Clinical Study Results

This summary reports the results of only one study. Researchers must look at the results of many types of studies to understand if a study medication works, how it works, and if it is safe to prescribe to study patients. The results of this study might be different than the results of other studies that the researchers review.

Sponsor:	Pfizer Inc.
Medicine(s) Studied:	Crisaborole (PF-06930164)
Protocol Number:	C3291038
Dates of Study:	26 June 2020 to 19 October 2021
Title of this Study:	Study Comparing Treatment Effects of Crisaborole Ointment with Vehicle Ointment (No Crisaborole) in Adults with Stasis Dermatitis [A Phase 2, Randomized, Double-Blind, Vehicle-Controlled, Proof-of-Concept Study to Evaluate the Efficacy, Safety, and Local Tolerability of Crisaborole Ointment, 2%, in Adult Participants with Stasis Dermatitis without Active Skin Ulceration]
Date(s) of this Report:	04 May 2022

– Thank You –

If you participated in this study, Pfizer, the Sponsor, would like to thank you for your participation.

This summary will describe the study results. If you have any questions about the study or the results, please contact the doctor or staff at your study site.

Why was this study done?

What is stasis dermatitis?

Stasis dermatitis is a skin condition that occurs on the lower legs because of slow or stopped blood flow. Its symptoms include redness, itch, pain, reduced comfort, swelling and not being able to perform daily activities. Stasis dermatitis mostly affects older people. Around 15 to 20 million people older than 50 years have stasis dermatitis in the United States.

What is crisaborole?

Crisaborole is an oil-based preparation (also referred to as 'ointment') which is applied onto the skin. Researchers think that crisaborole may help treat stasis dermatitis by decreasing inflammation in the skin. Inflammation is a type of defense mechanism the body has, which can lead to symptoms like redness and swelling.

Crisaborole ointment is approved in the US (EUCRISA™) and is available by prescription for treating mild to moderate atopic dermatitis (also known as atopic eczema which is a condition that causes the skin to become itchy, dry, and cracked). However, it is an investigational drug in this study because it is not approved for the treatment of stasis dermatitis.

What was the purpose of this study?

The purpose of this study was to compare the effects of crisaborole ointment and vehicle ointment to treat the symptoms of stasis dermatitis. The vehicle ointment is just like the crisaborole ointment, but it does not contain the active ingredient, crisaborole.

Researchers wanted to know:

Did the symptoms of stasis dermatitis decrease in participants treated with crisaborole ointment compared to participants treated with vehicle ointment?

What happened during the study?

How was the study done?

Researchers tested crisaborole on a group of adult participants to find out if participants taking crisaborole ointment (the test medicine) had improved symptoms of stasis dermatitis compared to participants taking the vehicle ointment.

Participants took part in this study at home. The study required a total of 3 home visits by home visiting clinicians. First, participants were screened by the clinician to make sure they had stasis dermatitis and did not have any other health problems to be able to join the study. This was known as the "screening period" and lasted up to 4 weeks. Participants who were able to join the study then entered a 6-week long treatment period. During the treatment period, participants were to apply the ointment twice a day to the areas of skin affected by the stasis dermatitis. Participants were asked to provide answers to questionnaires and to take pictures of the lower part of their legs (knees to feet only).

