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 with insomnia disorder

Thank you!

You took part in this clinical trial for the trial drug lemborexant, also called E2006. You and all of the participants helped researchers learn more about lemborexant to help adults with insomnia disorder. Insomnia disorder means that a person has trouble falling asleep and/or staying asleep over a long period of time. Symptoms of insomnia disorder 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 2016 and ended in January 2019.

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 971 participants from 101 sites in Canada, Finland, Germany, Italy, Japan, Mexico, New Zealand, Poland, the Republic of Korea, Romania, Spain, and the United States.

Of the 971 participants in this trial, 959 participants took at least 1 dose of trial treatment.

Why was the research needed?

Researchers were looking for a different way to treat people who have insomnia disorder. Lemborexant is different than most other medicines currently available to treat insomnia disorder. Researchers think lemborexant could help people with insomnia disorder get more sleep.

The researchers in this trial wanted to find out if lemborexant works in a large number of adults with insomnia disorder. 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:

- Did lemborexant decrease the amount of time it took a participant to fall asleep?
- Did lemborexant increase the percentage of time that participants were actually asleep during the time they spent in bed?
- Did lemborexant decrease the amount of time spent awake after falling asleep?
- Did lemborexant increase participants' sleepiness or alertness upon waking?
- 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 the questions above, researchers asked for the help of men and women like you. The participants in the trial were 18 to 88 years old. 31.8% of the participants were male, and 68.2% of the participants were female.

All of the participants in this trial had insomnia disorder. Insomnia disorder means that a person has trouble falling asleep and/or staying asleep for more than 3 nights a week for 3 months or more. People with insomnia disorder have trouble concentrating, have mood changes, and perform poorly at work or school.

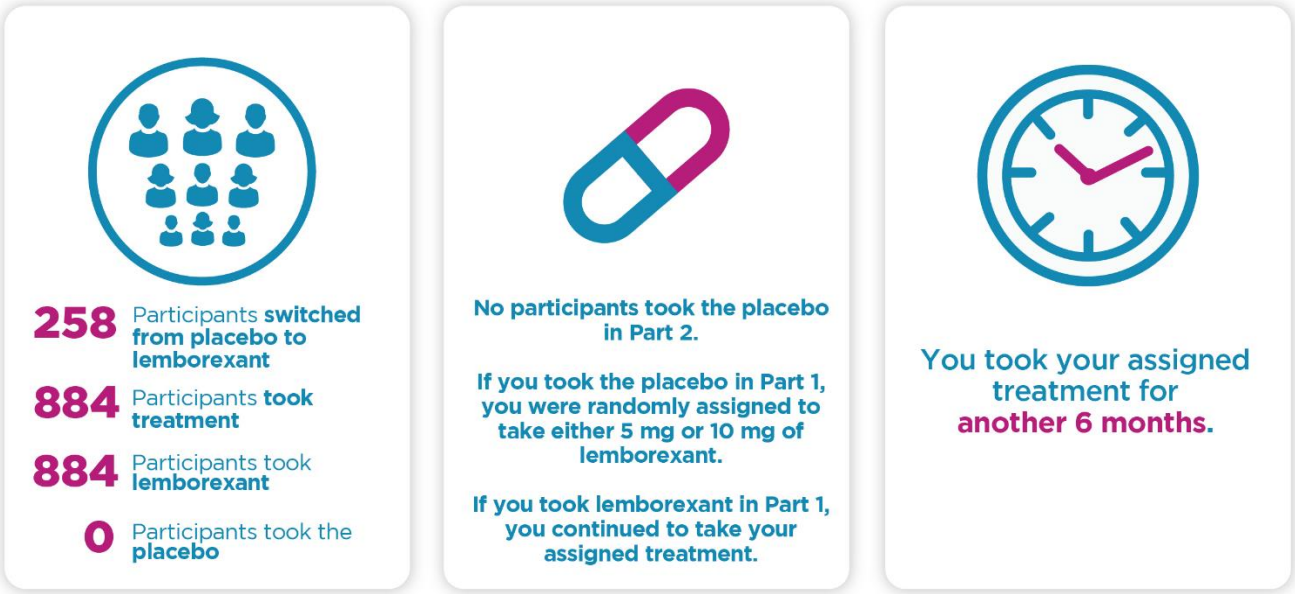
The first 2 weeks of the trial were "single-blind". This means that only the sponsor and the trial doctors and staff knew which trial drug the participants took. Each night during these first 2 weeks, you took a placebo by mouth. A placebo is a pill that looks like the trial drug pill but does not have any medicine in it.

