Clinical Study Results

Research Sponsor: Eisai Inc.
Drug Studied: Lecanemab, also called BAN2401
Short Study Title: A study to learn how well lecanemab works and its safety and risks in people with early Alzheimer's disease

Thank you

You took part in this clinical study for the study drug BAN2401, also called lecanemab. Everyone who participated helped researchers learn more about lecanemab and how it may help people with early Alzheimer's disease (AD). AD is a brain disorder that causes problems with memory, thinking, and behavior.

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 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?

It started in December 2012 and ended in July 2018.

The study included 856 participants from 117 study sites in the following countries:

Canada	France	Germany	Italy
Japan	Netherlands	South Korea	Spain
Sweden	United Kingdom	United States	

Out of 856 participants, 854 received one or more doses of study treatment (lecanemab or placebo). A placebo looks like lecanemab but does not have real medicine in it.

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 early AD. Previously, treatments for early AD included medicines that could help reduce some of its symptoms. But these medicines do not prevent the disease from getting worse.

The researchers in this study wanted to find out how well lecanemab works and its safety and risks in people with early AD. 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:

- Can lecanemab help slow down the worsening of AD, and if so, which dose of lecanemab is most effective?
- How well can participants tolerate lecanemab?
- What adverse events did participants receiving lecanemab 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 lecanemab 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 50 and 90 years old. Of these participants, 51% were male and 49% were female. The youngest was 50 years old, and the oldest was 90 years old.

All participants in this study had early AD. Some had mild memory or thinking problems likely caused by AD, while others had AD dementia. People with AD dementia have more noticeable memory loss and greater difficulty with daily activities.

This study was "double-blind". This means that the participants, the study doctors and staff, and the sponsor did not know which treatment group the participants were in.

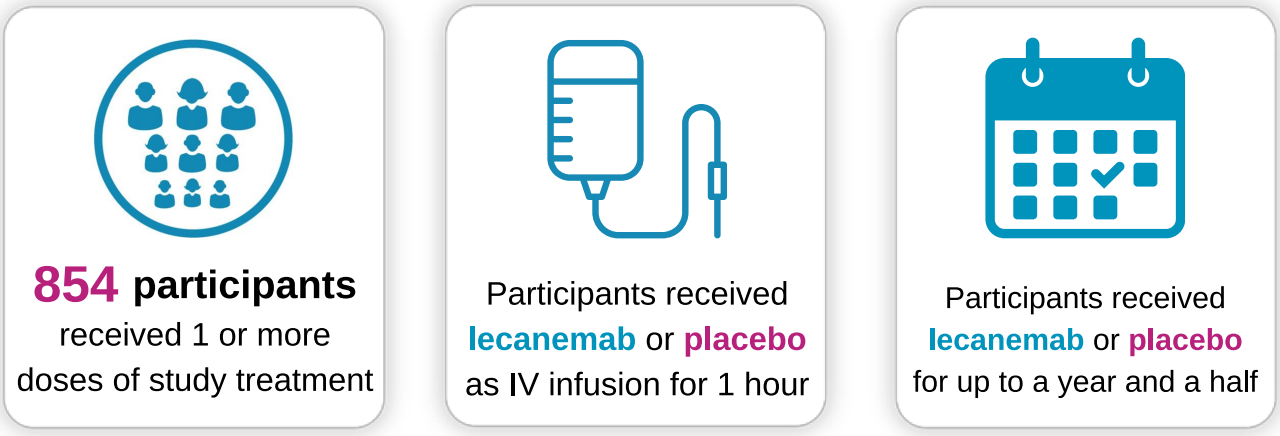
In this study, the study treatment (lecanemab or placebo) was measured in milligrams per kilogram of body weight (or mg/kg).

Participants were randomly divided into 6 treatment groups (like rolling a die):

- **Group 1**: participants received placebo.
- **Group 2**: participants received lecanemab 2.5 mg/kg every 2 weeks.
- **Group 3**: participants received lecanemab 5 mg/kg every 4 weeks.
- **Group 4**: participants received lecanemab 5 mg/kg every 2 weeks.
- **Group 5**: participants received lecanemab 10 mg/kg every 4 weeks.
- **Group 6**: participants received lecanemab 10 mg/kg every 2 weeks.

Participants in this double-blind study received lecanemab or placebo as an infusion into the vein (IV infusion) every 2 or 4 weeks for up to a year and a half (18 months).

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



What happened during the study?

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

The doctors or staff also:

- Confirmed that participants have early AD
- Analyzed blood and urine samples
- Obtained scans of participants' brains
- Completed different surveys to assess participants' early AD

During the treatment period, participants received their assigned dose of lecanemab or placebo for up to a year and a half (18 months).

