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: Xtandi® (enzalutamide [formerly MDV3100])

Protocol Number: MDV3100-10 (C3431013)

Dates of Study: 22 October 2013 to 31 August 2022

Title of this Study: Safety Study of Continued Enzalutamide Treatment in Prostate Cancer Patients (PLATO)

[A Phase 4, Randomized, Double-Blind, Placebo-Controlled Study of Continued Enzalutamide Treatment Beyond Progression in Patients With Chemotherapy-Naïve Metastatic Castration-Resistant Prostate Cancer]

Date(s) of this Report: 14 August 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 chemotherapy-naïve metastatic castration-resistant prostate cancer?

Prostate cancer is the name for cancer that starts in the prostate, which is a small, walnut-sized gland that lies at the base of the bladder in men and is part of the male reproductive system. Prostate cancer is a common cancer in men, and it is often a slow-growing cancer with few symptoms.

Chemotherapy is a specific type of treatment for cancer. "Chemotherapy naïve" means you have not received chemotherapy. "Metastatic" means that the cancer has spread to a part of the body beyond the prostate. In earlier stages of the disease, male hormones, or "androgens", are usually stimulating prostate cancer cells to grow. "Castration" means treatment that reduces androgen production from the testicles. "Castration-resistant" means that the prostate cancer continued to worsen despite castration, which usually occurs at a later stage of the disease.

What is enzalutamide?

Enzalutamide is a capsule that is swallowed and is approved to treat men with prostate cancer. Enzalutamide works by interfering with the connections between androgens (a type of hormone that plays a role in male traits and reproductivity) and androgen receptors (a protein in the body that attaches to androgens). This may help to slow the growth of prostate cancer.

Enzalutamide is approved by the United States (US) Food and Drug Administration (FDA) for men with advanced, castration-resistant, or metastatic castration-sensitive prostate cancer. "Castration-sensitive" means that the prostate cancer improved after castration. Enzalutamide is an experimental drug (still being tested) for earlier stage prostate cancer.

What was the purpose of this study?

The main purpose of this study was to help doctors decide whether enzalutamide may be a possible treatment for men with metastatic castration-resistant prostate cancer if abiraterone and prednisone are added to enzalutamide after blood levels of prostate-specific antigen (PSA) increased on enzalutamide alone. Abiraterone and prednisone are approved in the US, European Union, and other countries to treat men with metastatic castration-resistant prostate cancer. The study used several different tests to determine whether taking enzalutamide with abiraterone and prednisone was better than taking abiraterone and prednisone alone.

Researchers wanted to know:

- **How long did participants live without their prostate cancer getting worse after taking enzalutamide with abiraterone and prednisone compared to abiraterone and prednisone alone?**
- **What medical problems did participants have during the study?**

What happened during the study?

How was the study done?

Researchers tested enzalutamide on a group of participants to find out how long participants lived without their prostate cancer getting worse after taking enzalutamide with abiraterone and prednisone.

Researchers then compared the results of participants taking enzalutamide with abiraterone and prednisone to the results of participants taking a placebo with abiraterone and prednisone. A placebo does not have any medicine in it, but it looks just like the study medication.

All participants were "screened" to see if they qualified to be in the study.

The study had 2 parts:

Part 1

- All participants took enzalutamide (160 mg) once daily by mouth. The participants and researchers knew that participants received enzalutamide. This is known as an "open-label" treatment.
- At Week 13, blood levels of PSA were measured to see how the cancer was responding to enzalutamide. PSA is produced mainly by the prostate. Increased PSA levels may be a sign that the cancer is getting worse. Decreased PSA levels may be a sign that the cancer is getting better.
- At Week 13, if a participant's PSA went down or stayed the same level as before they started taking enzalutamide, they kept taking enzalutamide until their PSA went up to a certain level. At Week 13, if a participant's PSA went up, they stopped taking enzalutamide and had a safety follow-up visit about 30 days after stopping study treatment.
- When a participant's PSA went up after Week 13, the study doctor saw if they qualified for Part 2.

Part 2

- Participants were randomly assigned (similar to flipping a coin) to take either enzalutamide with abiraterone and prednisone or placebo with abiraterone and prednisone. The chance a participant got

placebo was 1 in 2, or 50%. The chance a participant got enzalutamide was also 1 in 2, or 50%. The participants and researchers did not know who took enzalutamide and who took the placebo. This is known as a "blinded" treatment. Participants were assigned to each group by chance alone.

