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:	Ervogastat and Danuglipron
Protocol Number:	C3421038
Dates of Study:	05 April 2021 to 08 November 2021
Title of this Study:	Study Looking at the Interactions Between Levels of Danuglipron and Ervogastat in the Body [A Phase 1, Open-Label Study to Evaluate the Pharmacokinetic Interactions Between PF-06882961 [Danuglipron] and PF-06865571 [Ervogastat] in Healthy Adult Participants (Part A) and Overweight Adults or Adults with Obesity Who are Otherwise Healthy (Part B)]
Date(s) of this Report:	30 October 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 Non-Alcoholic Steatohepatitis with Liver Fibrosis?

Non-Alcoholic Steatohepatitis (NASH) with liver fibrosis is a medical condition where there is a high amount of fat in the liver. Inflammation (swelling) and fibrosis (scarring) may also be present, which can cause a stiff liver. If someone develops a stiff liver, then their liver is not able to work properly, and this may make them ill.

What are danuglipron and ervogastat?

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

Ervogastat (err-vo-ga-stat, PF-06865571) is a new investigational medicine. It is not approved for use by health authorities. Ervogastat is taken by mouth. It blocks a specific enzyme (protein) called "DGAT2". This prevents the body from making certain types of fats. Too much fat in the liver is the first step toward developing NASH and liver scarring. Ervogastat decreases the storage of fat in the liver, which may help treat NASH with liver scarring.

What was the purpose of this study?

The purpose of this study was to compare the levels of danuglipron and ervogastat in participants' blood. The study drugs were given alone or as a combination, which means they were taken at the same time. The researchers did this because they wanted to see how the study drugs interact with one another.

Researchers wanted to know:

- **How does the amount of danuglipron or ervogastat in the blood change when these drugs are taken individually compared to when danuglipron and ervogastat are taken together?**
- **What medical problems did participants have during the study?**

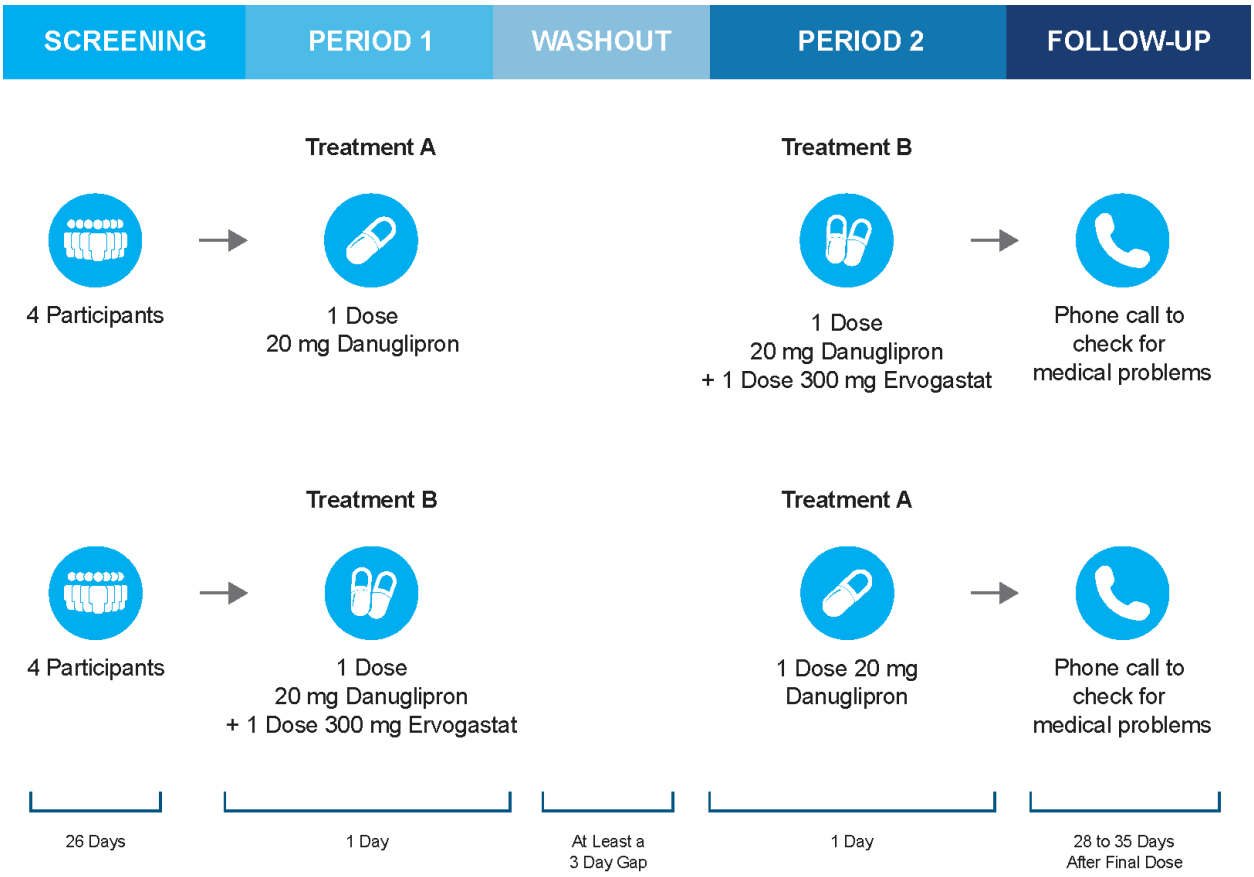
What happened during the study?

