NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the safety of LEE011 given with other cancer drugs in children and young adults with solid tumors

Thank you!

Thank you to the participants who took part in the clinical trial for **solid tumors**. 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: CLEE011Q12101

Drug studied: **LEE011**, also called **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 findings.

What was the main purpose of this trial?

The main purpose of this trial was to learn about the effects of **LEE011** given with other cancer drugs in children and young adults with **solid tumors**.

Solid tumors are lumps or masses of abnormal cells that form in organs or tissues.

The **solid tumors** studied in this trial include the following:

- **Rhabdomyosarcoma**: a rare cancer that starts in the muscles or soft tissues. It usually affects children and can grow in areas such as the head, neck, belly, arms, or legs.
- **High grade glioma**: a fast-growing brain tumor that starts in the cells that support and protect nerve cells. These tumors can affect how a child feels, moves, or thinks, depending on the location of the tumors in the brain.
- **Malignant rhabdoid tumor**: a rare and fast-growing cancer that usually affects young children. It can start in the kidneys, brain, or other parts of the body and can spread quickly.
- **Medulloblastoma**: a brain tumor that mainly affects children. It begins in the cerebellum, which is the part of the brain that helps with balance and coordination. Children may have trouble walking, feel dizzy, or get frequent headaches.
- **Neuroblastoma**: a cancer that begins in nerve cells, often in the adrenal glands. These small glands sit on top of each kidney and help control important body functions. In neuroblastoma, the nerve cells grow out of control and form a tumor.

Current treatments for solid tumors do not always work or may stop working over time. This is called **refractory disease**. Sometimes, cancer comes back after treatment - this is called a **relapse**. That is why researchers are looking for new treatment options.

This trial included children and young adults with solid tumors that were either refractory or relapsed.

The trial drug, **LEE011 (ribociclib)**, is approved for use in adults with certain types of breast cancer. It works by blocking the action of abnormal proteins and helps slow down cancer growth.

Drug
ribociclib

Pronounced as
RY-boh-SY-klib

In this trial, **LEE011** was given together with two approved other cancer drugs:

Topotecan

Temozolomide

Researchers tested increasing doses of **LEE011** to find a recommended dose that could be safely used for further study. They also carefully monitored all medical problems that happened during the trial and identified any that could cause changes in dosing. This type of research study is called a **dose escalation trial**.

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

- What was the recommended dose of **LEE011**, when given with other cancer drugs, for further testing?
- 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 December 2022 and ended in February 2025. The participants could receive trial treatment as long as they were benefiting from it.

The trial ended earlier than planned due to a decision by the sponsor.

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

Who was in this trial?

12 participants with **solid tumors** received treatment in this trial.

Participants' ages ranged from 4 to 20 years. Their average age was 14 years.

The number of participants by sex and race are shown below.

