AstraZeneca

# Clinical Study Results

**Research Sponsor:** AstraZeneca

**Drugs studied:** Durvalumab and olaparib

**Study Purpose:** This study was done to learn how well durvalumab and olaparib work together in people with advanced bladder cancer

**Protocol Number:** D933IC00003

## Thank you

Thank you for taking part in the clinical study for the study drugs durvalumab and olaparib.

You and all of the participants helped researchers learn more about durvalumab and olaparib to help people with advanced bladder cancer that can no longer be removed by surgery, also known as unresectable stage 4 urothelial 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 of this study

## Why was the research needed?

Researchers are looking for a better way to treat advanced bladder cancer that can no longer be removed by surgery. Before a treatment can be approved for people to get, researchers do clinical studies to find out how well it works and how safe it is.

## What treatments did the participants get?

The participants in this study got either durvalumab and olaparib, or durvalumab and a placebo. A placebo looks like a treatment but does not have any medicine in it.

## What were the results of this study?

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

- **Did durvalumab and olaparib together help the participants live longer with their cancer before it got worse?**

  No. The researchers compared the results for the participants who got durvalumab and olaparib with the results for those who got durvalumab and the placebo. Overall, the researchers found that the participants who got durvalumab and olaparib did not live longer with their cancer before it got worse, compared to the participants who got durvalumab and the placebo.

- **Did the participants feel that getting durvalumab and olaparib together helped with their symptoms and quality of life?**

  The researchers compared the results for the participants who got durvalumab and olaparib with the results for those who got durvalumab and the placebo. Overall, the researchers found that there were no meaningful differences in the symptoms and quality of life between the participants who got durvalumab and olaparib and the participants who got durvalumab and the placebo.

- **What medical problems did the participants have during this study?**

  There were 66.4% 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 having low levels of red blood cells, also called anemia.

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 these websites.

## Who took part in this study?

The researchers asked for the help of men and women with advanced bladder cancer that could no longer be removed by surgery. The participants in this study were 45 to 89 years old when they joined. All of the participants were not able to get a type of chemotherapy known as platinum-based chemotherapy because of safety problems with the chemotherapy.

The study included 154 participants in Canada, Russia, South Korea, Spain, Taiwan, the United States, and Vietnam.

## Why was the research needed?

Researchers are looking for a better way to treat people who have advanced bladder cancer that can no longer be removed by surgery. Before a treatment can be approved for people to get, researchers do clinical studies to find out how it works and how safe it is.

Advanced bladder cancer that can no longer be removed by surgery is called "unresectable stage 4 urothelial cancer". This includes cancer in other parts of the body near the bladder, such as the urinary tract. In people with cancer, the body is not able to control the growth of some cells. The extra cells can form tumors. When cancer progresses to an advanced stage, tumors spread to other parts of the body or grow beyond the organ where they started. Sometimes, there are too many tumors, or they are too difficult to remove by surgery.

Normally, the immune system can help stop tumors from growing. But, in some cases, the proteins on the tumor cells can interact with certain proteins on the immune cells. This may stop the immune cells from recognizing the tumor cells and being able to attack them.

The study drug durvalumab was designed to stop the tumor cells from interacting with some of these proteins on the immune cells. This lets the immune cells recognize the tumor cells again so the immune system can attack them. Durvalumab is available in some countries for other types of cancers. The study drug olaparib was designed to help stop the tumor cells from being able to repair

themselves when they are damaged. Olaparib is also available in some countries for other types of cancers.

In this study, the researchers wanted to find out if durvalumab with olaparib works better than durvalumab with the placebo in a small number of participants with advanced bladder cancer. 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:

- Did durvalumab and olaparib together help the participants live longer with their cancer before it got worse?
- Did the participants feel that getting durvalumab and olaparib together helped with their symptoms and 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 durvalumab with olaparib helps improve the health of people with advanced bladder cancer.

