Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: AZD1775

Study Title: A study to learn how AZD1775 works in patients with advanced solid tumors, and if AZD1775 is safe to take

Thank you

Thank you to the participants who took part in the clinical study for the study drug AZD1775. All of the participants helped researchers learn more about AZD1775 and if it can help patients with advanced solid tumors.

AstraZeneca 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?

The study started in July 2015 and ended in January 2018. The study included 92 participants in Canada 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 better ways to treat patients with advanced solid tumors. Before a drug can be approved for patients to take, researchers do clinical studies to find out if it works and how safe it is.

A solid tumor is a type of cancer that can form in different organs in the body.

“Advanced” means that the cancer is unlikely to be cured, and the cancer cells may have spread to other parts of the body.

Many cancer treatments are designed to directly stop cancer cells from growing. The study drug, AZD1775, is being developed to stop an enzyme in the body from working. An enzyme is a substance produced by the body that helps control bodily functions and activities. AZD1775 is being developed to target an enzyme that helps with the growth of both normal and cancer cells. Researchers think that stopping this enzyme from working may also help stop cancer cells from growing.

In this study, the researchers wanted to find out how AZD1775 works in patients with advanced solid tumors. They also wanted to find out if the participants had any medical problems during the study.

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

- How did AZD1775 affect participants’ tumors?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women who had advanced solid tumors and had received cancer treatment. The participants in the study were 28 to 83 years old when they joined.

What kind of study was this?

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

All of the participants took AZD1775 in pill form by mouth. The treatment doses were measured in milligrams, also called mg.

The participants took AZD1775 during treatment periods called “cycles”. Each participant could take part in as many treatment cycles as they wanted as long as their cancer did not get worse. If their cancer got worse, the participant stopped the treatment cycles. Each cycle lasted 3 weeks.

What happened during the study?

The study had 2 parts, Part A and Part B. Each participant was in only 1 of the 2 parts.

Before treatment, the study doctors did tests and exams to check the participants' health to make sure they could join the study. They also checked the participants' tumors. If the researchers then decided the participants could join the study, the participants were put into either Part A or Part B.

In Part A, the researchers wanted to find the highest dose of AZD1775 that could help treat participants' tumors without causing "dose-limiting toxicities", also called DLTs. A DLT is a medical problem that is severe enough to stop the researcher from increasing a participant's study drug dose.

There were 12 participants in Part A. All of the participants were scheduled to take 200 mg of AZD1775 twice a day for 3 days. These doses were scheduled to be taken at the beginning of weeks 1 and 2 of each cycle.

Three of the first 7 participants who took the 200 mg AZD1775 doses had DLTs before the other 5 participants were able to start their doses. So, the researchers lowered the treatment doses to 175 mg of AZD1775 for the other 5 participants after studying the results from the first 7 participants.

After the researchers studied all of the results from Part A, they began giving treatment to participants in Part B.

In Part B, 80 participants took 175 mg of AZD1775 twice a day for 3 days. They did this at the beginning of weeks 1 and 2 of each cycle.

After treatment, all of the participants visited their study site up to 12 times. At these visits, the doctors checked the participants' tumor growth and overall health. They also asked the participants how they were feeling.

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 changes.

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.

At the beginning of the study, the researchers determined that they could not accurately measure the tumors for 2 of the participants. So, some of the results below are for 90 of the 92 participants.

How did AZD1775 affect participants' tumors?

In this study, some of the participants had their tumors shrink or stay the same. But, the researchers could not determine if AZD1775 helped stop the tumors from growing. This was because the number of participants in the study was too small for the researchers to determine if AZD1775 helped control the participants' tumors.

To answer this question, the researchers measured:

