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: Danuglipron (PF-06882961)

Protocol Number: C3421047

Dates of Study: 25 October 2021 to 06 July 2022

Title of this Study: A Study on How Danuglipron Effects Blood Levels of Atorvastatin and Midazolam in Healthy Adults, and of Oral Contraceptives in Healthy Post-Menopausal Females

[A Phase 1, Open-Label, Two-Part Study to Evaluate the Effect of Two Steady-State Dose Levels of PF-06882961 on the Pharmacokinetics of Single Oral Doses of Atorvastatin and Midazolam in Healthy Adults and an Oral Contraceptive in Healthy Post-Menopausal Females]

Date(s) of this Report: 11 September 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?

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 properly use the insulin it makes. 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.

What is danuglipron?

Danuglipron (dah-noog-lih-pron, PF-06882961) is an experimental medicine that is taken by mouth and is not yet approved for use by health authorities. Danuglipron stimulates the glucagon-like peptide 1 (GLP-1) receptor and may help lower blood sugar levels by increasing insulin secretion. It may also increase the feeling of fullness and lower food intake and result in weight loss.

What was the purpose of this study?

The purpose of this study was to learn how danuglipron affects the levels of certain other medications in the blood. The other medications were:

- Atorvastatin (an approved/marketed drug used to treat high cholesterol)
- Midazolam (an approved/marketed drug used to treat anxiety), and
- Oral contraceptives (levonorgestrel and ethinyl estradiol)

In this study, the researchers gave danuglipron with atorvastatin, or danuglipron with midazolam, or danuglipron with oral contraceptives. They did this to see if danuglipron changed the amount of atorvastatin, midazolam, or oral contraceptives in the participant's blood. The researchers compared levels of these medications in blood when they were given with and without danuglipron.

This study was carried out in healthy participants and did not test if danuglipron helps participants with T2DM.

Researchers wanted to know:

- **How did danuglipron affect the levels of atorvastatin, midazolam, and oral contraceptives in the blood?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

There were 2 parts to this study, Part A and Part B.

In Part A, researchers looked at the interaction between danuglipron and atorvastatin and between danuglipron and midazolam in healthy adult participants.

In Part B, researchers looked at the interaction between danuglipron and the oral contraceptives levonorgestrel and ethinyl estradiol in healthy women who have gone through menopause or 'the change'. This means they no longer have monthly periods and cannot get pregnant.

Some people who take medicines that are similar to the study drug (danuglipron) can have problems like nausea, vomiting, and diarrhea, so these medicines are often started at a low dose with the dose increasing gradually over time. In this study, the dose of danuglipron started at started at 10 mg twice daily and quickly increased, every few days, to 120 mg twice daily, and then to 200 mg twice daily.

