Clinical Trial Results

Research Sponsor: Eisai Ltd.

Drug Studied: Lemborexant, also called Davigo™ or E2006

Short Trial Title: A trial to learn how lemborexant works and how safe it is in adults and elderly people with chronic insomnia

Thank you!

You took part in this clinical trial for the trial drug lemborexant. You and all of the participants helped researchers learn more about whether lemborexant can help adults and elderly people with chronic insomnia. Chronic insomnia means having sleep problems over a long period of time. Chronic insomnia symptoms also negatively affect the person's daily life.

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 Synchrogenix.

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

What has happened since the trial started?

The trial started in November 2013 and ended in April 2014.

The sponsor of the trial reviewed the data collected and created a report of the results. This is a summary of that report.

The trial included 291 participants from 22 sites in the United States.

Why was the research needed?

Researchers were looking for a different way to treat people who have chronic insomnia. Researchers think lemborexant could help patients with insomnia get more sleep.

The researchers in this trial wanted to find out if lemborexant works in adults and elderly people with chronic insomnia. 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:

- Which dose or doses of lemborexant increased sleep efficiency, also called SE, but did not increase sleepiness the next morning? SE refers to the amount of time a person is actually asleep during the time spent in bed trying to sleep.
- Which dose or doses of lemborexant also did not increase sleepiness the next morning?
- Which dose or doses of lemborexant increased SE?
- Which dose or doses of lemborexant decreased the time participants took to fall fully asleep?
- Which dose or doses of lemborexant decreased the amount of time awake after falling asleep?
- What adverse events did participants taking lemborexant have? An adverse event is a medical problem that may or may not 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 lemborexant works. But, these were not the main questions the trial was designed to answer.

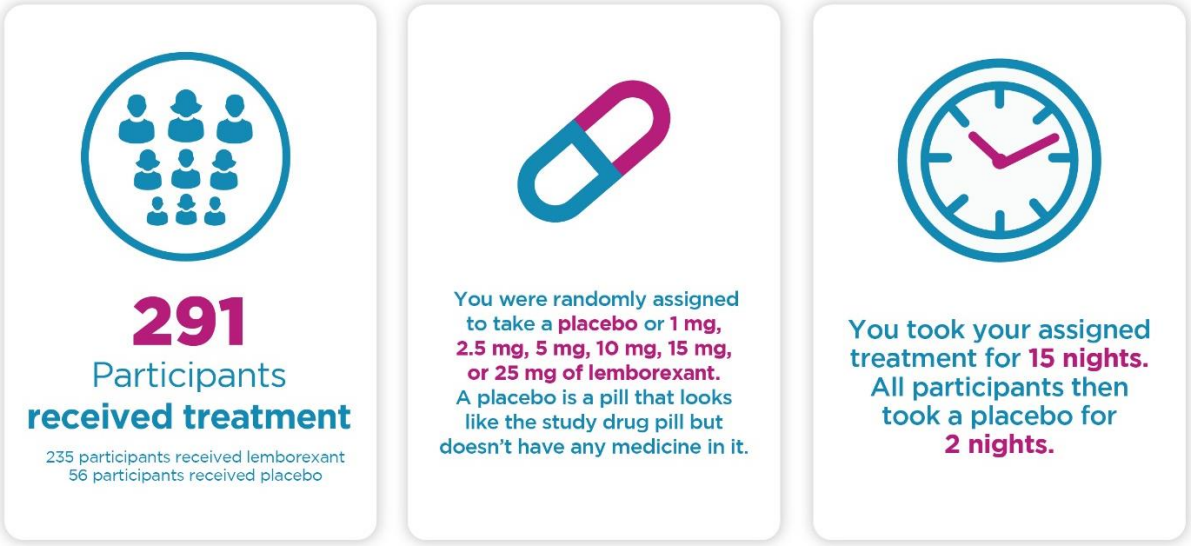
What kind of trial was this?

To answer these questions, researchers asked for the help of men and women like you. The participants in the trial were 19 to 80 years old. 37.5% of the participants were male, and 62.5% of the people were female.

