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-06823859

Protocol Number: C0251002

Dates of Study: 23 January 2018 to 28 November 2022

Title of this Study: A Study Looking at the Efficacy and Safety of PF-06823859 in Adults With Moderate to Severe Dermatomyositis

[A Phase 2 Double-Blind, Randomized, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Tolerability of PF-06823859 in Adult Subjects With Dermatomyositis]

Date of this Report: 30 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 dermatomyositis (DM)?

Dermatomyositis (dur-muh-toe-my-uh-SY-tis) is a rare disease that causes muscle weakness and/or inflammation and skin rashes. Symptoms can include a red skin rash around the eyelids, red bumps around the joints, and muscle weakness in the arms and legs. It is a type of myopathy (my-o-pa-thy). This is a general term referring to diseases that affect the muscles that connect to your bones.

What is PF-06823859?

The study drug (PF-06823859) is an investigational medicine. It is not currently approved for use by health authorities in countries where this study was held. PF-06823859 is given as an infusion in a vein of the arm. PF-06823859 targets a signaling protein in the immune system. A signaling protein tells the cells in the body how to respond, such as fighting infections. In a disease like DM, this signaling protein is found at high levels. It is thought that blocking this signaling protein may help treat DM. The researchers have been studying it as a potential treatment for DM. In future it may also be studied for the treatment of different / related conditions.

What was the purpose of this study?

There were 4 stages in this study. Adult DM participants with skin predominant disease participated in Stage 1, Stage 2 and amended Stage 2 (or Stage 2A). Adult DM participants with muscle predominant disease participated in Stage 3 of this study.

The main purpose of Stage 1, 2, and 2A of this study was to learn about the effects and safety of PF-06823859 in treating DM participants with skin predominant disease compared to a placebo while still taking their current

background medications for DM. A placebo does not have any medicine in it, but it looks just like the study medicine.

The main purpose of Stage 3 of this study was to learn about the effects, safety, and tolerability of PF-06823859 in DM participants with muscle predominant disease. "Tolerability" refers to how well participants can tolerate taking the study treatment.

Researchers wanted to know:

- **Skin predominant disease group: did the skin symptoms of DM participants taking PF-06823859 improve compared to participants taking placebo?**
- **Muscle predominant disease group: did the muscular symptoms of DM participants taking PF-06823859 improve compared to participants taking placebo?**
- **Did participants have any medical problems due to the study treatment?**

What happened during the study?

How was the study done?

Researchers conducted the study in 4 stages. The first three stages (Stage 1, 2, and 2A) included participants with DM who predominantly had skin disease, and Stage 3 included DM participants who predominantly had active muscle disease.

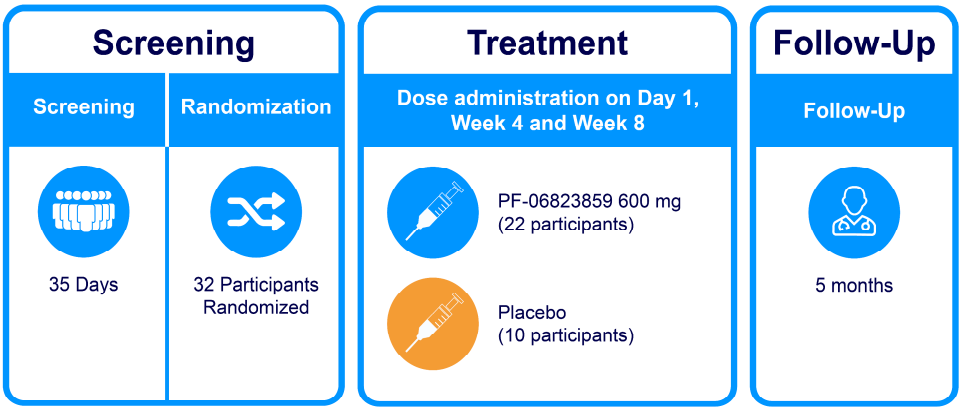
The participants and researchers did not know who received different doses of PF-06823859 and who received the placebo. This is known as a "blinded" study. Participants were assigned to 1 of the 3 treatment groups by chance to receive either PF-06823859 at a dose of 600 milligrams (mg), PF-06823859 at a dose of 150 mg, or a placebo. This known as a "randomized study".

