AstraZeneca

Clinical Trial Results

Research Sponsor: AstraZeneca

Drug Studied: Olaparib

Study Purpose: This trial was done to learn about the safety of olaparib and how it works in participants with advanced breast cancer.

Protocol Number: D0816C00018

Thank you

Thank you to the participants who took part in the clinical trial for the trial drug olaparib, also called AZD2281.

All of the participants helped researchers learn more about olaparib to help people with advanced breast cancer.

AstraZeneca sponsored this trial and believes it is important to share the results of this trial with the participants and the public. AstraZeneca reviewed the results of this trial when it ended and created a report of those results. This is a summary of that report.

An independent non-profit organization called CISCRP helped prepare this summary of the trial results. We hope it helps the participants understand and feel proud of their important role in medical research.

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

Overview of this trial

Why was the research needed?.....Page 3

Researchers are looking for a better way to treat advanced breast cancer. Before a drug can be approved for people to take, researchers do clinical trials to find out how it works and how safe it is.

What treatments did the participants take? .....Page 5

The participants in this trial took olaparib.

What were the results of this trial? .....Page 7

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

- **How long did the participants live without their cancer becoming worse after they started taking olaparib?**

  Overall, the participants lived for **8.2 months** without their cancer becoming worse after taking olaparib.

- **How long did the participants live after they started taking olaparib?**

  Overall, the participants lived for **24.9 months** after taking olaparib.

What medical problems did the doctors report as possibly related to the trial treatment? .....Page 8

There were **85.1%** of participants who had medical problems that the trial doctors reported as possibly being related to the trial drug. This was 217 out of 255 participants.

More details about the medical problems from this trial are included later in this summary.

Where can I learn more about this trial? .....Page 12

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

Who took part in this trial?

The researchers asked for the help of people with advanced breast cancer. The participants in this trial were 22 to 75 years old when they joined.

All of the participants had a change in either of 2 genes called "BRCA1" or "BRCA2". The participants' cancer was also classified as "HER2-ve". More details about this specific type of breast cancer can be found in the **"Why was this research needed?"** section.

Participants had also previously received either of 2 specific chemotherapy drugs called anthracycline and taxane, and their cancer had gotten worse after treatment with either of these 2 chemotherapy drugs.

This trial included 4 males and 251 females in 15 countries:

Country	Number of participants	Country	Number of participants
Bulgaria	7	Republic of Korea	16
Canada	13	Russian Federation	20
France	52	Spain	26
Germany	15	Taiwan	1
Hungary	2	Turkey	21
Italy	43	United Kingdom	24
Japan	2	United States	2
Poland	11		

Why was the research needed?

Researchers are looking for a better way to treat advanced breast cancer. Before a drug can be approved for people to take, researchers do clinical trials to find out how it works and how safe it is.

In people with breast cancer, the body is not able to control the growth of cancer cells in the breast. These cancer cells can form tumors in the breast and can also spread to other parts of the body. When breast cancer spreads to other parts of the body, this is called "metastatic" breast cancer, or "advanced" breast cancer.

There are many different types of breast cancer. Breast cancers with high levels of a protein called HER2 are called "HER2-positive". In HER2-positive cancer, HER2 causes the cancer cells to grow quickly. Breast cancers with normal levels of HER2 are called "HER2-ve". Drugs have been designed to treat HER2-positive breast cancer, but researchers are looking for better ways to treat HER2-ve breast cancer.

Tumor cells are normally able to fix their own DNA when it gets damaged, which lets them stay alive and grow. The trial drug, olaparib, was designed to kill tumor cells by stopping them from fixing their damaged DNA. Other trials have shown that olaparib worked well for the trial participants who had advanced HER2-ve breast cancer and changes in either the BRCA1 or BRCA2 gene. A change in a gene is also called a "mutation".

In this trial, the researchers wanted to find out more about how olaparib works and how safe it is.

What was the purpose of this trial?

This was a "Phase 3" trial. In this trial, the researchers wanted to find out if olaparib worked in a large number of participants with advanced breast cancer. They also wanted to find out if the participants had any medical problems during the trial.

The main questions researchers wanted to answer in this trial were:

- How long did the participants live without their cancer becoming worse after they started taking olaparib?
- How long did the participants live after they started taking olaparib?
- What medical problems did the doctors report as possibly related to the trial treatment?

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

What treatments did the participants take?

The participants in this trial took olaparib. The standard dose of olaparib was measured in milligrams, also called "mg".

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

The chart below shows the treatment plan for the participants.

	255 participants
	300 mg of olaparib
	Tablets taken by mouth
	Twice a day for as long as the trial doctor thought it was helping the participants, or until they left the trial

What happened during this trial?

The participants were in the trial until the trial doctors decided that olaparib was no longer helping them, or until they left the trial.

The trial started in January 2018 and the researchers stopped collecting results in October 2021.

The chart below shows what happened during the trial.