## What treatments did the participants get?

In this study, the participants got either durvalumab and olaparib, or durvalumab and a placebo that looked like olaparib. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure any of the effects they see in the participants who get the drug are actually caused by the drug.

This was a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew what treatments each participant was getting. Some studies are done this way because knowing what treatment the participants are getting can affect the results of the study. When the study ended, the research sponsor found out which treatments the participants got so they could create a report of the study results.

A computer program was used to randomly choose the treatments each participant got. 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.

Durvalumab was given as an injection into a vein, also known as an IV infusion. Olaparib and the placebo were taken as tablets by mouth. The doses of the study drugs were measured in milligrams, also known as mg.

The participants continued getting study treatment until their cancer got worse or until they left the study.

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

| | Durvalumab and olaparib | Durvalumab and placebo |
|---|---|---|
|  | 78 participants | 76 participants |
|  | 1,500 mg of durvalumab as an IV infusion | 1,500 mg of durvalumab as an IV infusion |
|  | 200 or 300 mg of olaparib as a tablet by mouth | Placebo as a tablet by mouth |
|  | • Durvalumab every 4 weeks<br>• Olaparib twice a day | • Durvalumab every 4 weeks<br>• Placebo twice a day |

## What happened during this study?

Each participant was in the study until their cancer got worse or until they left the study. The entire study took about 2.5 years to finish.

The study started in March 2018 and ended in October 2020.

The chart below shows what happened during the study.

## Before the participants got study treatment

**1 visit**

**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 exam and asked about the participants' medications and any medical problems
- took pictures of the participants' tumors using CT or MRI scans
- checked the participants' heart health using an electrocardiogram, also called an ECG
- if needed, used surgery to take a sample of the tumor, also known as a biopsy

Up to 4 weeks

## While the participants got study treatment

**Visits every 4 weeks**

**The study doctors:**

- did a physical exam and asked about the participants' medications and any medical problems
- gave the participants their doses of durvalumab by IV infusion every 4 weeks
- checked the participants' heart health using an ECG
- if needed, used surgery to take a sample of the tumor, also known as a biopsy
- took blood and urine samples

**The participants:**

- took their doses of olaparib or the placebo as tablets by mouth twice a day at home
- took pictures of the participants' tumors using CT or MRI scans at some visits
- answered questionnaires about their symptoms and quality of life

Until the participants' cancer got worse or they left the study

## After the participants got their last dose of study treatment

**Visits every 4 weeks**

**The study doctors:**

- asked about the participants' medications and any medical problems
- took blood and urine samples
- took pictures of the participants' tumors using CT or MRI scans at some visits

**The participants:**

- answered questionnaires about their symptoms and quality of life

As long as needed

# 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. 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.

## Did durvalumab and olaparib together help the participants live longer with their cancer before it got worse?

No. The researchers compared the results for the participants who got durvalumab and olaparib with the results for those who got durvalumab and the placebo. Overall, the researchers found that the participants who got durvalumab and olaparib did not live longer with their cancer before it got worse.

To answer this question, the study doctors took pictures of the participants' tumors using MRI or CT scans. MRI scans are also known as magnetic resonance imaging scans, and CT scans are also known as computed tomography 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 from when the participants started study treatment to when their cancer started spreading or growing.

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

- 4.2 months for the participants who got durvalumab and olaparib
- 3.5 months for the participants who got durvalumab and the placebo

Then, the researchers calculated the risk of the participants' cancer getting worse after starting study treatment. They compared the risk for the participants who got durvalumab and olaparib to the risk for the participants who got durvalumab and the placebo.

Compared to the participants who got durvalumab and the placebo, the participants who got durvalumab and olaparib had a 6.0% reduced risk of their cancer getting worse during the study.

Overall, this number was too small for the researchers to know if durvalumab and olaparib helped the participants live longer with their cancer before it got worse.

### Did the participants feel that getting durvalumab and olaparib together helped with their symptoms and quality of life?

