

Plain Language Summary of Study Results

Astellas is grateful to the people who took part in this clinical study.

Thank you!

What was the study called?

A study of enzalutamide in people with an advanced type of liver cancer called hepatocellular carcinoma.

Why was the study needed?

Your liver helps your body to digest food and store energy. It also helps remove poisons from the body. Hepatocellular carcinoma (or HCC for short) is the most common type of liver cancer. Advanced liver cancer means the cancer has spread from the liver where it first started to nearby tissue or lymph nodes. There are several treatments which are available for this cancer. They include: liver transplant or destroying cancer cells with heat or cold. Other treatments include x-rays and chemotherapy. These treatments do not work for everyone with HCC. Some people have their cancer come back after one of these anticancer treatments.

Researchers in this study were interested in finding better ways to treat HCC.

In this study, people with advanced HCC took enzalutamide or a placebo. Enzalutamide is approved in many countries for treatment of prostate cancer. The researchers studied enzalutamide as a possible treatment for people with advanced HCC. A placebo is a dummy capsule that looks like enzalutamide but does not have any medicine in it.

The study started in January 2016 and ended in February 2021. This was a 2-part study: the primary period lasted from start of the study until people stopped taking study medicine. The follow up period lasted up to 2 years after study medicine was stopped. The sponsor of this study (Astellas) reviewed all the study information and created reports of the results. This is a summary of those reports.

What were the main questions the study helped answer?

- How many people in each treatment group passed away? How long did they live?
- In this study, what medical problems did people have from taking enzalutamide?

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

This was a double-blinded study in the primary study period. That means that the people with hepatocellular carcinoma (HCC) and the study doctors did not know who took which of the study medicines. This helps make study results fair and unbiased. When the double-blinded period ended, people taking enzalutamide could then enter into an open-label study, if they wanted to do so. That means that the person with HCC and study doctors, knew that person took enzalutamide.

This study was conducted in adults 18 years or older who had confirmed HCC that had advanced. To be in the study a person had to have the following:

- The cancer was confirmed in tissue samples.
- It was advanced to a Barcelona Clinic Liver Cancer Stage B or C. Each stage is a combination of some characteristics of the disease. The last stage before death is D.
- These people were not able to receive other treatments. Or they had failed to improve on other treatments.
- They were able to manage with the liver cancer without requiring extreme treatment, such as liver transplant.
- They were active or they could perform light daily activities. They were expected to live at least 3 months.

The table below shows some information about the people in the study. 165 people were in the study.

	Number of People
Age Group	
65 years of age or less	91
66 years to 75 years of age	48
More than 75 years of age	26
Sex	
Men	144
Women	21

Where did the study take place?

This study took place at 37 clinics in several countries.

	Number of People
Clinic Location	
European Union Countries (<i>at the time of the study</i>)	72
Italy	47
Spain	6
United Kingdom	19
Outside European Union	93
Canada	5
Hong Kong	3
Province of Taiwan	10
Puerto Rico	2
Republic of Korea	59
United States	14

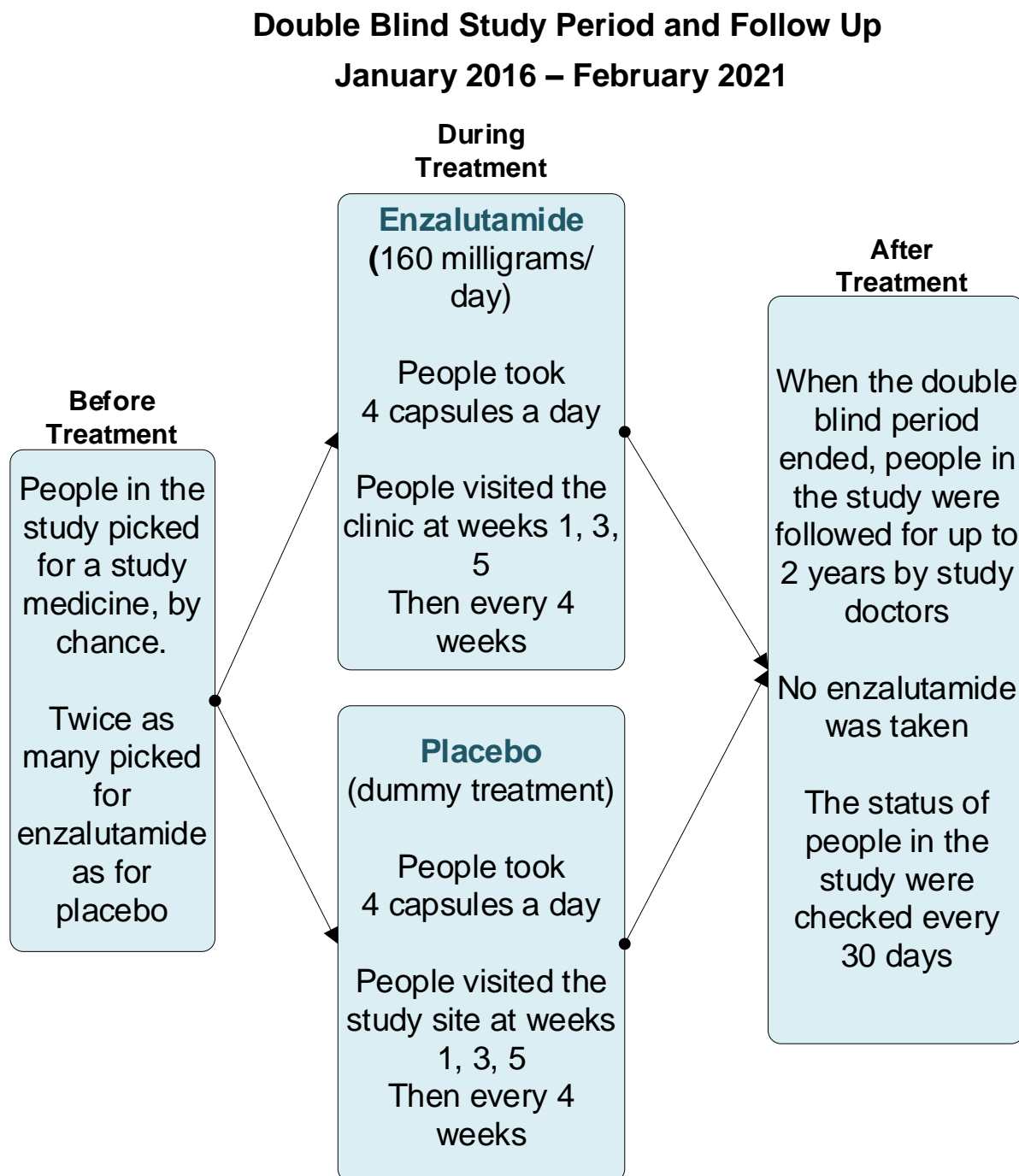
What happened during the study?

