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: C3421012

Dates of Study: 13 January 2021 to 18 February 2022

Title of this Study: Pharmacokinetic Study of PF-06882961 in Participants With Type 2 Diabetes Mellitus With Varying Degrees of Renal Impairment and in Participants Without Renal Impairment.

[A Phase 1, Open-Label, Single-Dose, Parallel Group Study to Evaluate the Pharmacokinetics of PF-06882961 in Participants With Type 2 Diabetes Mellitus With Varying Degrees of Renal Impairment Relative to Participants Without Renal Impairment]

Date(s) of this Report: 30 April 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 are Type 2 Diabetes Mellitus and Renal Impairment?

Type 2 diabetes mellitus (T2DM) is a disease where the body does not make enough insulin or does not respond properly to the insulin in the blood. Over time, T2DM can cause higher than normal levels of sugar in the blood which can result in health problems, including problems in the kidneys, heart, eyes, and nerves.

Renal impairment means that a person's kidneys are not functioning normally. People with renal impairment may not be able to remove some substances from the body as well as people with normal kidney 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 participants with T2DM who had problems with kidney function had the same or higher levels of danuglipron in their blood over time, compared to T2DM participants with normal kidney 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 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.

This report describes what happened during the study, what the results of the study are, and how participants can learn more about the study.

Researchers wanted to know:

- **If participants with T2DM who had problems with kidney function had the same or higher levels of danuglipron in their blood over time, compared to T2DM participants with normal kidney function?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested danuglipron on participants with T2DM with different levels of kidney impairment, and on participants with T2DM with normal kidney function and healthy volunteers of similar age, gender, and weight as participants with kidney impairment to learn how kidney impairment affected the way danuglipron acted in the body.

Participants were enrolled into the study, such that 5 groups depending on the status of their disease state and kidney function were included as given below:

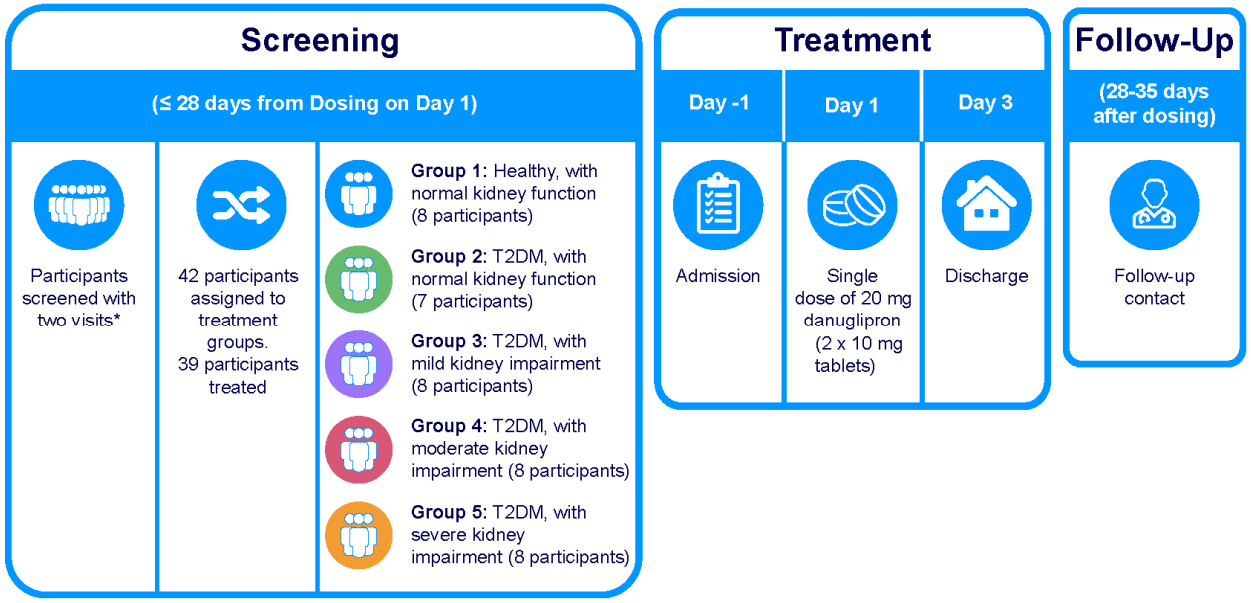
- Group 1: Healthy and normal kidney function
- Group 2: T2DM with normal kidney function
- Group 3: T2DM with mild kidney impairment

- Group 4: T2DM with moderate kidney impairment
- Group 5: T2DM with severe kidney impairment

In this study, participants received a single dose of 20 mg danuglipron by mouth (2 x 10 mg tablets), in the morning within about 10 minutes after completion of breakfast. This was an open-label study, which means that the participants and the researchers knew what treatment the participants received.