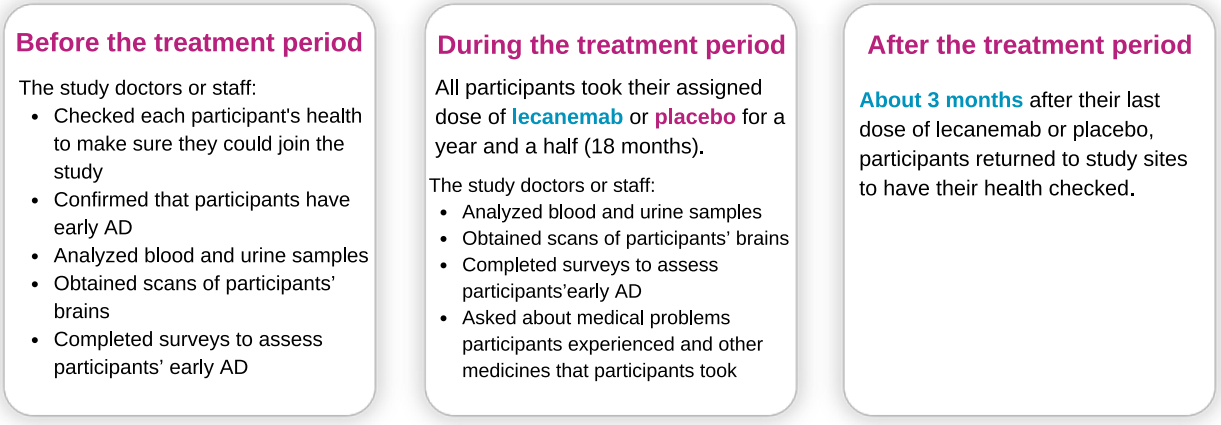
Throughout the study, the doctors:

- Analyzed blood and urine samples
- Obtained scans of participants' brains
- Completed different surveys to assess participants' early AD
- Asked about medical problems that participants experienced and other medicines that participants took

About 3 months after their last dose of lecanemab or placebo, participants returned to their study site to have their health checked.

The figure below shows how the study was done.

How did this study work?



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. A full report of the study results is available and 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.

Can lecanemab help slow down the worsening of AD, and if so, which dose of lecanemab is most effective?

To answer both questions, researchers checked the results of the following tests:

- **Alzheimer's Disease COMposite Score** (**ADCOMS**): A scoring tool that doctors use to check the participant's memory, thinking, and ability to do daily activities.
- **Brain amyloid scan**: A scan that shows the amount of amyloid in the brain. Amyloid is a protein that can build up in clumps and damage brain cells, making it harder for brain cells to communicate.
- **Clinical Dementia Rating – Sum of Boxes** (**CDR-SB**): A tool that doctors use to check how much a participant's ability to remember, think, and do daily activities is affected by dementia.
- **Alzheimer's Disease Assessment Scale – Cognitive Subscale** (**ADAS-Cog14**): A test that doctors use to check how well a participant's memory, thinking, and language skills are working.

Researchers calculated the changes in the results of each test before and after 18 months of treatment (12 months for ADCOMS). Researchers then compared the findings between participants who took lecanemab and those who took placebo.

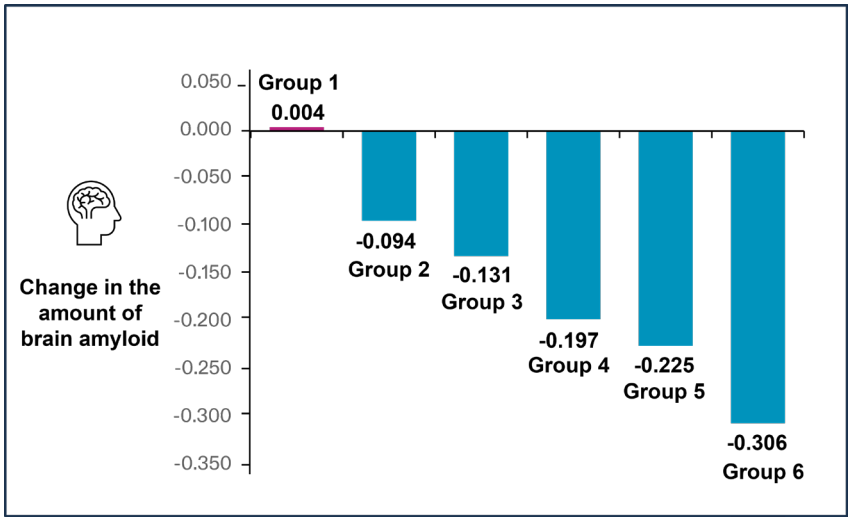
ADCOMS

After 12 months of treatment, participants in **Group 6** (lecanemab 10 mg/kg every 2 weeks) showed 35% slower worsening of AD based on the ADCOMS score compared with participants in **Group 1** (placebo).

