NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of ribociclib at a lower dose when given with hormone therapy in pre- and postmenopausal women with advanced breast cancer

Thank you!

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

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: CLEE011A2207
Drug studied: **ribociclib**, also called **LEE011**
Sponsor: Novartis

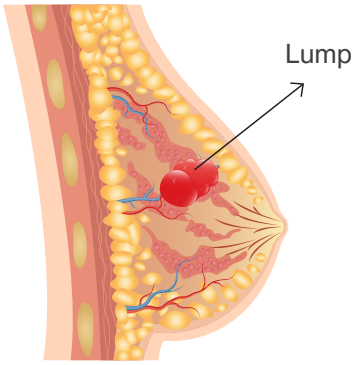
If you were a participant and have any questions about the results, please talk to the doctor or staff at the trial site.

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 main purpose of this trial was to learn about the effects of **ribociclib** given at a lower dose along with hormone therapy in pre- and postmenopausal women with **advanced breast cancer**.

In **advanced breast cancer**, cancer cells have spread from the breast and nearby areas to other parts of the body and cannot be removed through surgery. At this stage, the cancer may be controlled by treatment but is unlikely to be cured.



Breast Cancer

Common symptoms of **advanced breast cancer** are:

- Change in the size, shape, or appearance of one or both breasts
- Lump or swelling in the breast, chest, or armpits
- Pain
- Shortness of breath

The most common type of breast cancer is called **hormone receptor-positive (HR+)** and **human epidermal growth factor receptor 2-negative (HER2-) breast cancer**.

- **HR+:** Breast cancer cells have receptors (proteins) that use estrogen or progesterone to grow.
- **HER2-:** Breast cancer cells do not have the protein called **HER2**, which normally helps cells grow and divide. Treatments that target the **HER2** protein do not work to treat this type of breast cancer.

Advanced HR+/HER2- breast cancer can be treated with a few approved drugs, one of which is **ribociclib**, also called **LEE011.**

Ribociclib works by blocking the action of abnormal proteins and helps slow down cancer growth.

It is normally given in combination with drugs that lower estrogen activity in the body, such as:

Letrozole **Anastrozole** **Goserelin**

Drug
ribociclib

Pronounced as
RY-boh-SY-klib

Previous studies showed that **ribociclib** may cause certain medical problems at the approved dose of 600 milligrams (mg). In this trial, researchers wanted to check the safety of **ribociclib** given at a lower dose of 400 mg, while ensuring it could still help slow down cancer.

The main questions that researchers wanted to answer were:

- How many participants had their tumors shrink or disappear after treatment?
- 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 June 2019 and ended in August 2024. The participants received trial treatments as long as they were benefiting from them.

When the trial ended, researchers created a report of the trial results. This summary is based on that report.

Who was in this trial?

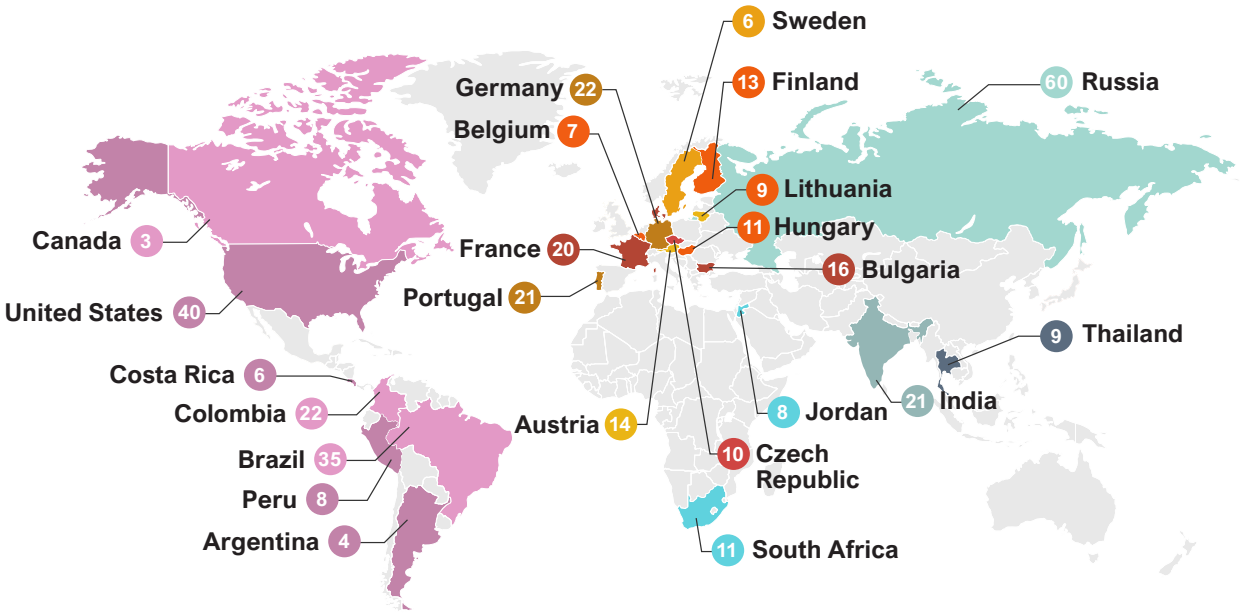
376 women with **advanced breast cancer** received treatment in this trial. Participants' ages ranged from 27 to 96 years. Their average age was 58 years.

