NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of LEE011 in people with advanced breast cancer

Protocol number: CLEE011XDE01

Thank you!

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. Thank you for taking part in this trial for the drug LEE011, also known as ribociclib. You helped researchers learn more about how LEE011 works in people with advanced breast cancer.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of a single clinical trial. Other clinical trials may have different findings. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Researchers are looking for a better way to treat **advanced breast cancer**. Advanced breast cancer is cancer that has spread from the breast, and areas around it, to another part of the body and cannot be removed with surgery.

LEE011 is a drug designed to treat many types of cancer, including advanced breast cancer that is both:

- **Hormone receptor-positive:** Breast cancer cells have receptors (proteins) that use estrogen or progesterone to grow
- **HER2-negative:** 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 is designed to be taken with **hormone therapy**, which blocks or lowers the level of estrogen in the body and may prevent cancer cells from using it to grow. Past trials had shown that LEE011 combined with hormone therapy could shrink or stop the growth of advanced breast cancer that was hormone receptor-positive and HER2-negative in women who no longer had periods (post-menopausal).

This trial was designed to learn about LEE011 combined with hormone therapy in a broader group of people with breast cancer than the past trials. This trial included:

- Women who had periods (**pre- and peri-menopausal**)
- Women who no longer had periods (**post-menopausal**)
- Men

During this trial, LEE011 was approved in the European Union and the United States to treat post-menopausal women with advanced, hormone receptor-positive, HER2-negative breast cancer.

Trial purpose

The main purpose of this trial was to learn about the effects and safety of LEE011 combined with hormone therapy in women and men with advanced breast cancer. It was also designed to confirm the results from past trials that included only post-menopausal women.

The main questions the researchers wanted to answer in this trial were:

- What percent of participants had tumors that shrank or stopped growing after 24 weeks of trial treatment?
- What medical problems did the participants have during the trial?

Trial treatments

The treatments in this trial were:

LEE011, also known as **ribociclib**, taken by mouth as tablets

Hormone therapy called **letrozole**, taken by mouth as tablets

For female participants who had periods (pre-menopausal), hormone therapy also included **goserelin** as an injection

How long was this trial?

This trial started in October 2016 and ended in February 2020. It was designed so that each participant could take part until they had a severe side effect, their cancer got worse, or they decided to leave the trial. On average, participants took their trial treatments for about 14 months.

The researchers completed this trial as planned. When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

502 participants took trial treatments – 497 women and 5 men. Participants' ages ranged from 29 to 90 years. They were 64 years old on average. Participants took part at 87 trial sites in Germany.

The participants could take part in this trial if their advanced breast cancer was:

- Hormone receptor-positive
- HER2-negative
- Not likely to be well treated with approved medicines

This trial included 2 groups of participants: Group A and Group B. The table below shows who was in each group.

	Group A	Group B
Women Pre-menopausal Peri-menopausal	**None**	**May or may not** have had previous treatment for advanced breast cancer
Women Post-menopausal	**No** previous treatment for advanced breast cancer	**Had** previous treatment for advanced breast cancer
Men	**No** previous treatment for advanced breast cancer	**Had** previous treatment for advanced breast cancer

What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment each participant took. In this trial, all participants took LEE011 and letrozole. Female participants who had periods also got goserelin.

What happened during this trial?

During screening

Up to 3 weeks before taking the trial treatments, trial doctors checked participants' health and breast cancer to make sure they could be in this trial. 504 participants could take part in this trial.
2 participants left before taking treatment.

During treatment

The participants took:

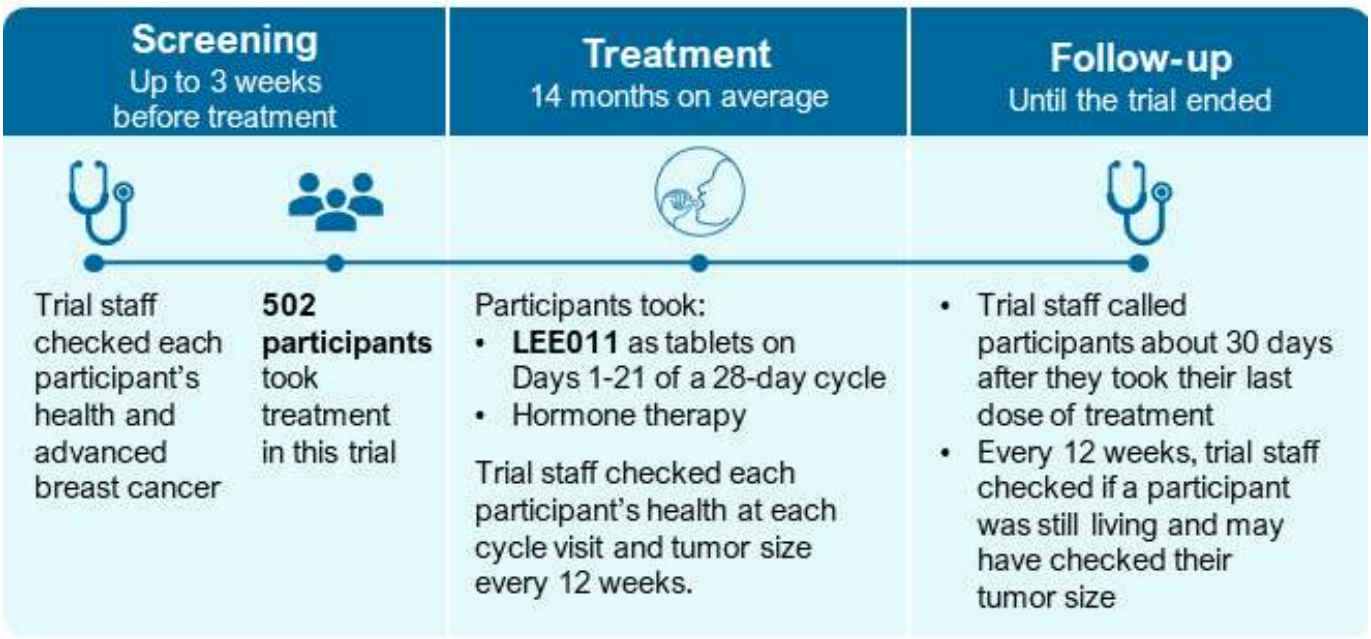
- **LEE011,** 600 milligrams (mg) taken by mouth as tablets once a day. The participants took LEE011 on Days 1-21 of a 28-day treatment cycle.
- **Letrozole,** 2.5 mg taken by mouth as tablets once a day