All of the people in this trial had chronic insomnia. Chronic insomnia means that a person has trouble getting to sleep or staying asleep for more than 3 nights a week for 3 months or more. People with chronic insomnia often have trouble concentrating, have mood changes, and perform poorly at work or school.

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

You took lemborexant or placebo by mouth. A placebo is a pill that looks like the study drug pill but does not have any medicine in it. The figure below shows how treatment was given in your trial.



What happened during the trial?

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

The doctors or study staff also:

- Asked what medications each participant was taking
- Took blood, urine, and saliva samples
- Checked each participant's heart health using an electrocardiogram, also called an ECG
- Did overnight tests to measure and record sleep
- Completed questionnaires

During the trial, participants were randomly assigned to take either lemborexant or a placebo. Participants took their assigned treatment for 15 nights and then all participants took a placebo for 2 nights.

Participants completed a Sleep Diary each day. Participants stayed overnight for tests at the study center for a total of 7 nights. While at the study center, they also completed questionnaires about their sleep and their moods.

Throughout the trial, the doctors or study staff**:**

- Continued to check the participants' health; asked what medications they were taking, and took blood, urine, and saliva samples
- Asked the participants how they were feeling and if they had any adverse events
- Checked each participant's heart health
- Did overnight tests to measure and record participants' sleep

After their last dose, all participants:

- Continued to complete their Sleep Diary each day
- Returned to the clinic approximately 12 days later for their final visit and tests

The figure below shows how the trial was done.

How did this trial work?

What were the results of the trial?

This is a summary of the main results of this trial up to April 2014. 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 these websites.

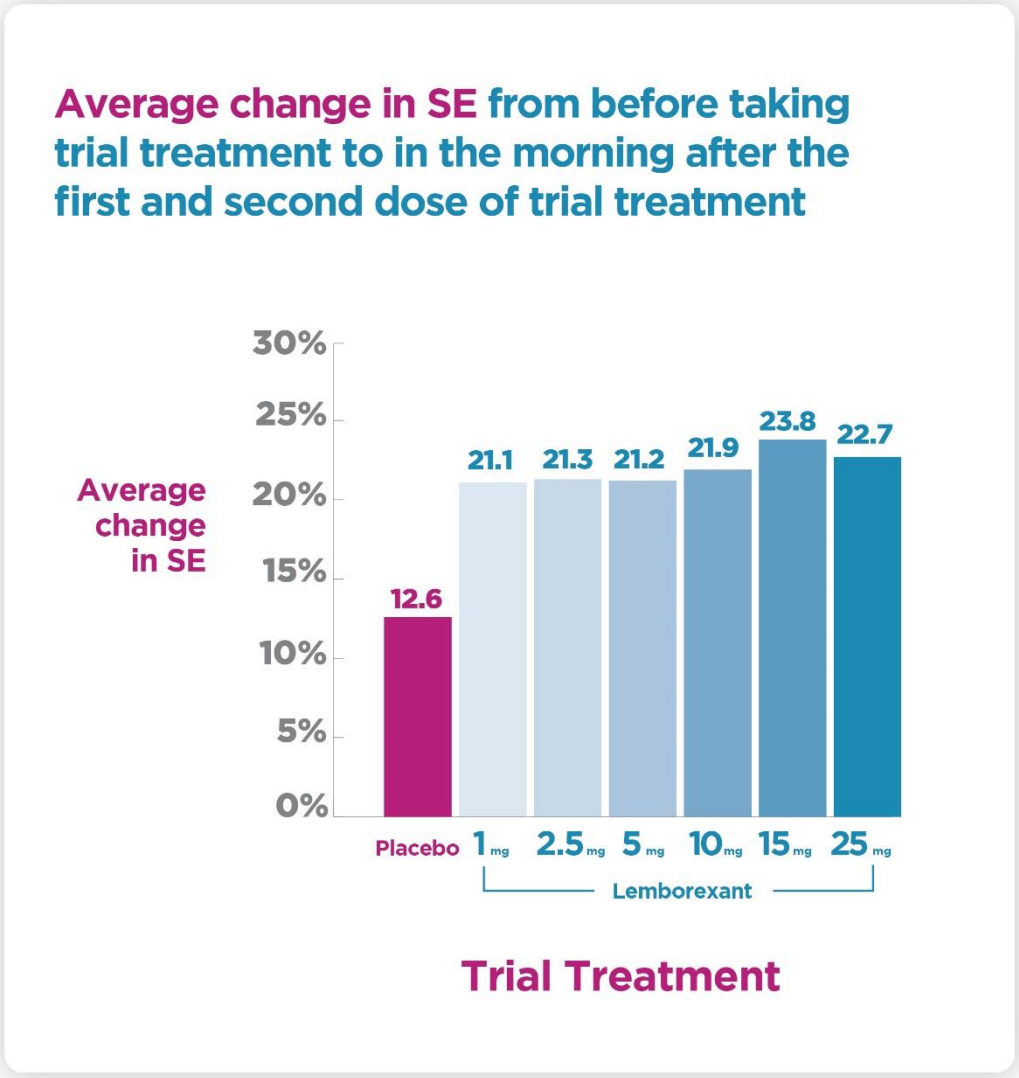
Researchers look at the results of many trials to decide which treatment options may work best and are well tolerated. Other trials may provide new information or different results. Always talk to a doctor before making any treatment decisions.