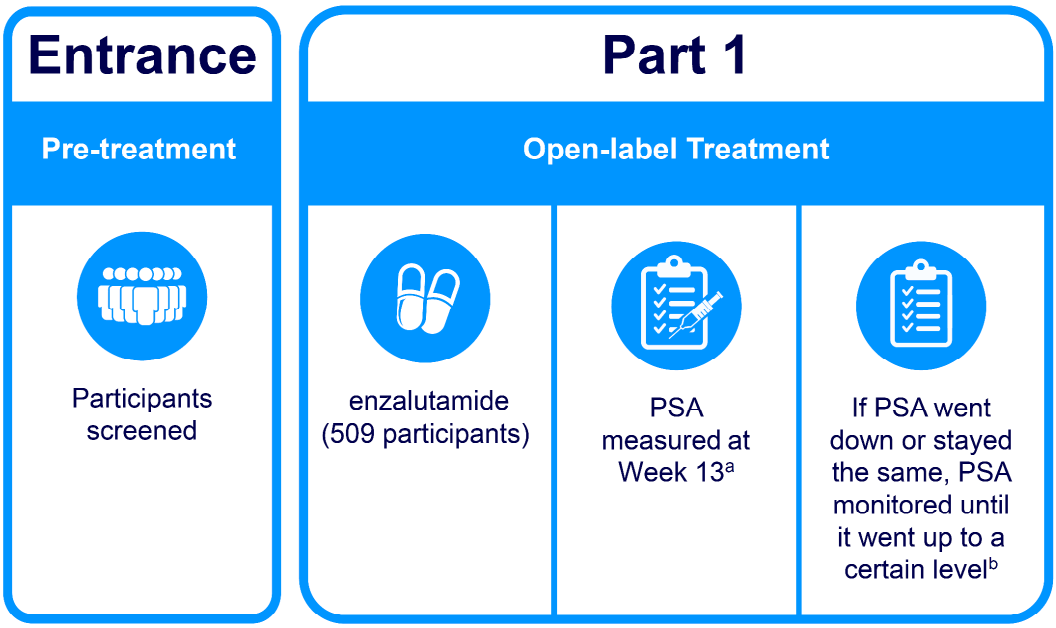
- Participants took either enzalutamide (160 mg) once daily by mouth or placebo once daily by mouth. All participants took abiraterone (1000 mg) once daily by mouth and prednisone (5 mg) twice daily by mouth (10 mg total per day).

Part 2 ended when the study doctor decided a participant should stop taking the study treatment or if the participant wanted to stop taking the study treatment. Participants had a safety follow-up visit about 30 days after stopping study treatment. Participants were also contacted every 4 weeks for up to 4 months after stopping study treatment to see if they started a new therapy for prostate cancer.

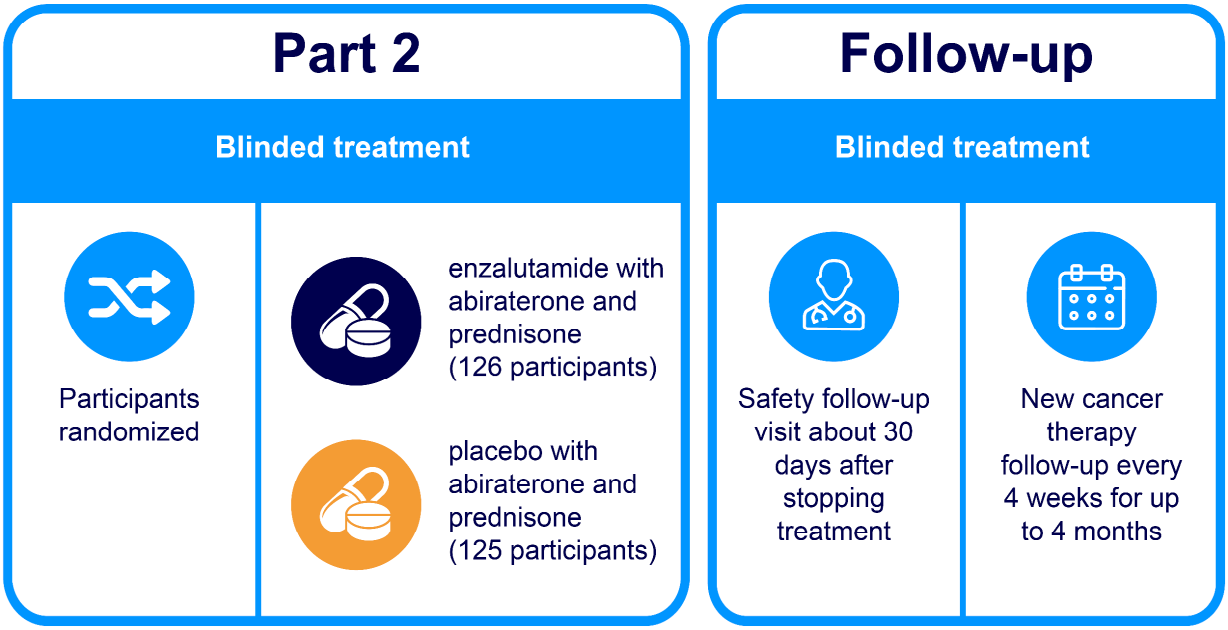
When entry into Part 2 closed, study doctors saw if participants that were still in Part 1 qualified to continue taking open-label enzalutamide or to switch to open-label abiraterone and prednisone. This part ended when the study doctor decided a participant should stop taking the study treatment or if the participant wanted to stop taking the study treatment. Participants had a safety follow-up visit about 30 days after stopping study treatment.