The rest of the 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 took. This trial had 2 parts. Part 1 started after the first 2 weeks of taking a placebo. Part 2 started 6 months later, immediately after Part 1. Both Part 1 and Part 2 lasted for 6 months each.

In Part 1, you took either lemborexant or a placebo by mouth. The figure below shows how treatment was given during Part 1 of your trial.

In Part 2, you took lemborexant by mouth. The figure below shows how treatment was given during Part 2 of your trial.

Part 2 of This Trial



What happened during the trial?

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

The trial doctors or staff also:

- Asked what medications each participant was taking
- Took blood and urine samples
- Checked each participant's heart health using an electrocardiogram, also called an ECG
- Asked participants to complete questionnaires

All participants also completed a Sleep Diary each day to record responses to questions about their sleep.

During the trial, all participants took a placebo each night for the first 2 weeks. The participants continued to record responses to questions about their sleep in a Sleep Diary each day.

Then, participants returned to the trial site for another visit. The trial doctors or staff took more blood and urine samples, checked each participant's heart health, checked the participants' Sleep Diaries, and asked participants to complete questionnaires.

Part 1 of the trial started after the first 2 weeks of taking a placebo. Participants were randomly assigned to take either 5 mg or 10 mg of lemborexant or a placebo each night. Part 1 of the trial lasted for 6 months.

Part 2 of the trial started right after Part 1 ended. Part 2 of the trial also lasted for 6 months. During this time,

- Participants who were randomly assigned to lemborexant in Part 1 continued to take lemborexant at their assigned dose each night.
- Participants who were randomly assigned to take the placebo in Part 1 were randomly assigned to take either 5 mg or 10 mg of lemborexant each night.

Throughout the trial, participants continued to complete their Sleep Diary each day. The trial doctors or staff:

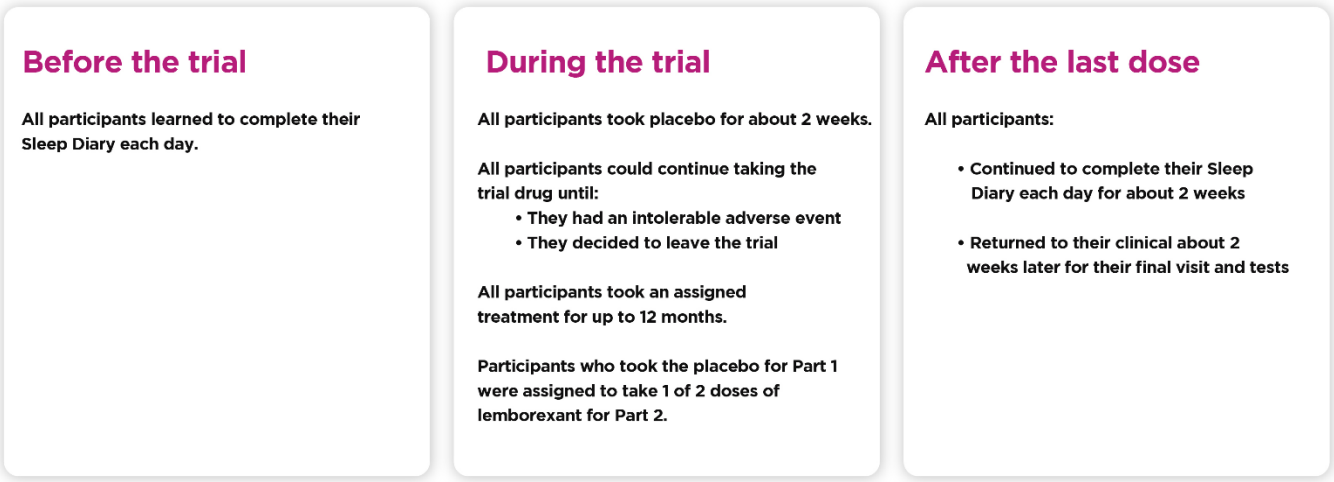
- Continued to check the participants' health, checked the participants' Sleep Diaries, asked what medications they were taking, and took blood and urine samples
- Asked the participants how they were feeling and if they had any adverse events
- Checked each participant's heart health

