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 study participants. The results of this study might be different than the results of other studies that the researchers review.

Sponsor: Pfizer Inc.

Medicine(s) Studied: Danuglipron (PF-06882961)

Protocol Number: C3421007

Dates of Study: 15 December 2020 to 13 May 2021

Title of this Study: Study to Compare How Two Different Doses of Danuglipron Affect the Level of Rosuvastatin and Midazolam in the Blood of Adult Participants With Obesity

[A Phase 1, Open-Label, Fixed Sequence Study to Evaluate the Effect of Two Steady State Dose Levels of PF-06882961 on the Pharmacokinetics of Single Oral Doses of Rosuvastatin and Midazolam in Otherwise Healthy Adult Participants With Obesity]

Date(s) of this Report: 10 July 2022

– 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. A person with T2DM either does not make enough insulin or their body cannot use the insulin it makes properly. Insulin is a hormone or chemical messenger that controls the amount of sugar in the blood after eating. Every person needs some sugar in the blood as their body uses this sugar for energy. If a person has T2DM, there is too much sugar in their blood and 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 can increase the risk of developing T2DM.

What is danuglipron?

Danuglipron, also known by the name PF-06882961, is a new type of glucagon-like peptide-1 (GLP-1) receptor agonist that is being developed. Some GLP-1 receptor agonists have been licensed for use in people with T2DM, and these are given by injection. Danuglipron is a tablet that is taken twice a day.

GLP-1 is a hormone produced by the body that increases the amount of insulin that is produced after a meal. The word agonist means the medicine needs to bind to something in the body to have an effect, which in this case is to mimic or copy GLP-1. GLP-1 receptor agonists cause the body to release more insulin, which may help control the amount of sugar in the blood in T2DM. GLP-1 receptor agonists also help to increase satiety, which means the person feels fuller after eating and may not eat as much at meals.

What was the purpose of this study?

The purpose of this study was to compare levels of rosuvastatin in the blood when 2 different doses of danuglipron were taken or when danuglipron was not taken with the rosuvastatin. Rosuvastatin is a medicine used to reduce cholesterol in the blood.

The researchers also wanted to compare levels of midazolam in the blood when 2 different doses of danuglipron were taken or when danuglipron was not taken with the midazolam. Midazolam is a medicine used to help with anxiety.

The medicines taken in a study are often called study treatment. The participants in this study were healthy adults and took danuglipron, rosuvastatin, and midazolam.

This is an early study that will help researchers plan future studies. This study did not test if danuglipron helps to improve control of blood sugar in T2DM.

Researchers wanted to know:

- **How did the amount of rosuvastatin and midazolam in the blood change when taken with 2 different doses of danuglipron?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested 2 different doses of danuglipron on a group of adult participants with obesity, but who were otherwise healthy, to learn how the amount of rosuvastatin and midazolam in the blood was changed when taken with danuglipron.

Participants were to stay at the study center for study periods 1 to 8 and were to take rosuvastatin (one 10 mg dose), midazolam (one 2 mg dose) and danuglipron (at different doses) as follows:

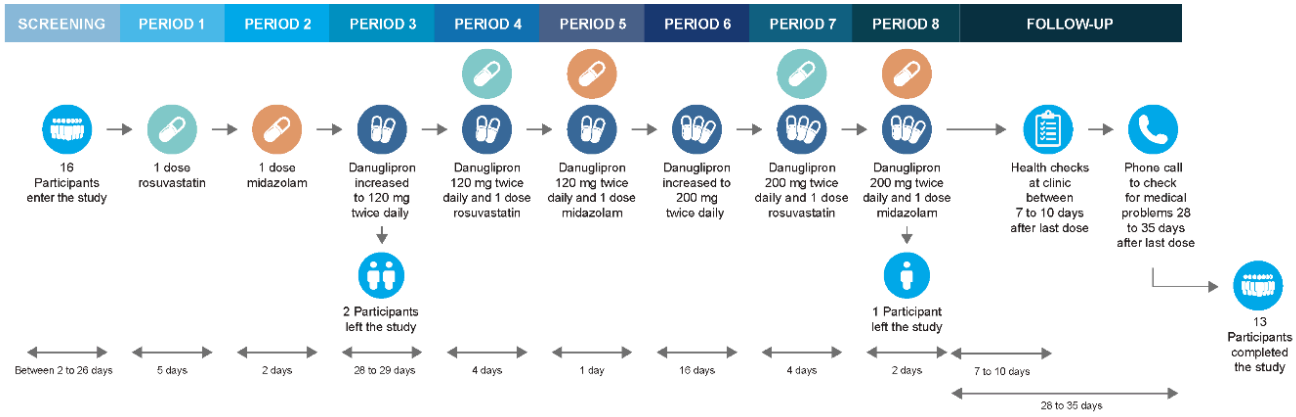
- Period 1 (5 days): one dose of 10 mg rosuvastatin only

