Summary of Results for Laypersons

What was the Study Called?

A Randomized, Double-blind, Phase 2 Efficacy and Safety Study of MDV3100 (ASP9785) vs. Bicalutamide in Castrate Men with Metastatic Prostate Cancer. This was also known as the TERRAIN study.

Why was this Study Needed?

Prostate cancer growth is dependent on male hormones or "androgens." An example of an androgen is testosterone. Prostate cancer that keeps growing even when the amount of testosterone in the body is reduced to very low levels is called castration-resistant prostate cancer (CRPC). Enzalutamide (also known as MDV3100 and Xtandi®) and bicalutamide are medicines that are used to treat patients with prostate cancer. Both stop the effect of androgens. For a while, they can stop or slow down the growth of prostate cancer. There is information on the anticancer effects of these medicines on CRPC. But these medicines have not yet been compared in a clinical study of patients with CRPC. Therefore, there was a need to study which of these medicines made the progression-free survival (PFS) of patients with CRPC longer. That is the length of time from the start of study medicine until the cancer got worse.

This study was conducted in patients with CRPC. The patients in this study took enzalutamide and placebo or bicalutamide and placebo. The section below describes what a placebo is. The main question this study helped to answer was which study medicine (enzalutamide or bicalutamide) made the PFS longer. It was also important to find out what unwanted effects these patients had from the study medicines.

The study started in March 2011 and ended in November 2017. When the study ended, the sponsor (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

What Kind of Study was This and Who Took Part in it?

This study had 2 parts: a "double-blinded" part, followed by an "open-label" part.

Double-blinded part: "Double-blinded" means that the patients and the researchers did not know who took which of the study medicines (enzalutamide and placebo or bicalutamide and placebo). A "placebo" is a dummy treatment such as a tablet or capsule that looks like a medicine, but does not have any medicine in it. Using a placebo helped make the study results fair and unbiased, because that way all patients took 4 capsules (enzalutamide or placebo) and 1 tablet (placebo or bicalutamide). The researchers and patients could not tell who was taking enzalutamide, and who was taking bicalutamide.

Open-label part: This part of the study started when the researchers were told which study medicines patients had been taking during the double-blinded part. "Open-label" means that all patients knew that they took enzalutamide.

Clinical studies have a list of requirements for patients who can be in a study ("inclusion" criteria) and patients who cannot take part in a study ("exclusion" criteria). The requirements for this study are listed below:

Men aged 18 years and older could be in the study if:

- Their doctor determined that they had prostate cancer. Their prostate cancer had spread from the prostate to other places in the body.
- Their testosterone level was ≤ 1.7 nmol/L (50 ng/dL). ("nmol/L" and "ng/dL" are units that measure the amount of the material in the blood. For example, a testosterone blood level of 1.7 nmol/L means that there is 1.7 nmol of testosterone in 1 L of blood.)
- They were taking hormonal therapy that blocks the effect of androgens and were planning to continue this therapy throughout the study or they had been castrated.
- They were fully active or they could perform light daily activities.
- They were expected to live for at least 1 year.

Men aged 18 years and older could not take part in this study if:

- They had a condition that the study doctor thought would make it hard for them to take part in the study or their condition would make it hard to evaluate their study results.
- They received chemotherapy for treatment of their prostate cancer.
- Their cancer had (probably) spread to the brain or the skull.
- They had abnormal hematology laboratory tests. Hematology laboratory tests examine blood formation and blood disorders. Patients could not receive growth factors or blood transfusions 7 days prior to the start of the study.
- They had abnormal liver or kidney function.

During the study, the study doctor did a check-up of the patients at several study visits. At the first visit, patients were checked to see if they could be in the study. Patients who could be in the study were picked for a treatment (enzalutamide or bicalutamide) by chance alone. The same number of patients received each treatment as described below.

- Enzalutamide: Patients took 160 mg (4 capsules) of enzalutamide once a day and 1 placebo tablet once a day.
- Bicalutamide: Patients took 50 mg (1 tablet) of bicalutamide once a day and 4 placebo capsules once a day.

The patients could take study medicine until their cancer got worse, they had unwanted effects they could not tolerate, they started a new cancer therapy or until the start of the open-label part. At the start of the open-label part, the study doctor determined which patients could benefit from enzalutamide treatment. Those patients took 160 mg (4 capsules) of enzalutamide once a day.

