NOVARTIS

Clinical Trial Results Summary

A clinical trial to learn more about the effects and safety of CTL019 given with pembrolizumab in people with diffuse large B-cell lymphoma (DLBCL)

Clinical trial protocol number: CCTL019J2101

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 **CTL019** works in people with **diffuse large B-cell lymphoma (DLBCL)** when given with another drug called pembrolizumab**.** 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 a better way to treat **diffuse large B-cell lymphoma (DLBCL).** DLBCL is the most common and a fast-growing type of non-Hodgkin lymphoma, which is a blood cancer. In DLBCL, white blood cells called B-cells grow too quickly and can form tumors (masses) throughout the body. **B-cells** are part of the body's immune system and make antibodies (proteins) to help fight infections.

CTL019 is a cancer treatment approved in some countries to treat people with certain types of B-cell cancers, including DLBCL that came back after previous treatments or did not respond to previous treatments. CTL019 is a type of chimeric antigen receptor (CAR) T-cell therapy. **CAR T-cell therapy** is a cancer treatment that uses a person's own T-cells (another type of white blood cell) to find and kill cancer cells. It has not been approved to be given with certain other cancer treatments, such as the immunotherapy called **pembrolizumab**.

Trial purpose

The main purpose of this trial was to learn about the safety and timing of CTL019 with pembrolizumab in people whose DLBCL came back after a previous treatment or did not respond to previous treatments. This trial also learned about the effects of CTL019 with pembrolizumab in people with DLBCL.

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

- When was the safest time to give pembrolizumab with CTL019 to participants?
- What medical problems did the participants have during the trial?

Trial treatments

The treatments in this trial were:

CTL019, also known as tisagenlecleucel: a type of CAR T-cell therapy. To prepare CTL019, trial doctors:

1. Take T-cells from a participant'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 participant through a vein (intravenous or IV infusion)

Pembrolizumab is a drug that blocks an immune system protein called PD-1. Blocking PD-1 allows immune cells to stop cancer cells. Pembrolizumab is approved in many countries to treat solid tumors, including certain skin, lung, and breast cancers. It is given as 200 milligrams (mg) every 3 weeks through an IV infusion.

How long was this trial?

This trial was designed so that each participant could take part for about 2 years.

The trial started in October 2018 and ended in July 2021. The researchers did not complete this trial as planned. This trial was designed to have 2 parts:

- Part 1 looked at the safest time to give pembrolizumab with CTL019
- Part 2 would have looked at the effect of the treatment on tumors

However, the sponsor decided to end this trial early during Part 1 and to stop enrolling participants. Each participant had the option to join a follow-up trial CTL019A2205B to have their general health and safety checked for up to 15 years after they received CTL019.

Why did this trial end early?

The reason was that the results from Part 1 didn't support more research on CTL019 with pembrolizumab. Also, new treatments that worked to treat DLBCL became available, such as other CAR T-cell therapies and immunotherapies. The decision to end the trial was not related to safety.

When the trial ended, the researchers collected information on the trial treatments and created a report of the trial results. This summary is based on that report.

Who was in this trial?

15 participants with **DLBCL** joined this trial. 3 participants left the trial before receiving treatment. This summary includes the 12 participants who received treatment in this trial. Participants' ages ranged from 35 to 79 years old. Their average age was 61 years.