Participants in the lecanemab group still got worsening of AD over time, but more gradually compared to those in the placebo group.

Brain Amyloid Scan

The figure below shows the change in the amount of brain amyloid after 18 months of treatment. A negative number means that the level of brain amyloid decreased after 18 months of treatment.



Based on the results above, lecanemab reduced the amount of brain amyloid, while placebo increased the amount of brain amyloid. The findings also showed that higher doses of lecanemab led to a greater reduction in the amount of brain amyloid.

CDR-SB

After 18 months of treatment, participants in **Group 6** (lecanemab 10 mg/kg every 2 weeks) showed 26% slower worsening of AD based on the CDR-SB score compared with participants in **Group 1** (placebo).

ADAS-Cog14

After 18 months of treatment, participants in **Group 6** (lecanemab 10 mg/kg every 2 weeks) showed 47% slower worsening of AD based on the ADAS-Cog14 score compared with participants in **Group 1** (placebo).

Based on the results above, researchers found that lecanemab 10 mg/kg every 2 weeks was the most effective dose in slowing down the worsening of AD.

How well can participants tolerate lecanemab?

To answer this question, researchers looked at all medical problems that participants experienced and all abnormal laboratory test results during the study.

Overall, participants tolerated all tested dose levels of lecanemab well.

More information about the safety and risks of lecanemab is presented below.

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.

Adverse Events in This Study

	Out of 245 participants who received placebo Total	Out of 609 participants who received lecanemab Total
How many participants had adverse events?	216 (88%)	552 (91%)
How many participants had serious adverse events?	43 (18%)	86 (14%)
How many participants stopped receiving lecanemab or placebo because of adverse events?	15 (6%)	92 (15%)

What were the most common serious adverse events?

In the **placebo group**, the most common serious adverse events – reported by a total of 2 participants or more – were the following:

- Fall – 4 participants
- Swelling and pain in the joints – 4 participants
- Fainting – 3 participants
- Bleeding between the brain and its outer covering – 2 participants

In the **lecanemab group**, the most common serious adverse events – reported by a total of 4 participants or more – were the following:

- Brain swelling seen on scan – 4 participants
- Chest pain not caused by a heart problem – 4 participants
- Mini-stroke – 4 participants

A total of 2 participants in **placebo** group and 5 participants in **lecanemab** group died because of adverse events. Study doctors thought that none of the adverse events that led to the death of a participant were caused by the study drug, except for 1 participant who had an abnormal tumor in the brain.

What were the most common adverse events?

The top 3 most common adverse events were the following:

- Reaction (such as redness) that happened during or soon after IV infusion
- Headache
- Infection of the parts of the body that collect and pass out urine

The table below shows the adverse events that happened in 10% or more of participants in the lecanemab group. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in This Study

	Out of 245 participants who received placebo Total	Out of 609 participants who received lecanemab Total
Reaction (such as redness) that happened during or soon after IV infusion	8 (3%)	109 (18%)
Headache	25 (10%)	96 (16%)
Infection of the parts of the body that collect and pass out urine	33 (13%)	69 (11%)
Nose and throat infection	41 (17%)	66 (11%)
Fall	32 (13%)	61 (10%)

How has this study helped patients and researchers?

In this study, researchers learned more about how well lecanemab works and its safety and risks in people with early AD.

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.

Lecanemab is an approved medicine for the treatment of early AD in many countries worldwide. Further clinical studies with lecanemab for early AD are ongoing.

Where can I learn more about the study?

You can find more information about this study on the websites listed below. A full report of the study results is available and can also be found here:

- http://www.clinicalstudiesregister.eu - Once you are on the website, click "**Home and Search**", then type **2012-002843-11** in the search box and click "**Search**".
- http://www.clinicalstudies.gov - Once you are on the website, type **NCT01767311** into the search box and click "**Search**".

Full study title: A Placebo-Controlled, Double-Blind, Parallel-Group, Bayesian Adaptive Randomization Design and Dose Regimen-finding Study With an Open-Label Extension Phase to Evaluate Safety, Tolerability and Efficacy of BAN2401 in Subjects With Early Alzheimer's Disease

Protocol number: BAN2401-G000-201

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

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.

CERTARA

Certara is a worldwide medical and regulatory writing organization and is not involved in recruiting participants or in conducting clinical studies
Certara Headquarters 4 Radnor Corporate Center Suite 350 Radnor, PA 19087
https://www.certara.com • 1-415-237-8272