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 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: Abrocitinib (PF-04965842)

Protocol Number: B7451092

Dates of Study: 21 October 2021 to 26 February 2022

Title of this Study: Study Investigating Blood Levels of Caffeine, Efavirenz, and Omeprazole When Taken Before and After Abrocitinib in Healthy Participants

[A Phase 1, Open-Label, Fixed-Sequence, 2-Period Study to Estimate the Effect of Multiple Dose Abrocitinib on the Pharmacokinetics of Single Doses of Caffeine, Efavirenz, and Omeprazole in Healthy Participants]

Date(s) of this Report: 25 August 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 atopic dermatitis?

Atopic dermatitis (or "AD"), also sometimes called atopic eczema, is a common skin disorder that causes patches of flaky, red, itchy skin. Some of the current medicines available for AD are not suitable for everyone and therefore researchers are looking for new treatments that are both safe and effective.

While researchers think that many things cause AD, it is made worse by the body's immune system. The immune system is the body's way of defending itself against infection and other substances that should not be there. In AD, the immune system is often abnormal, and this can trigger excess inflammation. The excess inflammation in the body is caused by special proteins called "cytokines". Inflammation is often seen as redness and swelling. Researchers think that medicines that modify the way these cytokines work could help treat patients with AD.

What is abrocitinib?

The treatment tested in this study was PF-04965842 (the original company name) or abrocitinib. Abrocitinib has been approved for sale in many countries around the world for the treatment of moderate to severe AD. It is a tablet that is swallowed. Abrocitinib blocks the activity of a protein called "Janus kinase 1", or JAK1, which acts like an on/off switch for the cells of the immune system that are abnormal in AD. By blocking JAK1 activity, the signal to the cells that triggers inflammation is reduced.

What was the purpose of this study?

The purpose of this study was to see if treatment with abrocitinib altered the amount of caffeine, efavirenz, and omeprazole in the blood. The results of this study provided researchers with information on how abrocitinib changes the amount of other commonly taken medicines. Caffeine is a natural stimulant found in tea, coffee, some drinks, etc. It is also included in some medicines. Efavirenz is an antiviral

medicine that prevents human immunodeficiency virus (HIV) from multiplying in the body and is used to treat HIV. Omeprazole is a medicine that reduces the amount of acid produced by the stomach and is often used to treat heartburn, acid reflux, and stomach ulcers. These 3 medicines were chosen as they might interact with abrocitinib.

Researchers wanted to know:

- **How did abrocitinib change the amount of caffeine, efavirenz, and omeprazole in the blood of participants?**
- **What medical problems did participants have during the study?**

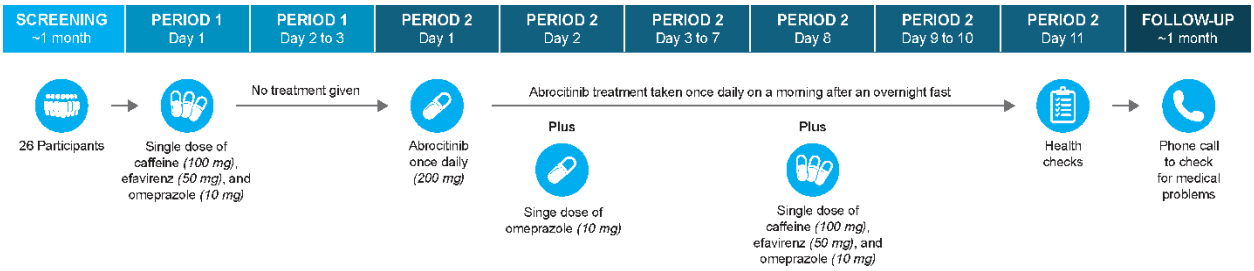
What happened during the study?

How was the study done?

Researchers tested caffeine, efavirenz, omeprazole, and abrocitinib on a group of healthy participants who did not have AD. They did this to learn if abrocitinib changed the amount of caffeine, efavirenz, and omeprazole in the blood of participants when these drugs were taken with abrocitinib. To do this, the researchers looked at the amount of caffeine, efavirenz, and omeprazole in the blood when taken without abrocitinib (e.g., before being given abrocitinib in this study) and compared this with the amount in the blood when taken with abrocitinib.

