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 Studied: PF-07209326

Protocol Number: C4071001

Dates of Study: 05 February 2020 to 07 July 2023

Title of this Study: Dose Escalation Study of PF-07209326 in Healthy Participants and Participants With Sickle Cell Disease

[A Randomized, Double-Blind, Placebo-Controlled Evaluation of Single Doses of PF- 07209326 in Healthy Participants (Safety, Tolerability, and Pharmacokinetics [PK]) Followed by an Open-Label, Repeat Dose Evaluation in Sickle Cell Disease Participants (Safety, Tolerability, PK, and Efficacy)]

Date of this Report: 27 February 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 sickle cell disease?

Sickle cell disease (SCD) is a common “inherited” red blood cell disorder. Inherited means it is passed down from parents to their children and runs in families. In the United States, approximately 100,000 people have SCD while around the world it is estimated that at least 5 million people have SCD. In SCD, many of the red blood cells have an abnormal shape (“sickled”), and these can cause swelling and pain.

Many people with SCD will develop a condition known as an “acute pain crisis” or “vaso-occlusive crisis” (VOC). This happens when white blood cells together with sickled red cells in blood vessels lead to a blockage. As a result, the blood flow and oxygen delivery to areas of the body is prevented, causing painful crises.

What is PF-07209326?

The study drug (PF-07209326) is an investigational medicine. It is not currently approved for use by health authorities in United States, where this study was held. PF-07209326 is administered as an injection under the skin (subcutaneous) or as an infusion into a vein through a needle (intravenous). PF-07209326 is an engineered protein also called a monoclonal antibody. Antibodies are proteins made by the body’s immune (defense) system. PF-07209326 is designed to block a naturally occurring protein known as “E-selectin” which is produced by the body during an immune response. It is thought that blocking this protein may help treat SCD. The researchers have been studying PF-07209326 as a potential treatment for SCD.

What was the purpose of this study?

The main purpose of this study was to learn about the safety and tolerability of PF-07209326 in healthy participants and participants with SCD. "Tolerability" refers to how well participants can tolerate receiving the study drug.

This was the first time that PF-07209326 was tested in healthy participants and participants with SCD. Researchers wanted to find out the safe (optimal) dose of the study drug that is tolerated by participants without causing any dangerous medical problems. This will help them decide what dose to give people in future studies.

Researchers wanted to know:

- **How safe and well tolerated was PF-07209326?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

The study was conducted in 2 parts: Part 1 and Part 2.

Part 1

Different doses of PF-07209326 were given to a group of healthy participants to better understand how PF-07209326 acts in the body.

Participants were assigned to receive single, increasing doses of subcutaneous (SC) or intravenous (IV) PF-07209326. Some participants received a matching SC and IV placebo dose instead of PF-07209326. A