How was the study done?

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

In Part A, researchers tested 20 mg danuglipron with or without 300 mg ervogastat in a group of healthy adult participants. They did this to learn how the amount of danuglipron in the blood changed when taken with or without ervogastat. There were 2 study periods (Periods 1 and 2) in this part of the study. Figure 1a shows when participants were to take single doses of 20 mg danuglipron and 300 mg ervogastat.

Figure 1a: Part A Study Plan

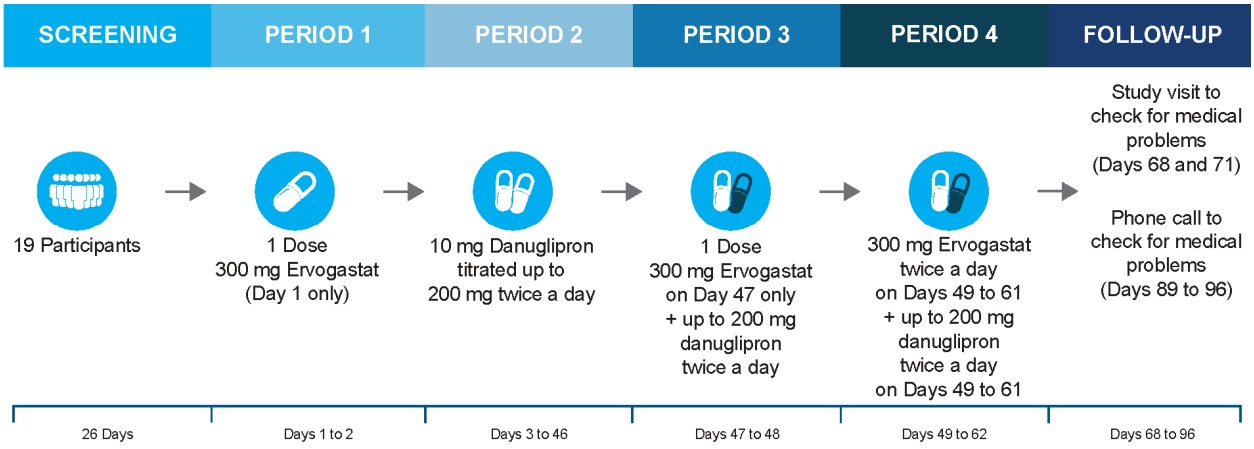


In Part B, researchers tested different doses of danuglipron and ervogastat. They did this in a group of healthy adults who were overweight or with obesity. The researchers wanted to learn how the amount of ervogastat in the blood changed when taken with danuglipron. They also wanted to see if the amount of danuglipron in the blood changed when taken with ervogastat.

In Part B, there were 4 study periods (Periods 1 to 4). Participants were to take a different treatment during each study period (Figure 1b). In Period 1, participants took 1 dose of 300 mg ervogastat on Day 1. In period 2, participants took 10 mg danuglipron twice a day. From Days 3 to 46, this was titrated up to 200 mg twice a day. Titrated means to increase the dose of a drug slowly. In Period 3, participants took 1 dose of 300 mg ervogastat on Day 47. They also took up to 200 mg

danuglipron twice a day on Days 47 and 48. In Period 4, participants took 300 mg ervogastat twice a day from Days 49 to 61. They also took up to 200 mg danuglipron twice a day from Days 49 to 61.