Female participants who had periods also got **goserelin,** 3.6 mg given as an injection every 4 weeks.

Each participant could continue to take the trial treatments until they had a severe side effect, their cancer got worse, or they decided to leave the trial. Trial staff checked each participant's health at each cycle visit and checked tumor size every 12 weeks.

During follow-up
Trial staff called participants about 30 days after they took their last dose of treatment to check their health. Until the trial ended, trial staff checked if a participant was still living every 12 weeks. If a participant's cancer had not gotten worse by the end of their treatment, trial staff also checked their tumor size every 12 weeks until the end of the trial or their cancer got worse.

How this trial was done:



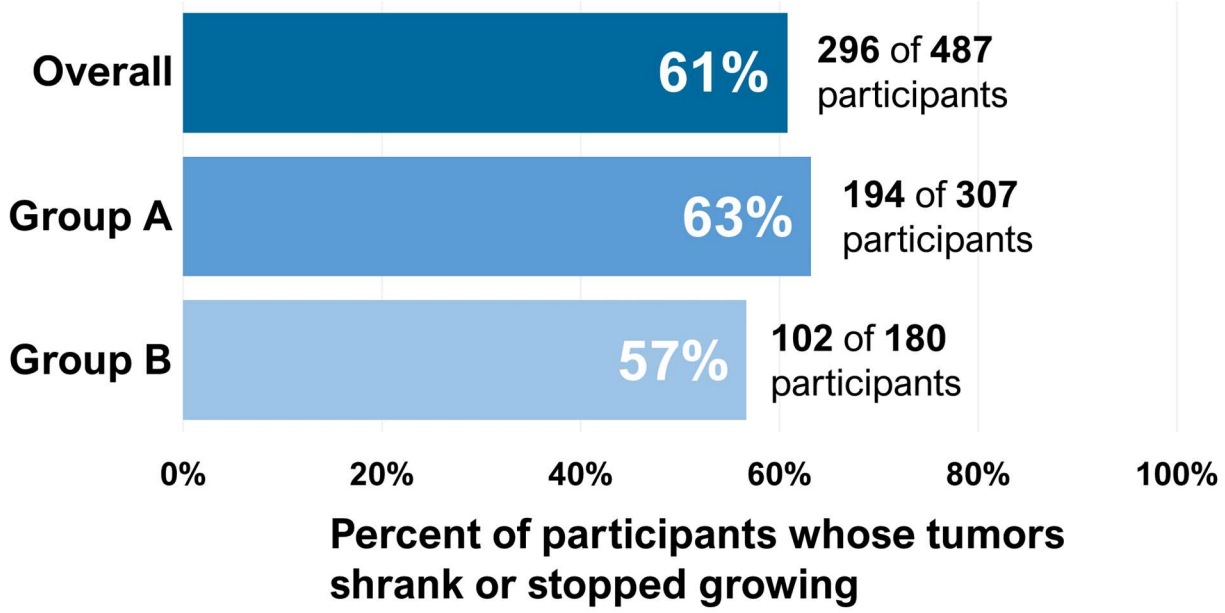
What were the main results of this trial?

What percent of participants had tumors that shrank or stopped growing after 24 weeks of trial treatment?

During certain visits to the trial site, trial staff used imaging scans to measure the size of participants' tumors. They used this information to calculate the **Clinical Benefit Rate (CBR)**, which is the percent of participants whose tumors shrank or stopped growing after taking the trial treatments.

After 24 weeks of trial treatment, about 61% of all participants had tumors that shrank or stopped growing. The percent was slightly higher for participants in Group A (63%) than in Group B (57%).

