



# CLINICAL TRIAL 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 medicine 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:** Enzalutamide/PF-04998299

**Protocol Number:** MDV3100-03 (C3431003)

**Dates of Trial:** 28 September 2010 to 8 February 2019

**Title of this Trial:** PREVAIL: A Multinational Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Chemotherapy-Naïve Patients With Progressive Metastatic Prostate Cancer Who Have Failed Androgen Deprivation Therapy

**Date of this Report:** 25 November 2019

— *Thank You* —

Pfizer, the Sponsor, would like to thank you for your participation in this clinical trial and provide you a summary of results representing everyone who participated. If you have any questions about the study or results, please contact the doctor or staff at your study site.

## WHY WAS THIS STUDY DONE?

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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.

Enzalutamide is a prescription medicine that is approved to treat men with prostate cancer that no longer responds to a medical or surgical treatment that lowers testosterone. 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.

The main goal of this study was to learn more about the use of enzalutamide in patients with prostate cancer that was spreading to other parts of the body, despite receiving treatment to block androgens. Researchers wanted to answer these research questions:

- How long did patients survive after receiving enzalutamide, compared to placebo?
- How long did patients survive without cancer getting worse after receiving enzalutamide, compared to placebo?

## WHAT HAPPENED DURING THE STUDY?

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This study compared 2 groups of patients to find out how long patients taking enzalutamide would survive, and how long they would survive without cancer getting worse, compared to patients taking a placebo. A placebo does not have any active medicine in it, but looks just like the medicine. The study included patients who had prostate cancer that was spreading to other parts of the body, despite receiving treatment to block androgens. The patients had either mild symptoms or no symptoms due to prostate cancer when the study began. To be eligible to join the study, patients must have never used a type of medicine called “cytotoxic chemotherapy”, which is used to destroy cancer cells.

Patients in this study were assigned to receive either enzalutamide or placebo. The patients and researchers did not know who took enzalutamide and who took the placebo. This is known as a “blinded” study. Patients were assigned to each treatment group by chance alone. This is known as a “randomized” study. Putting people into groups by chance helps make the groups more similar so they can be compared.

First, patients were checked by a study doctor to make sure they met the requirements to join the study. This was called the screening period.

During the treatment period, patients received the following treatments:

- Group 1: 871 patients received enzalutamide at a dose of 160 milligrams, taken by mouth each day
- Group 2: 844 patients received placebo, taken by mouth each day

During the treatment period, patients came to study visits every 4 weeks for the first 49 weeks, then every 12 weeks thereafter. At the study visits, imaging tests were done and patients were checked by study doctors to determine if prostate cancer was getting worse. Patients were also asked about any medical problems they were having.

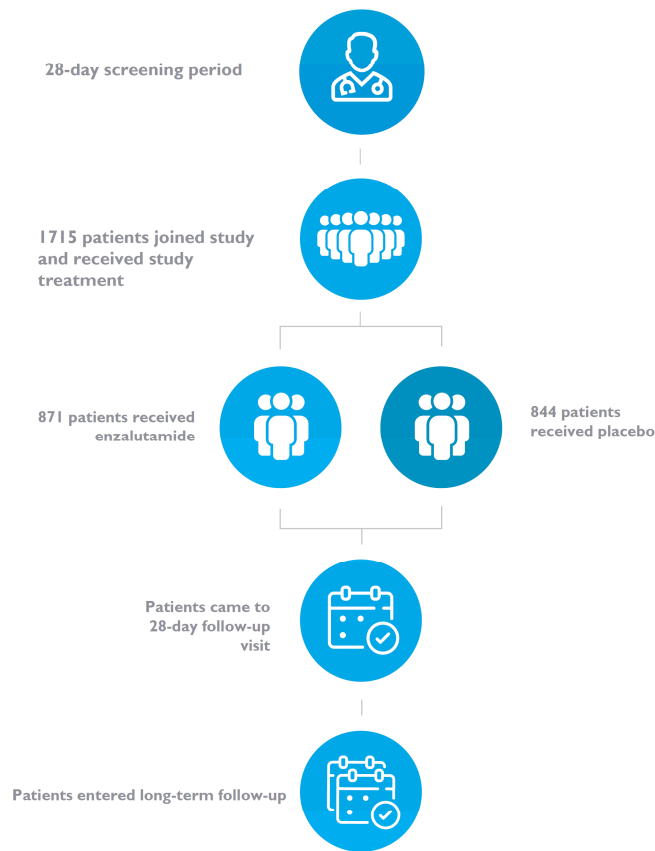
Patients continued taking enzalutamide or placebo as long as the medicine was tolerated and they continued to receive treatment to block androgens. Patients were to stop taking enzalutamide or placebo if:

- An imaging test showed that prostate cancer was getting worse
- Or they had complications caused by cancer spreading to the bone
- And they began taking either cytotoxic chemotherapy or an experimental drug for prostate cancer

Patients came to a follow-up visit 28 days after their last dose of enzalutamide or placebo. Next, patients had the option to enter the long-term follow-up study. During this time, patients were followed-up every 12 weeks.

In September 2013, the researchers finished gathering the information they needed to answer the research questions, and the main part of the study ended. Patients were then given the option to continue receiving enzalutamide (or switch to enzalutamide if they received placebo during the study).

The figure below shows what happened during this study.



The amount of time that patients were in the study varied, but the entire study took more than 8 years to complete, including both the main part of the study and the long-term follow-up part of the study. The sponsor ran this study at 207 locations in 22 countries in Asia, Australia, Europe, and North America. It began 28 September 2010 and ended 8 February 2019. 1,715 men joined study and received study treatment. All patients were between the ages of 42 and 93.

Patients were to enter the long-term follow-up part of the study after they stopped taking study treatment. Of the 1,715 patients who started the study and received study treatment, 428 patients (25%) were still receiving study treatment when the main part of the study ended in September 2013. 1,287 patients (75%) stopped taking study treatment by their choice, because a doctor decided it was best for a patient to

stop the study, because they had a medical problem, because prostate cancer got worse, or because they passed away.

When the study ended in February 2019, 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?**

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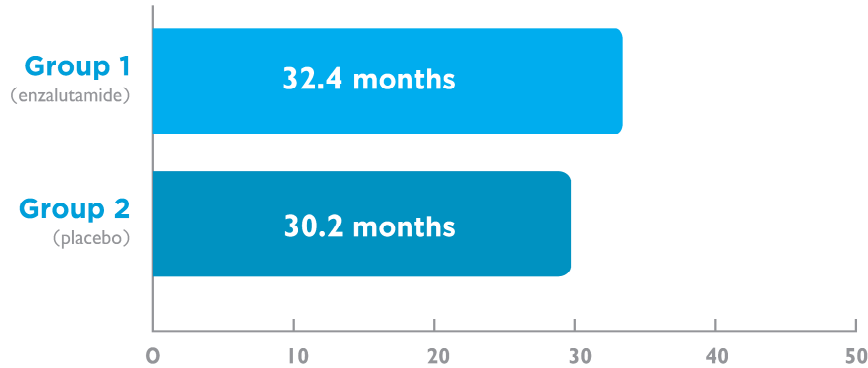
### **How long did patients survive after receiving enzalutamide, compared to placebo?**

To answer this question, the researchers looked at the median length of time that patients survived after receiving enzalutamide. A “median” is the middle number in a group of numbers. So, researchers looked at the length of time that each patient survived, in order from highest to lowest. The median is the middle number, and patients would have the same chance of surviving a longer time or a shorter time than this number.

The researchers first looked at data gathered from the beginning of the study until September 2013. During this time, the median length of time that patients survived after receiving enzalutamide was 32.4 months, while the median length of time that patients survived after receiving placebo was 30.2 months.

The researchers have determined that these results are not likely based on chance. The figure on the following page shows these study results.

### Median Survival Time: Beginning of Study Until September 2013



The researchers looked at the data again after all patients had been followed up with for at least 5 years (beginning of study until September 2017). During this time, the median length of time that patients survived after receiving enzalutamide was 35.5 months, while the median length of time that patients survived after receiving placebo was 31.4 months.

The researchers have determined that these results are not likely based on chance. The figure below shows these study results.

