AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Olaparib

Study Title: A study to learn how olaparib works and about its safety in men with metastatic castration-resistant prostate cancer compared with enzalutamide and abiraterone acetate

Thank you!

Thank you for taking part in the clinical study for the study drug olaparib.

You and all of the participants helped researchers learn more about olaparib to help men with metastatic castration-resistant prostate cancer.

AstraZeneca sponsored this study and believes it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. We hope it helps you understand and feel proud of your important role in medical research.

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

Overview

Why was the research needed?

Researchers are looking for a better way to treat metastatic castration-resistant prostate cancer, also called mCRPC. Before a drug can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

What treatments did the participants take?

The participants in this study took either olaparib, enzalutamide, or abiraterone acetate.

What were the results of the study?

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

> **Did olaparib help the participants live longer with their cancer before it got worse?**

Yes. Overall, the researchers found that the participants who took olaparib lived longer with their cancer before it got worse compared with those who took enzalutamide or abiraterone acetate.

> **Did olaparib help the participants' pain and health-related quality of life?**

Yes. Overall, the researchers found that olaparib helped the participants' pain and health-related quality of life compared with enzalutamide or abiraterone acetate.

> **What medical problems did the participants have during the study?**

There were 69.2% of participants who had medical problems that the study doctors thought might be related to the study treatments during the study. The most common medical problem was anemia. More information about the medical problems in this study can be found later in this summary.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

You can find out more information about this study on the websites listed on the last page. When a full report of the study results is available, it can also be found on those websites.

Who took part in the study?

The researchers asked for the help of men with mCRPC. The participants in this study were 47 to 91 years old when they joined.

The participants all had specific changes in the genetic code of their tumors. This means the genetic code of the tumor had changed from its original structure. The participants had tried a type of cancer treatment called a "new hormonal agent", but their cancer had still gotten worse.

The study included 387 participants in Argentina, Australia, Austria, Brazil, Canada, Denmark, France, Germany, Israel, Italy, Japan, the Netherlands, Norway, South Korea, Spain, Sweden, Taiwan, Turkey, the United Kingdom, and the United States.

Why was the research needed?

Researchers are looking for a better way to treat mCRPC. 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.

In this study, the researchers wanted to find out if olaparib works in a large number of participants with mCRPC. They also wanted to find out if the participants had any medical problems during the study.

In people with cancer, the body is not able to control the growth of cells. The extra cells can form tumors in the body's organs, such as the prostate. "Metastatic" means the cancer has spread to other parts of the body.

There are only a few available treatments for mCRPC, and these may not work for all patients. The study drug, olaparib, was designed to make it harder for tumor cells to grow and survive. In this study, the researchers wanted to compare olaparib to the mCRPC treatments enzalutamide and abiraterone acetate.

What was the purpose of this study?

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

- Did olaparib help the participants live longer with their cancer before it got worse?
- Did olaparib help the participants' pain and health-related quality of life?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if olaparib helps improve the health of people with mCRPC.

What treatments did the participants take?

In this study, the participants took either olaparib, enzalutamide, or abiraterone acetate. Enzalutamide and abiraterone acetate are each a type of treatment called a "new hormonal agent", also known as an NHA. Both of these treatments are already available for the treatment of mCRPC.

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

A computer program was used to randomly choose if the participants took olaparib or 1 of the NHA treatments. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible. For the participants who took 1 of the NHA treatments, the study doctors decided if each participant took enzalutamide or abiraterone acetate.

Each of the study treatments was taken as a tablet by mouth. The doses were measured in milligrams, also known as mg.

The participants who took abiraterone acetate also took the steroid prednisone or the steroid prednisolone.

The participants took the study treatments until their cancer got worse, they stopped taking the study treatment for other reasons, or they left the study.

The chart below shows the treatments the participants took.

	Olaparib (256 participants)	**NHA treatment** (131 participants)	
		Enzalutamide	**Abiraterone acetate**
Dose	• 300 mg • Twice a day	• 160 mg • Once a day	• 1,000 mg • Once a day **and** • 5 mg prednisone or prednisolone • Twice a day

What happened during the study?

The participants were in the study for up to 24 months. But, the entire study took 28 months to finish. The study started in February 2017 and the researchers stopped collecting information in June 2019 for the results presented here.

The chart below shows what happened during the study.

Before the participants took study treatment

2 visits

At these visits, the study doctors:

- checked the health of the participants to make sure they could join the study
- took blood and urine samples
- did a physical examination and asked about the participants' medications and any medical problems
- checked the participants' heart health using an electrocardiogram, also called an ECG
- asked the participants to complete a questionnaire and pain medication log
- took a tumor sample using surgery, also called a "biopsy"

Up to 4 weeks

While the participants took study treatment

Visits once every 4 weeks until week 24, then visits every 8 weeks

At some of the visits, the study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- asked the participants to complete questionnaires and a pain medication log
- took blood and urine samples
- checked the participants' ability to do their daily activities
- did an ECG to check the participants' heart health

The participants:

- did a bone scan and an MRI or CT scan to check the participants' tumors
- took daily doses of either olaparib or the NHA treatments

Up to 23 months

After the participants stopped taking study treatment

2 visits

At these visits, the study doctors:

- asked about the participants' medications, any medical problems and any additional cancer treatment
- did a bone scan and an MRI or CT scan to check the participants' tumors
- took blood samples
- asked the participants to complete questionnaires and a pain medication log
- checked the participants' ability to do their daily activities

30 days

Then, if the participants stopped taking study treatment because their cancer got worse, they continued having visits every 12 weeks. If they stopped taking study treatment for other reasons, they had visits every 8 weeks.

