NOVARTIS

Clinical Trial Results Summary

A trial to learn more about how well ECF843 works and how safe it is in participants with dry eye disease

Trial Number: CECF843A2201

Thank you

Thank you to the participants who took part in the clinical trial for the trial treatment ECF843. All of the participants helped the researchers learn about how well ECF843 works and how safe it is.

Novartis sponsored this trial and believes it is important to share what was learned from the results of this trial with the participants and the public.

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

What was the purpose of the trial?

There are currently limited treatment options available for doctors to give to people who have dry eye disease, also called “DED”. In this trial, the researchers wanted to learn more about how well ECF843 eye drops work compared to placebo eye drops, and how safe they are in participants with DED.

How do researchers think the trial treatment can help?

The trial treatment, ECF843, works by helping to provide moisture for the eye. This protects the surface of the eye by helping to stop it from becoming too dry. Researchers also think that ECF843 eye drops may help to reduce the levels of inflammation in the eye. Inflammation is one of the ways the immune system protects the body from disease and infection. But, too much inflammation in the eye can cause the eyes to become red, itchy, and painful.

ECF843 was designed to work the same as a protein found naturally in the body which provides moisture to the eye and joints. This protein is called “lubricin”.

What is Dry Eye Disease (DED)?

DED is a condition in which the eyes become dry, red, tired, and itchy.

Researchers think that DED has many different causes. These include:

- the eyes not producing enough tears to stop them from drying out
- the surface of the eye becoming damaged or having too much inflammation
- damage to the thin layer of fluid that covers the surface of the eye

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

- Did the participants’ DED symptoms become less severe after treatment with ECF843 eye drops compared to the placebo eye drops?
- Was there a difference in the participants’ corneal health after treatment with ECF843 eye drops compared to the placebo eye drops?

The cornea is the clear outer layer at the front of the eyeball that allows light into the eye. In people with DED, the cornea can sometimes become damaged.

- What medical problems happened during this trial?

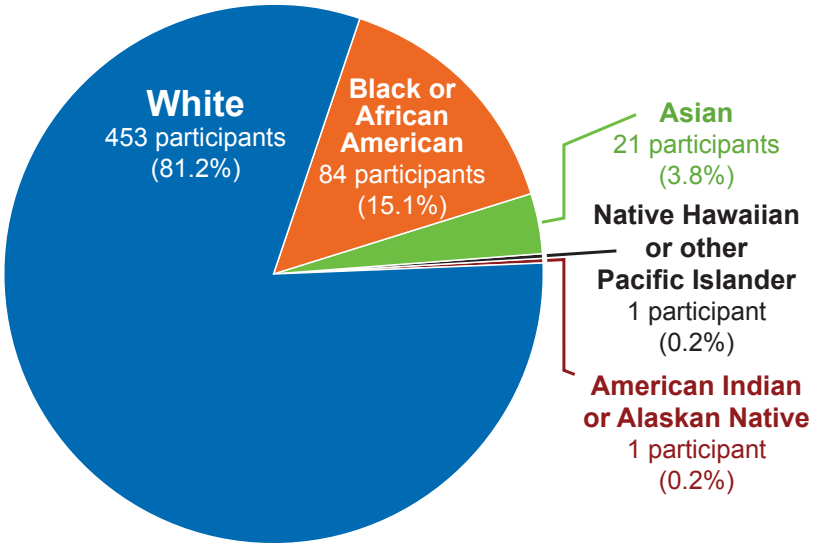
Who was in the trial?

To answer the questions in this trial, the researchers asked for the help of men and women who had DED for at least 6 months.

Everyone in this trial was 20 to 88 years old when they joined the trial. The charts below show the race and gender of the participants in this trial. There were 2 participants who reported more than 1 race.

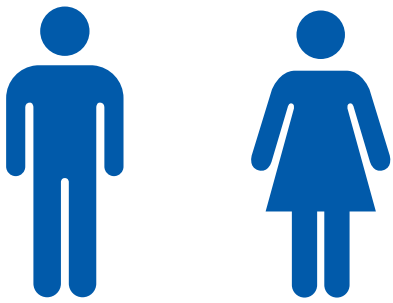
Participants' race

(out of 558 participants)



Participants' gender

(out of 558 participants)



Male
135 participants

Female
423 participants

All the participants in this trial were in the United States.

What treatments did the participants receive?

The participants in this trial received either ECF843 or the placebo as eye drops. The doses of ECF843 were measured in milligrams per milliliter, also called “mg/mL”.

The participants in this trial were split into 5 groups. The researchers used a computer program to randomly assign the treatment each participant received, and the dose level they received. This helped make sure the treatments were chosen fairly and comparing the results of the treatments was as accurate as possible.

This was a “double masked” trial. This means none of the participants, trial staff, or sponsor staff knew what trial treatment each participant received.

