Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: AZD1775

Study Title: A study to learn how different doses of AZD1775 affect patients with 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 and their family members helped researchers learn more about AZD1775 to help people with solid tumors.

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

If you or your family member participated in the study and have questions about the results, please speak with the doctor or staff at the study site.

What is happening with the study now?

The study started in December 2015 and ended in April 2018. The study included 62 participants in 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 patients with 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. 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 help stop cancer cells from growing.

In this study, the researchers wanted to find the "maximum tolerated dose" for AZD1775. The maximum tolerated dose is the highest dose of a drug that doesn't cause "dose-limiting toxicities", also called DLTs, in patients. A DLT is a medical problem that is severe enough to stop the researcher from increasing a participant's study drug dose. The researchers also wanted to find out how often participants could take the maximum tolerated dose for AZD1775 without developing DLTs.

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

- What was the maximum tolerated dose of AZD1775 for the participants?
- 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 solid tumors and had received cancer treatment. The participants in the study were 26 to 91 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 AZD1775 doses were measured in milligrams, also called mg.

This was also a "dose-escalation" study. This means that each group got only 1 dose amount of AZD1775 during the study. Different groups of participants were given different doses of AZD1775. The researchers carefully studied the results from each group before deciding whether or not to give the next higher dose to the next group of participants.

What happened during the study?

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.

During treatment, the participants joined 1 of 10 groups. Each group got treatment in 2-week or 3-week periods called "cycles". The participants could take part in as many treatment cycles as they wanted until their cancer got worse. If their cancer got worse, the participants stopped the treatment cycles.

The table below shows the treatment schedule for each group:

Group	AZD1775 treatment	Cycle length	Treatment schedule
Group 1 (6 participants)	125 mg twice a day	2 weeks	First 5 days of week 1
Group 2 (6 participants)	150 mg twice a day	2 weeks	First 5 days of week 1
Group 3 (5 participants)	200 mg once a day	2 weeks	First 5 days of week 1
Group 4 (6 participants)	200 mg once a day	3 weeks	First 5 days of weeks 1 and 2
Group 5 (4 participants)	250 mg once a day	2 weeks	First 5 days of week 1
Group 6 (3 participants)	250 mg once a day	3 weeks	First 5 days of weeks 1 and 2
Group 7 (10 participants)	250 mg once a day	3 weeks	First 5 days of weeks 1, 2, and 3
Group 8 (4 participants)	300 mg once a day	2 weeks	First 5 days of week 1
Group 9 (16 participants)	300 mg once a day	3 weeks	First 5 days of weeks 1 and 2
Group 10 (2 participants)	300 mg once a day	3 weeks	First 5 days of weeks 1, 2, and 3

After treatment, the participants visited their study site up to 8 times. At these visits, the doctors checked the participants' tumors 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.

What was the maximum tolerated dose of AZD1775 for the participants?

In this study, the researchers wanted to find the "maximum tolerated dose" for AZD1775. The maximum tolerated dose is the highest dose of a drug that doesn't cause "dose-limiting toxicities", also called DLTs, in participants. A DLT is a medical problem that is severe enough to stop the researcher from increasing a participant's study drug dose. The researchers also wanted to find out how often participants could take the AZD1775 maximum tolerated dose without developing DLTs.

In general, the researchers found that:

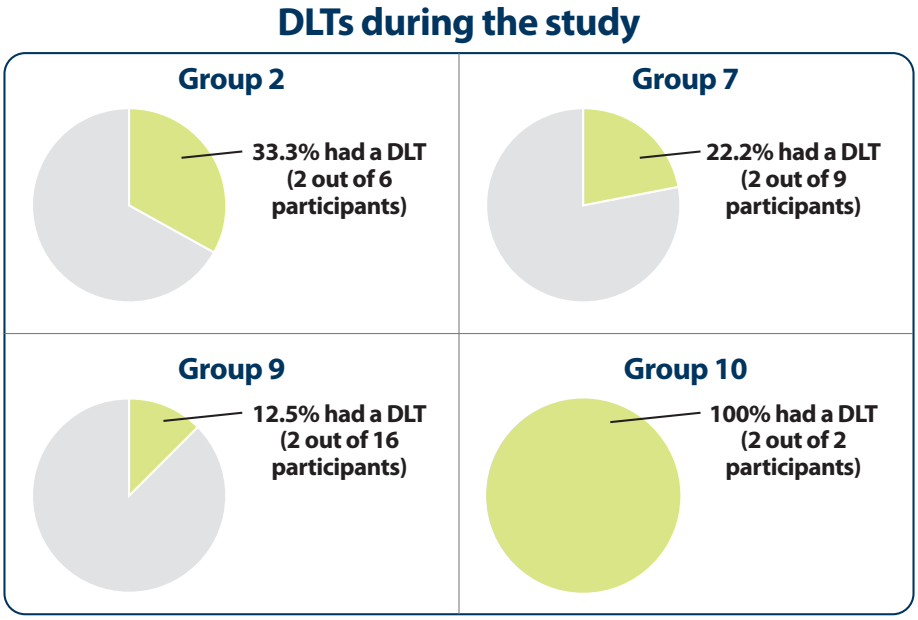
- Participants in Groups 1 and 2 had a maximum tolerated dose of 125 mg twice a day for AZD1775.
- Participants in Groups 3 through 10 had a maximum tolerated dose of 300 mg once a day for AZD1775.
- The overall maximum tolerated dose in the study was 300 mg once a day for AZD1775, taken for the first 5 days of weeks 1 and 2 during the 3-week treatment cycle.

