NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects of LEE011 in people with HR+ and HER2- advanced breast cancer

Thank you!

Thank you to the participants who took part in the clinical trial for HR+ and HER2- advanced breast cancer. Every participant helped the researchers learn more about the trial drug **LEE011**, also called ribociclib.

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

Trial information

Trial number: CLEE011A3201C

Novartis drug studied: LEE011, also known as ribociclib

Sponsor: Novartis

If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

This summary only shows the results of a single clinical trial. Other clinical trials may have different results.

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **LEE011** in people with a type of advanced breast cancer called hormone receptor positive, (HR+) and human epidermal growth factor receptor 2 negative (HER2-).

In this trial, researchers compared the effects of **LEE011** with hormone therapy to combination chemotherapy in women who had periods.

Advanced breast cancer is cancer that has spread from the breast to another part of the body and cannot be removed with surgery. It is also called locally advanced or metastatic. This trial included advanced breast cancer that was fast-growing and both:

- **Hormone receptor-positive (HR+):** Breast cancer cells have receptors (proteins) that use the hormones estrogen or progesterone to grow
- **Human epidermal growth factor receptor 2 negative (HER2-):** Breast cancer cells do not have the protein called HER2, which means treatments that target the HER2 protein don't work to treat this type of breast cancer

LEE011, also called **ribociclib**, is a drug designed to treat many types of cancer, including HR+, HER2- advanced breast cancer. **LEE011** is approved in certain countries to treat HR+, HER2- advanced breast cancer in women who do and don't have periods. It is approved in Asia, Europe, the Middle East, and the United States.

LEE011 is designed to be taken with hormone therapy.

Trial drug
LEE011 also called ribociclib

Pronounced as
RY-boh-SY-klib

Hormone therapy, also called endocrine therapy, blocks or lowers the level of estrogen in the body to prevent cancer cells from using estrogen to grow. Hormone therapy is a standard treatment but does not always work to treat advanced breast cancer.

Combination chemotherapy (chemo) is more than one chemotherapy medicine given together. Chemo is often used as a **standard treatment** for advanced breast cancer that is fast growing. Although chemo may shrink the tumors, it may not work for long and the cancer may get worse over time.

The trial's purpose was to answer these main questions:

- How long did participants live without their cancer getting worse?
- What medical problems, also called adverse events, happened during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial. Adverse events may or may not be caused by treatments in the trial.

How long was this trial?

The trial began in February 2019 and ended in May 2023. Participants were in this trial for up to 4 years.

Who was in this trial?

222 women with advanced breast cancer were in this trial. Participants' ages ranged from 26 to 58 years. Their average age was 43 years.
The number of participants by race is shown below.

