

Summary of Results for Laypersons

What was the Study Called?

The title of the study was: A Phase I Open-label Study to Evaluate the Effect of Multiple Doses of MDV3100 (ASP9785) on the Pharmacokinetics of Substrates for CYP2C8, CYP2C9, CYP2C19, and CYP3A4 in Patients with Castration-resistant Prostate Cancer.

Why was this Study Needed?

Some medicines are known or believed to interact with or interfere with other medicines a patient is taking. This study was done to find out if enzalutamide (previously called MDV3100 and also known by its brand name Xtandi®) has an effect on test medicines that are broken down by the body in a certain way. This was done by giving enzalutamide to patients along with test medicines that are known to be broken down by the body in a very specific way. Enzalutamide is a prescription medicine used to treat patients with prostate cancer.

Four prescription medicines were tested (test medicines) during this study:

- A test medicine commonly used to help control diabetes (pioglitazone) which is broken down by the body using a protein called CYP2C8
- A combination of 3 test medicines:
 - A commonly used blood thinner medicine (warfarin) which is broken down by the body using a protein called CYP2C9
 - A commonly used medicine to treat heartburn (omeprazole) which is broken down by the body using a protein called CYP2C19
 - A commonly used medicine to help people relax before surgery (midazolam) which is broken down by the body using a protein called CYP3A4

Also, it was important to find out what unwanted effects might happen if enzalutamide was taken together with the test medicines.

This study for enzalutamide took place at 2 clinics in South Africa between July 2011 and February 2012. 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 was a “drug-drug interaction” study. A drug-drug interaction study is used to determine if a medicine influences how the body breaks down another medicine that is in the body at the same time. For this study, patient blood samples were examined to see if the test medicine(s) is broken down by the body in the same way when it is given together with enzalutamide. The patients were given multiple doses of enzalutamide and:

- A single dose of pioglitazone
- A single dose of the combination of the 3 test medicines (warfarin, omeprazole, and midazolam)

A “washout period” is the time required to make sure all of the test medicine is out of the patient’s body. During this study, a washout period was used between pioglitazone and the combination of the 3 test medicines. The washout period was used to make sure that pioglitazone was out of the patient’s body before the combination of the 3 test medicines was given to the patient.

Only men were allowed to volunteer for this study. They were all over 18 years old. They had confirmed prostate cancer, were taking prescription medications to lower their male blood hormone levels, and their prostate cancer was getting worse. Patients could not take part in this study if any of the following was true:

- They were expected to live for less than 6 months.
- They were known to have a genetic make-up that made them process the test medicines slower than the average person.

The study lasted 104 to 162 days, including:

- 7 to 28 days to determine if the patient met the requirements of the study
- 97 days to do the study
- Possibly 37 more days if the patient’s prostate cancer was getting better and they were enrolled in another study allowing them to continue treatment with enzalutamide

Patients stayed overnight at the clinic when test medicines were given to them and for a certain amount of time afterwards. Patients did not eat for at least 10 hours before they were given the test medicines. On days that the patients were not sleeping at the clinic, a study nurse visited them at home. Blood samples were taken from patients at least once a day until all test medicines were out of their body.

From the 37 patients who volunteered for the study, 14 were enrolled into the study. Thirteen patients completed the study and the doctor decided to stop giving test medicine to 1 patient.

	Number of Patients
Age Group	
Aged 18 years and older	14
Men	14
EU Countries	0
Outside EU	14

What Were the Study Results?

The results of the study were as follows:

- Enzalutamide did not have any effect on how pioglitazone was broken down by the body
- Enzalutamide had a moderate effect on how warfarin was broken down by the body
- Enzalutamide had a moderate effect on how omeprazole was broken down by the body
- Enzalutamide had a strong effect on how midazolam was broken down by the body

Based on the results of this study, there is a better understanding of how enzalutamide, given in combination with other medicines, is broken down by the body. This information will help doctors treat prostate cancer patients who are taking 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 chart below shows the most common adverse reactions experienced by patients while taking part in this study.

Adverse Reactions	Number of patients (out of 14 patients)
Nausea	2
Constipation	2
Feeling tired	3
Feeling dizzy	2
Feeling hot for a brief moment	2

An adverse reaction is considered “serious” when it is life-threatening, causes lasting problems, or needs hospital care. Three patients had serious adverse reactions. One of those patients had convulsions and the study doctor decided to stop giving the patient test medicine.

Where Can I Learn More About This Study?

Astellas may perform additional studies to better understand enzalutamide.

This summary of the clinical study results is available 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. If you have questions about enzalutamide, please discuss these with your doctor.

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