Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD8154

Study Title: A study to learn about the safety of different doses and forms of AZD8154 in healthy participants

Thank you!

Thank you to the participants who took part in the clinical study for the study drug AZD8154. AstraZeneca AB 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.

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 2018 and ended in July 2019. It included 78 participants in Germany.

The study had 3 parts:

- Part A included 48 participants
- Part B included 6 participants
- Part C included 24 participants

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 who have asthma. 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.

Asthma is a condition that causes the airways to narrow, swell, and create extra mucus. This can cause symptoms such as wheezing, coughing, and difficulty breathing.

There are several inhaled treatments that doctors use to help patients control their asthma symptoms. But these treatments may not work for some people, and may cause medical problems.

The study drug, AZD8154, is an inhaled asthma treatment being developed to help patients control their asthma symptoms. In this study, the researchers wanted to find out about the safety of AZD8154 in healthy participants.

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

- Did the participants have changes in their safety results during the study?
- 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 AZD8154 improves the health of people who have asthma.

The researchers asked for the help of healthy men and women. The participants in this study were 18 to 44 years old when they joined.

What kind of study was this?

This study had 3 parts: Part A, Part B, and Part C. Each participant could only be in 1 part of the study.

Part A and Part C were “single-blind”. This means the researchers knew what the participants were taking during these parts, but the participants did not. These parts were also the “dose escalation” parts of the study. This means that the first group of participants in each part started out by getting a low dose of AZD8154. The study doctors carefully looked at the results from these participants, then decided whether to increase the dose in the next group of participants.

Part B of the study was “open-label”. This means the researchers and the participants knew which treatment the participants were taking during this part.

In Part A, the participants took 1 dose of either AZD8154 or a placebo through an inhaler. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to help make sure any of the effects they see in the participants who take the drug are actually caused by the drug.

Part B started after Part A. In Part B, the participants took AZD8154 through an inhaler or got it through a needle into their vein, also called an IV.

Part C started after Part B. In Part C, the participants took several doses of either AZD8154 or a placebo through an inhaler.

All of the AZD8154 doses in this study were measured in milligrams, also called mg.

A computer program was used to randomly choose the treatment each participant took during Part A and Part C. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

What happened during the study?

Before the participants took treatment, they visited their study site 2 times over the course of 4 weeks. At these visits, the study doctors checked to make sure the participants could join the study. The study doctors:

- did a physical examination
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG
- asked the participants about their medical history, how they were feeling, and what medicines they were taking
- explained how to take the inhaled treatments during the study

The study doctors also did these tests and measurements throughout the study.

Part A

During Part A, most of the participants visited their study site 1 time and stayed there for about 3 days. During this visit, they took 1 inhaled dose of either AZD8154 or the placebo. The doses of AZD8154 were made up of either small or large bits called "particles". Most of the AZD8154 doses were "small-particle" treatments, but 1 was a "large-particle" treatment. The researchers wanted to compare a small-particle and large-particle form of the same AZD8154 dose.

About 2 weeks after their first visit, 6 participants who took 1 of the doses of AZD8154 had another visit at their study site for about 3 days. During this visit, they took the same dose of AZD8154, but as a large-particle treatment.

Part B

The participants in Part B visited their study site 2 times over the course of about 3 weeks. During both visits, they stayed at their study site for about 3 days.

All 6 participants in Part B got the same treatments. During their first visit, they got 1 dose of AZD8154 through an IV. Then, they waited about 2 weeks before their next visit.

During their second visit, the participants took a small-particle treatment of AZD8154 through an inhaler.

Part C

The 24 participants in Part C visited their study site 1 time and stayed there for about 2 weeks. During this time, they took a small-particle treatment of AZD8154 or the placebo 11 times.

About 1 week after taking the last treatment, all of the participants visited their study site 1 time. At this visit, the study doctors checked the participants' overall health and lung health, and asked them how they were feeling.

What were the results of the study?

This is an overall summary of the main results from this study. 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 websites listed at the end of this summary may have a full report of the study results.

Did the participants have changes in their safety results during the study?

To answer this question, the researchers compared the results of specific tests and measurements that were done before the participants took treatment and throughout the study.

The researchers focused on the below tests and measurements:

- physical examinations
- blood and urine tests
- ECGs

Overall, the researchers found that there were some changes in the results of these tests and measurements during the study. But these changes were too small for the researchers to consider them significant.

The study doctors also kept track of the “adverse events” that the participants had during the study. An adverse event is any unwanted sign or symptom that participants have during a study.

Doctors keep track of all of the adverse events that happen in studies, even if they do not think the adverse events might be related to the study treatment. 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 websites listed at the end of this summary may have more information about the adverse events that happened during this study.

Serious adverse events

None of the participants had serious adverse events during the study.

None of the participants died during the study.

