NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn about the effects of CTL019 in children and young adults with non Hodgkin-lymphoma

Thank you!

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

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: CCTL019C2202

Drug studied: CTL019 or tisagenlecleucel

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.

Glossary

Clinical trial (simply called trial)

a research study in which people voluntarily participate to help evaluate the effects and safety of new drugs

Trial drug or trial treatment

a drug that researchers are studying in a clinical trial; **CTL019** in this trial

Researchers

someone who conducts a research study; in this summary, these include the trial scientists, the trial doctors, and their staff

Blood cancer

type of cancer that affects the normal function of blood cells

Non-Hodgkin lymphoma (NHL)

type of blood cancer that starts in the white blood cells

White blood cells

the cells of the immune system that help fight infections by attacking germs that attack the human body

Lymphocytes

type of white blood cells

Large B-cell lymphoma, Burkitt lymphoma and Burkitt leukemia

types of NHL or leukemia

Leukemia

cancerous white blood cells in the bone marrow

Bone marrow

a spongy tissue present inside the bones that helps make blood cells

B-cells and T-cells

types of lymphocytes

Tumor

mass of abnormal cells in the body

CAR T-cell therapy

uses a person's own T cells which are genetically modified to identify and fight cancer cells

Genetically modified

something whose genetic material has been changed by scientists, so it produces a desirable effect

Infusion

a way to put drugs or fluids directly into a vein using a tube attached to a needle

Chemotherapy

treatment with drugs that stop the growth of cancer cells, either by killing the cells or by stopping them from dividing

Inflammation

swelling, redness, heat, and/or pain due to a sore or injury

What was the main purpose of this trial?

The purpose of this trial was to learn about the effects of **CTL019** in children and young adults with non-Hodgkin lymphoma that had returned or did not respond to available treatments.

Non Hodgkin lymphoma (NHL) is a type of blood cancer that starts in the white blood cells called lymphocytes. In NHL, the lymphocytes grow abnormally and can form tumors throughout the body.

This trial included participants who had NHL or leukemia that affected their B-cells. These included large B-cell lymphoma, Burkitt lymphoma, and Burkitt leukemia.

CTL019 is a type of cancer treatment called chimeric antigen receptor (CAR) T-cell therapy.

CAR T-cell therapy uses a person's own T cells which are genetically modified to identify and fight cancer cells. These are then put back into the body.

Trial drug
CTL019 also called tisagenlecleucel

Pronounced as
tis-A-GEN-lec-leu-CEL

CTL019 is approved in some countries for the treatment of children and adults with certain types of NHL that had returned or did not respond to available treatments.

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The trial purpose was to answer these main questions:

- How many participants had at least 50% of their cancerous B-cells destroyed by **CTL019** by the end of the trial?
- What adverse events did the participants have during this trial?
  - ↳ An **adverse event** is any sign or symptom that participants have during a trial.

How long was this trial?

The trial began in February 2019 and ended in April 2023. It was planned for the participants to be in the trial for about 2 years after receiving the trial treatment.

Who was in this trial?

33 participants with NHL received treatment in this trial.
Participants' ages ranged from 3 to 22 years. Their average age was 13 years.
The number of participants by age group, gender, and race are shown below.

