Summary of Results for Laypersons

What was the Study Called?

A Phase 1 Open-label Study to Evaluate the Effect of Multiple Doses of Enzalutamide on the Pharmacokinetics of Substrates for CYP1A2 and CYP2D6 in Male Patients with Prostate Cancer.

Why was this Study Needed?

Enzalutamide is a medicine used to treat patients with prostate cancer. Enzalutamide used to be called MDV3100 and is also known by its brand name Xtandi®. Some medicines or substances 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 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 medicine used to treat patients with prostate cancer.

The 2 test medicines were:

- Caffeine which is known as a CYP1A2 substrate
- Dextromethorphan which is known as a CYP2D6 substrate

Caffeine is commonly found in coffee, tea, and chocolate. Dextromethorphan is a cough suppressant commonly found in over-the-counter cold and cough medicines.

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 1 clinic in Moldova. The study took place between October 2013 and February 2014. 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.

The patients were given the following:

- On day 1, a combination of 100 mg caffeine and 30 mg dextromethorphan was given to patients, followed by a washout period.
- On days 4 – 55, 160 mg enzalutamide was given to patients.
- On day 53, a combination of 100 mg caffeine and 30 mg dextromethorphan was given to patients.

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 to make sure that caffeine and

dextromethorphan were out of the patient's body before enzalutamide was given to the patient.

Patients were enrolled in the study if they met the following criteria:

- Aged 18 years or older.
- Confirmed prostate cancer.

Patients could not take part in this study if they were known to have any of the following:

- Liver or kidney issues.
- A genetic make-up that made them process the test medicines slower than the average person.

The study lasted up to 83 days, including:

- 28 days to determine if the patient met the requirements of the study
- 54 days to do the study

After day 55 and if the patient's prostate cancer was getting better, they were allowed to enroll in another enzalutamide study.

Patients stayed overnight at the clinic when test medicines were given to them and for a certain amount of time afterwards. Blood samples were taken from patients periodically until all test medicines were out of their body.

From the 37 patients who volunteered for the study, 14 were enrolled and received at least 1 dose of study medicine.

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

What Were the Study Results?

The study suggests that caffeine in combination with enzalutamide does not have an effect on CYP1A2. However, it appears that dextromethorphan in combination with enzalutamide may have a weak effect on CYP2D6. The combination of caffeine, dextromethorphan, and enzalutamide was safe and well tolerated.

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. Information from 14 patients who received at least 1 dose of study medicine is included in the table below.

Adverse Reactions	**Substrates Alone (out of 14 patients)**	**Enzalutamide Alone (out of 14 patients)**	**Substrates And Enzalutamide (out of 14 patients)**	**Total Enzalutamide (out of 14 patients)**
Lack of enough red blood cells (Anemia)	0	1	1	2
Fever	0	1	0	1
Increased blood level of a liver enzyme (gamma-glutamyl transferase [GGT])	1	0	0	0

An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or needs hospital care. No patients had serious adverse reactions during the study and no patients died during the study.

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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