# Clinical Trial Results

**Research Sponsor:** Eisai Ltd.

**Drug Studied:** Lemborexant, also called Davigo™ or E2006

**Short Trial Title:** A trial to learn how well lemborexant works and how safe it is in adults with insomnia disorder compared to placebo and zolpidem

## *Thank you!*

You took part in this clinical study 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 May 2016 and ended in January 2018.

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 1006 participants from 67 sites in Canada, Germany, Italy, Spain, United States of America, and United Kingdom.

# Why was the research needed?

Researchers were looking for a different way to treat people who have insomnia disorder. At the time of this trial, medicines available in the USA to treat insomnia disorder included zolpidem. But, these medications may not be as helpful in older people who have 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 time it took for participants to fall asleep?
- Did lemborexant increase the amount of time that participants were actually asleep during the time spent in bed?
- Did lemborexant decrease the amount of time that participants spent awake after falling asleep?
- Did lemborexant decrease the amount of time that participants spent awake during the second half of the night?
- 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 55 to 88 years old. 13.6% of the participants were male, and 86.4% of the participants were female.

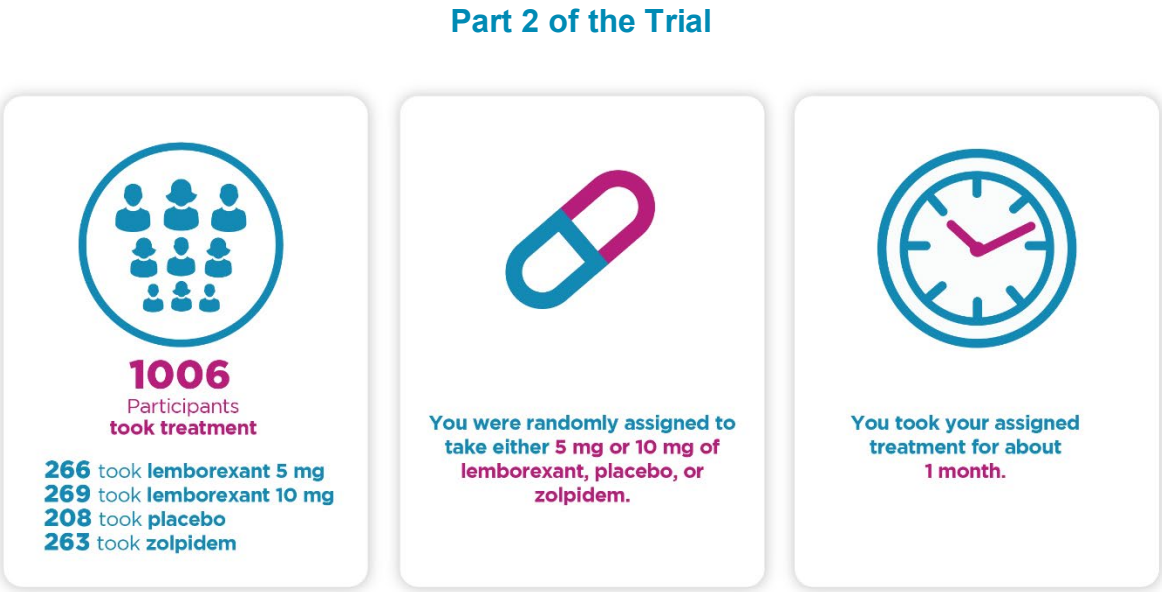
All of the participants in this trial had insomnia disorder. Insomnia disorder means that a person has trouble falling sleep and/or staying asleep for more than 3 nights a week for 3 months or more. People with insomnia disorder have trouble concentrating, have mood changes, and perform poorly at work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

**Part 1 of the trial was "single-blind".** This means that the trial doctors, trial staff, and the sponsor knew which trial drug the participants took, but the participants did not. Each night during Part 1, all participants took placebo by mouth for about 2 weeks. A placebo is a pill that looks like the trial drug pill but does not have any medicine in it.

The figure below shows how Part 1 of your trial was done.


**Part 2 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. Each night during Part 2, you took either 5 mg or 10 mg of lemborexant, placebo, or zolpidem by mouth for about 1 month.

The figure below shows how treatment was given in Part 2 of your trial.




# What happened during the trial?

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

- Asked what medications the participants were taking
- Checked the participants' overall health
- Checked the participants' heart health using an electrocardiogram, also called an ECG
- Took blood and urine samples
- Did overnight tests to measure and record the participants' sleep
- Asked the participants to complete their Sleep Diary each morning.