Age group

- 29 Under 18 years
- 4 18 years or above

Gender

- 23 Boys
- 10 Girls

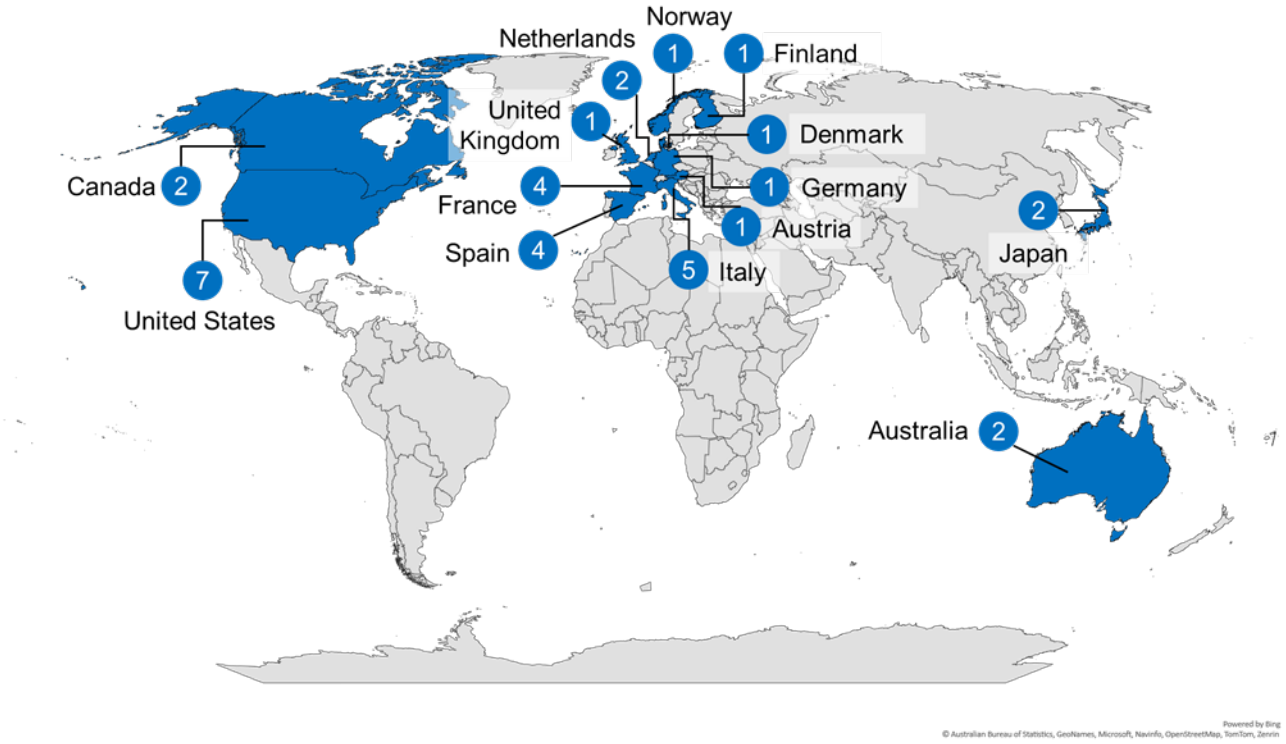
Race

- 2 Asian
- 1 Black or African American
- 28 White
- 2 Not provided

The participants could take part in this trial if they:

- were 25 years of age or younger and weighed at least 6 kilograms at the start of the trial
- had a confirmed diagnosis of B-cell NHL that had returned or did not respond to available treatments
- could at least engage in minimal play and keep busy with quieter activities if they were under 16 years old or do daily activities with or without help if they were 16 years or older

34 participants from 14 countries entered the trial, but 1 participant died before receiving the treatment. The map below shows the number of participants who took part in each country.



What treatments did the participants receive?

Participants received **CTL019**.

To manufacture **CTL019**, researchers:

Took some T-cells from each participant's blood

Genetically modified the T-cells in a laboratory so they could identify and fight cancer cells

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

What happened during this trial?

Before treatment — Up to 16 weeks

Trial doctors checked the participants' health and NHL to make sure they could be in this clinical trial.

- Trial doctors took participants' T-cells and manufactured each participant's CTL019 infusion. This could take up to 6 weeks. During this time, participants could receive their regular treatment for cancer if needed.
- Up to 2 weeks before treatment with CTL019, participants also received chemotherapy. It helped lower their T-cell levels to make room for the new CTL019 T-cells in their body.

During treatment — 1 day

33 participants received a single infusion of CTL019 into a vein.

After treatment — 2 years

Researchers checked the participants' NHL and general health till the end of the study.

Participants could join another trial, CCTL019A2205B, and continue being followed up for up to 15 years after receiving CTL019.

What were the main results of this trial?

In total, 33 participants received **CTL019**. However, the results of this trial were analyzed for 28 participants whose cancer could be measured before treatment.

How many participants had at least 50% of their cancerous B-cells destroyed by CTL019 by the end of the trial?

Overall, 32% of the participants (9 out of 28) had at least 50% of their cancerous B-cells destroyed by **CTL019** by the end of the trial.

To answer this question, researchers used different imaging scans which could include CT scan, MRI, and PET scan. 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.

What is 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 the treatment destroyed all cancer cells.
- A **partial response** means that the treatment destroyed at least 50% of the cancer cells.

32% of the participants (9 out of 28) had an **overall response** to treatment with CTL019

=

11% of the participants (3 out of 28) had a **complete response** to treatment with CTL019

+

21% of the participants (6 out of 28) had a **partial response** to treatment with CTL019

What were the other results of this trial?

To answer the following questions, researchers used the same tests listed above.

How long after receiving CTL019 did the participants live without their NHL getting worse?
Note: This is also known as **progression-free survival**.

After receiving **CTL019**, half of the participants lived for more than 2 and a half months, while others lived for a shorter duration, without their NHL getting worse.

How long did the participants live after receiving CTL019?
Note: This is also known as **overall survival**.

After receiving **CTL019**, half of the participants lived for more than 10 months, while others lived for a shorter duration.

What adverse events did the participants have?

