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 (formerly MDV3100)

Protocol Number: C3431010 (CRPC2)

Dates of Trial: 30 September 2009 to 02 November 2017

Title of this Trial: Safety and Efficacy Study of MDV3100 in Patients With Castration-Resistant Prostate Cancer Who Have Been Previously Treated With Docetaxel-based Chemotherapy (AFFIRM)

[AFFIRM: A Multinational Phase 3, Randomized, Double-Blind, Placebo-Controlled Efficacy and Safety Study of Oral MDV3100 in Patients With Progressive Castration-Resistant Prostate Cancer Previously Treated With Docetaxel-Based Chemotherapy]

Date of this Report: 16 April 2020

– 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?

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.

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 chemotherapy and treatment to block androgens. Chemotherapy is a type of medicine used to destroy cancer cells. Researchers wanted to answer this research question:

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

WHAT HAPPENED DURING THE STUDY?

This study compared 2 groups of patients to find out how long patients would survive after receiving enzalutamide, compared to 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 1 or 2 prior chemotherapy regimens, including at least 1 regimen with a chemotherapy medicine called docetaxel. These patients were also receiving treatment to block androgens.

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.

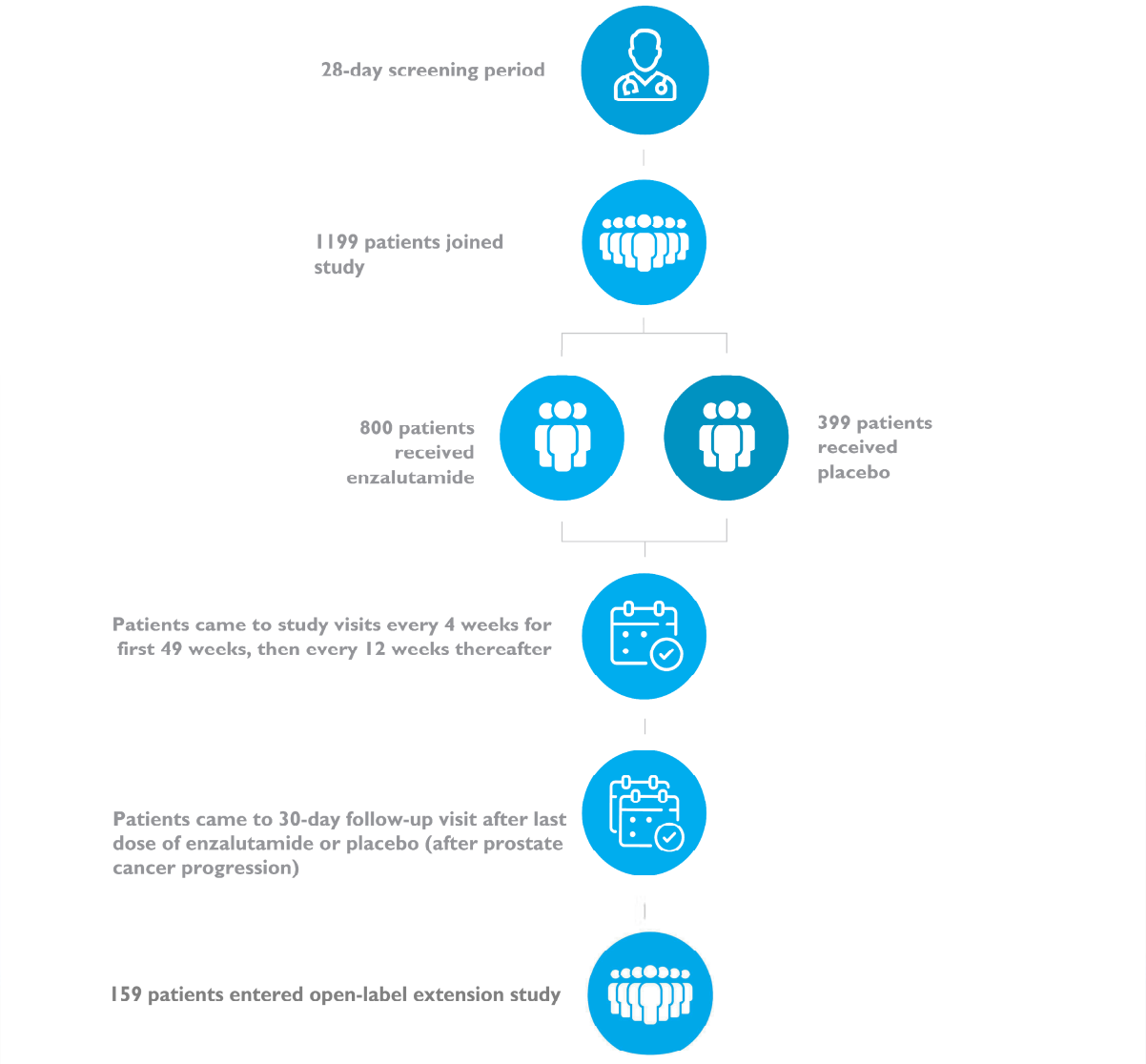
During the treatment period, patients received the following treatments:

- Group 1: 800 patients received enzalutamide at a dose of 160 milligrams, taken by mouth each day
- Group 2: 399 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 (known as prostate cancer "progression"). Patients were also asked about any medical problems they were having.

Patients came to a follow-up visit 30 days after their last dose of enzalutamide or placebo (after prostate cancer progression). Next, patients who were receiving placebo had the option to enter the "open-label extension" part of the study. During this part of the study, all patients received enzalutamide and were followed-up every 12 weeks. "Open-label" means that the patients and researchers knew which medicine the patients were taking.

The figure on the following page 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 open-label extension part of the study. The sponsor ran this study at 156 locations in 15 countries in Africa, Australia, Europe, North America, and South America. It began 30 September 2009 and ended 02 November 2017. 1,199 men joined the study and received study treatment. All patients were between the ages of 41 and 92 years.

Patients were to continue receiving study treatment until it was confirmed that their prostate cancer had gotten worse, and they were scheduled to begin taking another treatment for prostate cancer. Of the 1,199 patients who started the study, 250 patients (21%) were still receiving study treatment when the main part of the

study ended in September 2011. 949 patients (79%) 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. A total of 109 patients from the enzalutamide group and 50 patients from the placebo group entered the open-label extension part of the study.

When the study ended in November 2017, the Sponsor began reviewing the information collected. The Sponsor then created a report of the results. This is a summary of that report.

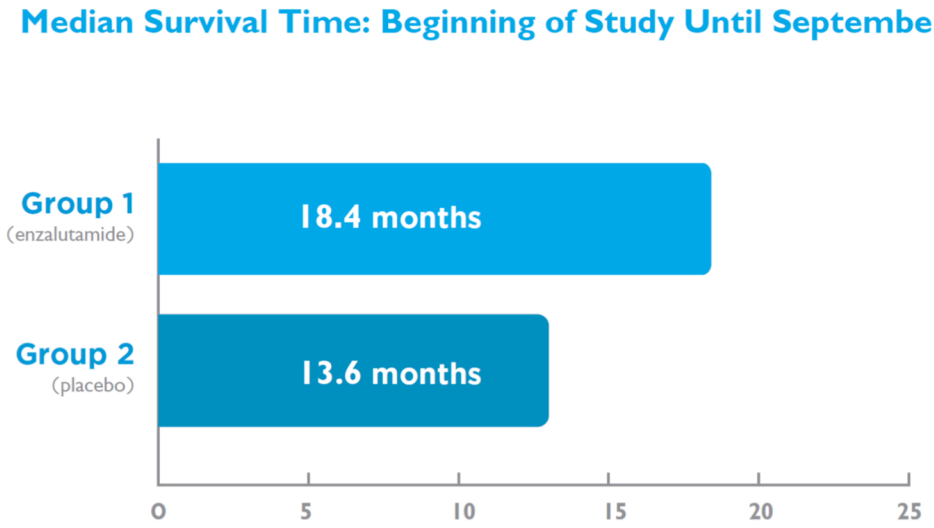
WHAT WERE THE RESULTS OF THE STUDY?