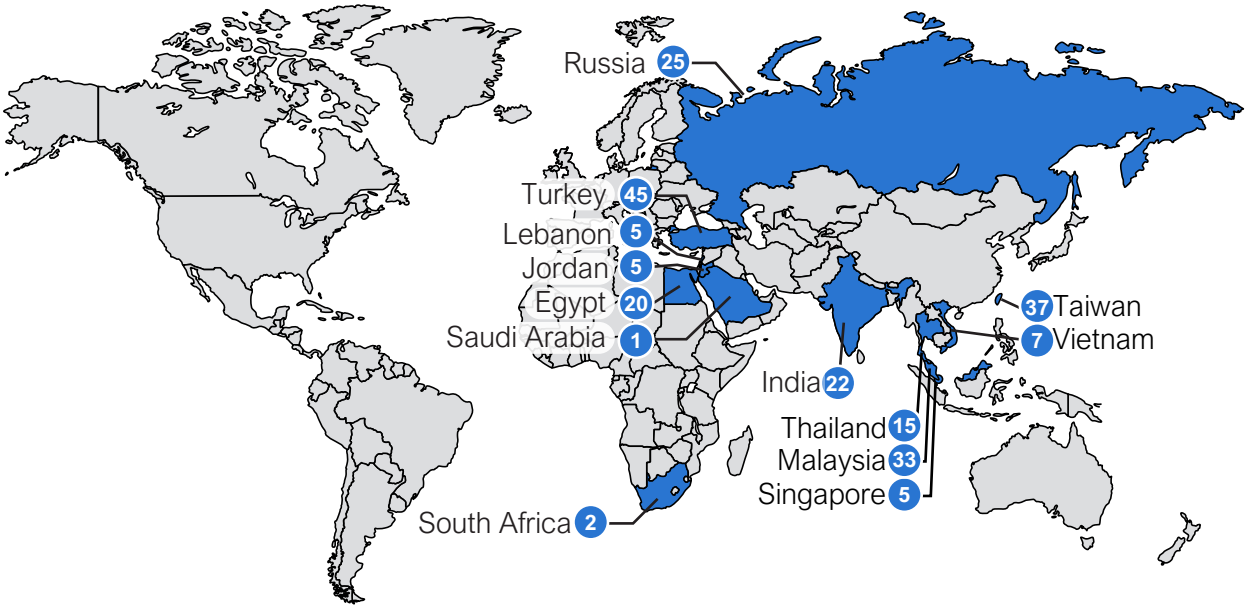
Race

118	Asian
1	Black or African American
103	White

The participants could take part in this trial if they:

- Had locally advanced or metastatic breast cancer that was fast-growing and both:
  - Hormone receptor-positive (HR+)
  - HER2-negative (HER2-)
- Had periods (pre- and peri-menopausal)
- Had not previously received chemotherapy or hormone therapy for their advanced breast cancer
- Did not have another type of cancer up to 3 years before joining the trial

222 participants joined this trial in 13 countries. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

The treatments in this trial were given as 28-day or 21-day cycles.
A **cycle** is a treatment period that is repeated. The treatments in this trial were:

LEE011, 600 milligrams (mg), which was taken by mouth as tablets once a day on Days 1-21 of a 28-day cycle. LEE011 was taken **with hormone therapy**, which included both of these:

- **Goserelin**, which was received as an injection on the first day of every 28-day cycle
- **Letrozole** or **anastrozole**, which was taken by mouth as tablets once every day in the 28-day cycle

Combination chemotherapy (chemo), which was given in 21-day cycles. Trial doctors chose 1 of 3 chemo options for each participant:

- Option 1: Docetaxel and capecitabine
- Option 2: Paclitaxel and gemcitabine
- Option 3: Capecitabine and vinorelbine

Researchers randomly assigned participants to **LEE011** with hormone therapy or chemo using a computer. Each participant received their treatments until their cancer got worse, they had certain side effects, or the trial doctor thought they were not benefitting from it.

In this trial, the participants and clinical trial team knew what treatment each participant received.

What happened during this trial?

Before treatment — **Up to about 1 month**

Trial staff checked the participants' health and breast cancer to make sure they could be in this clinical trial.

During treatment — **Up to 4 years**

222 participants were assigned to receive one of these treatments:

- **LEE011** with hormone therapy — 112 participants
- **Chemo** of the trial doctor's choice — 110 participants

10 participants assigned to receive chemo did not receive treatment because of the participant's or trial doctor's decision.

Trial staff checked the participants' breast cancer using imaging tests and general health throughout the trial. They also asked participants about their health-related quality of life.

After treatment — **Until the end of the trial**

Trial staff checked participants':

- Safety for up to 30 days after their last dose of trial treatment
- Health and survival every 4 months until the end of the trial

What were the main results of this trial?

Did participants who received LEE011 live longer without their cancer getting worse?

Overall, participants who received **LEE011** lived longer without their cancer getting worse compared to participants who received chemo.

To learn this, researchers kept track of when participants had their cancer get worse (grow or spread) or when participants died.

Length of time participants lived without their cancer getting worse

What were the other results of this trial?

How long did participants receive trial treatment before they had to stop treatment?

Overall, the time until participants had to stop trial treatment was:

- **19 months** for participants who received **LEE011**
- **9 months** for participants who received chemo

Participants who received **LEE011** continued treatment for longer compared to those who received chemo. About 2 times as many participants in the chemo group stopped treatment after 3 months compared to the **LEE011** group.

Researchers considered a participant to have stopped treatment when **any** of these happened:

- Their cancer got worse
- They died
- They started a different cancer treatment
- They stopped trial treatment for certain reasons

Did LEE011 have more effects on cancer compared to chemo?

Based on imaging tests, participants who received **LEE011** or chemo were similar in effects on:

- The number of participants who had tumors stop growing, shrink, or disappear
- The length of time until the tumors first shrank or disappeared

Researchers could not conclude how long participants lived overall in either group because most participants were still alive by the time the survival follow-up ended.

Did participants who received LEE011 rate their health-related quality of life higher than those who received chemo?

Overall, participants who received **LEE011** rated their health-related quality of life higher at most timepoints during the trial compared to those who received chemo.