Participants stayed overnight at the study center for 14 nights and were able to leave on the next day. The study plan is shown in Figure 1.

Figure 1. Study Plan



On Day 1 in Period 1, participants were given a single dose of 100 milligram (or mg) caffeine, 50 mg efavirenz, and 10 mg omeprazole. The participants then received 200 mg abrocitinib once daily (the highest approved dose) starting on Day 1 in Period 2. Participants continued to take abrocitinib daily until Day 10. During Period 2 when participants were taking abrocitinib, participants also received a single dose of 10 mg omeprazole on Day 2 and a single dose of 100 mg caffeine, 50 mg efavirenz, and 10 mg omeprazole on Day 8. All treatments were taken after an overnight fast (nothing to eat or drink except water).

During the study, researchers took samples of blood from participants and measured the amount of caffeine, efavirenz, and omeprazole in the blood. Researchers also took blood and urine samples to check the participants' health and asked them how they were feeling.

Where did this study take place?

The Sponsor ran this study at 1 location in the United States of America.

When did this study take place?

It began 21 October 2021 and ended 26 February 2022.

Who participated in this study?

The study included healthy adult participants.

- A total of 15 men participated

- A total of 11 women participated
- All participants were between the ages of 18 and 64 years

Of the 26 participants who started the study, all 26 participants finished the study.

How long did the study last?

Study participants were in the study for about 11 weeks including the time before they were treated, the time when they were staying in the study center, and the time after treatment when there were safety checks. The entire study took just over 4 months to complete.

When the study ended in February 2022, 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?

How did abrocitinib change the amount of caffeine, efavirenz, and omeprazole in the blood of participants?

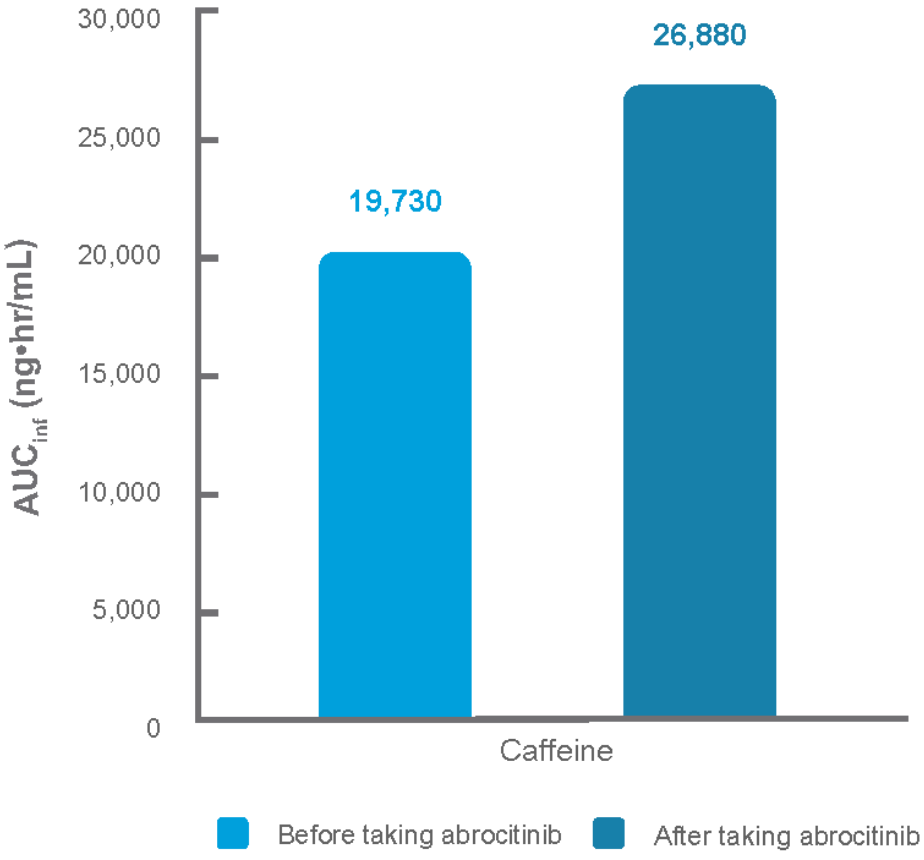
To answer this question, the researchers compared participants' blood test results from before and after participants had taken abrocitinib.

