# 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. |
| **Medicines Studied:** | PF-06753512 |
| **Protocol Number:** | B7791001 |
| **Dates of Study:** | 30 December 2015 to 23 February 2021<br>This study was terminated prematurely. |
| **Title of this Study:** | A Study to Determine the Safety and Effects of Increasing Doses of a Vaccine-Based Immunotherapy Regimen (VBIR) for Prostate Cancer (PF-06753512)<br>[A Phase 1 Study to Evaluate the Safety, Pharmacokinetics and Pharmacodynamics of Escalating Doses of a Vaccine-Based Immunotherapy Regimen (VBIR) for Prostate Cancer (PF-06753512)] |
| **Date(s) of this Report:** | 13 May 2022 |

# – 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 prostate cancer?

Prostate cancer is a common cancer in men that occurs in the prostate. The prostate is a small walnut-sized gland located beneath the bladder. Prostate cancer is the most common cancer in American men (except for skin cancers). Prostate cancer may cause no signs or symptoms in its early stages and if detected early, when it's still confined to the prostate gland, has the best chance for successful treatment. However, when it has spread to other parts of the patient's body (known as metastatic cancer), the chance of survival decreases. Most prostate cancer cells need androgens (male sex hormones) to grow. Treatments that target hormones decrease the androgen levels or block them thereby decreasing the prostate cancer cells' growth.

Treatments for prostate cancer includes:

- surgically removing the cancer or testicles (surgical castration)
- radiotherapy
- androgen-deprivation therapy to decrease the androgen levels, also known as chemical castration
- anti-androgen medications to stop androgens from working inside the prostate cancer cells

## What is PF-06753512?

Immunotherapy is a type of cancer therapy that helps the body's immune system fight cancer. There are 2 types of immunotherapies that are currently available for men with advanced prostate cancer: vaccines and medications. PF-06753512 or prostate cancer vaccine-based immunotherapy regimen (VBIR) combines a two-part immunotherapy vaccine (PF-06755992 or adenovirus C68) and plasmid DNA [pDNA (PF-06755990)] with injections of an immunotherapy medication (tremelimumab

alone or with PF-06801591) to activate the immune system's ability to fight the prostate cancer cells.

PF-06755992 is an adenovirus vaccine which uses 3 antigens that are specific for prostate cancer. These antigens are prostate specific antigen (PSA), prostate specific membrane antigen (PSMA) and prostate stem cell antigen (PSCA). A vaccination boost called pDNA or PF-06755990 delivers the PSA, PSMA and PSCA antigens to the immune system. The pDNA boost was administered using a device called the intramuscular TriGrid Delivery System (TDS-IM). The TDS-IM device "opened the pathway" into the cells, which allowed the pDNA to get into the cell.

Tremelimumab is a monoclonal antibody which is a laboratory-made protein that mimics or boosts the immune system's ability to fight off harmful pathogens. The immunotherapy vaccines teach the immune system what cancer cells look like so the immune system can find and kill them. The immunotherapy medications are known as checkpoint inhibitors. Cancer cells sometimes use molecules on cells called immune checkpoints to avoid attack by the immune system. Checkpoint inhibitors block these molecules so the immune system can find and kill the cancer cells.

## What was the purpose of this study?

The purpose of this research study was to learn about the safety and effects of VBIR, and when VBIR is given together with PF-06801591 in participants whose disease progressed after treatment with hormone medications such as abiraterone or enzalutamide (medications that are approved for the treatment of advanced or metastatic prostate cancer). Researchers also wanted to determine if VBIR and its combination with PF-06801591 has manageable side effects and provides long-term cancer control in men with prostate cancer. A "side effect" is something (expected or unexpected) that you feel was caused by a medicine or treatment you take.