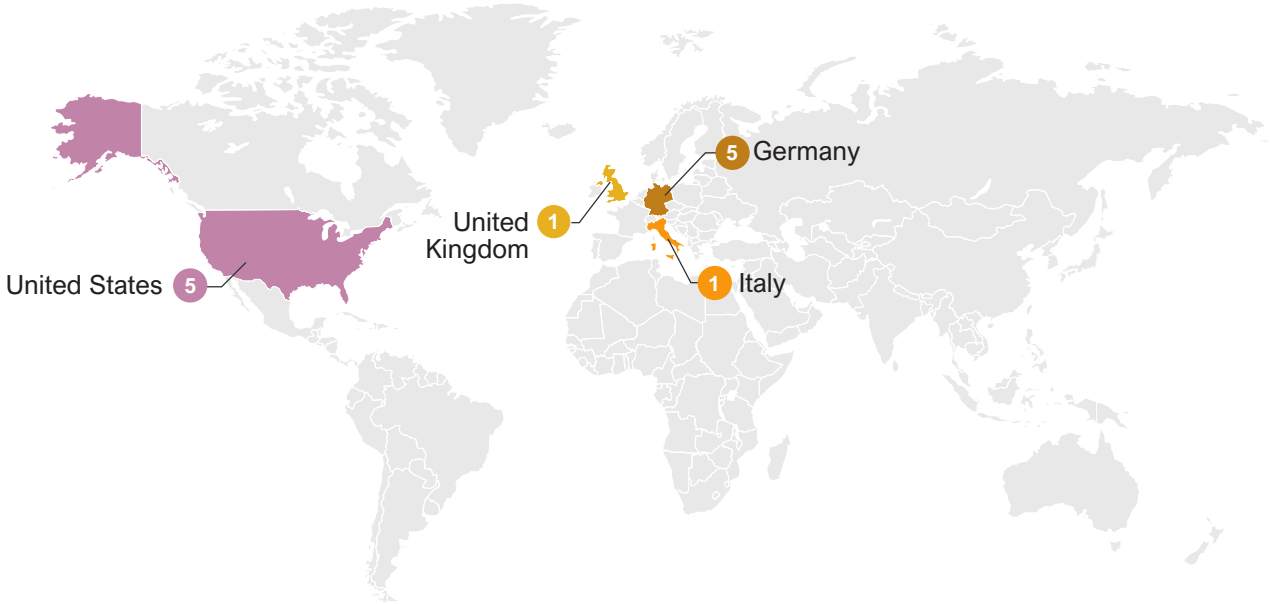
Sex

7 Females	5 Males

Race

10 White	1 Black or African American	1 Unknown

12 participants from **4 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 between 12 months and 21 years of age
- Had relapsed/refractory neuroblastoma or other **solid tumors** listed on page 2
- Did not have heart problems or other serious medical conditions

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.

LEE011: 100 or 200 milligrams per square meter per day (mg/m^2/day), provided as an oral solution, taken by mouth.

Milligrams per square meter (mg/m^2) is a unit for measuring the amount of trial drug based on a person's height and weight.

LEE011 was given along with **topotecan** and **temozolomide**.

Topotecan: 0.75 mg/m^2/day, given as an intravenous (IV) infusion, which is a drip through a tube directly into a vein.

Temozolomide: 150 or 100 mg/m^2/day, provided as capsules, taken by mouth.

Researchers also planned to use a **placebo** to study the effects of **LEE011**. A placebo looks like the trial drug but does not have any trial drug in it. However, the part of the study that would have included placebo was never done.

The participants, researchers, and trial staff knew what treatment the participants were receiving. The participants took **LEE011** with **topotecan** and **temozolomide**.

What happened during this trial?

Before treatment

Up to 4 weeks

The trial staff checked to make sure the participants could be in this trial.

During treatment

For as long as participants benefited from treatment

This trial was originally planned to be done in 3 parts. However as the trial ended early, only the 1st part was done - the **Dose Escalation**. The 2nd part would have further studied one of the doses in multiple groups **(Dose Expansion)**. The 3rd part would have compared treatment to placebo.

Dose Escalation

In this part, trial doctors wanted to find out the recommended dose of **LEE011** for further testing. They tested different doses of **LEE011** in separate groups of participants.

Researchers started by giving 200 mg/m²/day of **LEE011** to a small group of participants (Group 1). They received **LEE011** on Days 1 to 21 of the 28-day treatment cycle. After researchers reviewed the data and checked the safety of this dose, the next group received 100 mg/m²/day of **LEE011** on Days 6 to 21. The last group received 100 mg/m²/day of **LEE011** on Days 1 to 14. This process continued until the safety of each dose had been checked.

A total of 12 participants received treatment in this trial.

Group 1 2 particpants	**LEE011,** **200 mg/m²/day** Days 1 to 21	**Temozolomide,** **150 mg/m²/day** Days 1 to 5	**Topotecan,** **0.75 mg/m²/day** Days 1 to 5

↳ Safety check

Group 2 4 particpants	**LEE011,** **100 mg/m²/day** Days 6 to 21	**Temozolomide,** **150 mg/m²/day** Days 1 to 5	**Topotecan,** **0.75 mg/m²/day** Days 1 to 5

↳ Safety check

Group 3 6 particpants	**LEE011,** **100 mg/m²/day** Days 1 to 14	**Temozolomide,** **100 mg/m²/day** Days 1 to 5	**Topotecan,** **0.75 mg/m²/day** Days 1 to 5

In **Group 3**, the dose of **temozolomide** was lowered from 150 mg/m²/day to 100 mg/m²/day after participants had problems producing new blood cells. This is a known effect related to **temozolomide** treatment.

After treatment

Up to 30 days after the last dose

Participants were checked for adverse events for up to 30 days after the last dose.

Trial doctors checked participants for their overall health throughout the trial.

What were the main results of this trial?

What was the recommended dose of LEE011, when given with other cancer drugs, for further testing?

Researchers could not find a recommended dose of **LEE011** in combination with other cancer drugs studied for further testing. As a result, the trial ended early.

To find the recommended dose of **LEE011**, researchers closely monitored participants for any **dose-limiting toxicities (DLTs)** during the first treatment cycle.

DLTs are medical problems that:

- Trial doctors believe may be related to the trial treatment
- Require the treatment to be paused or the dose to be lowered

In this trial, if a participant received less than 75% of the planned dose due to various medical problems, it was also counted as DLT.