What was the total amount of caffeine, efavirenz, and omeprazole in the blood before and after participants took abrocitinib?

- The estimated total amount of caffeine in the blood from when caffeine was taken until caffeine was removed from the body is measured in nanogram hours per milliliter, also called ng•hr/mL. This is known as the area under the curve $(AUC)_{inf}$ and was 19,730 ng•hr/mL. When this was measured after participants had taken 200 mg abrocitinib, this was 26,880 ng•hr/mL. The amount of caffeine in the blood was about two-fifths (or 40%) higher when taken with abrocitinib. This is shown in Figure 2. Researchers think the

difference seen was not clinically significant. This means patients do not have to change how they use caffeine containing products when taking abrocitinib.

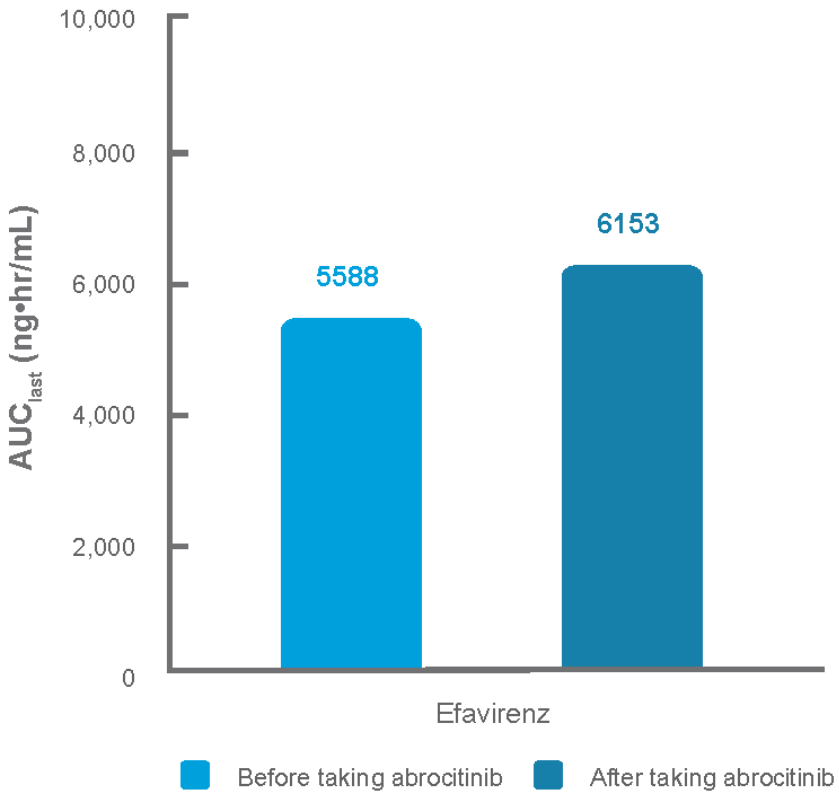
Figure 2. Blood Levels of Caffeine Before and After Participants Had Taken Abrocitinib



- The estimated total amount of efavirenz in the blood from when efavirenz was taken until the lowest amount of efavirenz was detected in the body was 5588 ng•hr/mL. This is known as the area under the curve $(AUC)_{last}$ and was calculated as the researchers were not able to estimate AUC_{inf}. When this was measured after participants had taken 200 mg abrocitinib, this was

