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:	Sisunatovir (PF-07923568)
Protocol Number:	C5241015
Dates of Study:	15 May 2023 to 30 October 2023
Title of this Study:	A Study to Investigate the Effects of Sisunatovir on the Heart Function of Healthy Adult Participants [A Phase 1, Randomized, Double-Blind, Sponsor-Open, Placebo- and Positive-Controlled Crossover Study to Investigate the Effect of Multiple Doses of Sisunatovir on QTc Interval in Healthy Adult Participants]
Date(s) of this Report:	20 May 2024

– 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 respiratory syncytial virus (RSV) infection?

Respiratory syncytial virus (RSV) is a virus that can cause an infection with symptoms that are similar to a bad cold, such as cough, fever, sore throat, and a runny nose. This infection can be serious in young children, older adults, and in those with underlying medical conditions. People with serious RSV infection may have trouble breathing and may need to be hospitalized.

What is Sisunatovir (PF-07923568)?

The study drug sisunatovir (see-sue-nah-toe-veer, PF-07923568) is an investigational medicine. It is taken as a capsule by mouth. An investigational medicine is one that is not approved for use outside of research studies. Researchers think sisunatovir may help the body's immune system defend against RSV infection. Sisunatovir blocks a protein in the RSV called the RSV-F protein. By blocking this protein, sisunatovir prevents the virus from entering the human cells and prevents the infection.

What was the purpose of this study?

The main purpose of this study was to see if taking sisunatovir has an effect on the heart function of healthy participants, compared to a placebo. A placebo does not have any medicine in it but looks just like the study medication.

In this study, researchers used a machine called an electrocardiogram or ECG, to measure heart function. The "QT interval" is a measurement made on the ECG that measures the electrical activity of the heart. To make sure the comparisons were accurate, researchers adjusted or "corrected" the QT interval using a special formula. The corrected QT

interval is called “QTc,” and the value used to describe the result is called “QTcF”.

The researchers wanted to see if there were any changes in QT interval after taking sisunatovir. Researchers mainly wanted to assess if sisunatovir caused “QT prolongation”. QT prolongation occurs when the heart takes longer than usual to contract and relax. This can affect the heart rhythm (beating of the heart) and can lead to life-threatening heart rhythm disorder.

The researchers gave moxifloxacin to some participants in the study. Moxifloxacin is an approved marketed drug with a known effect on the heart function (“QTc interval”). It is taken as a tablet by mouth. The researchers tested whether they were able to detect QT interval changes in this study by looking at their results for the participants who were given moxifloxacin. These participants were expected to have changes in their QT interval.

This study did not test if sisunatovir helps to improve RSV infection.

Researchers wanted to know:

- **Did participants have a clinically significant change in their heart function (measured by QT interval change) after taking sisunatovir?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested different doses of sisunatovir on a group of healthy participants to find out if study participants taking sisunatovir had a change in their heart function.

Participants were “screened” to see if they qualified to be in the study before they received the treatment.

The study had 3 treatment periods. Participants took one treatment in each period. The order (sequence) that participants took their treatment in was decided by chance. There were 6 treatment sequences.

Treatment A: Participants received sisunatovir 300 mg twice daily from Day 1 to Day 3.

Treatment B: Participants received placebo twice daily from Day 1 to Day 3.

Treatment C: Participants received placebo twice daily on Day 1 and Day 2, followed by a single dose of moxifloxacin 400 mg on Day 3. This treatment was administered to demonstrate that the study was able to successfully identify effects on heart function.

Researchers assessed the first 14 participants who took Treatment A. The dose from Treatment A was determined to be too low to achieve the required level of sisunatovir in the blood. Researchers wanted to see the effect of a higher level of sisunatovir in the participant’s blood. As a result, Treatment D was introduced as a higher dose to meet this requirement.

Treatment D: Participants received sisunatovir 350 mg twice daily from Day 1 to Day 3.

