AstraZeneca

Clinical Trial Results

Research Sponsor: AstraZeneca AB

Drug Studied: AZD5462

Trial Purpose: A trial to learn if AZD5462 is safe in healthy participants

Protocol Number: D9090C00001

Thank you

Thank you to the participants who took part in the clinical trial for the trial drug AZD5462.

AstraZeneca AB sponsored this trial and believes it is important to share the results of this trial with the participants and the public. AstraZeneca AB reviewed the results of this trial when it ended and created a report of those results. This is a summary of that report.

An independent non-profit organization called CISCRP helped prepare this summary of the trial results. We hope it helps the participants understand and feel proud of their important role in medical research.

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

Who took part in this trial?

The researchers asked for the help of healthy people. In this trial, "healthy" meant that the participants did not have any heart problems or any other serious or long-term health conditions. The participants in this trial were 20 to 50 years old when they joined.

This trial included 94 males and 4 females in the United States.

Why was the research needed?

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

Heart failure is a condition in which the heart does not pump blood as well as it should. This can cause damage to the heart muscle and to other organs. It can also cause fluid to build up in the arms and legs.

People with heart failure often have less blood flowing into their kidneys, a worsened ability to repair damaged heart tissues, and less flexible blood vessel walls that increase resistance to blood flow around the body.

People who have heart failure also often get tired quickly, have trouble breathing, and may get fluid around their lungs and in their stomach area. Currently, treatments for heart failure focus on better diet and exercise, and medications to help with swelling and improve heart function. However, because many of these treatments do not improve symptoms or outcomes well enough, new treatments are needed.

RXFP1 is a protein that is found on certain cells in the body. When the RXFP1 protein is active, it causes better blood flow in the kidneys and blood vessels, allows the heart to work better, and allows the body to better repair damage in the heart.

The trial drug, **AZD5462**, is designed to make the RXFP1 protein more active. Researchers think that this may help improve the lives of people with heart failure.

What was the purpose of this trial?

This was a "Phase 1" trial. In this trial, the researchers wanted to find out if the participants had any medical problems during the trial.

The main questions researchers wanted to answer in this trial were:

- How did the participants' overall health change during the trial?
- What medical problems did the doctors report as possibly related to the trial treatment?

The answers to these questions are important to know before other trials can be done to find out if AZD5462 helps improve the health of people with heart failure.

What treatments did the participants take?

The participants in this trial took AZD5462 or a placebo. 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. The doses of AZD5462 were measured in milligrams (mg).

In this summary, "trial treatment" means anything the participants took as part of the trial. This includes AZD5462 and the placebo. AZD5462 is the treatment that the researchers wanted to learn more about.

This was a "single-blind" trial. This means the sponsor and the pharmacist at the trial site knew what the participants were taking but the participants, trial doctors, and other trial staff did not.

A computer program was used to randomly choose the treatment each participant took. 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.

This was also a "first-in-human" trial. This means that this trial was the first time that AZD5462 was given to people.

This trial had 2 parts. In both parts, researchers gave increasing dose levels of AZD5462, or a placebo, to small groups of participants. In **Part A**, small groups of participants took a **single dose** of AZD5462 or a placebo. In **Part B**, separate small groups of participants took **multiple doses** of AZD5462 or a placebo for up to 10 days.

For some of the dose levels of AZD5462, researchers wanted to look at the results for participants of Japanese descent separately from other participants. This meant that for all the participants in these groups, the participants' biological parents and all their grandparents were Japanese. Researchers do this to see how AZD5462 affects people of different ethnicities. So, some of the groups below are labeled as only having participants of Japanese descent.

The charts below show the treatment plan for the participants.

Part A

	AZD5462 20 mg	**AZD5462 80 mg**	**AZD5462 400 mg**	**AZD5462 400 mg** (Japanese Group)	**AZD5462 750 mg**	**AZD5462 750 mg** (Japanese Group)	**AZD5462 1,000 mg**	**Placebo**
	6 participants	6 participants	6 participants	6 participants	6 participants	6 participants	6 participants	14 participants
	20 mg of AZD5462	80 mg of AZD5462	400 mg of AZD5462	400 mg of AZD5462	750 mg of AZD5462	750 mg of AZD5462	1,000 mg of AZD5462	Placebo
	As a liquid taken by mouth							
	1 time on their second visit							

