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-06835375
Protocol Number:	C1131001
Dates of Study:	17 November 2017 to 15 February 2022
Title of this Study:	Safety and Tolerability Study of PF-06835375 in Subjects with Seropositive Systemic Lupus Erythematosus or Rheumatoid Arthritis [A Phase 1, Randomized, Multi-Center, Double-Blind, Sponsor Open, Placebo-Controlled, Single and Multiple Dose-Escalation Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of PF-06835375 in Subjects with Seropositive Systemic Lupus Erythematosus or Rheumatoid Arthritis]
Date(s) of this Report:	09 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 are systemic lupus erythematosus and rheumatoid arthritis?

Systemic lupus erythematosus (also called lupus or SLE) and rheumatoid arthritis (or RA) are both types of "autoimmune disease". An autoimmune disease occurs when a person's immune system is overactive and attacks healthy parts of the body by mistake.

Some autoimmune diseases target only one organ or part of the body. In RA, the immune system attacks mainly the joints. In other diseases, like SLE, the whole body can be affected, including the skin, joints, heart, lungs, kidneys, and brain. SLE and RA can cause permanent damage to the tissues or joints if they go untreated.

What is PF-06835375?

PF-06835375 is an investigational medicine. It was not approved for general use at the time of this study. Researchers think that PF-06835375 can help to block the pathway of immune signals causing autoimmune diseases like SLE and RA.

In this study, PF-06835375 was given by injection in 2 ways: through a needle into the vein; known as "intravenously" (IV), or through a needle just underneath the skin; known as "subcutaneously" (SC). This study was the first time PF-06835375 was given to people and the dose needed to treat patients was not known.

During this study, participants also received tetanus/diphtheria and meningococcal B vaccine injections. Both of these vaccines have been approved for use in humans. When a vaccine is injected into a person's body, the body responds by making "antibodies", which are proteins that fight infections and help to prevent disease. This is known as the body's "immune response". The vaccines were given in this study to help learn more about the effect of PF-06835375 on the immune system.

What was the purpose of this study?

This study wanted to learn if PF-06835375 was safe to take for participants with SLE and RA compared to placebo. A placebo does not have any medicine in it, but it looks like the study medicine.

Researchers wanted to know:

- **How safe and well tolerated was PF-06835375?**
- **Did participants have any "dose-limiting toxicities"?**
- **What medical problems did participants have during the study?**

"Dose-limiting toxicities" (DLTs) are certain medical problems caused by taking study treatment which require the participant to lower the dose or stop taking the treatment (permanently or temporarily). Researchers collect information on DLTs to help find the recommended dose of a study treatment.

What happened during the study?

How was the study done?

There were 2 parts in this study, Part A and Part B. Each participant took part in either Part A or Part B, not both. Part B began before Part A was completed.

In Part A, all participants received a single dose of study treatment (PF-06835375 or placebo) on Day 1. The study treatment was given IV in Part A and the following doses were tested: 0.03 milligrams (mg), 0.1 mg, 0.3 mg, 1 mg, 3 mg, and 6 mg.

In Part B, participants received 2 doses of study treatment (PF-06835375 or placebo), 4 weeks apart (on Day 1 and Day 29). The study treatment was given SC in Part B and the following doses were tested: 0.3 mg, 1 mg, 3 mg, 6 mg, and 10 mg.

During both Part A and Part B, the participants and researchers did not know who took the different doses of PF-06835375 and who took the placebo. This is known as a "double-blinded" study. Participants were assigned to each group by chance alone. While PF-06835375 and placebo were given in a random order, the dose of PF-06835375 was gradually increased during both Part A and Part B. Each dose increase was made only after the current dose of PF-06835375 being tested was considered safe by the researchers.

Researchers took samples of blood and urine from the participants during the study and performed tests to measure each participant's immune system response. They checked the participants' health and asked them how they were feeling. Researchers also looked at the results of laboratory tests, blood pressure and 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.