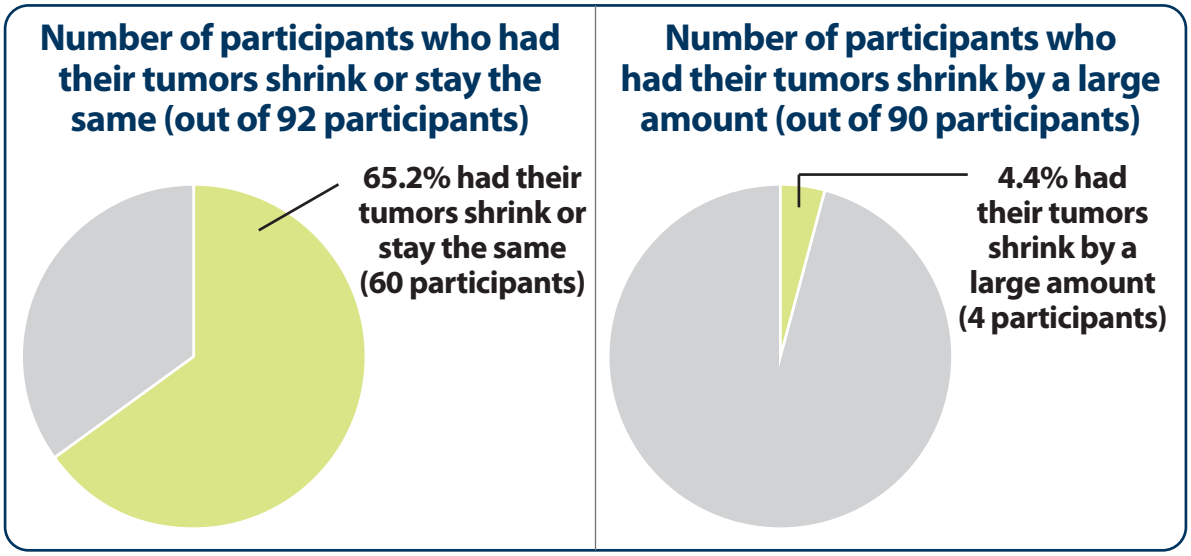
- the number of participants who had their tumors shrink or stay the same
- the number of participants who had their tumors shrink by a large amount
- how long it took for participants' tumors to grow after taking their first AZD1775 dose

The researchers considered a tumor to have shrunk by a large amount if it shrank by at least 30.0%. The researchers considered a tumor to have grown if it grew by at least 20.0%.

Overall, the researchers found that:

- 65.2% of participants had their tumors shrink or stay the same during the study. This was 60 out of 92 participants.
- 4.4% of participants had their tumors shrink by at least 30.0% during the study. This was 4 out of 90 participants.
- It took from 2.6 months to 4.1 months for participants' tumors to grow by at least 20.0% after taking their first AZD1775 dose.

The figures below show these results.



What medical problems did the participants have during the study?

This section is a summary of the medical problems the participants had during the study. Medical problems are considered “serious” when they are life-threatening, cause lasting problems, or require hospital care.

A medical problem that happens during a study is called an “adverse event”. An adverse event that the study doctors think might be related to the study drug is called an “adverse reaction”.

Adverse reactions may or may not be caused by the study drug. 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 additional information about the adverse events and adverse reactions that occurred during this study.

How many participants had adverse events?

A similar percentage of participants in Part A and Part B had adverse events.

A similar percentage of participants in Part A and Part B had serious adverse events.

None of the participants in Part A stopped treatment because of adverse events they had during the study. Some of the participants in Part B stopped treatment because of adverse events they had during the study.

The table below shows how many participants had adverse events during the study.

Adverse events during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
How many participants had adverse events during the study?	100.0% (7)	80.0% (4)	97.5% (78)	96.7% (89)
How many participants had serious adverse events during the study?	14.3% (1)	40.0% (2)	22.5% (18)	22.8% (21)
How many participants stopped treatment because of adverse events?	0.0% (0)	0.0% (0)	16.3% (13)	14.1% (13)

What serious adverse events did participants have?

There were 22.8% of participants who had serious adverse events during the study. This was 21 out of 92 participants.

The table below shows the serious adverse events that happened in at least 2 participants during the study. There were other serious adverse events, but those happened in fewer participants.

Serious adverse events during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
Anemia, which is a decrease in the amount of red blood cells in the blood	14.3% (1)	0.0% (0)	1.3% (1)	2.2% (2)
Stomach pain	0.0% (0)	20.0% (1)	1.3% (1)	2.2% (2)
Blockage in the small intestine only	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Dehydration	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Fainting because of decreased blood pressure	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Sepsis, which is swelling in the body from infection	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Vomiting	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)

What adverse events did the participants have?

The most common adverse event was diarrhea.

The adverse events in the table below happened in 15.0% or more of the participants overall. There were other adverse events, but those happened in fewer participants.

