Clinical Trial Results Summary

NOVARTIS

The safety and effects of the trial drug LML134 for people who work at night

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **LML134**. All of the participants helped the researchers learn more about how safe LML134 is to take.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public. An independent organization prepared this summary of the trial results.

We hope this helps the participants understand their important role in medical research.

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

Trial information

Trial number: CLML134X2201
Drug studied: LML134
Sponsor: Novartis

You can find **more information** about this trial by going to the websites listed on **page 9** of this summary.

Trial overview

What was the purpose of this trial?

Read more on **page 3**

This trial was designed to learn about the safety and effects of the trial drug LML134. This trial drug is designed to help people with a sleep-related disease called shift work disorder. This disease causes people to be overly sleepy while working at night and have trouble falling asleep during the day.

This trial was designed to answer these main questions:

- Were the participants less sleepy at night after they took LML134 compared to the placebo?
- What medical problems did the participants have during the trial? Keeping track of medical problems helped to learn about the safety of LML134.

Who was in this trial?

Read more on **page 3**

24 men and women began this clinical trial. Every participant in this trial worked night shifts that changed their usual sleep and awake times.

What treatments did the participants take?

Read more on **page 4**

The participants were assigned each of these treatments to take as pills during different time periods:

- LML134
- Placebo – looks like the trial drug but does not have any trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

What were the main results of this trial?

Read more on **page 6**

- The participants were less sleepy at night after they took LML134 compared to after they took the placebo
- The clinical trial team concluded that LML134 was safe for the participants in this trial. The most common medical problem was headache.

This trial had other results along with the main results. Read more on **page 7**

What was the purpose of this trial?

Researchers are looking for better ways to treat shift work disorder. **Shift work disorder** is a sleep-related disease that can happen to people whose work schedule changes their usual sleep and awake times, such as working night shifts. It causes people to be overly sleepy, especially during work times, and have trouble falling asleep during the day, when off work. Over time, it can impact their health and interfere with work or family life.

LML134 is a trial drug designed to help people feel less sleepy and more alert by increasing signals in the brain that control being awake. Before a drug can be approved to treat shift work disorder, researchers do many clinical trials to find out how safe it is and how it works.

This trial was designed to answer these questions:

- Were the participants less sleepy at night after they took LML134 compared to after they took the placebo?
- What medical problems did the participants have during the trial?

This trial was also designed to answer these questions:

- How did LML134 affect sleepiness over time?
- How much and how fast did LML134 get into the participants' blood?
- Did LML134 affect daytime sleep?

Who was in this trial?

24 participants began the trial – 20 men and 4 women. Everyone was 24 to 63 years old. Their average age was 41 years.

Every participant in this trial worked night shifts. Trial doctors measured each participant's sleepiness and sleep patterns to find out if night shifts impacted their sleep enough to mean they had shift work disorder. To measure sleepiness, trial staff used the **Multiple Sleep Latency Test**, also called the MSLT.

To be in this clinical trial, a person had to fall asleep in 8 minutes or less during the MSLT nap times. This shows that they were overly sleepy.

This trial took place in the United States.

What is the MSLT?

The MSLT is the standard way sleepiness is measured. It's done during an over-night stay at a clinic and measures how long it takes a person to fall asleep during 4 nap times, spaced 2 hours apart.
The sleepier someone is, the faster they fall asleep during the MSLT nap times.

For more information about who could and could not be in this trial, and the participants in this trial, visit novctrd.com. Use trial number **CLML134X2201** to find the scientific summary.

What treatments did participants take?

A computer program was used to randomly assign the order each participant took these treatments:

- **LML134**, 5 mg (milligram)
- **Placebo**: A placebo looks like the trial drug, but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug.

The participants took these treatments as pills.

Using a computer program to assign the treatments helped make sure the clinical trial team compared the results as fairly as possible.

The participants and the trial staff did not know what treatment each participant took during each treatment period. Some trials are done this way because knowing what treatment participants get can influence the results. Not knowing what treatment participants get helps make sure the results are looked at fairly.

What happened during this trial?

The trial began in July 2017 and ended in September 2018. The researchers stopped this trial early because the sponsor decided to stop all research on LML134 in people with sleep-related diseases. The decision to stop was not related to safety. 6 participants did not complete this trial.