The researchers also wanted to know how many DLTs participants had. There were 2 participants who died before receiving enough of the treatment for researchers to be able to study their DLT results. One of these participants was in Group 4, and 1 of these participants was in Group 7. So, the researchers could only study the DLT results for 60 of the 62 participants.

In this study, the researchers found there were 13.3% of participants who had DLTs. This was 8 out of 60 participants:

- 33.3% of participants in Group 2 had at least 1 DLT. This was 2 out of 6 participants.
- 22.2% of participants in Group 7 had at least 1 DLT. This was 2 out of 9 participants.
- 12.5% of participants in Group 9 had at least 1 DLT. This was 2 out of 16 participants.
- 100.0% of participants in Group 10 had at least 1 DLT. This was 2 out of 2 participants.
- None of the participants in Groups 1, 3, 4, 5, 6, or 8 had DLTs

The figure below shows 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 that the study doctors thought might be related to the study drug. 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 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 other information about adverse reactions or other medical problems that happened during this study.

How many participants had adverse reactions?

There were 90.3% of participants who had adverse reactions during the study. This was 56 out of 62 participants.

There were 6.5% of participants who stopped treatment because of adverse reactions they had during the study. This was 4 out of 62 participants.

The tables below and on the next page show how many participants had adverse reactions during the study.

Adverse reactions during the study (Groups 1 through 5)

	Group 1 (out of 6 participants)	Group 2 (out of 6 participants)	Group 3 (out of 5 participants)	Group 4 (out of 6 participants)	Group 5 (out of 4 participants)
How many participants had adverse reactions during the study?	100.0% (6)	100.0% (6)	100.0% (5)	100.0% (6)	50.0% (2)
How many participants had serious adverse reactions during the study?	0.0% (0)	33.3% (2)	0.0% (0)	16.7% (1)	0.0% (0)
How many participants stopped treatment because of adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)

Adverse reactions during the study (Groups 6 through 10)

	Group 6 (out of 3 participants)	Group 7 (out of 10 participants)	Group 8 (out of 4 participants)	Group 9 (out of 16 participants)	Group 10 (out of 2 participants)
How many participants had adverse reactions during the study?	100.0% (3)	80.0% (8)	50.0% (2)	100.0% (16)	100.0% (2)
How many participants had serious adverse reactions during the study?	33.3% (1)	0.0% (0)	25.0% (1)	12.5% (2)	0.0% (0)
How many participants stopped treatment because of adverse reactions?	0.0% (0)	10.0% (1)	25.0% (1)	0.0% (0)	50.0% (1)

How many participants had serious adverse reactions?

There were 11.3% of participants who had serious adverse reactions during the study. This was 7 out of 62 participants.

There were 53.2% of participants who died during the study. This was 33 out of 62 participants. The study doctors did not think that any of these deaths were related to AZD1775.

The tables below show the serious adverse reactions that happened during the study.