### Researchers wanted to know:

- **What side effects did participants have during the study?**

- **Was the VBIR safe in combination with PF-06801591 and did the participants tolerate it?**
- **Were there any Dose-Limiting Toxicities (DLTs)**
- **What doses from Part A of the study should be used in Part B of the study (see Figure 1)?**

# What happened during the study?

## How was the study done?

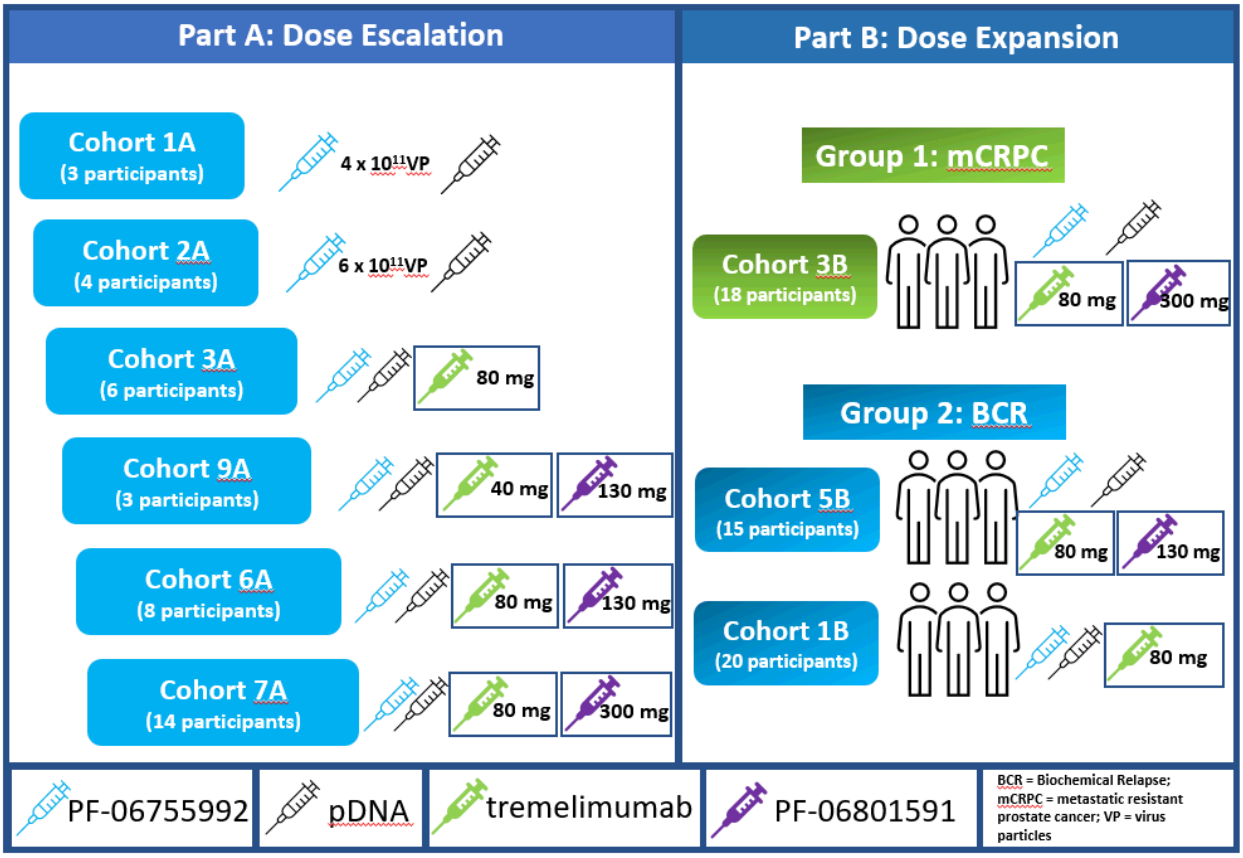
Figure 1 below shows Part A – Dose Escalation and Part B – Dose Expansion. Researchers tested increasing doses and combinations of VBIR components (PF-06755992, pDNA, tremelimumab) and PF-06801591 on participants to learn how the VBIR and PF-06801591 acted in the body. The cohorts (grouping) and dosing of the VBIR and PF-06801591 for the participants is shown.