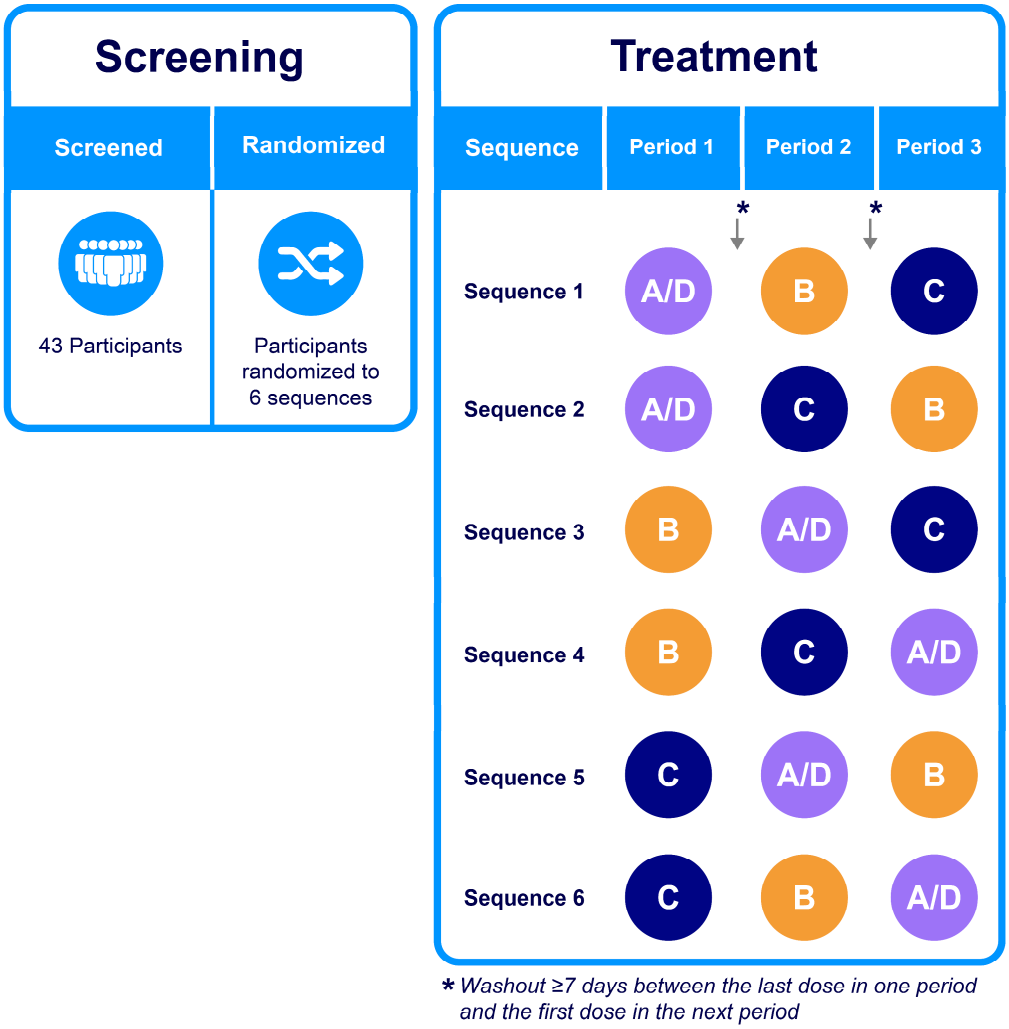
All treatments were given to participants with food, about 30 minutes after the start of a standard meal.

In between the treatment periods there were at least 7 days where participants did not receive any treatment. This was called a “washout”. It was done to allow all of the study medication to have left the participants’ body. During each treatment period, participants were admitted to the research unit 1 day prior to receiving the treatment and were required to reside until the completion of protocol assessments on Day 4. Participants were followed up for safety within 28 to 35 calendar days after the last dose of treatment.

In this study, treatment with sisunatovir and placebo was “blinded” to the participants and study doctor or study staff (except the pharmacy staff) but “open” to the Sponsor. This means that neither the participants nor the study doctors knew who received what treatment. Treatment with moxifloxacin was “unblinded” meaning both the participants and the study doctors knew which treatment was given.