The table below shows how many participants had DLTs during the first treatment cycle. The results cover 11 out of 12 participants because only those who completed the first cycle and had results available were included.

	Group 1	Group 2	Group 3
LEE011	**200 mg/m²/day**	**100 mg/m²/day**	**100 mg/m²/day**
Temozolomide	**150 mg/m²/day**	**150 mg/m²/day**	**100 mg/m²/day**
Topotecan	**0.75 mg/m²/day**	**0.75 mg/m²/day**	**0.75 mg/m²/day**
	2 participants	3 participants	6 participants
Participants who had DLTs during the first treatment cycle	2 of 2 **(100%)**	2 of 3 **(67%)**	2 of 6 **(33%)**

Below is a summary of the DLTs seen in each group.

Group 1:

- 2 participants from **Group 1** had a **low number of white blood cells called neutrophils** (neutropenia).
- These same 2 participants also had other medical problems that caused them to receive less than 75% of the planned dose.

Group 2:

- 1 participant had a **decrease in neutrophil levels**.
- This participant and one other (2 total) had medical problems that caused them to receive less than 75% of the planned dose.

Group 3:

- 1 participant had multiple DLTs which included **low blood pressure** (hypotension), **breathing difficulty** (dyspnea), **low levels of oxygen in the body** (hypoxia), and **lung failure** (respiratory failure).
- A second participant had medical problems that caused them to receive less than 75% of the planned dose.

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

Trial doctors also 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 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 **12 out of 12 participants (100%)** had adverse events.

- **6 out of 12 participants (50%)** had adverse events that were considered serious.
- **1 out of 12 participants (8%)** left the trial due to an adverse event.
- **1 out of 12 participants (8%)** died due to any cause, including from their solid tumor.

What serious adverse events did the participants have?

The table below shows all the serious adverse events that happened during the trial. Each serious adverse event happened in 1 participant.

	Group 1 2 participants	Group 2 4 participants	Group 3 6 participants
Neutrophil count decreased (a type of white blood cell)	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Fever with low levels of neutrophils Febrile neutropenia	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Non-cardiac chest pain	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Device-related infection	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Fall	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Platelet count decreased	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Pain in the arms and legs Pain in extremity	1 of 2 **(50%)**	0 of 4 **(0%)**	0 of 6 **(0%)**
Headache	1 of 2 **(50%)**	0 of 4 **(0%)**	0 of 6 **(0%)**
Breathing difficulty Dyspnea	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Low levels of oxygen in the body Hypoxia	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Lung failure Respiratory failure	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**
Low blood pressure Hypotension	0 of 2 **(0%)**	0 of 4 **(0%)**	1 of 6 **(17%)**

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.

	Group 1 2 participants	Group 2 4 participants	Group 3 6 participants
Low levels of red blood cells Anemia	2 of 2 **(100%)**	3 of 4 **(75%)**	6 of 6 **(100%)**
Nausea	2 of 2 **(100%)**	4 of 4 **(100%)**	4 of 6 **(67%)**
Vomiting	2 of 2 **(100%)**	2 of 4 **(50%)**	5 of 6 **(83%)**
Low levels of blood platelets Thrombocytopenia	2 of 2 **(100%)**	2 of 4 **(50%)**	2 of 6 **(33%)**
Neutrophil count decreased (a type of white blood cell)	0 of 2 **(0%)**	2 of 4 **(50%)**	4 of 6 **(67%)**
Platelet count decreased	0 of 2 **(0%)**	2 of 4 **(50%)**	4 of 6 **(67%)**
White blood cell count decreased	0 of 2 **(0%)**	2 of 4 **(50%)**	4 of 6 **(67%)**
Headache	1 of 2 **(50%)**	2 of 4 **(50%)**	3 of 6 **(50%)**

What was learned from this trial?

This trial helped researchers learn about the safety of **LEE011** given along with **topotecan** and **temozolomide** in children and young adults with **solid tumors**.

Researchers found that:

- Due to the number of participants who had DLTs in Part 1, researchers could not determine the recommended dose of **LEE011** in combination with other cancer drugs for further study. As a result, the trial ended early.

When this summary was written, the sponsor had no plans for future trials of **LEE011** in children or young adults with **solid tumors**.

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 **CLEE011Q12101**

For more information about this trial go to this website:

clinicaltrials.gov – search using the number **NCT05429502**

euclinicaltrials.eu/ – search using the number **2024-512095-35-00**

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

Full clinical trial title: Phase I/II Multicenter Study to Assess Efficacy and Safety of Ribociclib (LEE011) in Combination With Topotecan and Temozolomide (TOTEM) in Pediatric Patients With Relapsed or Refractory Neuroblastoma and Other Solid Tumors

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