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 Studied:	Talazoparib (Talzenna®) or PF-06944076
Protocol Number:	C3441021 (TALAPRO-2)
Dates of Study:	08 August 2017 to 16 August 2022
Title of this Study:	A Study of Talazoparib Given With Enzalutamide in Men Who Have Metastatic Castration-Resistant Prostate Cancer (mCRPC) [TALAPRO 2: A Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Talazoparib With Enzalutamide in Metastatic Castration Resistant Prostate Cancer]
Date(s) of this Report:	03 April 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 metastatic castration-resistant prostate cancer (mCRPC)?

Prostate cancer is a common cancer in men. It is often a slow-growing cancer with few symptoms. The prostate is a small gland that lies at the base of the bladder in men and is part of the male reproductive system.

"Metastatic" means that the cancer has spread to a part of the body beyond the prostate. In earlier stages of prostate cancer, male sex hormones (or "androgens") are usually stimulating the cancer cells to grow. "Castration-resistant" means that the prostate cancer continued to worsen despite receiving treatment that lessens androgen production from the testes.

Some men with mCRPC have specific changes in the genes that help cells to repair DNA damage. These changes in the genes may make it difficult for the cell to repair its DNA. This can make the cell become sensitive to some cancer treatments.

What is talazoparib?

The study medicine, talazoparib (Talzenna™), is a capsule taken by mouth. Talazoparib belongs to a class of medicines called "Poly (ADP-ribose) polymerases" (PARP) inhibitors.

> PARPs are proteins found in all normal and cancer cells. PARPs are needed to repair mistakes that can happen in DNA when cells divide. If the mistakes are not repaired, the cell will usually die and be replaced. Cells with mistakes in their DNA that do not die can become cancer cells.

A PARP inhibitor may help to kill cancer cells in 2 ways:

- It stops the PARP proteins from repairing the damaged DNA within cancer cells.
- It causes PARP proteins to remain attached or trapped to the DNA within cancer cells.

In this study, talazoparib was given together with enzalutamide. Researchers think giving talazoparib in combination with enzalutamide can help men with mCRPC better than enzalutamide alone. Earlier studies have shown that:

- Talazoparib blocks the repair of certain errors that may happen in the DNA when cells divide.
- Enzalutamide may shrink tumor size and slow tumor growth. It is often used to treat this form of prostate cancer.

What was the purpose of this study?

This study wanted to learn about talazoparib when given with enzalutamide to participants with mCRPC.

The purpose of each part of the study was:

- **Part 1:** To find the starting dose of talazoparib that can be given with enzalutamide.
- **Part 2:** To learn about the safety of the combination and effects of talazoparib when given with enzalutamide. Part 2 had 2 subgroups (also called "cohorts"). In both cohorts, men were assigned by chance to receive talazoparib with enzalutamide or placebo with enzalutamide.
    - **Cohort 1:** Men with mCRPC, regardless of whether or not their tumors have specific changes in DNA-repair genes.
    - **Cohort 2:** Men with mCRPC whose tumors must have specific changes in DNA-repair genes.

Researchers wanted to know:

1. **What was the starting dose of talazoparib that can be given with enzalutamide?**
2. **Did talazoparib with enzalutamide help Cohort 1 participants have more time without their prostate cancer getting worse?**
3. **Did talazoparib with enzalutamide help Cohort 2 participants have more time without their prostate cancer getting worse?**

The answers to Questions 1 and 2 are provided in this summary.

The answer to Question 3 is not in this summary. It will be provided at a later date once the results of Cohort 2 participants are available.

What happened during the study?

How was the study done?

This study had 2 parts.

In **Part 1**, a group of men with mCRPC signed up to take talazoparib with enzalutamide. The participants, study doctors, and researchers knew the treatments given during Part 1. This is known as an "open-label" study.

During Part 1, the study doctors wanted to find out the starting dose of talazoparib that can be given with enzalutamide. This starting dose was given to Part 2 participants.

In **Part 2**, two subgroups of men with mCRPC signed up.

- **Cohort 1:** Men with mCRPC, regardless of whether or not their tumors have specific changes in DNA-repair genes.
- **Cohort 2:** Men with mCRPC whose tumors must have specific changes in DNA-repair genes.