Participants stayed overnight for tests at the study center for a total of 7 nights. While at the study center, participants also completed questionnaires about their sleep, moods, and how tired they felt.

**During Part 1 of the trial,** all participants took placebo at bedtime for about 2 weeks. This part of the trial helped researchers find out which participants were able to continue on to the next part of the trial.

**During Part 2 of the trial,** participants were randomly assigned to take either 5 mg or 10 mg of lemborexant, placebo, or zolpidem. The participants took their assigned treatment at bedtime for about 1 month.

**Throughout the trial**, participants continued to complete their Sleep Diary each morning. Participants also continued to complete questionnaires about their sleep. The trial doctors or staff continued to:

- Check the participants' health, ask what medications they were taking, and take blood and urine samples
- Ask the participants how they were feeling
- Do overnight tests to measure and record the participants' sleep

**After their last dose,** all participants:

- Continued to complete their Sleep Diary each morning
- Returned to the study center about 14 days later for their final visit and tests

The figure below shows how the trial was done.

## How did this trial work?

### During the trial

**Participants could continue taking the trial drug until:**

- **They had an intolerable adverse event**
- **They decided to leave the trial**

**In Part 1 of the trial, participants took a placebo for about 2 weeks.**

**In Part 2 of the trial, participants took their assigned treatment for about 1 month.**

### After the last dose

**Participants:**

- **Continued to complete their Sleep Diary each morning for about 2 weeks**
- **Returned to the study center about 2 weeks later for their final visit and tests**

## 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.

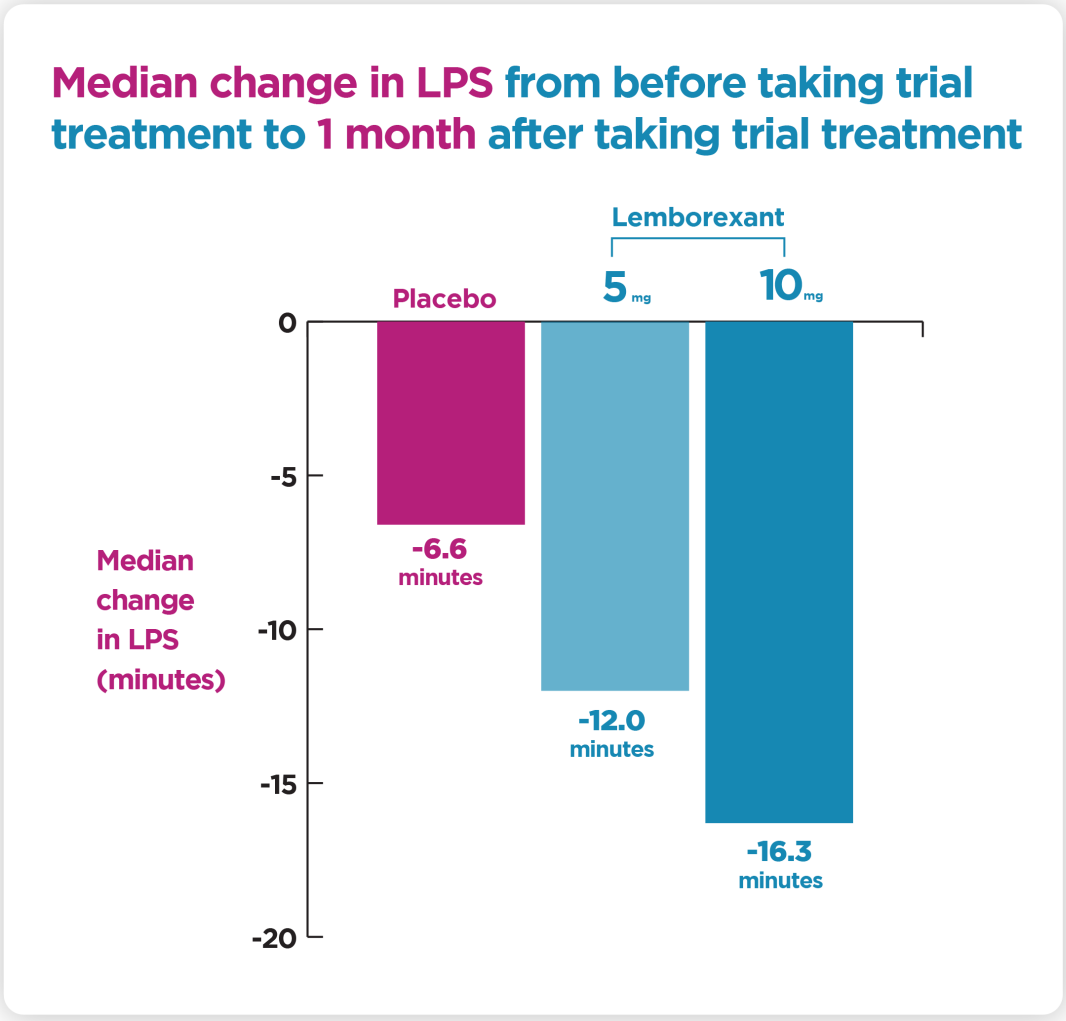
**Did lemborexant decrease the time it took for participants to fall asleep?**

