Clinical Trial Results

NOVARTIS

Research Sponsor:	Novartis
Location of Headquarters:	Basel, Switzerland
Drug Studied:	LFX453
Protocol #:	CLFX453X2201
Full Trial Title:	A randomized, vehicle controlled, active comparator, parallel group study to evaluate safety, tolerability, and preliminary efficacy of topical LFX453 formulations in patients with actinic keratosis
Full Scientific Summary:	www.novctrd.com
Trial Date:	March 2015 to January 2016

Thank you!

As a clinical trial patient, you belong to a large community of patients around the world. You helped researchers answer important health questions and test new medical treatments.

Thank you for taking part in the clinical trial for the drug LFX453. You helped researchers learn if LFX453 works in people with actinic keratosis. This trial started in March 2015 and ended in January 2016.

Novartis, the sponsor of this trial, thanks you for your help and thinks it is important for you to know the results of your trial. An independent non-profit organization called CISCRP prepared this summary of the trial results for you. We hope it helps you understand your important role in medical research.

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

What has happened since the trial ended?

You were in this trial for about 6 months, but the trial took close to 1 year to complete. The trial included 82 patients from 10 trial sites in Austria, Denmark, Germany, Iceland, and the United Kingdom. When the trial ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers were looking for a better way to treat actinic keratosis, also called AK. People with AK have thick, scaly patches of skin that can feel rough or dry. These patches are also called lesions. The lesions can appear on areas of the skin that have been exposed to a lot of sun or ultraviolet (UV) rays.

In this trial, researchers wanted to find out if the trial drug LFX453 can work with the body's immune system to help clear AK lesions. Researchers compared LFX453 with imiquimod and a placebo. Imiquimod, also known as Aldara™, is currently available to treat AK. A placebo looks like medicine but does not have any real medicine in it.

In your trial, researchers wanted to know:

- Did lesions completely clear in more patients who got LFX453 compared to patients who got the placebo?
- How much LFX453 got into the blood and how much was found in the skin?
- What medical problems did patients have during the trial?

To answer these questions, researchers asked for the help of men and women like you. The patients in this trial were 51 to 76 years old and had AK with lesions on their face, scalp, or both.

What kind of trial was this?

This trial was "double-blind". This means that none of the patients, trial doctors, trial staff, or sponsor staff knew if patients were getting LFX453 or the placebo.

Some trials are done this way because knowing what treatment each patient is getting can affect the results of the trial. Doing a trial this way helps make sure the results are looked at fairly.

Additionally, some patients got imiquimod and they were in an "open-label" part of the trial. This means that the patients, some trial doctors, and sponsor staff knew which patients were getting imiquimod. However, the medical staff that looked at each patient's skin did not know which treatment the patient got. This meant the results were looked at fairly.

When the trial ended, the research sponsor found out what all the patients got so they could create a report of the trial results.

What happened during the trial?

Before the trial started, the trial doctors did tests and asked about patients' AK symptoms to make sure they could join the trial.

During the trial, patients got one of the below study treatments for up to 8 weeks. Patients were randomly assigned, like flipping a coin, to get either:

- LFX453 Cream 1
- LFX453 Cream 2
- A placebo that looked like LFX453 Cream 1
- A placebo that looked like LFX453 Cream 2
- Imiquimod (Aldara™)

The chart below shows how many patients got each treatment.

