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 study participants. 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-04518600 and Utomilumab (PF-05082566)
Protocol Number:	B0601002
Dates of Study:	23 April 2015 to 25 November 2020
Title of this Study:	Study Of OX40 Agonist PF-04518600 Alone And In Combination With 4-1BB Agonist PF-05082566 [A Phase 1, Open-Label, Dose Escalation Study of PF-04518600 as a Single Agent and in Combination With PF-05082566 in Patients With Selected Locally Advanced or Metastatic Cancers]
Date(s) of this Report:	5 August 2021

– 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 locally advanced or metastatic cancer?

The term "metastatic" refers to cancer that has spread from the part of the body where it started to another part of the body. The term "locally advanced" refers to cancer that has spread from the part of the body where it started to a nearby part of the body. This study included participants with locally advanced or metastatic cancer that started in the head and neck, skin (melanoma), liver, kidney, lung, bladder, stomach, or cervix (lower part of womb).

What are PF-04518600 and utomilumab?

PF-04518600 is a type of protein known as an antibody, which may stimulate the immune system. PF-04518600 may produce an immune response against tumors by stimulating a molecule on immune cells called OX40. An immune response against tumor cells may help slow tumor growth by causing tumor cells to die. PF-04518600 is an investigational treatment, which means that it is still being studied and has not been approved for use outside of research studies. This study was the first time that PF-04518600 was given to people.

Utomilumab is another antibody treatment that may stimulate the immune system. Utomilumab may produce an immune response against tumors by stimulating a molecule on immune cells called 4-IBB. Utomilumab is an investigational treatment.

What was the purpose of this study?

The main purpose of this study was to learn more about the safety of PF-04518600 in people with locally advanced or metastatic cancer. Information about the safety of PF-04518600 was also needed so that researchers could determine the correct dose to use in the second part of this study and in future studies.

What happened during the study?

How was the study done?

This study was done in 2 parts. During Part 1, participants were given different doses of PF-04518600. Doses ranged from 0.01 milligrams per kilogram of weight (mg/kg) to 10 mg/kg IV (in the vein), or 30 mg or 250 mg IV. The dose given to participants was increased until the highest dose that could be safely tolerated was reached. This is called the maximum tolerated dose. The dose that each participant received stayed the same throughout the study, and depended on when they joined the study and how many participants had already been treated.

Some participants in Part 1 were in the "expansion group". These participants were required to have tumor biopsies (removal of cells or tissue) to look at the effect of PF-04518600 on the immune cells and cancer cells in their tumor, and to determine if specific cancer genes were turned on or off in the tumor. The first biopsy took place before the first dose of study drug, and a second biopsy took place about 6 weeks later. Some participants, including those with skin cancer (melanoma), also had a third biopsy about 6 weeks after the second biopsy.

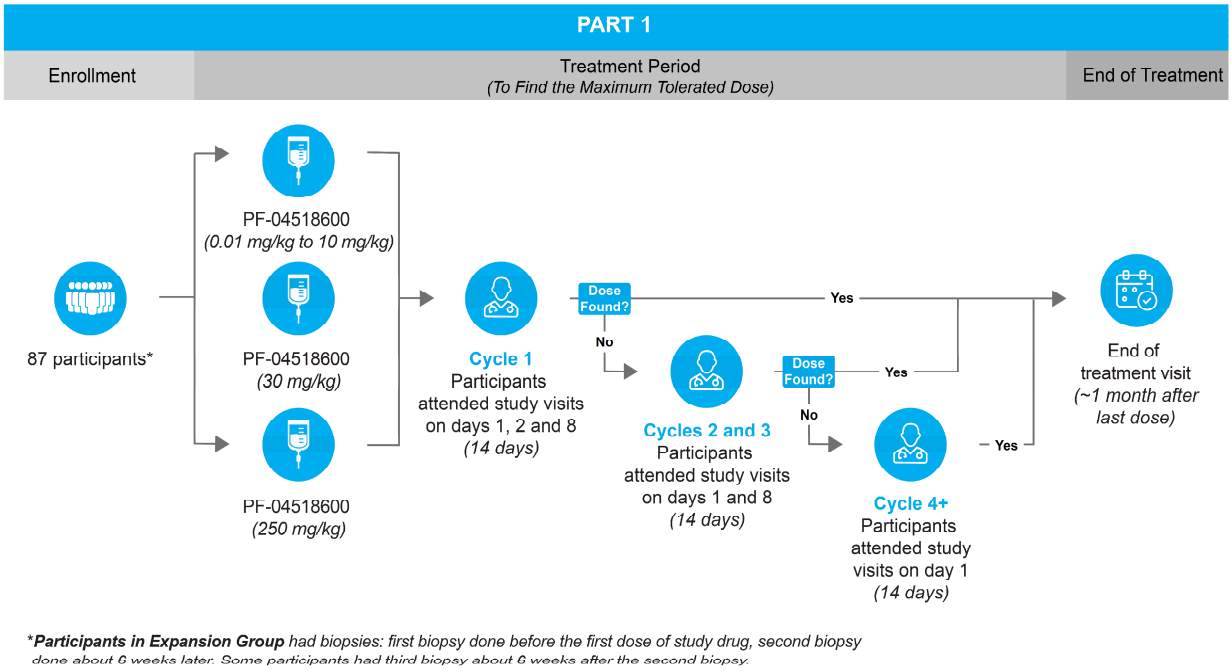
All participants in Part 2 received PF-04518600 doses closer to the maximum tolerated dose that was determined in the first part of the study (0.1 mg/kg to 3.0 mg/kg IV). They also received utomilumab, at a dose of 20 mg or 100 mg IV every 4 weeks. All participants in Part 2 were in the expansion group and were required to have tumor biopsies.