Which dose or doses of lemborexant increased the participants' SE but did not increase their sleepiness the next morning at the beginning of the trial?

To see if participants had in increase in SE after taking trial treatment, researchers measured participants' SE before they took trial treatment and then measured the average change in participants' SE in the morning after the first and second dose of trial treatment.

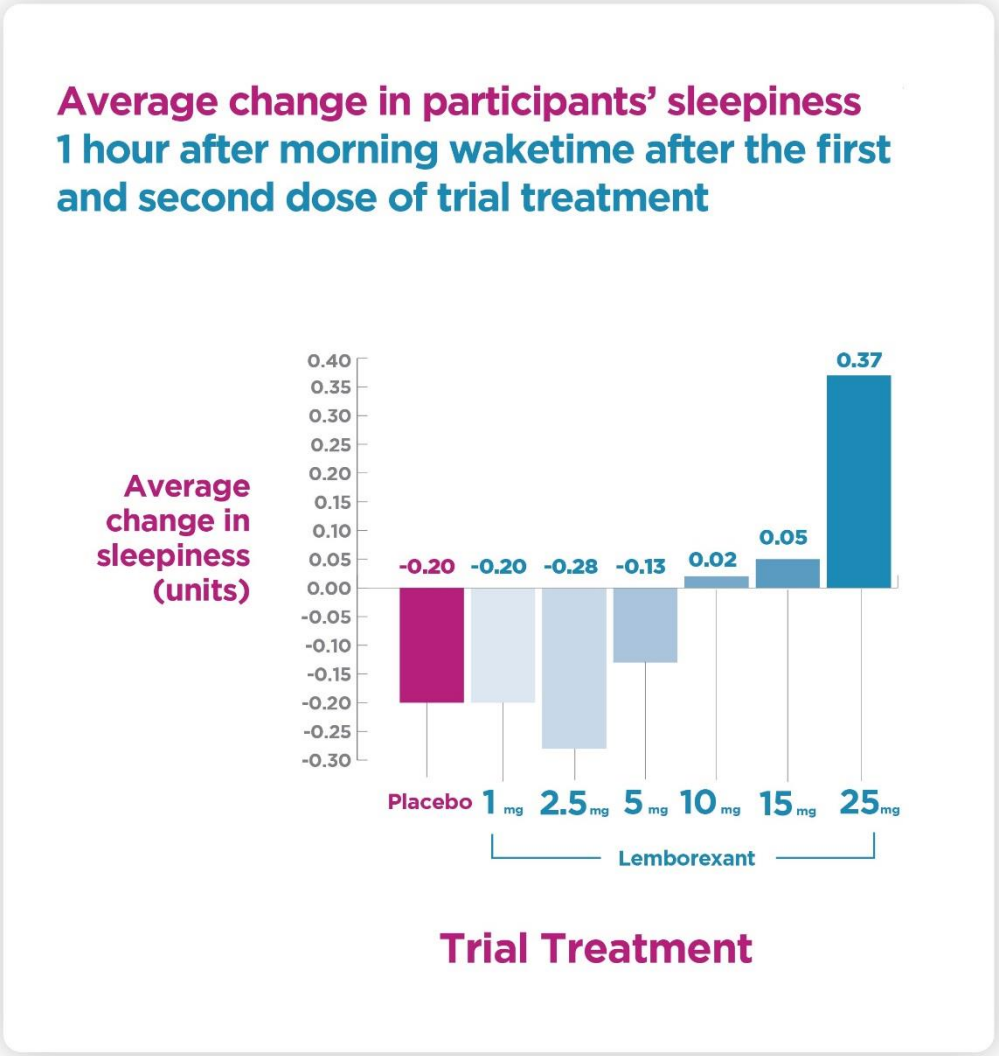
All of the doses of lemborexant significantly increased participants' SE in the morning after the first and second dose of trial treatment.

