NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the safety of Lu-FF58 in people with certain types of solid tumors

Thank you!

Thank you to the participants who took part in the clinical trial for 3 types of solid tumors. Every participant helped the researchers learn about the trial drug **Lu-FF58**, also called [^{177}Lu]Lu-FF58, and the trial tracer **Ga-FF58**, also called [^{68}Ga]Ga-FF58.

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: CAAA604A12101

Novartis drug studied: Lu-FF58, also called [^{177}Lu]Lu-FF58

Novartis tracer studied: Ga-FF58, also called [^{68}Ga]Ga-FF58

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 purpose of this trial was to learn about the safety of the trial drug **Lu-FF58** for the treatment of people with certain types of solid tumors. This trial was the first time that **Lu-FF58** was given to people. Before people received **Lu-FF58**, they had a PET (positron emission tomography) scan as an imaging test using the trial radioactive tracer **Ga-FF58**.

Solid tumors are cancers in organs and tissues, and not in body liquids such as blood. The 3 types of solid tumors in this trial were:

- **Pancreatic cancer**, which starts in the pancreas
- **Gastroesophageal (GE) cancer**, which starts in the stomach, esophagus (tube that connects the throat and stomach), or in the area where the stomach and esophagus meet
- **Glioblastoma multiforme (GBM)**, which is a fast-growing brain cancer

These types of tumors often have high levels of proteins on the surface of the cancer cells called **integrins**.

Lu-FF58, also called [^{177}Lu]Lu-FF58, is a trial drug that is a type of internal radiation therapy called radioligand therapy, or RLT.

Lu-FF58 is made of a radioactive substance called lutetium-177 (177Lu) attached to a molecule that recognizes (or finds) and attaches to integrins on cancer cells. After it attaches to integrins, the strong radiation of lutetium-177 kills cancer cells.

Ga-FF58, also called [^{68}Ga]Ga-FF58, is a trial radioactive tracer used to help doctors find tumors with high levels of integrins on the surface of their cells. **Ga-FF58** attaches to integrins on cancer cells and gives off weak radiation to show tumors on PET scan images – this radiation doesn't kill cancer cells.

PET is an imaging test (scan) that can show cells in the body that the radioactive tracer attached to. This can help doctors find specific cells, like tumor cells. However, some tumors may not appear on PET scans, based on the radioactive tracer used, even if other imaging tests have shown the tumors on scan images, such as computed tomography (CT) or magnetic resonance imaging (MRI).

As **Lu-FF58** had not been given to people before, the researchers had 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-FF58 for participants to receive?
- 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 October 2023 and ended in December 2024. Each participant was in the trial for up to 10 months. Participants whose tumors did not show up on PET scan images left the trial early.

This trial was designed to have 2 parts:

- **Part 1** looked at the safety of increasing doses of **Lu-FF58** in small groups of participants to find the recommended dose to give in Part 2.
- **Part 2** planned to look at the effects of the recommended dose of **Lu-FF58** in larger groups of participants. As the trial ended early, Part 2 was not started.

In December 2024, the sponsor decided to end this trial early after reviewing data from Part 1. This decision was not related to any safety concerns.

Who was in this trial?

24 participants with certain types of solid tumors joined this trial – 13 men and 11 women. Participants' ages ranged from 42 to 79 years. Their average age was 59 years.

The number of participants by race is shown below.