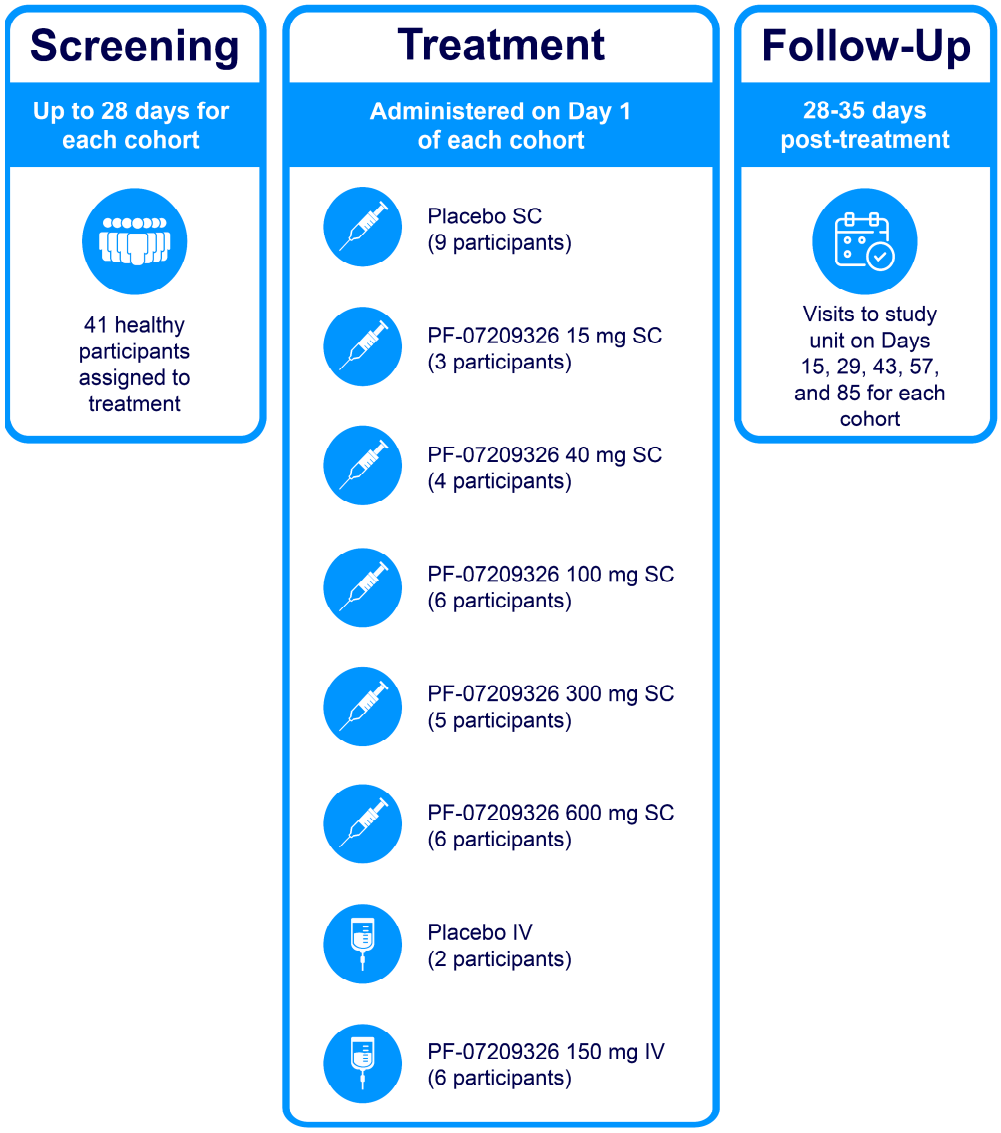
placebo does not have any medicine in it, but it looks just like the study medication. Each participant in Part 1 was treated once.

All participants were “screened” to see if they qualify to be in the study. Participants who qualified for treatment after screening entered the Treatment Period. They were required to stay in the study unit for 11 days during this period. Participants returned to the study unit on Days 15, 29, 43, 57, and Day 85 for follow-up visits as shown in the study design in Figure 1. Follow-up on Day 43 was done either by visiting the study unit or through a phone call.

Each group of participants treated with a particular dose of PF-07209326 or placebo is called a dosing cohort. The safety and tolerability of PF-07209326 was assessed and dose was increased for the next group of participants. As shown in Figure 1 below, participants received single dose of PF-07209326 or placebo on Day 1 of each cohort.

The participants and researchers did not know who received different doses of PF-07209326 and who received the placebo. This is known as a “blinded” study. Participants were assigned to each cohort by chance alone.