What medical problems, also called adverse events, happened during this trial?

Trial doctors keep track of all **adverse events** that happen in trials, even if they think the adverse events are not related to the trial treatments.

Many trials are needed to know if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened from the first dose of trial treatment up to 30 days after the last dose.

An **adverse event** is:

- Any **sign or symptom** that the participants have during a trial
- 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.

All the participants had adverse events. 33 participants had adverse events that were considered serious. 5 participants died due to cancer that got worse. 12 participants left the trial due to an adverse event. The researchers concluded there were no new safety concerns for **LEE011** in this trial.

How many participants had adverse events?

Participants who:	LEE011 112 participants	Chemo 100 participants
Had at least 1 **serious adverse event**	17 of 112	16 of 100
Had at least 1 **other adverse event**	112 of 112	100 of 100
Left the trial due to an adverse event	8 of 112	4 of 100
Died during the trial	5 of 112	0 of 100

What serious adverse events did the participants have?

33 participants had serious adverse events. 5 participants who received **LEE011** died due to breast cancer that got worse.

The table below shows the most common serious adverse events that happened in **3 or more** participants in either group. Additional serious adverse events happened in fewer participants.

	LEE011 112 participants	Chemo 100 participants
COVID-19	4 of 112 4%	0 of 100 0%
Trouble breathing Dyspnea	3 of 112 4%	0 of 100 0%

What other adverse events did the participants have?

212 participants had other adverse events.

The table below shows the other adverse events that happened in **30 or more** participants in either group. Additional adverse events happened in fewer participants.

	LEE011 112 participants	Chemo 100 participants
Low level of a type of white blood cell Neutropenia	73 of 112 65%	38 of 100 38%
Low level of red blood cells Anemia	40 of 112 36%	42 of 100 42%
A possible sign of liver damage Alanine aminotransferase increased	23 of 112 21%	30 of 100 30%
Throwing up Vomiting	7 of 112 6%	30 of 100 30%
Redness, swelling, and pain on the hands and feet from hand-foot syndrome Palmar-plantar erythrodysesthesia	3 of 112 3%	32 of 100 32%

What was learned from this trial?

Researchers learned about the effects of **LEE011** given with hormone therapy in people with fast-growing HR+, HER2- advanced breast cancer compared to combination chemotherapy (chemo).

The researchers concluded that, compared to those who received chemo, participants who received **LEE011** with hormone therapy:

- Lived longer without their cancer getting worse
- Received trial treatment for longer before they had to stop treatment
- Were similar in effects on the number of participants who had tumors stop growing, shrink, or disappear, and the length of time until the tumors first shrank or disappeared
- Rated their health-related quality of life higher at most timepoints during the trial

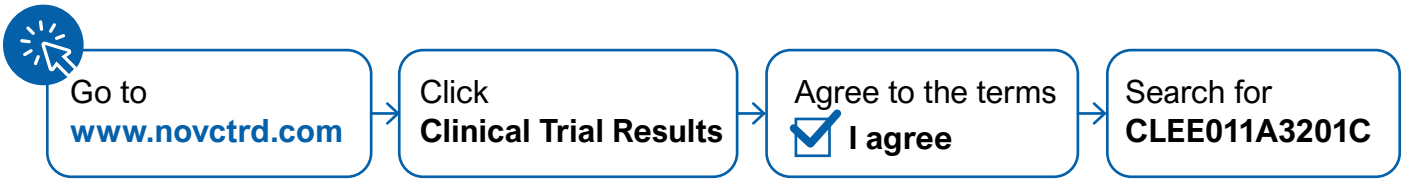
The researchers concluded there were no new safety concerns for **LEE011** in this trial.

When this summary was written, the sponsor had plans for future trials of **LEE011** in people with another type of breast cancer.

Where can I learn more about this trial?

More information about the results and adverse events in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website **www.novctrd.com**

Follow these steps to find the scientific summary:



For more information about this trial, go to this website:

- **clinicaltrials.gov** – search using the number **NCT03839823**

Other trials of **LEE011** may appear on the public website above. When there, search for LEE011 or ribociclib.

Full clinical trial title: A phase II randomized study of the combination of Ribociclib plus goserelin acetate with Hormonal Therapy versus physician choice chemotherapy in premenopausal or perimenopausal patients with hormone receptor-positive/ HER2-negative inoperable locally advanced or metastatic breast cancer

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1-888-669-6682 (US) | +41-61-324 1111 (EU)

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