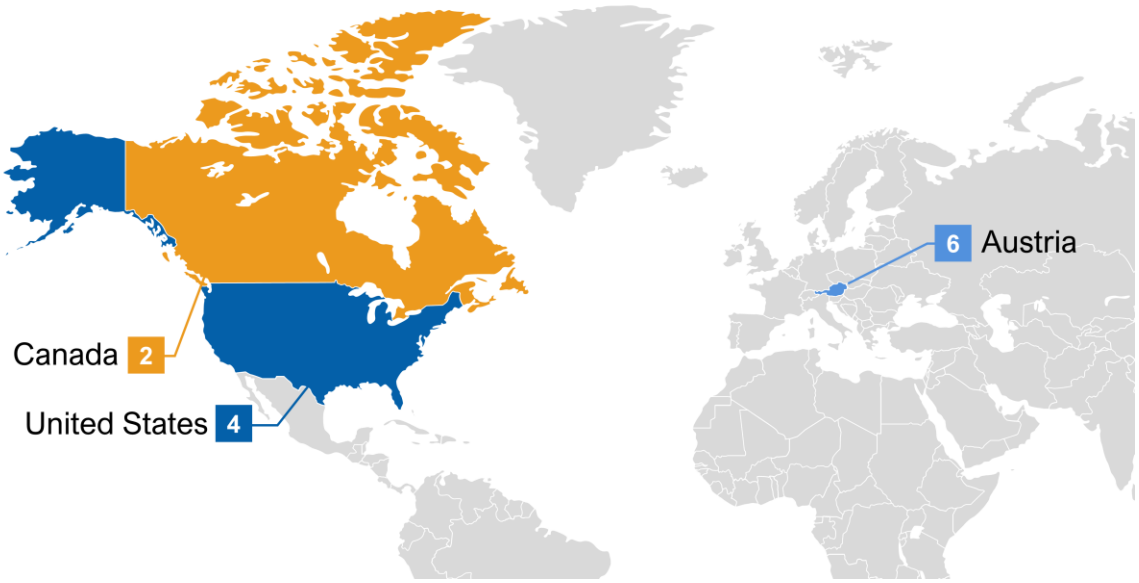
Participants reported their gender as:

Participants reported their race as:

The participants could take part in this trial if they had **DLBCL that was relapsed or refractory**, which means it came back after previous treatments or did not respond to previous treatments. They also had:

- DLBCL tumors that could be measured for their size
- Enough T-cells to prepare CTL019
- No other type of cancer or serious health condition
- Never taken certain other DLCBL treatments

Participants took part at 5 trial sites. The map below shows the number of participants who took part in each country.



What happened during this trial?

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 and pembrolizumab.

Up to **10 weeks** before treatment

During screening and before treatment

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

15 participants joined this trial. 3 participants left before receiving treatment with CTL019.

Trial doctors took participants' T-cells to prepare each participant's CTL019 infusion.

2 to 6 days before treatment, each participant received a drug to lower their T-cell levels to make room for the new CTL019 T-cells.

Up to **20 weeks** of treatment

During treatment

12 participants received 1 infusion of CTL019. Participants also received up to 6 infusions of pembrolizumab (once every 3 weeks).

The participants were assigned to one of these groups:

- Group 1 (4 participants): Started to receive pembrolizumab **15 days after** CTL019
- Group 2 (4 participants): Started to receive pembrolizumab **8 days after** CTL019
- Group 3 (4 participants): Started to receive pembrolizumab **1 day before** CTL019

Researchers first assigned participants to Group 1. After checking for safety concerns, the researchers then assigned participants to Groups 2 and 3.

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

Trial doctors checked the participants' DLBCL and general health throughout treatment.

Up to **2 years** after treatment

During follow-up

Participants returned to their trial site 15 times for researchers to check their general health:

- 8 times during the first month after receiving CTL019
- 5 times during the rest of the first year after receiving CTL019
- 2 times during the second year after receiving CTL019

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.

When was the safest time to give pembrolizumab with CTL019 to participants?

The researchers found that it was safe to give pembrolizumab with CTL019 at all of the 3 times. The researchers concluded there were no safety concerns for any of the 3 times participants received pembrolizumab.

To find this out, researchers kept track of the number of participants who had medical problems with too much risk of serious harm (called adverse events). All 12 participants took their treatments as instructed, and no participants reported medical problems with too much risk of serious harm.

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 up to 2 years 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?

8 participants had serious adverse events. 5 participants died during the up to 2-year follow-up after treatment. All of the deaths were related to their DLBCL getting worse.

The table below shows the **serious adverse events** that happened in each group. Each serious adverse event happened in only one participant.

