NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the safety of Lu-EVS459 in people with ovarian or lung cancer

Thank you!

Thank you to the participants who took part in the clinical trial for **ovarian and lung cancer**. Every participant helped to learn more about the trial drug **Lu-EVS459**, also called **[^{177}Lu]Lu-EVS459**, and the trial tracer **Ga-EVS459**, also called **[^{68}Ga]Ga-EVS459**.

Novartis sponsored this trial. We believe 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: CGIZ943A12101

Novartis drug studied: **Lu-EVS459,** also called **[^{177}Lu]Lu-EVS459**

Novartis tracer studied: **Ga-EVS459,** also called **[^{177}Ga]Ga-EVS459**

Sponsor: Novartis

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

This summary only shows the results of a single clinical trial.

What was the main purpose of this trial?

The purpose of this trial was to learn about the safety of **Lu-EVS459** for people with **ovarian or lung cancer**. Before people received **Lu-EVS459**, they had a PET (positron emission tomography) scan as an imaging test using the trial tracer **Ga-EVS459**.

Ovarian cancer starts in the ovaries. The ovaries are the organs in the female body that make eggs. The most common type of ovarian cancer is called **high grade serous ovarian cancer**, which grows in the lining around or near the ovaries.

Lung cancer starts in the lungs. The most common type of lung cancer is called **non-squamous non-small cell lung cancer**.

These types of cancers often have high levels of proteins on the surface of the cancer cells called **folate receptors**.

PET is an imaging test (scan) that uses a small amount of radiation called a tracer to show cells in the body. This can help doctors find specific cells, like cancer cells. In this trial, PET was used with other imaging tests, such as computed tomography (CT) or magnetic resonance imaging (MRI).

Ga-EVS459, also called **[68Ga]Ga-EVS459**, is a trial tracer (also called an imaging agent) used to help doctors find tumors with high levels of folate receptors on the surface of the cancer cells. **Ga-EVS459** differs from standard PET tracers because it attaches to folate receptors. After the tracer is injected into the body, it travels through the body and attaches to the proteins on cancer cells. The tracer gives off radiation signals that the PET scanner picks up to show these cells in scan images. This radiation doesn't kill cancer cells.

Lu-EVS459, also called **[^{177}Lu]Lu-EVS459**, is a trial drug that is a type of internal radiation therapy called radioligand therapy. **Lu-EVS459** is made of a radioactive substance called lutetium-177 (^{177}Lu) linked to a molecule that finds and attaches to folate receptors on cancer cells. After it attaches to the proteins, the radiation of lutetium-177 kills cancer cells.

This trial was the first time that **Lu-EVS459** was given to people. As **Lu-EVS459** had not been given to people before, the researchers planned to test increasing doses in different groups of participants in this trial to find the recommended dose. The researchers also needed to carefully check all the medical problems that happened during the trial and identify any that could cause changes in dosing.

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

- What was the recommended dose of Lu-EVS459 for participants to receive?
- What medical problems, also called adverse events, happened during this trial?
  - **Adverse events** reported are any sign or symptom that participants had during this trial. Adverse events **may** or **may not** be caused by treatments in this trial.

How long was this trial?

The trial began in September 2024 and ended in July 2025.

This trial was designed to have 2 parts:

- **Part 1** planned to look at the safety of increasing doses of **Lu-EVS459** in small groups of participants, starting with participants with **ovarian cancer**, to find the recommended dose to give in Part 2. Part 1 was not completed as planned because the trial ended early.
- **Part 2** planned to look at the effects of the recommended dose of **Lu-EVS459** in larger groups of participants. Part 2 did not start because the trial ended early.

The sponsor decided to end the trial early due to safety concerns in participants with **ovarian cancer** from Part 1. After this decision was made, the trial ended in July 2025. No participants with **lung cancer** joined the trial.

Novartis prepared a report of results. This summary is based on that report.

Who was in this trial?

4 female participants with **ovarian cancer** received treatment in this trial. Participants' ages ranged from 46 to 76 years. Their average age was 60 years.

The table below shows the number of participants by race.

Race	
White	4

The participants could take part in this trial if:

- They had one of these types of cancer:
  - High grade serous **ovarian cancer**
  - Non-squamous non-small cell **lung cancer** that had spread or could not be removed by surgery – the trial ended before any participants with **lung cancer** joined
- Their cancer had grown after previous treatment, or they could not continue receiving that treatment

4 participants from 2 countries received treatment.

The participants took part in:

- Israel | 2 participants
- Switzerland | 2 participants

What trial tracer and treatment did the participants receive?

Before participants received treatment in this trial, they had PET scans with:

Ga-EVS459, the trial tracer, which was received as an injection in a vein one time.

The treatment in this trial was:

Lu-EVS459, the trial drug, which was received through a needle in a vein called an intravenous (IV) infusion. **Lu-EVS459** was planned to be given once in each cycle. Because the trial ended early, each participant only received one infusion of **Lu-EVS459** on Day 1 of the first cycle.

What is a cycle?
A **cycle** is a treatment period that is repeated. In this trial, the cycle was 6 weeks.

The participants, researchers, and trial staff knew that the plan was for all participants to receive **Lu-EVS459** and **Ga-EVS459**.

What happened during this trial?

Before treatment with Lu-EVS459 — 7 weeks

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

4 participants with ovarian cancer had PET scans using the trial tracer **Ga-EVS459**. Researchers used the scans to learn how well **Ga-EVS459** showed participants' tumors.

During treatment with Lu-EVS459 — 6 weeks

Part 1

All 4 participants received one infusion of the trial drug **Lu-EVS459** for the first treatment cycle. After researchers did safety checks, all participants stopped treatment. No participants received another dose of **Lu-EVS459** for a second treatment cycle.