After their last dose, all participants:

- Continued to complete their Sleep Diary each day
- Returned to the clinic approximately 2 weeks 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. The results each participant had might be different and are not in this summary. But the results each participant 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.

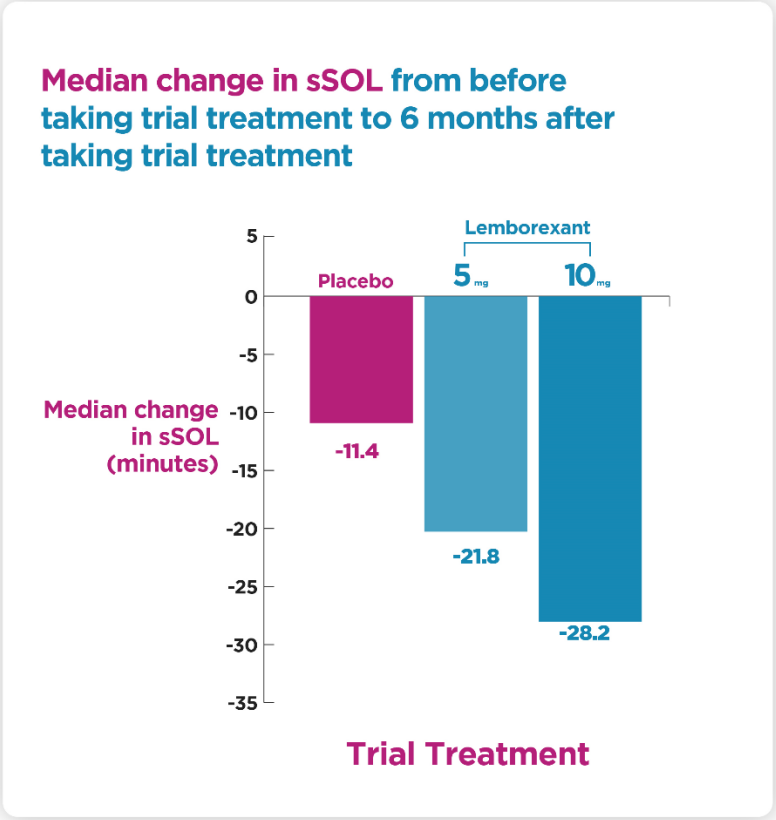
Did lemborexant decrease the amount of time it took a participant to fall asleep?

The amount of time that a participant recalls it took them to fall asleep is called subjective Sleep Onset Latency, or sSOL. “Subjective” means that the information the researchers collected came from what the participants recalled and recorded in their Sleep Diaries. The researchers wanted to know if lemborexant could decrease the participants’ sSOL after 6 months of trial treatment.

During the study, the participants recorded in their Sleep Diaries each morning how long they recalled it took them to fall asleep the night before. To see if participants’ sSOL decreased by the end of Part 1 of the trial, the researchers compared the participants’ sSOL before they took the trial treatment with the participants’ sSOL after 6 months of trial treatment.

Both doses of lemborexant significantly decreased participants’ sSOL more than placebo after 6 months of trial treatment.

