

Clinical Trial Results Summary

**A trial to learn how CLL442 works and about its safety
in participants with cutaneous squamous cell carcinoma in situ**

Research Sponsor: Novartis

Drug Studied: CLL442

Trial Number: CCLL442X2201

Thank you!



Thank you to the participants who took part in the clinical trial for the treatment CLL442. All of the participants helped the researchers learn about how CLL442 works and how safe it is to use.

Novartis sponsored this trial and reviewed the results of the trial when it ended. We at Novartis believe it is important to share what was learned from the results with the trial participants and the public. An independent organization prepared this summary of the trial results.

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 speak with the trial doctor or staff at your trial site.

You can find more information about this trial on the website listed on the last page of this summary.

Overview of this trial



What was the purpose of this trial?

In this clinical trial, the researchers studied how a treatment called CLL442 affected the skin in participants with cutaneous squamous cell carcinoma in situ, also known as SCCis.

The researchers also studied the safety of CLL442 in these participants.

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

- Did CLL442 reduce the size of a single lesion in the participants?
- Did CLL442 irritate the participants' skin?
- What medical problems did the participants have during the trial?

Keeping track of the participants' medical problems helped the researchers learn about the safety of CLL442.



Who was in the trial?

40 men and women with SCCis participated in this clinical trial.



What treatments did the participants use?

The participants in this trial applied CLL442 or a placebo on the skin. A placebo looks like the trial drug but does not have any trial drug in it.



What were the main results of the trial?

Overall, the researchers learned that:

- CLL442 did not reduce the size of a single lesion more than the placebo.
- CLL442 did not irritate the participants' skin more than the placebo.
- 60.0% of the participants had medical problems during this trial. This was 24 out of 40 participants. None of the medical problems were serious, and none caused a participant to leave the trial. Researchers concluded that CLL442 was safe for the participants in this trial.

More details about the results of this trial are included later in this summary.

What was the purpose of the trial?



Researchers are looking for a better way to treat patients with cutaneous squamous cell carcinoma in situ, also known as SCCis. Before a treatment can be approved for patients to take, researchers do clinical trials to find out how safe it is and how it works. In this trial, the researchers studied how the trial treatment, CLL442, affected the participants' skin. The researchers also studied the safety of CLL442.

SCCis is a type of skin cancer that is usually found on skin that has been exposed to the sun. It causes damaged areas of the skin called lesions. The current standard treatment for SCCis is surgery to remove the lesions. There are other treatments, but these may not help all patients.

CLL442 was designed to stop certain proteins that researchers think are involved in causing skin cancer. CLL442 is used as a cream that is applied to the skin. This was the first trial to study the effects of CLL442 in humans. The researchers in this trial studied how CLL442 affected healthy skin and skin with a lesion. This was because the researchers wanted to make sure that the cream would not cause problems in healthy skin.

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

- Did CLL442 reduce the size of a single lesion in the participants?
- Did CLL442 irritate the participants' skin?
- What medical problems did the participants have during the trial?

Who was in the trial?



To answer the questions in this trial, the researchers asked for the help of people with SCCis. Everyone in the trial was 55 to 90 years old when they joined. The average age of the participants was about 71 years old.

The trial included 40 participants in 3 countries: Australia, Belgium, and the United States.

What treatments did the participants use?






The clinical trial team used a computer program to randomly assign which treatment each participant used. This helped make sure that comparing the results of the treatments was as fair as possible.

The participants in this trial used either CLL442 or a placebo. A placebo looks like the trial drug but has no trial drug in it. Using a placebo helps researchers better understand the actual effects of a trial drug. The participants used the treatments through a cream they applied to their skin.

The doses of CLL442 were measured in milligrams per gram of body weight, also known as mg/g.

The chart below shows the treatments the participants used.

	Group 1	Group 2
	<ul style="list-style-type: none">• 30 participants used 2.5 mg/g of CLL442	<ul style="list-style-type: none">• 10 participants used the placebo
	<ul style="list-style-type: none">• Through a cream applied to the skin	
	<ul style="list-style-type: none">• Twice a day for 7 days on healthy skin• Then, twice a day on a skin lesion:<ul style="list-style-type: none">- until 14 days after the lesion was goneor- up to 84 days	

None of the participants, trial staff, or sponsor staff knew what treatment each participant applied. Some trials are done this way because knowing what treatment the participants are using can influence the results. Not knowing what treatment the participants used helps make sure the results are looked at fairly.

What happened during the trial?

The trial started in December 2017 and ended in November 2018. Each participant was in the trial for up to about 181 days. This trial was split into 2 time periods.

The chart below shows what happened during the trial.

Before the participants applied the treatment

The doctors checked the participants' health and their skin to make sure they could be in the trial.



