AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD4635

Study Purpose: This study was done to learn if taking fluvoxamine and/or smoking affected the amount of AZD4635 that got into the blood of healthy participants.

Protocol Number: D8730C00007

Thank you!

Thank you for taking part in the clinical study for the study drug AZD4635.

AstraZeneca AB sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

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

Who took part in the study?

The researchers asked for the help of healthy men and women. The participants in this study were 20 to 53 years old when they joined. Half of the participants were smokers and half of the participants were non-smokers. The smokers had a history of smoking more than 10 cigarettes per day for more than 6 months before they entered the study. The non-smokers had no history of smoking cigarettes. After being exposed to nicotine, the body makes a chemical called cotinine. The level of cotinine in a urine sample can be tested as evidence of recent smoking. In this study, the smokers provided a urine sample that was positive for cotinine before they entered the study. The non-smokers provided a urine sample that was negative for cotinine.

The study included 28 participants in the United Kingdom.

Why was the research needed?

Researchers are looking for a better way to treat cancer. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

The study drug, AZD4635, is being developed to treat some types of cancer, including prostate cancer. Some drugs need to be broken down before they can be removed from the body. How quickly the drug is broken down affects how much of it is in the blood. AZD4635 is removed from the body after being broken down by a liver protein called CYP1A2. Smoking can affect how CYP1A2 works. CYP1A2 can also be affected by some drugs, like a treatment for depression called fluvoxamine. Finding out if drugs or behaviours like smoking affect how much AZD4635 gets into the blood can help researchers learn how people should take AZD4635.

What was the purpose of this study?

In this study, the researchers wanted to learn if taking fluvoxamine and/or smoking affected the amount of AZD4635 that got into the blood of healthy participants.

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

- Did taking fluvoxamine and/or smoking affect how much AZD4635 got into the participants' blood?
- What medical problems did the participants have during the study?

This information is important to know before other studies can be done to help find out if AZD4635 improves the health of people who have cancer.

What treatments did the participants take?

In this study, all of the participants took:

- AZD4635 as capsules by mouth
- Fluvoxamine as tablets by mouth

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew which of these treatments each participant was taking during the study.

This study happened in 2 parts. In each part, half of the participants were smokers, and the other half were non-smokers.

Part 1 of the study lasted for 6 days. In Part 1, all of the participants took 1 dose of AZD4635 on day 1.

Part 2 of the study lasted for 11 days. In Part 2, all of the participants took fluvoxamine every day for 10 days. They also took 1 dose of AZD4635 on day 6.

The chart below shows the treatments and participant groups the researchers planned to study.

	28 participants in total • 14 participants were smokers • 14 participants were non-smokers
	• AZD4635 as capsules by mouth • Fluvoxamine as tablets by mouth
	Part 1: • 1 dose of AZD4635 Part 2: • Fluvoxamine every day for 10 days • 1 dose of AZD4635 with fluvoxamine

What happened during the study?

The study started in July 2020 and ended in December 2020.

Before the participants took study treatment, they visited their study site 1 time. This part of the study lasted for up to 4 weeks, because the participants joined at different times. At this visit, the study doctors made sure the participants could join the study. They also:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

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

While the participants took study treatment, they visited their study site 1 time and stayed overnight at the study site for 16 nights.

After the participants took the last study treatment, the study doctors called them 1 time about 6 to 9 days later. During this call, the study doctors checked the health of the participants.

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.

The websites listed at the end of this summary may have a full report of the study results.

Did taking fluvoxamine and/or smoking affect how much AZD4635 got into the participants' blood?

Overall, the researchers found that taking fluvoxamine increased how much AZD4635 got into the participants' blood. They also found that smoking did not affect how much AZD4635 got into the participants' blood.

To answer this question, the study doctors took blood samples throughout the study from the smokers and non-smokers. Samples were taken during Part 1 when the participants took AZD4635 alone and during Part 2 when the participants took AZD4635 and fluvoxamine. In these samples, they measured:

- the blood sample with the highest amount of AZD4635
- the total amount of AZD4635 in the participants' blood over time
- the total amount of AZD4635 in the participants' last blood sample

Based on the results from each participant, researchers calculated an average for each of these measurements. The researchers then compared the results of when the participants took only AZD4635 to when they took both AZD4635 and fluvoxamine. They also compared the results of the participants who were smokers to those who were non-smokers.

