Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD4785

Study Title: A study to learn about the safety of different doses of AZD4785 in participants with advanced solid tumors

Thank you!

Thank you to the participants who took part in the clinical trial for the study drug AZD4785. All of the participants helped researchers learn more about AZD4785 to help people with advanced cancer.

AstraZeneca AB sponsored this study and believes 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 participants were in the study for up to 8 months. However, the entire study took about 20 months to complete. The study started in May 2017 and ended in January 2019.

The researchers planned to include up to 50 participants in the study. But, the study ended earlier than expected because the sponsor decided not to continue the research into this drug. The study included 28 participants in the United Kingdom 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 people who have advanced cancer or cancer that has spread, and whose cancer is caused by a gene called KRAS. 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.

A solid tumor is a type of cancer that starts in an organ of the body. An “advanced” solid tumor usually means that the cancer has spread to other parts of the body. When there are changes in the KRAS gene, tumor cells can grow out of control. AZD4785 is designed to work by reducing the amount of protein made by the KRAS gene, and to slow the growth of tumor cells.

In this study, the researchers wanted to learn about the safety of different doses of AZD4785. They also wanted to learn what medical problems the participants had.

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

- Which dose of AZD4785 was safest?
- Which dose of AZD4785 would be best to test in future research?
- What medical problems did the participants have during the study?

To answer these questions, the researchers asked for the help of men and women with advanced cancer or cancer that had spread. Everyone in the study was 48 to 82 years old when they joined. All participants had cancer that was caused by a change in the KRAS gene. They had received treatment for their cancer, but their cancer had come back or had worsened after treatment.

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 in this study got AZD4785 through a needle into their vein, also called intravenous infusion. Doses were measured in milligrams, also called mg.

This was also a “dose escalation” study. This means that the first group of participants started out on a low dose of AZD4785. The doctors carefully looked at the results for these participants. Then, the researchers decided whether to increase the dose in the next group of participants. Researchers use dose escalation studies to learn about the safety of a specific dose before participants are given a higher dose.

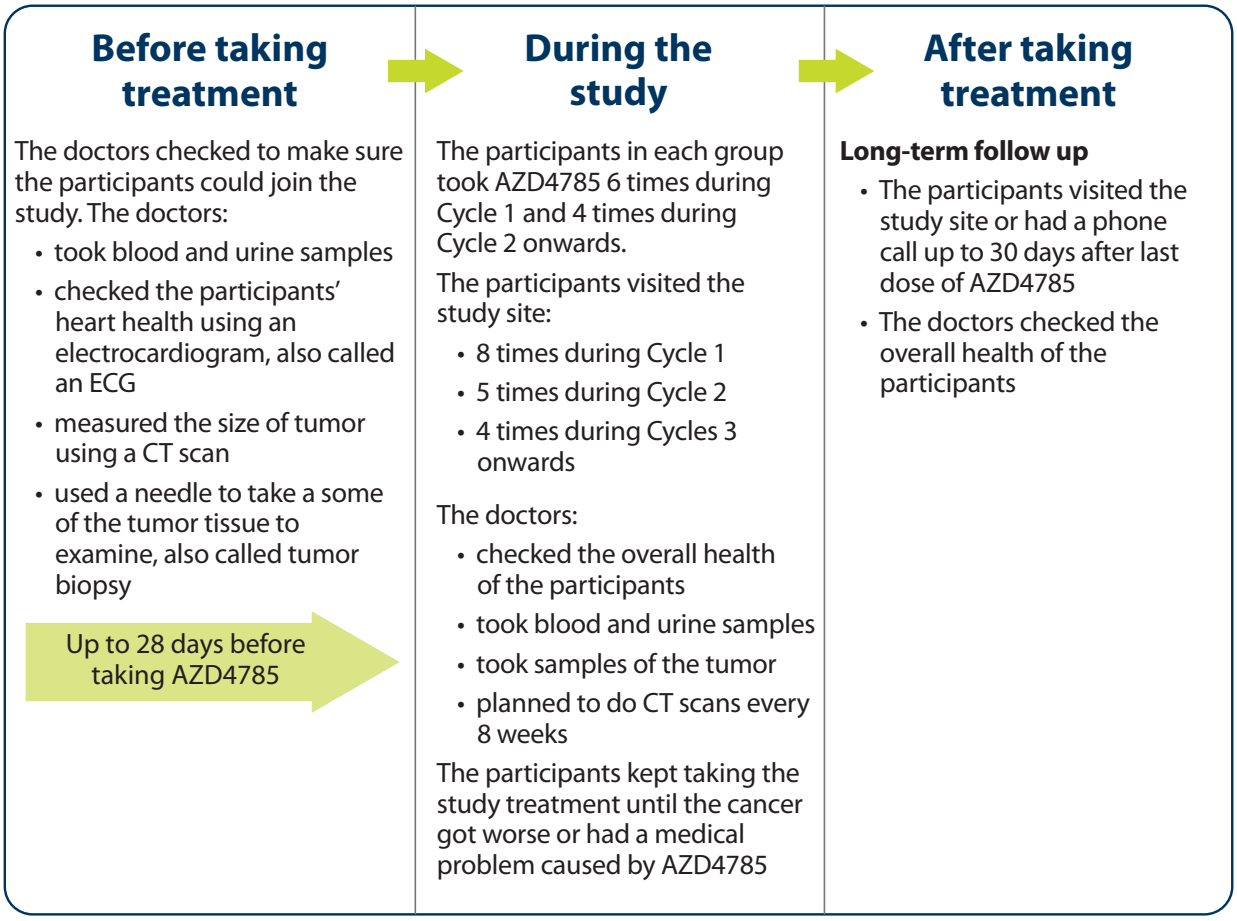
In this study, Part 1 was the dose escalation study. The researchers also planned to have a second part of the study. In this part, additional participants would be given a dose that had been well-tolerated in Part 1 of the study. However, the researchers decided to end the study after the first part. So, only the results from the first part are included in this summary. There were 7 dose treatment groups in this study. Each participant took part in 1 of the dose groups.

