NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the safety of LEE011 in people with high-risk early breast cancer

Protocol number: CLEE011G2301

Thank You!

Novartis, the sponsor of this clinical trial, would like to 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 high-risk early 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 **high-risk early breast cancer (EBC)**. EBC is cancer in the breast, and areas around it, that can be removed with surgery. “High risk” means that the breast cancer has a high chance of returning after surgery and spreading to other parts of the body.

LEE011 is a drug that is approved in some countries to be used combined with hormone therapy to treat certain types of breast cancer. **Hormone therapies** are drugs that block or lower estrogen in the body so cancer cells can’t use it to grow. LEE011 combined with hormone therapy is approved to treat breast cancer that is all 3 of these:

- **Advanced**: Breast cancer that has spread from the breast to another part of the body and cannot be removed with surgery
- **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 do not work to treat this type of breast cancer

Trial purpose

The main purpose of this trial was to learn if LEE011 was safe when combined with hormone therapy for people with hormone receptor-positive, HER2-negative high-risk EBC.

The main question the researchers wanted to answer in this trial was:

- What medical problems did the participants have during the trial?

Trial drugs

The drugs given in this trial were:

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

Placebo: looks like the trial drug, but does not have any trial drug in it. Using a placebo helps researchers better understand the effect of a trial drug.

Hormone therapy: participants took hormone therapy that is standard (usual) treatment for hormone receptor-positive and HER2-negative breast cancer. Each participant took 1 of these 4 hormone therapies by mouth as tablets:

- **Letrozole**
- **Anastrozole**
- **Exemestane**
- **Tamoxifen**

Later in the trial, the trial doctors switched participants who took tamoxifen to one of the other 3 hormone therapies. The reason was that other research showed tamoxifen combined with LEE011 may cause side effects on the heart.

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

How long was this trial?

This trial was designed so that each participant could take part for about 6 years. However, the sponsor decided to stop enrolling participants in this trial earlier than planned.

The trial started in June 2017 and ended in March 2020.

Why did enrollment end early?

The sponsor decided to begin a different trial to learn about LEE011 combined with hormone therapy in people with high-risk and medium-risk breast cancer through a single trial. The decision to end enrollment early was not related to safety.

When the sponsor decided to stop enrollment early, they also decided to focus the purpose on safety only. This means they no longer looked at how well LEE011 combined with hormone therapy worked to treat hormone receptor-positive, HER2-negative high-risk early breast cancer.

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?

The researchers designed this trial to include about 2,000 men and women with EBC. Because enrollment ended early, only 54 women and no men were in this trial.

The participants could take part in this trial if their EBC was:

- High risk
- Hormone receptor-positive
- HER2-negative
- Removed with surgery and treated with standard chemotherapy drugs

Participants had no other serious medical problems and had not received certain treatments.

Participants' ages ranged from 32 to 71 years. They were 56 years old on average. Most participants identified themselves as White. Other participants identified themselves as Black, Asian, Other, or Unknown.

This trial was planned to take place in several countries, but the sponsor stopped enrolling participants before anyone had taken part from outside of the United States. Participants took part at 33 trial sites in the United States.

What kind of trial was this?

This trial began as a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment the participants were taking. Some trials are done this way because knowing what treatment each participant is taking can affect the results of the trial. Doing a trial this way helps to make sure that the results are looked at with fairness towards all treatments.

When the sponsor stopped enrolling participants, they changed the trial to be open-label. This means that the participants and clinical trial team learned what treatment each participant took.

What happened during this trial?

During screening

Up to 4 weeks before taking the trial treatment, trial doctors checked participants' health and EBC to make sure they could be in this trial. 54 participants could take part in this trial. 4 participants left before taking treatment.

During treatment

The participants were randomly assigned to take 1 of 2 treatments:

- **LEE011,** 600 milligrams (mg) taken by mouth as tablets once a day
- **Placebo**, taken by mouth as tablets once a day

The participants took their assigned treatment on Days 1-21 of a 28-day cycle. The treatment period could last up to 26 cycles, or about 2 years.

In addition to 1 of the 2 treatments above, participants took 1 of these 4 **hormone therapies** by mouth as tablets:

- Letrozole
- Anastrozole
- Exemestane
- Tamoxifen – later in the trial, the trial doctors switched participants who took tamoxifen to one of the other 3 hormone therapies

