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-06730512
Protocol Number:	C0221002 (PODO)
Dates of Study:	15 October 2018 to 14 February 2023
Title of this Study:	A Study to Evaluate PF-06730512 in Adults With Focal Segmental Glomerulosclerosis (FSGS) [A Phase 2, 24-Week, Adaptive, Open Label, Sequential Cohort Trial to Evaluate the Efficacy, Safety, Tolerability and Pharmacokinetics of PF-06730512 Following Multiple Doses in Adult Subjects With Focal Segmental Glomerulosclerosis (FSGS)]
Date(s) of this Report:	11 January 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 focal segmental glomerulosclerosis?

Focal segmental glomerulosclerosis (FSGS) is a kidney disease that affects the tiny filters in the kidneys called glomeruli. These filters help remove waste products and excess fluid from the blood. In FSGS, certain parts (segments) of some glomeruli become scarred and damaged, and specialized cells called podocytes lose their normal shape. This results in leakage of proteins into the urine causing increased levels of protein in the urine.

What is PF-06730512?

PF-06730512 is a ROBO2 (recombinant human Roundabout Guidance Receptor 2)-human immunoglobulin (Ig) was developed for the treatment of FSGS. It attaches to the SLIT2 protein in the glomeruli and improves the structure of the podocyte in mice. In this way, PF-06730512 may reduce the levels of protein in the urine.

What was the purpose of this study?

The purpose of this research study was to learn about the effects, overall safety, how well participants can tolerate (tolerability) the study medication (PF-06730512), and to see how much study medication was in the blood (pharmacokinetics), following intravenous (IV) administration every 2 weeks up to 24 weeks. Intravenous administration means that the study medication is infused into one of your veins on your arm. The primary goal of this study was to see if the study medication could reduce the levels of protein (as measured by urine protein to creatinine ratio [UPCR]) in urine.

Researchers wanted to know:

How effective was the treatment with PF-06730512 to reduce the amount of protein in the urine (UPCR) in participants with Focal segmental glomerulosclerosis (FSGS)?

What happened during the study?

How was the study done?

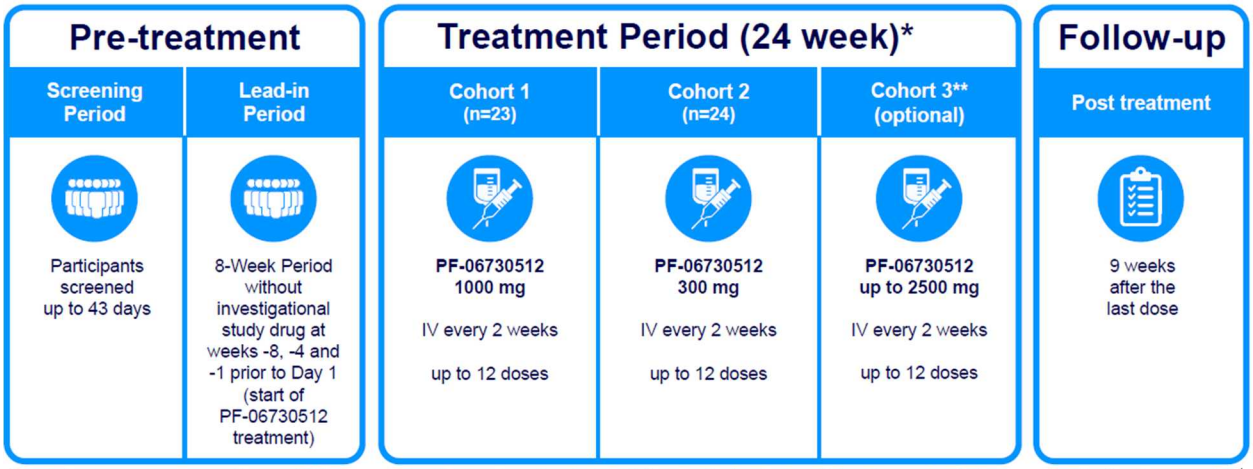
This was an “open-label” study. This means researchers and participants knew they were receiving the study medication, PF-06730512.

This study consisted of a Screening Period of up to 43 days, an approximately 8-week Lead-in Period (participants were monitored for stability of FSGS, but did not receive any study medication), up to a 24-week Treatment Period during which participants received PF-06730512 once every 2 weeks (Q2W), followed by an approximately 9-week Follow-up Period (participants did not receive any study medication, but were monitored). Figure 1 below shows the study design.

Researchers planned to test up to 3 doses of PF-06730512 in 3 cohorts of study participants to learn about the effects, overall safety of the study medication, and how well participants tolerate the study medication.

- Cohort 1 - PF-06730512 at 1000 mg Q2W IV.
- Cohort 2 - PF-06730512 300 mg Q2W IV.
- Cohort 3 (optional cohort) – PF-06730512 up to 2500 mg Q2W IV. Cohort 3 was not enrolled as the study was stopped after Cohort 2.

Figure 1: Study Flow Diagram



*Participants received a maximum of 12 doses during the treatment period (Initial study design had participants receive 6 doses during the treatment period)
**Cohort 3 was not enrolled as the study was stopped after Cohort 2.

Where did this study take place?

The Sponsor ran this study at 31 locations in 11 countries in the United States, Canada, Spain, Japan, Slovakia, United Kingdom, Poland, Germany, Czech Republic, Italy, and Mexico.

When did this study take place?