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

To answer this question, the researchers looked at data gathered from the beginning of the study until the main part of the study ended in September 2011. They 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.

During this time, the median length of time that patients survived after receiving enzalutamide was 18.4 months, while the median length of time that patients survived after receiving placebo was 13.6 months.

The researchers have determined that these results are clinically meaningful, and not likely based on chance. The figure on the following page 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?

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.

1,179 out of 1,199 patients (98%) had at least 1 medical problem. A total of 222 patients (19%) stopped taking study treatment because of medical problems. Out of the 50 patients who took placebo during the main part of the study and switched to enzalutamide during the open-label extension part of the study, 48 patients (96%) had

at least 1 medical problem. 12 (24%) of these patients stopped taking study treatment because of medical problems. The most common medical problems are listed below.

Most Common Medical Problems (Reported by More Than 10% of Patients)			
Medical Problem	Enzalutamide (800 Patients treated)	Placebo (399 Patients treated)	Placebo During Main Study/ Enzalutamide During Open-Label Extension (50 Patients treated)
Feeling tired	281 (35%)	117 (29%)	15 (30%)
Nausea	278 (35%)	167 (42%)	16 (32%)
Low appetite	246 (31%)	121 (30%)	9 (18%)
Back pain	229 (29%)	96 (24%)	9 (18%)
Constipation	210 (26%)	111 (28%)	7 (14%)
Joint pain	184 (23%)	71 (18%)	2 (4%)
Diarrhea	184 (23%)	70 (18%)	9 (18%)
Hot flush	165 (21%)	41 (10%)	1 (2%)
Feeling weak	151 (19%)	68 (17%)	9 (18%)
Vomiting	143 (18%)	88 (22%)	8 (16%)
Pain in hands or feet	139 (17%)	63 (16%)	5 (10%)
Low number of red blood cells	132 (17%)	76 (19%)	11 (22%)
Swelling caused by fluid build-up in lower limbs	121 (15%)	47 (12%)	4 (8%)
Pain in muscles, bones, and joints	121 (15%)	40 (10%)	3 (6%)

Bone pain	**110 (14%)**	**63 (16%)**	**2 (4%)**
Weight loss	**108 (14%)**	**42 (11%)**	**7 (14%)**
Headache	**101 (13%)**	**22 (6%)**	**1 (2%)**
Trouble breathing	**89 (11%)**	**40 (10%)**	**6 (12%)**
Pain or numbness caused by pressure on spinal cord	**59 (7%)**	**18 (5%)**	**5 (10%)**
Anxiety	**55 (7%)**	**16 (4%)**	**6 (12%)**
Fall	**44 (6%)**	**5 (1%)**	**6 (12%)**

WERE THERE ANY SERIOUS MEDICAL PROBLEMS?

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

During the main part of the study, 474 out of 1,199 patients (40%) had serious medical problems, including 319 patients (40%) in the enzalutamide group, and 155 patients (39%) in the placebo group. Out of the 50 patients who took placebo during the main part of the study and switched to enzalutamide during the open-label extension part of the study, 25 patients (50%) had serious medical problems after switching.

899 patients (75%) died during the main part of the study. Out of the 50 patients who took placebo during the main part of the study and switched to enzalutamide during the open-label extension part of the study, 21 patients (42%) died after switching. Most of these deaths were due to prostate cancer progression.

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.

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

www.clinicaltrials.gov	Use the study identifier **NCT00974311**
www.clinicaltrialsregister.eu	Use the study identifier **2009-013174-41**

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

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!