NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of a second treatment with CTL019 in children and young adults with acute lymphoblastic leukemia (ALL)

Clinical trial protocol number: CCTL019BUS03

Thank you!

Thank you to the participants who took part in the clinical trial for the drug **CTL019**, also known as **tisagenlecleucel**.

All of the participants helped the researchers learn more about how a second treatment with **CTL019** works in people with **acute lymphoblastic leukemia (ALL).** Novartis sponsored this trial and believes it is important to share what was learned from the results of the trial with the participants and the public.

We hope this helps the participants understand their important role in medical research.

If you participated in the trial and have questions about the results, please talk to the doctor or staff at your trial site.

Why was the research needed?

Researchers are looking for better ways to treat **acute lymphoblastic leukemia (ALL).** ALL is a type of cancer of blood and bone marrow (tissue inside of bones that helps make blood cells). It's the most common type of cancer in children.

In ALL, bone marrow makes too many immature white blood cells too fast, specifically B-cells. **B-cells** are part of the body's immune system and make antibodies (proteins) to help fight infections. The immature B-cells are not able to do their job to fight infections. They build up and crowd out healthy cells.

CTL019 is a type of cancer treatment called chimeric antigen receptor (CAR) T-cell therapy. **CAR T-cell therapy** is a cancer treatment that uses a person's own modified T-cells to find and kill cancer cells. **T-cells** are another type of white blood cell. To prepare CTL019, doctors:

1. Take T-cells from a person's blood
2. Change (genetically modify) their T-cells in the lab to help the T-cells find and kill cancerous B-cells
3. Give the changed T-cells (CTL019) to the person through a vein (intravenous or IV infusion)

CTL019 is approved in many countries to treat children and young adults with certain types of leukemia and adults with certain types of lymphoma. Researchers have studied the effects and safety of giving CTL019 to a person one time.

Trial purpose

The main purpose of this trial was to learn more about the effects and safety of giving CTL019 a second time to children and young adults with ALL.

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

- What percent of participants had their B-cell count go down within 9 months after a second treatment of CTL019?
- What medical problems did the participants have during the trial?

Trial treatment

The treatment in this trial was:

CTL019, also known as tisagenlecleucel: A cancer treatment that uses a person's own T-cells to find and kill cancer cells. Before joining this trial, all participants had already received one infusion of their own CTL019 and had remaining CTL019 for a possible, second infusion. In this trial, all participants received their remaining CTL019 as a second infusion.

How long was this trial?

This trial was designed so that each participant could take part for up to 1 year. The trial started in October 2020 and ended in October 2021.

The researchers did not complete this trial as planned. This trial was designed to have 54 participants. The sponsor ended this trial early after only 5 participants had joined due to difficulty finding children and young adults who met all the rules to join the trial. The decision to end the trial was not related to safety.

Who was in this trial?

5 participants with **ALL** were in this trial. Participants' ages ranged from 3 to 19 years old. All participants reported their race as White. Participants took part at 4 trial sites in the United States.

Participants' reported their gender as:

The participants could take part in this trial if they had already received one infusion of CTL019 and had:

- Their B-cell count go up after their first infusion
- An additional dose of CTL019 for a second infusion
- No other type of cancer or serious health condition
- Never received any other gene or T-cell therapy

What kind of trial was this?

This was an open-label trial, which means that the participants and clinical trial team knew what treatment each participant received. In this trial, all participants received CTL019.

What happened during this trial?

Up to **1 month** before treatment

During screening and before treatment

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

5 participants took part in this trial.

2 to 14 days before treatment, each participant received a drug to lower their T-cell levels to make room for the new CTL019 T-cells.

4 weeks of treatment

During treatment

All participants received a second infusion of their remaining CTL019. They stayed at or near the trial site for 4 weeks so the trial doctors could check their ALL and general health.

The participants also received approved medicines to treat possible side effects from the CTL019 infusion.

Up to **9 months** after treatment

During follow-up

Participants returned to their trial site up to 3 times after receiving the second infusion of CTL019. During the follow up visits, trial doctors checked the participants' ALL and general health.

End of trial

This trial ended early due to difficulty in finding children and young adults who could join this trial.

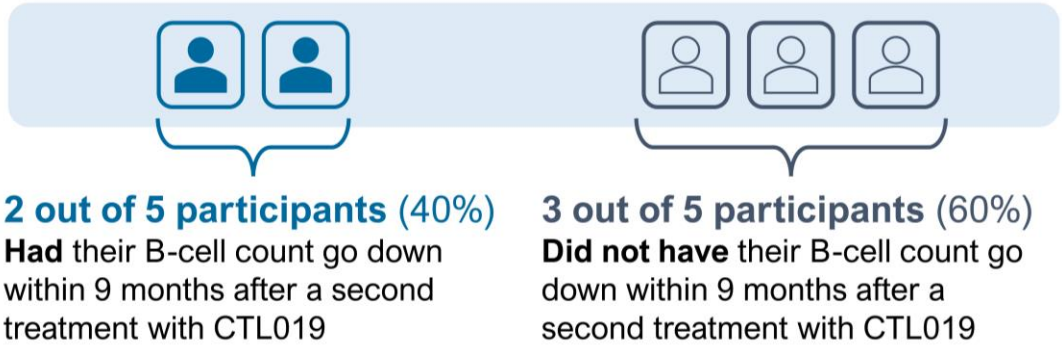
What were the main results of this trial?