The amount of time in minutes that it took a person to fall asleep is called “Latency to Persistent Sleep,” or LPS. The researchers wanted to know if lemborexant could decrease the participants’ LPS after 1 month of trial treatment.

To find out, researchers measured the participants’ LPS before taking trial treatment, and then measured the change in LPS after 1 month of trial treatment. One way to know about the change in LPS is to report the median values in minutes. Median is the middle number in a group of numbers that is sorted from lowest to highest. So, the median change in LPS is the middle number after each participant’s change in LPS was sorted from lowest to highest.

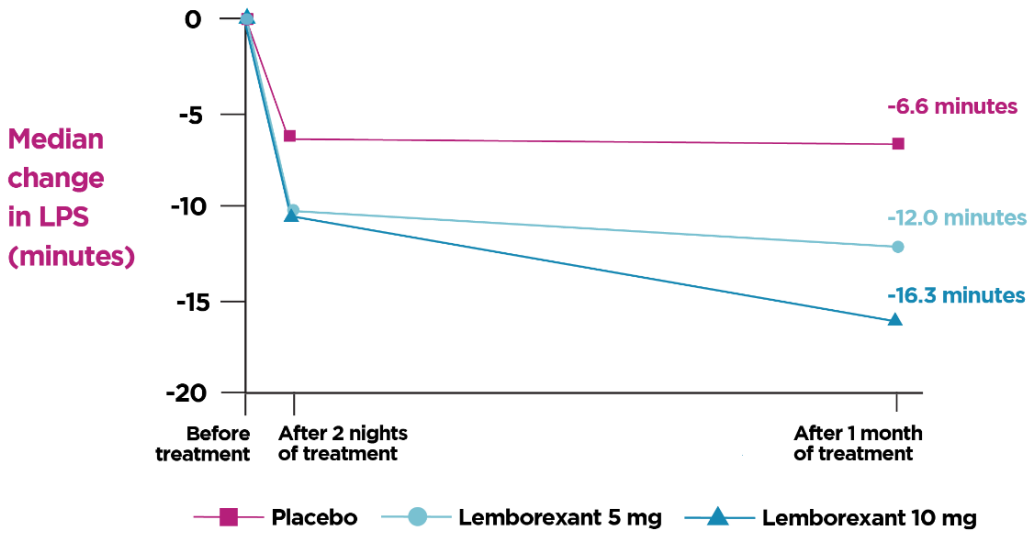
Both doses of lemborexant significantly decreased the participants’ LPS more than placebo after 1 month of trial treatment.

The chart below shows the median change in LPS after 1 month of trial treatment. A larger median decrease in LPS means that it took less time to fall fully asleep.



The chart below shows the median change in LPS from before taking trial treatment to 1 month after taking trial treatment. After 2 nights of trial treatment, the chart shows that both doses of lemborexant led to a larger median decrease in LPS compared to placebo. The results were similar after 1 month of trial treatment. A larger median decrease in LPS means that it took less time to fall fully asleep.

