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:	Lotiglipron (PF-07081532)
Protocol Number:	C3991003
Dates of Study:	22 December 2021 to 15 June 2022
Title of this Study:	Study Looking at Use of PF-07081532 in Adults with Type 2 Diabetes [Phase 1, Randomized, Double-Blind, Sponsor-Open, Placebo-Controlled Study to Assess the Safety, Tolerability, and Pharmacokinetics of Multiple Oral Doses of PF-07081532 in Adult Participants With Type 2 Diabetes Mellitus.]
Date(s) of this Report:	19 June 2023

– 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 and what is 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.

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.

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

What is lotiglipron?

Lotiglipron, which is also known as PF-07081523, is an investigational medicine. It is not approved for use by the health authorities. It is a tablet that is taken by mouth. Lotiglipron is a type of medicine known as a "glucagon-like peptide 1 receptor agonist". It is intended to keep blood sugar at healthy levels by increasing the amount of insulin released in the blood. These types of medicine also slow down the digestion of food and may increase the feeling of fullness after eating. This may lower food intake. Researchers think that lotiglipron may help lower blood sugar levels and reduce body weight if taken alongside appropriate diet and exercise.

What was the purpose of this study?

This was a Phase 1 study. This means the researchers are mainly looking to see if different doses of lotiglipron were safe when given to people with T2DM and people with obesity who do not have T2DM.

Researchers wanted to know:

- **Were the different does of lotiglipron safe when given to people with T2DM and to people with obesity who do not have T2DM?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

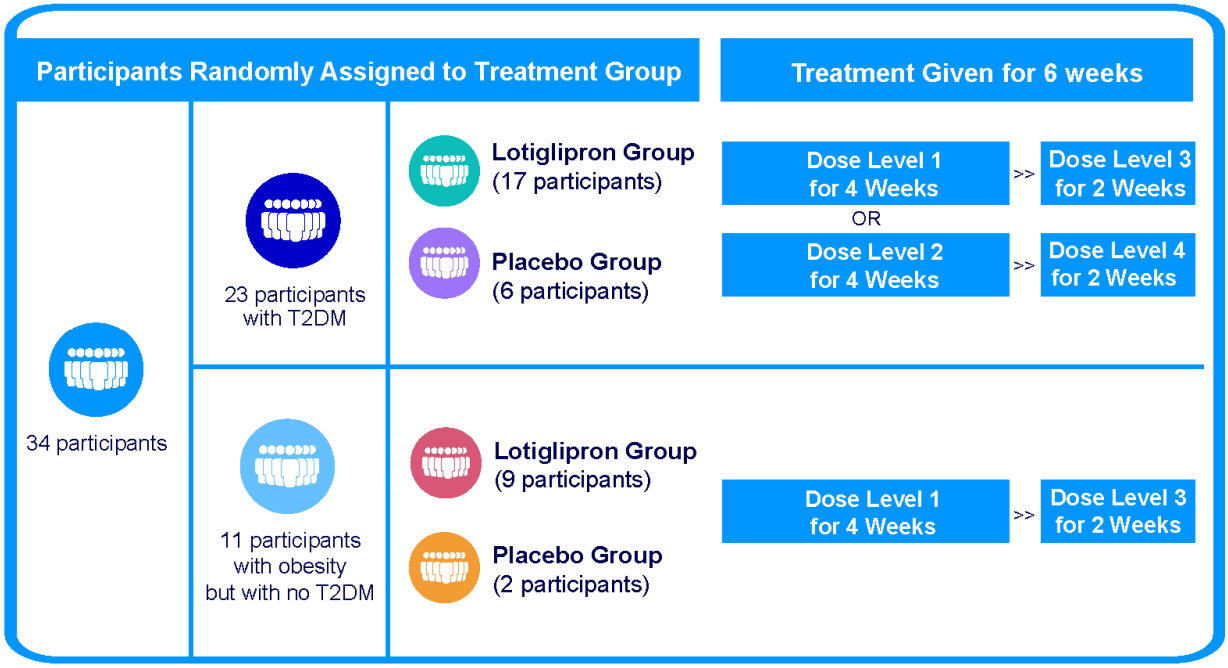
There were 2 different groups of participants in this study: participants with T2DM and participants with obesity who do not have T2DM.

In this study, participants were given either lotiglipron or placebo. A placebo does not have any medicine in it, but it looks just like the study medication. Researchers measured the effect of lotiglipron by comparing safety measurements and medical problems between participants who took different doses of lotiglipron and participants who took placebo.

Participants took lotiglipron or placebo once each day for a total of 6 weeks. They were given one dose level for the first 4 weeks and then had their dose increased. They took this new dose for a further 2 weeks. This is shown in Figure 1.