All participants in each stage of this study were "screened" to see if they qualified to be in the study. Participants who qualified for treatment after screening entered the "treatment period".

Stage 1

All participants entering Stage 1 of the study were screened for 35 days and 32 qualified participants entered the treatment period. Twenty-two participants received 600 mg of PF-06823859 and 10 participants received placebo on Day 1, Week 4 (visit 4), and Week 8 (Visit 5). They were required to visit the study unit on different days for dose administrations, efficacy and follow up assessments. Participants were followed up for safety assessment after the last dose for 5 months. Figure 1 shows the study design for Stage 1.

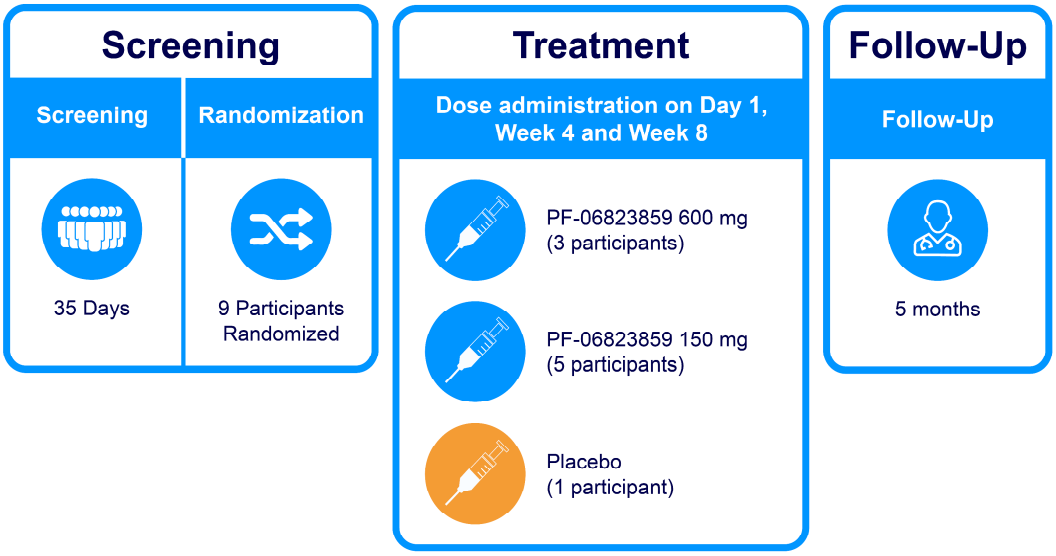
Figure 1: Study Design for Stage 1



Stage 2

Stage 2 included a lower dose of 150 mg to test and explore dose ranging. A total of 9 participants received 3 doses of either study drug or placebo on Day 1, Week 4 (visit 4), and Week 8 (visit 5). Participants could either receive 150 mg, 600 mg, or a placebo as shown in the study design Figure 2. After the last dose participants were assessed for efficacy at Week 12 (visit 6) and followed up for safety assessment for 5 months.

