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 Studied:	Lotiglipron (PF-07081532)
Protocol Number:	C3991041
Dates of Study:	22 February 2023 to 29 May 2023
Title of this Study:	A Study on How Itraconazole and Cyclosporine May Affect the Amount of PF-07081532 in the Blood [A Phase 1, Open-Label, Fixed-Sequence Study to Evaluate the Effect of Itraconazole and Cyclosporine on the Single-Dose Pharmacokinetics of PF-07081532 in Overweight or Obese Adult Participants]
Date of this Report:	24 March 2024

– 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 obesity?

Obesity is a long-term medical condition caused by excessive body fat and can cause serious health problems. People living with obesity have more body fat than those who are overweight.

People who are overweight or have obesity are at a higher risk of Type 2 diabetes, high blood pressure, heart disease, and other health problems.

What is lotiglipron?

Lotiglipron is also known as PF-07081532. It is an investigational medicine because it is not approved for use by the health authorities outside of research studies. It is taken by mouth (oral).

Lotiglipron is a type of medicine known as a "glucagon-like peptide 1 (GLP-1) receptor agonist". Medicines of this type are designed to keep blood sugar at healthy levels. They may also slow down the digestion of food and increase the feeling of fullness after eating, which can lead to lower food intake.

Researchers thought that lotiglipron may help lower blood sugar and reduce body weight if taken with proper diet and exercise. However, based on safety concerns observed in participants from other lotiglipron studies, the Sponsor decided to stop the development of lotiglipron. No future studies are planned with lotiglipron.

What was the purpose of this study?

The main purpose of this study was to see how medicines called itraconazole and cyclosporine may affect the amount of lotiglipron in the blood of participants who have excess body fat. Researchers chose itraconazole and cyclosporine for this study as these may interact with lotiglipron when they are taken together.

- Itraconazole is an approved medicine to treat fungal infections. It was given in the study as a liquid that was taken by mouth.
- Cyclosporine is an approved medicine that weakens the immune system and is given to patients who have received organ transplant to prevent organ rejection. It was given in the study as a capsule that was taken by mouth.

In this study, participants took a single oral dose of lotiglipron. This study was not designed to test the effect of lotiglipron on blood sugar levels or body weight.

Researchers wanted to know:

- **How did itraconazole and cyclosporine affect the amount of lotiglipron in the blood?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested lotiglipron, itraconazole, and cyclosporine in a group of participants to learn how itraconazole and cyclosporine may affect the amount of lotiglipron in the blood.

During the study, participants took:

- 1 dose of lotiglipron on 3 different days
- 1 dose of cyclosporine
- Multiple doses of itraconazole

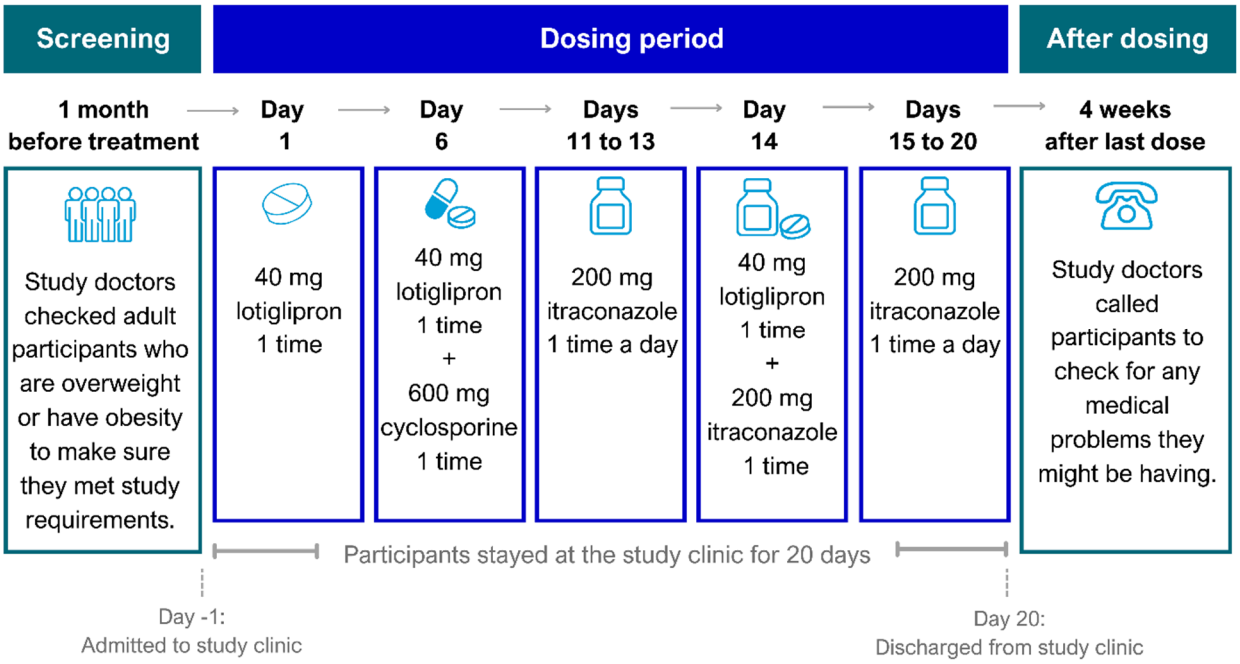
Participants stayed at the study clinic while they were taking lotiglipron, cyclosporine, and itraconazole. They stayed at the study clinic for a total of 20 days.

This was an open-label study. This means that researchers and participants knew the medications each participant was taking.