Participants were divided into groups to test the safety of VBIR and PF-06801591:

Group 1: Participants with metastatic castration-resistant prostate cancer (mCRPC) who had not taken anti-androgens or had cancer that did not respond to anti-androgens. mCRPC is an advanced form of prostate cancer that does not respond to other treatments and has spread to other parts of the body.

Group 2: Participants with non-metastatic hormone sensitive prostate cancer (HSPC) who had a biochemical relapse (rising PSA levels) before receiving androgen-deprivation therapy.

Figure 1. Overall study design




## Where did this study take place?

The Sponsor ran this study at 10-12 different research locations in the United States (US).

## When did this study take place?

It began 30 December 2015 and ended 23 February 2021.

## Who participated in this study?

The study included participants who met the inclusion criteria such as men over the age of 18 years, a diagnosis of prostate cancer, and those without any serious liver, adequate bone marrow or kidney problems.

A total of 91 men participated.

All participants were between the ages of 52 and 88 years.

Of the 91 participants who started the study, 44 finished the study and 47 participants were discontinued from the study. The main reason for discontinuation from the study phase was the participants refused further follow-up.

een participants left before the study was over by their own choice, their cancer got worse, or a doctor decided it was best for a participant to stop being in the study.

### How long did the study last?

Study participants were in the study for about 14 months (depended on the participants cohort). The entire study took around 5 years to complete.

The study was terminated on 20 August 2020 by the sponsor. The decision to terminate this study was based on a business decision and was not because of any safety or regulatory concerns with VBIR and PF-06801591.

When the study ended in February 2021 (last participant last visit), 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?

Results from this study suggest that the VBIR and PF 06801591 had manageable side effects in participants (Table 1).

### What side effects did participants have during the study?

The researchers recorded any side effects the participants had during the study. Participants could have had side effects for reasons not related to the study (for example, caused by an unknown underlying disease or by chance). Or side effects could also have been caused by a vaccine/study medication or by another medicine the participant was taking. Sometimes the cause of a side effect is unknown. By

comparing side effects across many vaccine groups in many studies, doctors try to understand what effects the vaccine/study medications might have on a participant.

Ninety out of 91 (99%) participants in this study had at least 1 side effect. A total of 27 participants discontinued the study treatment because of side effects. The most common side effects – those reported by at least 20% 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 side effects that were commonly reported during the study. All side effects reported in at least 20% of participants are listed.
- The **2nd** column tells how many of the 91 participants being administered the VBIR and PF-06801591 reported each side effect. Next to this number is the percentage of the 91 participants being administered the VBIR and PF-06801591 who reported the side effect.
- Using these instructions, you can see that 35 out of the 91 participants (38%) being administered the VBIR and PF-06801591 reported joint pain.

**Table 1. Commonly reported side effects by study participants**

| Side effects | VBIR and PF-06801591 (91 Participants) |
|---|---|
| **Low red blood cell count** | 28 out of 91 participants (31%) |
| **Loose stools (diarrhoea)** | 32 out of 91 participants (35%) |
| **Nausea** | 28 out of 91 participants (31%) |
| **Feeling tired** | 43 out of 91 participants (47%) |

| Table 1. Commonly reported side effects by study participants | |
|---|---|
| **Flu-like illness** | 29 out of 91 participants (32%) |
| **Amylase (enzyme that breaks down sugars) increased** | 19 out of 91 participants (21%) |
| **Liver test levels increased** | 20 out of 91 participants (22%) |
| **Lipase (enzyme that breaks down fat molecules) increased** | 21 out of 91 participants (23%) |
| **Decreased appetite** | 22 out of 91 participants (24%) |
| **Joint pain** | 35 out of 91 participants (38%) |
| **Back pain** | 20 out of 91 participants (22%) |
| **Headache** | 20 out of 91 participants (22%) |
| **Itching** | 19 out of 91 participants (21%) |

## Did study participants have any dose-limiting toxicities?

A DLT is a clinically significant side effect that occurs during a specific period after starting study treatment within the study (in the first 28 days after starting study treatment) and the side effects are graded based on a pre-defined grading scale.

