Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD1775, also called adavosertib

Study Title: A study to learn how AZD1775 and chemotherapy together work in participants with ovarian cancer, fallopian tube cancer, or peritoneal cancer

Thank you!

Thank you to the participants who took part in the clinical trial for the study drug adavosertib, also called AZD1775. All of the participants helped researchers learn more about AZD1775 to help people with ovarian cancer, fallopian tube cancer, or peritoneal cancer.

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

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?

Participants were in the study for up to 19 months, but the entire study took 4 years to finish. The study started in January 2015 and ended in December 2018.

The study included 94 participants in Canada, the Netherlands, and the United States.

The sponsor reviewed the data collected when the study ended and created a report of the results. This is a summary of that report.

Why was the research needed?

Researchers are looking for a better way to treat ovarian cancer in women whose cancer has come back after chemotherapy treatment. 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 find out if AZD1775 works in participants with ovarian cancer, fallopian tube cancer, or peritoneal cancer. All the participants had already had chemotherapy, but their cancer had come back. They also wanted to find out if the participants had any medical problems during the study.

A protein called WEE1 helps cancer cells to grow. AZD1775 slows the growth of cancer cells by stopping WEE1 from working. Researchers think that giving patients AZD1775 together with chemotherapy can help keep the cancer from coming back.

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

- How many participants had their tumors shrink or disappear?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of women over the age of 18 years with ovarian cancer, fallopian tube cancer, or peritoneal cancer. The participants in this study:

- were women 34 to 85 years old
- had advanced cancer and at least 1 tumor
- had their cancer come back after finishing prior chemotherapy

What kind of study was this?

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

There were 6 treatment groups in this study. Each participant was in only 1 of the groups. In each group, the participants got both AZD1775 and a specific type of chemotherapy. AZD1775 was taken as a pill by mouth. Doses were measured in milligrams, also called mg. Each type of chemotherapy was given through a needle into the vein, also called an IV infusion.

Chemotherapy treatment happens in cycles. At the end of a cycle, the patient either starts a new cycle or finishes treatment. The number of cycles depends on the type of chemotherapy the participant has.

The table below shows the different treatment groups in this study.

Treatment groups in this study

Group	AZD1775 treatment		Chemotherapy treatment	Cycle length
Group 1 (9 participants)	175 mg of AZD1775 once a day	• AZD1775 2 days a week for 3 weeks • No AZD1775 for 1 week	Gemcitabine for 3 weeks, then no chemotherapy for 1 week	4 weeks
Group 2 (38 participants)	225 mg of AZD1775 every 12 hours	• AZD1775 2.5 days a week for 3 weeks • No AZD1775 for 1 week	Paclitaxel for 3 weeks, then no chemotherapy for 1 week	4 weeks
Group 3 (23 participants)	225 mg of AZD1775 every 12 hours	• AZD1775 2.5 days a week for 1 week • No AZD1775 for 2 weeks	Carboplatin for 1 week, then no chemotherapy for 2 weeks	3 weeks
Group 4 (12 participants)	225 mg of AZD1775 every 12 hours	• AZD1775 2.5 days a week for 3 weeks	Carboplatin for 1 week, then no chemotherapy for 2 weeks	3 weeks
Group 5 (6 participants)	175 mg of AZD1775 every 12 hours	• AZD1775 2.5 days a week for 1 week • No AZD1775 for 3 weeks	• Pegylated liposomal doxorubicin, also called PLD • PLD for 1 week, then no chemotherapy for 3 weeks	4 weeks
Group 6 (6 participants)	225 mg of AZD1775 every 12 hours	• AZD1775 2.5 days a week for 1 week • No AZD1775 for 3 weeks	PLD for 1 week, then no chemotherapy for 3 weeks	4 weeks

What happened during the study?

Before the participants got any study treatment, the doctors checked the overall health of the participants to make sure that they could join the study. The doctors took blood and urine samples and took pictures of the participants' tumors using computerized tomography, also called CT scans, or magnetic resonance imaging, also called MRI scans.