The chart below show the average change in participants' SE in the morning after the first and second dose of trial treatment. A higher number meant that there was more of a change in SE.



To see if participants had an increase in sleepiness 1 hour after morning waketime after taking trial treatment, the researchers measured participants' sleepiness before they took trial treatment and then measured the average change in participants' sleepiness 1 hour after morning waketime after the first and second dose of trial treatment.

The chart below shows the average change in participants' sleepiness 1 hour after morning waketime after the first and second dose of trial treatment. A higher number meant that participants had an increase in sleepiness.



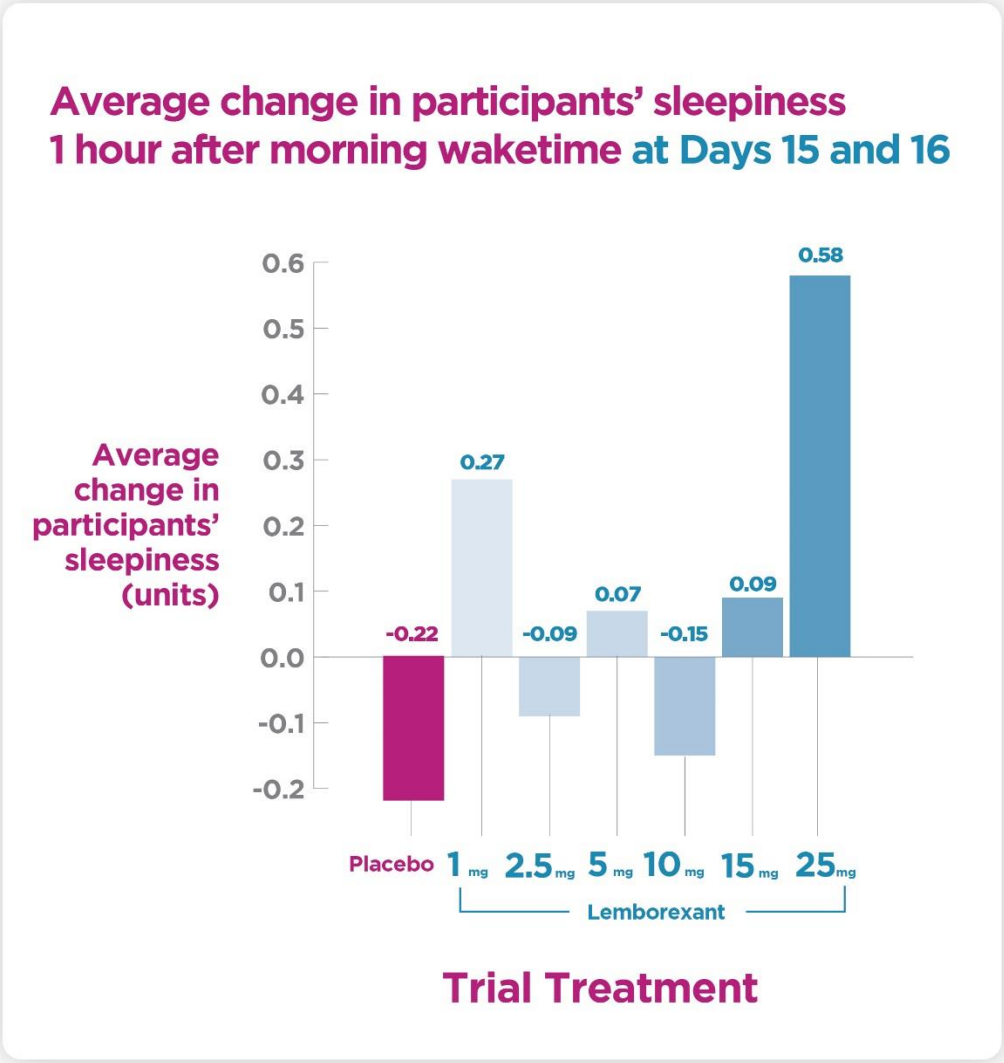
Then, the researchers combined the information from both of these charts together to see which dose or doses increased the participants' SE but did not increase their sleepiness the next morning.