Most common adverse events during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
Diarrhea	85.7% (6)	40.0% (2)	61.3% (49)	62.0% (57)
Nausea	100.0% (7)	40.0% (2)	50.0% (40)	53.3% (49)
Tiredness	71.4% (5)	60.0% (3)	42.5% (34)	45.7% (42)
Vomiting	85.7% (6)	60.0% (3)	22.5% (18)	29.3% (27)
Constipation	28.6% (2)	20.0% (1)	26.3% (21)	26.1% (24)
Decreased appetite	28.6% (2)	20.0% (1)	20.0% (16)	20.7% (19)
Difficulty breathing	0.0% (0)	20.0% (1)	22.5% (18)	20.7% (19)
Stomach pain	14.3% (1)	40.0% (2)	18.8% (15)	19.6% (18)
Back pain	42.9% (3)	20.0% (1)	12.5% (10)	15.2% (14)
Anemia, which is a decrease in the amount of red blood cells in the blood	14.3% (1)	0.0% (0)	16.3% (13)	15.2% (14)
Swelling in the legs	14.3% (1)	20.0% (1)	15.0% (12)	15.2% (14)
Dizziness	0.0% (0)	40.0% (2)	15.0% (12)	15.2% (14)

How many participants had adverse reactions?

A higher percentage of participants in Part A had adverse reactions compared to participants in Part B.

A higher percentage of participants in Part A had serious adverse reactions compared to participants in Part B.

None of the participants in Part A stopped treatment because of adverse reactions they had during the study. Some of the participants in Part B stopped treatment because of adverse reactions they had during the study.

The table below shows how many participants had adverse reactions during the study.

Adverse reactions during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
How many participants had adverse reactions during the study?	100.0% (7)	80.0% (4)	83.8% (67)	84.8% (78)
How many participants had serious adverse reactions during the study?	14.3% (1)	20.0% (1)	10.0% (8)	10.9% (10)
How many participants stopped treatment because of adverse reactions?	0.0% (0)	0.0% (0)	3.8% (3)	3.3% (3)

What serious adverse reactions did participants have?

There were 10.9% of participants who had serious adverse reactions during the study. This was 10 out of 92 participants.

There were 1.1% of participants in Part B who died during the study from the serious adverse reaction of a blood clot in the legs. This was 1 out of 92 participants. This serious adverse reaction was also an adverse event.

The table below shows the serious adverse reactions that happened during the study.

Serious adverse reactions during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
Anemia, which is a decrease in the amount of red blood cells in the blood	14.3% (1)	0.0% (0)	1.3% (1)	2.2% (2)
Dehydration	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Vomiting	0.0% (0)	0.0% (0)	2.5% (2)	2.2% (2)
Hypovolemia, which is a decrease in the amount of blood in the body	14.3% (1)	0.0% (0)	0.0% (0)	1.1% (1)
Blood clot in the legs	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Decrease in the amount of oxygen in the body	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Decrease in blood platelet count, which means the body cannot stop bleeding as well as it should	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Fainting because of decreased blood pressure	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Feeling very weak	0.0% (0)	20.0% (1)	0.0% (0)	1.1% (1)
Nausea	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Sepsis, which is swelling in the body from infection	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)
Urinary tract infection	0.0% (0)	0.0% (0)	1.3% (1)	1.1% (1)

What adverse reactions did the participants have?

The most common adverse reaction was diarrhea.

The adverse reactions in the table below happened in 10.0% or more of the participants overall. There were other adverse reactions, but those happened in fewer participants.

Most common adverse reactions during the study

	Part A 200 mg AZD1775 (out of 7 participants)	Part A 175 mg AZD1775 (out of 5 participants)	Part B 175 mg AZD1775 (out of 80 participants)	Total (out of 92 participants)
Diarrhea	85.7% (6)	40.0% (2)	56.3% (45)	57.6% (53)
Nausea	100.0% (7)	40.0% (2)	42.5% (34)	46.7% (43)
Tiredness	71.4% (5)	40.0% (2)	36.3% (29)	39.1% (36)
Vomiting	85.7% (6)	60.0% (3)	18.8% (15)	26.1% (24)
Decreased appetite	28.6% (2)	20.0% (1)	12.5% (10)	14.1% (13)

How has this study helped patients and researchers?

This study helped researchers learn more about how AZD1775 works in patients with advanced solid tumors, and what AZD1775 dose is safest to take.

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.

Other clinical studies with AZD1775 are ongoing at the time of the writing of this document.

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 **"NCT02482311"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6015C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase Ib, Open-Label, Multi-Centre Study to Assess the Safety, Tolerability, Pharmacokinetics, and Anti-tumour Activity of AZD1775 Monotherapy in Patients with Advanced Solid Tumours

AstraZeneca Protocol Number: D6015C00001

AstraZeneca sponsored this study and has its headquarters at 1800 Concord Pike in Wilmington, Delaware.

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.