Researchers took samples of blood and urine from participants during the study and measured the amount of danuglipron. Researchers then compared the amount of danuglipron in the urine and blood samples from participants with T2DM with different levels of kidney impairment to each other and to those with normal kidney function. Researchers also checked the participants' health during the study and asked them how they were feeling. There was a follow-up contact about 28-35 days after dosing with danuglipron.

The figure below shows what happened during this study.



*Screening Visit 2 was optional for participants with dialysis.
Note: Both screening visits were separated by at least 72 hours

Where did this study take place?

The Sponsor ran this study at 3 locations in the United States.

When did this study take place?

It began 13 January 2021 and ended 18 February 2022.

Who participated in this study?

The study included healthy adult participants with normal kidney function and adult participants with T2DM with normal kidney function and with different levels of kidney impairment, who also met the inclusion/exclusion criteria for categories such as age and weight.

- A total of 21 men participated
- A total of 18 women participated
- A total of 23 participants were between the ages of 45 and 64, and 16 participants were over the age of 65, inclusive
- A total of 8 participants were healthy with normal kidney function, 7 participants had T2DM with normal kidney function, 8 participants had T2DM with mild kidney impairment, 8 participants had T2DM with moderate kidney impairment, and 8 participants had T2DM with severe kidney impairment.

Of the 42 participants who started the study, 39 were treated with danuglipron and all 39 completed the study. Three (3) participants were not treated with danuglipron due to work conflict, use of prohibited medication, and family emergency.

How long did the study last?

Study participants were in the study for a minimum of about 5 weeks and a maximum of about 10 weeks. The entire study took 13 months to complete and was completed as planned.

When the study ended in February 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

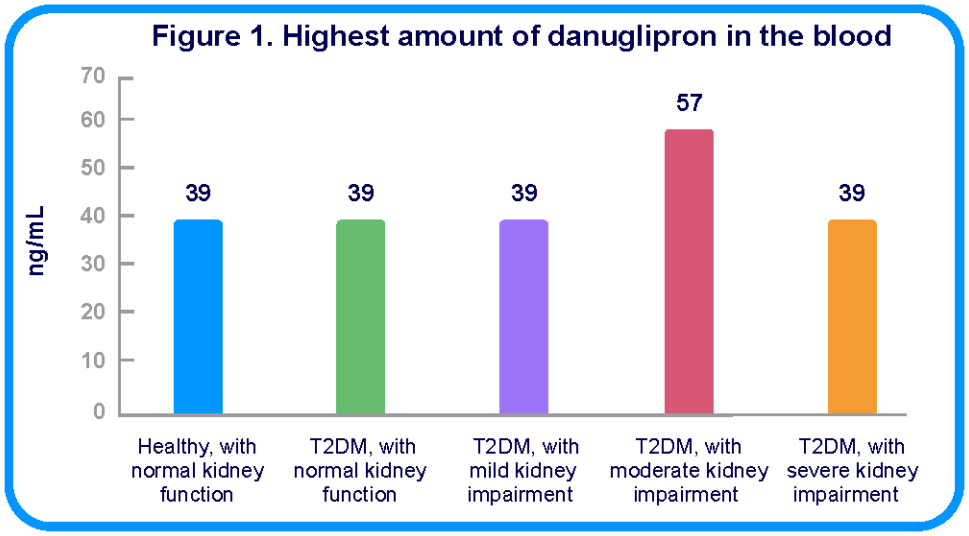
What were the results of the study?

What were the levels of danuglipron in the body of participants with T2DM with or without kidney impairment, compared to healthy participants with normal kidney function?