The 5-mg and 10-mg doses of lemborexant both increased the average participants' SE without significantly increasing sleepiness the next morning.Which dose or doses of lemborexant also did not increase sleepiness the next morning?

To see if participants had an increase in sleepiness 1 hour after morning waketime at the end of the trial, the researchers measured participants' sleepiness before they took trial treatment and then measured the average change in participants' sleepiness 1 hour after morning waketime at Days 15 and 16.

The 2.5 mg and 10 mg doses of lemborexant did not increase sleepiness 1 hour after morning waketime at Days 15 and 16. The 1 mg, 5 mg, 15 mg, and 25 mg doses of lemborexant increased sleepiness 1 hour after morning waketime at Days 15 and 16. These increases were not considered to be significant.

The chart below shows the average change in participants' sleepiness 1 hour after morning waketime at Days 15 and 16. A higher number meant that participants had an increase in sleepiness.

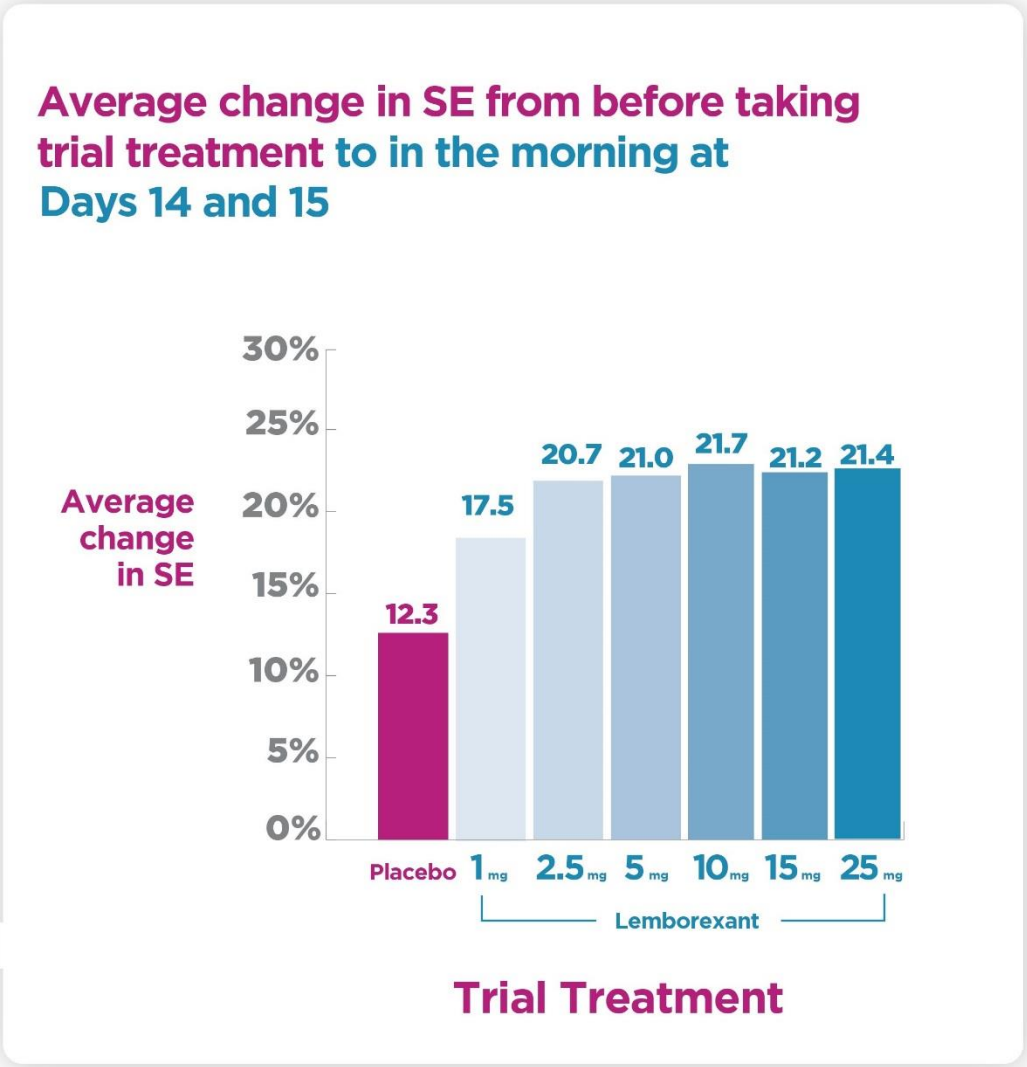


Which dose or doses of lemborexant increased SE?

To see if participants had an increase in SE after taking trial treatment, researchers measured participants' SE before they took trial treatment and then measured the average change in participants' SE in the morning at Days 14 and 15.

All of the doses of lemborexant increased participants' SE in the morning at Days 14 and 15.

The chart below shows the average change in participants' SE in the morning at Days 14 and 15. A higher number meant that there was more of a change in SE.



Which dose or doses of lemborexant decreased the time participants took to fall asleep?

To see if participants took less time to fall completely asleep after taking trial treatment at the beginning and end of the trial, researchers looked at how many minutes it took from the time participants went to bed and turned the lights off to the time that they were fully asleep. This time is called Latency to Persistent Sleep, or LPS. A decrease in LPS means that it took less time to fall fully asleep.