In Part A of the study, 1 participant (1%) experienced a DLT in the first 28 days after treatment with the vaccine, PF-06755992. The participant experienced a serious side effect of myositis (inflammation of the muscles that are used to move the body) and myasthenia gravis (a chronic autoimmune disorder in which antibodies destroy the communication between nerves and muscle, resulting in muscle weakness). Both the side effects were because of administration of the VBIR and resulted in the participant permanently stopping the administration of the VBIR.

# Did study participants have any serious side effects?

A side effect is considered "serious" when it is life-threatening, needs hospital care, or causes lasting problems.

Below are instructions on how to read Table 2.

### Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists serious side effects that were reported during the study. All serious side effects reported by at least 5% of participants are listed.
- The **2nd** column tells how many of the 91 participants being administered the VBIR and PF-06801591 reported each serious side effect. Next to this number is the percentage of the 91 participants being administered the VBIR and PF 06801591 who reported the serious side effect.
- Using these instructions, you can see that 4 out of the 91 participants (4%) being administered the VBIR and PF 06801591 reported inflammation of the colon.

**Table 2. Commonly reported serious side effects by study participants**

| Serious Side effects | VBIR and PF-06801591 (91 Participants) |
|---|---|
| **Autoimmune disease that affects the heart** | 1 out of 91 participants (1%) |
| **Inflammation of heart muscle** | 1 out of 91 participants (1%) |
| **Too little thyroid hormone (hypothyroidism)** | 1 out of 91 participants (1%) |
| **Abdominal pain** | 2 out of 91 participants (2%) |
| **Inflammation of the colon** | 4 out of 91 participants (4%) |
| **Loose stools (diarrhoea)** | 3 out of 91 participants (3%) |
| **Not enough blood flow to the intestine** | 1 out of 91 participants (1%) |

| Table 2. Commonly reported serious side effects by study participants | |
|---|---|
| **Increasing physiological dysfunction of two or more organ systems (multiple organ dysfunction syndrome)** | 1 out of 91 participants (1%) |
| **Fever** | 1 out of 91 participants (1%) |
| **Infection or inflammation of pouches in the intestines (diverticulitis)** | 1 out of 91 participants (1%) |
| **Broken thigh bone** | 1 out of 91 participants (1%) |
| **Liver test levels increased (alanine aminotransferase)** | 1 out of 91 participants (1%) |
| **Liver test levels increased (aspartate aminotransferase)** | 1 out of 91 participants (1%) |
| **Blood creatine phosphokinase increased (enzyme that indicates injury or stress to muscle tissue, heart, or brain)** | 1 out of 91 participants (1%) |
| **Low blood sodium** | 2 out of 91 participants (2%) |
| **Muscular weakness** | 2 out of 91 participants (2%) |
| **Inflammation of the muscles that are used to move the body** | 3 out of 91 participants (3%) |
| **Broken bones from osteoporosis** | 1 out of 91 participants (1%) |
| **Temporary loss of consciousness** | 1 out of 91 participants (1%) |
| **Severe kidney injury** | 2 out of 91 participants (2%) |
| **Blockage in one or both ureters** | 1 out of 91 participants (1%) |
| **Excess fluid around the outside of the lungs** | 1 out of 91 participants (1%) |
| **High blood pressure in the blood vessels that supply the lungs** | 2 out of 91 participants (2%) |

Six participants (7%) died during the study, of which 5 participants (5%) deaths were because of a serious side effect and in 2 of those participants (2%) deaths were considered related to the administration of the VBIR.

Increasing doses of the VBIR alone and in combination with increasing doses of PF-06801591 were well-tolerated in prostate cancer participants.

Based on these results, the researchers have decided that the results are not likely the result of chance. 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.

## 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:

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

www.clinicaltrials.gov
Use the study identifier **NCT02616185**

www.pfizer.com/research/research_clinical_trials/trial_results
Use the protocol number **B7791001**

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!