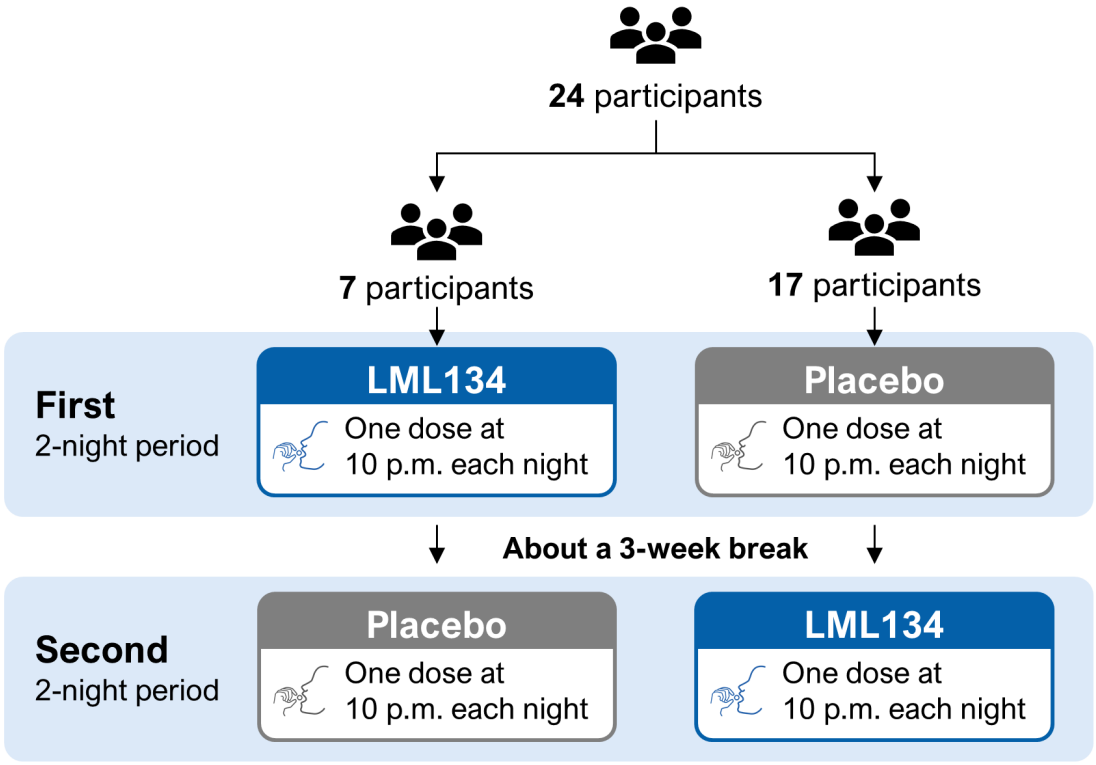
The chart on the following page shows how this trial was designed.

Here's how this trial was designed:

Before treatment

- The trial doctors checked each participant's health
- The trial doctors used the MSLT to measure each participant's sleepiness and confirm if they had shift work disorder
- Each participant kept a sleep diary for 2 weeks
- Each participant either worked night shifts for the 3 nights before treatment or for 2 nights and spent the third night at the trial site

During treatment



For each 2-night period, the trial staff:

- Measured each participant's sleepiness using the MSLT
- Took blood and urine samples and checked each participant's health

After treatment

- The trial doctors checked each participant's health after each 2-night period
- The trial staff called each participant to check on their health 30 days after their last visit to the trial site

What were the main results of this trial?

This is a summary of the overall results of this trial. Individual results from each participant may be different and are not included in this summary.

Researchers need many trials to learn if a drug or other treatment is safe and works well. Other trials may provide new information or different results. Always talk to a doctor before making any changes to your health care.

Were the participants less sleepy at night after they took LML134 compared to after they took the placebo?

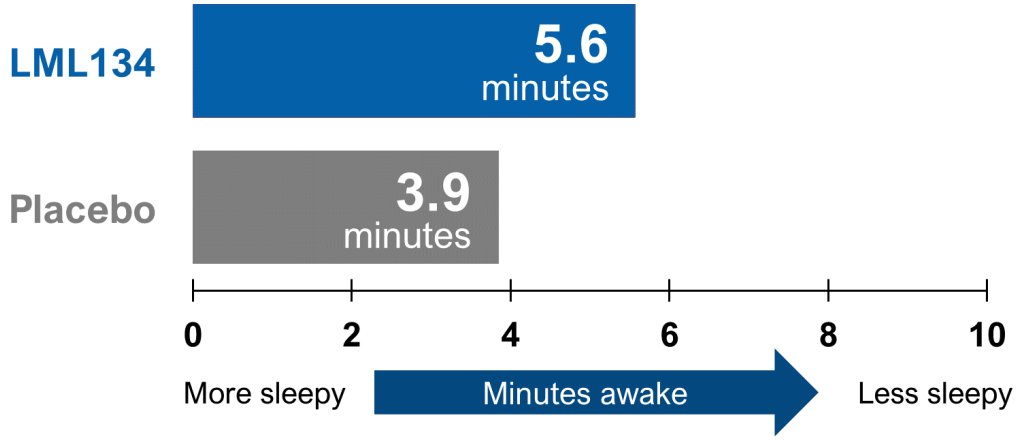
The participants were less sleepy at night after they took LML134 compared to after they took the placebo.