During the study, the participants in all groups visited their study site 3 times in each treatment cycle. At every visit, the doctors took blood samples and asked the participants what medical problems they had.

At the start of each new cycle, the doctors checked the participants' overall health and took blood and urine samples. After every 2 cycles, the doctors took a picture of the participants' tumors using CT or MRI scans.

The main reasons that participants stopped taking AZD1775 and chemotherapy were if:

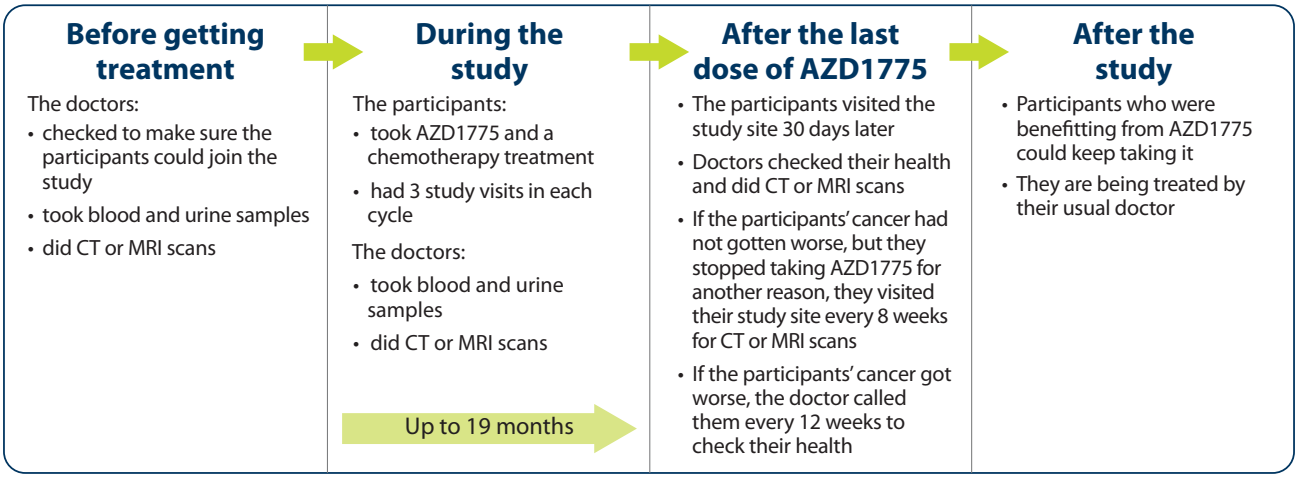
- their cancer got worse
- they had a medical problem that the doctors thought might be caused by AZD1775 and it would be dangerous for them to stay on treatment
- they wanted to leave the study or their doctor thought they should stop getting AZD1775

30 days after taking the last dose of AZ1775, the participants visited their study site. At this visit, the doctors checked their health and did CT or MRI scans. If a participant's cancer had not gotten worse during the study but they stopped taking AZD1775 for another reason, they visited the study site every 8 weeks. At these visits, the doctors did CT or MRI scans. The participants continued these visits until their cancer got worse or until the study ended.

If a participant's cancer got worse while they were taking study treatment or after their last dose, the doctors contacted the participant every 3 months to check their health. This could either be in person at a clinic or by phone. If the participant died, the doctor recorded when and how they died.

If a participant benefitted from AZD1775, they could keep taking it after the study ended and are being monitored by their doctor.

The chart below shows how the study was done.



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 researchers wanted to answer can be found on the websites listed at the end of this summary. If 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.

