Clinical Study Protocol Synopsis

A study to confirm the efficacy and safety of lecanemab in participants with preclinical Alzheimer's disease

Full Study Title:	AHEAD 3-45 Study: A Placebo-Controlled, Double-Blind, Parallel-Treatment Arm, 216 Week Study With an Extension Phase to Evaluate Efficacy and Safety of Treatment With BAN2401 in Subjects With Preclinical Alzheimer's Disease and Elevated Amyloid (A45 Trial) and in Subjects With Early Preclinical Alzheimer's Disease and Intermediate Amyloid (A3 Trial)		
EU Clinical Study Number:	2024-510888-39	**US Clinical Study Number:**	NCT04468659
Study Sponsor:	Eisai, Inc., Nutley, NJ, USA	Telephone number:	+1 201-692-1100

Why is this research needed?

Researchers are looking for a way to treat people who have preclinical Alzheimer's disease. **Alzheimer's Disease** (or **AD**) is a brain disorder that causes problems with memory, thinking, and behavior. People with preclinical AD have beta-amyloid in the brain but do not have symptoms of AD. **Beta-amyloid** is a toxic protein fragment which can disrupt communication between brain cells. **BAN2401** (also known as **lecanemab**) may help people with preclinical AD by preventing the formation of amyloid plaques.

In this study, researchers want to learn about the efficacy and safety of lecanemab in participants with preclinical AD who have certain levels of brain amyloid. Participants were divided into 2 groups (A3 or A45) depending on the levels of brain amyloid.

What treatment is being studied?

All participants will receive lecanemab or placebo for about 4 years as an injection through the vein. This type of injection is called intravenous infusion (or IV infusion). A placebo looks like lecanemab but does not have any medicine in it.

Doses of lecanemab will be measured in milligrams per kilogram of body weight.

No one involved in the study will know which treatment participants will receive. This is called a double-blind study.

What are the goals of this study?

The primary objective is to investigate how well lecanemab may work in preventing the worsening of memory, thinking, and behavior (main focus of A45) and in reducing brain amyloid after about 4 years of treatment (main focus of A3).

The secondary objectives are to investigate whether lecanemab can reduce brain amyloid (A45) and other toxic brain proteins after about 2 and 4 years of treatment (A3 and A45) and whether it can prevent the worsening of neurologic function using other tests after about 4 years of treatment (A45). Researchers will also investigate the safety of lecanemab (A3 and A45).

What are the measurements in this study?

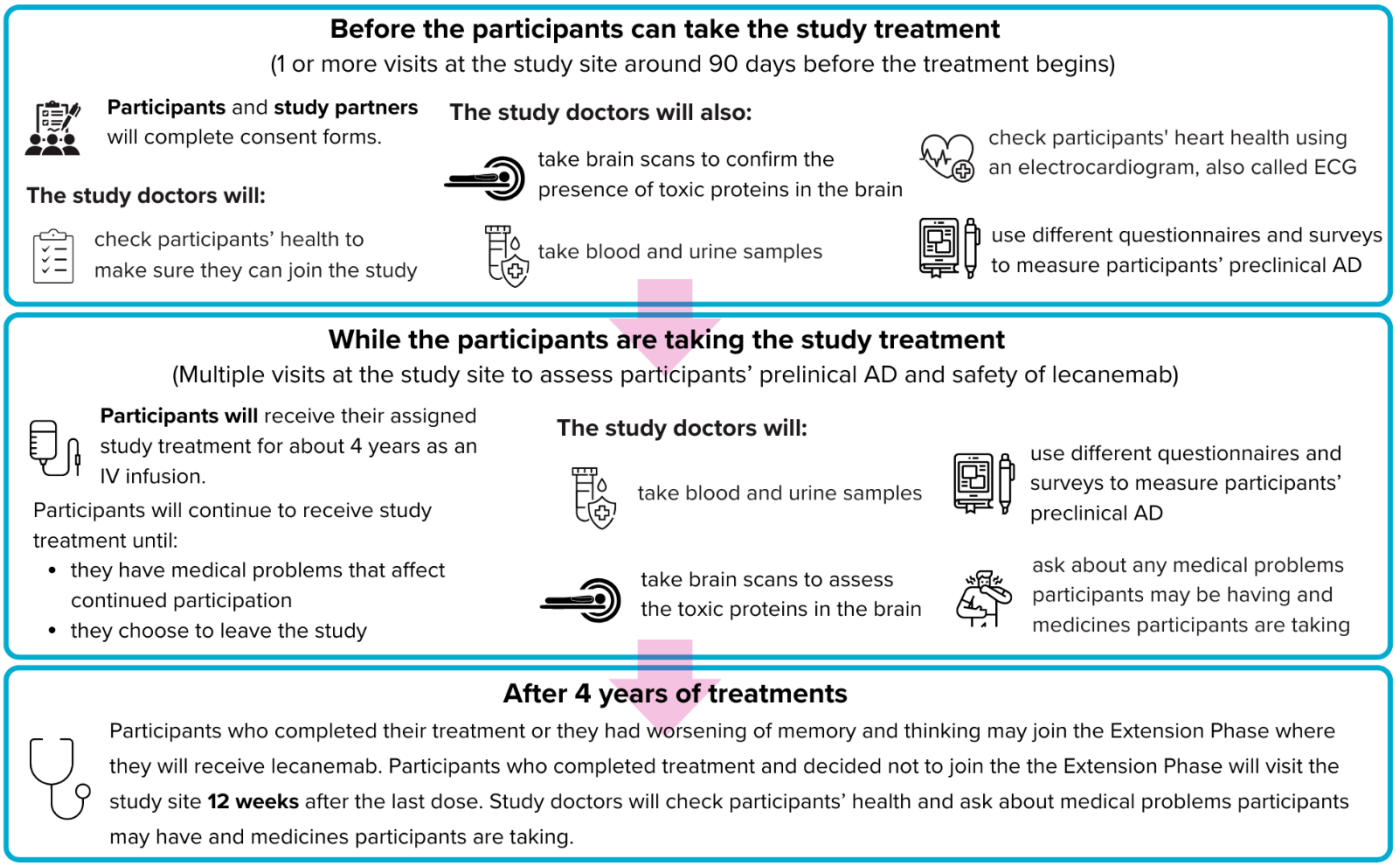
1. **Main measurement:** To investigate the primary objective, researchers will use a tool that measures memory, thinking, and behavior and brain scans to check the level of brain amyloid.
2. **Secondary measurements:** To investigate the secondary objectives, researchers will use other tools and questionnaires to measure neurologic function. They will also collect information on any medical problems that participants may have during the study.

The researchers will also collect other information about lecanemab. The measurements described above are the most important for this study.

What will happen during the study?

Before participants take part in the study, study doctors will explain the study to participants and their study partners and answer any questions they may have.

The chart below shows what will happen in the study.



Who can and cannot take part in this study?

People can take part in this study if they:

- Are 55 to 80 years old
- Have increased levels of brain amyloid without AD symptoms

People cannot take part in this study if they:

- Have any medical conditions that may affect study assessments/treatments or pose a safety risk

These are just some of the main requirements. Study doctors will check all requirements to see if a person can safely join this study. Participation in this study is voluntary. Participants can leave the study at any time.

What are the potential benefits and risks of taking part in this study?

Potential Benefits (Advantages): Lecanemab may help in treating participant's preclinical AD. The information collected in this study may help doctors learn more about lecanemab and preclinical AD, which could help people with AD.

Potential Risks (Disadvantages): Lecanemab may not help in treating participant's preclinical AD, or they might have side effects from lecanemab. There may be additional risks, which are unknown and unexpected.