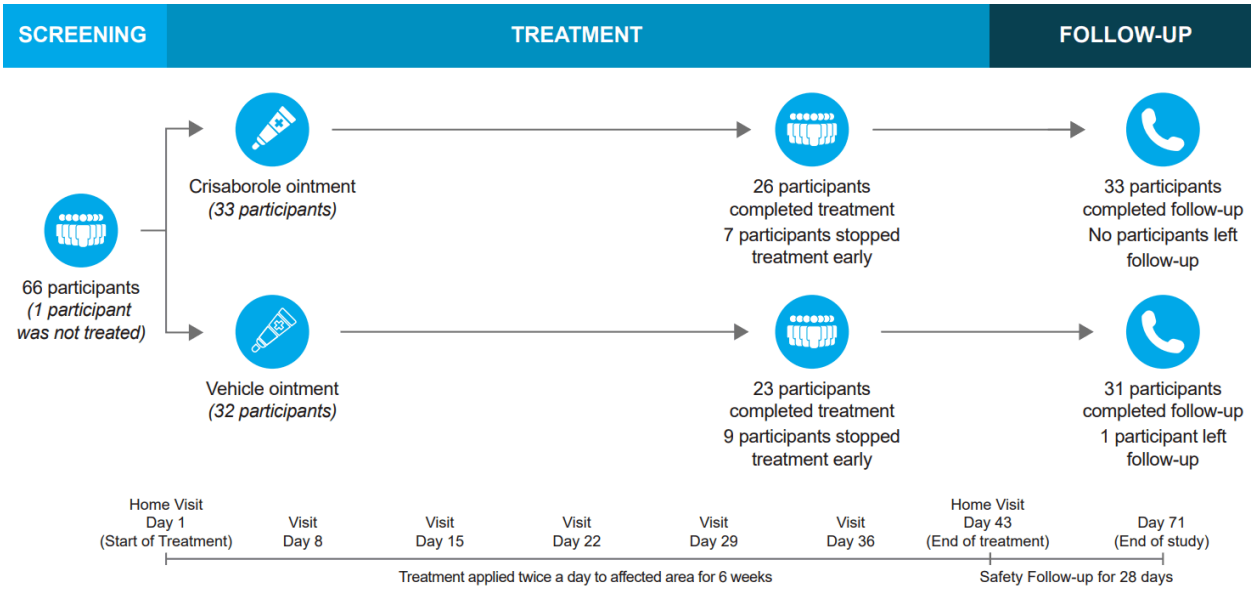
The study participants and researchers did not know who applied the crisaborole ointment and who applied the vehicle ointment. This is known as a "double-blinded" study. Participants were assigned by chance alone (like the flip of a coin), to receive the crisaborole ointment or vehicle ointment. Participants had a 50% (1 in 2) chance of receiving the crisaborole ointment and a 50% (1 in 2) chance of receiving the vehicle ointment. The ointments looked alike. No one (including the participants, the doctor, or the study team) was able to choose the group the participant was in.

This was done to make sure that the study results were not influenced by anyone in any way.

On Day 1 (the first day of treatment), participants were visited at home by the staff from the study site before they started their treatment. On Days 8, 15, 22, 29, and 36 during the treatment period, participants received telemedicine check-ups, which were audio and video calls to check for any medical problems. On Day 43 (end of treatment), participants were visited again at home. Participants then received a follow-up telemedicine check-up on Day 71. This was considered the end of the study.

The following figure shows what happened during the study.

Figure 1. Study Plan



Where did this study take place?

The Sponsor ran this study at 4 sites in the United States.

When did this study take place?

It began 26 June 2020 and ended 19 October 2021.

Who participated in this study?

The study included participants older than 45 years who had stasis dermatitis.

A total of 66 eligible participants were assigned to receive the study treatment; 32 participants in the vehicle group and 33 participants in the crisaborole group were treated. One (1) participant in the vehicle group was not treated because they decided not to use the study medication.

- A total of 35 men participated
- A total of 30 women participated
- All participants were between the ages of 48 years and 95 years.

Participants were to be treated for 6 weeks. Of the 65 participants who were treated with crisaborole or vehicle ointment, 49 out of the 65 participants finished their treatment. There were 64 out of 65 participants who finished the follow-up part of the study, 1 participant in the vehicle group was lost to follow-up after not continuing their treatment.

There were 16 participants (16 out of 65, or 25%) who did not finish treatment with crisaborole or vehicle ointment because of:

- Medical problems of which most were not related to the treatment (8 participants [12%])*.
- The participant was not diagnosed correctly according to study requirements (1 participant [2%]).
- The participant decided to stop treatment by choice (7 participants [11%]).

*One of the 8 participants had a medical problem which was present before the first dose of vehicle ointment, so it was not considered to be caused by the treatment or 'treatment emergent'.