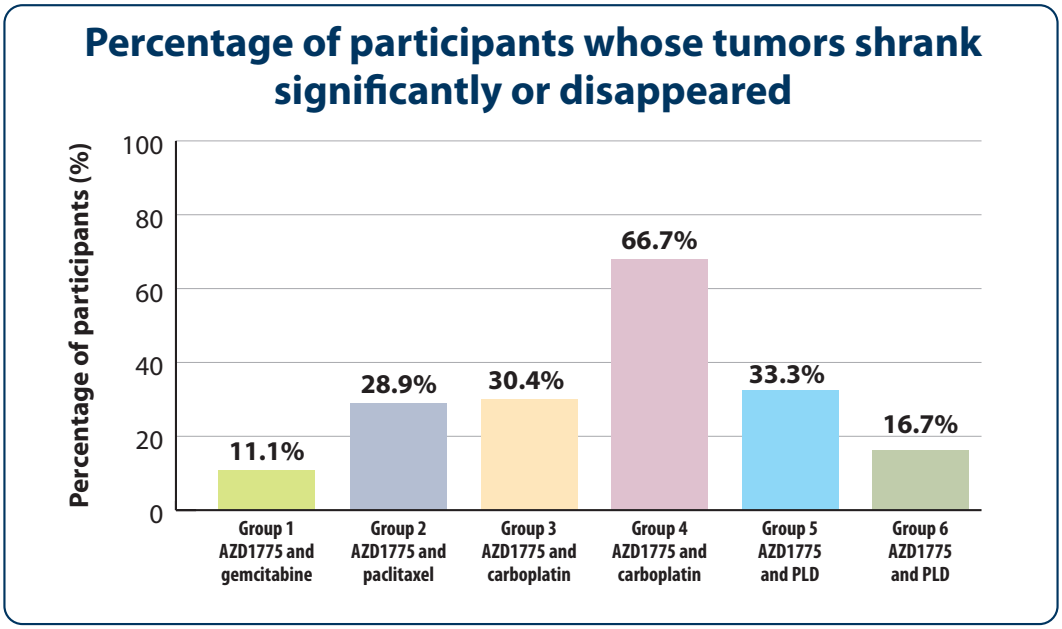
How many participants had their tumors shrink or disappear?

The researchers wanted to know how many participants had their tumors shrink significantly or disappear completely after getting AZD1775 and chemotherapy. To answer this question, they measured the size of the participants' tumors throughout the study. They did this using CT or MRI scans, and a measurement called Response Evaluation Criteria in Solid Tumors, also called RECIST.

The researchers found that overall, 31.9% of patients had their tumors shrink significantly or disappear after getting AZD1775 and chemotherapy. This was 30 out of 94 participants. The number of participants whose tumors shrank significantly or disappeared was:

- 11.1% in Group 1. This was 1 out of 9 participants.
- 28.9% in Group 2. This was 11 out of 38 participants.
- 30.4% in Group 3. This was 7 out of 23 participants.
- 66.7% in Group 4. This was 8 out of 12 participants.
- 33.3% in Group 5. This was 2 out of 6 participants.
- 16.7% in Group 6. This was 1 out of 6 participants.

The chart below summarizes the results.



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 AZD1775. These medical problems are called “adverse reactions”. An adverse reaction is considered “serious” when it is fatal, life-threatening, causes lasting problems, or requires hospital care.

These adverse reactions may or may not be caused by the study drugs. A lot of research is needed to know whether a drug causes an adverse reaction.

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.

How many participants had serious adverse reactions?

There were 27.7% of participants who had serious adverse reactions during the study. This was 26 out of 94 participants.

There was 1 participant who died from a serious adverse reaction during the study. This participant was in Group 2 and had a low level of white blood cells. This meant that the participant could not fight off an infection.