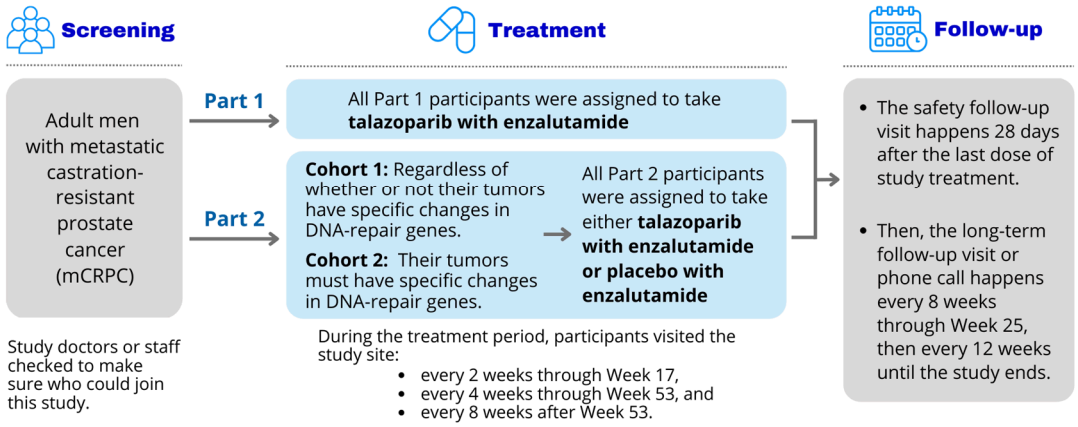
All Part 2 participants were assigned by chance to receive the study treatments. They received either talazoparib or placebo, which was given together with enzalutamide. A placebo does not have any medicine in it, but it looks just like talazoparib.

The participants, study doctors, and researchers did not know who took talazoparib and who took a placebo. This is known as a "double-blind" study. The participants, study doctors, and researchers knew that enzalutamide was given with talazoparib or placebo.

Researchers tested talazoparib given with enzalutamide on participants to find out if the study treatments helped with their prostate cancer. Then, researchers compared the results of participants given talazoparib with enzalutamide to the results of participants given a placebo with enzalutamide.

The figure below shows what happened in the study.

Figure 1. What happened in Part 1 and Part 2?



Throughout the study, study doctors or staff kept track of the participants' health. Participants had different tests to check if their prostate cancer was getting better or worse, such as:

- Computed tomography (CT) scan.
- Magnetic resonance imaging (MRI) scan.
- Bone scan.

In Parts 1 and 2, participants could continue taking the study treatments until:

- Their prostate cancer got worse as seen on a CT or MRI and bone scan.
- They were no longer being helped by the study treatments as judged by their study doctor.
- They stopped taking study treatments because of a medical problem they had during treatment.
- They left the study by their choice.
- They died.

Where did this study take place?

The Sponsor ran this study at 287 locations in 26 countries.

Argentina	Czech Republic	Japan	South Africa
Australia	Finland	Republic of Korea	Spain
Belgium	France	New Zealand	Sweden
Brazil	Germany	Norway	United Kingdom
Canada	Hungary	Peru	United States
Chile	Israel	Poland	
China	Italy	Portugal	

When did this study take place?

It began on 08 August 2017 and is ongoing as of 16 August 2022.

Who participated in this study?

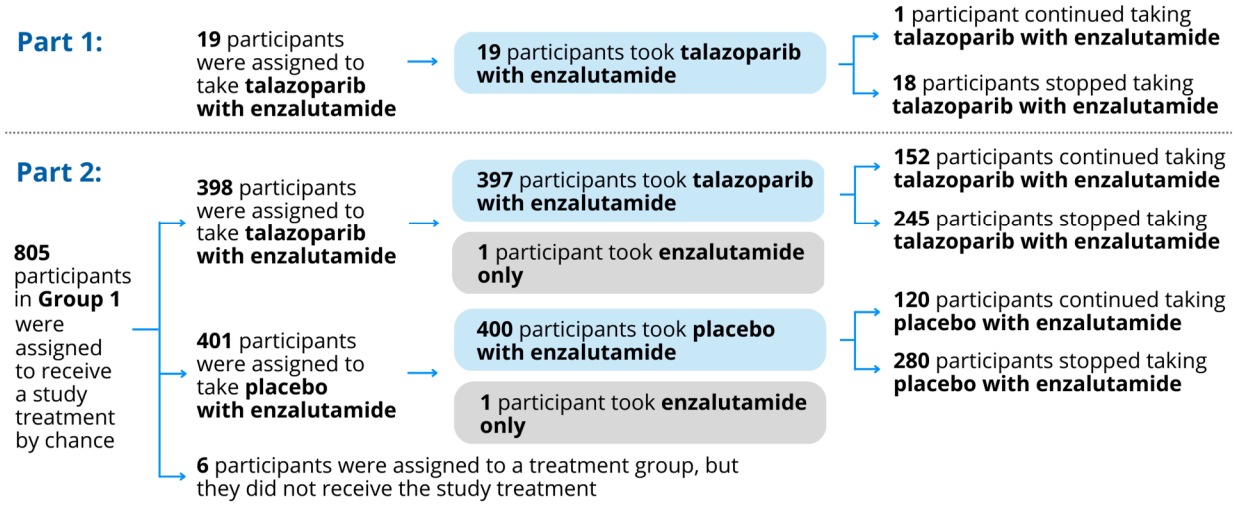
The study signed up adult men who met the study requirements, including:

