

Summary of Results for Laypersons

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

What was the Study Called?

A Study of Enzalutamide Plus Androgen Deprivation Therapy (ADT) Versus Placebo Plus ADT in Patients With Metastatic Hormone Sensitive Prostate Cancer (mHSPC). This is also known as the ARCHES study.

Why was this Study Needed?

Enzalutamide is a prescription medicine taken by mouth for treatment of metastatic prostate cancer. Metastatic means the cells have spread from the prostate to other parts of the body. The cancer cells could spread to the bones or to other body organs (called soft tissue). Prostate cancer growth is dependent on male hormones (called androgens). An example of an androgen is testosterone. One type of treatment for prostate cancer is to use medicines that block the production of male hormones (androgens). This type of therapy is called androgen deprivation therapy (or ADT for short).

Treatment with androgen deprivation therapy (ADT) may not work as well as desired in all men. There was a need to study other treatments or combinations of treatment to use in this kind of prostate cancer.

This study compared the length of time for radiographic progression-free survival in men in taking 2 different therapies. Progression-free survival is the length of time from the start of study treatment until the cancer got worse. Radiographic means that scans were taken. And these scans show if the cancer is getting worse. Men took either a combination of enzalutamide plus androgen deprivation therapy (ADT). Or they took androgen deprivation therapy (ADT) alone. To do that in a fair and unbiased way, the men who took only androgen deprivation therapy (ADT) also took placebo (please see section below for the explanation of placebo).

The study started in March 2016. The sponsor of this study (Astellas) did a review of study results in October 2018. The review showed that radiographic progression-free survival was longer with the combination of enzalutamide plus androgen deprivation therapy (ADT) than with ADT alone. Astellas then informed patients which therapy they were taking. Patients still in the study who had taken the combination of enzalutamide plus androgen deprivation therapy (ADT) could continue taking it. Patients still in the study who were taking placebo plus androgen deprivation therapy (ADT) could switch to the combination of enzalutamide plus androgen deprivation therapy (ADT), if they and their doctor were in agreement. As of 14 October 2018, 1146 men had taken study medicine. Astellas created a report of those study results. This is a summary of that report. The study still continues to follow the men who have remained in the study.

What Kind of Study was this and Who Took Part in It?

The study included 1150 adult men with metastatic prostate cancer. Those whose prostate cancer had spread to bones had this documented by positive bone scans. The men's prostate cancer that had spread to soft tissue was documented by scans of that soft tissue. Their cancer kept growing even when the amount of male hormones (androgens) in their body was reduced to very low levels by taking androgen deprivation therapy (ADT). Or their hormones were very low because they had been castrated. They were expected to live for at least a year or more. They were active or they could perform light daily activities.

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 study doctors did not know who took which of the 2 study treatments. To do this, the 2 therapies must look the same. Placebo was added to the androgen deprivation therapy (ADT) instead of enzalutamide. A "placebo" is a dummy treatment that looks like a medicine, but does not have any medicine in it. This helps make study results fair and unbiased.

During the double-blinded part, the study doctor did a check-up of the men at several study visits. At the first visit, they were checked to see if they could be in the study. Men who could be in the study were picked for 1 of 2 therapies by chance alone.

- Group 1 took 160 mg of enzalutamide once daily plus androgen deprivation therapy (ADT).
- Group 2 took placebo once daily plus androgen deprivation therapy (ADT). "Placebo" is a dummy treatment that looks like a medicine, but does not have any medicine in it.

During this double-blinded part, the men could continue taking treatment until their cancer got worse. Or they had unwanted effects they could not tolerate. Or they asked to stop treatment. Or the study doctor decided that continuing treatment was no longer in their best interest.

The double-blinded part of the study ended after scans showed the cancer had worsened in 287 men out of the 1150 men in the study. How well each group did in the double-blinded part was studied. Researchers and patients were told which study treatments the patients had been taking.

Open-label part: This part of the study was an "open-label" study. That means that each patient and the study doctors knew which study medicine that patient took.