The participants and the researchers at the study clinic did not know who took lotiglipron and who took the placebo. This is known as a "blinded" study. Participants were assigned to each group by chance alone.

Figure 1: Study Plan



To find out if lotiglipron was safe, the researchers used different tests and assessments. This included testing blood and urine throughout the study. Participants also had their heart rate, blood pressure, and the electrical activity of the heart monitored. To look at the electrical activity of the heart, the researchers used an electrocardiogram (ECG) machine. The researchers also checked the participants' health and asked them how they were feeling during the study.

Researchers then compared the results of participants taking lotiglipron with participants taking placebo.

This was done to help researchers try to understand if changes in the participant's health or medical problems they had during the study were related to the study medication or related to something else.

Where did this study take place?

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

When did this study take place?

It began 22 December 2021 and ended 15 June 2022.

Who participated in this study?

The study included 23 adult participants with T2DM as well as 11 adult participants who had obesity but who did not have T2DM and who were otherwise healthy.

- A total of 24 men participated
- A total of 10 women participated
- All participants were between the ages of 28 and 69 years

Of the 34 participants who started the study, 32 (94.1%) finished the study. There were 2 (5.9%) participants who did not finish the study. One of these took lotiglipron and the other took placebo. Both participants left the study for reasons which were not related to the study medication. There were no participants who left the study due to effects related to lotiglipron.

How long did the study last?

Study participants were in the study for up to 16 weeks. The entire study took almost 6 months to complete.

When the study ended in June 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?

Was lotiglipron safe?

To find out if treatment with lotiglipron was safe, the researchers looked at laboratory test results, blood pressure and pulse rate measurements, ECG assessments, and medical problems.

Note: Medical problems are discussed in this next section of this summary.

Were the different doses of lotiglipron safe when given to participants with T2DM and participants with obesity but who did not have T2DM?

The researchers did not have any concerns about the safety of lotiglipron at any of the doses tested. There were no harmful trends in the results of any safety tests done as part of this study. This included laboratory tests on blood and urine, blood pressure readings, pulse rates, or heart measurements using an ECG.

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 25 out of 34 (73.5%) participants in this study had at least 1 medical problem. No participants left the study because of medical problems. The most common medical problems – those reported by 2 or more participants – 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 in participants who had T2DM. All medical problems reported by 2 or more participants are listed.
- The **2nd** column tells how many of the 17 participants taking lotiglipron who reported each medical problem. Next to this number is the percentage of the 17 participants taking lotiglipron who reported the medical problem.

- The **3rd** column tells how many of the 6 participants taking placebo who reported each medical problem. Next to this number is the percentage of the 6 participants taking placebo who reported the medical problem.
- Using these instructions, you can see that 11 out of the 17 (64.7%) participants taking lotiglipron reported nausea. There were no participants taking placebo who reported nausea.

These instructions can also be followed to help you understand Table 2. Table 2 lists medical problems that were commonly reported during the study in participants who had obesity but who did not have T2DM. All medical problems reported by 2 or more participants are listed

Table 1. Commonly reported medical problems by study participants who had T2DM

Medical Problem	Lotiglipron (17 Participants)	Placebo (6 Participants)
Nausea	11 out of 17 participants (64.7%)	0
Diarrhea	5 out of 17 participants (29.4%)	4 out of 6 participants (66.7%)
Bloating or stomach bloating	7 out of 17 participants (41.2%)	0

Table 1. Commonly reported medical problems by study participants who had T2DM		
Medical Problem	**Lotiglipron (17 Participants)**	**Placebo (6 Participants)**
Indigestion	5 out of 17 participants (29.4%)	1 out of 6 participants (16.7%)
Constipation	5 out of 17 participants (29.4%)	0
Stomach acid reflux and heartburn	3 out of 17 participants (17.6%)	1 out of 6 participants (16.7%)
Belching or burping	2 out of 17 participants (11.8%)	1 out of 6 participants (16.7%)
Poor appetite	7 out of 17 participants (41.2%)	1 out of 6 participants (16.7%)
Headache	4 out of 17 participants (23.5%)	3 out of 6 participants (50.0%)
Feeling full too quickly when eating	3 out of 17 participants (17.6%)	0

Table 2. Commonly reported medical problems by study participants who had obesity but who did not have T2DM		
Medical Problem	**Lotiglipron (9 Participants)**	**Placebo (2 Participants)**
Nausea	4 out of 9 participants (44.4%)	0
Indigestion	4 out of 9 participants (44.4%)	0
Bloating or stomach bloating	3 out of 9 participants (33.3%)	0
Vomiting	3 out of 9 participants (33.3%)	0
Poor appetite	4 out of 9 participants (44.4%)	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.

There were no participants who had serious medical problems during the study.

There were no participants who 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 C3991003

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

www.clinicaltrials.gov	Use the study identifier **NCT05158244**

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!