The treatments assigned in each treatment period and the sequence in which the treatments were taken is shown in Figure 1 on the next page.

Figure 1. Study Design Schema



* *Washout ≥7 days between the last dose in one period and the first dose in the next period*

Participants had regular ECGs to monitor changes in their heart function. Researchers conducted other tests and collected blood samples to monitor safety. They also checked the level of sisunatovir in participants' blood. Participants were asked about how they were feeling, and their health was monitored periodically during 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 15 May 2023 and ended 30 October 2023.

Who participated in this study?

The study included healthy participants who met the inclusion/exclusion criteria for things such as age and weight.

- A total of 28 men participated
- A total of 15 women participated
- All participants were between the ages of 23 and 64 years

A total of 43 participants were treated in this study. Thirty-seven participants completed the treatment, and 6 participants did not complete the treatment due to:

- Unacceptable medical problems (2 participants [4.7%])
- A doctor decided it was best for a participant to stop being in the study (2 participants [4.7%])
- Participant left before the study was over by their choice (1 participant [2.3%])
- Participant no longer met the eligibility criteria (1 participant [2.3%])

How long did the study last?

Study participants were in the study for approximately 50 days. The entire study took 5 months and 16 days to complete.

When the study ended in October 2023, 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?

Did participants have a clinically significant change in their heart function (measured by QT interval change) after taking sisunatovir?

The results for healthy adult participants are shown below.

The study found that sisunatovir caused minimal changes in heart function, measured by QT interval change. None of these changes were of clinical concern to the researchers. Hence, the participants did not have a clinically significant change in their heart function after taking sisunatovir.

Did the study medication (sisunatovir) cause QTc prolongation?

The researchers compared QTc interval values before (baseline) and after taking sisunatovir and placebo. The difference in the before and after results was used to calculate the "placebo-adjusted change from baseline QTcF" (also referred to as "delta-delta QTcF" in this document). The values were measured in "milliseconds" (msec).

The researchers calculated these results for participants who took sisunatovir 300 mg and sisunatovir 350 mg. They also looked at the results for the participants who had a certain high level of sisunatovir in their blood. This level was called a "high clinical exposure".

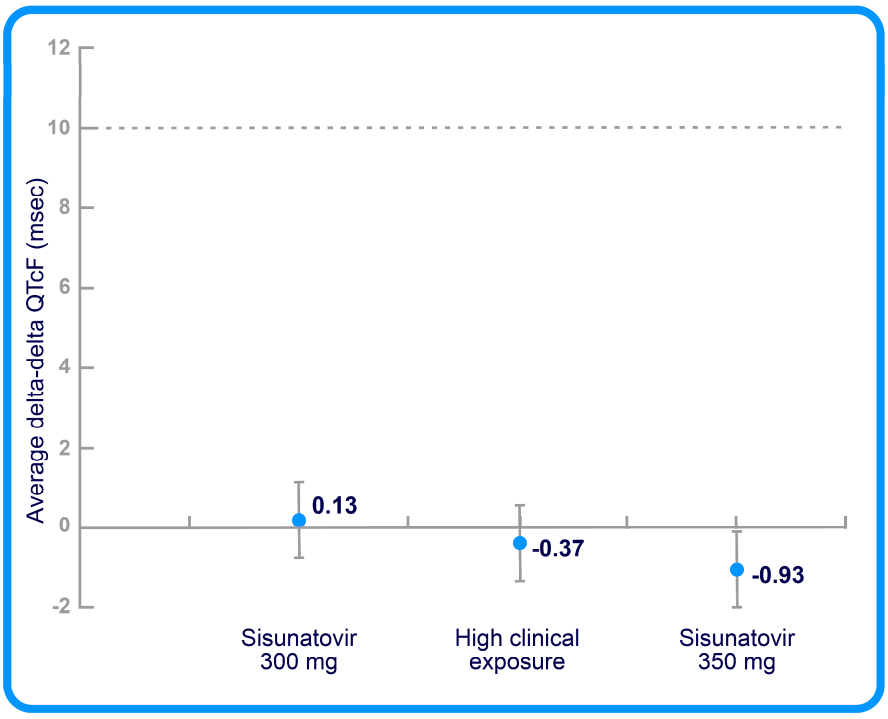
As shown in Figure 2, the average delta-delta QTcF was 0.13 msec after participants took sisunatovir 300 mg and -0.93 msec after taking sisunatovir 350 mg. The result for the high clinical exposure when sisunatovir 200 mg was taken along with an inhibitor of metabolism (a