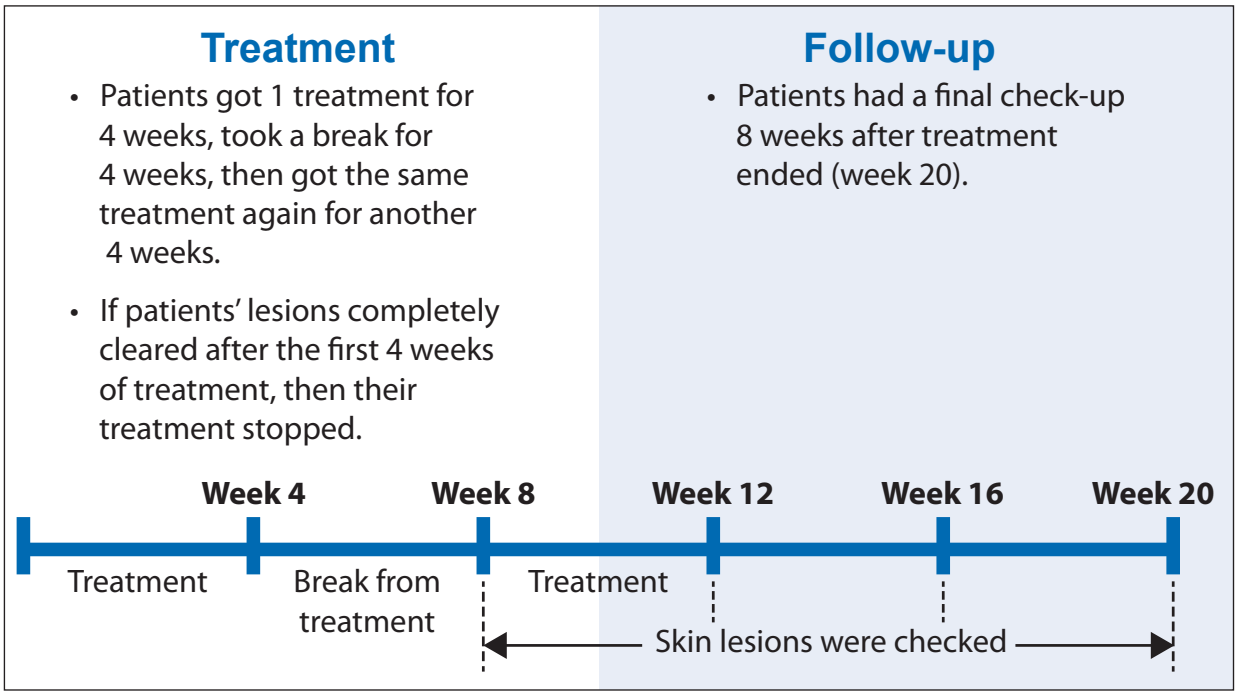
Treatment: 82 Patients
20 patients got LFX453 Cream 1 twice a day
20 patients got LFX453 Cream 2 twice a day
11 patients got the placebo for LFX453 Cream 1 twice a day
10 patients got the placebo for LFX453 Cream 2 twice a day
21 patients got imiquimod 3 times a week

Patients were given 1 of the treatments for 4 weeks, took a break for 4 weeks, and then got the same treatment again for another 4 weeks. If patients had their lesions completely clear after the first 4 weeks of treatment, then their treatment stopped.

At each trial site visit, the trial doctors did tests and checked the number of patients' skin lesions to see how well the creams were working. They did this by taking pictures and looking at the patients' skin.

After treatment ended, patients had a final check-up 8 weeks later.

The figure below shows how the trial was done and how often each treatment was applied to the skin:



What were the results of the trial?

This is a summary of the overall results of your trial, not your individual results. The results presented here are for a single trial. Researchers look at the results of many trials to decide which drugs work best and are safest for patients. Other trials may provide new information or different results. You should not make changes to your treatment based on the results of a single trial without first talking to your doctor.