To answer this question, the study doctors asked the participants to complete a questionnaire. This questionnaire was called the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30, also known as EORTC QLQ-C30.

The answers to the questionnaire were given "scores" based on the severity of the participants' symptoms and their quality of life. The researchers measured how much the participants' scores changed during the study.

The researchers compared the changes in the scores for the participants who got durvalumab and olaparib with those who got durvalumab and the placebo.

Overall, the researchers found that participants in both treatment groups had a little more fatigue and that their quality of life got a little worse during the study. But, there were no overall meaningful differences in symptoms and quality of life between the participants who got durvalumab and olaparib and the participants who got durvalumab and the placebo.

## 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 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 durvalumab and 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.

The results below are for the 152 out of 154 participants who got at least 1 dose of study treatment.

## Did any adverse reactions happen during this study?

| | Durvalumab and olaparib (out of 76 participants) | Durvalumab and placebo (out of 76 participants) |
|---|---|---|
| How many participants had adverse reactions? | 72.4% (55) | 60.5% (46) |
| How many participants had serious adverse reactions? | 14.5% (11) | 11.8% (9) |
| How many participants stopped taking study treatment due to adverse reactions? | 7.9% (6) | 6.6% (5) |

## What serious adverse reactions happened during this study?

The most common serious adverse reaction was having low levels of red blood cells, also called anemia. The table below shows the most common serious adverse reactions that happened in at least 2 participants during the study. There were other serious adverse reactions, but these happened in fewer participants.

### Most common serious adverse reactions

| Serious adverse reaction | Durvalumab and olaparib (out of 76 participants) | Durvalumab and placebo (out of 76 participants) |
|---|---|---|
| Low levels of red blood cells, also called anemia | 3.9% (3) | 1.3% (1) |
| Fatigue | 2.6% (2) | 0.0% (0) |
| Stomach pain | 1.3% (1) | 1.3% (1) |

None of the participants who got durvalumab and olaparib died because of serious adverse reactions during the study.

There were 1.3% of participants who got durvalumab and the placebo who died because of serious adverse reactions during the study. This was 1 out of 76 participants. The serious adverse reaction was having low levels of red blood cells, also called anemia.

## What adverse reactions happened during this study?

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

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

**Most common adverse reactions**

| Adverse reaction | Durvalumab and olaparib (out of 76 participants) | Durvalumab and placebo (out of 76 participants) |
|---|---|---|
| Low levels of red blood cells, also called anemia | 23.7% (18) | 13.2% (10) |
| Nausea | 19.7% (15) | 3.9% (3) |
| Diarrhea | 10.5% (8) | 2.6% (2) |
| Low appetite | 10.5% (8) | 2.6% (2) |
| Low levels of thyroid hormones | 9.2% (7) | 3.9% (3) |
| Itchiness | 7.9% (6) | 10.5% (8) |
| Rash | 7.9% (6) | 5.3% (4) |
| Dizziness | 6.6% (5) | 1.3% (1) |
| General weakness | 5.3% (4) | 1.3% (1) |

# How has this study helped patients and researchers?

This study helped researchers learn more about durvalumab and olaparib together in participants with advanced bladder 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 1 study. Other studies may provide new information or different results.

Further clinical studies with durvalumab and olaparib are ongoing and 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 **"NCT03459846"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search",** then type **"2017-004556-27"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D933IC00003"** into the search box, and click **"Find a Study"**.

**Full Study Title:** A Phase II, Randomized, Multicenter, Double-Blind, Comparative Global Study to Determine the Efficacy and Safety of Durvalumab in Combination With Olaparib for First-Line Treatment in Platinum-Ineligible Patients With Unresectable Stage IV Urothelial Cancer

**AstraZeneca Protocol Number:** D933IC00003

**National Clinical Trials Number:** NCT03459846

**EudraCT Number:** 2017-004556-27

**AstraZeneca** sponsored this study and has its headquarters at 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

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