Figure 2: Study Design for Stage 2



Stage 2A

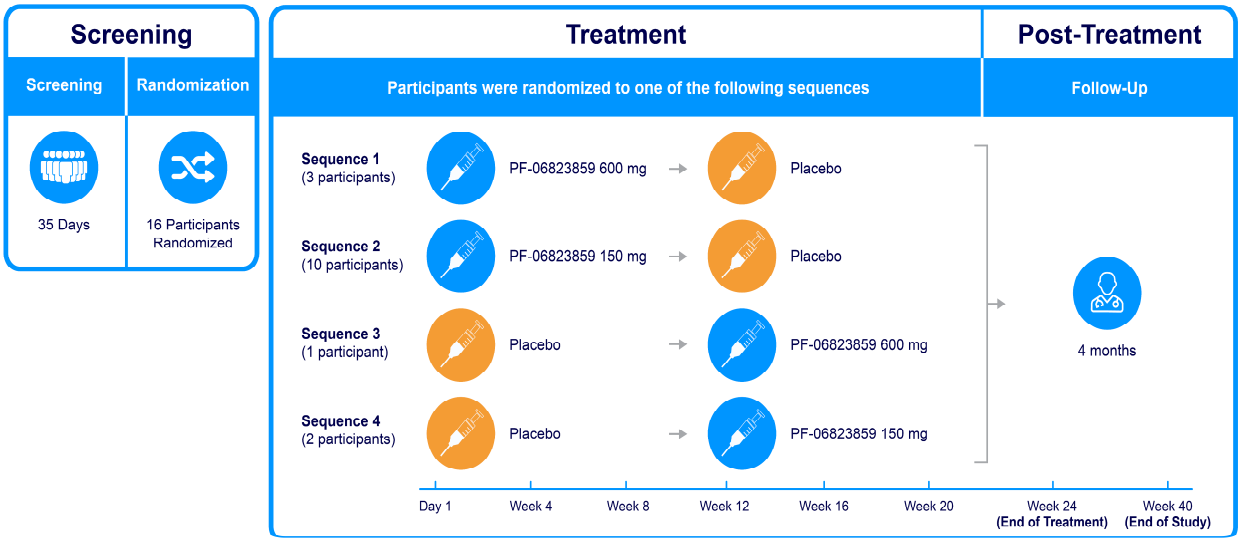
The study was further changed from Stage 2 to a fixed sequence design and was called amended Stage 2 (Stage 2A). Stage 2A included a switch at Week 12, participants who initially received placebo would then receive PF-06823859 and participants who initially received PF-06823859 switched to placebo. During this stage all participants received the study medicine, a total of 16 participants were assigned in to one of the 4 sequences:

- Three participants received PF-06823859 600 mg on Day 1, Week 4, and Week 8 followed by placebo at Week 12, Week 16, and Week 20

- Ten participants received PF-06823859 150 mg on Day 1, Week 4, and Week 8 followed by placebo Week 12, Week 16, and Week 20
- One participant received placebo on Day 1, Week 4, and Week 8 followed by PF-06823859 600 mg at Week 12, Week 16, and Week 20
- Two participants received placebo on Day 1, Week 4, and Week 8 followed by PF-06823859 150 mg at Week 12, Week 16, and Week 20

As shown in the study design Figure 3, participants received the last dose of either study treatment or placebo at Week 20 visit and treatment period ended at Week 24. Participants were then followed up for safety assessments for another of 4 months.

Figure 3: Study Design for Stage 2A



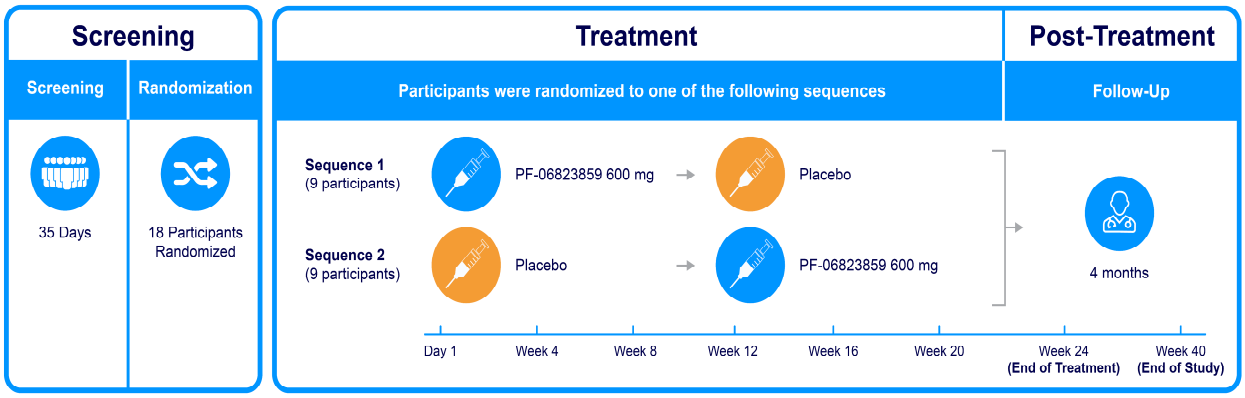
Stage 3

Stage 3 of this study was conducted in a similar manner as Stage 2A. A total of 18 participants with predominantly active muscle disease were randomized to either of the 2 sequences:

- Nine participants received PF-06823859 600 mg on Day 1, Week 4, and Week 8 followed by placebo at Week 12, Week 16, and Week 20
- Nine participants received placebo on Day 1, Week 4, and Week 8 followed by PF-06823859 600 mg at Week 12, Week 16, and Week 20

As shown in the study design Figure 4, participants received the last dose of either study treatment or placebo at Week 20 visit and treatment period ended at Week 24. Participants were then followed up for safety assessments for another 4 months.