The number of participants by race is shown below.

Race

290	Caucasian	24	Native American or Alaska Native	22	Asian
18	Unknown	17	Black	5	Other

376 participants from 23 countries received treatment. The map below shows the number of participants who took part in each country.



Participants **could take part** in this trial if they:

- Were at least 18 years old
- Were pre- or postmenopausal women
- Had **advanced HR+/HER2- breast cancer**
- Did not receive prior treatments for **advanced breast cancer**

What treatments did the participants receive?

Researchers studied the following treatments in a 28-day (4-week) cycle. A cycle is a treatment period that is repeated.

Ribociclib: 400 or 600 milligrams (mg), provided as tablets, taken by mouth, once a day for 3 weeks and one week off treatment.

Researchers used a computer to randomly assign participants to their treatment. Participants had an equal chance of receiving either 400 mg or 600 mg of **ribociclib**.

Ribociclib was given along with **letrozole** or **anastrozole**. Some participants also received **goserelin**.

Letrozole: 2.5 mg, provided as tablets, taken by mouth, once a day.

Anastrozole: 1 mg, provided as tablets, taken by mouth, once a day.

Goserelin: 3.6 mg, given as an injection into the muscle, once every 4 weeks.

Only pre-menopausal participants received **goserelin** along with other treatments.

The participants, researchers, and trial staff knew what treatment the participants were receiving.

What happened during this trial?

Before treatment

Up to 4 weeks

Trial doctors checked the participants' health and cancer status to make sure they could be in this clinical trial. This included physical exams, blood tests, and tumor images.

During treatment

For as long as participants benefited from treatment

A total of 376 participants received treatment with **ribociclib** along with other hormone drugs during this trial.

Participants were randomly assigned to 1 of 2 treatment groups based on the **ribociclib** dose they received:

Group 1 188 participants	**Ribociclib**, 400 mg once a day
Group 2 188 participants	**Ribociclib**, 600 mg once a day

Participants in both groups received **letrozole** or **anastrozole** and **ribociclib**. Participants received **goserelin** if they were pre-menopausal.

Participants continued treatment unless their condition got worse, they had unacceptable adverse events, they decided to stop treatment, or they died.

After treatment

Up to the end of the trial

Participants were checked:

- For adverse events, for up to 1 month after the last dose.
- For their cancer status until they could no longer be followed, or the trial ended.

Trial staff checked the participants' general health throughout the trial.

What were the main results of this trial?

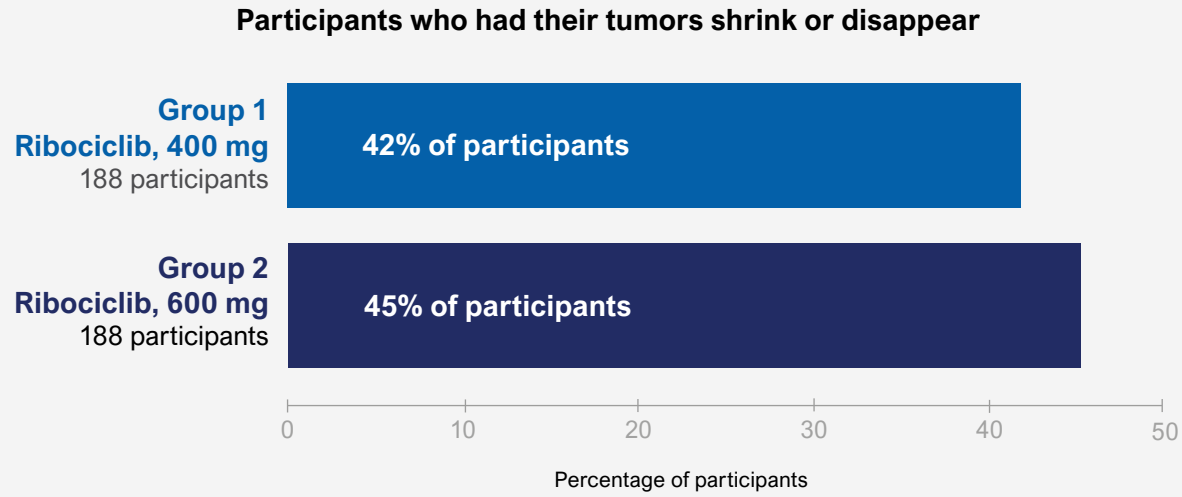
How many participants had their tumors shrink or disappear after treatment?