After Astellas had ended the study, the study doctor determined which patients would still benefit from the enzalutamide treatment. Those patients could continue enzalutamide treatment in a new extension study (9785-CL-0123).

This study took place at 84 clinics in several countries. 375 patients were in the study. Out of these patients, 372 patients took at least 1 dose of study medicine. 189 patients took bicalutamide. 192 patients took enzalutamide. Out of the 192 patients, 9 patients took both bicalutamide (during the double-blinded part) and enzalutamide (during the open-label part).

	Number of Patients
Age Group	
Aged less than 65 years	92
Aged between 65 and 75 years	165
Aged more than 75 years	118
Sex	
Men	375
Clinic Location	
European Union Countries (*at the time of the study*)	45
Belgium	6
Denmark	4
France	8
Germany	11
Romania	3
United Kingdom	13
Countries Outside European Union	39
Canada	7
US	32

What Were the Study Results?

The main question this study helped to answer was which study medicine (enzalutamide or bicalutamide) made the PFS of patients with CRPC longer. The study looked at the median PFS. That is the length of time from the start of study medicine until the time the cancer gets worse in half of the patients in each treatment group.

The results showed that from the start of study medicine, the cancer got worse in half of the patients after 15.7 months (478 days) in the enzalutamide group; and after 5.8 months (176 days) in the bicalutamide group.

A statistical test showed that the difference was not likely to be due to chance. The study showed that enzalutamide made the PFS of patients with CRPC longer than did bicalutamide.

What Adverse Reactions did Patients Have?

A lot of research is needed to know whether a medicine causes a medical problem. So when new medicines are being studied researchers keep track of all medical problems that patients have while they are in the study. These medical problems are called “adverse events” and are recorded whether or not they might be caused by the treatment taken. An “adverse reaction” is any medical problem or “adverse event” that is judged by the study doctor to be possibly caused by a medicine or treatment used in the study.

The table below shows the most common adverse reactions experienced by patients who took at least 1 dose of study medicine in this study.

Adverse Reaction	Enzalutamide (out of 192 patients)	Bicalutamide (out of 189 patients)
Any adverse reaction	129 (67.2%)	94 (49.7%)
Fatigue or tiredness	50 (26.0%)	29 (15.3%)
Feeling hot for a brief moment	25 (13.0%)	17 (9.0%)
Nausea or the urge to vomit	16 (8.3%)	17 (9.0%)
Headache or head pain	13 (6.8%)	7 (3.7%)
High blood pressure	10 (5.2%)	9 (4.8%)
Constipation	9 (4.7%)	6 (3.2%)
Decreased appetite	8 (4.2%)	7 (3.7%)
Enlargement of a man's breasts	8 (4.2%)	2 (1.1%)
Abnormal drowsiness or sluggishness, an unusual lack of energy	7 (3.6%)	4 (2.1%)
Decreased weight	7 (3.6%)	6 (3.2%)
Dizziness (or sensation of lightheadedness, unsteadiness or giddiness)	6 (3.1%)	11 (5.8%)
Feeling of weakness	5 (2.6%)	6 (3.2%)
Diarrhea	5 (2.6%)	6 (3.2%)

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems or needs hospital care.

19 patients experienced serious adverse reactions. The table below shows the most common serious adverse reactions.

Serious Adverse Reaction	Enzalutamide (out of 192 patients)	Bicalutamide (out of 189 patients)
Any serious adverse reaction	13 (6.8%)	6 (3.2%)
Belly pain	2 (1.0%)	0
Constipation	2 (1.0%)	0
Increased blood level of a liver enzyme (alanine aminotransferase)	1 (0.5%)	1 (0.5%)

14 patients died during the study: 11 patients who took enzalutamide and 3 patients who took bicalutamide. None of the patients who took bicalutamide died because of the study medicine. The death of 1 of the patients who took enzalutamide could have been related to the study medicine. This patient experienced a serious adverse reaction of inflammation of the entire body following lung infection.

Where Can I Learn More About This Study?

This document is a short summary of the main results from this study and reflects the information available as of October 2018. You can find this summary and more information about this study online at http://www.astellasclinicalstudyresults.com.

Please remember that researchers look at the results of many studies to find out how well medicines work and which adverse reactions they might cause. This summary only shows the results of this 1 study. If you have questions about the medicines used in this study, please discuss these with your doctor.

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