How long did the study last?

Study participants were in the study for about 14 weeks. The entire study took 15½ months to complete.

When the study ended in October 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

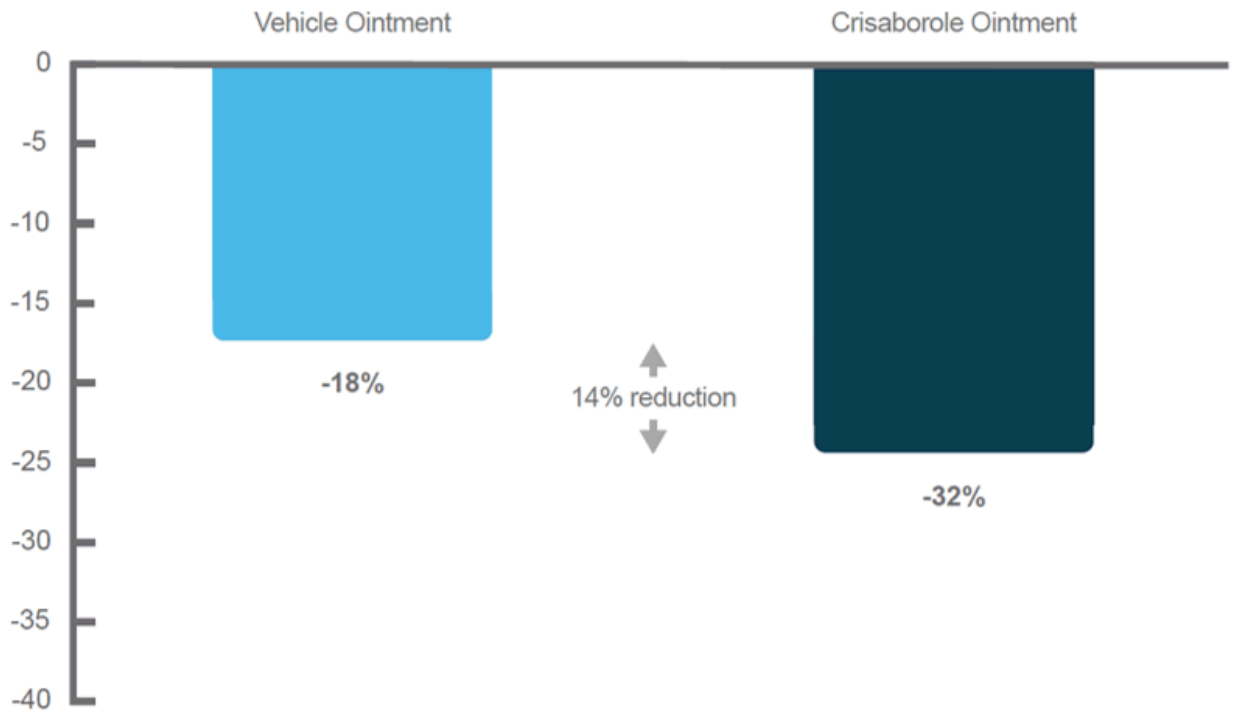
Did the symptoms of stasis dermatitis decrease in participants treated with crisaborole ointment compared to participants treated with vehicle ointment?

To answer this question, the researchers used a clinical tool to rate the severity of skin wounds caused by stasis dermatitis. This tool is called the Total Sign Score or TSS. The researchers compared the severity of symptoms from the time before participants started treatment to Day 43 (end of treatment). This gave the researchers the least square mean percent change in TSS from the start of the study on Day 1 to Day 43. Least square mean is a special way of calculating the average in some clinical studies. The least square mean percent change in TSS from Day 1 to Day 43 tells the researchers how the participant's stasis dermatitis had changed after 42 days of treatment in this study.

Did the study medication help improve the symptoms of stasis dermatitis compared to vehicle ointment?

On average, participants who used crisaborole had a least square mean percent decrease in TSS at Day 43 (Week 6) of 32% compared to 18% in participants who used the vehicle ointment (see Figure 2).

