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 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: C3421014

Dates of Study: 30 December 2020 to 10 January 2022

Title of this Study: A study to Compare the Pharmacokinetics of PF-06882961 in Adult Participants With Varying Degrees of Hepatic Impairment

[A Phase 1, Non-Randomized, Open-Label, Single-Dose, Parallel Cohort Study to Compare the Pharmacokinetics of PF-06882961 in Adult Participants With Varying Degrees of Hepatic Impairment Relative to Participants Without Hepatic Impairment.]

Date(s) of this Report: 03 February 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 hepatic impairment (abnormal liver function)?

The liver is an organ inside the body. It plays an important role in breaking down food, storing energy, and removing waste and toxic materials from the body. Abnormal liver function or liver disease can be caused due to several reasons, including heavy alcohol drinking, viral infections, autoimmune diseases, and use of certain medications. The liver can also be damaged when high levels of fat build up in the liver. The word "hepatic" is associated with liver. Hence, hepatic impairment refers to problems with liver function.

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 if patients who had problems with liver function had the same or higher levels of danuglipron in their blood over time, compared to participants with normal liver function. After danuglipron was swallowed, danuglipron entered the body and moved through the body. Danuglipron entered the blood and organs (for example, stomach, liver, and kidneys) when it moved through the body. Afterwards, danuglipron was removed from the body through urine and feces.

This study did not test if the drug helps to improve liver diseases and only focused on how danuglipron moves through the body and is affected by the liver and level of liver function.

Researchers wanted to know:

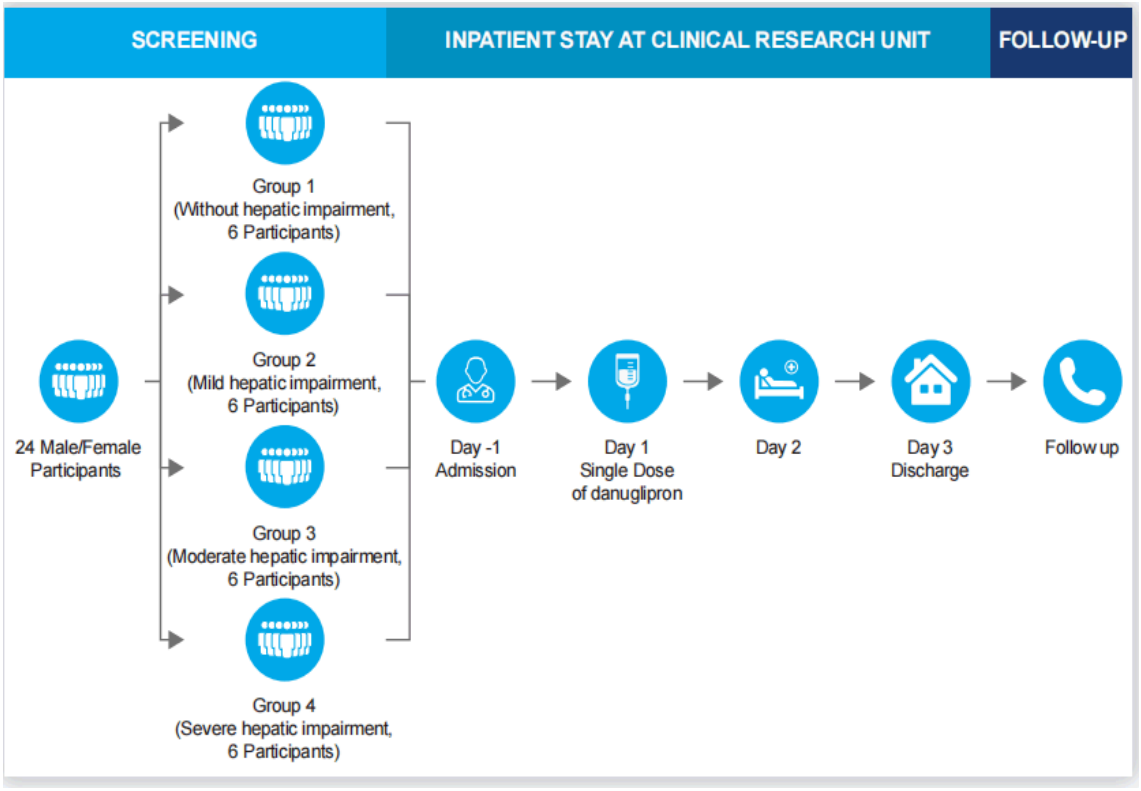
- **If patients who had problems with liver function had the same or higher levels of danuglipron in their blood over time, compared to participants with normal liver function?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

A group of 24 participants (18 participants with hepatic impairment and 6 with no liver disease) took a single dose of 20 mg of danuglipron. Participants were enrolled into the study, such that 4 equal groups based on severity of liver disease were included as given below:

- Group 1: No liver disease (6 participants)
- Group 2: Mild liver disease (6 participants)
- Group 3: Moderate Liver disease (6 participants)
- Group 4: Severe Liver disease (6 participants)



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

Researchers then compared the results of the amount of danuglipron in the blood of participants who had varying degrees of abnormal liver function (mild, moderate, severe) compared to people who had normal liver function.