During treatment

40 participants applied treatments in 2 periods

Up to 7 days

Period 1: Healthy skin

The participants:

- applied either CLL442 or placebo to an area of healthy skin 2 times a day
- had their overall health checked and gave blood and urine samples
- had their skin checked to see how the cream was affecting the skin
- answered questions about how they were feeling

Up to 84 days

Period 2: Skin lesion

The participants:

- applied either CLL442 or placebo to one of their skin lesions 2 times a day
- had their overall health checked and gave blood and urine samples
- had their skin checked to see how the cream was affecting the lesion
- answered questions about how they were feeling



After the participants applied the last treatment

- The trial doctors checked the participants' health and their skin 7 days later.
- The trial doctors called the participants and asked them about any medical problems they were having within 30 days of their last visit.

What were the main results of the trial?

This is a summary of the overall results from this trial. The individual results of each participant might be different and are not in this summary.

The results from several trials are needed to decide which treatments are safest and work best. Other trials may provide new information or different results. Always talk to a doctor before making any changes to your healthcare.

Did CLL442 reduce the size of a single lesion in the participants?



No. The researchers found that CLL442 did not reduce the size of a single lesion more than the placebo.

To answer this question, the trial doctors measured the size of a single skin lesion using 2 methods:

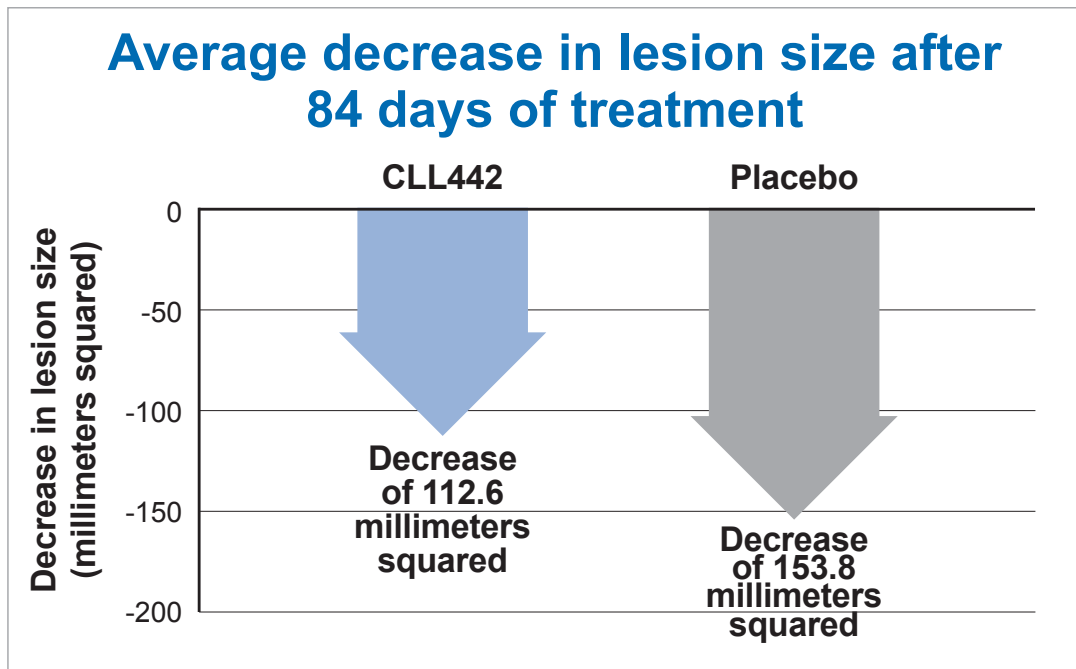
- taking pictures using a digital camera
- tracing the lesion onto paper and measuring the size with a ruler

The researchers then compared the size of the lesion before and after treatment. Each lesion was measured in millimeters squared. The researchers were able to measure the lesion size in 29 out of the 30 participants who applied CLL442. The researchers were able to measure the lesion size in all 10 participants who applied the placebo.

In both treatment groups, the size of the lesion decreased slightly after 84 days of treatment. But, the difference between the participants who applied CLL442 and those who applied the placebo was small. The researchers could not conclude that CLL442 affected the lesion size any more than the placebo. The researchers found that the lesion decreased by an average of:

- 112.6 millimeters squared in 29 participants who applied CLL442
- 153.8 millimeters squared in 10 participants who applied the placebo

The chart below shows these results.



Did CLL442 irritate the participants' skin?



No. The researchers found that CLL442 did not irritate the participants' skin more than the placebo.

To answer this question, the researchers studied skin irritation in 2 ways:

- severity of the participants' pain
- severity of the participants' skin symptoms

The researchers in this trial studied both healthy skin and skin with a lesion. This was because the researchers wanted to make sure that the cream would not cause problems in healthy skin.

The trial doctors asked the participants to rate their pain on a scale of 0 to 10. A 0 meant no pain, while a 10 meant the worst possible pain.

The trial doctors thoroughly examined the participants' skin in many ways, including looking at it, touching it, and checking the skin for symptoms.

Overall, the researchers found that both pain and skin symptoms were similar between the 2 treatment groups.