All participants in both Part A and Part B were followed for a minimum of 16 weeks after starting the study. If at this time, the effect of the study treatment on a participant's immune system had mostly disappeared and the researchers considered it safe for a participant to stop the study, they would have one subsequent phone visit and then leave the study. Otherwise, the participant would be asked to continue in the study and come to the study center for additional visits until the effect of the study treatment on their immune system had either stabilized or mostly disappeared and researchers considered it safe for them to leave the study. These study visits were about every 4 weeks until 1 year after the first dose of study treatment, and then every 12 weeks until the end of study.

Figure 1 (Part A) and Figure 2 (Part B) below show what happened during the study.

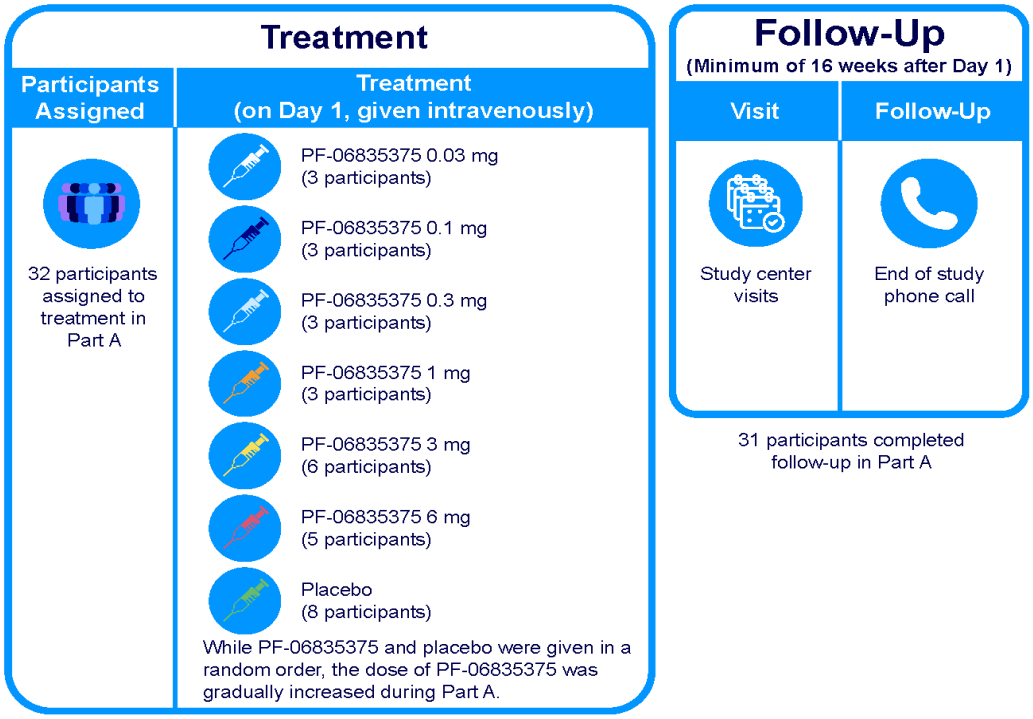
Where did this study take place?

The Sponsor ran this study at 11 locations in the United States.

When did this study take place?

It began 17 November 2017 and ended 15 February 2022.

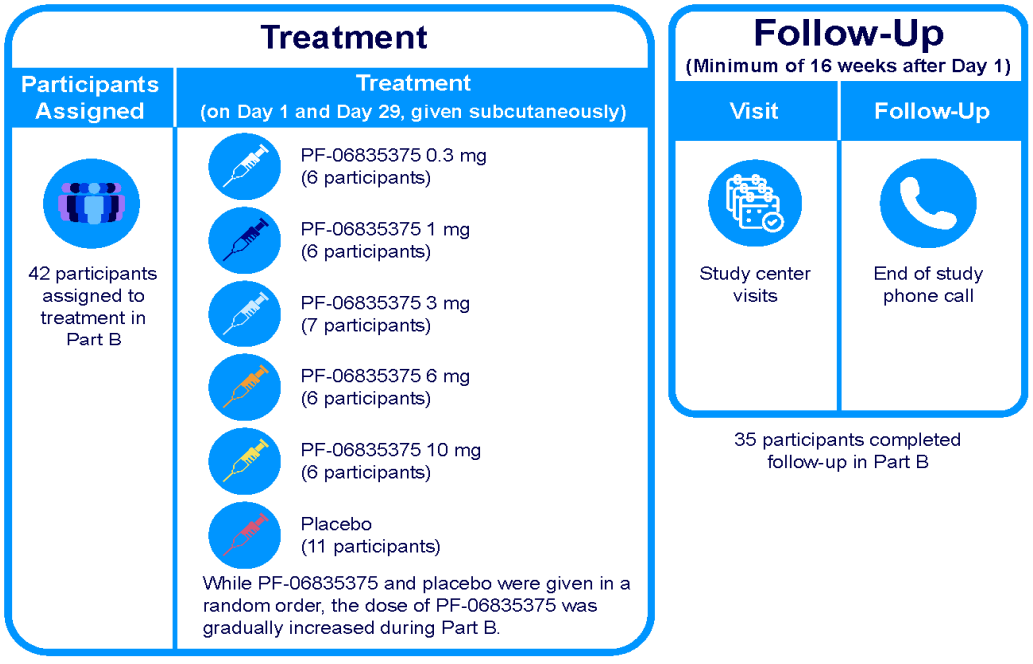
Figure 1. Study Design for Part A: Single dose