Figure 1: Study design for Part 1

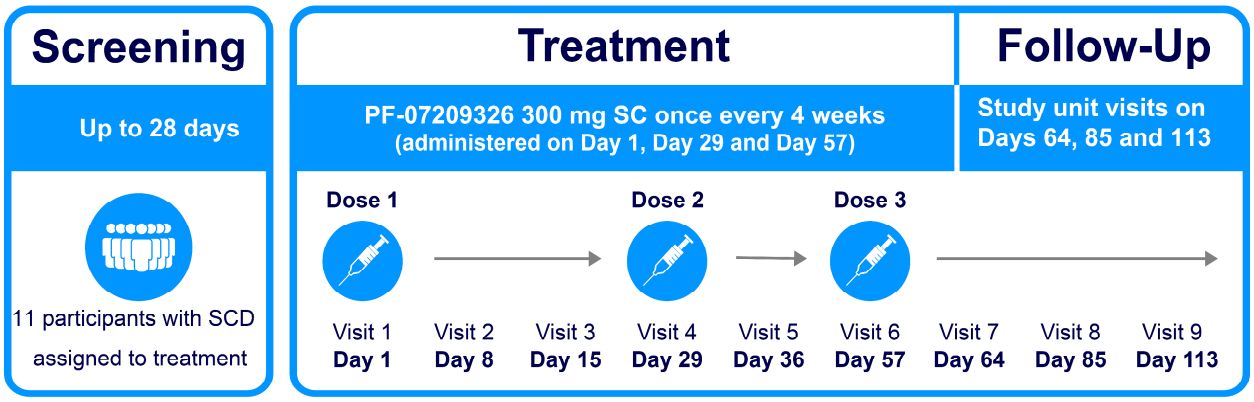


Part 2

In Part 2 of the study, researchers tested multiple doses of PF-07209326 in participants who had SCD. A total of 11 participants received a 300 mg SC dose of PF-07209326 once in every 4 weeks, on Days 1, 29, and 57. After screening, all participants returned to the study unit for their treatment and

follow-up visits. Figure 2 shows different visits to the study unit during treatment period and follow-up period.

Figure 2: Study design for Part 2



Part 2 was an "open-label" study. This means researchers and participants knew what study medication the participants received.

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

For Part 1, researchers then compared the results of participants who received different doses of PF-07209326. Researchers also compared results of participants who received PF-07209326 to those who received placebo. They did this to see if medical problems experienced during the study could be related to the study medication or something else. For Part 2, researchers evaluated the results of participants with SCD who were treated with 300 mg SC doses of PF-07209326.

Where did this study take place?

The Sponsor ran this study at 6 locations in the United States.

When did this study take place?

It began on 05 February 2020 and ended on 07 July 2023.

Who participated in this study?

For Part 1, the study included healthy participants who were between the ages of 18 to 55 years. In Part 2, participants with SCD who were between the ages of 16 to 70 years and who had experienced at least 2 but not more than 10 VOCs in the year before joining the study were included.

Part 1

A total of 41 participants were treated in Part 1 of the study.

- A total of 37 men participated
- A total of 4 women participated
- All participants were between the ages of 22 and 54 years

Of the 41 participants who were treated in Part 1 of the study, 40 participants completed the study. One participant discontinued the study due to death. This death was considered not related to the study drug.

Part 2

A total of 11 participants were treated in Part 2 of the study.

- A total of 9 men participated
- A total of 2 women participated
- All participants were between the ages of 21 and 62 years

All 11 participants who were treated in Part 2 completed the study.

How long did the study last?

Study participants were in the study for approximately 12 weeks in Part 1 and approximately 16 weeks in Part 2. The entire study took 3 years and 5 months to complete.

When the study ended in July 2023, the Sponsor reviewed 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 safe and well tolerated was PF-07209326?

In this study, researchers looked at the safety and tolerability of PF-07209326 for a range of single doses and as multiple doses (300 mg once every 4 weeks). The researchers did this by looking at the medical problems that participants had during the study. Researchers were specifically looking at the following reports:

- Results of laboratory tests, blood pressure, pulse rate, and electrocardiogram (ECG) tests. An ECG is a machine that looks at how well the heart is working when it pumps blood around the body.
- Medical problems related to infusion of the study medication (also called “infusion-related reactions” or IRRs).
- Medical problems related to the injection site. This is the place where the needle was inserted to give the study medication.