Figure 1b: Part B Study Plan



During the study, researchers took samples of blood from participants. They measured the amount of danuglipron and ervogastat in the samples. They also checked the participants' health during the study and asked them how they were feeling.

Where did this study take place?

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

When did this study take place?

It began 05 April 2021 and ended 08 November 2021.

Who participated in this study?

Part A included healthy adult participants. Part B included healthy adults who were overweight or with obesity.

In Part A:

- A total of 6 men participated
- A total of 2 women participated
- All participants were between the ages of 20 and 57 years

In Part B:

- A total of 18 men participated
- A total of 1 woman participated
- All participants were between the ages of 30 and 64 years

In Part A, all 8 participants finished the treatment and the follow-up period.

In Part B, of the 19 participants who started treatment, 3 did not finish the treatment. Two (2) of these stopped treatment because of medical problems (they developed Coronavirus Disease 2019 [Covid-19]) and 1 participant left by choice.

How long did the study last?

In Part A, participants were in the study for about 9 weeks. In Part B, participants were in the study for about 18 weeks. The entire study took just over 7 months to complete.

When the study ended in November 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?

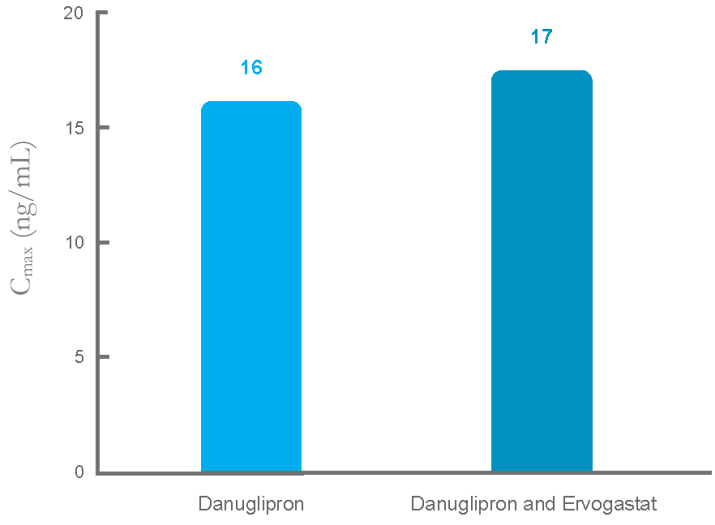
How does the amount of danuglipron or ervogastat in the blood change when these drugs are taken individually compared to when danuglipron and ervogastat are taken together?

In Part A, the researchers wanted to know if the amount of danuglipron was altered when this was taken with or without ervogastat.

How did the amount of danuglipron in the blood change when taken with ervogastat?

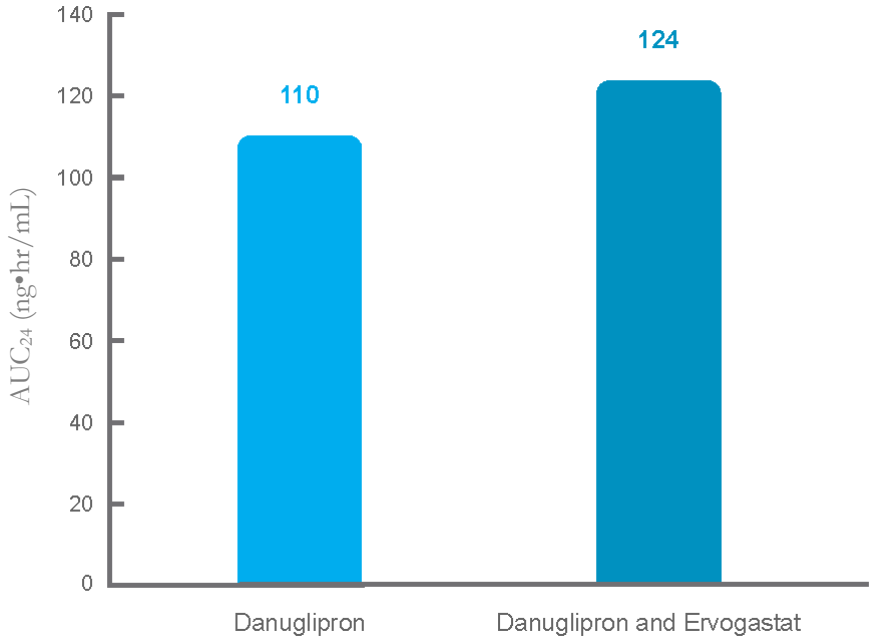
- When danuglipron was taken alone, the highest amount of danuglipron in the blood was 16 ng/mL (nanograms per milliliter) (Figure 2). This is known as C_{max}. The ng/mL is a unit used to measure the amount of drug in the blood. When danuglipron was taken with ervogastat, the highest amount of danuglipron in the blood was 17 ng/mL. Researchers considered the difference in the results as minor.