- Period 2 (2 days): one dose of 2 mg midazolam only on the first day
- Period 3 (28 to 29 days): gradual dosing of danuglipron up to 120 mg twice daily
- Period 4 (4 days): danuglipron 120 mg twice daily and one dose of 10 mg rosuvastatin on the first day
- Period 5 (1 day): danuglipron 120 mg twice daily and one dose of 2 mg midazolam
- Period 6 (16 days): gradual dosing of danuglipron up to 200 mg twice daily
- Period 7 (4 days): 200 mg danuglipron twice daily and one dose of 10 mg rosuvastatin on the first day
- Period 8 (2 days): 200 mg danuglipron twice daily and one dose of 2 mg midazolam on the first day

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

At the end of Period 8, participants had to return to the study center 7 to 10 days after their last dose of study medication for health checks. They then received a telephone call 28 to 35 days after their last dose of study medication to check on their health.

The study design is shown in the following figure.



Researchers compared the levels of rosuvastatin and midazolam in the blood of participants who had taken these medicines along with 2 different doses of danuglipron.

The participants and researchers knew who took each type of medicine. This is known as an "open-label" study.

Where did this study take place?

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

When did this study take place?

It began 15 December 2020 and ended 13 May 2021.

Who participated in this study?

This study included adult participants with obesity, but who were otherwise healthy.

- A total of 8 men participated
- A total of 8 women participated
- All participants were between the ages of 30 and 63 years

Of the 16 participants who started the study, 13 participants finished the study.

Three (3) participants stopped taking the study treatment by their choice or a doctor decided it was best for a participant to stop treatment. Two (2) of these participants stopped treatment, either permanently due to a fall or temporarily because of retching or dry heaving, and 1 participant stopped treatment because of other reasons.

How long did the study last?

Study participants were in the study for about 17 weeks. The entire study took around 5 months to complete.

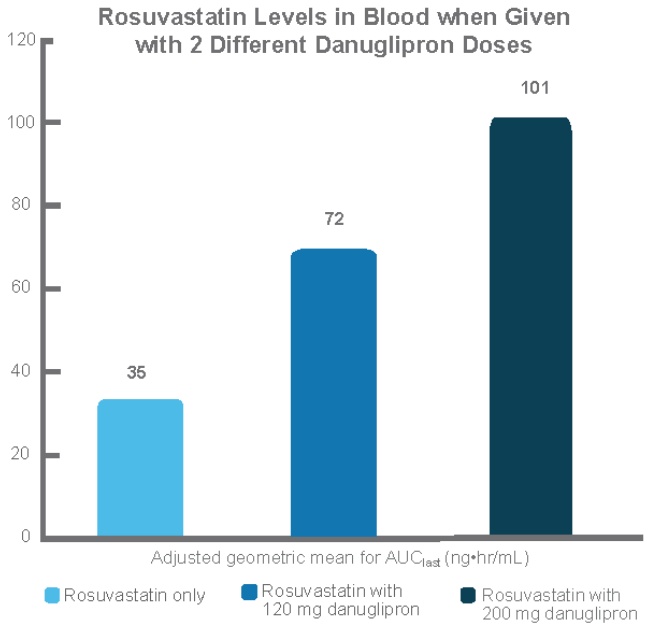
When the study ended in May 2021, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

What were the results of the study?

How did the amount of rosuvastatin and midazolam in the blood change when taken with 2 different doses of danuglipron?