## Median change in LPS from before taking trial treatment to 1 month after taking trial treatment



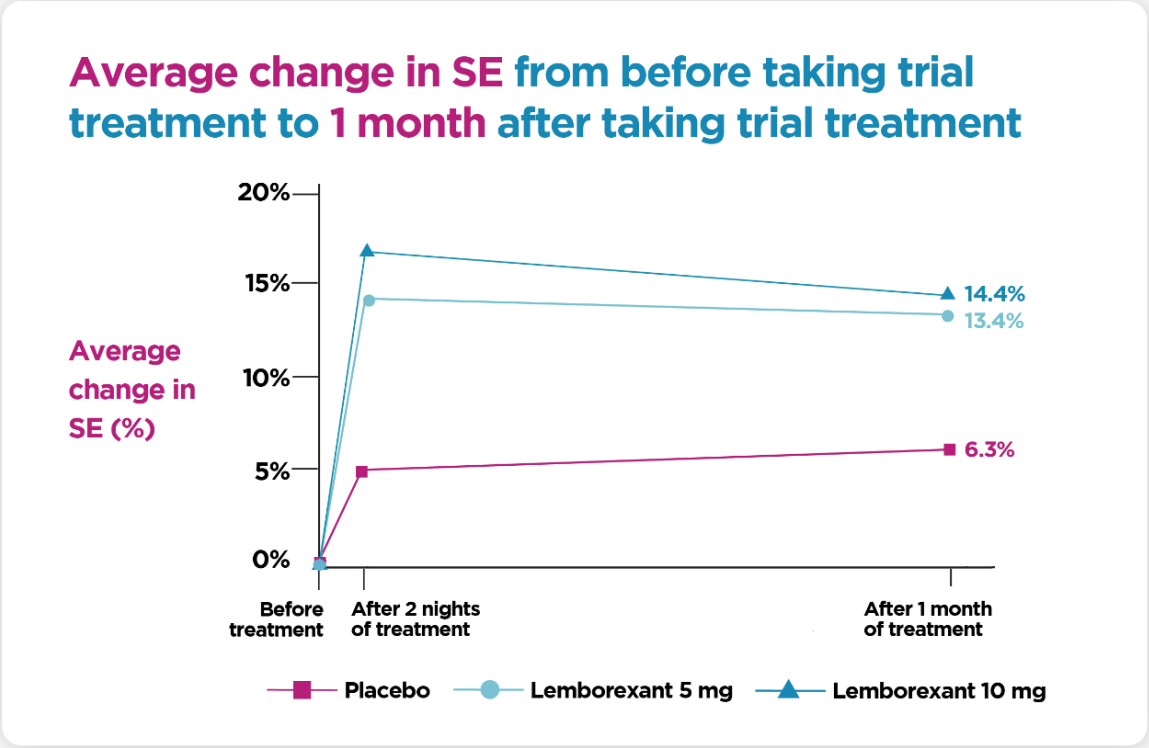
**Did lemborexant increase the amount of time that participants were actually asleep during the time spent in bed?**

The percentage of time that a person is actually asleep during the time they spent in bed trying to sleep is called “Sleep Efficiency,” or SE. The researchers wanted to know if lemborexant could increase the participants’ SE after 1 month of trial treatment.

To find out, researchers measured the participants’ SE before taking trial treatment, and then measured the average change in SE after 1 month of taking trial treatment.

Both doses of lemborexant significantly increased the participants’ SE more than placebo after 1 month of trial treatment.

The chart below shows the average change in SE from before taking trial treatment to 1 month after taking trial treatment. After 2 nights of trial treatment, the chart shows that both doses of lemborexant led to a larger average increase in SE more than placebo. The results were similar after 1 month of trial treatment. A larger average increase in SE means that more time in bed was spent asleep.



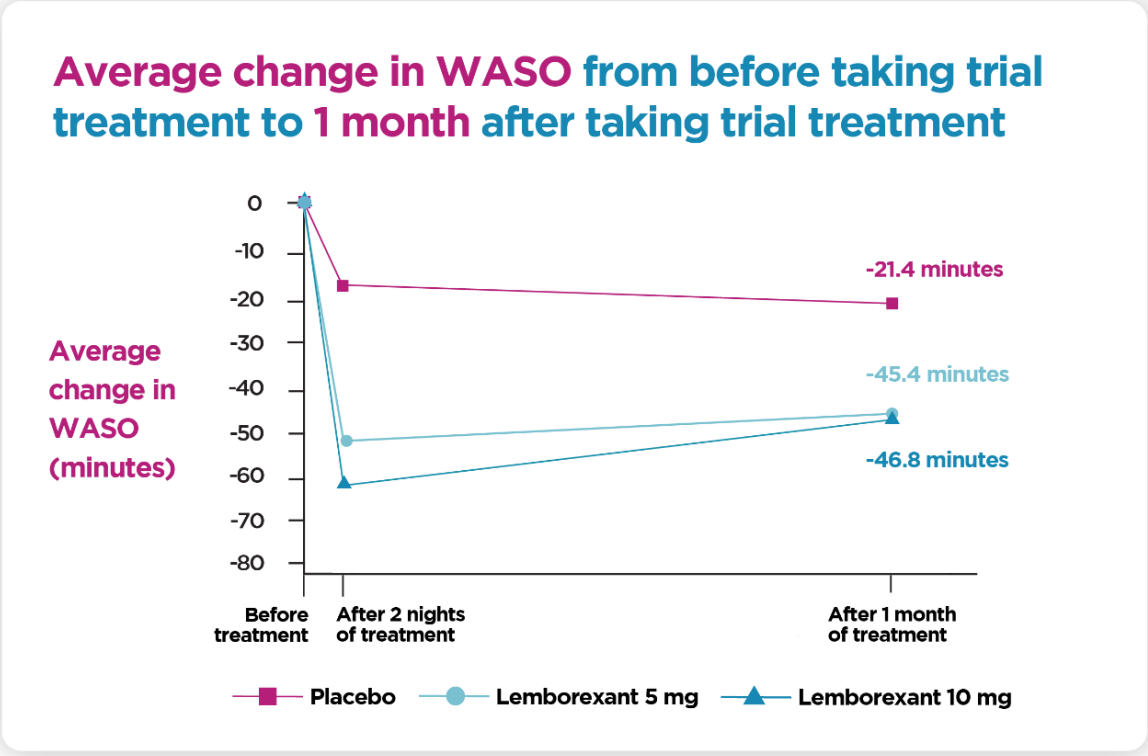
**Did lemborexant decrease the amount of time that participants spent awake after falling asleep?**