The treatment in this study was given in "cycles". Each cycle lasted for 28 days. If a participant's cancer was worse at the end of a cycle, or if the dose given was not tolerated by participants, treatment was stopped. If the treatment was tolerated, the participant could start a new cycle. The table below shows the different treatment groups in this study.

Group	AZD4785 treatment
Group 1 (3 participants)	Cycle 1 • 35 mg infusion of AZD4785 on days 1, 3, 5, 8, 15 and 22 Cycle 2 onwards • 35 mg infusion of AZD4785 once a week
Group 2 (3 participants)	Cycle 1 • 70 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 70 mg infusion of AZD4785 once a week
Group 3 (3 participants)	Cycle 1 • 140 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 140 mg infusion of AZD4785 once a week
Group 4 (3 participants)	Cycle 1 • 280 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 280 mg infusion of AZD4785 once a week
Group 5 (9 participants)	Cycle 1 • 560 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 560 mg infusion of AZD4785 once a week
Group 6 (5 participants)	Cycle 1 • 1,120 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 1,120 mg infusion of AZD4785 once a week
Group 7 (2 participants)	Cycle 1 • 900 mg infusion of AZD4785 on days 1, 3, 8, 15 and 22 Cycle 2 onwards • 900 mg infusion of AZD4785 once a week

What happened during the study?

The chart below shows how the study was done.



What were the results of the study?

Overall, this is a summary of the main results from this study. The individual results for each participant are not included 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 websites listed at the end of this summary may have a full report of the study results.

Which dose of AZD4785 was safest?

To answer this question, the study doctors counted the number of dose-limiting toxicities the participants had during the study. A dose-limiting toxicity is a medical problem that is severe enough to stop the study doctor from continuing to treat the participant on a dose of study treatment. A dose-limiting toxicity is also known as a DLT.

Overall, the researchers found that the results of the participants' tests and measurements did not change during the study. There were small differences in the results of these tests and measurements before and after getting AZD4785. But the differences were too small for the researchers to know if AZD4785 was the cause.

The researchers found that 1 out of 5 participants in Group 6 had a DLT. This was 20.0% of the participants in Group 6. None of the other participants in the study had a DLT.