Medical problems overall are described in the next section.

What was the result of laboratory tests after participants received PF-07209326 or placebo?

Researchers did not find any clinically important laboratory changes or abnormalities in the safety laboratory data during the study that were large enough to make a difference.

What was the result of blood pressure, pulse rate, and ECG tests after participants received PF-07209326 or placebo?

- All participants in Part 1 and Part 2 had blood pressure, pulse rate, and ECG tests during the study.
- None of the participants had blood pressure, pulse rate, and ECG values that met specific reporting criteria for important changes.
- No participants had changes in their blood pressure, pulse rate, and ECG values that were considered medically important or as medical problems.

Did participants experience any IRRs or medical problems related to injection or infusion site?

The following infusion/injection site medical problems were reported in Part 1 of the study:

- Discoloration at the injection site was reported by 1 participant who received the PF-07209326 40 mg SC dose.
- Skin redness at the injection site was reported by 2 participants each who received SC doses of placebo or PF-07209326 600 mg.
- Pain at the injection site was reported by 1 participant each who received SC doses of placebo, PF-07209326 300 mg, and PF-07209326 600 mg.

- Bleeding at injection site was reported by 2 participants who received the PF-07209326 600 mg SC dose.

Researchers considered these events mild in severity. All events except discoloration at the injection site were considered as related to study medication.

In Part 2 of the study, 1 event of skin redness at injection site and 2 events of itching at injection site were reported. Researchers considered these events mild and related to the study medication.

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 27 out of 41 (65.9%) participants in Part 1 and 8 out of 11 (72.7%) participants in Part 2 of this study had at least 1 medical problem. Eight (8) participants reported 12 medical problems related to study medication in Part 1 and 5 participants reported 9 medical problems related

to study medication in Part 2 of the study. No participants left the study because of medical problems. All medical problems reported by participants in Part 1 and Part 2 of the study – are described below.

Below are instructions on how to read Table 1, Table 2, and Table 3.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists medical problems that were reported by participants who received SC doses of PF-07209326 or SC doses of placebo during Part 1 of the study. All medical problems reported by participants are listed.
- The **2nd** column tells how many of the 9 participants who received placebo SC dose reported each medical problem. Below this number is the percentage of the 9 participants who received placebo SC dose that reported the medical problem.
- The **3rd** column tells how many of the 3 participants who received PF-07209326 15 mg SC dose reported each medical problem. Below this number is the percentage of the 3 participants who received PF-07209326 15 mg SC dose that reported the medical problem.
- The **4th** column tells how many of the 4 participants who received PF-07209326 40 mg SC dose reported each medical problem. Below this number is the percentage of the 4 participants who received PF-07209326 40 mg SC dose that reported the medical problem.
- The **5th** column tells how many of the 6 participants who received PF-07209326 100 mg SC dose reported each medical problem. Below this number is the percentage of the

6 participants who received PF-07209326 100 mg SC dose that reported the medical problem.

- The **6th** column tells how many of the 5 participants who received PF-07209326 300 mg SC dose reported each medical problem. Below this number is the percentage of the 5 participants who received PF-07209326 300 mg SC dose that reported the medical problem.
- The **7th** column tells how many of the 6 participants who received PF-07209326 600 mg SC dose reported each medical problem. Below this number is the percentage of the 6 participants who received PF-07209326 600 mg SC that reported the medical problem.
- Using these instructions, you can see that 1 out of the 6 (16.7%) participants who received PF-07209326 100 mg SC dose reported indigestion. No other participants who received PF-07209326 SC doses or placebo doses reported indigestion.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists medical problems that were reported by participants who received IV doses of PF-07209326 or IV doses of placebo during Part 1 of the study. All medical problems reported by participants are listed.
- The **2nd** column tells how many of the 2 participants who received placebo IV dose reported each medical problem. Next to this number is the percentage of the 2 participants who received placebo IV dose that reported the medical problem.

