepared this summary of the study and its results with a medical and regulatory writing organization called Certara.

If you and your caregiver participated in this study and 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 included 11 participants from 3 sites in the United Kingdom and the United States. Of the 11 participants, 8 received E2814 at least once.

It started in June 2021 and ended in May 2024.

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 thinking, learning, and memory problems related to DIAD. Standard treatments for people with DIAD include medicines that manage the symptoms of DIAD.

The researchers in this study wanted to better understand the safety and risks of E2814 and whether it reaches the brains of people with DIAD. They also wanted to find out if people had any medical problems during the study.

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

- Did participants with DIAD tolerate E2814 during the study?
- Did E2814 reach the brains of the participants with DIAD?
- What adverse events did participants receiving E2814 have? An adverse event is a medical problem that may or may not be caused by the study drug.

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 E2814 works, but these were not the main questions the study was designed to answer.

What kind of study was this?

To answer the main questions above, researchers asked for the help of participants who were between 49 and 68 years old and had been diagnosed with DIAD. Of these participants, 50% were male and 50% were female.

All participants in this study had thinking, learning, and memory problems related to DIAD.

The study was divided into 2 parts. Part 1 lasted for about 22 months (96 weeks) and was further divided into 2 parts: Part 1A and Part 1B.

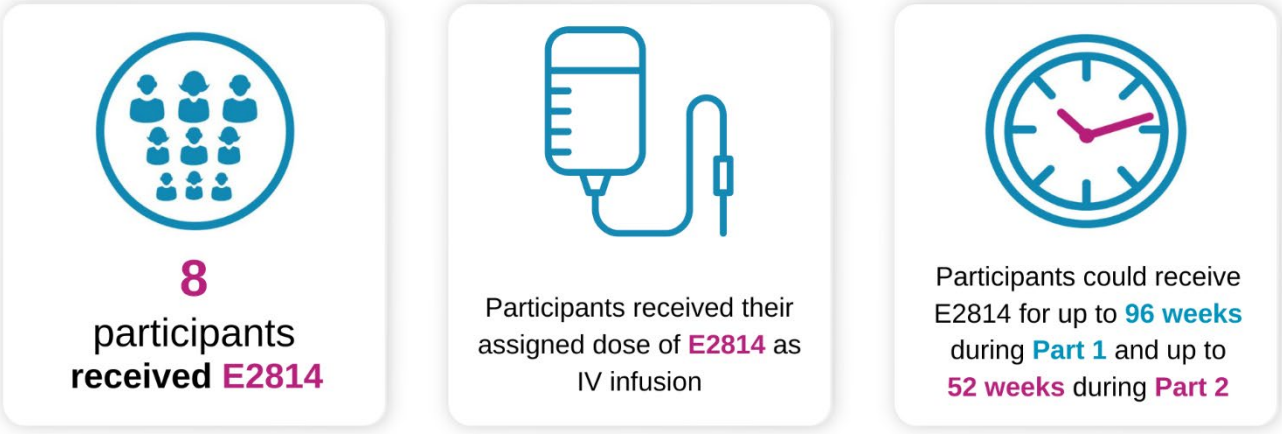
In **Part 1A**, participants received E2814 750 milligrams (mg) once every 4 weeks as an injection into the vein (IV infusion) for up to 12 weeks. Participants who tolerated E2814 750 mg could join Part 1B.

In **Part 1B**, participants received increasing doses of E2814 IV infusion. They started with 1500 mg once every 4 weeks. After 12 weeks, the dose increased to 3000 mg once every 4 weeks. Then, after another 12 weeks, they received 4500 mg once every 4 weeks for the remainder of the study.

In **Part 2**, participants received E2814 3000 mg IV infusion once every 4 weeks for up to 52 weeks.

This study was "open-label". This means that the participants, the study doctors and staff, and the sponsor knew that participants were receiving E2814.

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



What happened during the study?

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

The study doctors and staff also:

- Confirmed all participants had DIAD
- Took blood and urine samples for testing
- Completed a survey to check participants' ability to think, learn, and remember
- Performed brain scans to check participants' DIAD status

Before participants received E2814, study doctors did a spinal tap to collect fluid from the spinal cord called cerebrospinal fluid (CSF).