This is a summary of the overall results for all participants. It does not show the results of each individual participant. Results of individual participants could be different from the results of the total group of participants. More details on the results can be found on the websites listed at the end of this summary.

What percent of participants had their B-cell count go down within 9 months after a second treatment with CTL019?

2 of the 5 participants (40%) had their B-cell count go down within 9 months after a second treatment. Because the number of participants was so small, the researchers could not conclude if these results were meaningful.

The reason that B-cells go down after treatment with CTL019 is that CTL019 kills healthy and cancerous B-cells. **When CTL019 is working, the number of B-cells in the blood goes down, which is called B-cell aplasia.** Over time, the number of B-cells often goes back up as the body makes new, healthy B-cells.



What medical problems did the participants have during the trial?

Medical problems that happen in clinical trials are called "**adverse events**".

A lot of research is needed to know whether a drug causes an adverse event. So, when new drugs are being studied, researchers keep track of all adverse events the participants have, whether or not they are thought to be caused by the trial treatment.

This section is a summary of the adverse events that happened during treatment and about 9 months after treatment. The websites listed at the end of this summary have more information about the adverse events that happened in this trial.

An **adverse event** is an unwanted sign or symptom that participants have during a trial. An adverse event is considered "**serious**" when it is life-threatening, causes lasting problems, or the participant needs hospital care. These problems may or may not be caused by the trial treatment.

What were the serious adverse events?

There were no deaths reported during this trial.

3 of the 5 participants (60%) had 4 serious adverse events:

- **Fever** (pyrexia)
- **Flu-like symptoms from overactive T-cells** (cytokine release syndrome) – this happened after the participant received another T-cell therapy outside of this trial. It was a few months after they received CTL019.
- **Headache**
- **Tingling or prickling feeling** (paresthesia)

Each of these serious adverse events happened in only one participant.

What were the most common non-serious adverse events?

4 of the 5 participants (80%) had adverse events that were not considered serious.

The most common **non-serious adverse events** that happened in **3** out of **5** participants (60%) were:

- **Not as hungry as usual** (decreased appetite)
- **Back pain**

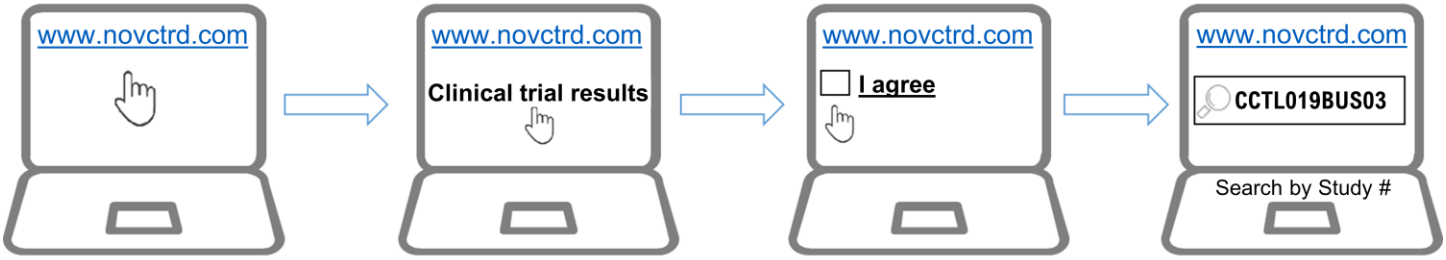
How has this trial helped?

This trial helped researchers learn how well a second infusion of CTL019 works and if it is safe to use in children and young adults with ALL. Because of the small number of participants in this trial, the researchers could not conclude if a second infusion of the participants' own CTL019 meaningfully lowered participants' B-cells. The researchers concluded the safety results from this trial were similar to past trials of one infusion of CTL019.

Please remember, this summary only shows the results of one clinical trial. Other clinical trials may have different results. Researchers and health authorities look at the results of many clinical trials to understand which drugs work and if they are safe. It takes many people in multiple clinical trials around the world to advance medical science and healthcare.

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).



You can find more information about this trial on this website:

- www.clinicaltrials.gov. Use the NCT identifier NCT04225676 in the search field.

Full clinical trial title: A phase II, open label, multi-center trial to determine the efficacy and safety of tisagenlecleucel re-infusion in Pediatric and Adolescent Young Adult (AYA) patients with acute lymphoblastic leukemia experiencing loss of B cell aplasia.

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of participants around the world. You helped researchers answer important health questions and test new medical treatments.

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

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