NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of tisagenlecleucel in people with follicular lymphoma

Thank you!

Thank you to the participants who took part in the clinical trial for **follicular lymphoma**. Every participant helped to learn more about the trial drug **tisagenlecleucel**, also called **CTL019**.

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: CCTL019E2202

Novartis drug studied: **tisagenlecleucel**, also called **CTL019**

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 effects of **tisagenlecleucel** for people with **follicular lymphoma** that had returned (relapsed) or did not respond to available treatments (refractory).

Follicular lymphoma (**FL**) is a type of non-Hodgkin lymphoma (NHL), which is a type of blood cancer. In **FL**, white blood cells called **B-cells** grow too quickly and can form tumors throughout the body. B-cells are part of the body's immune system and make antibodies (proteins) to help fight infections.

Tisagenlecleucel, also called **CTL019**, is a type of cancer treatment known as chimeric antigen receptor (CAR) T-cell therapy. CAR T-cell therapy uses a person's own **T-cells** (another type of white blood cell) which are taken from the blood and modified in the laboratory to find and fight cancer cells. These are then put back into the body.

Trial drug
Tisagenlecleucel
Pronounced as
tis-A-GEN-lec-leu-CEL

Tisagenlecleucel is approved in many countries to treat children and young adults with certain types of leukemia (another type of blood cancer) and adults with certain types of lymphoma.

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

- How many participants had no signs of cancer after treatment with **tisagenlecleucel**?
- 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 the trial.

How long was this trial?

The trial began in November 2018 and ended in May 2025. Each participant was in the trial for up to 5 years.

At the end of this trial, Novartis created a report of the trial results. This summary is based on that report.

Who was in this trial?

98 participants with **FL** joined the trial – 66 males and 32 females. Out of these, 97 participants received treatment in this trial, as 1 participant left before receiving **tisagenlecleucel** infusion. Participants' ages ranged from 29 to 73 years. Their average age was 57 years.

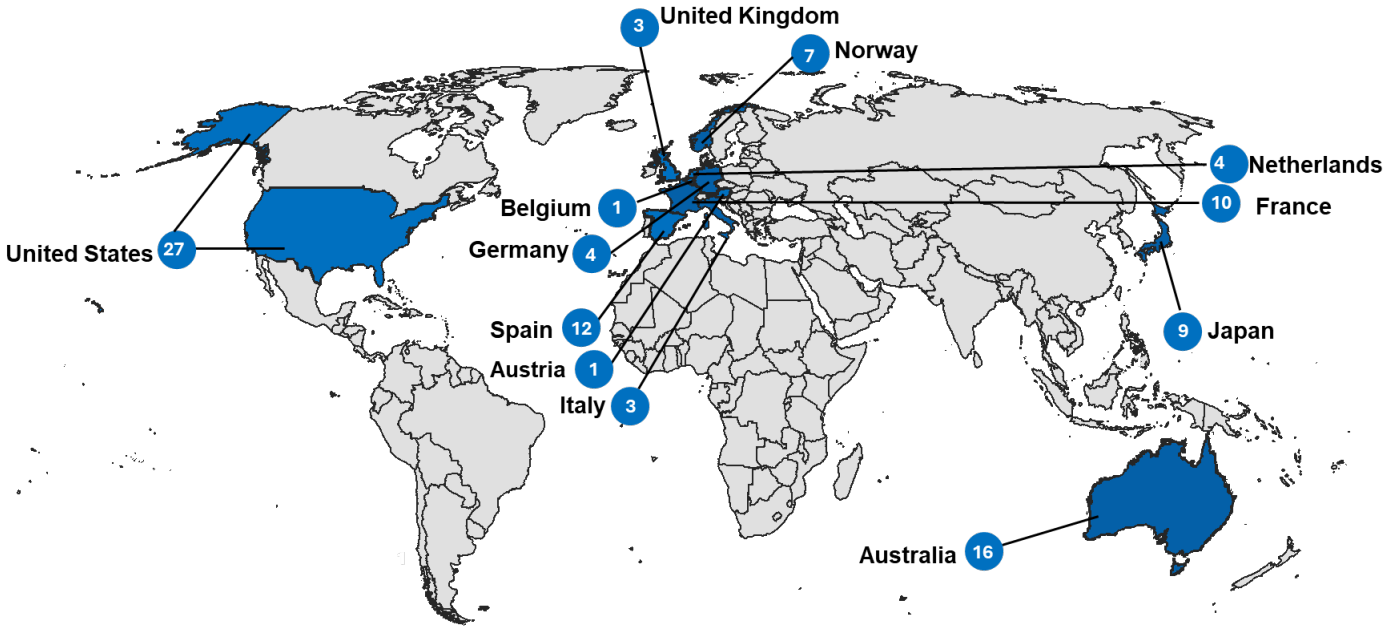
The table below shows the number of participants by race.