Race

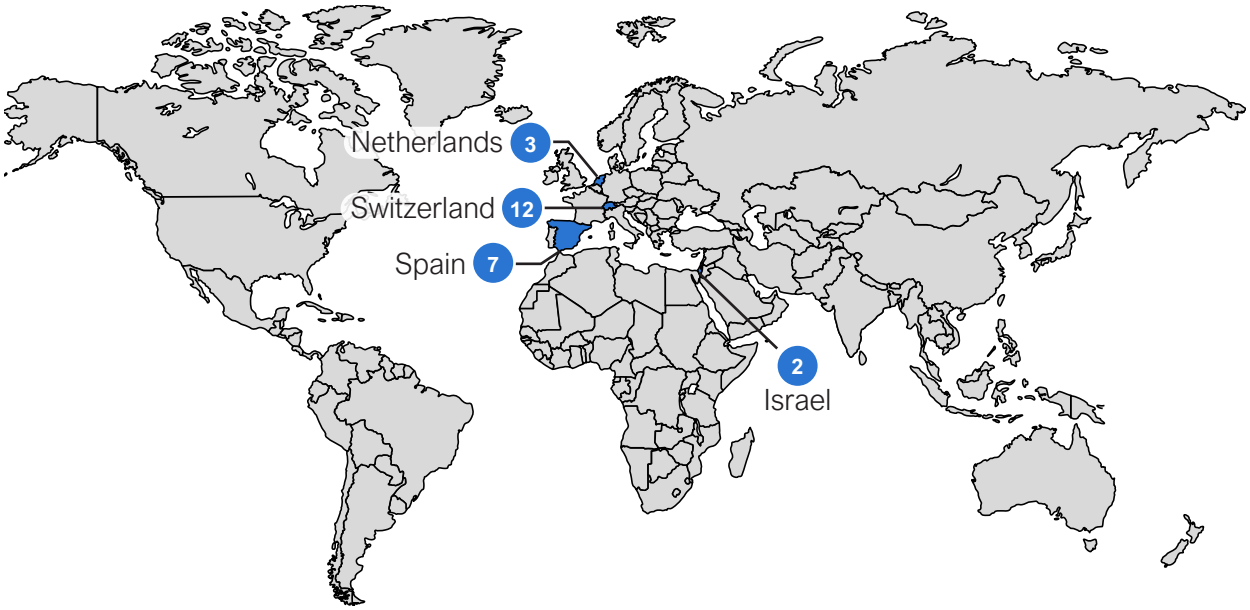
24	White

The participants could take part in this trial and receive the trial drug if:

- They had one of these types of solid tumors:
  - Pancreatic cancer that was advanced or metastatic
  - GE cancer that was advanced or metastatic
  - GBM that came back or kept growing after treatment
- **Ga-FF58** showed at least 1 tumor on their PET scan images

Advanced or metastatic means the cancer came back or spread to other parts of the body.

24 participants from 4 countries were in this trial. The map below shows the number of participants who took part in each country.



What trial tracer and treatment did the participants receive?

Before participants received treatment in this trial, they all had a PET scan with this trial radioactive tracer:

Ga-FF58, which was received once as an injection in a vein.

The treatment in this trial was:

Lu-FF58, which was received through a needle in a vein called an intravenous (IV) infusion on Day 1 of each 6-week cycle.

Participants received a low dose of **Lu-FF58** for their first treatment cycle. After researchers did safety checks, participants who had a second treatment cycle received a higher dose.

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

The participants could continue trial treatment as long as they were benefiting from it.

The participants, researchers, and trial staff knew that each participant received **Lu-FF58**.

What happened during this trial?

Before treatment — 6 weeks

The trial staff checked to make sure the participants could be in this trial. All of the participants had tumors based on other imaging tests, such as CT or MRI.

24 participants had a PET scan using **Ga-FF58** to confirm that the trial tracer showed at least 1 tumor.

18 participants did not have a tumor show up on the PET scan images using **Ga-FF58**. These participants left the trial before receiving **Lu-FF58**. Results from these participants helped researchers learn how **Ga-FF58** works as a radioactive tracer for PET scans.

During treatment — Up to 3 months

Part 1

6 participants whose tumors showed on PET scan images using **Ga-FF58** received a low dose of **Lu-FF58** in the first treatment cycle. Researchers did safety checks before starting the second treatment cycle with a higher dose of **Lu-FF58**. 4 participants left the trial before starting the second treatment cycle, and 2 participants received a higher dose of **Lu-FF58** in a second treatment cycle.

Part 2

Researchers planned to give more participants the recommended dose of **Lu-FF58** from Part 1. As the trial ended early, Part 2 was not started.

After treatment — 6 months

Trial staff checked participants for any medical problems for up to:

- 2 weeks after participants received **Ga-FF58**
- 6 months after participants' last dose of **Lu-FF58**

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-FF58 for participants to receive?