The participants in each group received 1 of the below treatments:

- **0.45 mg/mL** of **ECF843**, one drop in each eye 3 times per day (111 participants)
- **0.15 mg/mL** of **ECF843**, one drop in each eye 3 times per day (112 participants)
- **0.15 mg/mL** of **ECF843**, one drop in each eye 2 times per day (109 participants)
- **Placebo**, one drop in each eye 3 times per day (112 participants)
- **Placebo**, one drop in each eye 2 times per day (114 participants)

The participants received trial treatment during a treatment period that was 56 days long. The participants who received ECF843 eye drops received this treatment for up to 28 days during the 56-day treatment period. For the remaining days in the treatment period, these participants received the placebo eye drops.

The chart below shows the eye drop treatments that each group of participants received during Part 1 of the trial. There were 2 parts planned for this trial. But, the researchers decided to end the trial early before starting Part 2. This was because they could not conclude that ECF843 eye drops were helping the participants' DED symptoms and eye health more than the placebo eye drops in Part 1 of the trial.

	0.45 mg/mL of ECF843	0.15 mg/mL of ECF843	0.15 mg/mL of ECF843	Placebo	Placebo
	3 times per day for up to 28 days	3 times per day for up to 28 days	2 times per day for up to 28 days	3 times per day for up to 56 days	2 times per day for up to 56 days
	111 participants	112 participants	109 participants	112 participants	114 participants

What happened during this trial?

The trial started in October 2020 and ended in May 2021.The participants were in the trial for up to about 86 days.

There were 2 parts planned for this trial. But, after reviewing the data from the first part of this trial, the sponsor decided to end the trial early. This was because the difference in the results between ECF843 eye drops and the placebo eye drops was small. This meant that the researchers could not conclude that ECF843 eye drops were helping the participants' DED symptoms and eye health more than the placebo eye drops. The decision to stop the trial was not related to safety.

The chart below shows what happened during the first part of this trial.

Before the participants received treatment

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

On the first day of treatment

While the participants received treatment

The participants:

- visited their trial site 5 times
- filled out questionnaires to record their DED symptoms
- had tests done to check their eye health
- had their overall health checked and answered questions about any medical problems they were having

Up to 56 days

After the participants received treatment

- The doctors asked the participants questions about any medical problems they were having

Up to 30 days after their last dose

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.

Did the participants' DED symptoms become less severe after treatment with ECF843 eye drops compared to the placebo eye drops?

No. Overall, the difference between the treatments was too small for the researchers to know if ECF843 eye drops helped to make the participants' symptoms less severe compared to the placebo eye drops. The difference could have been due to chance.

To answer this question, the researchers asked the participants to record their DED symptoms using the SANDE questionnaire. They recorded their symptoms before they received treatment, and every day and evening before bedtime during treatment.

SANDE Questionnaire

The participants used the SANDE questionnaire to report their eye discomfort, including:

- the severity on a scale from "very mild" to "very severe"
- the frequency from "rarely" to "all the time"

Then, the researchers:

- calculated the average change in participants' SANDE scores from before they received treatment to the end of treatment
- if the participants' average change in score decreased, this meant their DED symptoms had improved after receiving treatment

The table below shows the average change in the participants' SANDE scores from before they received treatment to the end of the treatment period.

Average change in SANDE Scores after treatment				
0.45 mg/mL of ECF843 3 times per day	**0.15 mg/mL of ECF843** 3 times per day	**0.15 mg/mL of ECF843** 2 times per day	**Placebo** 3 times per day	**Placebo** 2 times per day
Decreased by 6.0	Decreased by 8.1	Decreased by 1.8	Decreased by 4.9	Decreased by 6.1

Was there a difference in the participants' corneal health after treatment with ECF843 eye drops compared to the placebo eye drops?

No. Overall, the difference between the results of the treatments was too small for the researchers to know if the participants' corneal health differed after treatment with ECF843 eye drops compared to the placebo eye drops. The difference could have been due to chance.

The cornea is the clear outer layer at the front of the eyeball that allows light into the eye. In people with DED, the cornea can sometimes become damaged.

To answer this question, the researchers used a medical test called "corneal fluorescein staining". Corneal fluorescein staining is a test where doctors put a colored dye into the eye and use a special type of blue light to detect damage to the cornea.

The colored dye stained any area of the cornea that was damaged. The researchers then scored how severe the damage was on a scale of 0 to 4:

- a **lower score** meant that the cornea had **less or no damage**
- a **higher score** meant that the cornea had **more damage**

The researchers scored how severe the damage to the participants' corneas was before they received treatment and at the end of treatment.

Then, the researchers used a mathematical formula to work out the average change in the participants' scores from before they received treatment to the end of treatment.

If the participants' average change in score decreased, this meant their corneal health had improved after receiving treatment.

Overall, the researchers found that the average change in the participants' scores from before they received treatment to 29 days after they received treatment was:

- -1.1 for the participants who received 0.45 mg/mL of **ECF843 3 times per day**
- -1.0 for the participants who received 0.15 mg/mL of **ECF843 3 times per day**
- -1.0 for the participants who received 0.15 mg/mL of **ECF843 2 times per day**
- -0.9 for the participants who received **the placebo 3 times per day**
- -1.1 for the participants who received **the placebo 2 times per day**

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 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.