Where did this study take place?

The Sponsor ran this study at 2 locations in the United States.

When did this study take place?

It began on 30 December 2020 and ended on 10 January 2022.

Who participated in this study?

The study included adult participants with or without abnormal liver function.

- A total of 13 men participated
- A total of 11 women participated
- All participants were between the ages of 45 and 70, inclusive.

Of the 24 participants who started the study, all of them finished the study.

How long did the study last?

Study participants were in the study for about 5 weeks to a maximum of 9 weeks. The entire study took 13 months to complete.

When the study ended in January 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?

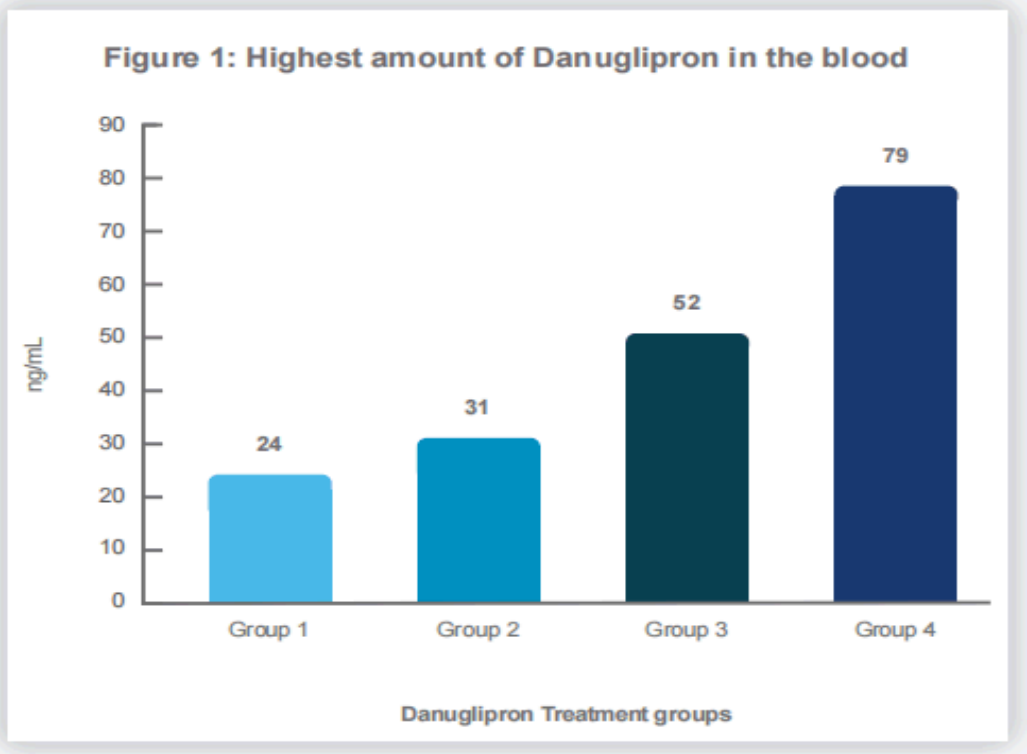
How did 20 mg danuglipron act in the body of participants with or without abnormal liver function?

To answer this question, the researchers compared the blood samples of participants with varying degrees of abnormal liver function (mild, moderate, severe) to people who had normal liver function.