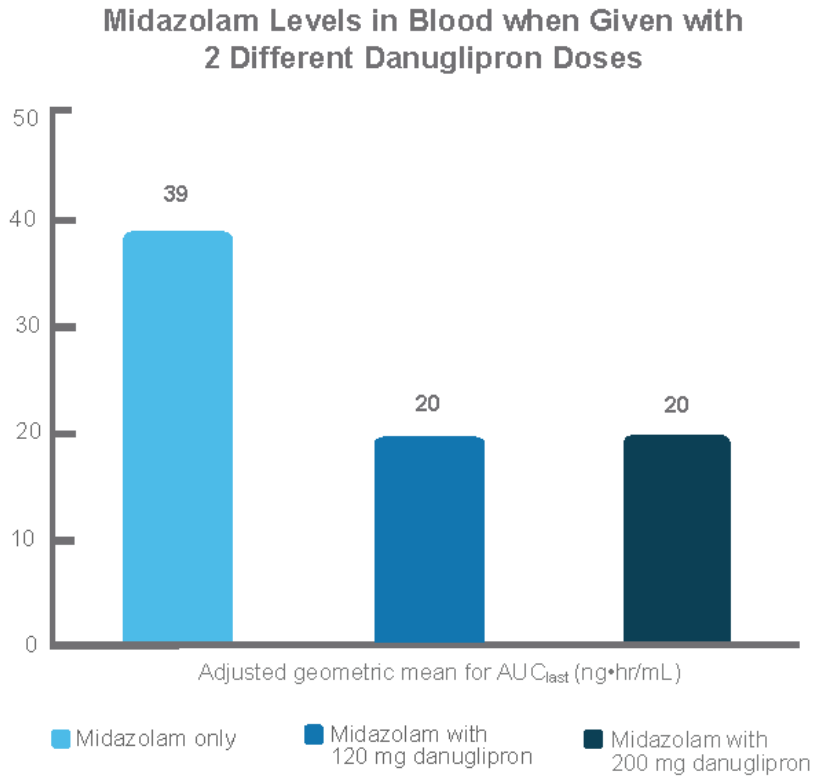
What was the amount of rosuvastatin in the blood before and after participants took 120 mg or 200 mg danuglipron?

- The total amount of rosuvastatin in the blood from when rosuvastatin was taken to the time when the lowest amount was detected in the blood was 35 nanogram hours per milliliter, also called ng•hr/mL. The ng•hr/mL is a unit used to measure total amount of drug over time in the blood. When rosuvastatin was taken while the participant was taking 120 mg danuglipron, this was increased to 72 ng•hr/mL, and when the participant was taking 200 mg danuglipron, this was further increased to 101 ng•hr/mL (see figure below).



What was the amount of midazolam in the blood before and after participants took 120 mg or 200 mg danuglipron?

- The total amount of midazolam in the blood from when midazolam was taken to the time when the lowest amount was detected in the blood was 39 ng•hr/mL. When midazolam was taken while the participant was taking 120 mg danuglipron, this was decreased to 20 ng•hr/mL, and when the participant was taking 200 mg danuglipron, this was still 20 ng•hr/mL (see figure below).



Based on these results, the researchers have determined that the results are not likely the result of chance. Rosuvastatin and midazolam may act differently in the body when taken alongside danuglipron.

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.

Fifteen (15) out of 16 (94%) participants in this study had at least 1 medical problem. There was 1 (6%) participant who stopped taking 120 mg danuglipron after a fall and the researchers did not think this fall was related to study medication. There was 1 (6%) participant who temporarily stopped taking 200 mg danuglipron because of retching or dry heaving. The researchers thought the retching or dry heaving was related to the study medication. There was 1 participant who left the study for other reasons. In total, there were 13 (81%) participants who completed the study. The most common medical problems – those reported by 2 or more participants at any point during the study – 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 at any point during the study. All medical problems reported by 2 or more participants are listed.
- The **2nd** column tells how many of the 16 participants in the study reported each medical problem. Next to this number is the percentage of the 16 participants in the study who reported the medical problem at any point during the study. Using these instructions, you can see that 13 out of the 16 (81%) participants in the study had nausea.

Table 1. Commonly reported medical problems by study participants during the study	
Medical Problem	**Overall (16 Treated Participants)**
Nausea	13 out of 16 participants (81%)
Constipation	12 out of 16 participants (75%)
Laboratory test showing kidneys not cleaning blood as fast as normal	11 out of 16 participants (69%)
Headache	7 out of 16 participants (44%)
Indigestion	6 out of 16 participants (38%)
Vomiting	6 out of 16 participants (38%)
Feeling full sooner than normal or after eating less than usual	5 out of 16 participants (31%)
Abdominal pain	4 out of 16 participants (25%)
Abdominal swelling	3 out of 16 participants (19%)
Dizziness	3 out of 16 participants (19%)
Feeling tired	3 out of 16 participants (19%)
Low blood sugar	3 out of 16 participants (19%)
Sleepiness	2 out of 16 participants (13%)
Decreased appetite	2 out of 16 participants (13%)

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.

One (1) participant (6%, or 1 out of 16 participants) had a serious medical problem. This was picked up during a routine blood test taken on the day the participant took their last dose of study medication. This test showed the liver function test results to be higher than normal. Liver function tests tell researchers how well the liver is working. This participant's liver function test results returned to normal when checked again. The researcher thought it was possible this serious medical problem was related to danuglipron. However, based on later information, the Sponsor thought this serious medical problem was not related to danuglipron.

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.clinicaltrials.gov Use the study identifier N**CT04621227**

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!