The study graphic in Figure 1 gives an overview of the study.

Figure 1. How Was the Study Done?



[a] If PSA increased, treatment stopped. Participants who stopped had a safety follow-up visit about 30 days after stopping treatment.
[b] When entry into Part 2 closed, 13 participants switched to abiraterone and prednisone. Participants who switched had a safety follow-up visit about 30 days after stopping treatment.



Where did this study take place?

The Sponsor ran this study at 51 locations in North America, Europe, and Australia.

When did this study take place?

It began 22 October 2013 and ended 31 August 2022.

Who participated in this study?

The study included adult male participants who had confirmed metastatic castration-resistant prostate cancer. Participants were not allowed to have had chemotherapy to treat their prostate cancer.

A total of 509 men joined the study. All participants were between the ages of 40 and 95 years.

- Of the 509 participants in the enzalutamide group, 245 (48.1%) stopped taking the study treatment. The most common reason for participants stopping study treatment was because their cancer got worse (92 participants [18.1%]).
- Of the 13 participants in the enzalutamide group switching to abiraterone and prednisone, 13 (100%) stopped taking the study treatment. The most common reason for participants stopping study treatment was because their cancer got worse (11 participants [84.6%]).
- Of the 126 participants in the enzalutamide with abiraterone and prednisone group, 125 (99.2%) participants stopped taking the study treatment. The most common reason for participants stopping study treatment was because their cancer got worse (104 participants [82.5%]). There was 1 (0.8%) participant that was assigned to this treatment but was not treated because their cancer got worse.

- Of the 125 participants in the placebo with abiraterone and prednisone group, 124 (99.2%) participants stopped taking the study treatment. The most common reason for participants stopping study treatment was because their cancer got worse (107 participants [85.6%]). There was 1 (0.8%) participant that was assigned to this treatment but was not treated because their cancer got worse.

How long did the study last?

The amount of time that participants were in the study varied. Initially, the study took less than 3 years to the primary completion date. After this, the study continued for participants who were still being treated. The entire study took about 8 years and 10 months to complete.

When the study ended in August 2022, the Sponsor began reviewing the information collected. The Sponsor then created a report of all of the safety results up to 31 August 2022. Before this, the Sponsor also created a report of the safety and efficacy (how well the medication worked) results from the information collected up to 07 October 2016 from Part 1 and Part 2. This is a summary of the 2 reports.

What were the results of the study?

How long did participants live without their prostate cancer getting worse after taking enzalutamide with abiraterone and prednisone compared to abiraterone and prednisone alone?

Researchers determined the length of time participants lived without their prostate cancer getting worse based on the information they collected up to October 2016.