The chart on the next page shows the median change in participants’ sSOL after 6 months of trial treatment. The median is the middle number in a group of numbers that is sorted from lowest to highest. So, the median change in sSOL is the amount of time in the middle of the smallest and the biggest changes in sSOL. The median is used when numbers fall into a particular pattern, which happened for the sSOL results in this trial. The median change in sSOL is shown in minutes. A larger decrease in sSOL means that it took participants less time to fall asleep.



The researchers also wanted to know if lemborexant could decrease the participants' sSOL by the end of Part 2 of the trial. The researchers found that for both doses of lemborexant, sSOL stayed lower after 12 months of trial treatment than before taking lemborexant. But, this was not the main question the trial was designed to answer. More information can be found on the websites provided at the end of this summary.

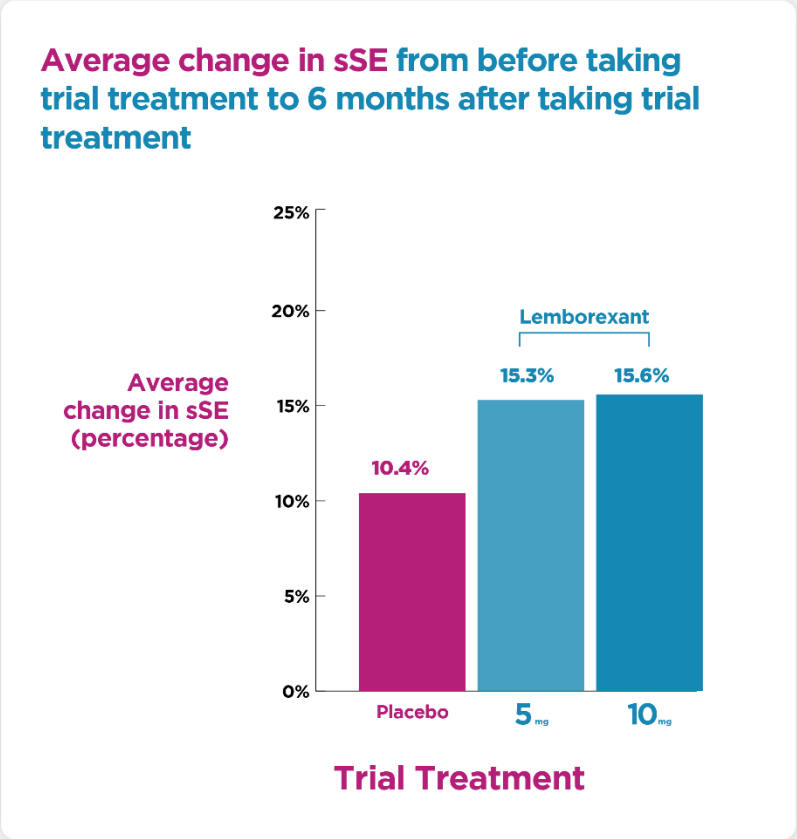
Did lemborexant increase the percentage of time that participants were actually asleep during the time they spent in bed?

The percentage of time that a participant recalls they were actually asleep during the time they spend in bed is called subjective Sleep Efficiency, or sSE. The researchers wanted to know if lemborexant could increase the participants' sSE after 6 months of trial treatment.

Each morning during the study, the participants recorded information in their Sleep Diaries, which allowed the researchers to calculate the participants' sSE. To see if participants' sSE increased by the end of Part 1 of the trial, the researchers compared the participants' sSE before they took trial treatment with the participants' sSE after 6 months of trial treatment.

Both doses of lemborexant significantly increased participants' sSE more than placebo after 6 months of trial treatment.

The chart below shows the average change in participants' sSE after 6 months of trial treatment. The average change in sSE is shown as a percentage. An increase in sSE means that a participant spent more of their time in bed asleep.



The researchers also wanted to know if lemborexant could increase the participants' sSE by the end of Part 2 of the trial. The researchers found that after 12 months of trial treatment, the results for sSE were similar to the results in Part 1. But, this was not the main question the trial was designed to answer. More information can be found at the websites provided at the end of this summary.