	Group 1	Group 2	Group 3
Number of participants who had serious adverse events	**2 of 4 participants** (50%)	**4 of 4 participants** (100%)	**2 of 4 participants** (50%)
Serious adverse events	• **Cancer cells spread to the tissue that covers the brain and spinal cord** (metastasis to meninges) • **Fainting** (syncope) • **Painful buildup of pus near the anus** (anal abscess) • **Swelling of the pancreas** (pancreatitis)	• **Buildup of fluid in tissue lining the lungs and chest** (pleural effusion) • **Fever and low levels of white blood cells** (febrile neutropenia) • **Chest pain** (musculoskeletal chest pain) • **Doesn't weigh as much as expected** (failure to thrive) • **Swelling of the liver** (hepatitis) • **Trouble breathing** (dyspnea) • **Stomach pain** (abdominal pain) • **Sudden, intense chest pain when breathing** (pleuritic pain)	• **Dark sticky stool with or without blood** (melena) • **Frequent, loose, or watery stool** (diarrhea) • **Fever** (pyrexia) • **Flu-like symptoms from overactive T-cells** (cytokine release syndrome) • **Swelling of the colon's inner lining** (colitis)

What were the most common non-serious adverse events?

12 participants had adverse events that were not considered serious.

The table below shows the **non-serious adverse events** that happened in 3 or more participants in any group.

	Group 1	Group 2	Group 3
	Number out of 4 participants (percent %)	**Number out of 4 participants** (percent %)	**Number out of 4 participants** (percent %)
Low levels of red blood cells Anemia	**2** (50%)	**2** (50%)	**3** (75%)
Low levels of white blood cells Neutropenia	**1** (25%)	**2** (50%)	**3** (75%)
Frequent, loose, or watery stool Diarrhea	**3** (75%)	**0** (0%)	**0** (0%)
Low levels of potassium in the blood Hypokalemia	**1** (25%)	**3** (75%)	**1** (25%)
Flu-like symptoms from overactive T-cells Cytokine release syndrome	**1** (25%)	**4** (100%)	**1** (25%)

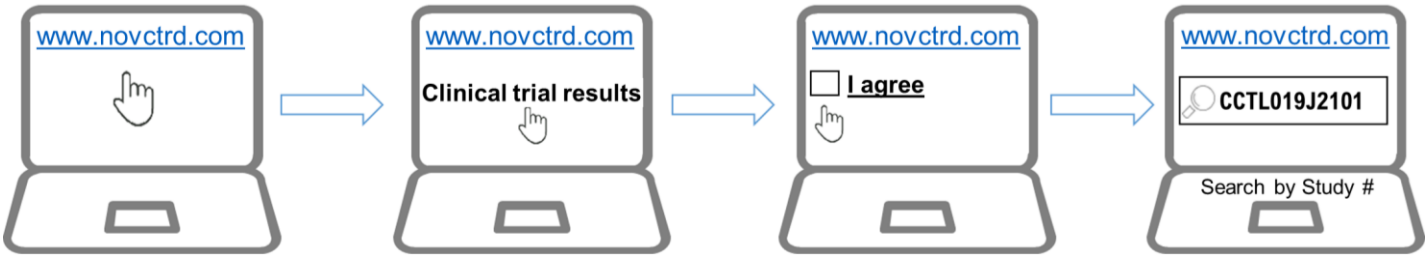
How has this trial helped?

This trial helped researchers learn if CTL019 is safe to give with pembrolizumab in people with DLBCL. The researchers found no safety concerns with giving pembrolizumab with CTL019 at any of the 3 different treatment times. Due to the small number of participants in each group and because the sponsor decided to end this trial early, the sponsor planned to collect more data on CTL019 in a long-term safety follow-up trial CCTL019A2205B. To learn more about trial CCTL019A2205B, go to www.clinicaltrials.gov and clinicaltrialsregister.eu.

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 NCT03630159 in the search field.

Full clinical trial title: Phase Ib study of tisagenlecleucel in combination with pembrolizumab in relapsed/refractory (r/r) Diffuse Large B-cell Lymphoma (DLBCL) patients.

Thank you

Our thanks to the participants who took part in this trial. All clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and test new medical treatments.

NOVARTIS

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);
www.novartisclinicaltrials.com