The open-label part started after the double-blinded part ended. Each man and his doctor decided whether or not he would continue taking enzalutamide plus androgen deprivation therapy (ADT) if he had been in group 1 during the double-blinded part. If he had been taking placebo plus androgen deprivation therapy (ADT) in group 2, he could switch to 160 mg enzalutamide daily plus androgen deprivation therapy (ADT) if he and his doctor agree.

During this open-label part, the men can continue taking treatment until their cancer gets worse. Or they have unwanted effects they cannot tolerate. Or they ask to stop treatment. Or the study doctor decides that continuing treatment is no longer in their best interest. The open-label part of the study is still continuing.

The double-blinded part of this study took place at 241 clinics in several countries. 1150 men were in the study and of those men, 1146 took at least 1 dose of study treatment, as of 14 October 2018. The open-label part of the study still continues.

Double-blinded Part of the Study	
	Number of Patients
Age Group	
Aged less than 65 years	300
Aged 65 years to 74 years	511
Aged 75 years or older	339
Clinic Location	
European Union Countries (<i>at the time of the study</i>)	546
Belgium	15
Denmark	62
Finland	39
France	44
Germany	10
Italy	68
Netherlands	54
Poland	47
Romania	57
Slovakia	81
Spain	55
Sweden	12
United Kingdom	2
Outside European Union	604
Argentina	10
Australia	47
Canada	41
Chile	52
Israel	23
Japan	92
New Zealand	23
Province of Taiwan	30
Republic of Korea	25
Russian Federation	139
United States	122

What Were the Study Results?

The double-blinded part of this study looked at the length of time from the start of study treatment until the cancer got worse. And it compared that length of time in men taking enzalutamide plus androgen deprivation therapy (ADT) to men taking androgen deprivation

therapy (ADT) alone. To measure that, both the study doctors and doctors who were independent of the study looked at scans taken of the bones or soft tissue during the study. The independent doctors decided if the cancer was worse or not.

They found that men who took enzalutamide plus androgen deprivation therapy (ADT) went longer before their cancer got worse than the men who took androgen deprivation therapy (ADT) plus placebo. (Placebo is a dummy treatment.)

The median (middle value in a sorted list of numbers) length of time until the cancer got worse was approximately 19 months in the placebo plus androgen deprivation therapy (ADT) group. The median was not available in the men who took enzalutamide plus androgen deprivation therapy (ADT) because there were fewer men whose cancer became worse. And the median was not reached.

The difference between the 2 groups was likely not to be due to chance.

The open-label part of the study is still continuing.

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.

In the double-blinded part of this study, 303 men (53.0%, or 303 out of 572 men) who took enzalutamide plus androgen deprivation therapy (ADT) experienced adverse reactions. 268 men (46.7%, or 268 out of 574 men) who took placebo plus androgen deprivation therapy (ADT) experienced adverse reactions. Placebo is a dummy treatment it has no medicine in it.

The table below shows the most common adverse reactions experienced by men who took at least 1 dose of study therapy, in the double-blinded part of this study.

Double-blinded Part of the Study		
Adverse Reaction	Enzalutamide+ADT (out of 572 men)	Placebo+ADT (out of 574 men)
Feeling hot for a brief moment	117 (20.5%)	104 (18.1%)
Fatigue or tiredness	85 (14.9%)	63 (11.0%)
Joint pain	29 (5.1%)	18 (3.1%)

ADT = androgen deprivation therapy.

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

In the double-blinded part of this study, men taking enzalutamide plus androgen deprivation therapy (ADT), 22 (3.8%, or 22 out of 572 men) experienced a serious adverse reaction. In the men taking placebo plus androgen deprivation therapy (ADT), 16 (2.8%, or 16 out of 574

men) experienced a serious adverse reaction in this study. (Placebo is a dummy treatment with no medicine in it.)

In the double-blinded part of this study, 84 men died during the study. 39 of the men were in the enzalutamide plus androgen deprivation therapy (ADT) group and 45 of the men were in the placebo plus androgen deprivation therapy (ADT) group. None of the deaths were caused by enzalutamide.

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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