Clinical Trial Results Summary

An extension trial to learn about the safety and effects of adriforant (ZPL389) in participants with moderate to severe atopic dermatitis who completed the CZPL389A2203 trial

Protocol number: CZPL389A2203E1

Thank You!

Novartis sponsored this trial and believes it is important to share the results of the trial with you and the public. Thank you for taking part in this trial for the drug ZPL389, also known as adriforant. You helped researchers learn more about the safety and effects of ZPL389 in people with moderate to severe atopic dermatitis, also known as eczema.

As a clinical trial participant, you belong to a large community of people around the world. Your invaluable contribution to medicine and healthcare is greatly appreciated.

This summary only shows the results of this extension trial. Other clinical trials may have different findings. It takes many people in multiple clinical trials around the world to advance medical science and healthcare. If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

How long was this trial?

This extension trial was planned so that an individual participant could take part for about 2 years. The trial started in April 2019 and ended in August 2020. The entire duration of this extension trial, from enrolling the first participant to the last participant completing the trial was about 1 year and 5 months.

The sponsor terminated this extension trial early because the core trial results indicated that the trial treatment did not show an effect in participants with moderate to severe atopic dermatitis. When this extension trial ended, the researchers collected information on the trial treatment (ZPL389) and created a report of the trial results. This summary is based on that report.

Why was the research needed?

Atopic dermatitis is a skin condition that is also known as eczema. Eczema causes inflammation of the skin and mainly affects the hands, feet, wrists, ankles, neck, and area behind the knees.

Symptoms of eczema include:

- rashes
- dry, itchy skin
- thickened, cracked, and scaly skin
- discharge of liquid from the affected areas of the skin

This skin condition is long lasting, commonly occurs in children and gets worse over the years. Eczema may have a negative impact on daily activities and emotional well-being.

Currently, available treatments for eczema include steroids, anti-allergics, and antiseptics that can be applied directly to the affected areas. However, these treatments are not effective for all patients and are not able to completely cure this skin condition.

In this extension trial, researchers wanted to know more about the safety and effects of ZPL389 in participants with moderate to severe eczema who completed the core trial.

Trial drugs

The drugs given in this trial were:

ZPL389: the trial drug, also known as adriforant, binds to a protein called histamine 4 receptor (H4R). Histamine, naturally produced in the body under certain circumstances, binds to H4R which causes inflammation and itching. When ZPL389 binds to H4R, it prevents histamine from binding to H4R. ZPL389 was expected to inhibit inflammatory responses and therefore itching. The participants received ZPL389 once a day as a capsule by mouth.

Topical treatment: Throughout the trial, the participants applied medicines on the skin called corticosteroids, and/or calcineurin inhibitors for sensitive areas, depending on the severity of their eczema. These medicines inhibit inflammation of the skin. They followed this treatment plan throughout the trial. Topical treatment was applied directly to the eczema-affected skin areas.

In addition to taking the trial drugs, researchers asked participants to also apply a basic skin moisturizer, called emollient, once a day on the entire body throughout the trial.

Participants could also take a high dose of topical corticosteroids to manage unbearable eczema symptoms when needed. This medicine was known as “rescue” medicine.

Trial purpose

The main question the researchers wanted to answer in this trial was:

What medical problems did the participants have during this trial?

Medical problems that happen in clinical trials are called “adverse events”. Adverse events are defined on Page 6 in this summary.

The other question researchers wanted to answer in this trial was:

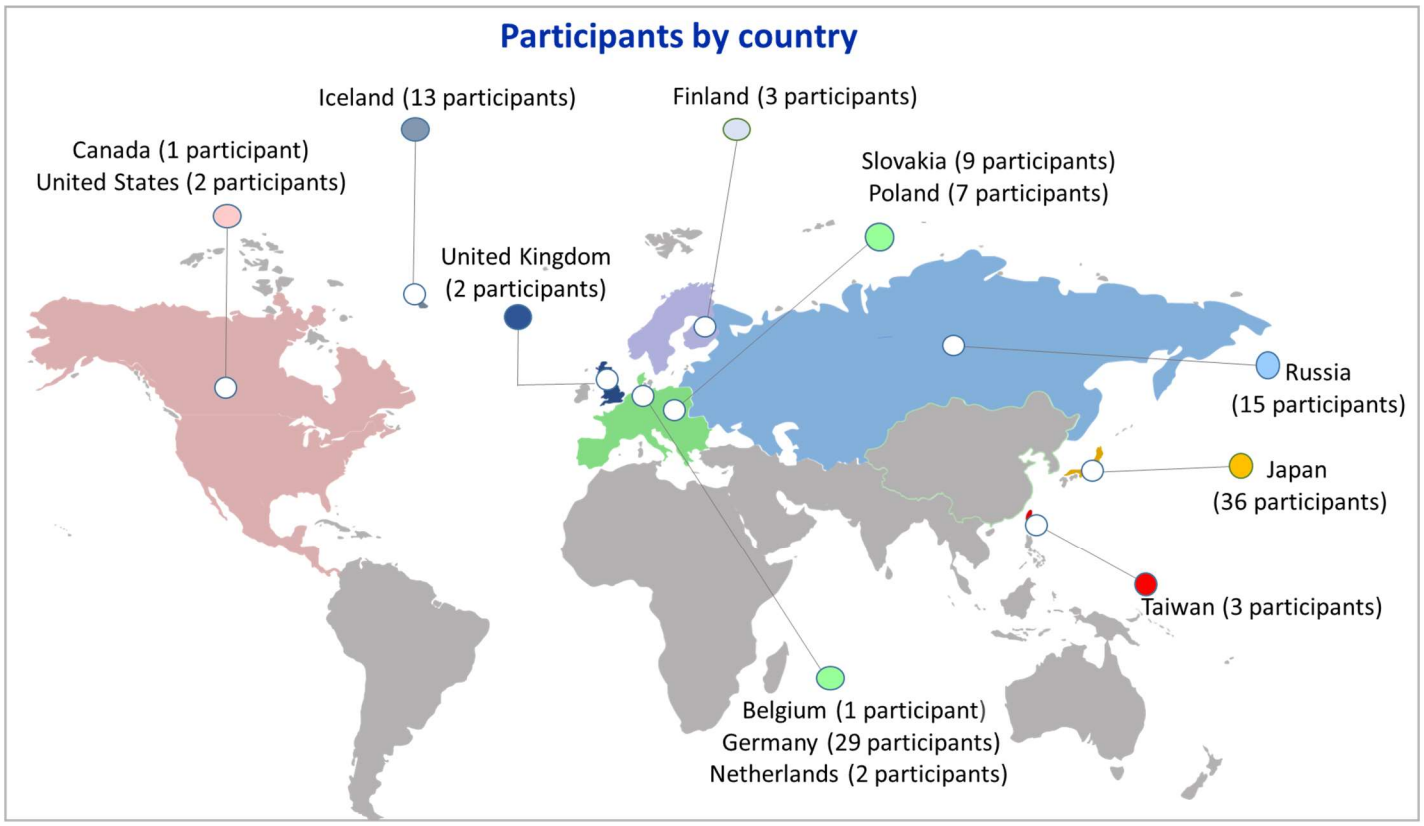
- Did ZPL389 reduce the symptoms of eczema over time?

Who was in this trial?

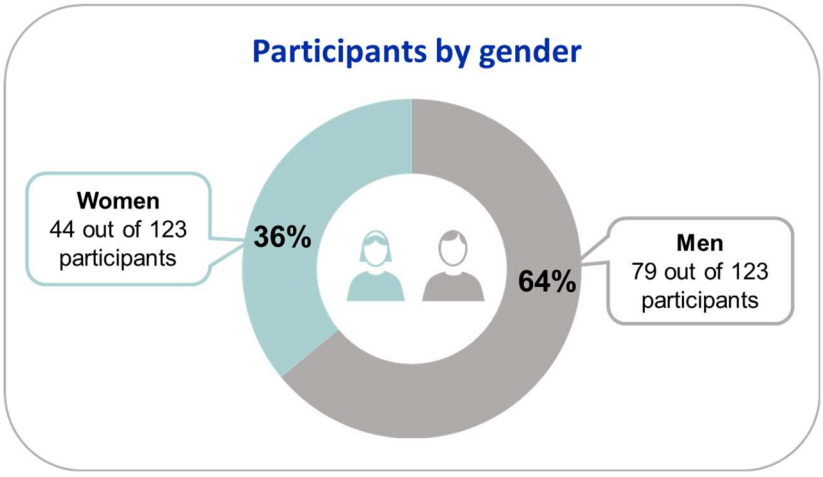
The participants could take part in this trial if they:

- had eczema and completed 16 weeks of treatment in the core trial, and
- did not have a history of any medical problems with the topical treatments used in this extension trial.

A total of 123 participants from 13 countries participated in this trial.



The average age of participants was 35 years. Participants' age ranged from 18 to 61 years. The majority of participants, 64% (79 out of 123) were men.



What kind of trial was this?