To find this out, the clinical trial team compared the average time it took the participants to fall asleep during the 4 MSLT nap times after they took each treatment. **The sleepier someone is, the faster they fall asleep during the MSLT nap times.**

For each 2-night period, the participants took their assigned treatment at 10 p.m. each night and stayed awake. After a few hours, trial staff asked them to take their first MSLT nap in a dark, quiet room. If a participant fell asleep during the nap time, trial staff woke them up after 15 minutes. The participant had to stay awake until the next MSLT nap time. This continued for 4 MSLT nap times in total.

The team found that the participants stayed awake longer during the nap times after they took LML134 compared to after they took the placebo.

Average minutes participants were awake during the 4 MLST nap times



What other results were learned?

The clinical trial team also learned more about:

- **How LML134 affected sleepiness over time**
  LML134 had less of an effect on sleepiness at the 4th nap time than at the earlier 3 nap times. The 4th nap time was about 9.5 hours after the participants took their assigned treatment.
- **How much and how fast LML134 got into the participants' blood**
  LML134 reached its highest levels in the participants' blood about 3 hours after they took it.
- **How LML134 affected daytime sleep**
  The data from this trial didn't show that LML134 affected the participants' daytime sleep, but more research is needed to know for sure.

What medical problems did the participants have during the trial?

Medical problems that happen during trials are called "adverse events". An **adverse event** is any unwanted sign or symptom that participants have during a trial. An adverse event is considered "**serious**" when it is life-threatening, causes lasting problems, the participant needs hospital care, or results in death.

Adverse events may or may not be caused by treatments in the trial. Many trials are needed to know if a drug or treatment causes an adverse event. Trial doctors keep track of all adverse events that happen in trials, even if they do not think the adverse events might be related to the trial treatments.

The clinical trial team concluded that LML134 was safe for the participants in this trial. The most common adverse event that the participants reported was headache.

Trial doctors looked for any adverse events when they checked the participants' health. Participants also reported adverse events. The clinical trial team compared the adverse events participants had when they took LML134 to when they took the placebo. Because 6 participants didn't complete this trial, the total number of the participants who took each treatment is different.

Adverse events during this trial

Participants who had:	LML134 (out of 21 participants)	Placebo (out of 23 participants)
Adverse events	24% (5)	13% (3)
Serious adverse events	0% (0)	0% (0)
Left this trial due to adverse events	10% (2)	0% (0)

What serious adverse events did the participants have?

During this trial, no participants reported serious adverse events and no participants died.

What types of adverse events did the participants have?

Some participants reported adverse events that were not serious. This section reports the types of adverse events the participants had during this trial.

Types of adverse events

	LML134 (out of 21 participants)	Placebo (out of 23 participants)
Headache	14% (3)	13% (3)
Anxiety	5% (1)	0% (0)
Cough	0% (0)	4% (1)
Feeling sick to the stomach Nausea	5% (1)	0% (0)
Joint pain Arthralgia	5% (1)	0% (0)
Mouth or throat pain Oropharyngeal pain	5% (1)	0% (0)
Viral infection	5% (1)	0% (0)
Throwing up Vomiting	5% (1)	0% (0)

What was learned from this trial?

This trial helped to learn about the effects and safety of LML134. The participants were less sleepy at night after they took LML134 compared to after they took the placebo. The clinical trial team concluded that LML134 was safe for the participants in this trial.

The results presented here are for one clinical trial. One trial cannot give a complete picture of the benefits and risks of a trial drug. The results of many trials are needed to find out which treatments can be used for people with shift work disorder. This summary shows only the main results from this trial. Other trials may provide new information or different results.

Where can I learn more about this and future clinical trials?

This is a summary of the results for one trial.

You can find detailed results and more information about this trial on the Novartis Clinical Trial Results website:

1. Visit novctrd.com
2. Click on “Clinical trial results and trial summary for patients” at the top right of the page
3. Read and scroll down, then click “I accept” to agree to use the information and the website
4. Select “Search by study number” on the bottom left of the page
5. Type **“CLML134X2201”** in the search box and click search

If you would like to view the website in a language other than English, you can click the “Google Translate” button on the top right of the page.

If you were in this trial and have questions about the results, please speak with the doctor or staff where you took part in this trial.

This clinical trial was registered on the following website:

- ClinicalTrials.gov – https://clinicaltrials.gov/

  To find this trial, type **CLML134X2201** in the **Other terms** search box

Full trial title:

A randomized, subject and investigator-blinded, placebo controlled, cross-over, multi-center Proof of Concept (PoC) study to assess the wakefulness promoting effect, safety, tolerability, and pharmacokinetics of LML134 in shift work disorder (SWD) patients.

Thank you!

Novartis would like to thank all of the people who participated in this clinical trial. The participants made this clinical trial possible and helped researchers answer important health questions and learn about a possible medical treatment. Many volunteers and many clinical trials are needed to advance medical science.

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