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:	PF-07304814
Protocol Number:	C4611001
Dates of Study:	09 September 2020 to 07 June 2021
Title of this Study:	First-in-human Study to Evaluate Safety, Tolerability, and Pharmacokinetics Following Single Ascending and Multiple Ascending Doses of PF-07304814 in Hospitalized Participants with COVID-19 [A Phase 1b, 2-Part, Double-Blind, Placebo-Controlled, Sponsor Open Study, to Evaluate the Safety, Tolerability and Pharmacokinetics of Single Ascending (24-Hour, Part 1) and Multiple Ascending (120-Hour, Part 2) Intravenous Infusions of PF-07304814 in Hospitalized Participants With COVID-19]
Date(s) of this Report:	17 October 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 COVID-19?

Corona**vi**rus **d**isease of 20**19** (COVID-19) is an infection that affects the nose, throat, and lungs. It is caused by a type of virus called the coronavirus. People who are infected by this virus can have mild to very severe symptoms. Some people may have no symptoms at all, while others can have severe symptoms of lung infection. Sometimes people with this infection may even lose their life.

What is PF-07304814?

PF-07304814 is a new investigational drug that is given to patients intravenously (in the vein through a thin plastic tube called a catheter). This drug has not yet been approved for use by health authorities. PF-07304814 blocks a specific enzyme (protein) called “severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) 3CL.” This protein is essential for the virus to multiply and grow. By decreasing the amount of virus in the body, PF-07304814 may help treat COVID-19 infection.

What was the purpose of this study?

The purpose of this study was to test the safety (the impact on the body) of PF-07304814 compared to a placebo. A placebo does not have any medicine in it, but it looks just like the study medication.

Researchers compared the effect of taking placebo to the effect of taking PF-07304814.

Researchers wanted to know:

- **How safe and well tolerated was PF-07304814?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

There were 2 parts to this study, Part 1 and Part 2. Each participant took part in either Part 1 or Part 2, not both.

- In Part 1, participants were given a single dose of study treatment (PF-07304814 or placebo). The study treatment was given by continuous infusion (drip) into the vein for 24 hours (1 day). The doses of PF-07304814 tested were 250 mg and 500 mg.
- In Part 2, participants were given PF-07304814 or placebo by continuous infusion (drip) into the vein for 120 hours (5 days). The doses of PF-07304814 tested were 250 mg and 500 mg per day.

During both Part 1 and Part 2, participant and researchers did not know who were given the different doses of PF-07304814 and who were given the placebo. This is known as a "double-blinded" study. Participants were assigned to each group by chance alone.

Participants were asked to stay in hospital for at least 3 days in Part 1, and at least 7 days in Part 2. After treatment, participants visited the hospital up to 4 times more for check-ups.

Figure 1 and Figure 2 below show what happened during the study.

Researchers took samples of blood and urine and took nose and throat swabs from participants during the study. Researchers tested the electrical activity of participants' hearts with "electrocardiograms" ("ECGs") during the study. They also checked the participants' health and asked them how they were feeling.

