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: C3991006

Dates of Study: 21 December 2022 to 15 March 2023

Title of this Study: A Study to Find Out What Happens to Lotiglipron in the Body of Healthy Men

[A Phase 1, Open-Label, 2-Period, Fixed Sequence Study to Investigate the Absorption, Distribution, Metabolism and Excretion of [^{14}C]PF-07081532 and to Assess the Absolute Bioavailability and Fraction Absorbed of PF-07081532 in Healthy Male Participants Using a [^{14}C]-Microtracer Approach]

Date of this Report: 18 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 are type 2 diabetes mellitus and obesity?

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

Obesity is a medical condition seen when a person has too much body fat that is damaging to their health. Obesity can increase the risk of developing T2DM.

Both T2DM and obesity raise the chance of getting many other health problems, such as heart disease, high blood pressure, high cholesterol, liver disease, breathing problems while sleeping, and certain cancers.

Some of the ways to treat T2DM and obesity include diet, exercise, and taking prescribed medications.

What is lotiglipron?

Lotiglipron, which is also known as PF-07081532, is an investigational medicine. It is not approved for use by the health authorities.

Lotiglipron is known as a “glucagon-like peptide 1 (GLP-1) receptor agonist”. It is meant to help the body produce a natural hormone called GLP-1, which is known to make people feel full. Lotiglipron is also meant to help the body release more insulin in the blood to keep the blood sugar at healthy levels.

In this study, lotiglipron was either taken orally (by mouth) or injected into the vein, also called intravenously (IV).

What was the purpose of this study?

The purpose of this study was to find out:

- how lotiglipron was taken up, moved through the body, broken down in the body, and removed from the body.
- how the body processed lotiglipron and how much of it was broken down or changed by the body. Researchers measured the amount of substances called metabolites, which are made as a drug is broken down by the body.

Participants in this study were healthy men. The study did not test if lotiglipron helps in treating T2DM or obesity.

Researchers wanted to know:

- **How much lotiglipron was found in the participants' urine and feces?**
- **How was lotiglipron broken down and changed into metabolites in the participants' blood, feces, and urine?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested lotiglipron in a group of healthy men. In this study, participants took a radiolabeled form of lotiglipron. A radiolabel is a substance with a tiny amount of radiation that is attached to lotiglipron. It allows researchers to measure the amount of lotiglipron that goes into the blood or leaves the body in the urine and feces.

Participants took part in Period 1 before moving to Period 2. In both periods, after having breakfast, participants received lotiglipron as described below.

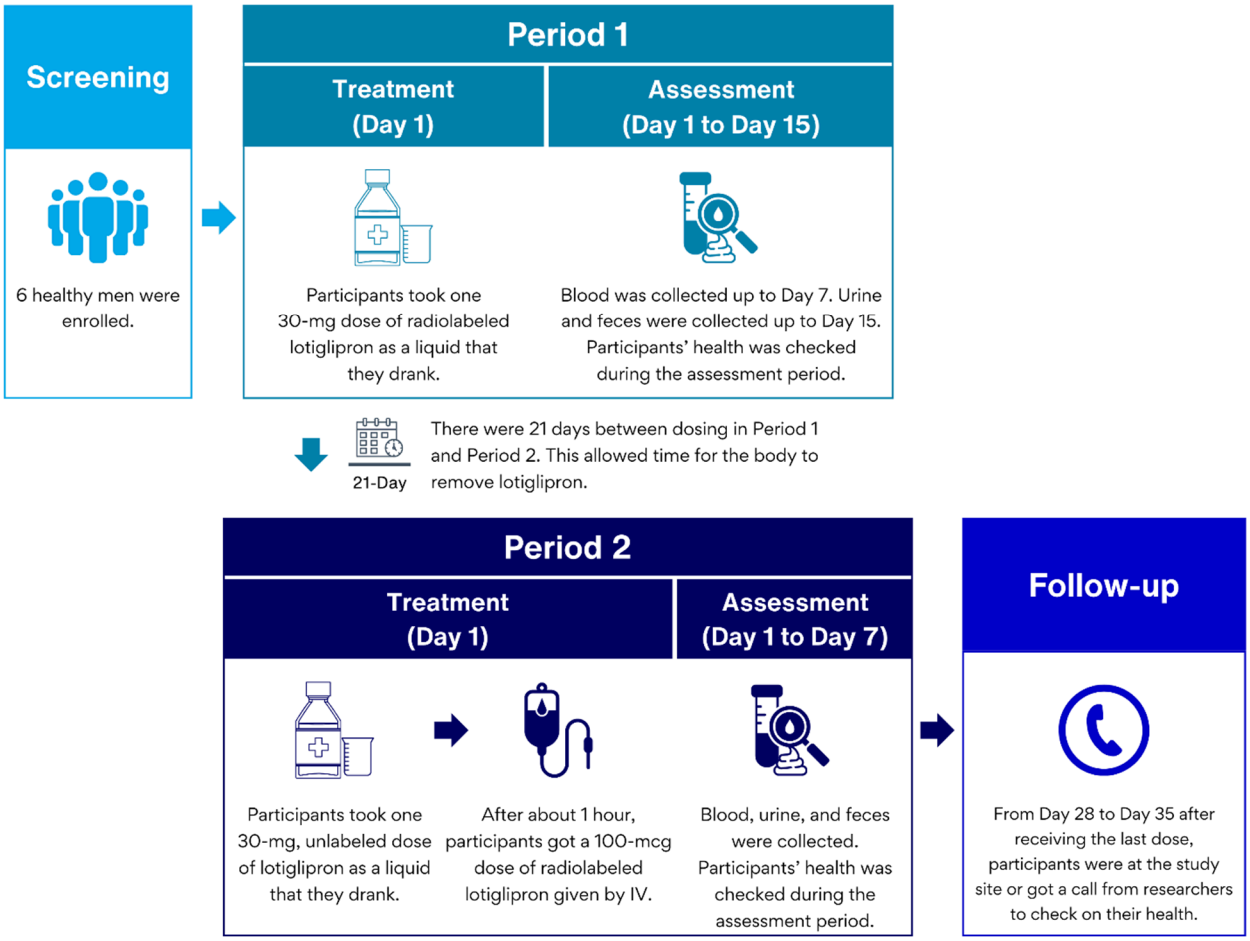
- On Day 1 of Period 1, participants took one 30-milligram (mg) dose of radiolabeled lotiglipron as a liquid that they drank.
- On Day 1 of Period 2, participants took one 30-mg, unlabeled dose of lotiglipron as a liquid that they drank. After about 1 hour, participants got a 100-microgram (mcg) dose of radiolabeled lotiglipron, which was given by IV (into a vein).