substance that blocks the breakdown of certain drugs or compounds in the body) was -0.37 msec.

Researchers decided beforehand on a specific cutoff value of 10 msec (shown as 'dotted' lines in Figure 2). This would help them identify if the change in QTc was significant or not.

All of the results were less than 10 msec as shown in Figure 2. This showed that sisunatovir did not have a clinically meaningful effect on QTc interval and did not cause QTc prolongation.

Figure 2. Summary of average delta-delta QTcF



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.

Twenty-five out of 43 (58.1%) participants in this study had at least 1 medical problem. A total of 2 participants (4.7%) left the study because of medical problems. The most common medical problems – those reported by 2 or more 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 participants are listed.
- The **2nd** column tells how many of the 42 participants who took sisunatovir 300 mg and 350 mg reported each medical problem. Below this number is the percentage of the 42 participants who took sisunatovir 300 mg and 350 mg that reported the medical problem.

- The **3rd** column tells how many of the 41 participants who took placebo reported each medical problem. Below this number is the percentage of the 41 participants who took placebo that reported the medical problem.
- The **4th** column tells how many of the 39 participants who took placebo and moxifloxacin 400 mg reported each medical problem. Below this number is the percentage of the 39 participants who took placebo and moxifloxacin that reported the medical problem.
- Using these instructions, you can see that 3 out of the 42 (7.1%) participants who took sisunatovir 300 mg and 350 mg reported abdominal pain. No participant who took placebo reported abdominal pain and 1 out of the 39 (2.6%) participants who took placebo and moxifloxacin 400 mg reported abdominal pain.

Table 1. Commonly reported medical problems reported for 2 or more study participants

Medical Problem	Sisunatovir 300 mg + 350 mg (42 Participants)	Placebo (41 Participants)	Placebo + Moxifloxacin 400 mg (39 Participants)
Abdominal pain	3 out of 42 participants (7.1%)	0	1 out of 39 participants (2.6%)
Constipation	5 out of 42 participants (11.9%)	1 out of 41 participants (2.4%)	0
Diarrhea	4 out of 42 participants (9.5%)	0	1 out of 39 participants (2.6%)
Nausea	3 out of 42 participants (7.1%)	0	1 out of 39 participants (2.6%)
Vomiting	4 out of 42 participants (9.5%)	1 out of 41 participants (2.4%)	1 out of 39 participants (2.6%)
Arm or leg pain	0	1 out of 41 participants (2.4%)	2 out of 39 participants (5.1%)

Table 1. Commonly reported medical problems reported for 2 or more study participants			
Medical Problem	**Sisunatovir 300 mg + 350 mg (42 Participants)**	**Placebo (41 Participants)**	**Placebo + Moxifloxacin 400 mg (39 Participants)**
Headache	5 out of 42 participants (11.9%)	1 out of 41 participants (2.4%)	1 out of 39 participants (2.6%)
Feeling faint	2 out of 42 participants (4.8%)	1 out of 41 participants (2.4%)	0
Sleepiness	2 out of 42 participants (4.8%)	1 out of 41 participants (2.4%)	1 out of 39 participants (2.6%)
Inflammation of a vein	0	2 out of 41 participants (4.9%)	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 any serious medical problems and no participant died during this 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.pfizer.com/research/ research_clinical_trials/trial_results	Use the protocol number C5241015

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

www.clinicaltrials.gov	Use the study identifier **NCT05878522**

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!