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

Most common serious adverse reactions during the study

	Group 1 AZD1775 and gemcitabine (Out of 9 participants)	Group 2 AZD1775 and paclitaxel (Out of 38 participants)	Group 3 AZD1775 and carboplatin (Out of 23 participants)	Group 4 AZD1775 and carboplatin (Out of 12 participants)	Group 5 AZD1775 and PLD (Out of 6 participants)	Group 6 AZD1775 and PLD (Out of 6 participants)
Low numbers of blood cells that help clotting	0.0% (0)	0.0% (0)	21.7% (5)	41.7% (5)	0.0% (0)	0.0% (0)
A fever and low numbers of blood cells that fight infection	0.0% (0)	13.2% (5)	4.3% (1)	8.3% (1)	0.0% (0)	0.0% (0)
Vomiting	0.0% (0)	2.6% (1)	8.7% (2)	8.3% (1)	16.7% (1)	0.0% (0)
Anemia (decrease in the number of red blood cells in the blood)	0.0% (0)	0.0% (0)	17.4% (4)	0.0% (0)	0.0% (0)	0.0% (0)
Nausea	0.0% (0)	2.6% (1)	8.7% (2)	0.0% (0)	16.7% (1)	0.0% (0)
Low numbers of blood cells that fight infection	0.0% (0)	2.6% (1)	4.3% (1)	16.7% (2)	0.0% (0)	16.7% (1)
Bacteria in the blood	0.0% (0)	2.6%(1)	0.0% (0)	8.3% (1)	0.0% (0)	0.0% (0)
Diarrhea	0.0% (0)	0.0% (0)	8.7% (2)	0.0% (0)	0.0% (0)	0.0% (0)
Blood clot in the lungs	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (2)	0.0% (0)	0.0% (0)

How many participants had adverse reactions?

There were 98.9% of participants who had adverse reactions during the study. This was 93 out of 94 participants.

There were 12.8% of participants who stopped taking AZD1775 because of adverse reactions they had during the study. This was 12 out of 94 participants.

What adverse reactions did the participants have?

The most common adverse reactions were diarrhea and nausea.

The table below shows the most common 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 during the study

	Group 1 AZD1775 and gemcitabine (Out of 9 participants)	Group 2 AZD1775 and paclitaxel (Out of 38 participants)	Group 3 AZD1775 and carboplatin (Out of 23 participants)	Group 4 AZD1775 and carboplatin (Out of 12 participants)	Group 5 AZD1775 and PLD (Out of 6 participants)	Group 6 AZD1775 and PLD (Out of 6 participants)
Diarrhea	22.2% (2)	76.3% (29)	65.2% (15)	50.0% (6)	16.7% (1)	83.3% (5)
Nausea	33.3% (3)	55.3% (21)	73.9% (17)	75.0% (9)	66.7% (4)	66.7% (4)
Low numbers of blood cells the fight infection	88.9% (8)	63.2% (24)	34.8% (8)	83.3% (10)	16.7% (1)	33.3% (2)
Feeling tired	33.3% (3)	60.5% (23)	65.2% (15)	58.3% (7)	33.3% (2)	66.7% (4)
Anemia (decrease in the number of red blood cells in the blood)	33.3% (3)	60.5% (23)	47.8% (11)	66.7% (8)	50.0% (3)	33.3% (2)
Low numbers of blood cells that help clotting	22.2% (2)	39.5% (15)	60.9% (14)	91.7% (11)	0.0% (0)	16.7% (1)
Vomiting	22.2% (2)	47.4% (18)	47.8% (11)	33.3% (4)	33.3% (2)	33.3% (2)
Reduced numbers of white blood cells	22.2% (2)	28.9% (11)	13.0% (3)	0.0% (0)	16.7% (1)	16.7% (1)
Reduced appetite	22.2% (2)	13.2% (5)	17.4% (4)	8.3% (1)	16.7% (1)	0.0% (0)
Altered sense of taste	11.1% (1)	10.5% (4)	8.7% (2)	16.7% (2)	16.7% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn how AZD1775 and chemotherapy worked together in participants with ovarian cancer, fallopian tube cancer, or peritoneal 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 AZD1775 are ongoing.

Where can I learn more about this study?

More information about this study is available on the website 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 this website, type **"NCT02272790"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2015-000886-30"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6010C00004"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Multicentre Phase II Study of AZD1775 plus Chemotherapy in Patients with Platinum-Resistant Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer

National Clinical Trials number: NCT02272790

AstraZeneca Protocol Number: D6010C00004

AstraZeneca AB sponsored this study and has its headquarters in Södertälje, Sweden.

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 participants.

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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