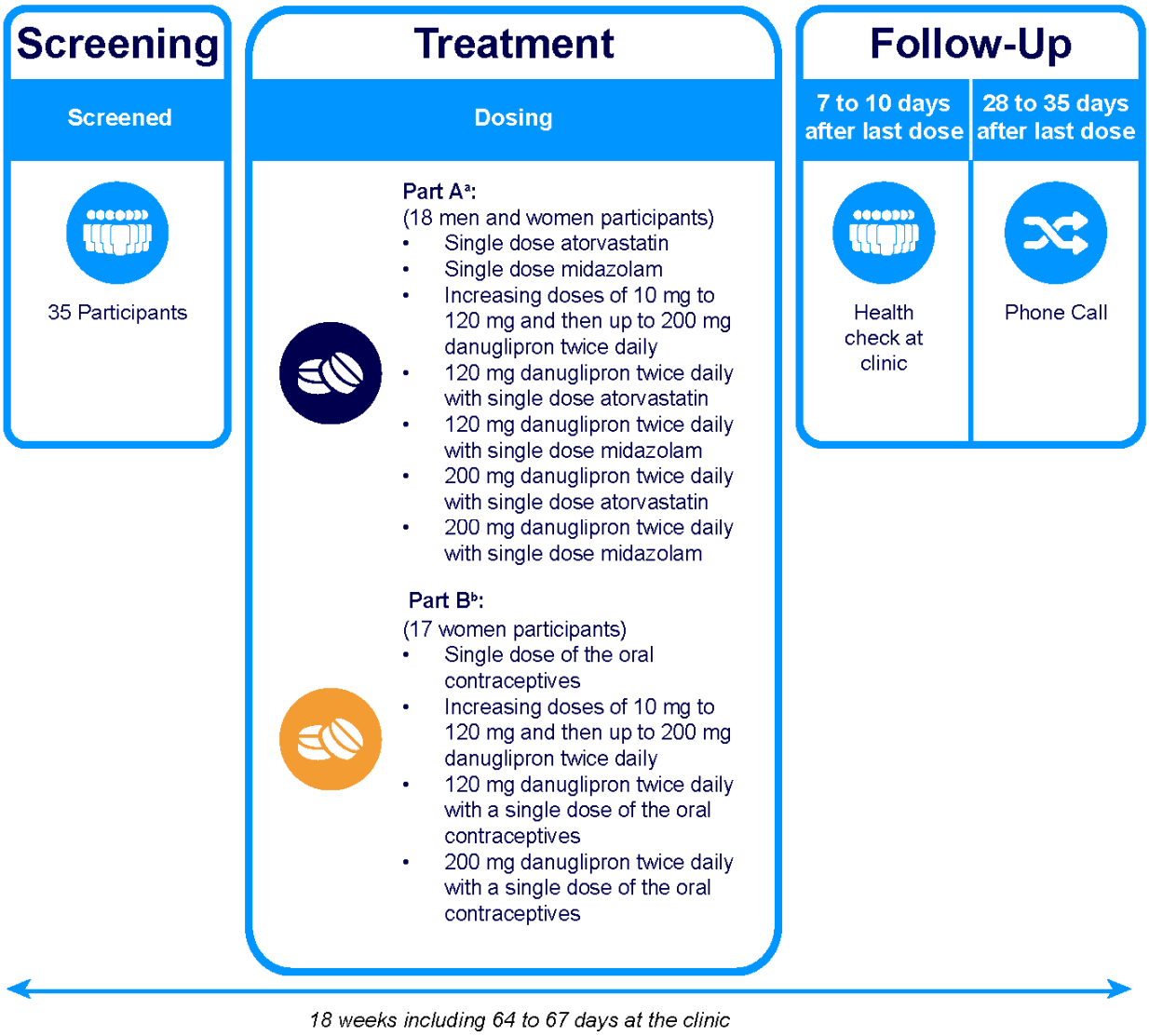
Researchers took samples of blood from participants during the study and measured the amount of the study drugs in the samples.

Researchers also checked the participants' health during the study and asked them how they were feeling.

Throughout the study, the participants and researchers knew which study drugs each participant was taking. This is known as an open-label study.

Figure 1 shows what happened in the study.

Figure 1: Study Design



a: Treatment given depended on the day of the study.

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 25 October 2021 and ended 06 July 2022.

Who participated in this study?

In Part A, the study included healthy participants

- A total of 16 men participated
- A total of 2 women participated
- All participants were between the ages of 24 and 62 years

In Part B, the study included healthy post-menopausal women

- A total of 17 women participated
- All participants were between the ages of 47 and 63 years

In Part A, 5 of 18 participants (27.8%) finished the study. The other 13 participants (72.2%) did not finish the study because:

- They had a positive COVID-19 test result (10 of 18 participants or 55.6%)
- The researcher decided they should stop the study (2 of 18 participants or 11.1%)
- The participant chose to leave the study (1 participant or 5.6%)

In Part B, 9 of the 17 participants (52.9%) finished the study. The other 8 participants (47.1%) did not finish the study because:

- They had unwanted medical problems (6 of 17 participants or 35.3%)
- The participant chose to leave the study (1 of 17 participants or 5.9%)

- The researcher decided they should stop the study because they were no longer suitable (1 participant or 5.9%)

How long did the study last?