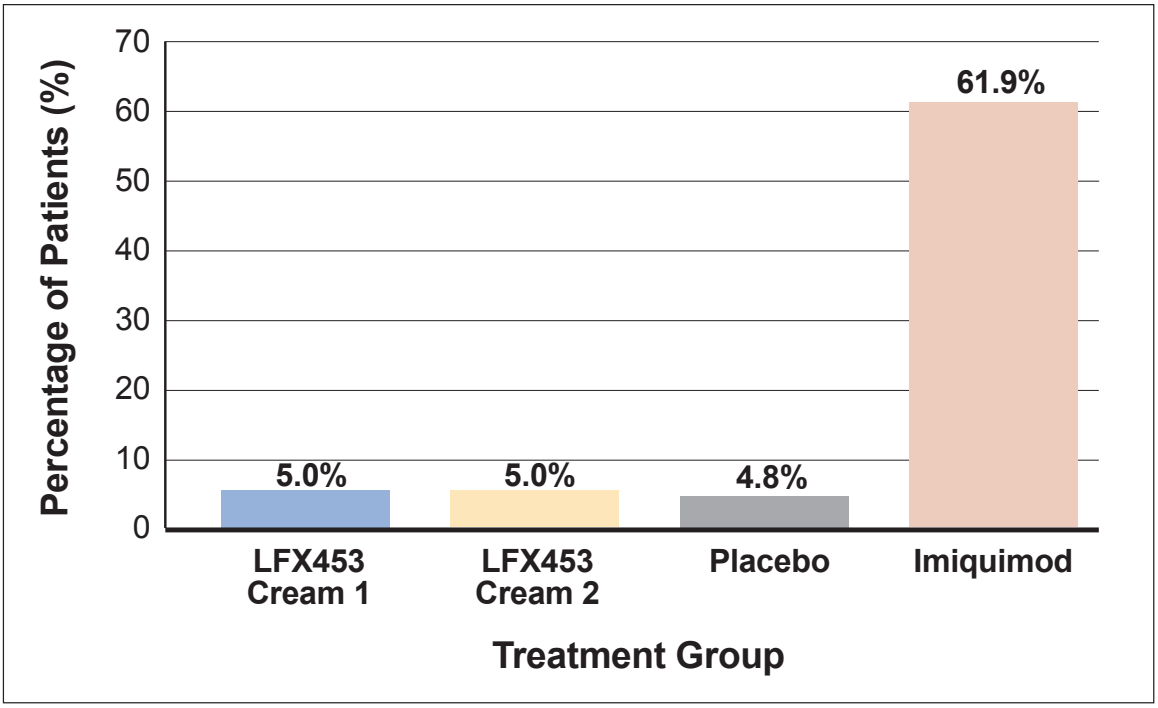
Did lesions completely clear in more patients who got LFX453 compared to patients who got the placebo?

No. Overall, the results did not show that lesions cleared more often in patients who got LFX453 compared to patients who got the placebo. Any differences between the treatment groups could have been due to chance.

When researchers looked at patients 8 weeks after treatment ended (week 20), they found that 1 of the 20 patients (5.0%) in each of the LFX453 groups and 1 out of the 21 patients (4.8%) in the 2 placebo groups had their lesions completely clear. In the imiquimod group, 13 of the 21 patients (61.9%) had their lesions completely clear at 8 weeks after treatment ended.

The chart below shows how many patients had their lesions completely clear 8 weeks after treatment ended.

Percentage of patients who had their lesions completely clear 8 weeks (week 20) after treatment ended



Researchers also looked at patients' lesions at week 8 and week 16.

At Week 8:

- None of the 40 patients (0.0%) who got LFX453 had their lesions completely clear.
- 1 of the 21 patients (4.8%) who got a placebo had their lesions completely clear.
- 3 of the 21 patients (14.3%) who got imiquimod had their lesions completely clear.

At Week 16:

- 1 of the 20 patients (5.0%) in each of the LFX453 groups had their lesions completely clear.
- 1 of the 21 patients (4.8%) who got a placebo had their lesions completely clear.
- 9 of the 21 patients (42.9%) who got imiquimod had their lesions completely clear.

How much LFX453 got into the blood and how much was found in the skin?

Researchers wanted to know how much LFX453 got into the blood and how much stayed in the skin. They found the following:

- Patients who got LFX453 Cream 1 or Cream 2 had very little LFX453 in their blood. The amount of LFX453 found in the blood was similar in patients that got Cream 1 and Cream 2.
- Within a week of getting either Cream 1 or Cream 2, LFX453 reached steady amounts in patients' blood.
- Patients who got Cream 1 had about 2 times more LFX453 in their skin compared to patients who got Cream 2.
- The amount of LFX453 in patients' skin was 6 times higher than the average amount of LFX453 in patients' blood.