The amount of time in minutes that a person spent awake after falling asleep is called "Wake After Sleep Onset," or WASO. The researchers wanted to know if lemborexant could decrease the participants' WASO after 1 month of trial treatment.

To find out, researchers measured the participants' WASO before taking trial treatment, and then measured the average change in WASO after 1 month of taking trial treatment.

Both doses of lemborexant significantly decreased the participants' WASO more than placebo after 1 month of trial treatment.

The chart below shows the average change in WASO from before taking trial treatment to 1 month after taking trial treatment. After 2 nights of trial treatment, the chart shows that both doses of lemborexant led to a larger average decrease in WASO compared to placebo after 2 nights of trial treatment. The results were similar after 1 month of trial treatment. A larger decrease in WASO means that there was less time spent awake after falling asleep.



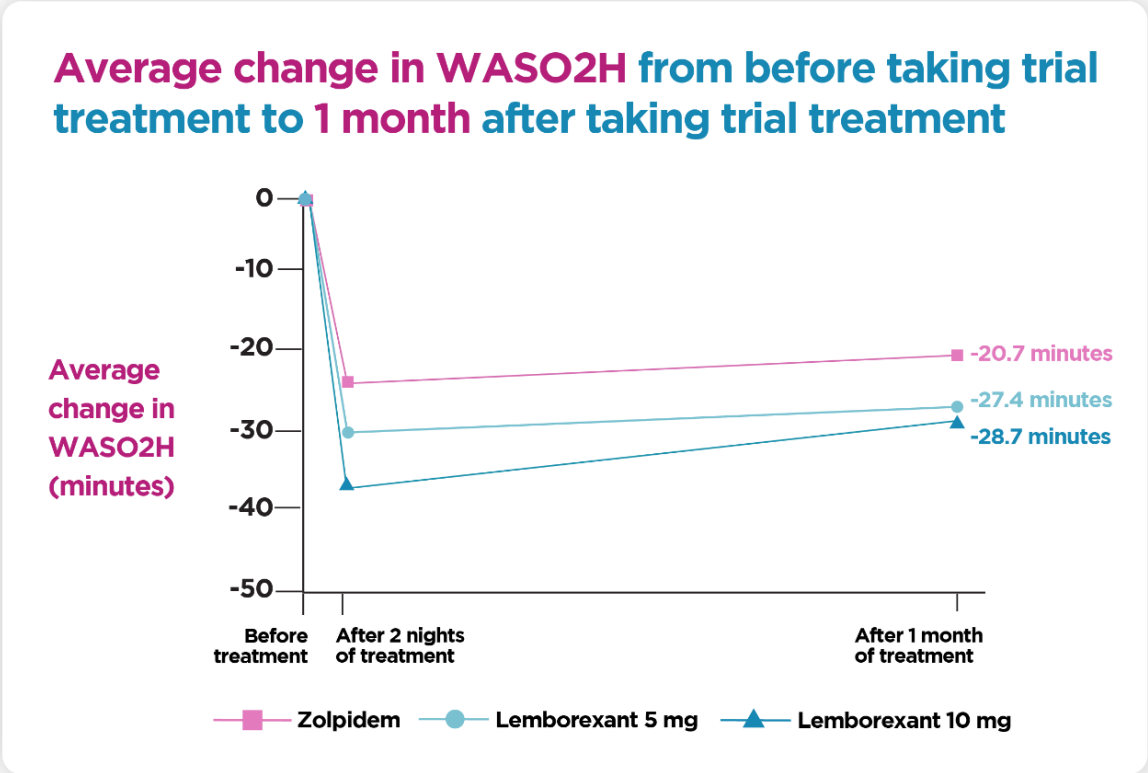
**Did lemborexant decrease the amount of time that participants spent awake during the second half of the night?**