31 participants completed follow-up in Part A

31 participants received treatment in Part A.
1 participant left Part A of the study before receiving any treatment.

Figure 2. Study Design for Part B: Two doses



35 participants completed follow-up in Part B

42 participants received treatment in Part B

Who participated in this study?

The study included adult participants between the ages of 18 and 70 with a confirmed diagnosis of SLE or RA. Participants had to have had symptoms of SLE or RA for at least 6 months before joining the study.

In Part A,

- A total of 2 men participated
- A total of 29 women participated
- All participants were between the ages of 28 and 68

In Part B,

- A total of 6 men participated
- A total of 36 women participated
- All participants were between the ages of 22 and 70

Of the 31 participants who started Part A and received treatment, all 31 participants completed follow-up in Part A.

Of the 42 participants who started Part B and received treatment, 41 participants completed treatment and 35 participants completed follow-up in Part B. One participant did not complete treatment in Part B due to taking another medicine which was not allowed. The most common reasons for not completing follow-up were because participants could not be contacted for follow-up or due to their own choice to leave the study.

How long did the study last?

The amount of time each participant was in this study varied. Participants were expected to be in the study for about 6 to 12 months. The entire study took about 4 years and 3 months to complete.

When the study ended in February 2022, 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-06835375?

The researchers assessed the safety and tolerability of PF-06835375 by looking at the medical problems participants had during the study. They also looked at the results of certain tests. Medical problems are discussed in full in the next section of this document.

What was the result of laboratory tests during the study?

- There were 3 out of 73 participants (4%) in the study (2 in Part A and 1 in Part B) who had abnormal laboratory test results that the researchers considered as medical problems and as "clinically significant" (could harm their health). One of the 3 participants (who received PF-06835375 1 mg IV in Part A) had increased liver enzymes levels that the researchers thought may be related to the study treatment.

What was the result of the blood pressure and pulse rate tests during the study?

- There were 3 out of 73 participants (4%) in the study who had abnormal blood pressure increases that the researchers considered as medical problems, as clinically significant, and as related to the study treatment. This included 1 participant in Part A (who received placebo IV) and 2 participants in Part B (1 who received 0.3 mg PF-06835375 SC and 1 who received 3 mg PF-06835375 SC).

- There were 3 out of 73 participants (4%) in the study who had abnormal blood pressure decreases that the researchers considered as medical

problems, as clinically significant, and as related to the study treatment. The participants were all in Part B (with 1 who received placebo SC and 2 who received 3 mg PF-06835375 SC).

What was the result of the ECG tests during the study?

- There were 3 out of 73 participants (4%) in the study (all in Part A) who had abnormal ECG results that the researchers considered as medical problems, as clinically significant, and as related to the study treatment. This included 2 participants (1 who received PF-06835375 0.1 mg IV and 1 who received 1 mg PF-06835375 IV) with increased heart rate, and 1 participant (who received 6 mg PF-06835375 IV) with abnormal electrical impulses in their ECG.

Did participants have any "dose-limiting toxicities"?

None of the participants had DLTs in either Part A or Part B of the study.

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.