Part 2

The trial ended early, and **Part 2** did not start.

After treatment with Lu-EVS459 — Up to 6 months

Trial staff checked participants for any medical problems and if their cancer grew or spread after trial treatment.

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

What were the main results of this trial?

What was the recommended dose of Lu-EVS459 for participants to receive?

The trial ended early, and the researchers did not recommend any dose of **Lu-EVS459** for participants.

To learn this, researchers kept track of how many participants had:

- **Dose limiting toxicities (DLTs)** during their first treatment cycle of **Lu-EVS459**. DLTs are medical problems that:
  - The trial doctors think could be related to the trial treatment
  - Prevent trial doctors from raising the dose of treatment
- **To pause trial treatment**, which means they stopped treatment for a period of time before they received it again. This is called a dose interruption.
- **To lower the dose of trial treatment**, which means they received a smaller amount or received it less often. This is called a dose reduction.

Number of participants who had a DLT

3 of the 4 participants had at least 1 DLT during their first (and only) treatment cycle of **Lu-EVS459**. The DLTs were:

	Lu-EVS459 4 participants
Very low level of a type of white blood cell Agranulocytosis	**2 of 4** 50%
Low level of red blood cells Anemia	**2 of 4** 50%
Low level of red blood cells, white blood cells, and platelets Pancytopenia	**1 of 4** 25%
Lower level of white blood cells White blood cell counts decreased	**1 of 4** 25%
Lower level of a type of white blood cell Neutrophil count decreased	**1 of 4** 25%

None of the participants paused treatment, or had the dose of **Lu-EVS459** lowered.

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 do this even if they think the adverse events are not related to the trial treatments.

Researchers need results from many trials to decide if a drug or treatment causes an adverse event.

This section is a summary of the adverse events that happened after participants received the trial tracer and treatment.

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, requires hospital care, or results in death

Treatments in the trial **may** or **may not** cause adverse events.

1 out of the 4 participants who received **Ga-EVS459** had a serious adverse event. None of the participants who received **Ga-EVS459** had other adverse events.

3 out of the 4 participants who received **Lu-EVS459** had adverse events, including serious and other adverse events.

- 3 participants had serious adverse events.
- 3 participants died due to any cause, including cancer getting worse.

Due to safety results for **Lu-EVS459**, the researchers ended this trial early.

What adverse events did the participants have?

The table below shows the most common adverse events.

	4 participants	
	Ga-EVS459 Trial tracer	**Lu-EVS459** Trial drug
Very low level of a type of white blood cell Agranulocytosis	**0 of 4** 0%	**2 of 4** 50%
Low level of red blood cells Anemia	**0 of 4** 0%	**2 of 4** 50%

What serious adverse events did the participants have?

The table below shows the serious adverse events.

	4 participants	
	Ga-EVS459 Trial tracer	**Lu-EVS459** Trial drug
Very low level of a type of white blood cell Agranulocytosis	**0 of 4** 0%	**2 of 4** 50%
Fever Pyrexia	**1 of 4** 25%	**0 of 4** 0%
Low level of red blood cells, white blood cells, and platelets Pancytopenia	**0 of 4** 0%	**1 of 4** 25%
Intestines cannot push or move waste out of the body Ileus	**0 of 4** 0%	**1 of 4** 25%
Blocked intestines prevent waste from moving through Intestinal obstruction	**0 of 4** 0%	**1 of 4** 25%
Blood clot in the lungs Pulmonary embolism	**0 of 4** 0%	**1 of 4** 25%

What was learned from this trial?

Researchers planned to learn about the safety of **Lu-EVS459** in people with **ovarian or lung cancer**.

The trial ended early due to safety concerns with **Lu-EVS459** in participants with **ovarian cancer**.

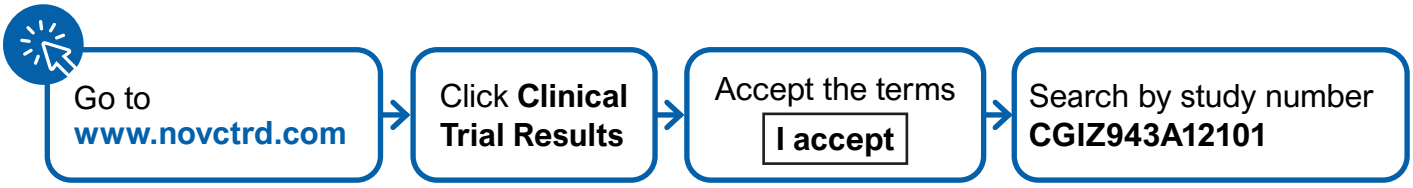
The researchers did not recommend any dose of **Lu-EVS459**.

When this summary was written, Novartis had no plans for future trials of **Lu-EVS459** in people with **ovarian or lung cancer**.

Where can I learn more about this trial?

To learn more about the results and adverse events in this trial, read the scientific summary of the results. It is 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 any of these websites:

- **clinicaltrials.gov** – search using the number **NCT06376253**
- **euclinicaltrials.eu** – search using the number **2023-507674-41-00**

Other trials of **Lu-EVS459** or **Ga-EVS459** may appear on the public websites above. When there, search for **Lu-EVS459**, **[^{177}Lu]Lu-EVS459**, **Ga-EVS459**, or **[^{68}Ga]Ga-EVS459**.

Full clinical trial title: A phase I, open-label, multi-center study to evaluate the safety, tolerability, dosimetry, and preliminary activity of [^{177}Lu]Lu-EVS459 in patients with ovarian and lung cancers

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