What medical problems did patients have?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs are being studied, researchers keep track of all medical problems that patients have. These medical problems are called "adverse events". An adverse event is any sign or symptom that may or may not be caused by the trial drug.

How many patients had adverse events during the trial?

Some patients in each treatment group had adverse events. Slightly more patients in the imiquimod group had adverse events compared to the other treatment groups.

The table below shows how many patients had adverse events during this trial.

Adverse events in this trial

	LFX453 Cream 1 Out of 20 patients	LFX453 Cream 2 Out of 20 patients	Placebo for LFX453 Cream 1 Out of 11 patients	Placebo for LFX453 Cream 2 Out of 10 patients	Imiquimod Out of 21 patients
How many patients had adverse events?	10 (50.0%)	15 (75.0%)	9 (81.8%)	8 (80.0%)	18 (85.7%)
How many patients had serious adverse events?	1 (5.0%)	1 (5.0%)	1 (9.1%)	1 (10.0%)	1 (4.8%)
How many patients stopped taking the treatment because of adverse events?	1 (5.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	2 (9.5%)

Did any patients have serious adverse events?

Some patients also had serious adverse events. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or leads to hospitalization. During the trial, all serious adverse events were reported and written down, whether or not they were caused by the trial drug. No patients died during the trial.

In this trial, there were 6 serious adverse events that happened in 5 patients:

- 1 patient who got LFX453 Cream 1 had depression that got worse.
- 1 patient who got LFX453 Cream 2 had an abdominal hernia, or bulging of the stomach through a weakness in the abdominal wall muscle.
- 1 patient who got the placebo for LFX453 Cream 1 had an irregular or quick heartbeat as well as a stroke.
- 1 patient who got the placebo for LFX453 Cream 2 had diarrhea that got worse.
- 1 patient who got imiquimod had a fracture at the top of the thigh bone.

The trial doctors did not think any of the serious adverse events were related to the drugs used in this trial.

What were the most common side effects?

Researchers also looked at the most common adverse events caused by the trial drugs, also known as "side effects". The most common side effect was redness of the skin where the treatment was given. This side effect only happened in the imiquimod treatment group.

The table below show the most common side effects caused by the trial drugs that happened to more than 1 patient in the trial.

Most common side effects in this trial

Most common side effect	LFX453 Cream 1 Out of 20 patients	LFX453 Cream 2 Out of 20 patients	Placebo for LFX453 Cream 1 Out of 11 patients	Placebo for LFX453 Cream 2 Out of 10 patients	Imiquimod Out of 21 patients
Redness of the skin where the treatment was given	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	5 (23.8%)
Flu-like illness	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)
Chills	0 (0.0%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	1 (4.8%)
Scab where the treatment was given	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)
Itchy skin where the treatment was given	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (9.5%)

Where can I learn more about this trial?

Researchers look at the results of many trials to decide which drugs work best and are safest for patients. It takes volunteers in many trials all around the world to advance medical science.

More information about the results and the full list of adverse events that happened in this trial can be found in the scientific summary of the results available on the Novartis Clinical Trial Results website (www.novctrd.com). Once on the site, click **"Clinical trial results"** at the bottom of the page. After agreeing to enter the Novartis website, type **CLFX453X2201** into the keyword search box and click "Search". If you have questions about the results, please speak with the trial doctor or staff at your trial site.

This trial was registered on the following websites:

- Clinical Trials.gov (https://clinicaltrials.gov/) - National Clinical Trial # NCT02404389
- EU clinical register (https://www.clinicaltrialsregister.eu) - EU Clinical Trial # 2014-003613-28

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical trials, nor is it involved in conducting clinical trials.

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