Figure 2: C_{max} for danuglipron when a single dose was taken with and without ervogastat



- When danuglipron was taken alone, the total amount of danuglipron in the blood during the 24 hours after participants took danuglipron was 110 ng•hr/mL (nanogram hours per milliliter) (Figure 3). This is known as AUC_{24}. The ng•hr/mL is a unit used to measure total amount of drug over time in the blood. When participants took danuglipron with ervogastat, the total amount of danuglipron in the blood during the 24 hours after participants took these study drugs was 124 ng•hr/mL. Researchers considered the difference in the results as minor.

Figure 3: AUC_{24} for danuglipron when a single dose was taken with and without ervogastat

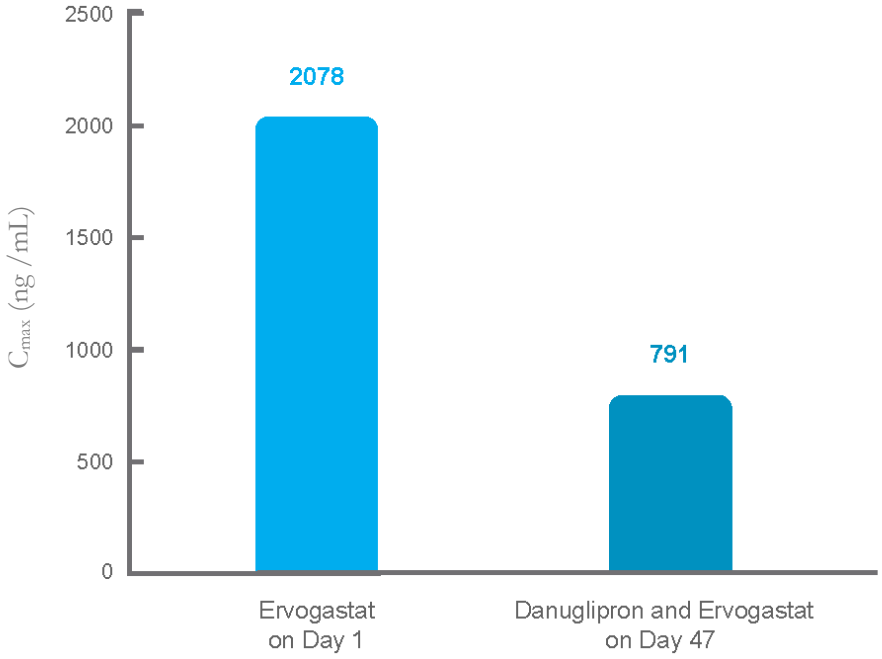


In Part B, the researchers wanted to know if the amount of ervogastat was altered when this was taken with many doses of danuglipron. The researchers also wanted to see if the amount of danuglipron changed when this was taken with many doses of ervogastat.

How did the amount of ervogastat in the blood change when taken with danuglipron on Day 47?