Figure 1. Study Plan Part 1

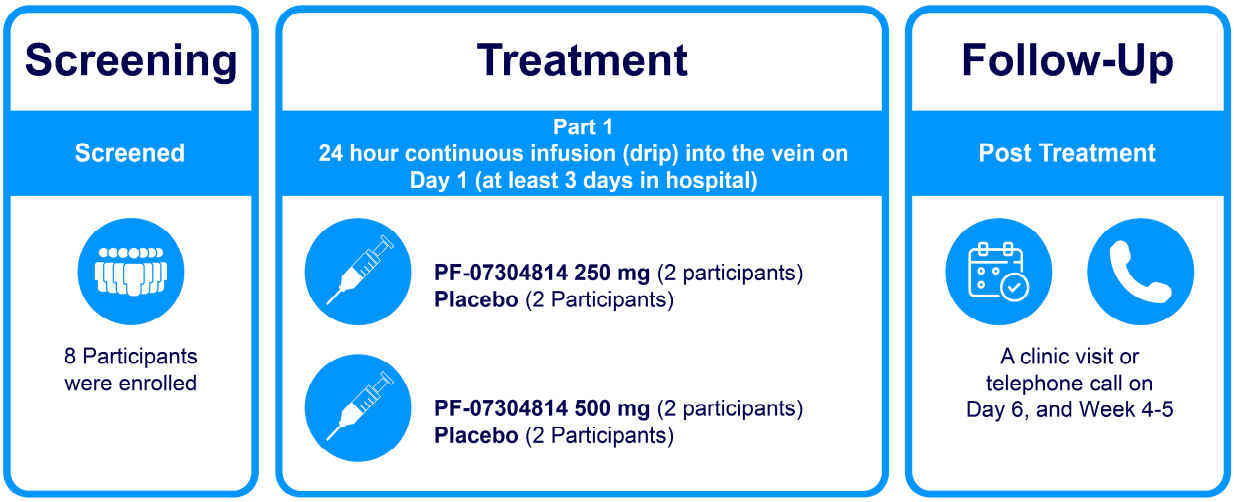
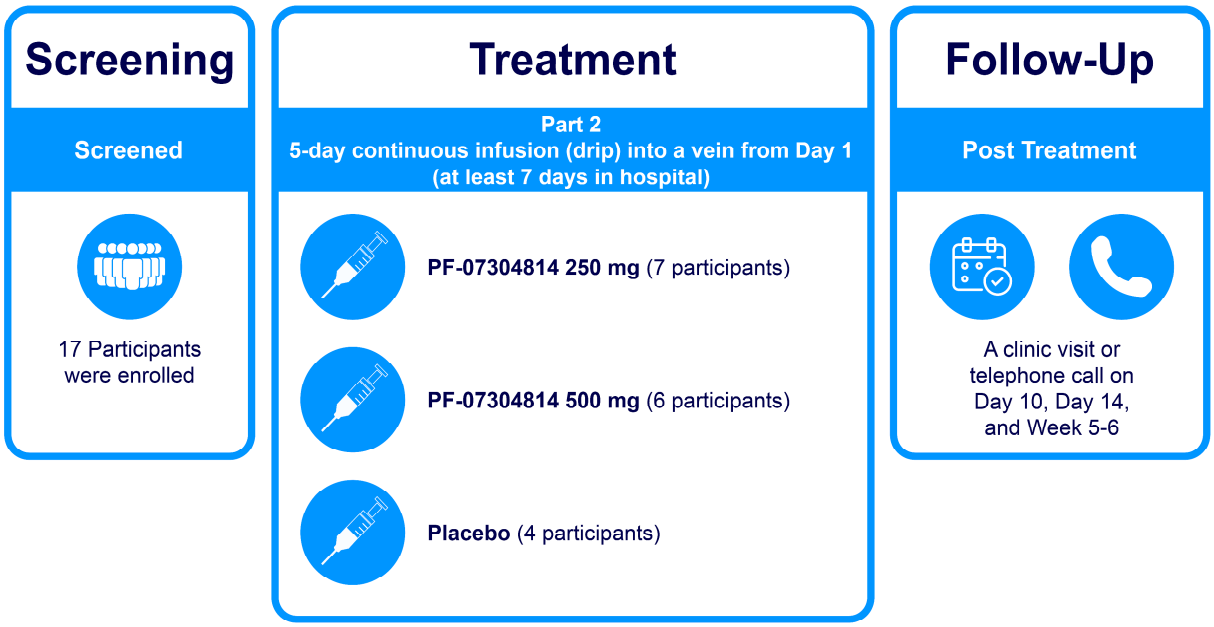


Figure 2. Study Plan Part 2



Where did this study take place?

The Sponsor ran this study at 8 locations in 3 countries in Europe and North America.

When did this study take place?

It began 09 September 2020 and ended 07 June 2021.

Who participated in this study?

The study included adult participants who had a confirmed COVID-19 infection, had COVID-19 symptoms, and met the study's body weight criteria. Only participants who were hospitalized could take part in the study.