The researchers had planned to have a second part of the study, where additional participants were to be given a dose that had been well-tolerated in part 1 of the study. However, the study was stopped because the sponsor decided not to do any more research into this drug. So, no dose of AZD4785 was chosen.

Which dose of AZD4785 would be best to test in future research?

To answer this question, the researchers compared the results of the tests and measurements that the doctors did before and after the participants got AZD4785. The researchers also collected information about how many "adverse events" the participants had.

An adverse event is any medical problem that happens during the study. Adverse events are considered "serious" when they are life-threatening, cause lasting problems, or require hospital care. Adverse events may or may not be caused by the study drug. This section includes information about the adverse events that the study doctors did not think were related to the study drug.

How many participants had adverse events not thought to be related?

- 21.4% of participants had at least 1 adverse event that was not related to the study drug. This was 6 out of 28 participants.
- 10.7% of participants had at least 1 serious adverse event that was not related to the study drug. This was 3 out of 28 participants.
- There were 10.7% of participants who stopped taking the study drug because of adverse events. This was 3 out of 28 participants. 1 participant stopped taking the study drug because of adverse events that were not related to the study drug.

What serious adverse events did the participants have that were not thought to be related?

The table below shows the serious adverse events that the participants had during this study that the study doctors did not think were related to the study drug.

Serious adverse events not thought to be related to study drug

Serious adverse events	Group 1 (35 mg AZD4785) out of 3 participants	Group 2 (70 mg AZD4785) out of 3 participants	Group 3 (140 mg AZD4785) out of 3 participants	Group 4 (280 mg AZD4785) out of 3 participants	Group 5 (560 mg AZD4785) out of 9 participants	Group 6 (1,120 mg AZD4785) out of 5 participants	Group 7 (900 mg AZD4785) out of 2 participants
Inflammation of lung tissue	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	0.0% (0)
Inflammation affecting the whole body	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	0.0% (0)
Collapsed lung	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	0.0% (0)
Sepsis	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	0.0% (0)
Nerve damage to arm and shoulder	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	20.0% (1)	0.0% (0)

There were 11 participants who died during the study due to reasons not related to the study drug.

- 35.7% of participants died due to cancer getting worse. This was 10 out of 28 participants.
- 3.6% of participants died for reasons unknown to the doctors. This was 1 out of 28 participants.

What were the most common adverse events not thought to be related?

The most common adverse event was dizziness.

The table below shows adverse events that:

- happened in 15% or more of all the study participants
- the study doctors did not think were related to the study drug

Some participants may have had more than 1 adverse event. There were other adverse events, but these happened in fewer participants.

Most common adverse events not thought to be related to study drug

Adverse events	Group 1 (35 mg AZD4785) out of 3 participants	Group 2 (70 mg AZD4785) out of 3 participants	Group 3 (140 mg AZD4785) out of 3 participants	Group 4 (280 mg AZD4785) out of 3 participants	Group 5 (560 mg AZD4785) out of 9 participants	Group 6 (1,120 mg AZD4785) out of 5 participants	Group 7 (900 mg AZD4785) out of 2 participants
Dizziness	33.3% (1)	66.7% (2)	0.0% (0)	0.0% (0)	33.3% (3)	0.0% (0)	50.0% (1)
Anemia, which is a low level of red blood cells	33.3% (1)	0.0% (0)	66.7% (2)	33.3% (1)	11.1% (1)	20.0% (1)	0.0% (0)
Constipation	33.3% (1)	0.0% (0)	33.3% (1)	0.0% (0)	33.3% (3)	20.0% (1)	0.0% (0)
Difficulty swallowing	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	33.3% (3)	40.0% (2)	0.0% (0)
Weight loss	33.3% (1)	66.7% (2)	33.3% (1)	0.0% (0)	22.2% (2)	0.0% (0)	0.0% (0)
Tiredness	33.3% (1)	0.0% (0)	33.3% (1)	0.0% (0)	33.3% (3)	0.0% (0)	0.0% (0)
Pain in the abdomen	33.3% (1)	33.3% (1)	0.0% (0)	33.3% (1)	22.2% (2)	0.0% (0)	0.0% (0)
Back pain	66.7% (2)	0.0% (0)	0.0% (0)	33.3% (1)	22.2% (2)	0.0% (0)	0.0% (0)
Dehydration	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	44.4% (4)	0.0% (0)	0.0% (0)

What medical problems did participants have during the study?

