AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Capivasertib

Study Purpose: This study was done to learn about the safety of capivasertib given with existing medicines in men who had prostate cancer that had spread to other parts of the body.

Protocol Number: D3618C00002

Thank you

Thank you for taking part in the clinical study for the study drug capivasertib, also called AZD5363.

AstraZeneca AB sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.

Who took part in this study?

The researchers asked for the help of men with prostate cancer. The participants in this study were 49 to 82 years old when they joined.

The participants had prostate cancer that had spread to other parts of the body and could no longer be treated by lowering the levels of a hormone called "testosterone". When they joined the study, the participants had been treated with at least 1 other type of treatment for prostate cancer

The study included 27 participants. This included 11 participants from Spain and 16 participants from the United States.

Why was the research needed?

Researchers are looking for a better way to treat prostate cancer. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works with existing medicines.

In people with cancer, the body is not able to control the growth of some cells. The extra cells can form tumors and can also spread to other parts of the body.

The study drug, capivasertib, is designed to stop one of the proteins in the body that helps tumors to grow and spread.

What was the purpose of this study?

In this study, the researchers wanted to learn about the safety of capivasertib when given with some of the existing medicines for prostate cancer.

The main questions the researchers wanted to answer in this study were:

- What signs and symptoms did the participants have during the study?
- What medical problems happened during this study?

The answers to these questions are important to know before other studies can be done to find out if capivasertib helps improve the health of men who have prostate cancer that has spread to other parts of the body.

What treatments did the participants take?

In this study, all of the participants took capivasertib and another drug called abiraterone. The participants were already getting treatment for their prostate cancer called "androgen deprivation therapy", also called ADT. Abiraterone is an approved treatment for prostate cancer. All of the participants also took a steroid tablet to reduce the chance of having medical problems caused by abiraterone.

Before the study started, the researchers had planned that some participants would take capivasertib with another approved prostate cancer drug called enzalutamide. This part of the study did not happen because there was a change in the drug development plans.

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was taking.

Study treatment doses were measured in milligrams, also called "mg".

This study had 2 parts. Participants were in either Part 1 or Part 2 of the study. In **Part 1** of the study, the study doctors used the results to help them choose the right dose of capivasertib for the participants of **Part 2** to take. The results showed that the dose used in Part 1 did not cause too many medical problems, so the same dose was used in Part 2 without the need to test other doses of capivasertib.

Each week in both parts of the study, the participants took capivasertib 2 times a day every day for 4 days and then did not take it for 3 days. Abiraterone and steroid tablets were taken every day. The participants carried on taking ADT. The participants took the study treatments in 4-week periods called "cycles". The participants were in the study until their cancer got worse, the study doctors thought they should stop taking study treatment, or they left for another reason.

Because all of the participants took the same doses of capivasertib and abiraterone, their results will be presented together as a single group. The chart below shows the treatments the participants took.

	Parts 1 and 2
	27 participants
	• 800 mg of capivasertib, taken as 200 mg tablets • 1,000 mg of abiraterone, taken as 500 mg tablets • 10 mg of steroid, taken as a single 10 mg tablet
	• 2 capivasertib tablets, 2 times a day • 2 abiraterone tablets, once a day • 1 steroid tablet, once a day, taken with abiraterone

What happened during this study?

The study started in August 2019 and ended in June 2021.

Before the participants took study treatment, they visited their study site within the 28 days before starting study treatment. At this visit, the study doctors made sure the participants could join the study. They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- checked how well the participants were able to do their daily activities
- took blood and urine samples
- took pictures of the participants' tumors using CT or MRI scans
- checked the participants' heart health using an electrocardiogram, also known as an "ECG"
- checked how well the participants' hearts were pumping blood using an echocardiogram, also called an "ECHO" or a multigated acquisition scan, also called a "MUGA" scan

The study doctors also did these tests and measurements throughout the study, although ECHO or MUGA scans were only done if study doctors felt they were necessary.

While the participants took study treatment, they visited their study site up to 4 times in the first cycle, and then 1 time every cycle until they stopped taking study treatment.

When the participants stopped taking study treatment, they visited their study site 1 additional time so the study doctors could check their health.

About 30 days after the participants stopped taking study treatment, they visited their study site 1 time. At these visits, the study doctors checked the health of the participants.

What were the results of this study?

This is a summary of the main results from this study overall. The results each participant had might be different and are not in this summary.

Researchers look at the results of many studies to decide which treatments work best and are safest. Other studies may provide new information or different results. Always talk to a doctor before making any treatment changes.

The websites listed at the end of this summary may have more information about the study results.

What signs and symptoms did the participants have during the study?