- All participants in the study were between the ages of 33 and 77

Part 1

- A total of 5 men participated
- A total of 3 women participated

Of the 8 participants who started Part 1 of the study, all completed their treatment. After treatment, 7 of the participants completed follow-up and finished the study. One participant could not be contacted.

Part 2

- A total of 14 men participated
- A total of 3 women participated

Of the 17 participants who started Part 2 of the study, 16 participants finished their treatment. There was 1 participant in the placebo group who stopped treatment early because of a medical problem.

There was 1 participant in the placebo group who did not finish the follow-up part of the study. This was because they passed away. The researchers did not believe that the death was related to study medication.

How long did the study last?

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

When the study ended in June 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 safe and well-tolerated was PF-07304814?

What was the result of laboratory tests during the study?

Part 1

A total of 2 out of 8 participants (25.0%) who had abnormal laboratory test results that the researchers considered as medical problems and as “clinically significant” (could harm their health).

- Both of these participants were in a placebo group.

Part 2

A total 2 out of 17 participants (11.8%) who had abnormal laboratory test results that the researchers considered as medical problems or “clinically significant”.

- One of these participants was in the placebo group and this participant stopped treatment early
- One of these participants was in the PF-07304814 250 mg group.

None of these abnormal laboratory results in Part 1 or Part 2 were believed to be related to PF-07304814 treatment.

Researchers also tested participant’s blood for results that showed how much their blood was likely to clot and cause a medical problem. Medical problems are described in the next section.

What was the result of blood pressure, pulse rate, temperature, and breathing rate during the study?

No participants had changes in blood pressure, pulse rate, temperature, or breathing rate that the researchers considered as medical problems, or "clinically significant".

What were the results for oxygen support needed during the study?

Oxygen levels in the blood were monitored in the study. Below is a summary of extra oxygen given to participants whose oxygen level in the blood was less than 94%.

Part 1

A total of 4 out of 8 (50.0%) participants were given extra oxygen throughout the study.

- One of these participants was in the PF-07304814 250 mg group
- One of these participants was in the PF-07304814 500 mg group
- Two of these participants were in the placebo groups.

There was 1 other participant was given extra oxygen at some point during the study (i.e., not all the time). This participant was in the placebo group.

Part 2

A total of 8 out of 17 (47.1%) participants were given extra oxygen throughout the study.

- Three of these participants were in the PF-07304814 250 mg group

- Four of these participants were in the PF-07304814 500 mg group
- One of these participants was in the placebo group.

Four other participants were given extra oxygen at some point during the study (i.e., not all the time).

- One of these participants was in the PF-07304814 250 mg group
- One of these participants was in the PF-07304814 500 mg group
- Two of these participants were in the placebo group.

Some of the participants who needed extra oxygen in the study needed it because they had medical problems. None of those medical problems were believed to be related to PF-07304814 treatment.

What were the results of the ECG tests during the study?

No participants had ECG results that the researchers considered as a medical problem, or "clinically significant".

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 unknown 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.

Part 1 medical problems

A total of 6 out of 8 (75.0%) participants in Part 1 of this study had at least 1 medical problem.

No participants left the study because of medical problems. Medical problems are described in Table 1 below.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists all medical problems that were reported during Part 1 of the study.
- The **2nd** column tells how many of the 2 participants who were given PF-07304814 250 mg reported each medical problem. Next to these numbers is the percentage of the 2 participants in this group who reported the medical problem.

- The **3rd** column tells how many of the 2 participants who were given PF-07304814 500 mg reported each medical problem. Next to these numbers is the percentage of the 2 participants in this group who reported the medical problem.
- The **4th** column tells how many of the 2 participants who were given 250 mg placebo reported each medical problem. Next to these numbers is the percentage of the 2 participants in this group who reported the medical problem.
- The **5th** column tells how many of the 2 participants who were given 500 mg placebo reported each medical problem. Next to these numbers is the percentage of the 2 participants in this group who reported the medical problem.
- Using these instructions, you can see that, 1 out of the 2 participants (50.0%) taking PF-07304814 250 mg reported problems with blood clotting. There were 0 participants in the other groups who reported problems with blood clotting.