Study participants were in the study for about 18 weeks. The entire study took approximately 9 months to complete. There were no interruptions, nor was the study discontinued.

When the study ended in July 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?

How did danuglipron affect the levels of atorvastatin, midazolam, and oral contraceptives in the blood?

Overall, this study showed:

- Blood levels of atorvastatin were slightly higher when given with danuglipron than when atorvastatin was given alone
- Blood levels of midazolam were slightly lower when given with danuglipron than when midazolam was given alone
- Blood levels of one of the oral contraceptives, levonorgestrel, were slightly higher when given with danuglipron than when given alone
- Blood levels of one of the oral contraceptives, ethinyl estradiol, were similar when given with danuglipron and when given alone

Clinical trials like this one are designed to include the number of people that the researchers need to study to give reliable results. As mentioned on the previous page, more than 70% of the participants who joined Part A did not complete the study (most left due to a positive COVID-19 test

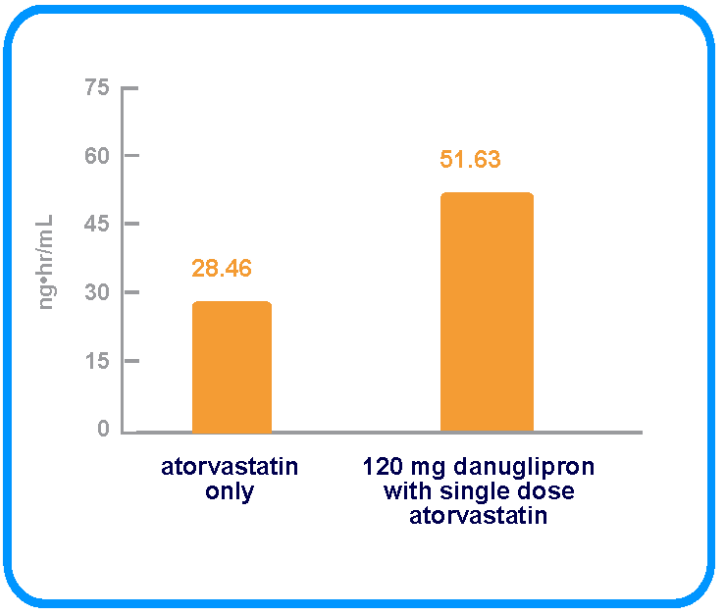
result). This meant that only a small number of participants were given the 200 mg dose of danuglipron in Part A and so the results seen with this dose may not be reliable. Because of this, the results on blood levels of atorvastatin and midazolam with 200 mg danuglipron are not included in this document.

The total amount of atorvastatin in the blood from when atorvastatin was taken to the time when the lowest amount was detected in the blood is known as AUC_{last}. The ng•hr/mL (nanogram hours per milliliter) is a unit used to measure the total amount of drug over time in the blood. Sometimes if the amount of drug is lower, pg•hr/mL (picogram hours per milliliter) is used instead of ng•hr/mL.

What was the amount of atorvastatin in the blood when it was taken with or without danuglipron?

- As shown in Figure 2:
    - On average, the AUC_{last} for atorvastatin when taken alone was 28.46 ng•hr/mL
    - On average, the AUC_{last} for atorvastatin when taken with 120 mg danuglipron was 51.63 ng•hr/mL