After being fully asleep, the amount of time in minutes that a person spent awake during the second half of the night is called “Wake After Sleep Onset during the Second Half of the night,” or WASO2H. The researchers wanted to know if lemborexant could decrease the participants’ WASO2H after 1 month of trial treatment.

To find out, researchers measured the participants’ WASO2H before taking trial treatment, and then measured the average change in WASO2H after 1 month of taking trial treatment.

Both doses of lemborexant significantly decreased the participants’ WASO2H more than zolpidem after 1 month of trial treatment.

The chart below shows the average change in WASO2H from before taking trial treatment to 1 month after taking trial treatment. After 2 nights of trial treatment, the chart shows that both doses of lemborexant led to a larger average decrease in WASO2H compared to zolpidem. The results were similar after 1 month of trial treatment. A larger decrease in WASO2H means that there was less time spent awake during the second half of the night, as measured after falling asleep.



# 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, 302 out of 1006 participants (30.0%) had adverse events.

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

**Adverse Events in This Trial**

| | Out of 209 participants who took placebo | Out of 263 participants who took zolpidem | Out of 266 participants who took 5 mg of lemborexant | Out of 268 participants who took 10 mg of lemborexant |
|---|---|---|---|---|
| How many participants had adverse events? | 53 (25.4%) | 93 (35.4%) | 74 (27.8%) | 82 (30.6%) |
| How many participants had serious adverse events? | 0 (0%) | 4 (1.5%) | 2 (0.8%) | 0 (0.0%) |
| How many participants stopped taking the trial drug because of adverse events? | 2 (1.0%) | 7 (2.7%) | 2 (0.8%) | 3 (1.1%) |

### 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.

In this trial, 6 out of 1006 participants (0.6%) had serious adverse events.

- 4 out of 263 participants (1.5%) who took zolpidem had serious adverse events. These included heart disease, intestinal blockage, chest pain, lung infection, back pain, and disease of the blood vessels.
- 2 out of 266 participants (0.8%) who took 5 mg of lemborexant had serious adverse events. These included hernia of the abdomen and viral stomach flu.

Each serious adverse event happened in 1 participant.

None of the participants died during this trial.

### What were the most common adverse events?

In this trial, 302 out of 1006 participants (30.0%) had adverse events.

The most common adverse events were headache, sleepiness, and urinary tract infection.

The table below shows the adverse events that happened in 2% or more in participants who took either 5 mg or 10 mg of lemborexant. There were other adverse events, but these happened in fewer participants.

**Most Common Adverse Events in This Trial**

| | Out of 209 participants who took placebo | Out of 263 participants who took zolpidem | Out of 266 participants who took 5 mg of lemborexant | Out of 268 participants who took 10 mg of lemborexant |
|---|---|---|---|---|
| **Headache** | 13 (6.2%) | 14 (5.3%) | 17 (6.4%) | 13 (4.9%) |
| **Sleepiness** | 4 (1.9%) | 4 (1.5%) | 11 (4.1%) | 19 (7.1%) |
| **Urinary tract infection** | 2 (1.0%) | 2 (0.8%) | 3 (1.1%) | 9 (3.4%) |
| **Common cold** | 3 (1.4%) | 1 (0.4%) | 7 (2.6%) | 1 (0.4%) |
| **Infection of the nose, throat, or voice box** | 4 (1.9%) | 2 (0.8%) | 6 (2.3%) | 1 (0.4%) |

# 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 have 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.clinicaltrialsregister.eu - Once you are on the website, click "**Home and Search**", then type **2015-004347-39** in the search box and click "**Search**".
- http://www.clinicaltrials.gov - Once you are on the website, type **NCT02783729** into the search box and click "**Search**".

**Full trial title:** A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Active Comparator, Parallel-Group Study of the Efficacy and Safety of Lemborexant in Subjects 55 Years and Older With Insomnia Disorder

**Protocol number:** E2006-G000-304

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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