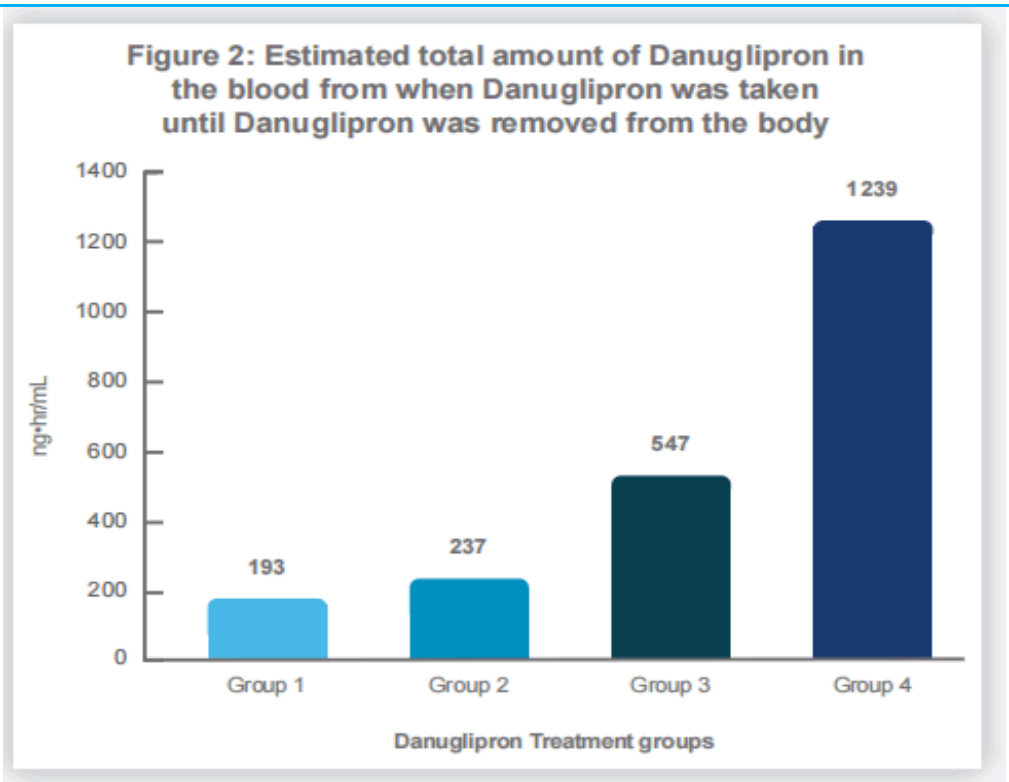
What was the amount of danuglipron in the blood after participants took 20 mg of danuglipron?

- The highest level of danuglipron reached in the blood after participants took 20 mg of danuglipron is shown in Figure 1. The amount of drug in the blood was measured in nanograms per milliliter, also called ng/mL. In this

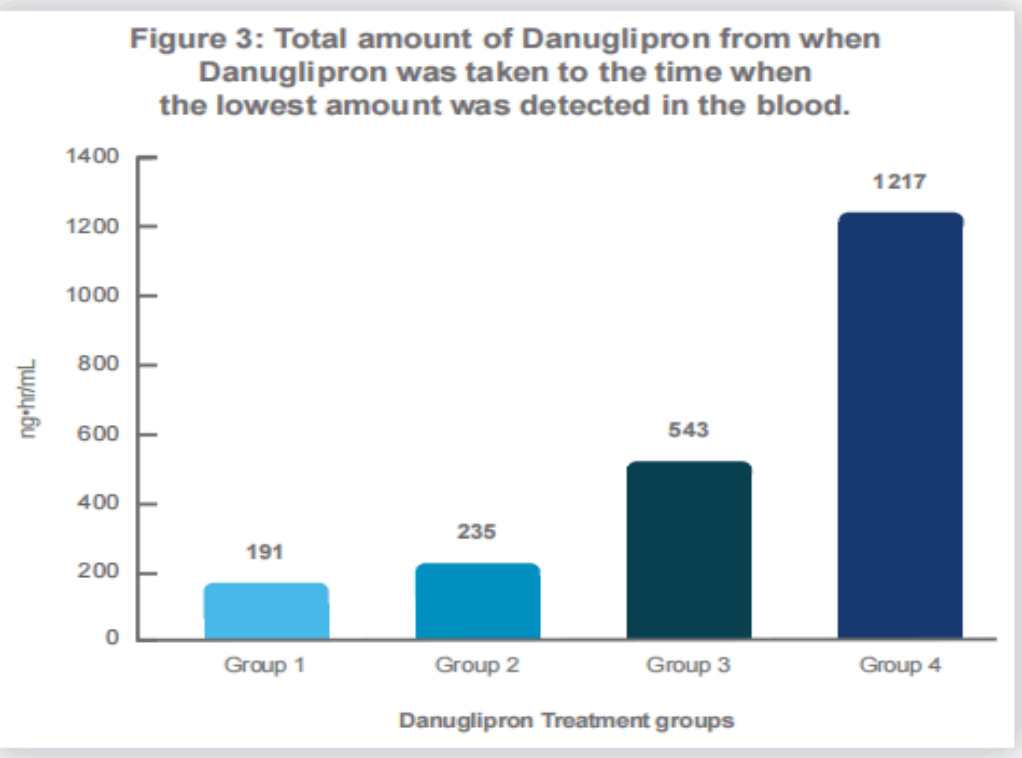
study, the amount of danuglipron measured in the blood was highest in participants with severe abnormal liver function (Group 4).