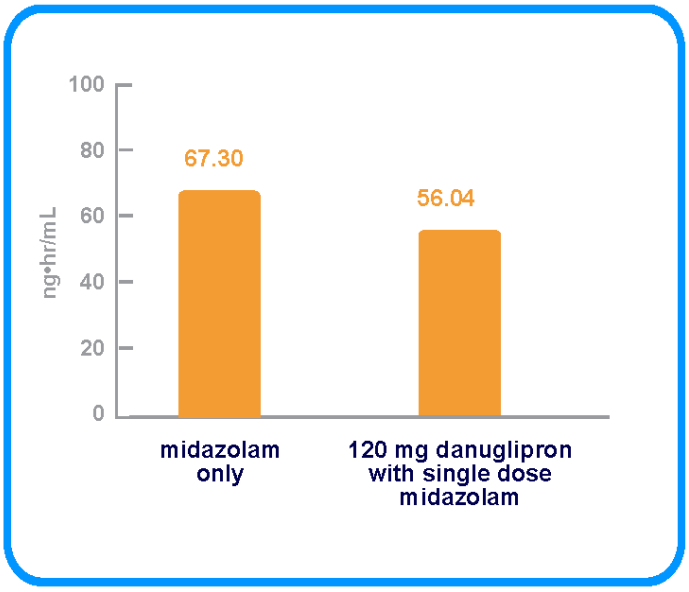
Figure 2: Average Amounts of Atorvastatin in Blood



What was the amount of midazolam in the blood when it was taken with or without danuglipron?

- As shown in Figure 3:
  - On average, the AUC_{last} for midazolam when taken alone was 67.30 ng•hr/mL
  - On average, the AUC_{last} for midazolam when taken with 120 mg danuglipron was 56.04 ng•hr/mL

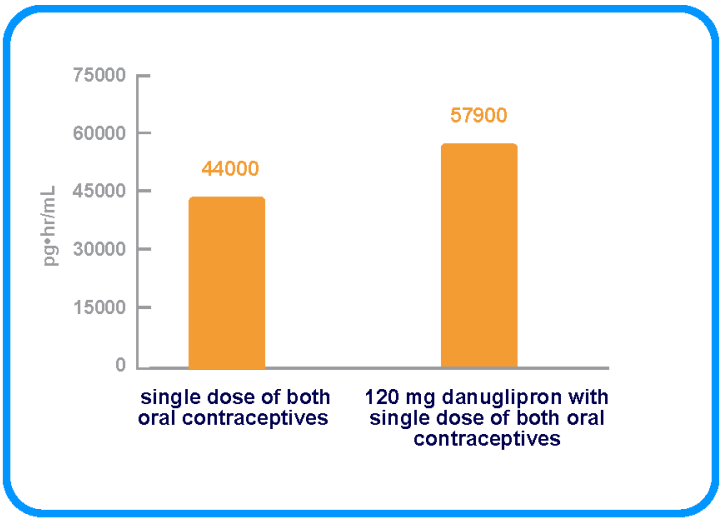
Figure 3: Average Amounts of Midazolam in Blood



What was the amount of levonorgestrel in the blood when it was taken with or without danuglipron?

- Participants received an oral contraceptive containing levonorgestrel and ethinyl estradiol.
- As shown in Figure 4:
  - On average, the AUC_{last} for levonorgestrel when taken with ethinyl estradiol but not with danuglipron was 44,000 pg•hr/mL (picogram hours per milliliter).
  - On average, the AUC_{last} for levonorgestrel when taken with ethinyl estradiol and 120 mg danuglipron was 57,900 pg•hr/mL.

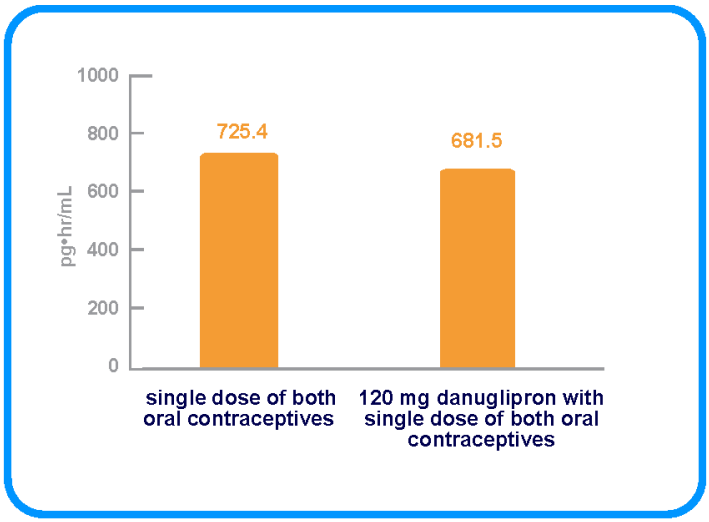
Figure 4: Average Amounts of the Oral Contraceptive, Levonorgestrel, in Blood



What was the amount of ethinyl estradiol in the blood when it was taken with or without danuglipron?