Figure 4: Study Design for Stage 3



Researchers used two different tests to measure the severity of participants' DM at the beginning of the study and at Week 12 of the treatment. For participants with skin predominant disease in Stage 1, Stage 2, and Stage 2A researchers used the cutaneous dermatomyositis disease area and severity index (CDASI) scale to assess the DM skin related activity. This scale measured the severity of participants' skin disease and was used at most visits during the study. Negative values on a change in CDASI indicates improvement from baseline and positive values indicate less or no improvement from baseline.

In Stage 3, researchers assessed the active muscle disease by the total improvement score (TIS) on a scale of 0-100 at Week 12. On a TIS scale 0

indicates no improvement from baseline and positive values indicate increased improvement from a baseline. TIS is a sum of improvement scores of the following 6 set of measurements:

- Patient global assessment (PtGA).
- Physician global assessment (PhGA).
- Manual muscle testing-8 (MMT-8) is a scale used to measure the muscle strength of participants.
- A personal health assessment questionnaire – disability index (HAQ- DI) form completed by participants.
- Extramuscular activity from the myositis disease activity assessment tool (MDAAT) which is a tool to measure participants' disease activity of various organ systems.
- Participant's most abnormal muscle enzyme at the start of the study.

Where did this study take place?

The Sponsor ran this study at 25 locations in 5 countries in North America and Europe.

When did this study take place?

It began on 23 January 2018 and ended on 28 November 2022.

Who participated in this study?

Stage 1, 2 and 2A of this study included DM participants with skin predominant disease who had:

- CDASI activity score equal to 14 or more.
- History of at least 1 medication for DM that did not work.

Stage 3 included DM participants with muscle predominant disease who had one of the following:

- MMT-8 score of less than or equal to 136 out of 150 and PhGA (greater than or equal to 3 centimeters [cm] on 0-10 cm visual analog scale [VAS]). 'PhGA' stands for physician global assessment completed by the study doctor or the physician.
- Sum of PhGA, PtGA of myositis and extramuscular global assessment of ≥10 cm (using 0-10 cm VAS scale for each).

Overall, a total of 75 participants joined this study: 32 participants in Stage 1, 9 Participants in Stage 2, 16 participants in Stage 2A, and 18 participants in Stage 3.

In Stage 1,

- A total of 3 men and 29 women participated.
- All participants were between the ages of 25 and 78.

In Stage 2,

- A total of 0 men and 9 women participated.
- All participants were between the ages of 24 and 71.

In Stage 2A,

- A total of 1 man and 15 women participated.
- All participants were between the ages of 34 and 67.

In Stage 3,

- A total of 5 men and 13 women participated.
- All participants were between the ages of 21 and 68.

Of the 32 participants who started Stage 1 and received treatment, 3 participants (9.4%) stopped the treatment. Two participants (6.3%) stopped due to a medical problem, meaning that the participant or their doctor thought it was best for the participant to stop treatment. One participant (3.1%) stopped the treatment by his own choice. Of the 9 participants who started Stage 2 and received treatment, none of the participants discontinued the study treatment.

Of the 16 participants who started Stage 2A and received treatment, 2 participants (12.5%) stopped the treatment. Two participants (12.5%) discontinued the study during the follow-up period. One participant (6.3%) was lost to follow-up and another participant (6.3%) withdrew from the study by his own choice.

Of the 18 participants who started Stage 3 and received treatment, 2 participants (11.1%) stopped the treatment. One participant (5.6%) stopped due to a medical problem, meaning that the participant or their doctor thought it was best for the participant to stop treatment. One participant (5.6%) stopped the treatment by his own choice. One participant (5.6%) died during the follow-up period of the study.

How long did the study last?

The entire study took about 4 years and 10 months to complete. When the study ended in November 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?