What were the results of the 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. A full list of the questions the researchers wanted to answer can be found on the websites listed at the end of this summary. When a full report of the study results is available, it can also be found on these websites.

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. This summary is only for your information. Please talk to your doctor if you need any medical advice.

In this study, the researchers wanted to learn how the study treatments affected tumors with specific changes in the genetic code. These changes were in the following genes:

- Breast cancer type 1, also known as BRCA1
- Breast cancer type 2, also known as BRCA2
- Ataxia telangiectasia mutated, also known as ATM

So, the results below include information for the 245 participants who had cancers with these genetic changes.

Did olaparib help the participants live longer with their cancer before it got worse?

Yes. Overall, the researchers found that the participants who took olaparib lived longer with their cancer before it got worse compared with the participants who took the NHA treatments.

To answer this question, the researchers took pictures of the participants' tumors using MRI or CT scans. To measure tumor growth, they used a set of rules called Response Evaluation Criteria in Solid Tumors, also known as RECIST. Then, the researchers counted the number of months between the participants taking study treatment and their cancer spreading or growing. They compared these results in the participants who took olaparib and in those who took the NHA treatments.

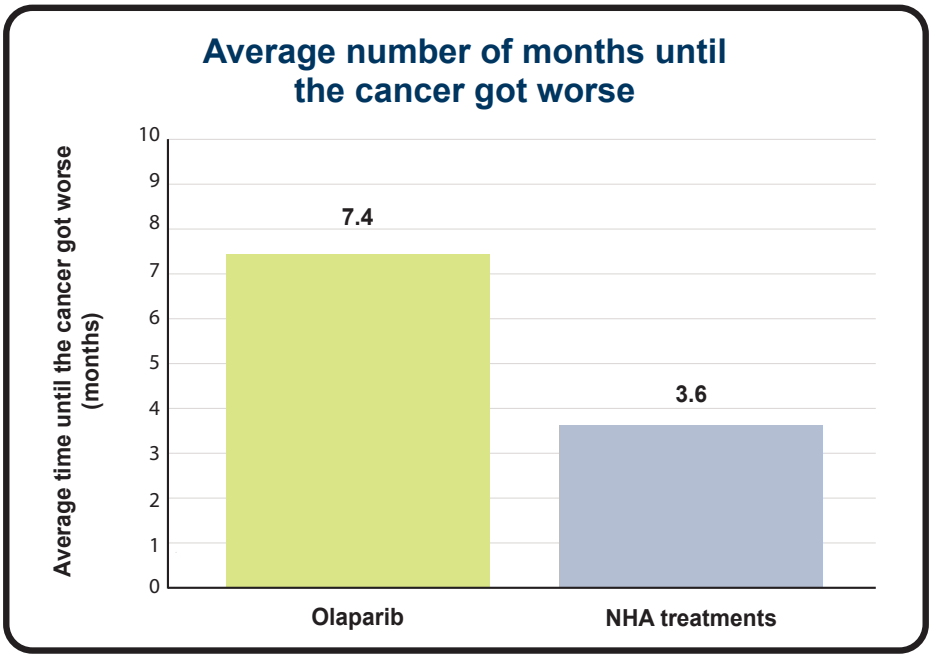
Overall, the researchers found that the average number of months until the participants' cancer got worse was:

- 7.4 months for the participants who took olaparib
- 3.6 months for the participants who took the NHA treatments

The researchers calculated the risk of the participants' cancer getting worse after starting study treatment. They compared the risk between the participants who took olaparib and those who took the NHA treatments.

The participants who took olaparib had a 66% reduced risk of their cancer getting worse compared with the participants who took the NHA treatments.

The graph below shows the average number of months until the participants' cancer got worse.



Did olaparib help the participants' pain and health-related quality of life?

Yes. Overall, the researchers found that olaparib helped the participants' pain and health-related quality of life compared with the participants who took the NHA treatments.

Pain

The researchers found that 12 months after starting study treatment, fewer participants had their pain get worse in the group that took olaparib than in the group that took the NHA treatments.

To answer this question, the study doctors asked the participants to complete a questionnaire called "Brief Pain Inventory - Short Form", also known as BPI-SF. In this questionnaire, the participants had to rate their pain on a scale from 1 to 10.

The study doctors also counted the number of participants who had to use strong painkillers to help their pain. The researchers calculated the percentage of the participants who did not have their pain get worse 12 months after starting study treatment. They compared the results in the participants who took olaparib and in those who took the NHA treatments.

