Clinical Study Results

Research Sponsor: AstraZeneca

Drugs Studied: Adavosertib and olaparib

Study Title: A study to learn about the safety of adavosertib with olaparib in participants with solid tumors or small-cell lung cancer

Thank you

Thank you for taking part in the clinical study for the study drug adavosertib together with olaparib. Adavosertib is also called AZD1775. You and all the other participants helped the researchers learn about using adavosertib and olaparib to help people with solid tumors or small-cell lung cancer, also called SCLC.

AstraZeneca sponsored this study and thinks 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 doctor or staff at your study site.

What is happening with the study now?

The study started in August 2015 and ended in April 2019. The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

The study included 120 participants with solid tumors and 10 participants with SCLC in the United States and Canada.

Why was the research needed?

Researchers are looking for a better way to treat patients with solid tumors, including patients with SCLC. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

In this study, the researchers wanted to learn about the safety of adavosertib taken together with olaparib in participants with solid tumors and participants with SCLC. The researchers also wanted to know if the participants had any medical problems during the study.

A solid tumor is a type of cancer that starts in an organ of the body. SCLC is an uncommon cancer of the lung. All of the participants in this study had already tried cancer treatments, but their cancer had come back or gotten worse.

In people whose cancer has not gotten better after previous treatment, certain proteins help cause the tumor to grow. Adavosertib was designed to stop one of these proteins from letting the tumor grow and to cause tumor cells to die.

Olaparib is available as a treatment for people with advanced ovarian cancer and metastatic breast cancer. It works by stopping a protein in the body from allowing the tumor to grow.

Previous studies have shown that treatment with a combination of adavosertib and olaparib may be beneficial for people with solid tumors, including people with SCLC, who have already tried other treatments that did not help their cancer.

In this study, the researchers wanted to learn how many participants had dose-limiting toxicities after getting adavosertib and olaparib. Dose-limiting toxicities are also called DLTs. These are medical problems that are severe enough to prevent the study doctor from increasing the dose of the study treatment in the study.

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

- How many participants had DLTs after getting adavosertib and olaparib?
- Did the participants' safety results change after taking adavosertib with olaparib?
- 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 that help find out if adavosertib taken together with olaparib improves the health of people with certain cancers.

The researchers asked for the help of men and women with solid tumors and men and women with SCLC. They had already tried treatments but their cancer had started growing again. Everyone in the study was 26 to 80 years old when they joined.

What kind of study was this?

This was a an “open-label” study. This means the researchers and the participant knew what the participant was taking.

In this study, treatment happened in 21-day periods called “cycles”. The participants took part in the study until their cancer got worse, they decided to stop taking part in the study, the study doctors stopped their participation, or the study finished. So, the participants each had a different number of treatment cycles.

There were 2 parts to this study:

- Part A included participants with solid tumors. There were different groups of participants who took adavosertib and olaparib at different doses and on different schedules.
- Part B included participants with SCLC, who had not previously taken part in Part A of the study. All of the participants in Part B took the same dose of adavosertib and olaparib on the same schedule throughout Part B.

The participants took adavosertib and olaparib tablets by mouth at home. The doses were measured in milligrams, also called mg.

At the beginning of the study, only a few participants joined each of the treatment groups. The study doctors looked at the results for these participants. Then, the researchers decided whether or not to include more participants in each treatment group.

Each participant stayed on the same dose of adavosertib and olaparib throughout the study.

There were 2 participants, 1 in Part A and 1 in Part B, who joined the study but never took any study treatment. So, this summary includes information about 119 participants in Part A, and 9 participants in Part B.

The tables below show the different treatments in each part of the study.