What medical problems happened during the trial?

Medical problems that happen in clinical trials are called “**adverse events**”. An adverse event is any 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.

Adverse events may or may not be caused by the treatments in the trial.

A lot of research is needed to know whether a treatment causes an adverse event. Doctors keep track of all the adverse events that happen in trials, even if they do not think the adverse events might be related to the treatments.

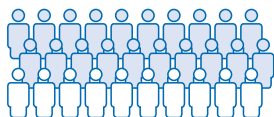
This section is a summary of the adverse events that happened during this trial.



60.0% of the participants had adverse events during this trial. This was 24 out of 40 participants. None of the adverse events were serious and none caused a participant to leave the trial. Researchers concluded that CLL442 was safe for the participants in this trial.

How many participants had adverse events?

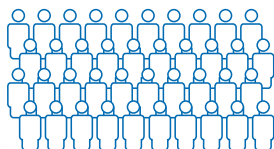
Summary of adverse events



- 66.7% of the participants who applied CLL442 had adverse events. This was 20 out of 30 participants.



- 40.0% of the participants who applied the placebo had adverse events. This was 4 out of 10 participants.



- None of the participants had serious adverse events.
- None of the participants left the trial because of adverse events.

What were the most common serious adverse events?

During this trial, none of the participants had serious adverse events.

None of the participants died during this trial.

What were the most common adverse events?

The adverse events below happened in 2 or more participants during the trial. There were other adverse events, but these happened in fewer participants.

Most common adverse events in this trial

	CLL442 (Out of 30 participants)	Placebo (Out of 10 participants)	Total (Out of 40 participants)
Infection of the upper airways	20.0% (6)	0.0% (0)	15.0% (6)
A type of skin cancer called basal cell carcinoma	6.7% (2)	10.0% (1)	7.5% (3)
Itching where the cream was applied	6.7% (2)	0.0% (0)	5.0% (2)
High blood pressure	6.7% (2)	0.0% (0)	5.0% (2)
Sores in the mouth	3.3% (1)	10.0% (1)	5.0% (2)
Itching	6.7% (2)	0.0% (0)	5.0% (2)

The trial doctors also looked at the adverse events that they thought may be related to the trial drug. The trial doctors decided whether the adverse events were related to the trial drug before they knew which treatment the participants applied to their skin.

The table below shows all of the adverse events the trial doctors thought may be related to the trial drug.

Adverse events thought to be related to the trial drug			
	CLL442 (Out of 30 participants)	Placebo (Out of 10 participants)	Total (Out of 40 participants)
Itching where the cream was applied	6.7% (2)	0.0% (0)	5.0% (2)
Abnormal dreams	3.3% (1)	0.0% (0)	2.5% (1)
Redness where the cream was applied	3.3% (1)	0.0% (0)	2.5% (1)
Flaky skin where the cream was applied	3.3% (1)	0.0% (0)	2.5% (1)
Pain where the cream was applied	3.3% (1)	0.0% (0)	2.5% (1)
Sores in the mouth	0.0% (0)	10.0% (1)	2.5% (1)
Sore in a mucus-producing tissue	3.3% (1)	0.0% (0)	2.5% (1)
Numbness in the mouth	3.3% (1)	0.0% (0)	2.5% (1)

For more information about the adverse events in this trial, please see the scientific summary that can be found on the website noted at the end of the summary.

What was learned from this trial?

The information described above helped researchers learn about CLL442 and its safety in participants with SCCis.

More research is needed to find out which treatments can be used for patients with SCCis. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

Where can I learn more about this trial?



More information about the results of this trial can be found in the scientific results summary available on the Novartis Clinical Trial Results website.

- Go to www.novctrd.com.
- Once on the site, click “**Clinical trial results and trial summary for patients**” at the top right of the page.
- After accepting the terms, go to the bottom left of the page and click “**Search by study number**”.
- Type “**CCLL442X2201**” into the keyword search box and click “**Search**”.

If you would like to view the website in a language other than English, you can click the “**Google Translate**” button on the top right of the page.



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

If more clinical trials are planned, they will be listed on the above public websites or www.novartisclinicaltrials.com. Search for “**CLL442**” or “**SCCis**”.

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type “**CCLL442X2201**” into the “**Other terms**” search box, and click “**Search**”.
- www.clinicaltrialsregister.eu Once you are on the website, click “**Home and Search**”, then type “**CCLL442X2201**” in the search box, and click “**Search**”.

Full trial title: A randomized, investigator-and patient-blind, placebo-controlled, parallel group first in human and proof of concept study to evaluate the safety, tolerability, and efficacy of CLL442 in patients with Cutaneous Squamous Cell Carcinoma in situ (SCCis)

Protocol number: CCLL442X2201

Thank you!

Clinical trial participants belong to a large community of participants around the world. They help researchers answer important health questions and study new medical treatments.



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) • +41613241111 (EU) • novartisclinicaltrials.com