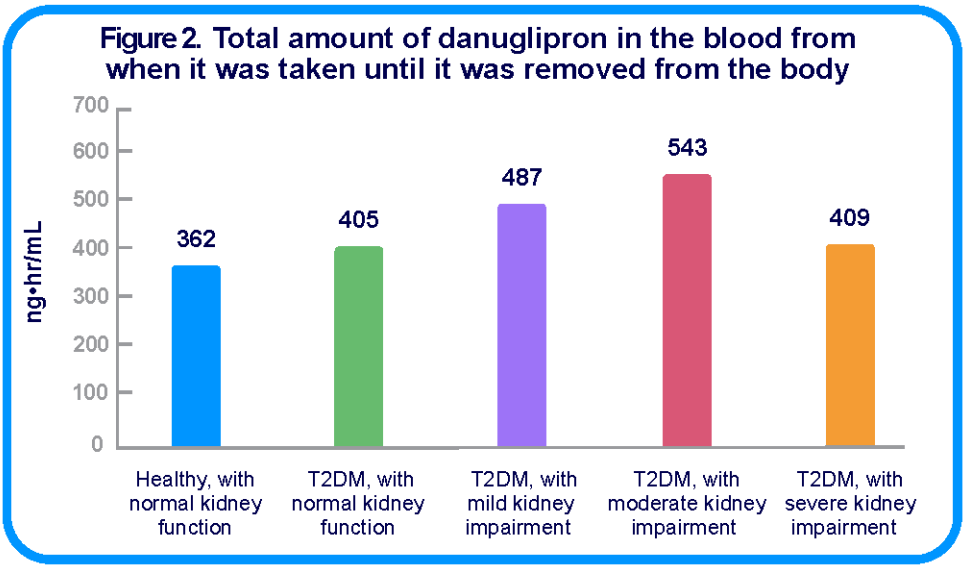
To answer this question, the researchers compared the blood samples of participants with T2DM with normal kidney function and T2DM with different levels of kidney impairment (mild, moderate, severe) to each other and to healthy people who had normal kidney function. The results are shown below.

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

- The highest amount of danuglipron measured in the blood after a single dose of 20 mg danuglipron is shown in Figure 1. The amount of danuglipron in the blood was measured in nanograms per milliliter, also called ng/mL. Researchers considered the differences in the results as minor.



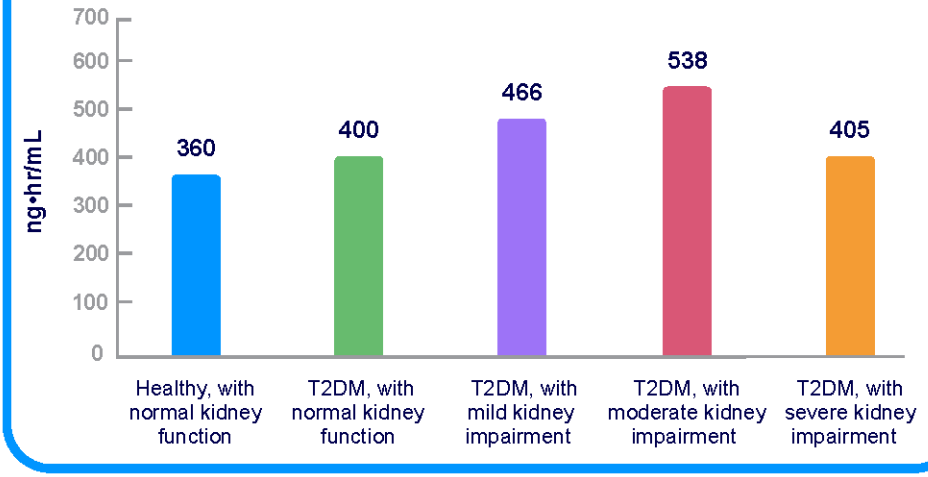
- The estimated total amount of danuglipron in the blood from when it was taken until it was removed from the body is shown in Figure 2. The total amount of danuglipron in the blood over time was measured in nanogram hours per milliliter, also called ng•hr/mL. Researchers considered the differences in the results as minor.