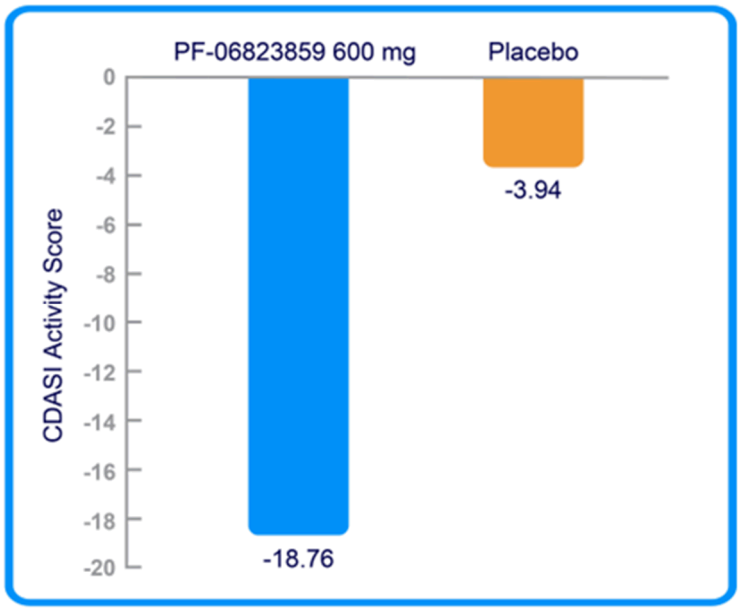
Skin predominant disease group: did the skin symptoms of DM participants taking PF-06823859 improve compared to participants taking placebo?

To answer this question, researchers measured the severity of each participant's DM during Stage 1, Stage 2, and Stage 2A using CDASI activity score. Researchers measured the severity at the beginning of the study and at Week 12. The difference in severity was used to decide if participants' DM had improved or not. A successful treatment is defined as the decrease in CDASI activity score and therefore the outcome of the treatment is in negative (-) values.

Stage 1

In Stage 1 of this study, participants in PF-06823859 600 mg treatment group had greater decrease in the CDASI activity score (-18.76), compared to the placebo group (-3.94) as shown in Figure 5. The difference in the severity between participants in PF-06823859 600 mg group and placebo was observed as -14.82. Based on this result, researchers found that participants taking PF-06823859 600 mg had improved DM skin symptoms compared to placebo.

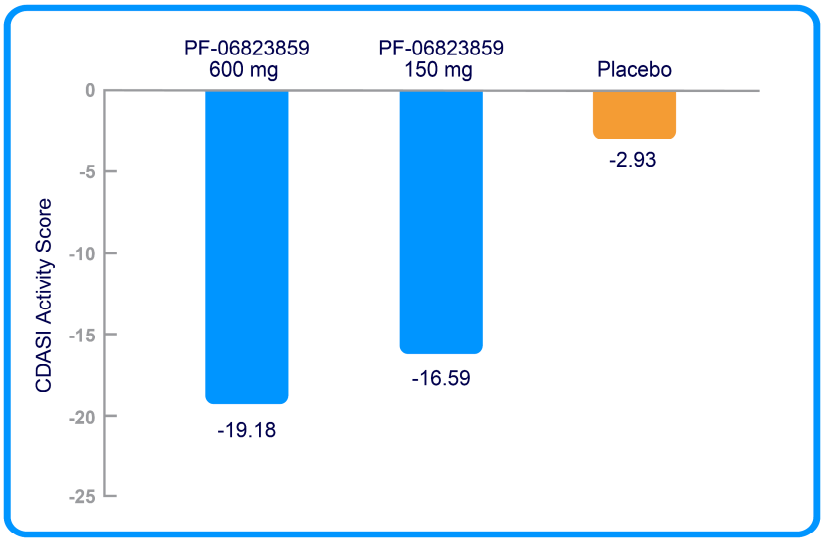
Figure 5: Average change of CDASI activity score at Week 12 for Stage 1



Stage 1, Stage 2, and Stage 2A (skin predominant disease group)

The results from Stage 1, Stage 2, and Stage 2A were combined and analysed together for participants who had skin predominant disease. As shown in Figure 6, participants in both the PF-06823859 600 mg and PF-06823859 150 mg treatment groups had greater decrease in CDASI activity score compared to the placebo group. Based on this result, researchers found that participants taking PF-06823859 600 mg and 150 mg had improved DM skin symptoms compared to placebo.