Race	
81	White or Caucasian
13	Asian
1	Black or African American
3	Not reported

The participants could take part in this trial if they:

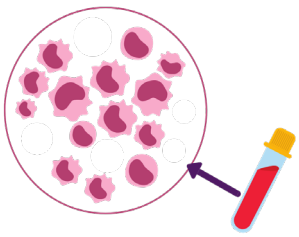
- Were at least 18 years of age
- Had confirmed diagnosis of **FL** that had returned or did not respond to available treatments
- Had **FL** that could be measured on imaging scans
- Had never received any other gene or T-cell therapy
- Were fully active or able to perform light physical activity

97 participants from 12 countries received treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

All participants received **tisagenlecleucel**. To make **tisagenlecleucel**, researchers:



Took the participants' blood and collected T-cells

Modified the T-cells in a laboratory so they could find and fight cancer cells

Gave the modified T-cells to the participants as an infusion into a vein

The participants, researchers, and trial staff knew that all participants received **tisagenlecleucel**.

What happened during the trial?

Before treatment — Approximately 6 weeks

The trial staff checked the participants' health and **FL** to make sure the participants could be in this trial.

- Trial doctors took participants' blood and collected T-cells. T-cells were then modified to make each participant's **tisagenlecleucel** infusion. This could take around 3 to 4 weeks. During this time, participants could receive their regular treatment for cancer if needed.
- 2 to 6 days before **tisagenlecleucel** treatment, participants also received chemotherapy. Chemotherapy was given before the **tisagenlecleucel** infusion to lower the number of existing T-cells in the body. This helped to make space for the **tisagenlecleucel** T-cells and helped them grow and work better.

During treatment — 1 day

97 participants received a single infusion of **tisagenlecleucel** directly into a vein. Participants may also have received approved medicines to treat medical problems from the **tisagenlecleucel** infusion.

After treatment — Up to 5 years

Trial staff checked participants' general health and for any medical problems for up to 5 years after they received **tisagenlecleucel**. If face-to-face follow-up visits were not possible, participants were also contacted via telephone every 3 months until end of the trial.

After completion of follow-up visits for this trial, participants could join another trial, CCTL019A2205B, and continue being followed up for up to 15 years after receiving **tisagenlecleucel**.

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

What were the main results of this trial?

How many participants had no signs of cancer after treatment with tisagenlecleucel?

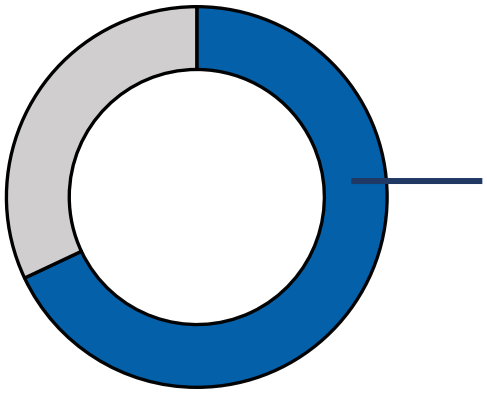
Overall, **68%** (**64** out of **94**) of participants had no signs of cancer after treatment with **tisagenlecleucel**.

To answer this question, researchers measured the **complete response rate (CRR)** using different imaging scans including PET scan, CT scan, and MRI. They also studied the bone marrow tissue samples from the participants where applicable. Bone marrow is present inside the bones and helps make blood cells.

The results are available for 94 participants who had measurable disease before receiving **tisagenlecleucel** treatment.

What is complete response rate (CRR)?
CRR is the percentage of participants who had no signs of cancer on scans or from tissue samples after they received **tisagenlecleucel**. This was measured from the time **tisagenlecleucel** was given until the participants' cancer got worse or they started a new cancer treatment, whichever happened first.

Percentage (number) of participants who had no signs of cancer after treatment



68% (**64** out of **94**) of participants had no signs of cancer after treatment

What were the other results of this trial?

To answer the following questions, researchers used imaging scans (such as PET, CT, and MRI scans) and, when needed, examined bone marrow samples from the participants.

