

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 Multicenter, Single-arm, Open-label, Postmarketing Safety Study to Evaluate the Risk of Seizure Among Subjects with Metastatic Castration-Resistant Prostate Cancer (mCRPC) Treated with Enzalutamide Who Are at Potential Increased Risk of Seizure. This is also known as the UPWARD study.

Why was this Study Needed?

Enzalutamide is a prescription medicine for treatment of metastatic prostate cancer. Metastatic means the cells have spread from the prostate to another part of the body. These men may have a higher risk of having a seizure. For example, cancer cells in the brain can cause a seizure. Enzalutamide can also cause seizures. In some early studies of enzalutamide, 0.1 to 0.9 % of the participants experienced seizure. However, these early studies did not include men who had known risks of seizure. There was a need to learn the seizure rate in men with risk factors for seizure, when they are treated with enzalutamide.

This study was conducted in men with metastatic prostate cancer. They also had an increased risk for a seizure. The study looked at how many men had at least 1 seizure during the first 4 months of treatment with enzalutamide. It was also important to find out what other unwanted effects men had from the study medicine.

The study started in September 2013 and ended in January 2019. When the study ended, 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 Kind of Study was this and Who Took Part in It?

This was an “open-label” study. This means that each patient and the study doctors knew the patient took enzalutamide.

The study included men with metastatic prostate cancer. Their prostate cancer kept growing even when the amount of male hormones (called androgens) in their body was reduced to very low levels. Or even after removal of the testes. This is called castration-resistant prostatic cancer. The men had at least 1 risk factor for a seizure. Risk factors included: a history of seizures (but not one within 12 months of study start); a history of stroke; or small strokes that come and go quickly and leave no effect; a history of brain or head injury with loss of consciousness; unexplained loss of consciousness within the last 12 months; a wound or diseased patch in the brain; a history of abnormal connection between arteries and veins so the blood bypasses tissue in the brain; a history of brain infection; use of medicine for seizures; Alzheimer’s; other brain diseases from prostate cancer. They were active or they could perform light daily activities. Or they were able to walk and were capable of all self-care, but unable to carry out any work activities. And they were up and about more than half of the time that they were awake. Each seizure that was reported during the study was confirmed by a group of independent doctors who agreed the man had a seizure.

During the study, the study doctor did a check-up of the men at several study visits. At the first visit, the men were checked to see if they could be in the study. The men who could be in the study took enzalutamide by mouth: 160 mg (four 40-mg capsules) once a day. They took enzalutamide for 4 months. At the end of the 4 months, the men could remain on enzalutamide treatment for an extended period. They could continue 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 the patients' best interest.

This study took place at 73 clinics in 20 countries. 424 men were in the study. Out of these men, 423 took at least 1 dose of study medicine.

	Number of Men
Age Group	
Aged less than 65 years	66
Aged 65 years or older	357
Clinic Location	
European Union Countries (<i>at the time of the study</i>)	149
Belgium	6
Czech Republic	17
Finland	23
France	3
Germany	9
Hungary	3
Italy	25
Spain	48
Sweden	6
United Kingdom	9
Outside European Union	274
Argentina	36
Australia	16
Canada	5
Chile	57
Israel	60
New Zealand	3
Republic of Korea	12
Singapore	1
Taiwan	8
United States	76

What Were the Study Results?

This study was in men with metastatic prostate cancer and with increased risk of seizures. It looked at how many men had at least 1 confirmed seizure during the first 4 months of treatment with enzalutamide.

1.1% (4 out of 366 men) had a seizure within the first 4 months of treatment with enzalutamide.

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 men who took at least 1 dose of study medicine in this study.

Adverse Reaction	Enzalutamide (out of 423 men)
Any adverse reaction	217 (51.3%)
Fatigue or tiredness	74 (17.5%)
Weakness; lack of energy and strength	44 (10.4%)

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

37 men (8.7%, or 37 out of 423 men) experienced a serious adverse reaction in this study.

58 men died during the study. The majority of the deaths (23 out of the 58), were due to disease progression. 6 deaths were due to general health deterioration. The deaths of 6 of the men could have been related to enzalutamide.

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 July 2019. 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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