Researchers took blood samples from participants throughout the study. Researchers also checked the participants' health and asked them how they were feeling.

Figure 1 on the next page shows how the study was done.

Figure 1. How was this study done?



Where did this study take place?

The Sponsor ran this study at 1 study clinic in the United States.

When did this study take place?

It began on 22 February 2023 and ended on 29 May 2023.

Who participated in this study?

The study included adults who have a body mass index (BMI) of 25 or greater. The BMI is calculated using height and weight. It helps estimate a person's total body fat.

BMI Categories:

- Below 18.5 = underweight
- 18.5 to 24.9 = normal weight
- 25 to 29.9 = overweight
- 30 or greater = obesity

In the study,

- A total of 11 men and 5 women participated.
- All participants were from 18 to 56 years old.

All 16 participants who took part in the study completed the study.

How long did the study last?

Each participant was in the study for about 76 days (about 2 and a half months). The entire study took about 3 months to complete.

When the study ended in May 2023, 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 itraconazole and cyclosporine affect the amount of lotiglipron in the blood?

To answer this question, study doctors took blood samples from participants throughout the study. They measured the total amount of lotiglipron in the blood over time in nanogram hours per milliliter (ng•hr/mL).

Researchers compared the amount of lotiglipron in participants' blood:

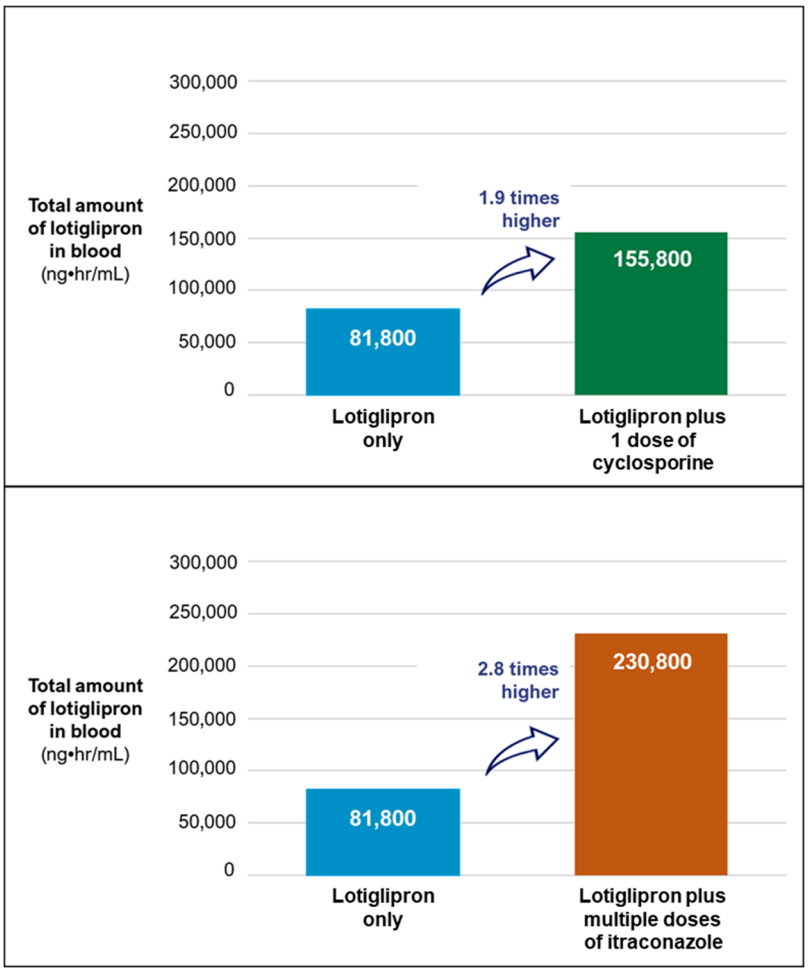
- On days when participants took lotiglipron only, and
- On days when they took lotiglipron with cyclosporine or itraconazole.

Study results showed that the amount of lotiglipron in the blood was higher when it was taken with cyclosporine or itraconazole than when it was taken alone.

Figure 2 below shows that compared to when lotiglipron was taken alone:

- The amount of lotiglipron in the blood was 1.9 times higher when lotiglipron was taken with 1 dose of cyclosporine.
- The amount of lotiglipron in the blood was 2.8 times higher when lotiglipron was taken with multiple doses of itraconazole.

Figure 2. How much lotiglipron was in the blood when it was taken with and without cyclosporine or itraconazole?



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.

A total of 11 out of 16 participants (68.8%) 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 in the study – those reported by more than 2 participants in total – are described in Table 1 on the next page.

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 2 participants in total are listed.
- The **2nd** column tells how many of the total participants reported each medical problem. Next to this number is the percentage of the total participants who reported the medical problem.
- For example, using these instructions, you can see that 7 out of the 16 participants (43.8%) reported feeling sick or queasy.

Table 1. Commonly reported medical problems by study participants	
Medical Problem	**All Participants (16 Participants)**
Feeling sick or queasy (also known as nausea)	7 out of 16 participants (43.8%)
Feeling hot	6 out of 16 participants (37.5%)
Loss of appetite	4 out of 16 participants (25.0%)
Indigestion	4 out of 16 participants (25.0%)
Headache	4 out of 16 participants (25.0%)
Diarrhea	3 out of 16 participants (18.8%)

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.

None of the participants had a serious medical problem. None of the 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:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C3991041**

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

www.clinicaltrials.gov	Use the study identifier **NCT05745701**

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!