Researchers found that **42% of participants** who took **ribociclib** at a dose of **400 mg** and **45% of participants** who took **ribociclib** at a dose of **600 mg** had their tumors shrink or disappear after treatment.

Although the results between the two groups were close, the results showed that this difference could be due to chance alone.

Researchers wanted to find out how well the lower dose of **ribociclib (400 mg)** worked compared to the standard **600 mg** dose. To do this, they looked at how many participants had their tumors shrink or disappear after treatment.

The results were reported for participants who took **ribociclib** along with other drugs. The table below shows the number of participants who had their tumors shrink or disappear.



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

Trial doctors keep track of all medical problems, also called adverse events, that happen in trials. They track **adverse events** 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 start of the treatment **up to 1 month 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.

A total of **362 out of 376 participants (96%)** had adverse events.

- **75 out of 376 participants (20%)** had adverse events that were considered serious.
- **45 out of 376 participants (12%)** left the trial due to an adverse event.
- **11 out of 376 participants (3%)** died due to any cause.

There were no new or unexpected safety concerns with **ribociclib**.

How many participants had adverse events?

Participants who:	Ribociclib 400 mg 188 participants	Ribociclib 600 mg 188 participants
Had at least **1 adverse event (including serious and other)**	180 of 188 (96%)	182 of 188 (97%)
Had at least **1 serious adverse event**	38 of 188 (20%)	37 of 188 (20%)
Left the trial due to an adverse event	21 of 188 (11%)	24 of 188 (13%)

What serious adverse events did the participants have?

The table below shows the most common serious adverse events that happened during the trial.

	Ribociclib 400 mg 188 participants	Ribociclib 600 mg 188 participants
Lung infection Pneumonia	2 of 188 (1%)	3 of 188 (2%)
COVID related lung infection COVID pneumonia	3 of 188 (2%)	1 of 188 (1%)
COVID-19	2 of 188 (1%)	2 of 188 (1%)
Back pain	2 of 188 (1%)	2 of 188 (1%)
Fluid around the lungs Pleural effusion	2 of 188 (1%)	2 of 188 (1%)
Shortness of breath Dyspnea	0 of 188 (0%)	4 of 188 (2%)

What other (not including serious) adverse events did the participants have?

The table below shows the most common other adverse events that happened during the trial.

	Ribociclib 400 mg 188 participants	Ribociclib 600 mg 188 participants
Low levels of of neutrophils Neutropenia	100 of 188 (53%)	125 of 188 (66%)
Increased level of liver protein in the blood Alanine aminotransferase increased	49 of 188 (26%)	47 of 188 (25%)
Low levels of white blood cells Leukopenia	40 of 188 (21%)	52 of 188 (28%)
Increased level of liver protein in the blood Aspartate aminotransferase increased	41 of 188 (22%)	40 of 188 (21%)
Low red blood cells Anemia	31 of 188 (16%)	49 of 188 (26%)
Nausea	31 of 188 (16%)	44 of 188 (23%)
Tiredness Fatigue	22 of 188 (12%)	40 of 188 (21%)
Joint pain Arthralgia	31 of 188 (16%)	28 of 188 (15%)

What was learned from this trial?

This trial helped researchers learn about the effects of **ribociclib** given along with **letrozole** or **anastrozole** and **goserelin** in women with **HR+/HER2- advanced breast cancer**.

The researchers concluded that:

- Overall, 42% of participants who received 400 mg of **ribociclib** had their tumors shrink or disappear, compared to 45% in the 600 mg group.
- Although the results between the two groups were close, the results showed that this difference could be due to chance alone.
- There were fewer safety issues with the 400 mg dose than the 600 mg dose of **ribociclib**. There were no new or unexpected safety concerns with **ribociclib**. The safety results were similar to those seen in previous trials.

When this summary was written, other trials of **ribociclib** were still ongoing.

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:

Go to **www.novctrd.com** → Click **Clinical Trial Results** → Accept the terms **I accept** → Search for **CLEE011A2207**

For more information about this trial, go to any of these websites:

- clinicaltrials.gov – search using the number **NCT03822468**
- clinicaltrialsregister.eu – search using the number **2018-004234-15**

Other trials with **ribociclib** appear on the public websites above. When there, search for **ribociclib** or **LEE011**.

Full clinical trial title: A phase II, multicenter, randomized, open-label study to evaluate the safety and efficacy of 400 mg of ribociclib in combination with non-steroidal aromatase inhibitors for the treatment of pre- and postmenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer who received no prior therapy for advanced disease

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