- Participants received an oral contraceptive containing levonorgestrel and ethinyl estradiol.
- As shown in Figure 5:
  - On average, the AUC_{last} for ethinyl estradiol when taken with levonorgestrel but not with danuglipron was 725.4 pg•hr/mL
  - On average, the AUC_{last} for ethinyl estradiol when taken with levonorgestrel and 120 mg danuglipron was 681.5 pg•hr/mL

Figure 5: Average Amounts of the Oral Contraceptive, Ethinyl Estradiol, in Blood



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 Part A, 17 out of 18 (94.4%) participants had at least 1 medical problem. A total of 10 (55.6%) participants stopped taking the study drug because they had a positive COVID-19 test result. There were no other participants who stopped taking the study drug in Part A.

In Part B, 16 out of 17 (94.1%) participants had at least 1 medical problem.

In both Part A and Part B, the researchers thought that most (over 90%) of the medical problems were mild.

A total of 6 (35.3%) participants stopped taking the study drug because of medical problems. This included 4 participants who stopped taking the study drug because of nausea. The most common medical problems – those reported by more than 2 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. All medical problems reported by more than 2 participants are listed.
- The **2nd** column tells how many of the 18 participants in Part A reported each medical problem. Next to this number is the percentage of the 18 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 17 participants in Part B reported each medical problem. Next to this number is the percentage of the 17 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 11 out of the 18 (61.1%) participants in Part A reported nausea. There

were 15 out of 17 (88.2%) participants in Part B of the study who reported nausea.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Part A: Atorvastatin or Midazolam and/or Danuglipron (18 participants)	Part B: Oral Contraceptives and/or Danuglipron (17 participants)
Nausea	11 out of 18 participants (61.1%)	15 out of 17 participants (88.2%)
Stomach pains	8 out of 18 participants (44.4%)	12 out of 17 participants (70.6%)
Headache	8 out of 18 participants (44.4%)	12 out of 17 participants (70.6%)
Constipation	8 out of 18 participants (44.4%)	11 out of 17 participants (64.7%)
Feeling full sooner than expected, or after eating less than usual	0	14 out of 17 participants (82.4%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Part A: Atorvastatin or Midazolam and/or Danuglipron (18 participants)**	**Part B: Oral Contraceptives and/or Danuglipron (17 participants)**
Vomiting	6 out of 18 participants (33.3%)	7 out of 17 participants (41.2%)
Positive COVID-19 Test	13 out of 18 participants (72.2%)	0
Decreased appetite	6 out of 18 participants (33.3%)	5 out of 17 participants (29.4%)
Dizziness	4 out of 18 participants (22.2%)	4 out of 17 participants (23.5%)
Indigestion	1 out of 18 participants (5.6%)	4 out of 17 participants (23.5%)
Laboratory test showing kidneys not cleaning blood as fast as normal	1 out of 18 participants (5.6%)	4 out of 17 participants (23.5%)

Table 1. Commonly reported medical problems by study participants		
Medical Problem	**Part A: Atorvastatin or Midazolam and/or Danuglipron (18 participants)**	**Part B: Oral Contraceptives and/or Danuglipron (17 participants)**
Unable to sleep (insomnia)	1 out of 18 participants (5.6%)	4 out of 17 participants (23.5%)
Diarrhea	0	4 out of 17 participants (23.5%)
Bite from a bug, insect, or spider	0	3 out of 17 participants (17.6%)

Note: In this study, the dose of danuglipron started at 10 mg twice daily and increased every few days. Increasing the dose quickly over a short period of time may have affected how well the participants tolerated the study drugs.

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.

No participants had serious medical problems.

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 C3421047

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

www.clinicaltrials.gov

Use the study identifier **NCT05093205**

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!