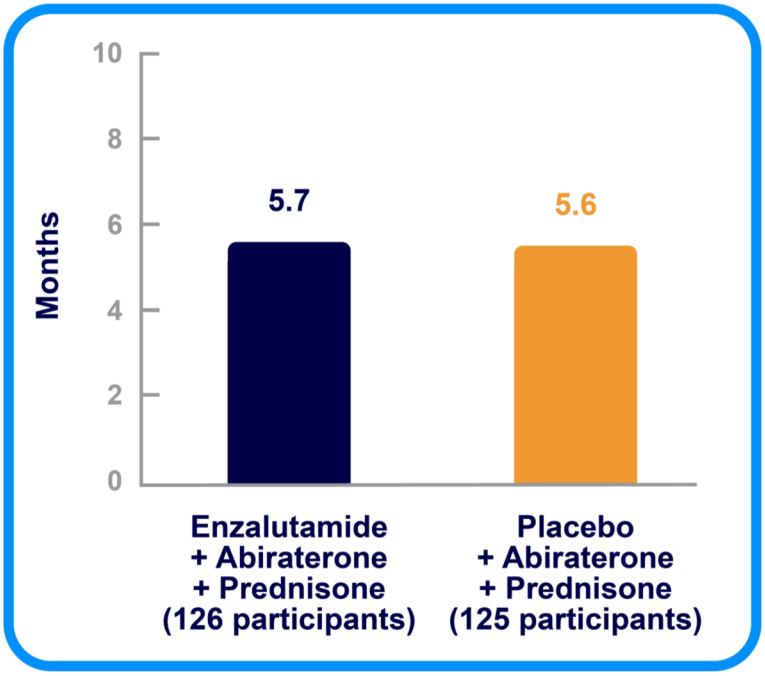
Medical problems are summarized based on the information collected up to August 2022 and are shown in the next section.

Did enzalutamide with abiraterone and prednisone help participants live longer without their prostate cancer getting worse compared to placebo with abiraterone and prednisone?

To answer this question, the researchers looked at the median length of time that participants lived without their cancer getting worse after receiving study treatment. A “median” is the middle number in a group of numbers. So, researchers looked at the length of time that each participant lived without their cancer getting worse, in order from highest to lowest. The median is the middle number, and participants would have the same chance of living a longer time or a shorter time than this number without their cancer getting worse.

The median length of time that participants lived without their cancer getting worse after taking enzalutamide with abiraterone and prednisone was 5.7 months, while the median length of time that participants lived without their cancer getting worse after taking placebo with abiraterone and prednisone was 5.6 months.

Figure 2. Median Time Without Cancer Getting Worse



Based on these results, the researchers concluded that the results were similar between enzalutamide with abiraterone and prednisone and placebo with abiraterone and prednisone. The study results did not show that one treatment was better than another at helping participants live longer 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, doctors try to understand what effects a study medication might have on a participant.

In the enzalutamide group, 476 out of 509 (93.5%) participants had at least 1 medical problem. In the enzalutamide group switching to abiraterone and prednisone, 13 out of 13 (100%) participants had at least 1 medical problem. In the enzalutamide with abiraterone and prednisone group, 114 out of 125 (91.2%) participants had at least 1 medical problem. In the placebo with abiraterone and prednisone group, 115 out of 124 (92.7%) participants had at least 1 medical problem. A total of 59 participants discontinued the treatment because of medical problems. The medical problems did not include the participants who were not treated because their cancer got worse. The most common medical problems – those reported by more than 15% of participants in any group – 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 15% of participants in any group are listed.

- The **2nd** column tells how many of the 509 participants in the enzalutamide group reported each medical problem. Next to this number is the percentage of the 509 participants who reported the medical problem.
- The **3rd** column tells how many of the 13 participants in the enzalutamide group switching to abiraterone and prednisone reported each medical problem. Next to this number is the percentage of the 13 participants who reported the medical problem.
- The **4th** column tells how many of the 125 participants in the enzalutamide with abiraterone and prednisone group reported each medical problem. Next to this number is the percentage of the 125 participants who reported the medical problem.
- The **5th** column tells how many of the 124 participants in the placebo with abiraterone and prednisone group reported each medical problem. Next to this number is the percentage of the 124 participants who reported the medical problem.
- Using these instructions, you can see that:
    - In the enzalutamide group, 101 out of the 509 (19.8%) participants reported nausea.
    - In the enzalutamide switching to abiraterone and prednisone group, 0 out of the 13 (0.0%) participants reported nausea.

- In the enzalutamide with abiraterone and prednisone group, 23 out of the 125 (18.4%) participants reported nausea.
- In the placebo with abiraterone and prednisone group, 12 out of the 124 (9.7%) participants reported nausea.