### Median Survival Time: Beginning of Study Until September 2017

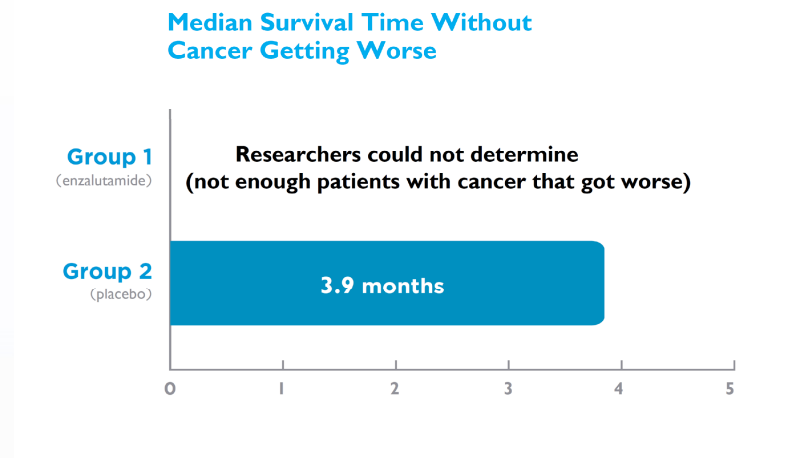




## How long did patients survive without prostate cancer getting worse after receiving enzalutamide, compared to placebo?

To answer this question, the researchers looked at imaging tests done between the beginning of the study and September 2013, to see if prostate cancer had gotten worse. During this time, the median length of time that patients survived without prostate cancer getting worse after receiving placebo was 3.9 months. The researchers were not able to determine the median length of time that patients survived without prostate cancer getting worse after receiving enzalutamide, because not enough patients had worsening prostate cancer during this time.

The researchers have determined that these results are not likely based on chance. The figure below shows these study results.



This does not mean that everyone in this study had these results. Other studies may produce different results, as well. These are just some of the main findings of the study, and more information may be available at the websites listed at the end of this summary.

## WHAT MEDICAL PROBLEMS DID PATIENTS HAVE DURING THE STUDY?

Researchers looked at medical problems that happened from the beginning of the study until the end of the long-term follow-up part of the study in February 2019.

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 the side effects of an experimental drug might be.

1,648 out of 1,715 patients (96%) had at least 1 medical problem. A total of 426 patients (25%) stopped taking study treatment because of medical problems. The most common medical problems are listed below.

<b>Most Common Medical Problems (Reported by More Than 10% of Patients)</b>		
<b>Medical Problem</b>	<b>Enzalutamide (871 Patients treated)</b>	<b>Placebo (844 Patients treated)</b>
Feeling tired	333 (38%)	220 (26%)
Back pain	283 (33%)	189 (22%)
Constipation	223 (26%)	147 (17%)
Nausea	213 (25%)	192 (23%)
Joint pain	205 (24%)	137 (16%)
Low appetite	183 (21%)	140 (17%)
Diarrhea	160 (18%)	121 (14%)
Hot flush	159 (18%)	66 (8%)
High blood pressure	149 (17%)	36 (4%)



Fall	142 (16%)	45 (5%)
Pain in hands or feet	124 (14%)	98 (12%)
Weight loss	122 (14%)	72 (9%)
Feeling weak	122 (14%)	69 (8%)
Swelling caused by fluid build-up in lower limbs	115 (13%)	71 (8%)
Pain in muscles, bones, and joints	113 (13%)	74 (9%)
Headache	102 (12%)	59 (7%)
Bone pain	101 (12%)	118 (14%)
Blood in urine	95 (11%)	49 (6%)
Cough	93 (11%)	58 (7%)
Trouble breathing	88 (10%)	61 (7%)
Low number of red blood cells	86 (10%)	71 (8%)

## WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

A medical problem is considered “serious” when it is life-threatening, needs hospital care, or causes lasting problems.

611 out of 1,715 patients (36%) had serious medical problems. 382 patients (44%) in the enzalutamide group, and 229 patients (27%) in the placebo group had serious medical problems.

1,382 patients (81%) died during the study. Most of these deaths were due to prostate cancer progression. Study doctors determined that 4 patients (less than 1%) died for reasons related to study treatment.

## WHERE CAN I LEARN MORE ABOUT THIS STUDY?

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If you have questions about the results of your study, please speak with the doctor or staff at your study site.

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

[www.clinicaltrials.gov](http://www.clinicaltrials.gov)

Use the study identifier **NCT01212991**

[www.clinicaltrialsregister.eu](http://www.clinicaltrialsregister.eu)

Use the study identifier **2010-020821-41**

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

**Again, thank you for volunteering.**  
We do research to try to find the  
best ways to help patients, and you  
helped us to do that!