Part A treatments

Group number	Number of participants out of 119 participants	Treatment
1	3 participants	• 125 mg adavosertib twice daily for 6 days per cycle • 100 mg olaparib twice daily for 14 days per cycle
2	3 participants	• 150 mg adavosertib twice daily for 6 days per cycle • 100 mg olaparib twice daily for 14 days per cycle
3	4 participants	• 175 mg adavosertib twice daily for 6 days per cycle • 100 mg olaparib twice daily for 14 days per cycle
4	7 participants	• 150 mg adavosertib twice daily for 6 days per cycle • 200 mg olaparib twice daily for 14 days per cycle
5	7 participants	• 175 mg adavosertib twice daily for 6 days per cycle • 200 mg olaparib twice daily for 14 days per cycle
6	14 participants	• 175 mg adavosertib twice daily for 6 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
7	14 participants	• 175 mg adavosertib twice daily for 9 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
8	5 participants	• 175 mg adavosertib twice daily for 6 days per cycle • 300 mg olaparib twice daily for 14 days per cycle
9	8 participants	• 250 mg adavosertib once daily for 10 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
10	7 participants	• 200 mg adavosertib once daily for 10 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
11	16 participants	• 250 mg adavosertib once daily for 6 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
12	4 participants	• 250 mg adavosertib once daily for 9 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
13	3 participants	• 300 mg adavosertib once daily for 6 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
14	13 participants	• 200 mg adavosertib once daily for 6 days per cycle • 200 mg olaparib twice daily for 21 days per cycle
15	11 participants	• 200 mg adavosertib once daily for 6 days per cycle • 300 mg olaparib twice daily for 21 days per cycle

Part B Treatments

Group number	Number of participants out of 9 participants	Treatment
16	9 participants	• 200 mg adavosertib once daily for 6 days per cycle • 200 mg olaparib twice daily for 21 days per cycle

The study drug doses and schedule used in Group 14 in Part A were the same doses and schedule used in Group 16 in Part B.

What happened during the study?

Before the participants took study treatment, they visited the study site 1 time. This was up to 4 weeks before they started the study. At this visit, the study doctors checked the participants' overall health to make sure that they could join the study. The study doctors:

- did a physical exam and checked vital signs
- took blood samples
- asked about the participants' medical history
- checked the participant's heart health using an electrocardiogram, also called an ECG
- measured the participants' tumors using CT or MRI scans
- looked at a sample of each participant's tumor
- asked the participants about any medications they were taking

The study doctors also did physical exams, ECGs, and CT or MRI scans throughout the study. They also took blood samples and asked the participants about their medications throughout the study.

During the study, the participants took study treatment based on their treatment group. They visited the study site up to 5 times per cycle. At some site visits, the study doctors took urine samples and used a needle to take a sample of the tumor tissue. This is also called a tumor biopsy.

After taking the last dose of study treatment, the participants visited their study site at least 2 more times over the next month.

At the first of these visits, the study doctors checked the participants' health, asked them about their medications, and took blood and urine samples.

At the next visit, the study doctors asked about the participants' health and medications and checked the size of their tumors using a CT scan.

After this, the participants visited the study site or received phone calls from the study site every 6 weeks or 3 months after their last dose. This happened until they started a new cancer treatment, their cancer got worse, or they left the study.

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.

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 change.

The website listed at the end of this summary may have a full report of the study results.

How many participants had DLTs after getting adavosertib and olaparib?

To help answer this question, the researchers counted the number of dose limiting toxicities the participants had during Part A of the study.

Counting the number of DLTs helps researchers determine the safety of different doses of a treatment. This helps them find the highest dose that the participants can take. The researchers in this study wanted to determine what dose to give participants in future studies using adavosertib and olaparib together.

The researchers did not count the number of DLTs in Part B of the study, since the dose did not change during that part.

In Part A, 11.8% of the participants had a DLT. This was 14 out of 119 participants. Some participants had more than 1 DLT.

The table below shows the number of participants who had a DLT in each treatment group during Part A of the study:

Dose-limiting toxicities

Group number	Number of participants out of 119 participants	Part A Adavosertib and olaparib (Out of 119 participants)
1	3 participants	0.0% (0)
2	3 participants	0.0% (0)
3	4 participants	0.0% (0)
4	7 participants	0.0% (0)
5	7 participants	0.0% (0)
6	14 participants	7.1% (1)
7	14 participants	14.3% (2)
8	5 participants	20.0% (1)
9	8 participants	25.0% (2)
10	7 participants	28.6% (2)
11	16 participants	6.3% (1)
12	4 participants	25.0% (1)
13	3 participants	33.3% (1)
14	13 participants	7.7% (1)
15	11 participants	18.2% (2)

The most common DLTs were a decrease in the number of a type of white blood cell called neutrophils, and a decrease in the number of blood-clotting fragments called platelets.