- Confirmed prostate cancer that had spread to other parts of the body and is getting worse.
- Had castration by surgery or medical treatment.

All participants were male and between the ages of 36 and 91 years.

The figure below shows how many participants continued or stopped taking the study treatments as of 16 August 2022.

Figure 2. How many participants took the study treatments?



The most common reasons participants stopped taking the study treatments were:

- They had medical problems during treatment (in Part 1).
- Their prostate cancer got worse (in Part 2).

How long did the study last?

The study started on 08 August 2017. As of 16 August 2022, the study has been ongoing for about 5 years. It is scheduled to end in November 2024.

The Sponsor reviewed the information collected as of 16 August 2022. The Sponsor then created a report of the results. This is a summary of that report.

This summary describes the results for participants in Part 1 and Cohort 1 participants in Part 2.

What were the results of the study?

What was the starting dose of talazoparib that can be given with enzalutamide?

The starting dose of talazoparib was **0.5 mg once daily** when given with enzalutamide. This was the starting dose of talazoparib given with enzalutamide to Part 2 participants.

To answer this question, researchers looked at the results of Part 1 participants. At the start of Part 1, participants took talazoparib 1 milligram (mg) once daily with enzalutamide 160 mg once daily.

The study doctors checked the participants' safety and lab test results on scheduled visits. After 5 weeks of treatment, study doctors measured the amount of talazoparib and enzalutamide in the blood. Then, based on these results, they determined that the starting dose of talazoparib should be lowered to 0.5 mg once daily.

Did talazoparib with enzalutamide help Cohort 1 participants have more time without their prostate cancer getting worse?

To answer this question, researchers looked at the records of Cohort 1 participants in Part 2.

An independent group of experts looked at the participants' CT or MRI and bone scan results. This expert group checked if the participants' prostate cancer got worse. Then, researchers measured how long the participants lived without their prostate cancer getting worse after starting the study treatments.

In this study, researchers found that:

- Participants who got talazoparib with enzalutamide had more time without their prostate cancer getting worse compared to those who got a placebo with enzalutamide.
- Participants who got talazoparib with enzalutamide were **37% less likely** to have worsening prostate cancer or to die of any cause, compared to those who got a placebo with enzalutamide.

Based on these results, researchers have decided that the results are not likely due to chance. Talazoparib given with enzalutamide may help men with mCRPC have more time without their cancer getting worse.

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, researchers try to understand what effects a study medication might have on a participant.

The results are described for:

- All participants in Part 1.
- Cohort 1 participants in Part 2.

The results include participants who had at least 1 medical problem while taking the study treatment.

Part 1:

All 19 (100%) participants had a medical problem.

In total, 3 participants left Part 1 because of a medical problem.

Table 1 shows the most common medical problems seen in more than 40% of participants in Part 1.

Below are instructions on how to read Table 1.

Instructions for Understanding Table 1.

- The **1st** column of Table 1 lists the most common medical problems seen in Part 1. It lists all medical problems seen in more than 40% of participants.
- The **2nd** column tells how many of the 19 participants taking the study treatments had each medical problem. Next to this number is the percentage of the 19 participants taking the study treatments who had medical problem.
- Using these instructions, you can see that 14 of 19 participants (74%) taking the study treatments had low number of red blood cells.

Table 1. What were the most common medical problems in Part 1?