Table 1. Medical problems reported by study participants in Part 1				
Medical Problem	PF-07304814 250 mg (2 Participants)	PF-07304814 500 mg (2 Participants)	250 mg placebo (2 participants)	500 mg Placebo (2 Participants)
Problems with blood clotting	1 out of 2 participants (50.0%)	0	0	0
Rapid heartbeat	0	0	0	1 out of 2 participants (50.0%)
Abdominal pain	0	0	0	1 out of 2 participants (50.0%)
Diarrhea	0	1 out of 2 participants (50.0%)	0	1 out of 2 participants (50.0%)
Indigestion	0	0	1 out of 2 participants (50.0%)	0

Table 1. Medical problems reported by study participants in Part 1				
Medical Problem	PF-07304814 250 mg (2 Participants)	PF-07304814 500 mg (2 Participants)	250 mg placebo (2 participants)	500 mg Placebo (2 Participants)
Swelling, fluid retention	0	0	1 out of 2 participants (50.0%)	0
Covid-19 lung infection	0	0	1 out of 2 participants (50.0%)	0
Infection of hair follicle (hair root pocket)	0	1 out of 2 participants (50.0%)	0	0
Fungal skin infection called “tinea cruris”	0	0	0	1 out of 2 participants (50.0%)
Low proportion of red blood cells	0	0	0	1 out of 2 participants (50.0%)

Table 1. Medical problems reported by study participants in Part 1				
Medical Problem	PF-07304814 250 mg (2 Participants)	PF-07304814 500 mg (2 Participants)	250 mg placebo (2 participants)	500 mg Placebo (2 Participants)
Low red blood cells	0	0	0	1 out of 2 participants (50.0%)
Abnormal liver tests	0	0	1 out of 2 participants (50.0%)	0
Increased liver enzymes in blood	0	0	0	1 out of 2 participants (50.0%)
Pain in arm or leg	0	0	0	1 out of 2 participants (50.0%)
Blood in the urine	0	0	1 out of 2 participants (50.0%)	0

Table 1. Medical problems reported by study participants in Part 1				
Medical Problem	**PF-07304814 250 mg (2 Participants)**	**PF-07304814 500 mg (2 Participants)**	**250 mg placebo (2 participants)**	**500 mg Placebo (2 Participants)**
Lungs not working properly	1 out of 2 participants (50.0%)	0	0	0
Blood clot in the subclavian vein (a vein that carries blood from the upper part of the body to the heart)	0	1 out of 2 participants (50.0%)	0	1 out of 2 participants (50.0%)

Part 2 medical problems

A total of 9 out of 17 (52.9%) participants in Part 2 of this study had at least 1 medical problem. One participant left Part 2 of the study because of medical problems. Medical problems are described in Table 2 below.

Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists all medical problems that were reported during Part 2 of the study.
- The **2nd** column tells how many of the 7 participants who were given PF-07304814 250 mg reported each medical problem. Next to these numbers is the percentage of the 7 participants in this group who reported the medical problem.
- The **3rd** column tells how many of the 6 participants who were given PF-07304814 500 mg reported each medical problem. Next to these numbers is the percentage of the 6 participants in this group who reported the medical problem.
- The **4th** column tells how many of the 4 participants who were given placebo reported each medical problem. Next to these numbers is the percentage of the 4 participants in this group who reported the medical problem.
- Using these instructions, you can see that 1 out of the 7 participants (14.3%) taking PF-07304814 250 mg reported low blood platelets. Platelets help blood to clot. There were 0 participants in the other groups who reported “low blood platelets”

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	**PF-07304814 250 mg (7 Participants)**	**PF-07304814 500 mg (6 Participants)**	**Placebo (4 Participants)**
Low blood platelets (platelets help blood to clot)	1 out of 7 participants (14.3%)	0	0
Slow heart rate	1 out of 7 participants (14.3%)	0	0
Hole in ear drum	1 out of 7 participants (14.3%)	0	0
Stomach pain	1 out of 7 participants (14.3%)	0	0
Discomfort	1 out of 7 participants (14.3%)	0	0