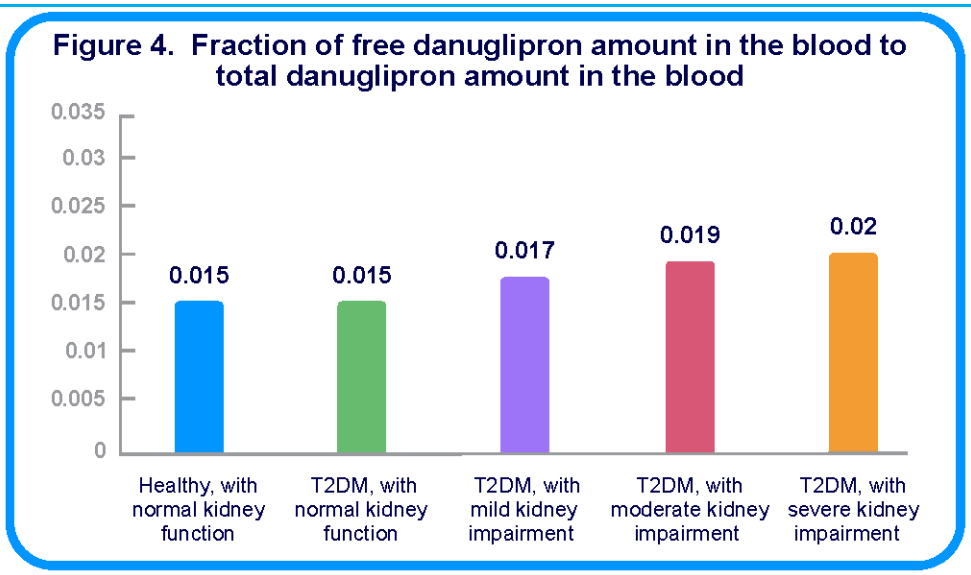
- The estimated total amount of danuglipron from when it was taken to the time when the lowest amount was detected in the blood is shown in Figure 3.

It is measured in ng•hr/mL. Researchers considered the differences in the results as minor.

Figure 3. Total amount of danuglipron in the blood from when it was taken to the time when the lowest amount was detected in the blood



- 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 amount in the blood to total danuglipron amount in the blood is shown in Figure 4. In this study, the fraction of unbound danuglipron in the blood was slightly increased in T2DM participants with kidney impairment, compared with T2DM participants without kidney impairment, and the researchers did not believe the results are likely the result of chance.



Overall, the amount of danuglipron in the blood was generally similar across all kidney function groups in T2DM participants and in healthy participants with normal kidney 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.

A total of 12 out of 39 participants (31%) in this study had at least 1 medical problem. No participants left the study because of medical problems. The most common medical problems reported by 2 or more of the total 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 2 or more of the total participants are listed.
- The **2nd to 6th** column tells how many of the 39 participants taking the study medication in the healthy with normal kidney function group, T2DM with normal kidney function group, and T2DM with mild, moderate or severe kidney impairment groups reported each medical problem. Next to this number is the percentage of the 39 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 1 out of 8 participants (13%) taking danuglipron in the healthy and normal kidney function group, 1 out of 7 participants (14%) in the T2DM with normal kidney function group, 1 out of 8 participants (13%) in T2DM with moderate kidney impairment group, and 1 out of 8 participants (13%) in T2DM with severe kidney impairment group reported nausea.

Table 1. Commonly reported medical problems by study participants					
Medical Problem	Danuglipron (39 Participants)				
	Healthy and Normal Kidney Function	T2DM with Normal Kidney Function	T2DM with Mild Kidney Impairment	T2DM with Moderate Kidney Impairment	T2DM with Severe Kidney Impairment
Nausea	1 out of 8 participants (13%)	1 out of 7 participants (14%)	0 out of 8 participants (0%)	1 out of 8 participants (13%)	1 out of 8 participants (13%)
Diarrhoea	0 out of 8 participants (0%)	0 out of 7 participants (0%)	0 out of 8 participants (0%)	2 out of 8 participants (25%)	0 out of 8 participants (0%)
Excessive urine production	0 out of 8 participants (0%)	2 out of 7 participants (29%)	0 out of 8 participants (0%)	0 out of 8 participants (0%)	0 out of 8 participants (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 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.

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

www.clinicaltrials.gov
Use the study identifier **NCT04616027**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number **C3421012**

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!