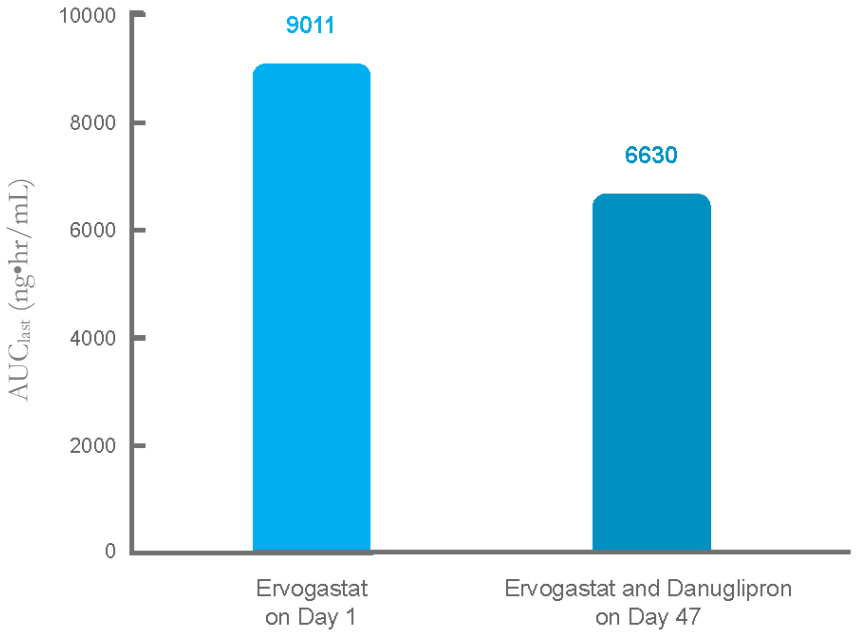
- When ervogastat was taken regularly alone, the highest amount of ervogastat in the blood or C_{max} was 2078 ng/mL (Figure 4). When ervogastat was taken regularly with danuglipron, the highest amount of ervogastat in the blood was 791 ng/mL. Researchers considered the amount of ervogastat in the blood was reduced by danuglipron and was not likely the result of chance.

Figure 4: C_{max} for ervogastat when taken regularly with and without danuglipron



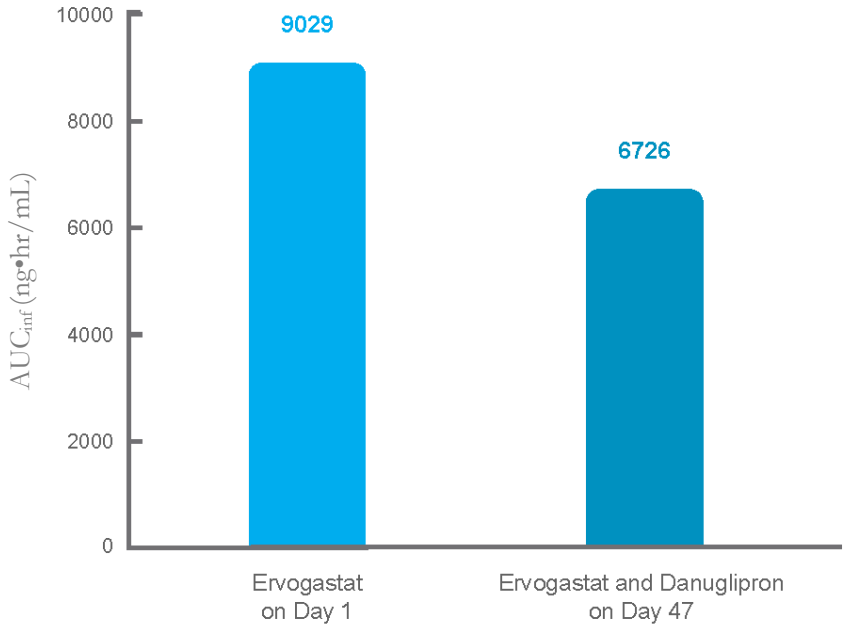
- When ervogastat was taken regularly alone, the total amount of ervogastat from when ervogastat was taken to the time when the lowest amount was detected in the blood was 9011 ng•hr/mL (Figure 5). This is known as AUC_{last}. When ervogastat was taken regularly with danuglipron, the total amount of ervogastat in the blood from when ervogastat was taken to the time when the lowest amount was detected in the blood was 6630 ng•hr/mL. Researchers considered the amount of ervogastat in the blood was reduced by danuglipron and was not likely the result of chance.

Figure 5: AUC_{last} for ervogastat when taken regularly with and without danuglipron



- When ervogastat was taken regularly alone, the estimated total amount of ervogastat in the blood from when ervogastat was taken until ervogastat was removed from the body was 9029 ng•hr/mL (Figure 6). This is known as AUC_{inf}. When ervogastat was taken regularly with danuglipron, the estimated total amount of ervogastat in the blood from when ervogastat was taken until ervogastat was removed from the body was 6726 ng•hr/mL. Researchers considered the amount of ervogastat in the blood was reduced by danuglipron and was not likely the result of chance.