How long after receiving tisagenlecleucel did the participants live without their FL getting worse?

After receiving **tisagenlecleucel**, half of the participants lived for around 4 years and 4 months without their **FL** returning or getting worse.

Researchers kept track of the length of time from when participants received the trial treatment until their cancer returned, got worse, or they died due to any cause. This is called **progression-free survival**, or **PFS**. They then calculated the median **PFS** for participants. Median **PFS** is the length of time from the start of the trial until half of the participants had their cancer return or get worse, which means tumors grew, new tumors appeared, or they died due to any cause.

How many participants had at least a 50% reduction in their tumors after treatment with tisagenlecleucel?

Overall, 86% (81 out of 94) of participants had at least a 50% reduction in their tumors after treatment with **tisagenlecleucel**.

Researchers calculated the number of participants who achieved **overall response**. The **overall response** is the sum of participants who had a **complete response** or a **partial response** to treatment. A **complete response** means that participants had no signs of cancer after treatment. A **partial response** means that participants had at least a 50% reduction in their tumors after treatment.

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 from the day participants started the trial treatment until 5 years after 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.

96 out of 97 participants had adverse events, including serious and other adverse events.

- 52 participants had serious adverse events.
- 22 participants died due to any cause, including **FL** at any time during the trial.

The researchers concluded there were no new safety concerns for **tisagenlecleucel** in this trial.

What serious adverse events did the participants have?

52 participants had serious adverse events.

The table below shows the most common serious adverse events.

	Tisagenlecleucel 97 participants
A serious immune reaction that may cause fever, nausea, headache, rash, dizziness, and difficulty breathing Cytokine release syndrome	19 of 97 20%
Lung infection Pneumonia	15 of 97 16%
Low number of neutrophils with fever Febrile neutropenia	8 of 97 8%
COVID-19	4 of 97 4%
Fever Pyrexia	3 of 97 3%

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

The table below shows the most common other adverse events.

	Tisagenlecleucel 97 participants
Low number of white blood cells called neutrophils Neutropenia	43 of 97 44%
A serious immune reaction that may cause fever, nausea, headache, rash, dizziness, and difficulty breathing Cytokine release syndrome	30 of 97 31%
Low red blood cell count Anaemia	26 of 97 27%
Diarrhea	24 of 97 25%
Headache	23 of 97 24%
Number of white blood cells goes down White blood cell count decreased	22 of 97 23%

What was learned from this trial?

Researchers learned about the effects of **tisagenlecleucel** in people with **follicular lymphoma (FL)** that had returned or did not respond to available treatments.

The researchers concluded that:

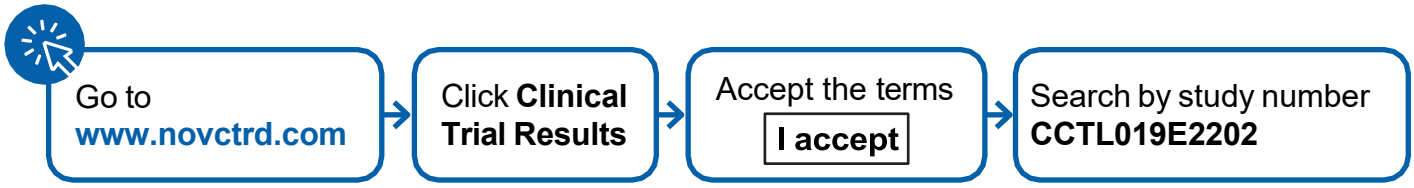
- 68% of participants had their cancer completely disappear after treatment with **tisagenlecleucel**.
- Half of participants lived for around 4 years and 4 months without their **FL** returning or getting worse.
- 86% of participants had at least a 50% reduction in their tumors after treatment with **tisagenlecleucel**.
- No new safety concerns for **tisagenlecleucel** were found in this trial.

When this summary was written, another trial CCTL019A2205B was ongoing for the participants who completed this trial.

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 the following websites:

- **clinicaltrials.gov** – search using the number **NCT03568461**
- **euclinicaltrials.eu** – search using the number **2023-508127-13-00**

Other trials of **tisagenlecleucel** may appear on the public websites above. When there, search for **tisagenlecleucel** or **CTL019**.

Full clinical trial title: A phase II, single arm, multicenter open label trial to determine the efficacy and safety of tisagenlecleucel (CTL019) in adult patients with refractory or relapsed follicular lymphoma

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