Before the participants took trial treatment

2 visits

The trial doctors:

- checked the health of the participants to make sure they could join the trial
- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- took pictures of some of the participants' tumors using MRI or CT scans
- used surgery to take a sample of some of the participants' tumors

Up to 1 month

While the participants took trial treatment

1 visit every 4 weeks up to week 12,
then 1 visit every 6 weeks up to week 48,
then 1 visit every 12 weeks

The trial doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood samples
- checked to see if the cancer had gotten better or gotten worse
- took pictures of some of the participants' tumors using MRI or CT scans

The participants:

- took their trial treatment

Until the cancer got worse, or they left the trial for another reason

After the participants took trial treatment

1 or more visits

The trial doctors:

- asked about the participants' medical problems
- took blood samples

The participants:

- began taking new cancer treatments if necessary
- took their trial treatment

Until the end of the trial

What were the results of this trial?

This is a summary of the main results from this trial overall. The individual results of each participant might be different and are not in this summary. A full list of the questions that researchers wanted to answer can be found on the websites listed at the end of this summary. When a full report of the trial results is available, it can also be found on these websites.

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

For the 2 main questions below, the researchers only looked at participants who were **born with** BRCA1 or BRCA2 mutations. There were only 3 participants whose BRCA1 or BRCA2 mutations happened later in life, so their results are not included. So, the results below are for 252 of 255 participants.

How long did the participants live without their cancer becoming worse after they started taking olaparib?

The researchers found that the participants lived for a median of **8.2 months** without their cancer becoming worse after taking olaparib.

To find this out, the researchers counted the number of months each participant lived without their cancer becoming worse, and then calculated the median number of months for all participants. The "median" is the middle number in a group of numbers when ordered from lowest to highest.

How long did the participants live after they started taking olaparib?

The researchers found that the participants lived for a median of **24.9 months** after taking olaparib.

To determine this, the researchers counted the number of months each participant lived after taking olaparib, and then calculated the median number of months for all participants.

What medical problems did the doctors report as possibly related to the trial treatment?

This section is a summary of the medical problems that the participants had during this trial that the doctors reported as **possibly related** to the trial 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. The results from several trials are needed to decide if a treatment causes an adverse reaction.

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

Did any adverse reactions happen during this trial?

There were 85.1% of participants who had adverse reactions in this trial. This was 217 out of 255 participants.

	Olaparib (out of 255 participants)
How many participants had serious adverse reactions?	3.9% (10)
How many participants had adverse reactions?	85.1% (217)
How many participants stopped taking olaparib due to adverse reactions?	4.3% (11)

What serious adverse reactions happened during this trial?

The most common serious adverse reaction was **low levels of red blood cells, also called anemia**.

Serious adverse reaction	Olaparib (out of 255 participants)
Low levels of red blood cells, also called anemia	2.4% (6)
A fever and low levels of neutrophils, a type of white blood cell, also called febrile neutropenia	0.4% (1)
A type of cancer caused by poorly developed blood cells, also called myelodysplastic syndrome	0.4% (1)
A condition where fluid collects around the heart, also called pericardial effusion	0.4% (1)
Inflammation around the lungs, also called pleurisy	0.4% (1)

None of the participants died during this trial because of serious adverse reactions.

What adverse reactions happened during this trial?

The most common adverse reaction was **nausea**.

The adverse reactions below happened in 10 or more participants. There were other adverse reactions, but each of these happened in fewer participants.

Adverse reaction	Olaparib (out of 255 participants)
Nausea	47.8% (122)
Low levels of red blood cells, also called anemia	34.5% (88)
Physical weakness or low energy, also called asthenia	20.8% (53)
Fatigue	18.0% (46)
Vomiting	17.6% (45)
Low levels of neutrophils, a type of white blood cell, also called neutropenia	15.3% (39)
Diarrhea	11.0% (28)
Low levels of white blood cells, also called leukopenia	7.8% (20)
Headache	7.5% (19)
Decreased appetite	7.1% (18)
Indigestion, also called dyspepsia	7.1% (18)
Having a changed sense of taste, also called dysgeusia	5.5% (14)
Dizziness	4.7% (12)
Disorder that affects taste	4.3% (11)
Upper belly pain	4.3% (11)
Decreased levels of neutrophils, a type of white blood cell	4.3% (11)

What did researchers learn from this trial?

This trial helped researchers learn more about how olaparib affects people with advanced breast cancer.

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

At the time this summary was made and approved by the sponsor, further clinical trials with olaparib were ongoing.

Where can I learn more about this trial?

You can find more information about this trial on the websites listed below. When a full report of the trial results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03286842"** into the **"Other terms"** search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-001054-34"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D0816C00018"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase IIIb, Single-arm, Open-label Multicentre Study of Olaparib Monotherapy in the Treatment of HER2-ve Metastatic Breast Cancer Patients with Germline or Somatic BRCA1/2 Mutations

AstraZeneca Protocol Number: D0816C00018

National Clinical Trials Number: NCT03286842

EudraCT Number: 2017-001054-34

AstraZeneca sponsored this trial and has its headquarters in Cambridge, United Kingdom.

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

Thank you

Clinical trial 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 trials, nor is it involved in conducting clinical trials.

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