In both periods, researchers took blood, urine, and fecal samples from participants. Researchers also checked the participants' health during the study and asked them how they were feeling.

The participants and researchers knew what treatments the participants received. This is known as an "open-label" study.

Figure 1 shows what happened in the study.

Figure 1. Overall study design



Where did this study take place?

The Sponsor ran this study at 1 location in the Netherlands.

When did this study take place?

It began on 21 December 2022 and ended on 15 March 2023.

Who participated in this study?

The study included 6 healthy men.

- All participants were between the ages of 18 and 60 years.
- All 6 participants finished the study.

How long did the study last?

Participants were in the study for up to 12 weeks. The entire study took about 3 months to complete.

When the study ended in March 2023, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

No future studies are planned with lotiglipron.

What were the results of the study?

How much lotiglipron was found in the participants' urine and feces?

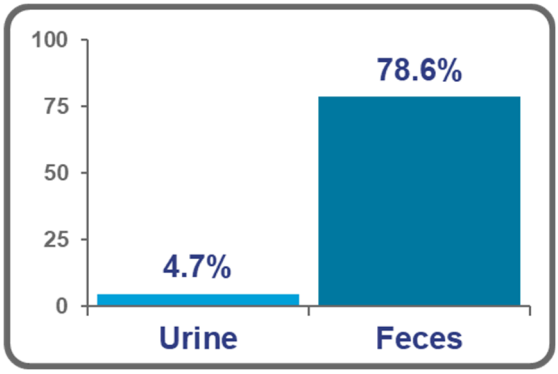
To answer this question, researchers checked the amount of lotiglipron that left the body of participants in Period 1 in the urine and feces.

Over 15 days (or 360 hours) after participants took lotiglipron in Period 1, about 83% of radiolabeled lotiglipron had left the body.

- Most of the radiolabeled lotiglipron left in the feces (78.6%).
- Some of the radiolabeled lotiglipron left in the urine (4.7%).

Figure 2 shows the amount of radiolabeled lotiglipron found in the participant's urine and feces.

Figure 2. How much radiolabeled lotiglipron left the body in the urine and feces?



How was lotiglipron broken down and changed into metabolites in the participants' blood, feces, and urine?

After lotiglipron entered the body, some of it was unchanged, while some of it was broken down by the body to produce substances called metabolites.

Researchers checked the amount of lotiglipron and its metabolites in the blood, feces, and urine of participants in Period 1.

Over 15 days (or 360 hours) after participants took lotiglipron in Period 1, the 2 most common metabolites seen were the following:

- 9% of lotiglipron was broken down into a metabolite called PF-07943285, which was found in the blood.
- 14% of lotiglipron was broken down into a metabolite called PF-07943283, which was found in the feces.

A very small amount of lotiglipron left the body in the urine. Researchers found some other metabolites in the blood, feces, and urine, but these were in small amounts.

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.

In Period 1, 4 out of 6 participants (67%) had at least 1 medical problem.
In Period 2, 2 out of 6 participants (33%) had at least 1 medical problem.
No participants left the study because of a medical problem.

The medical problems reported by more than 1 participant in the study are described in Table 1.

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 reported during the study by more than 1 participant.
- The **2nd** column tells how many of the participants reported each medical problem after receiving lotiglipron in Period 1. Next to this number is the percentage of the participants who reported the medical problem after receiving lotiglipron in Period 1.
- The **3rd** column tells how many of the participants reported each medical problem after receiving lotiglipron in Period 2. Next to this number is the percentage of the participants who reported the medical problem after receiving lotiglipron in Period 2.
- Using these instructions, you can see that, for example:
    - 2 out of 6 participants (33%) had a headache after receiving lotiglipron in Period 1.
    - 1 out of 6 participants (17%) had a headache after receiving lotiglipron in Period 2.

Table 1. Medical problems reported by more than 1 participant		
Medical Problem	**Period 1 (30-mg, radiolabeled, oral lotiglipron) (6 Participants)**	**Period 2 (30-mg, unlabeled, oral lotiglipron plus 100-mcg, radiolabeled, IV lotiglipron) (6 Participants)**
Headache	2 out of 6 participants (33%)	1 out of 6 participants (17%)
Queasy feeling or nausea	2 out of 6 participants (33%)	0 out of 6 participants (0%)

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 in the study had serious medical problems.

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:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C3991006**

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

www.clinicaltrials.gov	Use the study identifier **NCT05652647**

This study is also identified using the EU clinical trial registration number 2022-003311-29.

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!