- The **3rd** column tells how many of the 6 participants who received PF-07209326 150 mg IV dose reported each medical problem. Next to this number is the percentage of the 6 participants who received PF-07209326 150 mg IV dose that reported the medical problem.
- Using these instructions, you can see that 1 out of the 6 (16.7%) participants treated with a single 150 mg IV dose of PF-07209326 were reported to have a disorder that affects the white part of the eye. No participants who received placebo IV dose reported this disorder.

Instructions for Understanding Table 3.

- The **1st** column of Table 3 lists medical problems that were reported during Part 2 of the study. All medical problems reported by study participants in Part 2 are listed.
- The **2nd** column tells how many of the 11 participants who received PF-07209326 300 mg SC dose in Part 2 reported each medical problem. Next to this number is the percentage of the 11 participants who received PF-07209326 300 mg SC dose in Part 2 that reported the medical problem.
- Using these instructions, you can see that 1 out of the 11 (9.1%) participants who received PF-07209326 300 mg SC dose in Part 2 reported high levels of blood clotting cells.

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
Indigestion	0	0	0	1 out of 6 participants (16.7%)	0	0
Nausea	1 out of 9 participants (11.1%)	0	0	0	0	0
Tooth loss	0	0	0	0	1 out of 5 participants (20.0%)	0
Bruise at the site of injection	0	0	1 out of 4 participants (25.0%)	0	0	0
Redness at the site of application	1 out of 9 participants (11.1%)	0	0	0	0	0
Irritation at the site of application	0	0	1 out of 4 participants (25.0%)	0	0	0

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
Death	0	0	0	1 out of 6 participants (16.7%)	0	0
Feeling tired	0	0	1 out of 4 participants (25.0%)	0	0	0
Discolor-ation at injection site	0	0	1 out of 4 participants (25.0%)	0	0	0
Redness at injection site	2 out of 9 participants (22.2%)	0	0	0	0	2 out of 6 participants (33.3%)
Bleeding at injection site	0	0	0	0	0	2 out of 6 participants (33.3%)
Pain at injection site	1 out of 9 participants (11.1%)	0	0	0	1 out of 5 participants (20.0%)	1 out of 6 participants (16.7%)

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
Common cold	1 out of 9 participants (11.1%)	0	0	0	0	0
Soft tissue injury	0	0	0	0	1 out of 5 participants (20.0%)	0
SARS-CoV-2 test positive	0	0	0	0	1 out of 5 participants (20.0%)	0
Joint pain	0	0	0	1 out of 6 participants (16.7%)	0	0
Muscle pain	0	0	0	0	1 out of 5 participants (20.0%)	0
Arm or leg pain	0	0	0	1 out of 6 participants (16.7%)	0	1 out of 6 participants (16.7%)

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
Headache due to drug withdrawal	0	0	1 out of 4 participants (25.0%)	0	0	0
Headache	0	1 out of 3 participants (33.3%)	1 out of 4 participants (25.0%)	0	1 out of 5 participants (20.0%)	0
Excessive sleepiness	1 out of 9 participants (11.1%)	0	0	0	0	0
Muscle contraction involuntary	0	0	1 out of 4 participants (25.0%)	0	0	0
Difficulty falling asleep	0	0	1 out of 4 participants (25.0%)	0	0	0
Fear of medical or surgical procedures	0	0	0	0	0	1 out of 6 participants (16.7%)

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
resulting in distress						
Kidney stone	0	0	0	1 out of 6 participants (16.7%)	0	0
Runny nose	0	0	1 out of 4 participants (25.0%)	0	0	0
Blocked nose	0	0 out of 3 participants (33.3%)	0	0	1 out of 5 participants (20.0%)	0
Red, inflamed skin due to touching a certain substance	0	0	0	0	0	1 out of 6 participants (16.7%)
Bruise	0	0	0	0	0	1 out of 6 participants (16.7%)

