

## Plain Language Summary of Study Results

Astellas is grateful to the men who took part in this clinical study. Thank you.

### What was the study called?

A Randomized Study of Enzalutamide in Patients with Localized Prostate Cancer Undergoing Active Surveillance. This is also known as the ENACT study.

### Why was the study needed?

Localized prostate cancer means the cancer has not spread outside of the prostate. This cancer may grow very slowly in some men. Doctors can choose between several options to treat this type of cancer. One option is called ‘interventional’. Interventional options include surgery on the prostate, radiation (x-rays) directed at the prostate, or ultrasound directed at the prostate. These procedures can carry the risk of impotence. This is the inability to have or maintain an erection during sexual intercourse. Or a man can have problems with controlling the flow of urine from his bladder. A second option is called active surveillance. Active surveillance (or AS, for short) means the doctor closely monitors the man at regular checkups. Blood tests and prostate exams are done. Biopsies or scans may be done every 1 to 3 years also. Interventional options and the AS option may not work well for all men with localized prostate cancer. It is worthwhile to explore additional options. One possible option is treating localized prostate cancer with a medicine normally used to treat more advanced prostate cancer.

In this study, men were treated with enzalutamide. Enzalutamide is a prescription medicine. It is used for treatment of castration-resistant prostate cancer (metastatic and nonmetastatic). And for treatment of metastatic castration-sensitive prostate cancer. Metastatic means the cancer cells have spread from the place where they first formed to another part of the body. Castration-resistant means the prostate cancer keeps growing even when the amount of testosterone (a hormone) in the body is reduced to very low levels.

The study started in June 2016 and ended in August 2020. The sponsor of this study (Astellas) reviewed all the study information and created a report of the results. This is a summary of that report.

### What were the main questions the study helped answer?

How long did it take for the prostate cancer to progress in men who took enzalutamide? And how did this compare to men who were under active surveillance alone?

It was also important to find out what medical problems these men had from taking enzalutamide.

## What kind of study was this and who took part in it?

This was an “open-label” study. That means that each man with prostate cancer and the study doctors knew which treatment group the man was assigned to, enzalutamide or continued active surveillance.

This study was conducted in men 18 years or older with localized prostate cancer. Their prostate cancer had been confirmed with a biopsy done within 6 months of the first study visit. Their cancer was either low risk or intermediate risk of getting worse. The level of risk was judged using criteria from National Comprehensive Cancer Network. The men were under active surveillance before starting the study. They were expected to live for more than 5 years.

The following table describes the age of the men who participated in the study. They either took the study medicine or had active surveillance.

	Number of Men
<b>Age Group</b>	
Aged less than 65 years	99
Aged 65 years to less than 75 years	95
Aged 75 years or more	33

## Where did the study take place?

This study took place at 66 clinics in the US and Canada.

227 men were in the study.

- 114 men were in the study medicine (enzalutamide) group.
- 113 men were in the active surveillance group.

## What happened during the study?

During the study, the study doctor did a check-up of the men at several study visits. At the first visit, men were checked to see if they could be in the study.

The men who could be in the study were assigned to either take enzalutamide or to continue on active surveillance, by chance alone.

Men who were assigned to the enzalutamide treatment group took 160 milligrams of enzalutamide by mouth once a day for 1 year. The study doctor checked them every 3 months. After the first year was up, they stopped taking the study medicine.

Men who were assigned to the active surveillance (AS) group took no study medicine in the first year. The study doctor checked them also every 3 months.

After the first year of the study, men in both groups continued to be followed by the study doctors for at least another year. The men were checked by the study doctors every

3 months. After 2 years, the men were checked every 6 months up to 3 years, until the man's prostate cancer progressed or until the study ended.

## **What were the study results?**

The main question this study wanted to answer was:

### **How long did it take for the prostate cancer to progress in men who took enzalutamide? And how did this compared to men who were under active surveillance alone?**

Cancer that progressed means the cancer became worse. Study doctors compared the results of tests and tissue samples done at the start of the study to those done after the first year of the study.

Prostate cancer progressed after the first year of the study in:

- 28.1% (32 men out of 114) who took enzalutamide.
- 37.2% (42 men out of 113) who had active surveillance.

The study doctors checked the time it took for the cancer to progress. The expected median time of the cancer progressing was not reached in either group of men. The median is a middle value in a sorted list of numbers. The range is the upper and lower values. This means that the study doctors could not calculate the median number of months with an appropriate range.

Men who took enzalutamide had 46% less risk of their cancer progressing compared to men in the active surveillance group.

The odds that a man's prostate cancer would progress after 1 year was 70% lower for the enzalutamide group than for the active surveillance group.

Although no study medicine was given in the 2<sup>nd</sup> year of the study, the researchers looked at the odds for the cancer getting worse after the 2<sup>nd</sup> year. The odds that a man's prostate cancer would worsen after the 2<sup>nd</sup> year or at the end of the study were the same for both groups of men.

## **What adverse reactions did men have in this study?**

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 people 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.

114 men were assigned to the enzalutamide treatment group. Out of these, 112 men took at least 1 dose of the study medicine. 99 men (88.4%, or 99 out of 112 men) had adverse reactions in this study.

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

<b>Adverse Reaction</b>	<b>Enzalutamide (out of 112 men)</b>
Fatigue or tiredness	59 (52.7%)
Enlarged breasts in males	41 (36.6%)
Nipple pain	34 (30.4%)
Breast tenderness	28 (25.0%)
Impotence or the inability to have or maintain an erection during sexual intercourse	17 (15.2%)

Men in the active surveillance group also had medical problems. These were not caused by study medicine because these men did not receive any study medicine.

### **Did any of the men in this study have serious adverse reactions?**

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

3 men who received enzalutamide (2.7%, or 3 out of 112) experienced a serious adverse reaction in this study.

3 men passed away during the study. None of the deaths were thought to be caused by enzalutamide nor were due to prostate cancer.

### **Where can I learn more about this study?**

This document is a short summary of the main results from this study. 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. Your doctor may help you understand more about the results of this study.

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