The researchers measured participants' LPS before they took trial treatment and then measured the average change in participants' LPS in the morning after the first and second dose of trial treatment and in the morning at Days 14 and 15.

In the morning after the first and second dose of trial treatment and in the morning at Days 14 and 15, the 2.5-mg, 5-mg, 10-mg, 15-mg, and 25-mg doses of lemborexant all significantly decreased the average LPS.

Which dose or doses of lemborexant decreased the amount of time awake after falling asleep?

To see if participants spent less time awake after falling asleep after taking trial treatment at the beginning and end of the trial, researchers looked at how many minutes of time awake after falling asleep participants had after they were fully asleep. This time is called Wake after Sleep Onset, or WASO. A decrease in WASO means that there was less time awake after falling asleep.

The researchers measured participants' WASO before they took trial treatment, and then measured the average change in participants' WASO in the morning after the first and second dose of trial treatment and in the morning at Days 14 and 15.

In the morning after the first and second dose of trial treatment, the 10-mg, 15-mg, and 25-mg doses of lemborexant all significantly decreased the average WASO.

In the morning at Days 14 and 15, the 15-mg and 25-mg doses of lemborexant significantly decreased the average WASO.

What medical problems did participants have?

Medical problems that happen in clinical trials are called "adverse events". An adverse event 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 events that happened during this trial. These medical problems may or may not be caused by the trial drug. 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 events?

In this trial, 139 out of 291 participants (47.8%) had adverse events during the trial.