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	PF-07304814 250 mg (7 Participants)	PF-07304814 500 mg (6 Participants)	Placebo (4 Participants)
Inflammation	0	0	1 out of 4 participants (25.0%)
Injected fluid leaking into the surrounding skin	0	1 out of 6 participants (16.7%)	0
Non-cardiac chest pain	0	1 out of 6 participants (16.7%)	0
Limb swelling (with fluid)	0	1 out of 6 participants (16.7%)	0
Bacterial infection of the larger airways	0	0	1 out of 4 participants (25.0%)

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	**PF-07304814 250 mg (7 Participants)**	**PF-07304814 500 mg (6 Participants)**	**Placebo (4 Participants)**
Covid-19 lung infection	0	0	1 out of 4 participants (25.0%)
Lung infection	1 out of 7 participants (14.3%)	0	0
Deep infection of skin cells at an opening into the abdomen (“stoma”)	1 out of 7 participants (14.3%)	0	0
Fall	0	0	1 out of 4 participants (25.0%)

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	**PF-07304814 250 mg (7 Participants)**	**PF-07304814 500 mg (6 Participants)**	**Placebo (4 Participants)**
Increased amount of a blood clot protein ("fibrin d-dimer" in the blood	0	0	1 out of 4 participants (25.0%)
Abnormal liver function test	0	0	1 out of 4 participants (25.0%)
High blood sugar	1 out of 7 participants (14.3%)	0	0
Joint pain	0	0	1 out of 4 participants (25.0%)
Low urine output	1 out of 7 participants (14.3%)	0	0

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	**PF-07304814 250 mg (7 Participants)**	**PF-07304814 500 mg (6 Participants)**	**Placebo (4 Participants)**
Lungs not working properly due to fluid in lungs	1 out of 7 participants (14.3%)	0	0
Shortness of breath	1 out of 7 participants (14.3%)	0	0
Lack of oxygen getting to the body	0	0	1 out of 4 participants (25.0%)
Blood clot in the lung	0	1 out of 6 participants (16.7%)	1 out of 4 participants (25.0%)
Frequent interruption of breathing during sleep	1 out of 7 participants (14.3%)	0	0

Table 2. Medical problems reported by study participants in Part 2			
Medical Problem	**PF-07304814 250 mg (7 Participants)**	**PF-07304814 500 mg (6 Participants)**	**Placebo (4 Participants)**
Rash	1 out of 7 participants (14.3%)	0	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.

Part 1

A total of 3 out of 8 participants (37.5%) in Part 1 of the study had serious medical problems.

- One participant in the PF-07304814 500 mg group had a **blood clot in the subclavian vein** (a vein that carries blood from the upper body to the heart).
- One participant in the 500 mg placebo group had a **blood clot in the subclavian vein**.
- One participant in the 250 mg placebo group had **infection of the lung caused by COVID-19**.

Part 2

A total of 4 out of 17 participants (23.5%) in Part 2 of the study had serious medical problems.

- One participant in the PF-07304814 500 mg group had a **blood clot in the lung**.
- One participant in the PF-07304814 250 mg group had a **lung infection**, and **difficulty breathing due to fluid in the lungs**.
- One participant in the PF-07304814 250 mg group had **shortness of breath**.
- One participant in the placebo group had a **blood clot in the lung**, and a **lack of oxygen getting to the body**.

Researchers do not believe any of the serious medical problems reported by participants in Part 1 and Part 2 were related to study medications.

One participant died during Part 2 of the study, from a lack of oxygen getting to the body (hypoxia). The death was not believed to be related to the study medications. This participant was in the placebo group.

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 C4611001

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

www.clinicaltrials.gov	Use the study identifier **NCT04535167**
www.clinicaltrialsregister.eu	Use the study identifier 2020-003905-73

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!