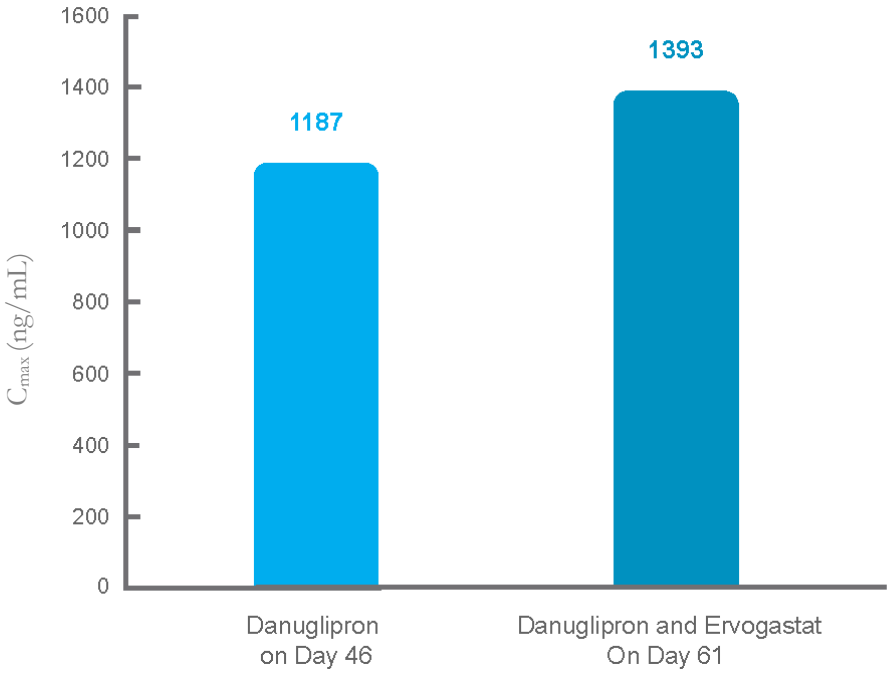
Figure 6: AUC_{inf} for ervogastat when taken regularly with and without danuglipron



How did the amount of danuglipron in the blood change when taken with ervogastat on Day 61?

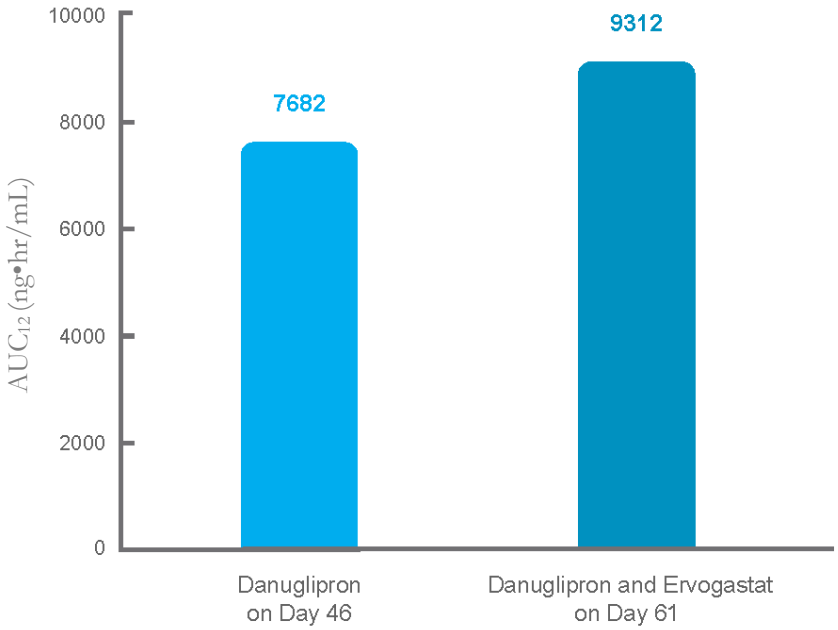
- When danuglipron was taken regularly alone, the highest amount of danuglipron in the blood or C_{max} was 1187 ng/mL (Figure 7). When danuglipron was taken regularly with ervogastat, the highest amount of danuglipron in the blood was 1393 ng/mL. Researchers considered the difference in the results as minor.