In this trial, the adverse events were split into those that happened **within the eye**, and those that happened **to other organs of the body**.

This section is a summary of the adverse events that happened while the participants received treatment during this trial.

An adverse event is:

- any unwanted sign or symptom that the participants have during a trial.
- considered serious when it is life-threatening, results in death, causes lasting problems, or the participant needs hospital care.

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

- 8.2% of the participants had adverse events during this trial. This was 46 out of 558 participants.
- 2 adverse events were serious.
- 0.4% of the participants left the trial due to an adverse event. This was 2 out of 558 participants.

What were the serious adverse events?

There were no serious adverse events that happened **within the eye**.

There were 2 serious adverse events that happened **to other organs of the body:**

- A stroke caused by a lack of blood flow to the brain happened in 1 participant who received **the placebo eye drops 2 times per day**. This was 1 out of 114 participants (0.9%) in that group.
- Pelvic mass, a group of abnormal cells growing in the pelvis happened in 1 participant who received **the placebo eye drops 3 times per day**. This was 1 out of 112 participants (0.9%) in that group.

No participants died during the treatment period of this trial.

What were the most common adverse events that happened within the eye?

The adverse events below that happened **within the eye** happened in more than 2 participants overall. There were other adverse events that happened within the eye, but those happened in fewer participants.

Most common adverse events that happened inside the eye

Adverse event	0.45 mg/mL of ECF843 3 times per day	0.15 mg/mL of ECF843 3 times per day	0.15 mg/mL of ECF843 2 times per day	Placebo 3 times per day	Placebo 2 times per day
	(percentage and number of participants)				
Pain in the eye	1 of 111 **0.9%**	2 of 112 **1.8%**	0 of 109 **0.0%**	0 of 112 **0.0%**	0 of 114 **0.0%**
Blurred vision	1 of 111 **0.9%**	1 of 112 **0.9%**	0 of 109 **0.0%**	1 of 112 **0.9%**	1 of 114 **0.9%**
Chalazion, which is a small lump on the eyelid caused by a gland in the eyelid becoming blocked	0 of 111 **0.0%**	0 of 112 **0.0%**	0 of 109 **0.0%**	1 of 112 **0.9%**	2 of 114 **1.8%**
Conjunctival hyperemia, which is eye inflammation caused by high levels of blood flow to the conjunctiva, the tissue that covers the surface of the eye	0 of 111 **0.0%**	1 of 112 **0.9%**	0 of 109 **0.0%**	0 of 112 **0.0%**	2 of 114 **1.8%**

What were the most common adverse events that happened outside the eye?

The adverse event below that happened **outside the eye** happened in more than 2 participants overall. There were other adverse events that happened outside the eye, but those happened in fewer participants.

Most common adverse events that happened outside the eye

Adverse event	0.45 mg/mL of ECF843 3 times per day	0.15 mg/mL of ECF843 3 times per day	0.15 mg/mL of ECF843 2 times per day	Placebo 3 times per day	Placebo 2 times per day
	(percentage and number of participants)				
Headache	0 of 111 **0.0%**	3 of 112 **2.7%**	0 of 109 **0.0%**	0 of 112 **0.0%**	1 of 114 **0.9%**

What was learned from this trial?

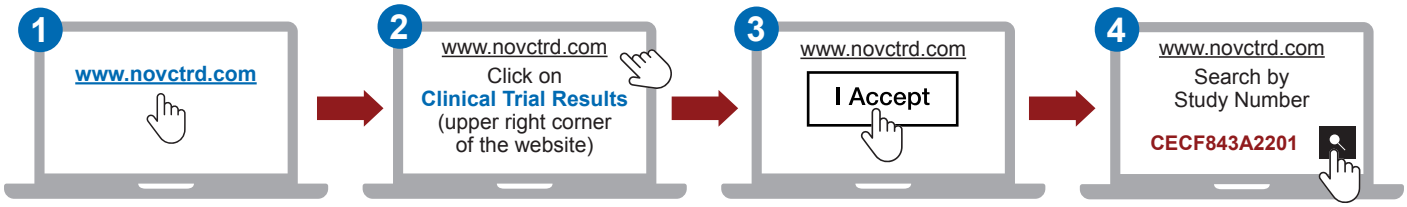
The researchers learned that ECF843 eye drops did not help to make the participants' DED symptoms less severe compared to the placebo eye drops. The researchers found that there was no difference in the participants' corneal health after treatment with ECF843 eye drops compared to the placebo eye drops. The researchers also learned more about the safety of ECF843 eye drops.

The results presented here are for a single trial. This summary shows only the main results from this one trial. If you have any questions, please talk to the doctor or staff at your trial site.

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, www.novctrd.com.

Please follow the below steps:



You can find more information about this trial on the following websites:

- https://www.clinicaltrials.gov/. Use the NCT identifier NCT04391894 in the search field.

Full trial title: A randomized, double-masked, multicenter study to evaluate the safety and efficacy of ECF843 vs Vehicle in subjects with dry eye disease

Protocol number: CECF843A2201

ClinicalTrials.gov number: NCT04391894

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.

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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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