Clinical Study Protocol Synopsis

A study to learn how well E2086 may work, its safety profile, and how the bodies of adult participants with narcolepsy handle E2086

Full Study Title:	A Randomized, Double-Blind, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of E2086 in Adults with Narcolepsy
EU Clinical Study Number:	2025-523503-30
US Clinical Study Number:	NCT07493265
Study Sponsor:	Eisai Inc., Nutley, NJ, USA Telephone number: +1 888-274-2378

Why is this research needed?

Researchers are looking for a different way to treat people who have narcolepsy. **Narcolepsy** is a disorder associated with daytime sleepiness. There are 2 types of narcolepsy: type 1 (NT1) and type 2 (NT2). The key difference is having **cataplexy**, which is the sudden weakening of muscles usually caused by strong emotions like laughter. People with NT1 have cataplexy, while those with NT2 do not.

Standard treatments for people with narcolepsy include medicines that help them stay awake and alert. E2086 may help to treat people with narcolepsy by acting like the substance in the brain that helps control wakefulness.

This study tests different doses of E2086 to learn how well it may work in participants with NT1 or NT2.

What treatment is being studied?

Participants will take E2086 or placebo as tablets once daily during the treatment period.

A **placebo** looks like E2086 but does not have any medicine in it.

Participants will take low, middle, and high doses of E2086 or placebo, each for 4 weeks, with a 7-day break between dose strengths.

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

What are the goals of this study?

Primary Objective	Main Secondary Objective	Other Secondary Objectives
To find out if E2086 can help to improve wakefulness in participants with NT1 and NT2 compared with placebo	To find out if E2086 can help to reduce cataplexy in participants with NT1 compared with placebo	To learn more about how well E2086 works and its safety profile, how it affects blood pressure, and how the body handles it

What are the measurements in this study?

1. **Primary measurement:** Researchers will compare how long participants can stay awake before treatment and after 4 weeks of treatment.

2. **Main secondary measurement:** Researchers will compare the number of weekly cataplexy events during 4 weeks of treatment for participants with NT1.

   Other secondary measurements: Researchers will check how often participants feel sleepy, any medical problems they may have, their average blood pressure, and the amount of E2086 in the blood.

The researchers will also collect other information about E2086, but the measurements described above are the most important for this study.

What will happen during the study?

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

The chart below shows what will happen in each part of the study.

Before the participants take study treatment

1 or more visits at the study site during the 4 weeks before the treatment begins

All participants will complete consent forms.

The study doctors will:

Check participants' health to make sure they can join the study

The study doctors will also:

Ask participants to record sleep information in their diaries. Participants with NT1 will also record cataplexy information in their diaries.

Take blood and urine samples

Check participants' heart health using an electrocardiogram, also called ECG

Do tests to measure how quickly participants fall asleep and how sleepy they feel during the day

While the participants are taking study treatment

Multiple visits at the study site to assess the goals of this study

Participants will take E2086 or placebo as tablets once daily during treatment period.

The study doctors will:

Do tests to measure how quickly participants fall asleep and how sleepy they feel during the day

The study doctors will also:

Ask participants to continue completing their diaries

Check participants' heart health using ECG

Take blood and urine samples

Ask about medical problems participants may have and medicines participants are taking

After the participants finish or stop taking study treatment

After **treatment ends**, participants will have a follow-up period (about 14 days) without taking E2086 but will continue completing their diaries. Then there will be a final study visit. If a **participant stops treatment early**, they will have an early visit (within 7 days after their last dose) and may continue follow-up checks or have an early final study visit about 2 weeks later.

Who can and cannot take part in this study?

People can take part in this study if they:

- are 18 years old or older
- have NT1 or NT2

People cannot take part in this study if they:

- are pregnant or breastfeeding women
- have certain medical conditions that require treatment

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

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

Potential Benefits (Advantages): E2086 may help to treat narcolepsy. The information collected in this study may help doctors learn more about E2086 that could help people with narcolepsy.

Potential Risks (Disadvantages): E2086 may not help to treat narcolepsy, or participants might have side effects from E2086. Being part of a study can burden participants (for example, participants must make time to visit the study site and be admitted overnight on scheduled days). There may be other risks that are unknown and unexpected.