Overall, the researchers found that the average percentage of participants who did not have their pain get worse 12 months after starting study treatment was:

- 76.5% for the participants who took olaparib
- 43.1% for the participants who took the NHA treatments

The researchers calculated the risk of the participants' pain getting worse after starting study treatment. They compared the risk between the participants who took olaparib and those who took the NHA treatments.

The participants who took olaparib had a 56% reduced risk of their pain getting worse compared with the participants who took the NHA treatments.

Health-related quality of life

Overall, the researchers found that the participants who took olaparib reported that it helped their health-related quality of life compared with the NHA treatments.

To answer this question, the study doctors asked the participants to complete a questionnaire called the "Functional Assessment of Cancer Therapy – Prostate", also known as FACT-P. Based on the participants' responses in this questionnaire, the study doctors calculated a FACT-P score for each participant. The researchers calculated the average change in this score throughout the study. They compared these results in the participants who took olaparib and in those who took the NHA treatments. A smaller change in the FACT-P score meant that the participants' health-related quality of life was better.

The researchers found that the average change in the FACT-P score was a:

- 6.2 point decrease for the participants who took olaparib
- 12.4 point decrease for the participants who took the NHA treatments

What medical problems happened during the 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 treatments. 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 treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for the study treatments.

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.

There was 1 participant in the NHA treatment group who did not take any study treatment. So, the results below are for 386 out of 387 participants.

Did any adverse reactions happen during this study?

	Olaparib (out of 256 participants)	NHA treatments (out of 130 participants)
How many participants had adverse reactions?	80.5% (206)	46.9% (61)
How many participants had serious adverse reactions?	13.7% (35)	3.8% (5)
How many participants stopped taking study treatment due to adverse reactions?	12.5% (32)	4.6% (6)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was anemia.

The table below shows the serious adverse reactions that happened in more than 1 participant during the study. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions

Serious adverse reaction	Olaparib (out of 256 participants)	NHA treatments (out of 130 participants)
Anemia	6.3% (16)	0.0% (0)
Decreased numbers of a type of white blood cell called neutrophils	1.2% (3)	0.0% (0)
Decreased numbers of blood cells that help form blood clots	1.2% (3)	0.0% (0)
Vomiting	1.2% (3)	0.0% (0)
Lung infection	0.8% (2)	0.0% (0)
Blood clot in the lungs	0.8% (2)	0.0% (0)
General weakness	0.4% (1)	0.8% (1)

There were 0.5% of participants who died because of serious adverse reactions. This was 2 out of 386 participants.

- 0.4% of participants who took olaparib died because of serious adverse reactions. This was 1 out of 256 participants.
- 0.8% of participants who took 1 of the NHA treatments died because of serious adverse reactions. This was 1 out of 130 participants.
- Both of these deaths were because of lung problems.

What adverse reactions happened during this study?

The most common adverse reaction was anemia.

The table below shows the adverse reactions that happened in 10 or more participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Olaparib (out of 256 participants)	NHA treatments (out of 130 participants)
Anemia	37.1% (95)	2.3% (3)
Nausea	35.2% (90)	9.2% (12)
Decreased appetite	22.3% (57)	6.2% (8)
Fatigue	21.5% (55)	11.5% (15)
Diarrhea	13.7% (35)	1.5% (2)
General weakness	10.9% (28)	7.7% (10)
Vomiting	10.5% (27)	3.1% (4)
Decreased numbers of blood cells that help form blood clots	6.3% (16)	0.0% (0)
Altered sense of taste	5.5% (14)	1.5% (2)
Decreased numbers of a type of white blood cell called neutrophils	5.1% (13)	0.0% (0)
Constipation	4.3% (11)	1.5% (2)
Acid reflux	4.3% (11)	0.0% (0)
Inflammation of the mouth and lips	4.3% (11)	0.0% (0)
Decreased weight	3.9% (10)	1.5% (2)
Breathlessness	3.1% (8)	1.5% (2)
Swelling in the arms and legs	2.3% (6)	3.1% (4)

How has this study helped patients and researchers?

This study helped researchers learn more about olaparib for people with metastatic castration-resistant prostate cancer.

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 olaparib 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 **"NCT02987543"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search",** then type **"2016-000300-28"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D081DC00007"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase III, Open Label, Randomized Study to Assess the Efficacy and Safety of Olaparib (Lynparza™) Versus Enzalutamide or Abiraterone Acetate in Men with Metastatic Castration-Resistant Prostate Cancer Who Have Failed Prior Treatment with a New Hormonal Agent and Have Homologous Recombination Repair Gene Mutations (PROfound)

AstraZeneca Protocol Number: D081DC00007

National Clinical Trials number: NCT02987543

EudraCT number: 2016-000300-28

AstraZeneca sponsored this study and has its headquarters in Cambridge, UK.

The phone number for the AstraZeneca Information Center is +1-877-240-9479 and the email is information.center@astrazeneca.com.

Thank you!

Clinical study participants and their families 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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