AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Olaparib

Study Purpose: This study was done to learn how well olaparib works in people with advanced ovarian cancer who had received chemotherapy that had worked partly or completely

Protocol Number: D0816L00003

Thank you

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

The participants helped researchers learn more about olaparib to help people with ovarian cancer who had previously received chemotherapy. The participants had completely or partly responded to chemotherapy treatment.

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 of this study

Why was the research needed?

Researchers are looking for a way to stop ovarian cancer from getting worse or coming back after it has been treated with chemotherapy. Before a drug can be approved for people to take, researchers do clinical studies to find out how well it works and how safe it is.

What treatment did the participants take?

271 of the 272 participants in this study took olaparib after having at least 1 round of chemotherapy.

What were the results of this study?

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

- **When the participants took olaparib, how many had a treatment response?**

  Overall, the researchers found that 37.4% of the participants had a treatment response during the study. This was 101 out of 270 participants.

- **What medical problems happened during the study?**

  There were 93.0% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. This was 252 out of the 271 participants who took olaparib. The most common medical problem was nausea.

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

Who took part in this study?

The researchers asked for the help of people with ovarian cancer. The participants in this study were 35 to 91 years old when they joined.

Most of the participants had already received a type of cancer treatment known as "platinum-based" chemotherapy that had shrunk their ovarian cancer completely or partly.

The study included 272 participants in Canada and the United States.

Why was the research needed?

Researchers are looking for a way to stop ovarian cancer from getting worse or coming back after it has been treated with chemotherapy. Before a drug can be approved for people to take, researchers do clinical studies to find out how well it works and how safe it is.

In this study, the researchers wanted to find out how well olaparib worked in a small number of participants with ovarian cancer. In people with cancer, the body is not able to control the growth of cells. These cells can form tumors. In people with ovarian cancer, tumors typically form in the ovaries, or they may form in other nearby places, such as:

- the lining of the inside of the abdomen
- the lining of the uterus
- the fallopian tubes that connect the ovaries to the uterus

In adults with ovarian cancer, it is rare for tumors to form outside of the ovaries.

The study drug, olaparib, was designed to help stop tumor cells from repairing themselves when they are damaged. This makes it harder for tumor cells to grow and survive.

In this study, the researchers wanted to find out if olaparib helped stop the participants' cancer from coming back or getting worse after it had been treated with chemotherapy. They also wanted to find out if the participants had any medical problems during the study.

What was the purpose of this study?

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

- When the participants took olaparib, how many had a treatment response?
- 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 ovarian cancer.

What treatments did the participants take?

In this study, all of the participants took olaparib.

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

The participants took olaparib as tablets by mouth. The dose of olaparib was measured in milligrams, also known as "mg". The study doctors could reduce the dose of olaparib for participants if they had any medical problems during the study. The participants took olaparib until their cancer got worse or came back, until the study doctors thought they should stop study treatment, or until they left the study for another reason.

The chart below shows the treatment the researchers planned to study.

	272 participants
	600 mg total of olaparib a day, as 2 tablets twice daily by mouth
	Olaparib twice a day until their cancer got worse or came back, until the study doctors thought they should stop study treatment, or until they left the study for another reason

What happened during this study?

The study started in December 2016 and ended in December 2020. This summary includes the study results as of August 2019.

Before the participants took study treatment, the study doctors did genetic tests on their blood samples and tumor samples. This was done to find out if the participants had mutations in common cancer genes called "BRCA1" and "BRCA2". The BRCA mutations that were found in the blood samples could be inherited mutations, also called "germline" mutations. Or they could be mutations in their tumor cells, also called "somatic" mutations or "acquired" mutations.

The study doctors also tested the tumor samples to see if the cancer cells had gene mutations that make it difficult for the cells to repair themselves when they are damaged. This reduced ability is also called homologous recombination deficiency also known as "HRD".

Based on the results of these tests, the participants were placed into 1 of the following 5 groups:

- **Group 1:** Participants with an **inherited mutation** in their BRCA1 or BRCA2 genes
- **Group 2:** Participants with an **acquired mutation** in their tumor BRCA1 or BRCA2 genes, and normal inherited BRCA1 and BRCA2 genes
- **Group 3:** Participants **with tumor-cell HRD** and normal BRCA1 and BRCA2 genes
- **Group 4:** Participants **without tumor-cell HRD** and with normal BRCA1 and BRCA2 genes
- **Group 5:** Participants with missing or unavailable information on their tumor-cell HRD and/or BRCA gene mutations

The participants were in the study until one of the following happened:

- the participant chose to stop taking part
- the participant died
- the study team could not contact the participant

The chart below shows what happened during the study.