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”. This section is a summary of the adverse reactions the participants had during the study. 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 serious adverse reactions?

There were 17.9% of participants who had serious adverse reactions during the study. This was 5 out of 28 participants.

There were 2 participants who died due to the serious adverse reaction of the continuous shutting down of the nervous system. This happened in:

- 11.1% of participants in Group 5. This was 1 out of 9 participants in Group 5.
- 50.0% of participants in Group 7. This was 1 out of 2 participants in Group 7.

The table below shows the serious adverse reactions that happened during the study. There was 1 patient who experienced 2 serious adverse reactions.

The table includes the 2 participants who died due to continuous shutting down of the nervous system.

Serious adverse reactions during the study

Serious adverse reaction	Group 1 (35 mg AZD4785) out of 3 participants	Group 2 (70 mg AZD4785) out of 3 participants	Group 3 (140 mg AZD4785) out of 3 participants	Group 4 (280 mg AZD4785) out of 3 participants	Group 5 (560 mg AZD4785) out of 9 participants	Group 6 (1,120 mg AZD4785) out of 5 participants	Group 7 (900 mg AZD4785) out of 2 participants
Continuous shutting down of the nervous system	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	50.0% (1)
Chest pain	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	0.0% (0)	0.0% (0)
Infusion-related reaction	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	20.0% (1)	0.0% (0)
Damage to the nerves outside of the brain and spinal cord	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	20.0% (1)	0.0% (0)

How many participants had adverse reactions?

- 78.6% of participants had at least 1 adverse reaction. This was 22 out of 28 participants.
- 7.1% of participants stopped taking study drug because of adverse reactions. This was 2 out of 28 participants.

What adverse reactions did the participants have?

The most common adverse reaction was tiredness.

The table below shows the most common adverse reactions that happened in more than 15% of all participants during the study. Some participants may have had more than 1 adverse reaction. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reaction	Group 1 (35 mg AZD4785) out of 3 participants	Group 2 (70 mg AZD4785) out of 3 participants	Group 3 (140 mg AZD4785) out of 3 participants	Group 4 (280 mg AZD4785) out of 3 participants	Group 5 (560 mg AZD4785) out of 9 participants	Group 6 (1,120 mg AZD4785) out of 5 participants	Group 7 (900 mg AZD4785) out of 2 participants
Tiredness	0.0% (0)	0.0% (0)	0.0% (0)	100% (3)	22.2% (2)	80.0% (4)	50.0% (1)
Diarrhea	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	33.3% (3)	80.0% (4)	50.0% (1)
Nausea	33.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (3)	60.0% (3)	100% (2)
Anemia, which is a low level of red blood cells	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	55.6% (5)	20.0% (1)	0.0% (0)
Blood test showing raised levels of a liver enzyme (AST)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	22.2% (2)	80.0% (4)	50.0% (1)
Decreased appetite	33.3% (1)	33.3% (1)	0.0% (0)	0.0% (0)	22.2% (2)	40.0% (2)	0.0% (0)
Blood test showing raised levels of a liver enzyme (ALT)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	11.1% (1)	60.0% (3)	50.0% (1)
Infusion-related reaction	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	22.2% (2)	60.0% (3)	0.0% (0)
Itchy skin	0.0% (0)	0.0% (0)	0.0% (0)	33.3% (1)	11.1% (1)	40.0% (2)	50.0% (1)
Fever	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	22.2% (2)	40.0% (2)	50.0% (1)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of AZD4785 in participants with advanced cancer or cancer that has spread.

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 AZD4785 are not 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 this website, type **"NCT03101839"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D8360C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase I, Open-Label, Multicentre Dose-Escalation Study to Investigate the Safety and Pharmacokinetics of AZD4785 in Patients with Advanced Solid Tumours Where KRAS May Be an Important Driver of Tumour Survival

National Clinical Trials number: NCT03101839

AstraZeneca Protocol Number: D8360C00001

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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