In Part A, 30 out of 31 participants (97%) had at least 1 medical problem, and 15 participants (48%) had a medical problem that was thought to be related to the study treatment. None of the participants left the study in Part A because of medical problems.

In Part B, 32 out of 42 participants (76%) had at least 1 medical problem, and 16 participants (38%) had a medical problem that was thought to be related to the study treatment. One (2%) participant left the study in Part B because of a medical problem.

Table 1 (Part A) and Table 2 (Part B) show the most common medical problems – those reported by a total of 3 or more participants in either part of the study.

Below are instructions on how to read Tables 1 and 2.

Instructions for Understanding Tables 1 and 2.

- The **1st** column of Tables 1 and 2 lists medical problems that were commonly reported during the study. They list all medical problems reported by 3 or more participants overall in either Part A or Part B of the study.
- The **2nd** column tells how many of the participants taking PF-06835375 were reported to have each medical problem. Next to this number is the percentage of participants taking PF-06835375 who reported the medical problem.
- The **3rd** column tells how many of the participants taking placebo were reported to have each medical problem. Next to this number is the percentage of the participants taking placebo who reported the medical problem.
- For example, using these instructions, you can see that:
    - In Part A, a total of 8 out of 23 participants (35%) taking PF-06835375 reported headache. One participant (13%) taking placebo in Part A reported headache.
    - In Part B, a total of 7 out of 31 participants (23%) taking PF-06835375 reported headache. Two participants (18%) taking placebo in Part B reported headache.

Table 1. Most common medical problems in Part A of the study		
Medical Problem	**PF-06835375 0.03 to 6 mg IV (23 Participants)**	**Placebo IV (8 Participants)**
Headache	8 out of 23 participants (35%)	1 out of 8 participants (13%)
Infection of nose, sinuses, throat, voice box or windpipe	4 out of 23 participants (17%)	2 out of 8 participants (25%)
Feeling like about to vomit (nausea)	4 out of 23 participants (17%)	1 out of 8 participants (13%)
Fever	4 out of 23 participants (17%)	1 out of 8 participants (13%)
Infection of the kidney, bladder, or urethra	5 out of 23 participants (22%)	0
Diarrhoea	3 out of 23 participants (13%)	1 out of 8 participants (13%)
Back pain	1 out of 23 participants (4%)	2 out of 8 participants (25%)
Shortness of breath	2 out of 23 participants (9%)	1 out of 8 participants (13%)
High blood pressure	2 out of 23 participants (9%)	1 out of 8 participants (13%)

Table 2. Most common medical problems in Part B of the study		
Medical Problem	**PF-06835375 0.3 to 10 mg SC (31 Participants)**	**Placebo SC (11 Participants)**
Headache	7 out of 31 participants (23%)	2 out of 11 participants (18%)
Fever	5 out of 31 participants (16%)	1 out of 11 participants (9%)
Chills	4 out of 31 participants (13%)	1 out of 11 participants (9%)
Redness at vaccination site	2 out of 31 participants (6%)	3 out of 11 participants (27%)
Infection of the kidney, bladder, or urethra	4 out of 31 participants (13%)	0
Vaccination complication	3 out of 31 participants (10%)	1 out of 11 participants (9%)
Diarrhoea	3 out of 31 participants (10%)	0
Feeling like about to vomit (nausea)	3 out of 31 participants (10%)	0
Skin reaction causing redness or rash	2 out of 31 participants (6%)	1 out of 11 participants (9%)
High blood pressure	2 out of 31 participants (6%)	1 out of 11 participants (9%)
Low blood pressure	2 out of 31 participants (6%)	1 out of 11 participants (9%)

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.

In Part A, 3 out of 31 participants (10%) had at least 1 serious medical problem:

- 1 participant who received placebo IV had a heart attack, disease of the arteries leading to the heart, back pain, and neck pain.
- 1 participant who received PF-06835375 0.03 mg IV had chest pain.
- 1 participant who received 0.3 mg PF-06835375 IV had high blood pressure.

None of these serious medical problems were considered to be related to study treatment.

In Part B, no participants (0%) had serious medical problems.

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 **NCT03334851**
www.clinicaltrialsregister.eu	Use the study identifier **2017-003077-34**
www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number **C1131001**

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!