Before the participants took study treatment

1 visit

The study doctors:

- checked the health of the participants to make sure they could join the study
- tested for the type of mutation in the participants' ovarian cancer
- did a physical exam and asked about the participants' medications and any medical problems
- took pictures of the participants' tumors using CT or MRI scans
- took blood and urine samples
- if needed, used surgery to take a sample of the tumor, also known as a biopsy

Up to 4 weeks

While the participants took study treatment

Visits about every 4 weeks for the first 12 months, then visits every 12 weeks

The study doctors:

- asked about the participants' medications and any medical problems, until the participants stopped study treatment
- took blood and urine samples
- took pictures of the participants' tumors using CT or MRI scans every 8 weeks. This was until the participants' cancer got worse

The participants:

- took their doses of olaparib as tablets by mouth twice a day at home

Until the participants' cancer got worse

1 week after the participants took their last dose of study treatment

1 visit

The study doctors:

- asked about the participants' medications and any medical problems
- took blood and urine samples

4 weeks after the participants took their last dose of study treatment

1 visit

The study doctors:

- asked about the participants' medications and any medical problems
- took blood and urine samples

Then, participants were contacted every 12 weeks until they died or until the study ended

What were the results of this study?

This is a summary of the main results from this study overall as of August 2019. The results each participant had 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 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.

There were 270 participants who took olaparib and had their cancer measured at the start of the study. So, the results below include only 270 of the 272 participants.

When the participants took olaparib, how many had a treatment response?

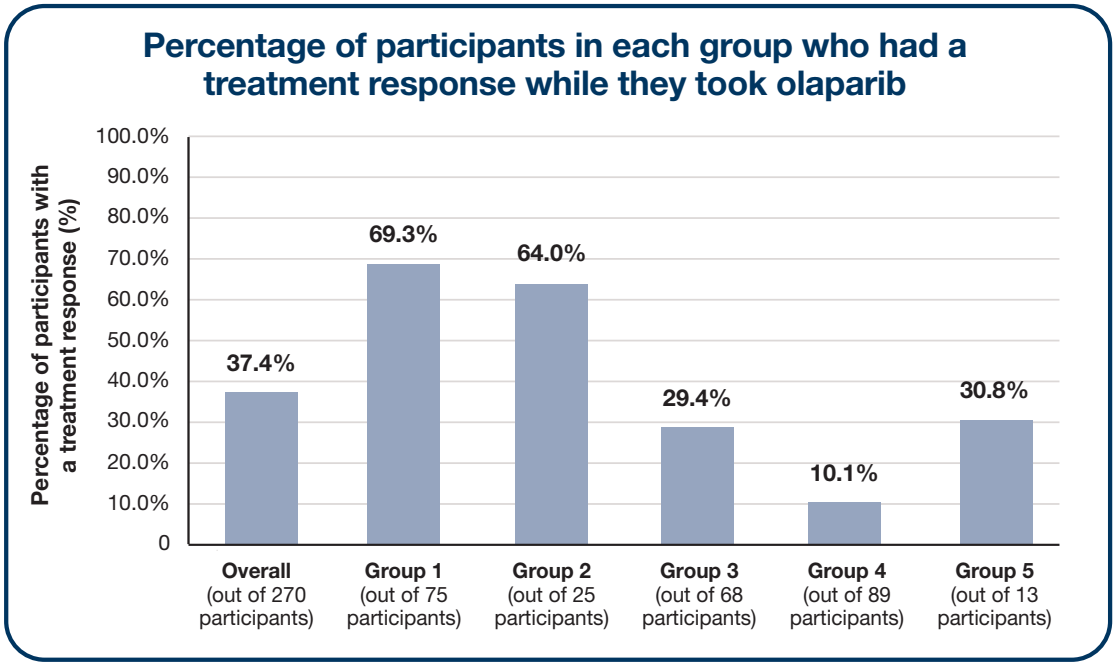
To answer this question, the study doctors took pictures of the participants' tumors using MRI or CT scans. To measure tumor growth, they used a set of rules called Response Evaluation Criteria in Solid Tumors, also known as "RECIST". Then, the researchers calculated how many of the participants had their tumors shrink partly or completely. This is also known as a complete or partial response.