Did the participants' safety results change after taking adavosertib and olaparib?

This was the main question that the researchers wanted to answer in Part B. This is because all of the participants in Part B took 200 mg of adavosertib once daily for 6 days per cycle and 200 mg olaparib twice daily.

To help answer this question, the researchers compared the results of the participants' vital signs and blood tests before and after the participants took study treatment in Part B.

Overall, the researchers found that there was no change in the participants' vital signs before and after treatment in this part.

They found that there were some changes in the participants' blood cell counts, blood proteins, and blood minerals compared to before they took study treatment. These changes were similar to results in earlier studies with adavosertib and olaparib.

Adverse events

The doctors also kept track of the "adverse events" that the participants had in Part B. 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 treatments.

Later in this document, there will be a summary of the adverse events that the study doctors thought might be related to the study treatments. This section is a summary of all the adverse events in Part B, whether they might be related to the study treatments 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.

The table below includes a summary of the adverse events the participants had in Part B:

	Part B Adavosertib and olaparib (Out of 9 participants)
How many participants in Part B had adverse events?	100% (9)
How many participants in Part B had serious adverse events?	33.3% (3)
How many participants in Part B stopped taking 1 of the study treatments because of adverse events?	0.0% (0)
How many participants died due to serious adverse events?	11.1% (1)

The most common adverse events were low numbers of blood-clotting fragments called platelets, and low numbers of red blood cells. This is also called anemia.

There were 3 participants who had serious adverse events during Part B of the study. These were fever in a participant with low numbers of white blood cells, a urinary tract infection, and pneumonia.

What medical problems did participants have 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.

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

How many participants had serious adverse reactions?

There were 13.3% of participants who had serious adverse reactions during the study. This was 17 out of 128 participants.

There were 13.4% of participants who had serious adverse reactions during Part A of the study. This was 16 out of 119 participants.

There were 11.1% of participants who had serious adverse reactions during Part B of the study. This was 1 out of 9 participants.

The only serious adverse reaction that happened in more than 2 participants during the study overall is listed in the table below.

Serious adverse reaction	Part A (Out of 119 participants)	Part B (Out of 9 participants)	Total (Out of 128 participants)
Fever in a participant with low numbers of white blood cells	2.5% (3)	1.1% (1)	3.1% (4)

There were other serious adverse reactions but they each happened in fewer participants. Some participants had more than one serious adverse reaction.

There were 0.8% of participants who died during the study due to serious adverse reactions. This was 1 out of 119 participants. This participant was in Group 9 in Part A. Participants in this group took 250 mg of adavosertib once daily for 10 days per cycle and 200 mg olaparib twice daily.

How many participants had adverse reactions?

There were 93.0% of participants who had adverse reactions during the study. This was 119 out of 128 participants.

There were 93.3% of participants who had adverse reactions during Part A of the study. This was 111 out of 119 participants.

There were 88.9% of participants who had adverse reactions during Part B of the study. This was 8 out of 9 participants.

There were 1.6% of participants who stopped taking both study treatments because of adverse reactions they had during the study. This was 2 out of 128 participants. All of these participants stopped taking the study treatments during Part A of the study.

What adverse reactions did participants have?

The most common adverse reactions in Part A of the study were diarrhea, nausea, and fatigue.

The most common adverse reactions in Part B of the study were a decrease in the number of blood-clotting fragments called platelets, and a decrease in the number of red blood cells. This is also called anemia.

Part A

The tables below and on the next page show the most common adverse reactions that happened in 20% or more of the participants during this part of the study. This means the adverse reactions happened in 23 or more participants.