Table 1. Commonly reported medical problems by study participants

Medical Problem	Enzalutamide (509 Participants)	Enzalutamide Switching to Abiraterone + Prednisone (13 Participants)	Enzalutamide + Abiraterone + Prednisone (125 Participants)	Placebo + Abiraterone + Prednisone (124 Participants)
Nausea	101 out of 509 participants (19.8%)	0 out of 13 participants (0.0%)	23 out of 125 participants (18.4%)	12 out of 124 participants (9.7%)
Constipation	85 out of 509 participants (16.7%)	0 out of 13 participants (0.0%)	22 out of 125 participants (17.6%)	14 out of 124 participants (11.3%)
Feeling tired	206 out of 509 participants (40.5%)	0 out of 13 participants (0.0%)	21 out of 125 participants (16.8%)	19 out of 124 participants (15.3%)

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Medical Problem	Enzalutamide (509 Participants)	Enzalutamide Switching to Abiraterone + Prednisone (13 Participants)	Enzalutamide + Abiraterone + Prednisone (125 Participants)	Placebo + Abiraterone + Prednisone (124 Participants)
Fall	55 out of 509 participants (10.8%)	2 out of 13 participants (15.4%)	15 out of 125 participants (12.0%)	10 out of 124 participants (8.1%)
Rib fracture	5 out of 509 participants (1.0%)	2 out of 13 participants (15.4%)	1 out of 125 participants (0.8%)	1 out of 124 participants (0.8%)
Decreased appetite	83 out of 509 participants (16.3%)	2 out of 13 participants (15.4%)	15 out of 125 participants (12.0%)	11 out of 124 participants (8.9%)
Back pain	113 out of 509 participants (22.2%)	1 out of 13 participants (7.7%)	27 out of 125 participants (21.6%)	28 out of 124 participants (22.6%)
Joint pain	79 out of 509 participants (15.5%)	3 out of 13 participants (23.1%)	22 out of 125 participants (17.6%)	16 out of 124 participants (12.9%)

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Medical Problem	Enzalutamide (509 Participants)	Enzalutamide Switching to Abiraterone + Prednisone (13 Participants)	Enzalutamide + Abiraterone + Prednisone (125 Participants)	Placebo + Abiraterone + Prednisone (124 Participants)
Muscular weakness	21 out of 509 participants (4.1%)	2 out of 13 participants (15.4%)	6 out of 125 participants (4.8%)	6 out of 124 participants (4.8%)
Muscle spasms	10 out of 509 participants (2.0%)	2 out of 13 participants (15.4%)	4 out of 125 participants (3.2%)	9 out of 124 participants (7.3%)
Hot flush	90 out of 509 participants (17.7%)	1 out of 13 participants (7.7%)	8 out of 125 participants (6.4%)	3 out 124 participants (2.4%)
High blood pressure	52 out 509 participants (10.2%)	0 out of 13 participants (0.0%)	25 out of 125 participants (20.0%)	11 out of 124 participants (8.9%)

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.

- In the enzalutamide group, 163 out of 509 (32.0%) participants had serious medical problems. The most common serious medical problem was blood in the urine (11 out of 509 [2.2%] participants).
- In the enzalutamide group switching to abiraterone and prednisone, 4 out of 13 (30.8%) participants had serious medical problems. The serious medical problems were joint pain (1 participant [7.7%]), stomach flu (1 participant [7.7%]), decreased blood flow to the heart (1 participant [7.7%]), and cancerous or non-cancerous growths getting worse (1 participant [7.7%]).
- In the enzalutamide with abiraterone and prednisone group, 47 out of 125 (37.6%) participants had serious medical problems. The most common serious medical problem was pressure on the spinal cord (5 participants [4.0%]).
- In the placebo with abiraterone and prednisone group, 37 out of 124 (29.8%) participants had serious medical problems. The most common serious medical problem was pneumonia (3 participants [2.4%]).

A total of 57 participants died during the study. The number of participants that died during the study included all enrolled participants whether or not the study treatment was taken. In the enzalutamide group, 32 out of 509 (6.3%) participants died. Most of these deaths were due to other reasons. In the enzalutamide group switching to abiraterone and prednisone, 1 out of 13 (7.7%) participants died. This death was due to a medical problem.

In the enzalutamide with abiraterone and prednisone group, 14 out of 126 (11.1%) participants died. Most of these deaths were due to the participant's cancer getting worse. In the placebo with abiraterone and prednisone group, 10 out of 125 (8.0%) participants died. Most of these deaths were due to the participant's cancer getting worse.

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 **C3431013**

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

www.clinicaltrials.gov	Use the study identifier **NCT01995513**
www.clinicaltrialsregister.eu	Use the study identifier **2013-000722-54**

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!