Study treatment was broken up into 14 day "cycles". Treatment was given on Day 1 of each cycle. Participants were watched closely for any medical problems throughout the study. Participants were expected to attend the following visits at the study center:

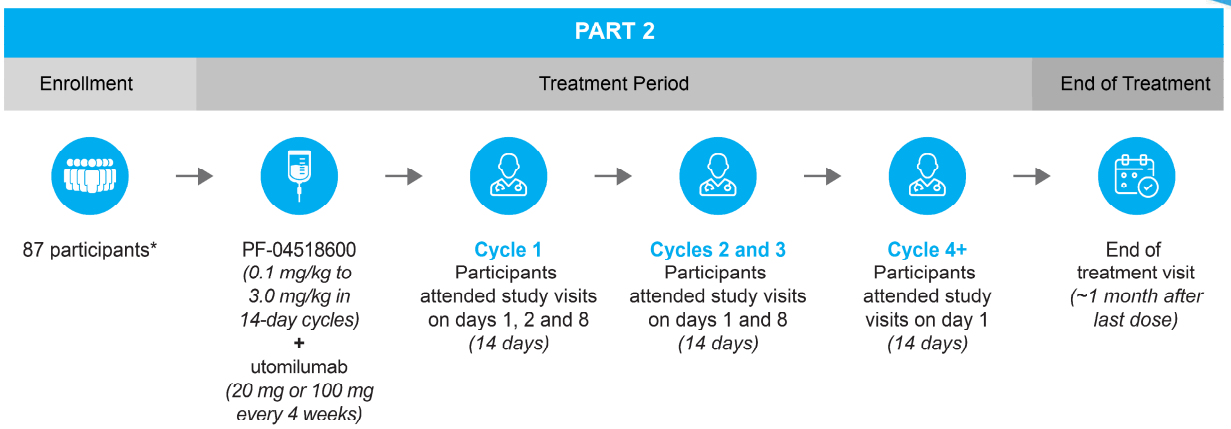
- Days 1, 2, and 8 of the first 14 day cycle
- Days 1 and 8 of the second and third cycle
- Day 1 of each remaining cycle
- An "End of Treatment" visit about 1 month after they stopped taking study treatment

There was no maximum number of treatment cycles. Participants could continue in the study as long as treatment was safely tolerated and their cancer was not getting worse. This was an "open-label" study, which means that the study doctors and participants knew which treatment and dose was given.

The figures below show what happened during the study.



*__Participants in Expansion Group__ had biopsies: first biopsy done before the first dose of study drug, second biopsy done about 6 weeks later. Some participants had third biopsy about 6 weeks after the second biopsy.



All Participants *had biopsies: first biopsy done before the first dose of study drug, second biopsy done about 6 weeks later. Some participants had third biopsy about 6 weeks after the second biopsy.*

Where did this study take place?

The Sponsor ran this study at 14 locations in France, Netherlands, Japan, and the United States.

When did this study take place?

It began 23 April 2015 and ended 25 November 2020.

Who participated in this study?

This study included adult participants who:

- had locally advanced or metastatic cancer that started in the head and neck, skin (melanoma), liver, kidney, lung, bladder, stomach, or cervix
- had tried standard cancer treatments without adequate results, or had declined standard cancer treatments
- had at least 1 tumor that could be measured
- were examined by the study doctor and determined to be healthy enough to participate in the study

During Part 1:

- A total of 75 men participated
- A total of 12 women participated
- All participants were between the ages of 23 and 81 years

During Part 2:

- A total of 50 men participated
- A total of 37 women participated
- All participants were between the ages of 22 and 85 years

Participants could continue in the study as long as treatment was safely tolerated and their cancer was not getting worse. Of the 87 participants who started Part 1, 14 (16%) completed the study. 73 participants (84%) did not finish the study because they died or chose to leave the study. Of the 87 participants who started Part 2, 1 (1%) completed the study. 86 participants (99%) did not finish the study because they died or chose to leave the study.

How long did the study last?

The amount of time that participants were in the study varied. The entire study took more than 5 years to complete. In October 2018, the Sponsor decided to stop enrolling participants in this study due to business reasons. This decision was not due to any safety concerns. Participants already enrolled in the study continued as planned.