During the treatment period, participants received their assigned dose of E2814 IV infusion.

Throughout the treatment period, the study doctors and staff:

- Took blood and urine samples for testing
- Performed brain scans to check participants' DIAD status
- Did a spinal tap to collect CSF

After their last dose, the study doctors and staff followed up on participants for up to 12 weeks to check their health.

The figure below shows how the study was done.

How did this study work?

Before the study started

The study doctors or staff:

- Checked each participant's health to make sure they could join the study
- Confirmed all participants had DIAD
- Took blood and urine samples
- Performed brain scans
- Did spinal tap to collect CSF

During the treatment period

All 8 participants received their assigned dose of E2814 IV infusion.

The study doctors or staff:

- Performed brain scans to check participants' DIAD status
- Did spinal tap to collect CSF
- Asked if participants were having medical problems and other medicines participants were taking

After the treatment period

About 12 weeks after the last dose, study doctors or staff followed up on participants.

During this period, the study doctors or staff also asked participants about medical problems they were having and other medicines they were taking.

What were the results of the study?

This is a summary of the main results of this study. Each participant's individual results were different and unique to them. Individual results are not given separately in this summary, but all participants' results are summarized together here. 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.

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

Did participants with DIAD tolerate E2814 during the study?

After reviewing all of the results, overall, participants tolerated all tested doses of E2814, except for 1 participant who experienced a serious medical problem—a blood clot in a vein in the brain—which led to the stopping of E2814 during the study.

More information about the safety and risks of E2814 can be found below.

Did E2814 reach the brains of the participants with DIAD?

To answer this question, researchers collected CSF using a spinal tap to check the amount of E2814.

Researchers were able to measure the amount of E2814 in the CSF, confirming that E2814 reached the brains of participants with DIAD.

What medical problems did participants have?

Medical problems that happen to participants in clinical studies are called “adverse events”. If the study doctors thought an adverse event was caused by the study drug, it is called an “adverse reaction”. Adverse events or reactions are considered “serious” if the participant needs to be admitted to a hospital, if they are life-threatening, or if they cause lasting health problems.

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

How many participants had adverse events?

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

Adverse Events in This Study

	Out of 8 participants who received E2814
How many participants had adverse events?	8 (100%)
How many participants had serious adverse events?	3 (38%)
How many participants died because of adverse events?	0 (0%)
How many participants had adverse reactions	3 (38%)
How many participants stopped receiving E2814 because of adverse events?	3 (38%)

What were the most common serious adverse events?

In this study, there were no common serious adverse events. The serious adverse events were blood clot in the veins of the brain, seizure, lung infection, and joint pain.

What were the most common adverse events?

In this study, the most common adverse events were COVID-19 (2 participants) and nose and throat infection (2 participants). Other adverse events happened in 1 participant each.

What were the most common adverse reactions?

In this study, there were no common adverse reactions. The adverse reactions were swelling of the legs and arms, pain in extremity, blood clot in the veins of the brain, vomiting, and inflammation of blood vessels.

How has this study helped patients and researchers?

In this study, researchers learned more about how E2814 may have helped people with DIAD.

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 E2814 are either ongoing or planned.

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:

- http://www.clinicalstudiesregister.eu - Once you are on the website, click "**Home and Search**", then type **2020-005728-12** in the search box and click "**Search**".
- http://www.clinicalstudies.gov - Once you are on the website, type **NCT04971733** into the search box and click "**Search**".

Full study title: An Open-Label Phase 1b/2 Study to Assess Safety and Target Engagement of E2814 in Subjects with Mild to Moderate Cognitive Impairment Due to Dominantly Inherited Alzheimer's Disease

Protocol number: E2814-G000-103

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 numbers for general information are +1-888-274-2378 (USA) and +44-845-676-1400 (UK).

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 "to give first thought to patients and the people in the daily living domain, and increase the benefits that health care provides to them as well as meet diverse healthcare needs worldwide", 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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