This was a double-blind trial. This means that none of the participants, trial doctors, or trial staff knew what treatment participants were receiving. Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Conducting a trial this way helps to make sure that the results are looked at objectively regardless of the treatment type.

What happened during this extension trial?

During treatment (up to 100 weeks, in addition to the 16 weeks of treatment in the core trial)

The participants who received ZPL389 30 mg or 50 mg in the core trial, continued to receive the same dose of ZPL389 along with topical treatment in this extension trial.

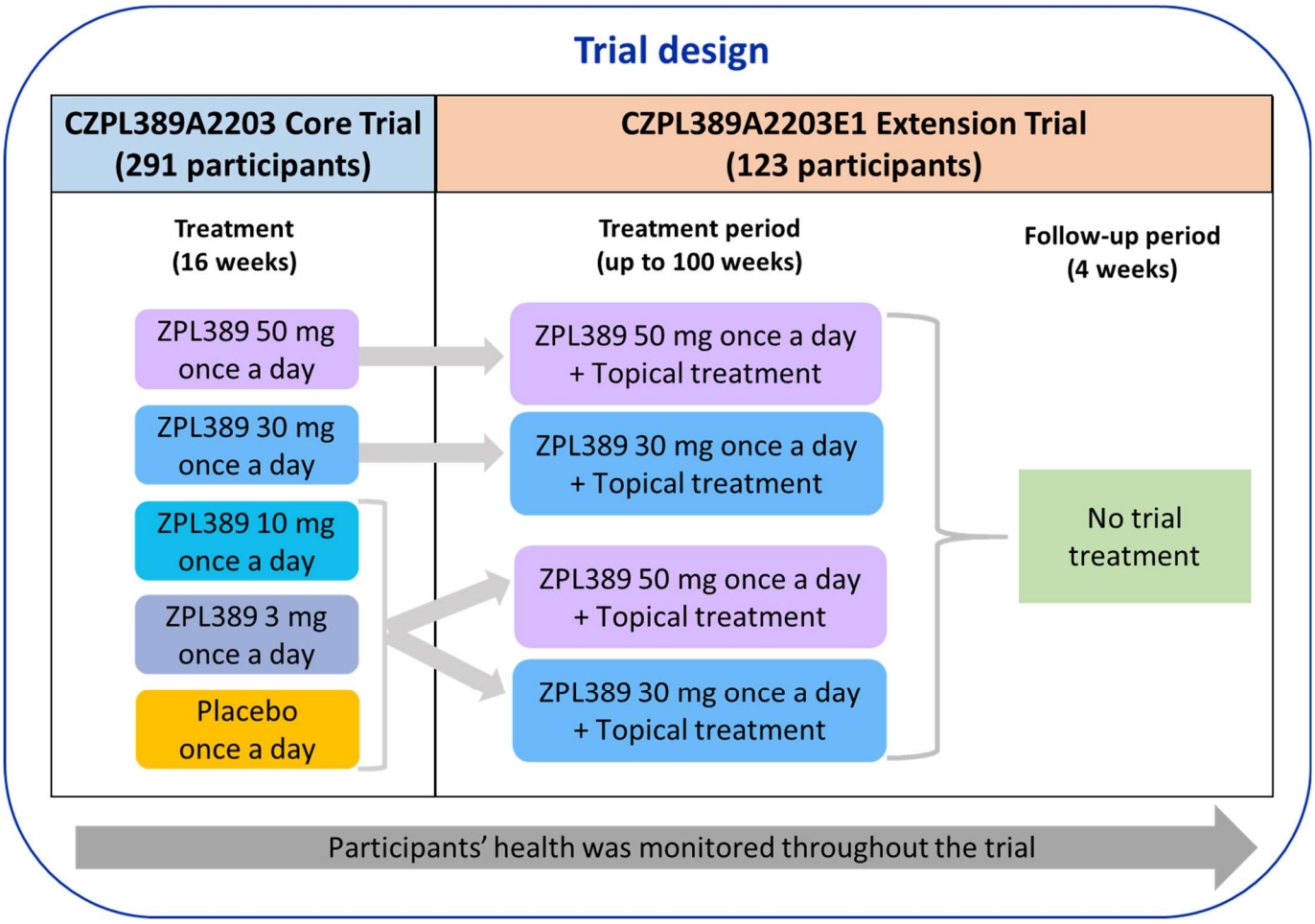
The participants who received ZPL389 3 mg or 10 mg, or placebo in the core trial, were randomly assigned to receive ZPL389 30 mg or 50 mg along with topical treatment in this extension trial. This means that these participants could end up in either treatment group. This process is called randomization.

ZPL389 was planned to be taken for up to 100 weeks.