To answer this question, the study doctors did tests and measurements before and after the participants took capivasertib. The doctors did physical exams and tested the participants' blood and urine samples to check their overall health.

Overall, the researchers found that there were some small changes in the results of these tests and measurements but, the researchers did not consider these changes to be clinically important.

The study doctors also kept track of the "adverse events" that the participants had.

An adverse event is any sign or symptom that participants have during a study. Doctors keep track of all the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatment.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatment. This section is a summary of all the adverse events, whether they might be related to the study treatment or not. An adverse event is considered "serious" when it is life-threatening, causes lasting problems, or the participant needs hospital care.

Adverse events may or may not be caused by the treatments in the study. A lot of research is needed to know whether a treatment causes an adverse event.

	Parts 1 and 2 (out of 27 participants)
How many participants had adverse events?	100.0% (27)
How many participants had serious adverse events?	37.0% (10)
How many participants stopped taking study treatment due to adverse events?	40.7% (11)

There were 3.7% of participants who died because of adverse events. This was 1 out of 27 participants. This adverse event was not thought to be related to the study drug.

The serious adverse events were:

- Sudden kidney damage
- Diarrhea
- A rash with flat and bumpy parts on the skin
- Adrenal glands not making enough hormones
- Allergic reaction to the study drug
- Fatigue
- Fever
- Fungi or yeasts in the blood
- High blood sugar
- Infection with a type of bacteria called pseudomonas
- Pain in the abdomen
- The tubes in the kidneys stop working properly
- Urinary infection

The most common adverse events were:

- Diarrhea
- Low numbers of red blood cells
- Nausea
- Fatigue
- Feeling weak
- A rash with flat and bumpy parts on the skin
- Decreased appetite
- High blood sugar
- Sudden kidney damage

The study doctors also counted the number of dose limiting toxicities the participants had during the study. A dose limiting toxicity is also known as a "DLT". A DLT is an adverse event that is severe enough to stop the study doctor from giving the participants their study treatment.

None of the participants had a DLT during the study.

What medical problems happened during this study?

This section is a summary of the medical problems the participants had during the study that the study doctors thought might be related to the study drug. These medical problems are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study drug. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for capivasertib.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this study.

Did any adverse reactions happen during this study?

	Parts 1 and 2 (out of 27 participants)
How many participants had adverse reactions?	92.6% (25)
How many participants had serious adverse reactions?	18.5% (5)
How many participants stopped taking study treatment due to adverse reactions?	18.5% (5)

What serious adverse reactions happened during this study?

The table below shows the serious adverse reactions that happened during the study.

Serious adverse reactions	
Serious adverse reaction	**Parts 1 and 2** (out of 27 participants)
Allergic reaction to the study drug	3.7% (1)
Diarrhea	3.7% (1)
Fatigue	3.7% (1)
High blood sugar	3.7% (1)
A rash with flat and bumpy parts on the skin	3.7% (1)
Sudden kidney damage	3.7% (1)
The tubes in the kidneys stop working properly	3.7% (1)

What adverse reactions happened during this study?

The most common adverse reaction was diarrhea.

The table below shows the adverse reactions that happened in 5 or more of participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions	
Adverse reaction	**Parts 1 and 2** (out of 27 participants)
Diarrhea	44.4% (12)
Fatigue	22.2% (6)
Nausea	22.2% (6)
High blood sugar	18.5% (5)
A rash with flat and bumpy parts on the skin	18.5% (5)

How has this study helped patients and researchers?

This study helped researchers learn more about the safety of capivasertib when given with some of the existing medicines in men with prostate cancer that had spread to other parts of the body.

Researchers look at the results of many studies to decide which treatments work best and are safest. This summary shows only the main results from this one study. Other studies may provide new information or different results.

Further clinical studies with capivasertib are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT04087174"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2019-000071-17"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D3618C00002"** into the search box and click **"Find a Study"**.

Full Study Title: A Phase I, Open-label, Multi-centre Study to Assess the Safety, Tolerability, and Pharmacokinetics of Capivasertib (AZD5363) in Combination with Novel Agents in Patients with Metastatic Castration Resistant Prostate Cancer

AstraZeneca AB Protocol Number: D3618C00002

National Clinical Trials Number: NCT04087174

EudraCT Number: 2019-000071-17

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, Sweden.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you

Clinical study participants belong to a large community of people who take part in clinical research around the world. They help researchers answer important health questions and find medical treatments for patients.

CISCRP

The Center for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organization focused on educating and informing the public about clinical research participation. CISCRP is not involved in recruiting participants for clinical studies, nor is it involved in conducting clinical studies.

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