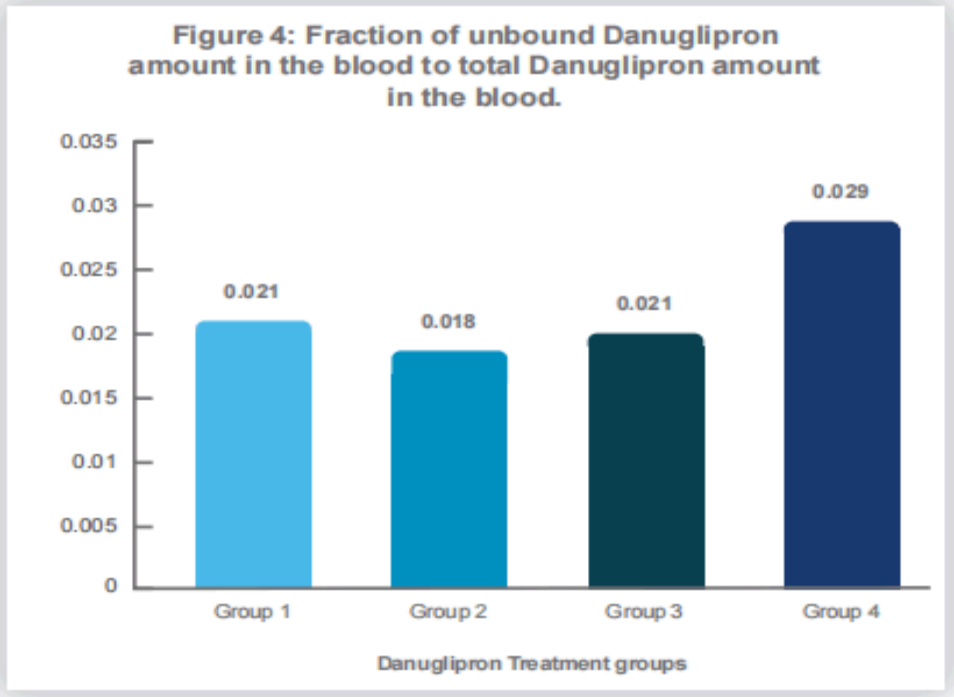
- The estimated total amount of danuglipron in the blood over time is shown in Figure 2. The ng•hr/mL (nanogram hours per milliliter) is a unit used to measure the total amount of drug over time in the blood. In this study, the total amount of danuglipron in the blood from when it was taken until danuglipron was removed from the body was highest in participants with severe abnormal liver function (Group 4).



- The total amount of danuglipron from when it was taken to the time when the lowest amount was detected in the blood is shown in Figure 3. In this study, the total amount of danuglipron from when it was taken to the time when the lowest amount was detected in the blood was highest in participants with severe abnormal liver function (Group 4).



- A drug is called 'free' or 'unbound' when it is not attached to anything (for example, protein) in the blood. The fraction of unbound danuglipron in the blood is shown in Figure 4. The fraction of unbound danuglipron in the blood was almost similar for Group 1, Group 2, and Group 3; and slightly higher in Group 4 participants with severe abnormal liver function.



In general, patients who had moderate or severe liver problems (Group 3 and 4) had higher levels of danuglipron in their blood over time compared to participants with normal liver function (Group 1). Results were similar for patients with mild liver problems (Group 2) compared to participants with normal liver function.

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 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.

Four (4) out of 24 (17%) participants in this study had at least 1 medical problem. None of the participants left the study because of medical problems. Medical problems reported by 1 or more participants are described below.

Below are instructions on how to read 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 1 or more participants are listed.
- The **2nd to 4th** column tells how many of the 24 participants in Group 1 to 4 reported each medical problem. Next to this number is the percentage of the 24 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 3 out of the 24 participants taking the danuglipron reported nausea.

Table 1. Commonly reported medical problems by study participants				
Medical Problem	Danuglipron Group 1 (6 Participants)	Danuglipron Group 2 (6 Participants)	Danuglipron Group 3 (6 Participants)	Danuglipron Group 4 (6 Participants)
Nausea (feeling like about to vomit)	0 out of 6 participants (0%)	0 out of 6 participants (0%)	2 out of 6 participants (33%)	1 out of 6 participants (17%)
Diarrhoea (loose stools)	0 out of 6 participants (0%)	1 out of 6 participants (17%)	0 out of 6 participants (0%)	0 out of 6 participants (0%)
Vomiting (being sick)	0 out of 6 participants (0%)	0 out of 6 participants (0%)	0 out of 6 participants (0%)	1 out of 6 participants (17%)

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 in this study had serious medical problems, and 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:

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

www.clinicaltrials.gov — Use the study identifier **NCT04604496**

www.pfizer.com/research/research_clinical_trials/trial_results — Use the protocol number C3421014

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!