When the study ended in November 2020, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

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.

All participants (100%) in Part 1 had at least 1 medical problem. A total of 9 participants (10%) in Part 1 stopped taking study treatment because of medical problems, and 2 of these participants stopped taking study treatment because of medical problems that were considered to be related to the study treatment (heart failure and liver injury).

All participants (100%) in Part 2 had at least 1 medical problem. A total of 11 participants (13%) in Part 2 stopped taking study treatment because of medical problems, and 2 of these participants stopped taking study treatment because of medical problems that were considered to be related to the study treatment (reaction to IV infusion and rash).

The most common medical problems – those reported by at least 15% of participants – are described below.

Below are instructions on how to read Tables 1 to 4.

Instructions for Understanding Tables 1 to 4.

- The **1st** column of Table 1 lists medical problems that were commonly reported during Part 1. All medical problems reported by at least 15% of participants are listed.
- The **2nd** column tells how many of the 87 participants taking the study medication reported each medical problem. Next to this number is the percentage of the 87 participants taking the study medication who reported the medical problem.
- Using these instructions, you can see that 31 out of the 87 participants (36%) taking the study medication reported feeling tired.

Table 1. Commonly reported medical problems by study participants during Part 1

Medical Problem	PF-04518600 (87 Participants)
Feeling tired	31 out of 87 participants (36%)
Liver enzyme (AST) increased	21 out of 87 participants (24%)
Decreased appetite	20 out of 87 participants (23%)
Nausea	19 out of 87 participants (22%)
Abdominal pain	17 out of 87 participants (20%)
Itching	17 out of 87 participants (20%)
Trouble breathing	16 out of 87 participants (18%)
Low number of red blood cells	15 out of 87 participants (17%)

Table 1. Commonly reported medical problems by study participants during Part 1	
Medical Problem	**PF-04518600 (87 Participants)**
Fever	15 out of 87 participants (17%)
Diarrhea	14 out of 87 participants (16%)
Vomiting	14 out of 87 participants (16%)

Table 2. Commonly reported medical problems by study participants during Part 2	
Medical Problem	**PF-04518600 + Utomilumab (87 Participants)**
Feeling tired	25 out of 87 participants (29%)
Decreased appetite	23 out of 87 participants (26%)
Low number of red blood cells	22 out of 87 participants (25%)
Nausea	20 out of 87 participants (23%)
Constipation	18 out of 87 participants (21%)
Diarrhea	16 out of 87 participants (18%)

How many participants had "dose-limiting toxicities"?

"Dose-limiting toxicities" 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). No participants in this study had dose-limiting toxicities. The participants who stopped taking study treatment (9 participants in Part 1 and 11 participants in Part 2) did so for other medical problems.

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.

29 out of 87 participants (33%) in Part 1 had at least 1 serious medical problem.
30 out of 87 participants (35%) in Part 2 had at least 1 serious medical problem. The most common medical problems – those reported by more than 1 participant – are described below.

Table 3. Commonly reported serious medical problems by study participants during Part 1

Serious Medical Problem	PF-04518600 (87 Participants)
Pain	2 out of 87 participants (2%)
Fever	2 out of 87 participants (2%)
Infection of the biliary tract	2 out of 87 participants (2%)
Urinary tract infection	2 out of 87 participants (2%)
High blood sugar	2 out of 87 participants (2%)
Worsening cancer	2 out of 87 participants (2%)

Table 4. Commonly reported serious medical problems by study participants during Part 2

Serious Medical Problem	PF-04518600 + Utomilumab (87 Participants)
Worsening medical condition	2 out of 87 participants (2%)
Trouble breathing	2 out of 87 participants (2%)
Back pain	2 out of 87 participants (2%)
Fever	2 out of 87 participants (2%)
Serious skin infection (cellulitis)	2 out of 87 participants (2%)
Increased calcium level in the blood	2 out of 87 participants (2%)
Worsening cancer	2 out of 87 participants (2%)
Decreased sodium level in the blood	2 out of 87 participants (2%)

For Part 1, a total of 57 (66%) participants died:

- 44 deaths were due to cancer
- 13 deaths were due to unknown or other reasons
- None of the deaths were related to study treatment
- 2 participants died during the study or within 28 days of finishing study treatment

For Part 2, a total of 65 (75%) participants died:

- 44 deaths were due to cancer
- 2 deaths were due to toxicity from study treatment
- 19 deaths were due to unknown or other reasons
- 9 participants died during the study or within 28 days of finishing study treatment

This does not mean that everyone in this study had these results. These are just some of the main findings of this study. Other studies may have different results.

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.clinicaltrials.gov

Use the study identifier
NCT02315066

Please remember that researchers look at the results of many studies to find out which medicines can work and are safe for study participants.

Again, if you participated in this study,
thank you for volunteering.
We do research to try to find the
best ways to help study participants, and you
helped us to do that!