It began 15 October 2018 and ended 14 February 2023.

Who participated in this study?

The study included participants who were at least 18 years old with a kidney biopsy-confirmed diagnosis of FSGS, having the measure of how well the kidneys filter blood (estimated glomerular filtration rate [eGFR] greater than or equal to 45 mL/min/1.73 m^2; or eGFR 30-45 mL/min/1.73 m^2 along with a recent report of kidney tissue examination [biopsy] showing less than 50% tissue deposition on the kidney [tubule-interstitial fibrosis]) and amount of protein in the urine (UPCR) greater than 1.5 g/g at Screening.

- A total of 25 men participated.
- A total of 22 women participated.
- All participants were between the ages of 21 and 75 years.

Participants were to be treated until:

- they left the study by their own choice,
- they had unacceptable medical problems,
- they had behavior issues,
- the study ended, or
- they were unable to follow the study-required visits or procedures at study site.

Of the 47 participants who started the study, 10 participants including 1 in Cohort 1, and 9 in Cohort 2, stopped the study medication early. One (1) participant in Cohort 1 stopped the study medication due to a medical problem. None of participants in Cohort 2 stopped the study medication due to a medical problem. In Cohort 2, 5 participants stopped the study medication due to study termination, 2 participants stopped the study medication by their own choice, and 1 participant each stopped the study medication due doctor's choice and lack of effectiveness with the study medication.

How long did the study last?

Study participants were in the study for approximately 11 months. The entire study took approximately 4.5 years to complete.

The researchers decided to close the study due to lack of effectiveness with the 1000 mg (Cohort 1) and 300 mg (Cohort 2) doses on 05 December 2022. The decision to close the study was not related to a

safety concern. Follow-up was continued for the participants after the study treatment was completed or terminated in the study.

When the study ended in February 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?

How effective was the treatment with PF-06730512 to reduce the amount of protein in the urine (UPCR) in participants with Focal segmental glomerulosclerosis (FSGS)?

According to the 24-hour urine collection, the mean percentage change from baseline in UPCR at Week 13 was -12.283% for Cohort 1 and -0.045% for Cohort 2.

This means the study results did not show that study medication has clinically meaningful effect in reducing the amount of protein in the urine (UPCR) in participants with FSGS.

> 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 37 out of 47 (78.7%) participants in this study had at least 1 medical problem. One (1) participant in Cohort 1 stopped the study medication due to a medical problem. The most common medical problems – those reported by more than 5% of participants in the study – 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 23 participants in Cohort 1 taking PF-06730512 1000 mg IV reported each medical problem. Next to this number is the percentage of the 23 participants taking the study medication who reported the medical problem.
- The **3rd** column tells how many of the 24 participants in Cohort 2 taking PF-06730512 300 mg IV reported each medical problem. Next to this number is the percentage of the 24 participants taking the study medication who reported the medical problem.

- The **4th** column tells how many of the total 47 participants in the study (Cohort 1 + Cohort 2) reported each medical problem. Next to this number is the percentage of the 47 participants who reported the medical problem.
- Using these instructions, you can see that 5 out of the 47 (10.6%) participants taking the study medication reported feeling tired.

Table 1. Commonly reported medical problems reported by more than 5% of the total study participants

Medical Problem	Cohort 1 PF-06730512 1000 mg IV (23 Participants)	Cohort 2 PF-06730512 300 mg IV (24 Participants)	Total (47 Participants)
Feeling tired	3 out of 23 participants (13.0%)	2 out of 24 participants (8.3%)	5 out of 47 participants (10.6%)
Headache	2 out of 23 participants (8.7%)	3 out of 24 participants (12.5%)	5 out of 47 participants (10.6%)

Table 1. Commonly reported medical problems reported by more than 5% of the total study participants

Medical Problem	Cohort 1 PF-06730512 1000 mg IV (23 Participants)	Cohort 2 PF-06730512 300 mg IV (24 Participants)	Total (47 Participants)
COVID (SARS-Cov-2) infection (with symptoms)	1 out of 23 participants (4.3%)	3 out of 24 participants (12.5%)	4 out of 47 participants (8.5%)
Positive COVID (SARS-Cov-2) test with or without symptoms	2 out of 23 participants (8.7%)	2 out of 24 participants (8.3%)	4 out of 47 participants (8.5%)
Loose stools	2 out of 23 participants (8.7%)	2 out of 24 participants (8.3%)	4 out of 47 participants (8.5%)
Vomiting	2 out of 23 participants (8.7%)	1 out of 24 participants (4.2%)	3 out of 47 participants (6.4%)
Acute kidney injury	2 out of 23 participants (8.7%)	1 out of 24 participants (4.2%)	3 out of 47 participants (6.4%)

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.

4 out of 47 participants (2 in Cohort 1 and 2 in Cohort 2) had serious medical problems. All serious medical problems were not related to the study medication.

Cohort 1

- 1 participant had kidney failure (renal impairment) and fluid overload (extra fluid in the body).
- 1 participant had acute kidney injury and loose stools.

Cohort 2

- 1 participant had serious medical problem of coronavirus disease (COVID) infection.
- 1 participant had disease progression of FSGS.

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.

For more details on your study protocol, please visit:

www.pfizer.com/research/research_clinical_trials/trial_results	Use the protocol number C0221002

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

www.clinicaltrials.gov	Use the study identifier **NCT03448692**
www.clinicaltrialsregister.eu	Use the study identifier 2019-003607-35

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!