Figure 6: Average change of CDASI activity score at Week 12 for skin predominant disease group



Did participants have any medical problems during the study?

In stage 3, researchers looked at the safety and tolerability of PF-06823859 at Week 12. The researchers did this by looking at the medical problems that the participants had at Week 12 during the study. Researchers were specifically interested in seeing if the participants had the following:

- Medical problems and their severity during the course of the study.
- Most common medical problems at Week 12.
- Viral infections.

Medical problems overall are described in the next section.

A total of 12 out of 18 (66.7%) participants reported at least one medical problem at Week 12 during Stage 3 of the study. Seven out of 9 (77.8%) participants who received placebo then 600 mg of PF-06823859 had at least one medical problem and 5 out 9 (55.6%) participants who received

600 mg of PF-06823859 then placebo had at least one medical problem. The most common medical problems were related to stomach and intestine (gastrointestinal disorders).

- Upper stomach pain, diarrhoea, nausea, and vomiting were reported in one participant (11.1%) each who received 600 mg of PF-06823859 then placebo.
- Pain when swallowing was reported by one (11.1%) participant who received placebo then 600 mg of PF-06823859.

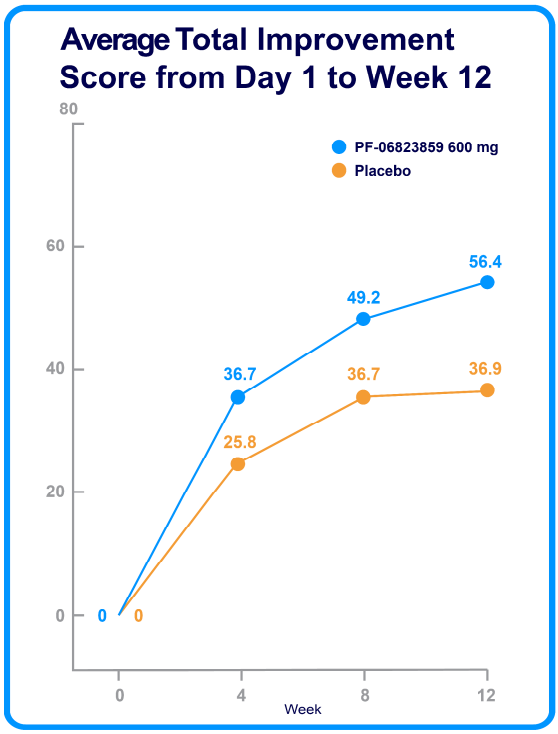
Researchers found that all these medical problems were similar between the PF-06823859 groups and placebo groups, and they were mild to moderate in severity. Researchers also found that there were no cases of shingles or oral herpes reported by study participants.

Muscle predominant disease group: did the muscular symptoms of DM participants taking PF-06823859 improve compared to participants taking placebo?

To answer this question, researchers measured TIS of participants with muscle disease at the beginning of the study and at Week 12. TIS is a continuous measure ranging from 0-100, where 0 indicates no improvement from baseline and positive numbers indicate increased improvement from baseline. The average difference in the TIS between treatment group and placebo group was used to decide if participants had improved DM muscle symptoms or not.

As shown in Figure 7, participants in PF-06823859 600 mg treatment group had greater TIS from Week 4 to Week 12 compared to the placebo group. Based on this result, researchers found that participants taking PF-06823859 600 mg had an overall improvement in the DM muscle symptoms compared to placebo.

Figure 7: Average TIS from Day 1 to Week 12 for muscle predominant disease group



Based on these results for all 4 stages of the study, researchers have decided that results are not likely the results of chance. PF-06823859 may be effective compared to placebo in treating adults with DM who had skin and muscle disease.

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.

Sixty-five out of 75 (86.7%) participants in this study had at least 1 medical problem. A total of 2 participants, one participant from Stage 1 and the other from Stage 3 left the study because of medical problems. The most common medical problems – those reported by more than 5% of 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 more than 5% of participants are listed.
- The **2nd** column tells how many of the 45 participants who received a placebo reported each medical problem. Next to this number is the percentage of the 45 participants who received placebo that reported the medical problem.