Overall, the researchers found that 37.4% of the participants had a treatment response while taking olaparib. This was 101 out of 270 participants.

The number of participants who had a treatment response in the different groups was as follows:

- 69.3% of participants in Group 1. This was 52 out of 75 participants.
- 64.0% of participants in Group 2. This was 16 out of 25 participants.
- 29.4% of participants in Group 3. This was 20 out of 68 participants.
- 10.1% of participants in Group 4. This was 9 out of 89 participants.
- 30.8% of participants in Group 5. This was 4 out of 13 participants.

The graph below shows these results.



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 olaparib. 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 olaparib. 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 olaparib.

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 who did not take the study drug, so the results below include only 271 of the 272 participants.

Did any adverse reactions happen during this study?

	Olaparib (out of 271 participants)
How many participants had adverse reactions?	93.0% (252)
How many participants had serious adverse reactions?	7.4% (20)
How many participants stopped taking olaparib due to adverse reactions?	3.3% (9)

What serious adverse reactions happened during this study?

The most common serious adverse reaction was low levels of iron in the blood.

The table below shows the serious adverse reactions that happened during the study. None of the participants died because of serious adverse reactions.

Serious adverse reactions

Serious adverse reaction	Olaparib (out of 271 participants)
Low levels of iron in the blood	1.1% (3)
Inflammation in the lungs	0.7% (2)
Pain in the abdomen	0.7% (2)
Blockage of the intestine	0.4% (1)
Clot in a large vein that carries blood to the heart from other areas of the body	0.4% (1)
Clot in a blood vessel in the lungs	0.4% (1)
Diarrhea	0.4% (1)
Dizziness	0.4% (1)
Hole in the upper part of the small intestine	0.4% (1)
Headache	0.4% (1)
Infection in the lungs	0.4% (1)
Large red blood cells and not enough normal red blood cells	0.4% (1)
Long-term kidney disease	0.4% (1)
Low levels in the blood of platelets, which are cells that help blood to clot	0.4% (1)
Muscle weakness	0.4% (1)
Nausea	0.4% (1)
Redness of the navel	0.4% (1)
Scarring of the lungs	0.4% (1)
Vomiting	0.4% (1)

What adverse reactions happened during this study?

There were 93.0% of participants who had medical problems that the study doctors thought might be related to the study drug during the study. This was 252 out of 271 participants. The most common adverse reaction was nausea.

The table below shows the adverse reactions that happened in 5.0% or more of participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Olaparib (out of 271 participants)
Nausea	60.5% (164)
Fatigue	53.9% (146)
Low levels of iron in the blood	23.6% (64)
Vomiting	23.6% (64)
Decreased appetite	17.0% (46)
Sense of taste change	14.0% (38)
Diarrhea	12.9% (35)
Headache	11.8% (32)
Increased levels in the blood of a substance called "creatinine", which helps show how well the kidneys are working	11.8% (32)
Indigestion	10.0% (27)
Dizziness	8.5% (23)
Constipation	7.7% (21)
Cough	7.0% (19)
Stomach acid flowing back into the tube connecting the mouth and stomach	6.3% (17)
Loss of hair	5.9% (16)
Shortness of breath	5.9% (16)

How has this study helped patients and researchers?

The results of this study so far have helped researchers learn more about olaparib for people with ovarian cancer that had responded to treatment completely or partly.

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 or ongoing.

Where can I learn more about this study?

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

- www.clinicaltrials.gov. Once you are on the website, type **"NCT02983799"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D0816L00003"** into the search box, and click **"Find a Study"**.

Full Study Title: Non-Randomized, Open-Label Phase II Study to Assess Olaparib Tablets as a Treatment for Subjects with Different HRD Tumor Status and with Platinum-Sensitive, Relapsed, High-Grade Serous or High-Grade Endometrioid Ovarian, Fallopian Tube, or Primary Peritoneal Cancer That Have Received at Least 1 Prior Line of Chemotherapy (LIGHT Study)

AstraZeneca Protocol Number: D0816L00003

National Clinical Trials Number: NCT02983799

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

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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

Version 1.0 2021_12_09