There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during Part A

Groups 1 through 8 (adavosertib and olaparib)

	Group 1 (Out of 3 participants)	Group 2 (Out of 3 participants)	Group 3 (Out of 4 participants)	Group 4 (Out of 7 participants)	Group 5 (Out of 7 participants)	Group 6 (Out of 14 participants)	Group 7 (Out of 14 participants)	Group 8 (Out of 5 participants)
Diarrhea	66.7% (2)	66.7% (2)	75.0% (3)	28.6% (2)	28.6% (2)	50.0% (7)	42.9% (6)	80.0% (4)
Nausea (feeling sick)	100.0% (3)	33.3% (1)	25.0% (1)	42.9% (3)	71.4% (5)	50.0% (7)	50.0% (7)	60.0% (3)
Fatigue	33.3% (1)	66.7% (2)	50.0% (2)	42.9% (3)	42.9% (3)	64.3% (9)	71.4% (10)	80.0% (4)
Decrease in the number of red blood cells (anemia)	33.3% (1)	0.0% (0)	50.0% (2)	28.6% (2)	42.9% (3)	35.7% (5)	64.3% (9)	20.0% (1)
Vomiting	0.0% (0)	33.3% (1)	0.0% (0)	57.1% (4)	28.6% (2)	21.4% (3)	35.7% (5)	60.0% (3)
Decrease in the number of blood-clotting fragments called platelets	33.3% (1)	33.3% (1)	0.0% (0)	0.0% (0)	14.3% (1)	21.4% (3)	50.0% (7)	40.0% (2)
Decreased appetite	0.0% (0)	0.0% (0)	0.0% (0)	14.3% (1)	14.3% (1)	50.0% (7)	14.3% (2)	60.0% (3)

Groups 9 through 15 (adavosertib and olaparib)

	Group 9 (Out of 8 participants)	Group 10 (Out of 7 participants)	Group 11 (Out of 16 participants)	Group 12 (Out of 4 participants)	Group 13 (Out of 3 participants)	Group 14 (Out of 13 participants)	Group 15 (Out of 11 participants)	Total (Out of 119 participants)
Diarrhea	50.0% (4)	71.4% (5)	62.5% (10)	75.0% (3)	33.3% (1)	38.5% (5)	54.5% (6)	52.1% (62)
Nausea (feeling sick)	25.0% (2)	42.9% (3)	56.3% (9)	25.0% (1)	33.3% (1)	30.8% (4)	54.5% (6)	47.1% (56)
Fatigue	37.5% (3)	14.3% (1)	50.0% (8)	75.0% (3)	0.0% (0)	15.4% (2)	36.4% (4)	46.2% (55)
Decrease in the number of red blood cells (anemia)	25.0% (2)	42.9% (3)	56.3% (9)	25.0% (1)	33.3% (1)	46.2% (6)	63.6% (7)	43.7% (52)
Vomiting	12.5% (1)	14.3% (1)	25.0% (4)	50.0% (2)	33.3% (1)	15.4% (2)	18.2% (2)	26.1% (31)
Decrease in the number of blood-clotting fragments called platelets	25.0% (2)	28.6% (2)	12.5% (2)	0.0% (0)	66.7% (2)	15.4% (2)	9.1% (1)	21.8% (26)
Decreased appetite	12.5% (1)	14.3% (1)	12.5% (2)	25.0% (1)	0.0% (0)	30.8% (4)	27.3% (3)	21.8% (26)

Part B

The table below shows the most common adverse reactions that happened in 20% or more of the participants during this part of the study. This means the adverse reactions happened in 2 or more participants.

There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during Part B

	Group 16 Adavosertib and olaparib (Out of 9 participants)
Decrease in the number of blood-clotting fragments called platelets	66.7% (6)
Decrease in the number of red blood cells (also called anemia)	55.6% (5)
Decreased appetite	22.2% (2)
Decrease in the number of white blood cells called leukocytes	22.2% (2)
Decrease in the number of white blood cells called neutrophils	22.2% (2)
Vomiting	22.2% (2)
Diarrhea	22.2% (2)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of adavosertib when taken with olaparib in participants with solid tumors and SCLC.

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 the study drugs are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If 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 "**NCT02511795**" into the search box, and click "**Search**".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6010C00005"** into the search box and click **"Find a Study"**.

Full Trial Title: A Phase Ib Study of Adavosertib and Olaparib in Patients with Refractory Solid Tumours

National Clinical Trials number: NCT02511795

AstraZeneca Protocol Number: D6010C00005

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

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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