Trial doctors keep track of all **adverse events** that happen in trials, 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 up to 2 years after receiving the trial treatment.

Information on adverse events was available for all 33 participants who received **CTL019**.

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 participants had adverse events. 24 participants had adverse events that were considered serious. 17 participants died – 15 due to worsening of their cancer and 2 due to other reasons. The researchers concluded that there were no new safety concerns about CTL019 from this trial.

How many participants had adverse events?

Participants who:	CTL019 33 participants
Had at least 1 adverse event	**33 of 33** 100%
Had at least 1 serious adverse event	**24 of 33** 73%
Died during the trial	**17 of 33** 52%

What serious adverse events did the participants have?

24 participants had serious adverse events. The table below shows the most common serious adverse events that happened in **5% or more** participants.

	CTL019 33 participants
Inflammation in the body due to an overactive immune system Cytokine release syndrome	**8 of 33** 24%
Fever Pyrexia	**7 of 33** 21%
A build-up of excess fluid in the lungs Pleural effusion	**3 of 33** 9%
A fever with extremely low levels of neutrophils - a type of white blood cells Febrile neutropenia	**2 of 33** 6%
Decreased ability to move and feel due to nerve damage Peripheral sensorimotor neuropathy	**2 of 33** 6%
Decreased ability to perceive and respond Depressed level of consciousness	**2 of 33** 6%
Seizure	**2 of 33** 6%
Stomach pain Abdominal pain	**2 of 33** 6%
Sudden kidney damage Acute kidney injury	**2 of 33** 6%

What other adverse events did the participants have?

All participants had other adverse events. The table below shows the most common other adverse events that happened in **20% or more** participants.

	CTL019 33 participants
Inflammation in the body due to an overactive immune system Cytokine release syndrome	**16 of 33** 48%
Fever Pyrexia	**14 of 33** 42%
Vomiting	**13 of 33** 39%
A low number of red blood cells to carry oxygen around the body Anemia	**11 of 33** 33%
A low number of neutrophils Neutrophil count decreased	**10 of 33** 30%
A low number of platelets - a type of blood cell Platelet count decreased	**9 of 33** 27%
Feeling sick Nausea	**9 of 33** 27%
A low number of white blood cells White blood cell count decreased	**8 of 33** 24%
Headache	**8 of 33** 24%
A condition in which neutrophils are too low Neutropenia	**7 of 33** 21%
Stomach pain Abdominal pain	**7 of 33** 21%

What was learned from this trial?

Researchers learned about the effects of **CTL019** in children and young adults with NHL that had returned or did not respond to available treatment.

Researchers found that 32% of the participants (9 out of 28) had at least 50% of their cancerous B-cells destroyed by **CTL019** by the end of the trial.

They also found that half of the participants lived for more than:

- 2 and a half months after receiving **CTL019** without their NHL getting worse
- 10 months after receiving **CTL019**

They did not find any new safety concerns with the use of **CTL019** in this trial.

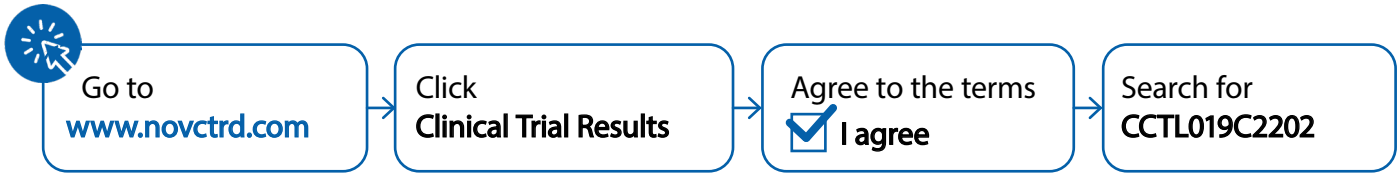
Findings from this study could help develop a treatment option for this age group.

Other trials with **CTL019** are ongoing. The follow-up trial, CCTL019A2205B, for participants who received **CTL019** in this trial is also ongoing.

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 **NCT03610724**
- **clinicaltrialsregister.eu/ctr-search/search** – search using the number **2017-005019-15**

If more trials are planned, they will appear on the public websites above. When there, search for CTL019, tisagenlecleucel, or non-Hodgkin lymphoma.

Full clinical trial title: A Phase II, single arm, multicenter open label trial to determine the safety and efficacy of tisagenlecleucel in pediatric patients with relapsed or refractory mature B-cell non-Hodgkin lymphoma (NHL) (BIANCA)

Novartis is a global healthcare company based in Switzerland that provides solutions to address the evolving needs of patients worldwide.

1-888-669-6682 (US) | +41-61-324 1111 (EU)

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