Figure 2. Least Square Mean Percent Change From Baseline in TSS at Day 43 (Week 6 [End of Treatment]) in Participants with Stasis Dermatitis



Based on these results, the researchers have decided that the results are not likely the result of chance. The crisaborole ointment may help improve the symptoms of stasis dermatitis.

This does not mean that everyone in this study had these results. This is a summary of just some of the main results of this study.

What medical problems did participants have during the study?

The researchers recorded any medical problems the participants had during the study. Participants could have had medical problems for reasons not related to the study (for example, caused by an underlying disease or by chance). Or, medical problems could also have been caused by a study treatment or by another medicine the participant was taking. Sometimes the cause of a medical problem is unknown. By comparing medical problems across many treatment groups in many studies, doctors try to understand what effects a study medication might have on a participant.

A total of 27 out of 65 participants (42%) in this study had at least 1 medical problem. There were 7 out of the 65 participants (11%) who stopped taking the treatment because of medical problems but decided to continue in the study. No participants left the study because of medical problems. The most common medical problems reported by more than 5% of participants in either group are described below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were commonly reported during the study. All medical problems reported by more than 5% of participants in either group are listed.
- The **2nd** column tells how many of the 33 participants taking the crisaborole ointment reported each medical problem. Next to this number is the percentage of the 33 participants taking the crisaborole ointment who reported the medical problem.
- The **3rd** column tells how many of the 32 participants taking the vehicle ointment reported each medical problem. Next to this number

is the percentage of the 32 participants taking the vehicle ointment who reported the medical problem.

- Using these instructions, you can see that 2 out of the 33 participants (6%) taking the crisaborole ointment reported an infection of the kidneys, bladder, or urethra. A total of 1 out of the 32 participants (3%) taking the vehicle ointment reported an infection of the kidneys, bladder, or urethra.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Crisaborole Ointment (33 Participants)	Vehicle Ointment (32 Participants)
Infection of the kidneys, bladder, or urethra	2 out of 33 participants (6%)	1 out of 32 participants (3%)
Headache	2 out of 33 participants (6%)	1 out of 32 participants (3%)
Skin rash	2 out of 33 participants (6%)	1 out of 32 participants (3%)
Redness of skin	2 out of 33 participants (6%)	2 out of 32 participants (6%)
Itch	3 out of 33 participants (9%)	1 out of 32 participants (3%)

Did study participants have any serious medical problems?

A medical problem is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

Five (5) participants (8%, or 5 out of 65 participants) had serious medical problems.

- One (1) participant in the crisaborole ointment group had cellulitis. Cellulitis is a serious infection of the skin caused by a germ (bacteria). This serious medical problem happened just before treatment had finished and the participant got better. The doctor and the researcher did not think this was related to the crisaborole ointment.
- Four (4) participants in the vehicle ointment group had serious medical problems. Each of these are listed below:
    - One (1) participant had cellulitis. This serious medical problem happened just before treatment had finished and the participant got better. The doctor and the researcher did not think this was related to the vehicle ointment.
    - One (1) participant had muscular dystrophy before joining the study, which then worsened during the study. Muscular dystrophy causes muscle weakness. The participant did not get better at the time of the last report. The doctor and the researcher did not think this was related to the vehicle ointment.
    - One (1) participant had a mass in their throat at the screening visit and was diagnosed with throat cancer during the study. The participant did not get better at the time of the last report. The doctor and the researcher did not think this was related to the vehicle ointment.
    - One (1) participant had cystitis. Cystitis is an infection of the bladder caused by a germ (bacteria). This serious medical problem happened

during the treatment period and the participant got better. The doctor and the researcher did not think this was related to the vehicle ointment.

No participants died during the study.

Where can I learn more about this study?

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

For more details on your study protocol, please visit:

The full scientific report of this study is available online at:

www.clinicaltrials.gov
Use the study identifier **NCT04091087**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number **C3291038**

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for study patients.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help study patients, and you
helped us to do that!