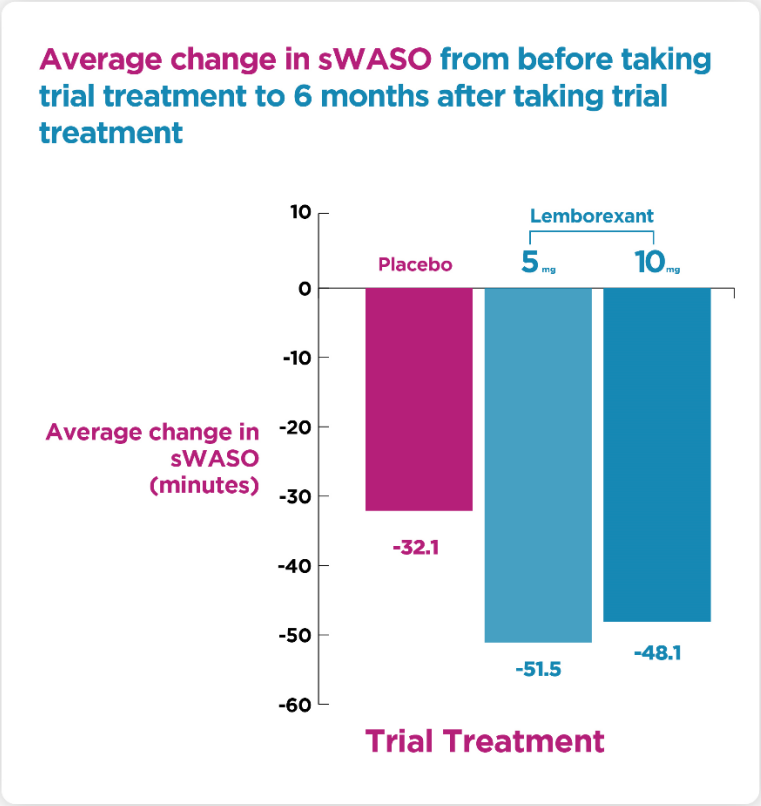
Did lemborexant decrease the amount of time spent awake after falling asleep?

The amount of time that a participant recalls they spent awake after falling asleep is called subjective Wake After Sleep Onset, or sWASO. The researchers wanted to know if lemborexant could decrease the participants' sWASO after 6 months of trial treatment.

Each morning during the study, the participants recorded information in their Sleep Diaries, which allowed the researchers to calculate the participants' sWASO. To see if participants' sWASO decreased at the end of Part 1 of the trial, the researchers compared the participants' sWASO before they took trial treatment with the participants' sWASO after 6 months of trial treatment.

Both of the doses of lemborexant significantly decreased participants' sWASO more than placebo after 6 months of trial treatment.

The chart below shows the average change in participants' sWASO after 6 months of trial treatment. The average change in sWASO is shown in minutes. A decrease in sWASO means that there was less time spent awake after falling asleep.



The researchers also wanted to know if lemborexant could decrease the participants' sWASO by the end of Part 2 of the trial. The researchers found that for both doses of lemborexant, sWASO stayed lower after 12 months of trial treatment than before taking lemborexant. But, this was not the main question the trial was designed to answer. More information can be found at the web sites provided at the end of this summary.

Did lemborexant increase participants' sleepiness or alertness upon waking?