As the trial ended early, researchers did not find the recommended dose of **Lu-FF58** for participants to receive.

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

- **Dose limiting toxicities (DLTs)**, which 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.

None of the participants who received Lu-FF58 had a DLT, paused treatment, or had the dose of Lu-FF58 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 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 receiving **Ga-FF58** until 2 weeks after
- From the start of treatment until 6 months after participants' last dose of **Lu-FF58**

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.

4 of 24 participants who received **Ga-FF58** had adverse events.

4 of 6 participants who received **Lu-FF58** had adverse events, including serious and other adverse events.

- 4 participants who received **Lu-FF58** had adverse events that were considered serious
- No participants left the trial due to an adverse event
- 5 participants who received **Lu-FF58** died during the trial due to cancer getting worse

The researchers concluded there were no unexpected safety concerns for **Lu-FF58** or **Ga-FF58** in this trial.

How many participants had adverse events?

	Ga-FF58 24 participants	**Lu-FF58** 6 participants
Had **any adverse event**	**4 of 24**	**4 of 6**
Had at least 1 **serious adverse event**	**0 of 24**	**4 of 6**
Died during the trial	**0 of 24**	**5 of 6**

What serious adverse events did the participants have?

No participants had serious adverse events after receiving **Ga-FF58**.

4 participants had serious adverse events after receiving **Lu-FF58**. These serious adverse events happened in 1 participant each:

- **Brain swelling** (brain edema)
- **Heavy bleeding in the esophagus, stomach, or small intestine** (upper gastrointestinal hemorrhage)
- **Weakness or being unable to move on one side of the body** (hemiparesis)
- **Pattern of behaviors that cause problems, such as in work or social situations** (behavior disorder)

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

The table below shows the most common adverse events, which happened in 2 participants who received **Ga-FF58** or **Lu-FF58**.

	Ga-FF58 24 participants	**Lu-FF58** 6 participants
Back pain	**2 of 24** 8%	**0 of 6** 0%
Too much of the stress hormone cortisol in the body Cushingoid	**0 of 24** 0%	**2 of 6** 33%

What was learned from this trial?

Researchers learned about the safety of **Lu-FF58** for people with certain types of solid tumors. After reviewing data from Part 1, the sponsor decided to end this trial early. This decision was not related to any safety concerns.

As the trial ended early, researchers did not find the recommended dose of **Lu-FF58** for participants to receive.

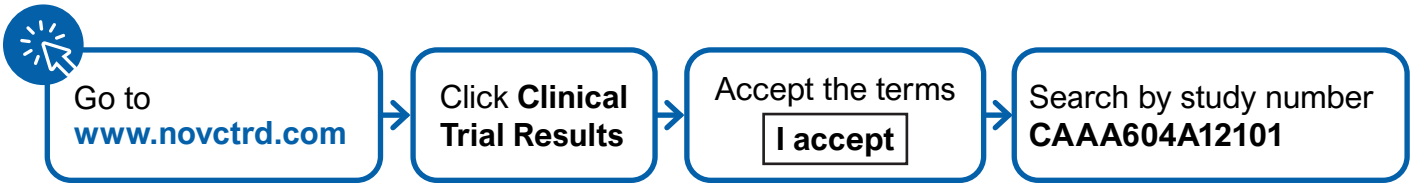
The researchers concluded there were no unexpected safety concerns for **Lu-FF58** or **Ga-FF58** in this trial.

When this summary was written, the sponsor had no plans for future trials of **Lu-FF58** or **Ga-FF58** in people with pancreatic cancer, gastroesophageal (GE) cancer, or glioblastoma multiform (GBM).

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:



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

- **clinicaltrials.gov** – search using the number **NCT05977322**
- **euclinicaltrials.eu** – search using the number **2022-502367-37-00**

Other trials of **Lu-FF58** and **Ga-FF58** may appear on the public websites above. When there, search for **Lu-FF58,** [^{177}Lu]Lu-FF58, **Ga-FF58**, or [^{68}Ga]Ga-FF58.

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-FF58 in patients with selected advanced solid tumors

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