Serious adverse reactions during the study (Groups 1 through 5)

	Group 1 (out of 6 participants)	Group 2 (out of 6 participants)	Group 3 (out of 5 participants)	Group 4 (out of 6 participants)	Group 5 (out of 4 participants)
Fever with decrease in number of white blood cells (may increase the risk of illness)	0.0% (0)	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)
Dehydration	0.0% (0)	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)
Pneumonia	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Decrease in number of blood platelet cells (may increase the risk of bleeding)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Decrease in number of red blood cells in the body	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

Serious adverse reactions during the study (Groups 6 through 10)

	Group 6 (out of 3 participants)	Group 7 (out of 10 participants)	Group 8 (out of 4 participants)	Group 9 (out of 16 participants)	Group 10 (out of 2 participants)
Fever with decrease in number of white blood cells (may increase the risk of illness)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Dehydration	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Pneumonia	33.3% (1)	0.0% (0)	0.0% (0)	6.3% (1)	0.0% (0)
Decrease in number of blood platelet cells (may increase the risk of bleeding)	0.0% (0)	0.0% (0)	25.0% (1)	0.0% (0)	0.0% (0)
Decrease in number of red blood cells in the body	0.0% (0)	0.0% (0)	0.0% (0)	6.3% (1)	0.0% (0)

What adverse reactions did the participants have?

The most common adverse reaction was diarrhea. The adverse reactions below (Groups 1 through 5) and on the next page (Groups 6 through 10) happened in 3 or more participants in any treatment group. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study (Groups 1 through 5)

	Group 1 (out of 6 participants)	Group 2 (out of 6 participants)	Group 3 (out of 5 participants)	Group 4 (out of 6 participants)	Group 5 (out of 4 participants)
Diarrhea	33.3% (2)	83.3% (5)	20.0% (1)	33.3% (2)	25.0% (1)
Nausea	50.0% (3)	50.0% (3)	20.0% (1)	66.7% (4)	0.0% (0)
Tiredness	83.3% (5)	66.7% (4)	20.0% (1)	16.7% (1)	0.0% (0)
Vomiting	16.7% (1)	33.3% (2)	0.0% (0)	50.0% (3)	0.0% (0)
Dehydration	33.3% (2)	66.7% (4)	0.0% (0)	16.7% (1)	0.0% (0)
Decreased appetite	33.3% (2)	33.3% (2)	0.0% (0)	16.7% (1)	0.0% (0)
Decrease in number of red blood cells in the body	0.0% (0)	16.7% (1)	0.0% (0)	33.3% (2)	0.0% (0)
Decrease in number of blood platelet cells (may increase risk of bleeding)	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Muscle pain	16.7% (1)	0.0% (0)	20.0% (1)	50.0% (3)	0.0% (0)
Decrease in number of white blood cells (may increase the risk of illness)	0.0% (0)	33.3% (2)	20.0% (1)	0.0% (0)	0.0% (0)
Indigestion	50.0% (3)	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)
Muscle spasms	50.0% (3)	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)

Most common adverse reactions during the study (Groups 6 through 10)

	Group 6 (out of 3 participants)	Group 7 (out of 10 participants)	Group 8 (out of 4 participants)	Group 9 (out of 16 participants)	Group 10 (out of 2 participants)
Diarrhea	66.7% (2)	70.0% (7)	0.0% (0)	56.3% (9)	100.0% (2)
Nausea	66.7% (2)	20.0% (2)	50.0% (2)	43.8% (7)	100.0% (2)
Tiredness	66.7% (2)	20.0% (2)	25.0% (1)	50.0% (8)	0.0% (0)
Vomiting	66.7% (2)	10.0% (1)	0.0% (0)	25.0% (4)	50.0% (1)
Dehydration	33.3% (1)	20.0% (2)	0.0% (0)	6.3% (1)	0.0% (0)
Decreased appetite	0.0% (0)	20.0% (2)	0.0% (0)	25.0% (4)	0.0% (0)
Decrease in number of red blood cells in the body	33.3% (1)	10.0% (1)	0.0% (0)	37.5% (6)	0.0% (0)
Decrease in number of blood platelet cells (may increase risk of bleeding)	33.3% (1)	30.0% (3)	25.0% (1)	18.8% (3)	50.0% (1)
Muscle pain	0.0% (0)	20.0% (2)	25.0% (1)	6.3% (1)	0.0% (0)
Decrease in number of white blood cells (may increase the risk of illness)	0.0% (0)	10.0% (1)	0.0% (0)	25.0% (4)	50.0% (1)
Indigestion	0.0% (0)	0.0% (0)	0.0% (0)	12.5% (2)	0.0% (0)
Muscle spasms	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about which AZD1775 dose is safest to take to help patients with solid tumors.

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 **"NCT02610075"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D6015C00003"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase Ib Study to Determine the Maximum Tolerated Dose (MTD) of AZD1775 Monotherapy in Patients with Locally Advanced or Metastatic Solid Tumours

AstraZeneca Protocol Number: D6015C00003

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 and their families 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.