Clinical Benefit Rate (CBR) after 24 weeks of trial treatment



Note: This graph includes 487 of the 502 participants who took treatment.

What were the other results of this trial?

The clinical trial team also answered these questions:

Did the participants who had previously been treated for breast cancer have a different CBR?
The CBR was about the same for participants who had and had not previously been treated for breast cancer.

Were participants who had been previously treated for breast cancer more likely to have their tumor shrink or disappear?
Participants who were previously treated for breast cancer were less likely to have their tumors shrink or disappear than those who were not previously treated.

How long did participants live without their cancer getting worse?
The average time participants lived without their cancer getting worse ranged from about 9 months to 22 months after starting treatment. Participants who were previously treated for breast cancer had their cancer get worse sooner than those who were not previously treated.

How long did participants live?
The clinical trial team tracked each participant's survival until the trial ended for all participants. About 80% to 90% of participants were still living about 16 months after starting treatment.

Did participants' quality of life change during the trial?
To measure the participants' quality of life, the clinical trial team asked participants to answer sets of questions at the start of treatment and during treatment. Then, they looked for changes in participants' answers over time. The team found that, on average, participants reported their quality of life went down by 10% at about 3 or 4 months of treatment. Overall, participants reported no large changes to their quality of life during the trial.

What medical problems did the participants have during the trial?

Medical problems that happen in clinical 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, or the participant needs hospital care. These problems may or may not be caused by the trial drug.

A lot of research is needed to know whether a drug causes an adverse event. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. So, when new drugs are being studied, researchers keep track of all adverse events the participants have.

This section is a summary of the adverse events that happened during and 30 days after treatment. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the most common serious adverse events?
147 participants had serious adverse events, and 12 of these participants died during treatment.

Serious adverse events that happened in at least 1.5% (8 out of 502) of participants:

	Group A	Group B
	Percent % (out of 319 participants)	**Percent %** (out of 183 participants)
Shortness of breath Dyspnea	**3%** (9)	**2%** (3)
Infection in the lungs Pneumonia	**3%** (8)	**1%** (2)
Feeling sick to the stomach Nausea	**2%** (7)	**1%** (2)
Low red blood cell levels Anemia	**1%** (4)	**2%** (4)
Blood clot in the lungs Pulmonary embolism	**2%** (7)	**1%** (1)

What were the most common non-serious adverse events?

496 participants had adverse events that were not considered serious.

Non-serious adverse events that happened in at least 25% (125 out of 502) of participants:

	Group A	Group B
	Percent % (out of 319 participants)	**Percent %** (out of 183 participants)
Low white blood cell (neutrophil) levels Neutropenia	**51%** (162)	**48%** (88)
Feeling sick to the stomach Nausea	**41%** (130)	**42%** (77)
Feeling tired Fatigue	**39%** (123)	**40%** (74)
Hair loss Alopecia	**37%** (119)	**31%** (57)
The common cold Nasopharyngitis	**29%** (94)	**27%** (49)
Diarrhea	**27%** (85)	**22%** (40)

How has this trial helped?

After 24 weeks of trial treatment, about 61% of all participants had tumors that shrank or stopped growing. This result confirmed results from past trials that included fewer groups of people with breast cancer.

The clinical trial team found no safety concerns for LEE011 when combined with hormone therapy. The adverse events that the participants had in this trial were similar to those reported in other trials of LEE011 with hormone therapy.

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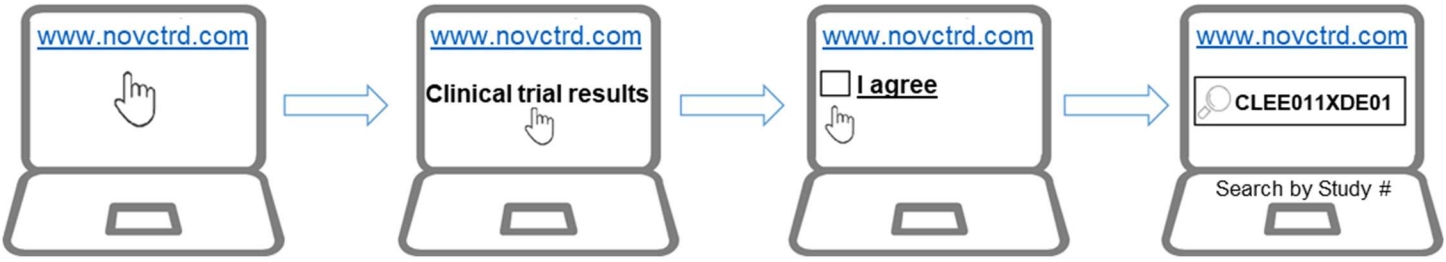
Where can I learn more about this trial?

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).



You can find more information about this trial on the following websites:

- www.clinicaltrials.gov. Use the NCT identifier **NCT03096847** in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search. Use the EudraCT identifier **2016-002556-24** in the search field.

Full clinical trial title: A national phase IIIb, multi-center, open label study for women and men with hormone-receptor positive, HER2-negative locally advanced or metastatic breast cancer treated with ribociclib (LEE011) in combination with letrozole

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

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Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

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