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:	C3991007
Dates of Study:	29 August 2022 to 20 July 2023
Title of this Study:	A Study on How Lotiglipron Is Processed in Adults With Diabetes and Kidney Dysfunction [A Phase 1, Open-Label, Single-Dose, Parallel-Group Study to Evaluate the Pharmacokinetics of PF-07081532 in Adult Participants With Type 2 Diabetes Mellitus With Varying Degrees of Renal Impairment Relative to Participants Without Renal Impairment]
Date of this Report:	11 June 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 Type 2 diabetes mellitus?

Type 2 diabetes mellitus (T2DM) is a common form of diabetes. Over time, T2DM can cause higher than normal levels of sugar in the blood. This may harm the health of the person with T2DM.

Insulin is a hormone or chemical messenger that controls the amount of sugar in the blood after eating. A person with T2DM either does not make enough insulin or their body cannot properly use the insulin it makes. Every person needs some sugar in the blood as their body uses this sugar for energy. If a person has T2DM, and there is too much sugar in their blood, this can cause lots of different health problems, including stroke, and may even lead to death.

Some people with T2DM can control the amount of sugar in their blood with diet, but others will need medicine to help them do this.

What is lotiglipron?

Lotiglipron is also known as PF-07081532. It is an investigational medicine, which means health authorities have not approved its use outside of research studies. It is taken by mouth.

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.

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 T2DM and different degrees of kidney dysfunction compared to those with properly working kidneys.

> Kidney dysfunction happens when the kidneys are not working well enough to perform their functions. People with kidney dysfunction may process substances, including medicines, differently from people with properly working kidneys.

This study did not test if lotiglipron helped participants with T2DM or kidney dysfunction.

Researchers wanted to know:

- **Was lotiglipron processed differently in participants with kidney dysfunction compared to those with properly working kidneys?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers planned to test lotiglipron in 4 groups of participants with T2DM to see how the amount of lotiglipron in the blood differs between those with properly working kidneys and those with kidney dysfunction of different severities:

Group 1: Participants with properly working kidneys.

Group 2: Participants with **mild** kidney dysfunction.

Group 3: Participants with **moderate** kidney dysfunction.

Group 4: Participants with **severe** kidney dysfunction.

> The study ended early and before people with T2DM and properly working kidneys were enrolled. Because of this, only participants with T2DM and kidney dysfunction of different severities were signed up.

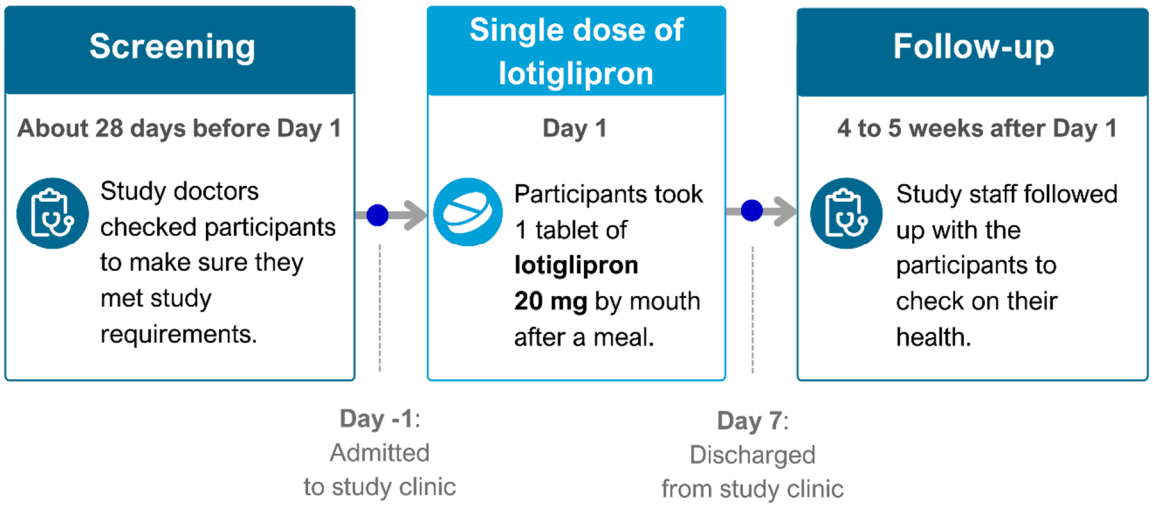
Participants took 1 tablet of lotiglipron 20 milligrams (also known as mg) by mouth as a single dose on Day 1. Participants took lotiglipron after a meal. The participants, study doctors and staff, and researchers knew that participants took lotiglipron. This is called an “open-label” study.

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 below 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 29 August 2022 and ended on 20 July 2023.

The Sponsor decided to stop this study early because of safety concerns observed in participants from other lotiglipron studies (where lotiglipron was given in multiple doses).

Who participated in this study?

The study included adults 18 years or older who met the following study requirements:

- Have T2DM
- Either have properly working kidneys or have mild, moderate, or severe kidney dysfunction

A total of 18 participants started and took a single dose of lotiglipron.

- A total of 11 men and 7 women participated.
- All participants were from 52 to 83 years old.

Of the 18 participants who started the study, 17 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?

Participants were in the study for about 6 to 10 weeks. The entire study took about 11 months to complete.

When the study ended in July 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 kidney dysfunction compared to those with properly working kidneys?

The study ended early and before people with T2DM and properly working kidneys were enrolled. Because of this, the study could not answer whether lotiglipron was processed differently in people with T2DM and kidney dysfunction compared to those with T2DM but with properly working kidneys.

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 4 out of 18 participants (22.2%) had at least 1 medical problem in this study. The following list shows the medical problems experienced by these participants.

Mild kidney dysfunction group (out of 5 participants)	**Moderate kidney dysfunction group** (out of 5 participants)	**Severe kidney dysfunction group** (out of 8 participants)
One (1) participant had headache.	One (1) participant had queasy feeling (also called nausea). One (1) participant had headache and vomiting.	One (1) participant had COVID-19.

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 or died during the study.

In this study, a single dose of lotiglipron 20 mg was found to be safe in and well tolerated by participants with T2DM who also have kidney dysfunction of different severities.

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 **C3991007**

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

www.clinicaltrials.gov	Use the study identifier **NCT05510245**

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!