The researchers measured the extent and severity of eczema symptoms using standard measurements scores at defined time points. The participants' health was monitored throughout the trial.

During treatment-free follow-up period (4 weeks)

After completing the treatment period, participants continued to be monitored even though they did not receive any trial treatment. They could still apply basic skin moisturizer to their skin.



What were the key results of this trial?

This is a summary of the average results for all participants in different treatment groups. 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. A detailed presentation of the results can be found on the websites listed at the end of this summary.

What medical problems did the participants have during this 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. During a trial, all adverse events are recorded, whether or not they are thought to be caused by the trial drug. When new drugs are being studied, researchers keep track of all adverse events participants have.

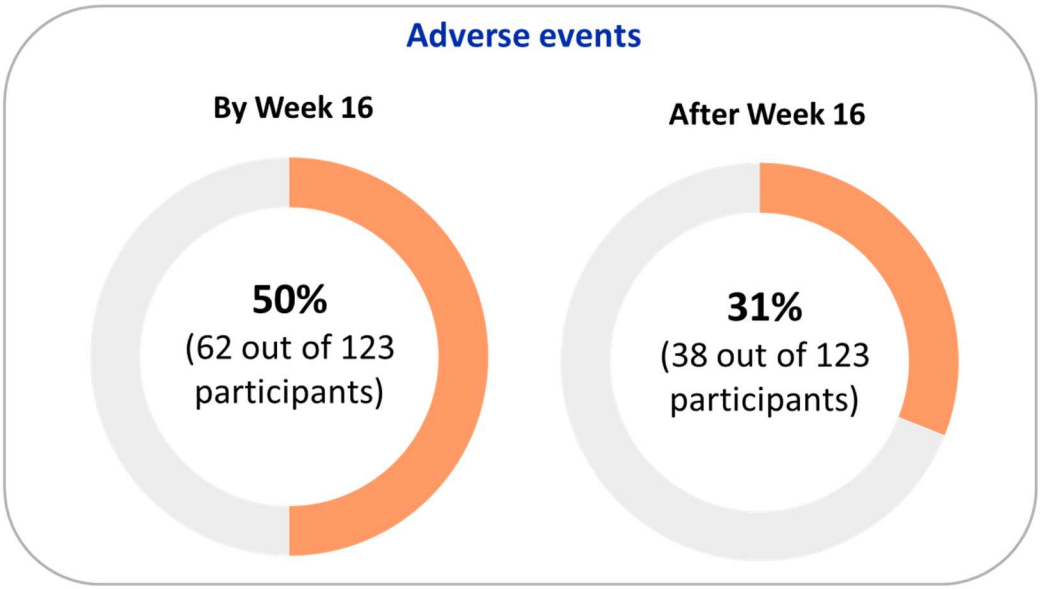
This section is a summary of the adverse events that happened during this trial. The websites listed at the end of this summary may have more information about all the adverse events that happened in this trial.

An adverse event is an unwanted sign, symptom, or disease 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 drug.

The researchers looked at the adverse events by time point:

- **Short-term (by Week 16):** Adverse events that happened during the first 16 weeks of treatment in this extension trial, or during the first 32 weeks of treatment if considering the first 16 weeks of core trial treatment.
- **Long-term (after Week 16):** Adverse events that happened after the first 16 weeks of treatment in this extension trial, or after 32 weeks of treatment if considering the first 16 weeks of core trial treatment.



How many participants had adverse events?

By Week 16: 62 out of 123 participants (50%) had 1 or more adverse events. During the trial, 5 out of 123 participants (4%) stopped the trial treatment because of adverse events. Serious adverse events happened in 7 out of 123 participants (6%) in the trial.

After Week 16: 38 out of 123 participants (31%) had 1 or more adverse events. During the trial, 1 out of 123 participants (1%) stopped the trial treatment because of adverse events. Serious adverse events happened in 2 out of 123 participants (2%) in the trial.

No participant died during this trial.

Number of participants (%) with adverse events by Week 16 and after Week 16

	By Week 16		After Week 16	
	ZPL389 30 mg (Out of 60 participants)	**ZPL389 50 mg** (Out of 63 participants)	**ZPL389 30 mg** (Out of 60 participants)	**ZPL389 50 mg** (Out of 63 participants)
At least 1 adverse event	29 (48%)	33 (52%)	18 (30%)	20 (32%)
At least 1 serious adverse event	2 (3%)	5 (8%)	0	2 (3%)
Stopped drug due to adverse event	2 (3%)	3 (5%)	0	1 (2%)

What were the most common non-serious adverse events?