Figure 7: C_{max} for danuglipron when taken regularly with and without ervogastat



- When danuglipron was taken regularly alone, the total amount of danuglipron in the blood during the 12 hours after participants took danuglipron was 7682 ng•hr/mL (Figure 8). This is known as AUC_{12}. When danuglipron was taken regularly with ervogastat, the total amount of danuglipron in the blood during the 12 hours after participants took danuglipron was 9312 ng•hr/mL. Researchers considered the difference in the results as minor.

Figure 8: AUC_{12} for danuglipron when taken regularly with and without ervogastat



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 with danuglipron and/or ervogastat 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 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, there were no medical problems reported by participants.

In Part B, 18 out of 19 (95%) participants had at least 1 medical problem. A total of 2 (11%) participants left the study because of medical problems (due to testing positive for COVID-19). The most common medical problems – those reported by more than 30% of participants overall – 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 Part B of the study. All medical problems reported by more than 30% of participants are listed.
- The **2nd** column tells how many of the 19 participants taking 300 mg ervogastat reported each medical problem. Next to this number is the percentage of the 19 participants taking 300 mg ervogastat who reported the medical problem.

- The **3rd** column tells how many of the 19 participants taking danuglipron titrated up to 200 mg twice a day reported each medical problem. Next to this number is the percentage of the 19 participants taking danuglipron titrated up to 200 mg twice a day who reported the medical problem.
- The **4th** column tells how many of the 16 participants taking 300 mg ervogastat with up to 200 mg danuglipron twice a day reported each medical problem. Next to this number is the percentage of the 16 participants taking 300 mg ervogastat with up to 200 mg danuglipron twice a day who reported the medical problem.
- The **5th** column tells how many of the 16 participants taking 300 mg ervogastat twice a day with up to 200 mg danuglipron twice a day reported each medical problem. Next to this number is the percentage of the 16 participants taking 300 mg ervogastat twice a day with up to 200 mg danuglipron twice a day who reported the medical problem.
- Using these instructions, you can see that 12 out of 19 participants (63%) taking danuglipron titrated up to 200 mg twice a day reported a feeling of sickness compared with 6 out of 16 participants (38%) taking 300 mg ervogastat twice a day and up to 200 mg danuglipron twice a day, 1 out of 19 participants (5%) taking ervogastat 300 mg, and 1 out of the 16 participants (6%) taking 300 mg ervogastat twice a day and up to 200 mg danuglipron twice a day.

Table 1. Commonly reported medical problems by study participants in Part B of the study				
Medical Problem	**300 mg Ervogastat (19 Participants) Day 1 only**	**Danuglipron titrated up to 200 mg twice a day (19 Participants) Days 3 to 46**	**300 mg Ervogastat and up to 200 mg danuglipron twice a day (16 Participants) Days 47 to 48**	**300 mg Ervogastat and up to 200 mg danuglipron (both twice a day) (16 participants) Days 49 to 62**
Feeling of sickness	1 out of 19 participants (5%)	12 out of 19 participants (63%)	1 out of 16 participants (6%)	6 out of 16 participants (38%)
Vomiting	0	7 out of 19 participants (37%)	3 out of 16 participants (19%)	6 out of 16 participants (38%)
Reduced desire to eat	0	10 out of 19 participants (53%)	0	0
Indigestion		8 out of 19 participants (42%)		2 out of 16 participants (12%)
Feeling sleepy	0	8 out of 19 participants (42%)	0	1 out of 16 participants (6%)

Table 1. Commonly reported medical problems by study participants in Part B of the study				
Medical Problem	**300 mg Ervogastat (19 Participants) Day 1 only**	**Danuglipron titrated up to 200 mg twice a day (19 Participants) Days 3 to 46**	**300 mg Ervogastat and up to 200 mg danuglipron twice a day (16 Participants) Days 47 to 48**	**300 mg Ervogastat and up to 200 mg danuglipron (both twice a day) (16 participants) Days 49 to 62**
Constipation	0	6 out of 19 participants (32%)	1 out of 16 participants (6%)	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.

No participants had serious medical problems. No participants died in 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.

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

www.clinicaltrials.gov	Use the study identifier NCT04839393
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C3421038

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!