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:	C3991009
Dates of Study:	01 August 2022 to 05 April 2023
Title of this Study:	A Study on How Lotiglipron is Processed in Adults With Liver Impairment Compared to Adults Without Liver Impairment [A Phase 1, Open-Label, Single-Dose, Parallel Group Study to Compare the Pharmacokinetics of PF-07081532 in Adult Participants With Varying Degrees of Hepatic Impairment Relative to Participants Without Hepatic Impairment]
Date of this Report:	16 April 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 liver impairment?

The liver is a body organ that helps break down food and rid the body of waste. The liver also plays an important role in breaking down other substances, such as medicines.

Liver damage or impairment happens when the liver is not working well enough to perform its functions. People with liver impairment may process substances, including medicines, differently from people with a properly working liver.

What is lotiglipron?

Lotiglipron is also known as PF-07081532. It is an investigational medicine because health authorities have not approved its use outside of research studies.

Lotiglipron is 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.

At the time of this study, researchers were studying lotiglipron as a possible treatment for people with Type 2 diabetes. 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 learn if the amount of lotiglipron in the blood over time was different in people who have liver impairment compared to people with a properly working liver.

This study did not test if lotiglipron helped participants with liver impairment.

Researchers wanted to know:

- **Was lotiglipron processed differently in participants with liver impairment compared to those with a properly working liver?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested lotiglipron in 4 groups of participants to see how the amount of lotiglipron in the blood differs between those with a properly working liver and those with liver impairment of different severities:

Group 1: Participants with a properly working liver.

Group 2: Participants with mild liver impairment.

Group 3: Participants with moderate liver impairment.

Group 4: Participants with severe liver impairment.

Participants took 1 tablet of lotiglipron 20 milligrams (also known as mg) by mouth as a single dose. Participants took lotiglipron after a meal. The

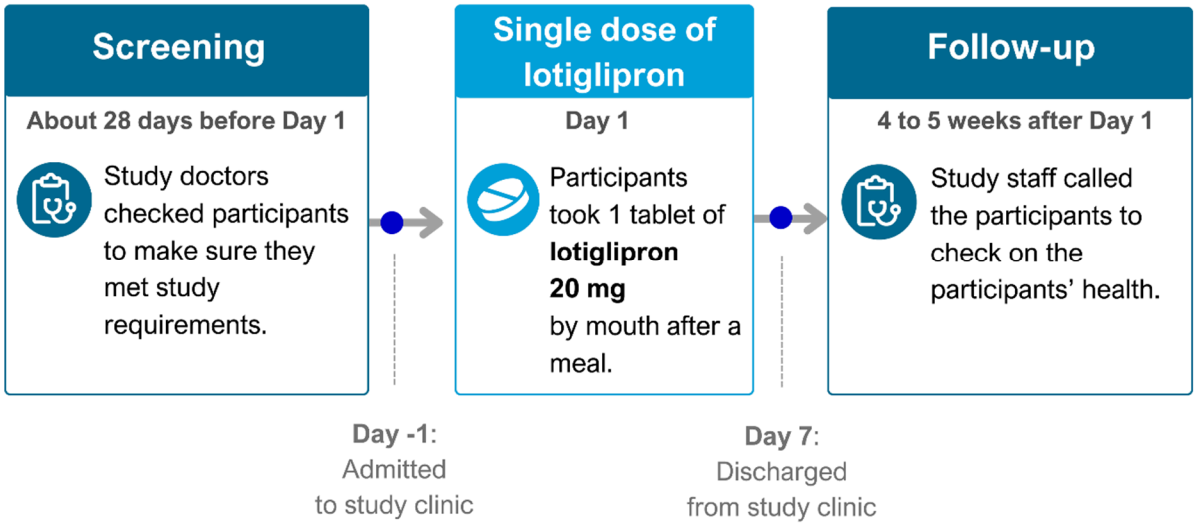
participants, study doctors and staff, and researchers knew that participants took lotiglipron. This is called an “open-label” study.

Participants stayed at the study clinic for 7 nights, starting the day before they took lotiglipron. Study staff then followed up with the participants 4 to 5 weeks after they took lotiglipron on Day 1 to check on them.

Researchers took blood and urine samples from participants throughout the study. Researchers also checked the participants’ health using other tests and asked them how they were feeling.

Figure 1 shows how the study was done.

Figure 1. How was this study done?



Where did this study take place?

This study ran at 2 locations in the United States.

When did this study take place?

It began on 01 August 2022 and ended on 05 April 2023.

Who participated in this study?

The study included adults who have a properly working liver and adults who have mild, moderate, or severe liver impairment.

- A total of 18 men and 6 women participated.
- All participants were from 36 to 71 years old.

Of the 24 participants who started the study and took lotiglipron, 23 participants completed the study. One (1) participant did not finish the study because of their own decision to stop taking part in the study.

How long did the study last?

Study participants were in the study for about 5 to 9 weeks. The entire study took about 8 months to complete.

When the study ended in April 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?

Was lotiglipron processed differently in participants with liver impairment compared to those with a properly working liver?

To answer this question, study doctors looked at the results of participants' blood tests. Researchers checked for the following:

- amount of lotiglipron in the blood over time from the day the participants took lotiglipron up to the time when they left the study clinic 7 days later.
- the free fraction of lotiglipron in the blood over time.

The **free fraction** of a medicine is the portion of a medicine that does not attach to anything, for example a protein, in the blood.

Researchers then compared the results of participants with liver impairment of different severities to that of participants with a properly working liver.

Results in this study showed that there was no big difference in the amount of lotiglipron in the blood between participants with liver impairment of different severities and those with a properly working liver.

- The total amount of lotiglipron in the blood over time (from the day they took lotiglipron to the time when the lowest amount was found in the blood) was about similar across groups.
- The highest amount, also called maximum concentration, of lotiglipron in the blood was about 30% lower in participants with severe liver impairment compared to those with a properly working liver. The maximum concentration of lotiglipron in the blood was about similar in those with mild and moderate liver impairment and those with a properly working liver.

Results also showed that the fraction of free lotiglipron was:

- higher in participants with severe liver impairment compared to other groups.
- about similar in those with mild and moderate liver impairment and those with a properly working liver.

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 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 2 out of 24 participants (8%) had at least 1 medical problem in this study.

- One (1) had low blood sugar levels. This participant was from the group with a properly working liver.
- One (1) had nausea (queasy feeling), vomiting, and dizziness. This participant was from the group with severe liver impairment.

None of the participants left the study because of medical problems.

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 **C3991009**

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

www.clinicaltrials.gov	Use the study identifier **NCT05478603**

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!