During the study, the study doctor did a check-up of the people at several study visits. At the first visit, people were checked to see if they could be in the study. People were picked for either enzalutamide or placebo, by chance. This study had a screening period, primary treatment period, and a follow up period.

People could continue to take their study medicine until: they had medical problems; or their cancer got worse; or the study doctor decided that person should stop treatment; or they asked to stop treatment.

When people stopped taking the study medicine for any reason they continued to be followed for up to 2 years.

The following diagram provides an overview of the study.



After the double blind treatment period ended, the sponsor decided to allow an open-label period. In this period, people who wanted to take enzalutamide could do so. It was optional. Only 1 person entered the open-label period. At a later time that person's disease got worse and they left the study.

What were the study results during the study?

- How many people in each treatment group passed away?

165 people entered the study. 110 were assigned to enzalutamide and 55 were assigned to placebo.

	Enzalutamide Group 110 People	Placebo Group 55 People
How many people passed away during the study?	75 people (68.2%, 75 out of 110 people)	38 people (69.1%, 38 out of 55 people)

- How long did they live?

How long did people live?	About 8 months	About 8 months
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A statistical test showed that the difference between the groups was likely to be due to chance. Enzalutamide did not help people with hepatocellular carcinoma (HCC) live longer.

None of the deaths were judged by the study doctor to be possibly caused by enzalutamide

What adverse reactions did people 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 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.

Out of the 165 people in the study, 162 of them took at least 1 dose or part of a dose of either enzalutamide or placebo.

- 68 people (63.6%, or 68 out of 107 people) who took enzalutamide had adverse reactions in this study.
- 24 people (43.6%, or 24 out of 55 people) who took placebo had adverse reactions in this study.

The table below shows the most common adverse reactions experienced by people in the primary study period.

	Enzalutamide (out of 107 people)	Placebo (out of 55 people)
Fatigue or tiredness	28 (26.2%)	6 (10.9%)
Decreased appetite	14 (13.1%)	5 (9.1%)
Diarrhea	4 (3.7%)	7 (12.7%)
Nausea or the urge to vomit	14 (13.1%)	5 (9.1%)

Did any of the people 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. The number of people in this study with serious adverse reactions was:

- 7 people (6.5%, or 7 out of 107 people) who took enzalutamide had serious adverse reactions in this study.
- 3 people (5.5%, or 3 out of 55 people) who took placebo had serious adverse reactions in this study.

Where can I learn more about this study?

This document is a short summary of the main results from this study.

The full name for the study is: A phase 2, randomized, double-blind, placebo-controlled study to assess the efficacy and safety of enzalutamide in subjects with advanced hepatocellular carcinoma.

You can find this summary and more information about this study at

<https://astellasclinicalstudyresults.com/>

Further information can be found at the following websites:

<https://clinicaltrials.gov/> ClinicalTrials.gov Identifier: NCT02528643

<https://clinicaltrialsregister.eu> EudraCT number: 2014-004283-37

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.

Sponsor contact details:

Astellas Pharma Global Development Inc.
1 Astellas Way
Northbrook, IL 60062
USA