Table 1. Medical problems reported by study participants in Part 1

	SC cohorts of PF-07209326 in Part 1					
Medical Problem	**Placebo SC (9 participants)**	**PF-07209326 15 mg SC (3 participants)**	**PF-07209326 40 mg SC (4 participants)**	**PF-07209326 100 mg SC (6 participants)**	**PF-07209326 300 mg SC (5 participants)**	**PF-07209326 600 mg SC (6 participants)**
Redness	0	0	0	0	0	1 out of 6 participants (16.7%)
Rash	0	0	0	0	1 out of 5 participants (20.0%)	0
Skin redness	0	0	0	0	1 out of 5 participants (20.0%)	0
Increased blood pressure	0	0	0	0	0	1 out of 6 participants (16.7%)

Table 2. Medical problems reported by study participants in Part 1		
	IV cohorts of PF-07209326 in Part 1	
Medical Problem	Placebo IV (2 participants)	PF-07209326 150 mg IV (6 participants)
Disorder that affects the white eye part	0	1 out of 6 participants (16.7%)
Constipation	0	1 out of 6 participants (16.7%)
Difficulty swallowing	0	1 out of 6 participants (16.7%)
Discoloration at application site	0	1 out of 6 participants (16.7%)
Insect bite	2 out of 2 participants (100%)	0
Liver test enzyme (alanine amino-transferase) increased	0	1 out of 6 participants (16.7%)
Neck pain	0	1 out of 6 participants (16.7%)

Table 2. Medical problems reported by study participants in Part 1		
	IV cohorts of PF-07209326 in Part 1	
Medical Problem	Placebo IV (2 participants)	PF-07209326 150 mg IV (6 participants)
Arm or leg pain	0	1 out of 6 participants (16.7%)
Dizziness	0	1 out of 6 participants (16.7%)
Feeling of worry or fear	0	1 out of 6 participants (16.7%)
Shortness of breath	0	1 out of 6 participants (16.7%)
Red, inflamed skin due to touching a certain substance	0	1 out of 6 participants (16.7%)
Itching	0	1 out of 6 participants (16.7%)

Table 3. Medical problems reported by study participants in Part 2	
Medical Problem	**PF-07209326 300 mg SC (11 participants)**
High level of blood clotting cells	1 out of 11 participants (9.1%)
Eye discomfort	1 out of 11 participants (9.1%)
Toothache	1 out of 11 participants (9.1%)
Tiredness	1 out of 11 participants (9.1%)
Skin redness at injection site	1 out of 11 participants (9.1%)
Itching at injection site	2 out of 11 participants (18.2%)
Swelling of the tissues in the sinuses	1 out of 11 participants (9.1%)
Presence of germs in the urine	1 out of 11 participants (9.1%)
Skin rashes due to fungal infection	1 out of 11 participants (9.1%)
Covid-19 infection	1 out of 11 participants (9.1%)
Cold sores	1 out of 11 participants (9.1%)

Table 3. Medical problems reported by study participants in Part 2	
Medical Problem	**PF-07209326 300 mg SC (11 participants)**
A result from a blood test that indicates the blood is taking longer than normal to clot	1 out of 11 participants (9.1%)
Increase in liver enzyme	1 out of 11 participants (9.1%)
Joint pain	1 out of 11 participants (9.1%)
Headache	1 out of 11 participants (9.1%)
Collapse of the whole or part of a lung	1 out of 11 participants (9.1%)

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.

One participant (2.4% or 1 out of 57 participants) who received PF 07209326 100 mg SC died during Part 1 of the study. The participant died on Day 76 of the study. The reason for the death was unknown and has not been reported. Researchers concluded that the death was not related to the study medication.

There were no other serious medical problems reported in the study.

Based on these results, researchers concluded that different SC and IV doses of PF-07209326 tested in healthy participants and participants with SCD were found to be safe and well tolerated.

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 C4071001

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

www.clinicaltrials.gov	Use the study identifier **NCT04255875**

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!