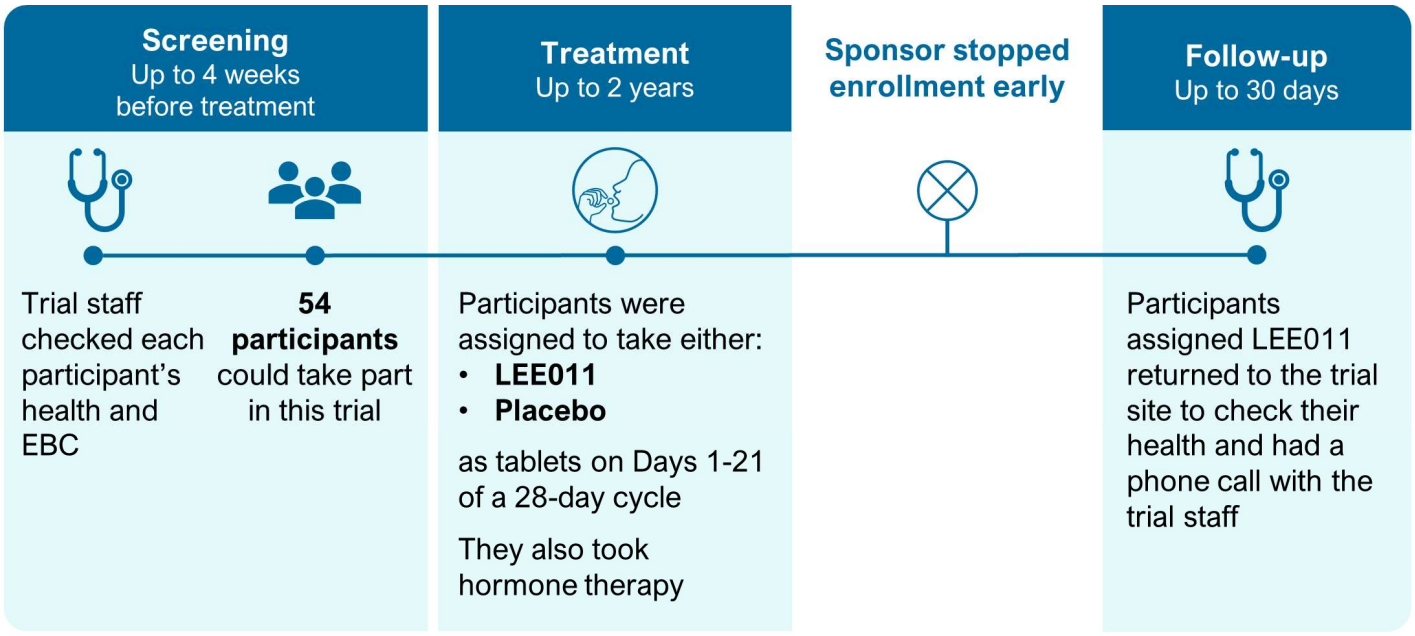
When the sponsor stopped enrollment early, participants who were assigned LEE011 and hormone therapy had the option to finish their trial treatments. Participants who were assigned the placebo stopped and left the trial.

Researchers checked the participants' EBC and general health throughout the trial.

During follow-up

Participants returned to their trial site within 15 days after taking their last dose of treatment for an end-of-treatment visit to check their health. Trial staff also called the participants on the phone 30 days after their last day of treatment.

How this trial was done:



What were the main results of this trial?

This is a summary of the overall results for all participants in both treatment groups. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

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 an 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. 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 the treatment period. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

What were the serious adverse events?

There were no deaths reported during this trial. A total of 6 participants (12% of all participants who took treatment) had serious adverse events, which are listed in the table below.

	LEE011 and hormone therapy	**Placebo** and hormone therapy
	Percent % (out of 26 participants)	**Percent %** (out of 24 participants)
Skin infection Cellulitis	**4%** (1)	**4%** (1)
Cancer of blood and bone marrow Acute myeloid leukaemia	**4%** (1)	**0%** (0)
Skin infection on the breast Breast cellulitis	**4%** (1)	**0%** (0)
Congestive heart failure Cardiac failure congestive	**4%** (1)	**0%** (0)
A condition causing blood clots Disseminated intravascular coagulation	**4%** (1)	**0%** (0)
Blood clot in the lungs Pulmonary embolism	**4%** (1)	**0%** (0)
Seizure	**0%** (0)	**4%** (1)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 8 participants (16% of all participants who took treatment) are listed in the table below.

	LEE011 and hormone therapy	Placebo and hormone therapy
	Percent % (out of 26 participants)	**Percent %** (out of 24 participants)
Feeling sick to the stomach Nausea	**46%** (12)	**25%** (6)
Low level of white blood cells Neutropenia	**54%** (14)	**0%** (0)
Feeling tired Fatigue	**46%** (12)	**4%** (1)
Joint pain Arthralgia	**23%** (6)	**29%** (7)
Lower level of white blood cells White blood cell count decreased	**38%** (10)	**0%** (0)
Cough	**27%** (7)	**8%** (2)
Hair loss Alopecia	**27%** (7)	**4%** (1)

How has this trial helped?

The clinical trial team found that most of the adverse events that the participants had in this trial could be managed by adjusting the dose of the trial drugs. The adverse events were similar to those reported in other trials of LEE011 combined with hormone therapy.

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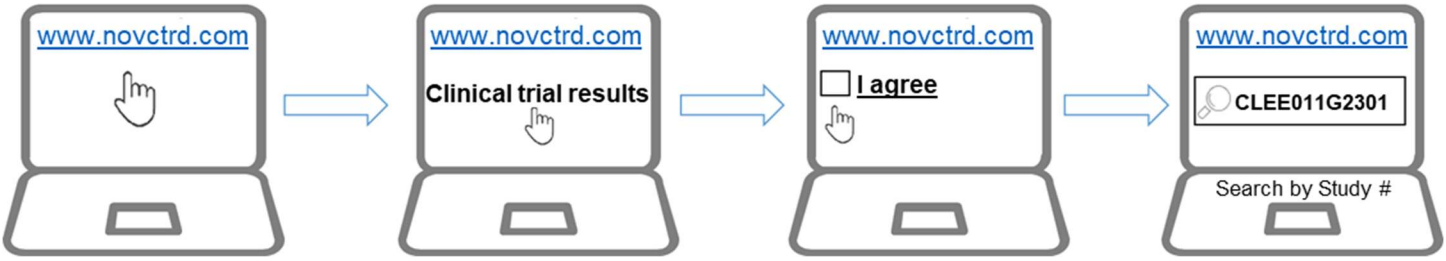
Where can I learn more about this trial?

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 these websites:

- www.clinicaltrials.gov. Use the NCT identifier 03078751 in the search field.
- www.clinicaltrialsregister.eu/ctr-search/. Use the EudraCT identifier 2014-001795-53 in the search field.

Full clinical trial title: An open label, multi-center protocol for U.S. patients enrolled in a study of ribociclib with endocrine therapy as an adjuvant treatment in patients with hormone receptor-positive, HER2-negative, high risk early breast cancer

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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