The most common non-serious adverse events that happened in at least 5% (5 out of 100) of participants in any group are shown below.

Number (%) of participants with most common non-serious adverse events

ZPL389 Total number of participants in group	By Week 16 30 mg 60	By Week 16 50 mg 63	After Week 16 30 mg 60	After Week 16 50 mg 63
Nose and throat infection (Nasopharyngitis)	6 (10%)	4 (6%)	8 (13%)	3 (5%)
Worsening of eczema (Dermatitis atopic)	1 (2%)	4 (6%)	1 (2%)	3 (5%)

What were the serious adverse events?

The serious adverse events that happened in any group are shown in the next table.

Number (%) of participants with serious adverse events by Week 16

ZPL389 Total number of participants in group	30 mg 60	50 mg 63
Infection of the prostate gland, located between the bladder and the penis (Prostatitis)	1 (2%)	0
Inflammed and narrowed airways in the lungs (Asthma)	1 (2%)	0
Inflammation of the larger tubes, which carry air to and from the lungs (Bronchitis)	0	1 (2%)
Stomach Pain (Abdominal pain)	0	1 (2%)
Worsening of eczema (Dermatitis atopic)	0	1 (2%)
Fluid-filled sac in the ovary (Ovarian cyst)	0	1 (2%)
Sudden collapse of the lungs (Pneumothorax spontaneous)	0	1 (2%)
Inflammation of the small tubes of the lungs (Bronchiolitis)	0	1 (2%)

After Week 16: 2 out of 123 (2%) participants had serious adverse events: one (1%) participant had inflammation along with build-up of fat in the liver (steatohepatitis), and one (1%) participant had ankle fracture. Both participants were in the ZPL389 50 mg group.

How many participants stopped trial drug due to adverse events?

By Week 16: 5 out of 123 (4%) participants stopped trial drug early due to adverse events such as stomach pain (abdominal pain), feeling tired (fatigue), fluid-filled sac in the ovary (ovarian cyst), and worsening of eczema (dermatitis atopic).

After Week 16: 1 out of 123 (1%) participants stopped trial drug early due to worsening of eczema (dermatitis atopic).

What were the other results of this trial?

Did ZPL389 reduce the symptoms of eczema over time?

In this trial, researchers measured the extent and severity of symptoms of eczema in all participants using standard measurement scores. After starting treatment in this trial, researchers could not find a meaningful reduction in the extent and severity of symptoms of eczema in either dose group. The trial treatment did not show an effect in participants with moderate to severe eczema.

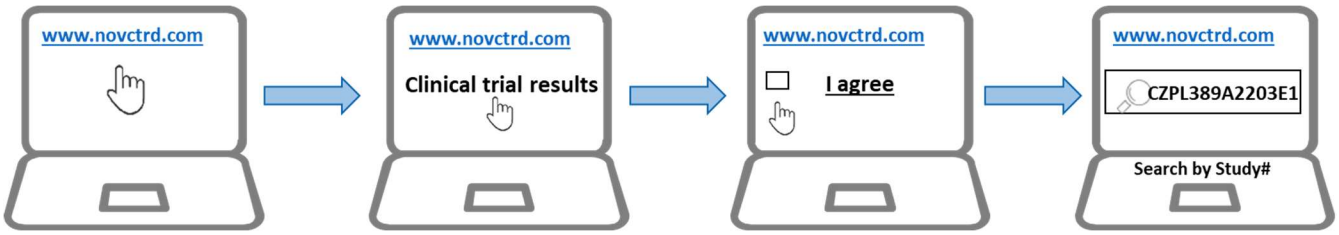
How was this trial useful?

This trial was planned to help researchers learn about the safety and effects of ZPL389 in people with eczema. The sponsor ended this trial early because the core trial results indicated that the trial treatment did not show an effect in participants with moderate to severe eczema. Results from this trial may be used in other clinical trials for people with moderate to severe eczema.

If you have any questions about these trial results, please talk to the doctor or staff at your trial site.

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 the following websites:

- www.clinicaltrials.gov Use the NCT identifier NCT03948334 in the search field.
- https://www.clinicaltrialsregister.eu/ctr-search/search Use the EudraCT identifier 2018-000595-15 in the search field.

Full clinical trial title: A randomized, double blind, multicenter extension to CZPL389A2203 dose-ranging study to assess the short-term and long-term safety and efficacy of oral ZPL389 with concomitant or intermittent use of TCS and/or TCI in adult patients with atopic dermatitis (ZEST Extension)

Thank you

Thank you for taking part in this trial. As a clinical trial participant, you belong to a large community of people 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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