- The **3rd** column tells how many of the 17 participants who received PF-06823859 150 mg reported each medical problem. Next to this number is the percentage of the 17 participants who received PF-06823859 150 mg that reported the medical problem.
- The **4th** column tells how many of the 47 participants who received PF-06823859 600 mg reported each medical problem. Next to this number is the percentage of the 47 participants who received PF-06823859 600 mg that reported the medical problem.
- Using these instructions, you can see that 1 out of the 17 participants who received PF-06823859 150 mg reported low red blood cell count. Neither of the participants who received placebo or PF-06823859 600 mg reported low red blood cell count.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Placebo (45 Participants)	PF-06823859 150 mg (17 Participants)	PF-06823859 600 mg (47 Participants)
Low red blood cell count	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Rapid heartbeat	1 out of 45 participants (2.2%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Placebo (45 Participants)**	**PF-06823859 150 mg (17 Participants)**	**PF-06823859 600 mg (47 Participants)**
Abdominal pain	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	1 out of 47 participants (2.1%)
Diarrhoea	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	3 out of 47 participants (6.4%)
Nausea	2 out of 45 participants (4.4%)	0 out of 17 participants (0%)	3 out of 47 participants (6.4%)
Feeling tired	4 out of 45 participants (8.9%)	1 out of 17 participants (5.9%)	1 out of 47 participants (2.1%)
Stuffy nose	3 out of 45 participants (6.7%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Tooth infection	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Upper respiratory tract infection	1 out of 45 participants (2.2%)	0 out of 17 participants (0%)	4 out of 47 participants (8.5%)
Fall	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	2 out of 47 participants (4.3%)
Infusion related reaction	2 out of 45 participants (4.4%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)

Table 1. Commonly reported medical problems by study participants

Medical Problem	Placebo (45 Participants)	PF-06823859 150 mg (17 Participants)	PF-06823859 600 mg (47 Participants)
Accidental skin cuts	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Blood potassium decreased	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	1 out of 47 participants (2.1%)
Covid-19 infection	4 out of 45 participants (8.9%)	0 out of 17 participants (0%)	1 out of 47 participants (2.1%)
Weight increased	1 out of 45 participants (2.2%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Joint pain	1 out of 45 participants (2.2%)	2 out of 17 participants (11.8%)	3 out of 47 participants (6.4%)
Muscle pain	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Neck pain	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Tumour in the parathyroid gland that is non-cancerous	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Headache	7 out of 45 participants (15.6%)	3 out of 17 participants (17.6%)	6 out of 47 participants (12.8%)

Table 1. Commonly reported medical problems by study participants			
Medical Problem	**Placebo (45 Participants)**	**PF-06823859 150 mg (17 Participants)**	**PF-06823859 600 mg (47 Participants)**
Reduced sensation to touch pain and temperature	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Mental impairment	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Bleeding in vagina	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Long-term cough	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	1 out of 47 participants (2.1%)
Hair loss	1 out of 45 participants (2.2%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Dermatomyositis*	1 out of 45 participants (2.2%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)
Itching	5 out of 45 participants (11.1%)	1 out of 17 participants (5.9%)	1 out of 47 participants (2.1%)
Redness, swelling and bumps in the face	0 out of 45 participants (0%)	1 out of 17 participants (5.9%)	0 out of 47 participants (0%)

*Worsening

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.

A total of 5 participants had 10 serious medical problems during the study. Four (8.5%) participants in PF-06823859 600 mg group and one participant in the placebo group reported these medical problems. Researchers do not believe any of the serious medical problems reported by participants were related to study medication. The following serious medical problems were reported during the study:

- Inflammation of the large intestine, swelling and pain in the joints, fracture in the upper arm bone, low levels of white blood cells, low number of cells in the blood, increased liver enzymes, hyper-inflammatory disorder of the immune system, high blood levels of bilirubin (a breakdown product of red blood cells, indicates liver problems), yellowing of the eyes (sign of jaundice) and injury or abnormality in the brain and spinal cord.

One participant died 133 days after receiving the last dose of the study medication, during the follow up period of the study. Researchers considered this death was not due to the study medication.

Researchers concluded that overall, PF-06823859 was generally safe and well tolerated in all stages of 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.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C0251002

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

www.clinicaltrials.gov	Use the study identifier **NCT03181893**
www.clinicaltrialsregister.eu	Use the study identifier **2020-004228-41**

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!