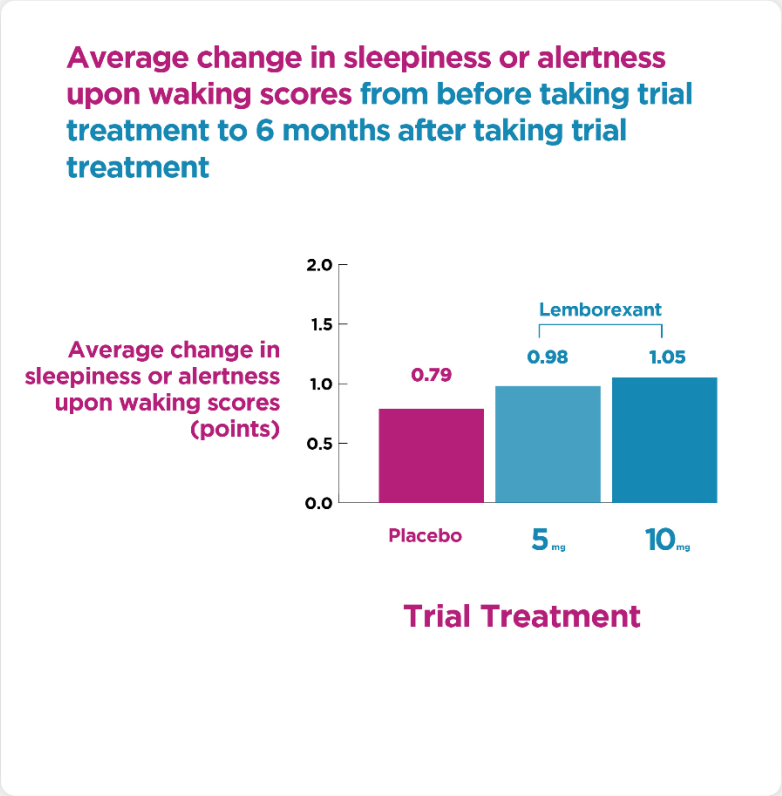
The researchers wanted to find out if participants who took lemborexant felt sleepier or more alert upon waking. They wanted to know how participants felt after 6 months of treatment.

To see if participants felt sleepier or more alert upon waking by the end of Part 1 of the trial, the participants rated their sleepiness or alertness upon waking on a scale of 1 to 9. The higher the score, the more alert the participant.

Participants completed this rating scale before, during, and after the trial. Then, the researchers measured the average change in participants' scores after 6 months of trial treatment.

Both doses of lemborexant increased participants' alertness upon waking more than placebo after 6 months of trial treatment. However, this change was only significant for participants who took 10 mg lemborexant.

The chart below shows the average change in participants' sleepiness or alertness upon waking scores after 6 months of trial treatment. The average change is shown in points. A higher score means that the participants felt more alert.



The researchers also wanted to know if lemborexant could increase the participants' sleepiness or alertness upon waking, as measured by the end of Part 2 of the trial. The researchers found that after 12 months of trial treatment, participants' alertness upon waking stayed higher for both doses of lemborexant. But, this was not the main question the trial was designed to answer. More information can be found at the websites provided at the end of this summary.

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 Part 1 of this trial,

- 200 out of 319 participants (62.7%) who took the placebo had adverse events.
- 379 out of 628 participants (60.4%) who took lemborexant had adverse events.

The table below shows how many participants had adverse events in Part 1 of this trial.

Adverse Events in Part 1 of This Trial

	Placebo (N=319) n (%)	Lemborexant 5 mg (N=314) n (%)	Lemborexant 10 mg (N=314) n (%)
How many participants had adverse events?	200 (62.7%)	192 (61.1%)	187 (59.6%)
How many participants had serious adverse events?	5 (1.6%)	7 (2.2%)	9 (2.9%)
How many participants stopped taking the trial drug because of adverse events?	12 (3.8%)	13 (4.1%)	26 (8.3%)

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

Among participants in Part 2 who took the placebo in Part 1,

- 73 out of 133 participants (54.9%) who switched from placebo to 5 mg lemborexant had adverse events.
- 71 out of 123 participants (57.7%) who switched from placebo to 10 mg lemborexant had adverse events.

Among participants in Part 2 who continued to take lemborexant from Part 1,

- 122 out of 251 participants (48.6%) who took 5 mg lemborexant had adverse events.
- 109 out of 221 participants (49.3%) who took 10 mg lemborexant had adverse events.