Overall, the researchers found that the average amounts of AZD4635 in the blood were higher when the participants took it with fluvoxamine. This means that fluvoxamine increased the amount of AZD4635 that got into the participants' blood. This is likely to be because fluvoxamine affected CYP1A2. Based on these results the researchers think other drugs that affect CYP1A2 may also affect the amount of AZD4635 that gets into the blood.

Overall, the researchers found that the average amounts of AZD4635 in the blood were not different in the participants who were smokers compared with those who were non-smokers. This means that smoking did not affect the amount of AZD4635 that got into the participants' blood.

What medical problems happened during this 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 AZD4635. 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 AZD4635. A lot of research is needed to know whether a drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for AZD4635.

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.

There was 1 participant who was a non-smoker who stopped taking study treatment in Part 2 before they got AZD4635. This was due to an adverse reaction thought to be related to fluvoxamine. So, the results for the non-smokers below are for 13 out of the 14 participants in that group.

None of the other participants stopped taking study treatment due to adverse reactions.

Did any adverse reactions happen during this study?

A summary of the adverse reactions thought to be related to AZD4635 is shown below.

Part 1

AZD4635

- There were 42.9% of smokers who had adverse reactions. This was 6 out of 14 participants.
- There were 50.0% of non-smokers who had adverse reactions. This was 7 out of 14 participants.

Part 2

AZD4635 and fluvoxamine

- There were 64.3% of smokers who had adverse reactions. This was 9 out of 14 participants.
- There were 76.9% of non-smokers who had adverse reactions. This was 10 out of 13 participants.

What serious adverse reactions happened during this study?

None of the participants had serious adverse reactions during this study.

What adverse reactions happened during this study?

The most common adverse reactions were dizziness, nausea, and insomnia.

The table below shows the most common adverse reactions thought to be related to AZD4635. It shows the adverse reactions that happened in 2 or more participants during the study. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

Adverse reaction	Part 1: AZD4635		Part 2: AZD4635 and fluvoxamine	
	Smokers (out of 14 participants)	**Non-smokers** (out of 14 participants)	**Smokers** (out of 14 participants)	**Non-smokers** (out of 13 participants)
Dizziness	14.3% (2)	35.7% (5)	14.3% (2)	38.5% (5)
Nausea	7.1% (1)	14.3% (2)	42.9% (6)	15.4% (2)
Insomnia	0.0% (0)	0.0% (0)	21.4% (3)	38.5% (5)
Headache	14.3% (2)	0.0% (0)	0.0% (0)	15.4% (2)
Increased energy	21.4% (3)	0.0% (0)	0.0% (0)	7.7% (1)
Stomach pain	7.1% (1)	0.0% (0)	0.0% (0)	15.4% (2)
Anxiety	0.0% (0)	7.1% (1)	7.1% (1)	15.4% (2)
Decreased appetite	0.0% (0)	0.0% (0)	14.3% (2)	7.7% (1)
Twitching muscles	0.0% (0)	0.0% (0)	0.0% (0)	15.4% (2)
Tremor	7.1% (1)	0.0% (0)	0.0% (0)	7.7% (1)
Feeling bloated	7.1% (1)	0.0% (0)	0.0% (0)	7.7% (1)

How has this study helped patients and researchers?

This study helped researchers learn if taking fluvoxamine and/or smoking affected how much AZD4635 got into the blood of 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 AZD4635 are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. If more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT04478513"** into the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D8730C00007"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase I, Open-label, Non-randomized Study to Assess the Effect of Fluvoxamine (CYP1A2 Inhibitor) and Smoking (CYP1A2 Inducer) on the Pharmacokinetics of a Single Oral Dosing of AZD4635 in Healthy Volunteers

AstraZeneca Protocol Number: D8730C00007

National Clinical Trials Number: NCT04478513

AstraZeneca AB sponsored this study and has its headquarters at 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.

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.

CISCRP | One Liberty Square, Suite 1100 • Boston, MA 02109 | 1-877-MED-HERO | www.ciscrp.org

Version 1.0 2021_09_09