Medical Problem	Talazoparib With Enzalutamide (19 Participants)
Low number of red blood cells	14 of 19 participants (74%)
Loss of appetite	10 of 19 participants (53%)
Tiredness	10 of 19 participants (53%)
Queasy feeling (nausea)	9 of 19 participants (47%)
Low number of a white blood cell called neutrophil	8 of 19 participants (42%)

Part 2:

The following participants had a medical problem:

- 392 of 398 participants (99%) who got talazoparib with enzalutamide.
- 379 of 401 participants (95%) who got a placebo with enzalutamide.

In total, 35 participants left Part 2 because of a medical problem.

Table 2 shows the most common medical problems seen in more than 20% of participants in Part 2.

Below are instructions on how to read Table 2.

Instructions for Understanding Table 2.

- The **1st** column of Table 2 lists the most common medical problems seen in Part 2. It lists all medical problems seen in more than 20% of participants.
- The **2nd** column tells how many of the 398 participants taking talazoparib with enzalutamide had each medical problem. Next to this number is the percentage of the 398 participants taking talazoparib with enzalutamide who had the medical problem.
- The **3rd** column tells how many of the 401 participants taking a placebo with enzalutamide had each medical problem. Next to this number is the percentage of the 401 participants taking a placebo with enzalutamide who had the medical problem.
- Using these instructions, you can see how many had low number of red blood cells:
  - 262 of 398 participants (66%) taking talazoparib with enzalutamide.
  - 70 of 401 participants (18%) taking a placebo with enzalutamide.

Table 2. What were the most common medical problems in Part 2?		
Medical Problem	Talazoparib With Enzalutamide (398 Participants)	Placebo With Enzalutamide (401 Participants)
Low number of red blood cells	262 of 398 participants (66%)	70 of 401 participants (18%)
Low number of a white blood cell called neutrophil	142 of 398 participants (36%)	28 of 401 participants (7%)
Tiredness	134 of 398 participants (34%)	118 of 401 participants (29%)
Low number of a type of blood cells called platelets	98 of 398 participants (25%)	14 of 401 participants (4%)
Back pain	88 of 398 participants (22%)	72 of 401 participants (18%)
Low number of white blood cells	88 of 398 participants (22%)	18 of 401 participants (5%)
Loss of appetite	86 of 398 participants (22%)	63 of 401 participants (16%)
Queasy feeling (nausea)	82 of 398 participants (21%)	50 of 401 participants (13%)

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.

The results include participants who had at least 1 serious medical problem while taking the study treatment.

Part 1:

Overall, 9 of 19 participants (47%) had a serious medical problem. The most common serious medical problem was low number of red blood cells. This serious medical problem was seen in 2 of 19 participants (11%).

In total, 3 of 19 participants (16 %) had a serious medical problem that study doctors thought could be related to the study treatment.

Overall, 7 of 19 participants (37%) who received study treatment died during Part 1. Of these participants, study doctors thought the death of 1 participant could be related to the study treatment.

Part 2:

The following participants had a serious medical problem:

- 157 of 398 participants (39%) who got talazoparib with enzalutamide.
- 107 of 401 participants (27%) who got a placebo with enzalutamide.

Table 3 shows the most common serious medical problems seen in 2% or more participants in Part 2.

Instructions on how to read Table 3 are similar to those written in Table 2.

Table 3. What were the most common serious medical problems in Part 2?		
Serious Medical Problem	**Talazoparib With Enzalutamide (398 Participants)**	**Placebo With Enzalutamide (401 Participants)**
Low number of red blood cells	55 of 398 participants (14%)	1 of 401 participants (less than 1%)
Blood in the urine	10 of 398 participants (3%)	4 of 401 participants (1%)
UTI or urinary tract infection	9 of 398 participants (2%)	3 of 401 participants (less than 1%)

In Part 2, the following participants had a serious medical problem that study doctors thought could be related to the study treatment:

- 78 of 398 participants (20%) who got talazoparib with enzalutamide.
- 12 of 401 participants (3%) who got a placebo with enzalutamide.

Study doctors and staff followed up on 805 participants who joined Part 2.

Overall, 252 of 805 participants (31%) who received the study treatments died during Part 2. Of these participants:

- 123 of 402 participants (31%) got talazoparib with enzalutamide, and 129 of 403 participants (32%) got a placebo with enzalutamide.
- The most common cause of death was worsening of prostate cancer.
- For one of the participants who died in Part 2, study doctors thought the death was due to a medical problem that could be related to study treatment. This participant received a placebo with enzalutamide.

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 **C3441021**

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

www.clinicaltrials.gov — Use the study identifier **NCT03395197**

www.clinicaltrialsregister.eu — Use the study identifier **2017-003295-31**

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!