Adverse events

Part A

- 27.8% of participants who took AZD8154 had an adverse event during Part A. This was 10 out of 36 participants.
- 41.7% of participants who took the placebo had an adverse event during Part A. This was 5 out of 12 participants.

Part B

- 33.3% of participants had an adverse event after getting AZD8154 through an IV or an inhaler during Part B. This was 2 out of 6 participants.

Part C

- 55.6% of participants who took AZD8154 had an adverse event during Part C. This was 10 out of 18 participants.
- 50.0% of participants who took the placebo had an adverse event during Part C. This was 3 out of 6 participants.

None of the participants stopped treatment due to an adverse event during the study.

Most common adverse events

The most common adverse event that happened during the study was headache.

The tables below and on the next page show the adverse events that happened in at least 2 participants during Part A and Part C. There were other adverse events that happened during Part A and Part C, but those happened in fewer participants. No adverse events happened in more than 1 participant during Part B.

Most common adverse events during Part A

	Headache	Irritation in the throat	Chest pain	Dry throat
0.08 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
0.29 mg of AZD8154 (Out of 6 participants)	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)
0.88 mg of AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)	0.0% (0)	0.0% (0)
2.7 mg of small-particle AZD8154 (Out of 6 participants)	16.7% (1)	0.0% (0)	16.7% (1)	0.0% (0)
2.7 mg of large-particle AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)	0.0% (0)	16.7% (1)
5.4 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
7.7 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)
Placebo (Out of 12 participants)	8.3% (1)	8.3% (1)	8.3% (1)	8.3% (1)

Most common adverse events during Part C

	Headache	Cough	Local skin reaction
0.6 mg of AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)	0.0% (0)
1.8 mg of AZD8154 (Out of 6 participants)	50.0% (3)	16.7% (1)	33.3% (2)
3.1 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	0.0% (0)
Placebo (Out of 6 participants)	16.7% (1)	0.0% (0)	0.0% (0)

What medical problems did the participants have during the study?

This section is a summary of the adverse events the participants had during the study that the study doctors thought might be related to the study treatments. These adverse events are called “adverse reactions”. An adverse reaction is considered “serious” when it is life threatening, causes lasting problems, or requires hospital care.

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 websites listed at the end of this summary may have other information about adverse reactions that happened during this study.

All of the adverse reactions listed in this section are also included in the list of adverse events above.

How many participants had adverse reactions?

Part A

- 27.8% of participants who took AZD8154 had an adverse reaction during Part A. This was 10 out of 36 participants.
- 41.7% of participants who took the placebo had an adverse reaction during Part A. This was 5 out of 12 participants.

Part B

- 16.7% of participants had an adverse reaction after getting AZD8154 through an IV or an inhaler during Part B. This was 1 out of 6 participants.

Part C

- 44.4% of participants who took AZD8154 had an adverse reaction during Part C. This was 8 out of 18 participants.
- 50.0% of participants who took the placebo had an adverse reaction during Part C. This was 3 out of 6 participants.

None of the participants stopped treatment due to an adverse reaction during the study. None of the participants had serious adverse reactions or died during the study.

What adverse reactions did the participants have?

The most common adverse reaction during the study was headache.

The tables below show the adverse reactions that happened in at least 2 participants during Part A and Part C. There were other adverse reactions that happened during Part A and Part C, but those happened in fewer participants. No adverse reactions happened in more than 1 participant during Part B.

Most common adverse reactions during Part A

	Headache	Irritation in the throat	Chest pain	Dry throat
0.08 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
0.29 mg of AZD8154 (Out of 6 participants)	16.7% (1)	0.0% (0)	0.0% (0)	0.0% (0)
0.88 mg of AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)	0.0% (0)	0.0% (0)
2.7 mg of small-particle AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)
2.7 mg of large-particle AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)	0.0% (0)	16.7% (1)
5.4 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
7.7 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)	16.7% (1)	0.0% (0)
Placebo (Out of 12 participants)	8.3% (1)	8.3% (1)	8.3% (1)	8.3% (1)

Most common adverse reactions during Part C

	Headache	Cough
0.6 mg of AZD8154 (Out of 6 participants)	16.7% (1)	16.7% (1)
1.8 mg of AZD8154 (Out of 6 participants)	50.0% (3)	16.7% (1)
3.1 mg of AZD8154 (Out of 6 participants)	0.0% (0)	0.0% (0)
Placebo (Out of 6 participants)	16.7% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of different doses and forms of AZD8154 in healthy participants.

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 AZD8154 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 **"NCT03436316"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D8900C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase 1 Study to Assess the Safety, Tolerability and Pharmacokinetics of AZD8154 Following Single and Multiple Ascending Dose Administration in Healthy Subjects

AstraZeneca Protocol Number: D8900C00001

AstraZeneca AB sponsored this study and has its headquarters at 151 85 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 patients.