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

Adverse Events in This Trial

	Placebo (N=56) n (%)	Lemborexant					
		1 mg (N=32) n (%)	2.5 mg (N=27) n (%)	5 mg (N=38) n (%)	10 mg (N=32) n (%)	15 mg (N=56) n (%)	25 mg (N=50) n (%)
How many participants had adverse events?	21 (37.5%)	11 (34.4%)	11 (40.7%)	16 (42.1%)	19 (59.4%)	31 (55.4%)	30 (60%)
How many participants had serious adverse events?	1 (1.8%)	0	0	0	0	0	1 (2.0%)
How many participants stopped receiving the trial drug because of adverse events?	0	0	0	0	0	0	1 (2.0%)

N is the number of participants in each group.
% is the percentage of participants with the adverse event in each group.
n = number of participants with the adverse event in each group.

What were the most common serious adverse events?

In this trial, 2 out of 291 participants (0.69%) had serious adverse events.

The table below shows the serious adverse events that happened.

Serious Adverse Events in This Trial

	Placebo (N=56) n (%)	Lemborexant					
		1 mg (N=32) n (%)	2.5 mg (N=27) n (%)	5 mg (N=38) n (%)	10 mg (N=32) n (%)	15 mg (N=56) % n (%)	25 mg (N=50) n (%)
High level of potassium in the blood	1 (1.8%)	0	0	0	0	0	0
Seizure	0	0	0	0	0	0	1 (2.0%)

N is the number of participants in each group.
% is the percentage of participants with the adverse event in each group.
n = number of participants with the adverse event in each group.

In this trial, 0 out of 291 participants died due to serious adverse events.

What were the most common adverse events?

In this trial, 139 out of 291 participants (47.8%) had adverse events.

The most common adverse events were sleepiness, headache, and being temporarily unable to move or speak while falling asleep or upon waking.

The table below shows the adverse events that happened in 2% or more of all participants or 5% or more in any lemborexant dose group. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in This Trial

	Placebo (N=56) n (%)	Lemborexant						
		1 mg (N=32) n (%)	2.5 mg (N=27) n (%)	5 mg (N=38) n (%)	10 mg (N=32) n (%)	15 mg (N=56) n (%)	25 mg (N=50) n (%)	Total (N=235) n (%)
Sleepiness	0	1 (3.1%)	1 (3.7%)	2 (5.3%)	4 (12.5%)	10 (17.9%)	11 (22.0%)	29 (12.3%)
Headache	3 (5.4%)	3 (9.4%)	3 (11.1%)	3 (7.9%)	3 (9.4%)	6 (10.7%)	5 (10.0%)	23 (9.8%)
Temporarily unable to move or speak while falling asleep or upon waking	0	0	0	1 (2.6%)	3 (9.4%)	4 (7.1%)	2 (4.0%)	10 (4.3%)
Sleep abnormalities recorded during overnight sleep tests	2 (3.6%)	0	2 (7.4%)	1 (2.6%)	1 (3.1%)	3 (5.4%)	2 (4.0%)	9 (3.8%)
Nightmare	0	0	0	1 (2.6%)	3 (9.4%)	4 (7.1%)	0	8 (3.4%)
Abnormal dreams	0	2 (6.3%)	0	1 (2.6%)	3 (9.4%)	0	0	6 (2.6%)

N is the number of participants in each group.
% is the percentage of participants in each group with the adverse event.
n is the number of participants in each group with the adverse event.

How has this trial helped patients and researchers?

In this trial, researchers learned more about how lemborexant may have helped people with chronic insomnia.

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 lemborexant are planned.

Where can I learn more about the trial?

You can find more information about this trial on the websites listed below. If a full report of the trial results is available, it can also be found here:

- http://www.clinicaltrials.gov - Once you are on the website, type **NCT01995838** into the search box and click "**Search**".

Full trial title: A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Bayesian Adaptive Randomization Design, Dose-Response Study of the Efficacy of E2006 in Adults and Elderly Subjects with Chronic Insomnia

Protocol number: E2006-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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