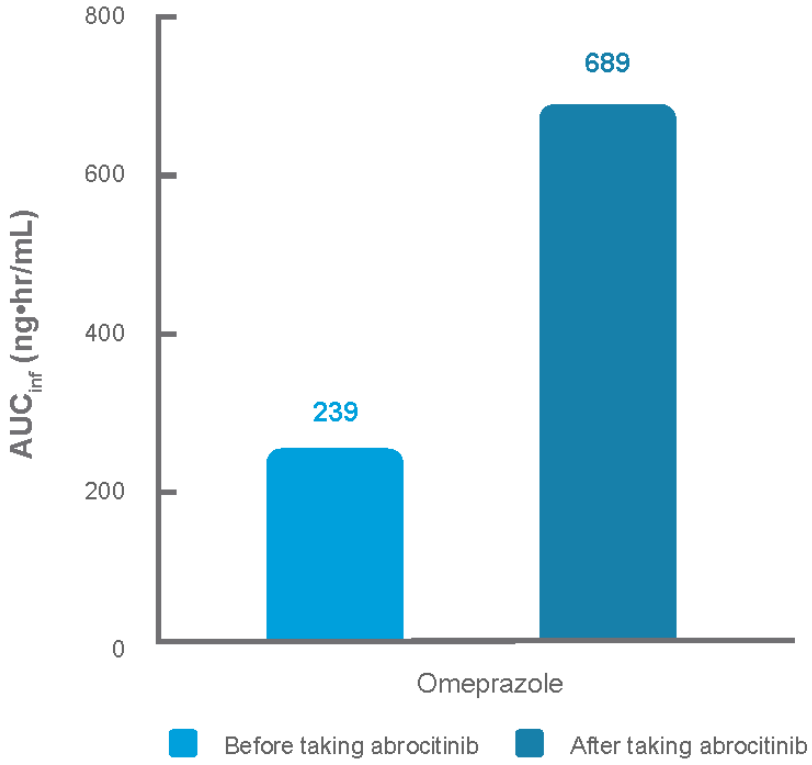
6153 ng•hr/mL. This is shown in Figure 3. Researchers considered the difference in the results as minor.

Figure 3. Blood Levels of Efavirenz Before and After Participants Had Taken Abrocitinib



- The estimated total amount of omeprazole in the blood from when omeprazole was taken until the omeprazole was removed from the body was 239 ng•hr/mL. When this was measured after participants had taken 200 mg abrocitinib, this was 689 ng•hr/mL. This is shown in Figure 4. Researchers considered the amount of omeprazole in the blood was almost double (189% higher) when taken with abrocitinib.

Figure 4. Blood Levels of Omeprazole Before and After Participants Had Taken Abrocitinib



Based on these results, the researchers have decided that the results are not likely the result of chance. Researchers considered the difference in the amount of caffeine and efavirenz in the blood that was seen before taking abrocitinib compared with after taking abrocitinib was not clinically significant. The level of omeprazole in the blood was higher after taking abrocitinib and this is likely to be clinically significant. These differences could have been due to chance.

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. Other studies may have different results.

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 unknown 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.

Seven out of 26 (27%) participants in this study had at least 1 medical problem. None of the participants left the study because of medical problems. The most common medical problems – those reported by at least 2 out of 26 participants (8%) – 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 at least 2 participants (8%) are listed.
- The **2nd** column tells how many of the 26 participants taking caffeine, efavirenz, and omeprazole reported each medical problem. Next to this number is the percentage of the 26 participants taking caffeine, efavirenz, and omeprazole who reported the medical problem.
- The **3rd** column tells how many of the 26 participants taking caffeine, efavirenz, and omeprazole after abrocitinib reported each medical problem. Next to this number is the percentage of the 26 participants

taking caffeine, efavirenz, and omeprazole after abrocitinib who reported the medical problem.

- Using these instructions, you can see that 0 out of 26 (0%) participants taking caffeine, efavirenz, and omeprazole reported increased blood pressure. A total of 2 out of 26 (8%) participants taking caffeine, efavirenz, and omeprazole after abrocitinib reported increased blood pressure.

Table 1. Commonly reported medical problems by study participants

Medical problem	100 mg Caffeine, 50 mg Efavirenz, and 10 mg Omeprazole (26 Participants)	100 mg Caffeine, 50 mg Efavirenz, and 10 mg Omeprazole after 200 mg Abrocitinib (26 Participants)
Increased blood pressure	0 out of 26 participants (0%)	2 out of 26 participants (8%)
Shaking	2 out of 26 participants (8%)	1 out of 26 participants (4%)

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.

There were no participants with serious medical problems and no participants died during this 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 **NCT05067439**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number B7451092

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

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