The table below shows how many participants had adverse events in Part 2 of this trial.

Adverse Events in Part 2 of This Trial

	Participants who took placebo in Part 1		Lemborexant 5 mg (N=251) n (%)	Lemborexant 10 mg (N=221) n (%)
	Lemborexant 5 mg (N=133) n (%)	Lemborexant 10 mg (N=123) n (%)		
How many participants had adverse events?	72 (54.9%)	71 (57.7%)	122 (48.6%)	109 (49.3%)
How many participants had serious adverse events?	4 (3.0%)	6 (4.9%)	8 (3.2%)	2 (0.9%)
How many participants stopped taking the trial drug because of adverse events?	6 (4.5%)	10 (8.1%)	4 (1.6%)	4 (1.8%)

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

What were the most common serious 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.

None of the participants died during this trial.

In Part 1 of this trial,

- 5 out of 319 participants (1.6%) who took the placebo had serious adverse events.
- 16 out of 628 participants (2.5%) who took lemborexant had serious adverse events.

Each serious adverse event happened in 1 participant.

Among participants in Part 2 who took the placebo in Part 1,

- 4 out of 133 participants (3.0%) who switched from placebo to 5 mg lemborexant and had serious adverse events.
- 6 out of 123 participants (4.9%) who switched from placebo to 10 mg lemborexant had serious adverse events.

Among participants in Part 2 who continued to take lemborexant from Part 1,

- 8 out of 251 participants (3.2%) who took 5 mg lemborexant had serious adverse events.
- 2 out of 221 participants (0.9%) who took 10 mg lemborexant had serious adverse events.

The most common serious adverse event in Part 2 of this trial was arthritis. This happened in 1 out of 133 participants (0.8%) who switched from placebo to 5 mg lemborexant and in 2 out of 123 participants (1.6%) who switched from placebo to 10 mg lemborexant. There were other serious adverse events, but these happened in 1 participant each.

What were the most common adverse events?

In Part 1 of this trial, the most common adverse events were sleepiness, common cold, headache, and flu.

The table on the next page shows the adverse events in Part 1 that happened in 5% or more of participants in any lemborexant dose group. There were other adverse events, but these happened in fewer participants.

Most Common Adverse Events in Part 1 of This Trial

	Placebo (N=319) n (%)	Lemborexant	
		5 mg (N=314) n (%)	10 mg (N=314) n (%)
Sleepiness	5 (1.6%)	27 (8.6%)	41 (13.1%)
Common cold	40 (12.5%)	30 (9.6%)	29 (9.2%)
Headache	21 (6.6%)	28 (8.9%)	21 (6.7%)
Flu	15 (4.7%)	15 (4.8%)	16 (5.1%)

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.

In Part 2 of this trial, the most common adverse events were common cold, sleepiness, and headache.

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

Most Common Adverse Events in Part 2 of This Trial

	Participants who took placebo in Part 1		Lemborexant 5 mg (N=251) n (%)	Lemborexant 10 mg (N=221) n (%)
	Lemborexant 5 mg (N=133) n (%)	Lemborexant 10 mg (N=123) n (%)		
Common Cold	8(6.0%)	6 (4.9%)	18 (7.2%)	15 (6.8%)
Sleepiness	8 (6.0%)	15 (12.2%)	5 (2.0%)	6 (2.7%)
Headache	8 (6.0%)	3 (2.4%)	10 (4.0%)	10 (4.5%)

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 whether lemborexant may have helped people with insomnia disorder.

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. The results of earlier trials with lemborexant helped to inform the design of this trial. Future 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 **NCT02952820** into the search box and click "**Search**".
- http://www.clinicaltrialsregister.eu – Once you are on the website, type **2015-001463-39** into the search box and click "**Search**".

Full trial title: A Long-Term Multicenter, Randomized, Double-Blind, Controlled, Parallel-Group Study of the Safety and Efficacy of Lemborexant in Subjects With Insomnia Disorder

Protocol number: E2006-G000-303

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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