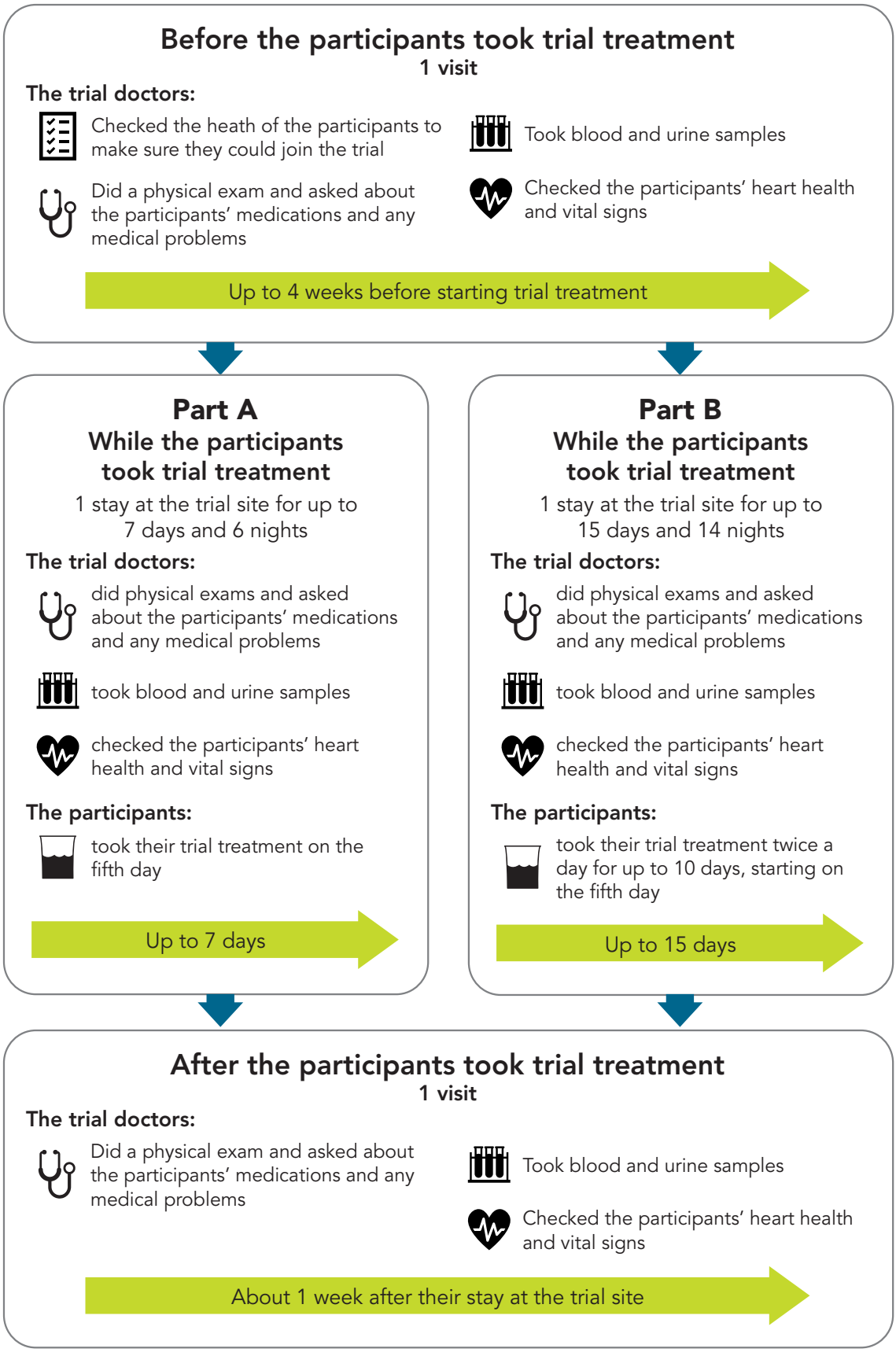
Part B						
	AZD5462 40 mg	**AZD5462 120 mg**	**AZD5462 250 mg**	**AZD5462 500 mg**	**AZD5462 500 mg** (Japanese Group)	**Placebo**
	6 participants	6 participants	7 participants	6 participants	7 participants	10 participants
	40 mg of AZD5462	120 mg of AZD5462	250 mg of AZD5462	500 mg of AZD5462	500 mg of AZD5462	Placebo
	As a liquid taken by mouth					
	Twice a day for up to 10 days					

What happened during this trial?

The participants in Part A were in the trial for up to about 6 weeks, and the participants in Part B were in the trial for up to about 7 weeks. But, the entire trial took 1 year and 2 months to finish.

The trial started in July 2021 and ended in September 2022.

The chart below shows what happened during the trial.



What were the results of this trial?

This is a summary of the main results from this trial overall. The individual results of each participant might be different and are not in this summary.

Researchers look at the results of many trials to decide which treatments work best and are safest. Other trials may provide new information or different results. Always talk to a doctor before making any treatment changes.

How did the participants' overall health change during the trial?

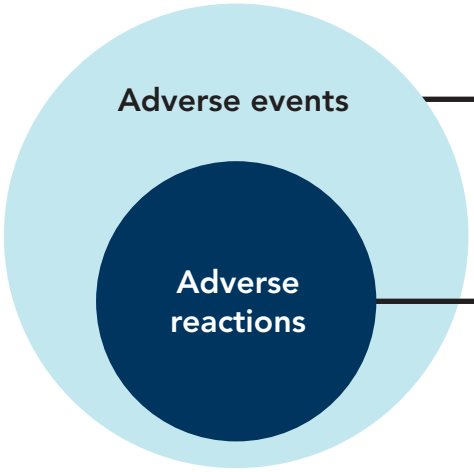
To answer this question, the doctors did tests and measurements of the participants' health throughout this trial. The doctors took blood and urine samples, did physical exams, checked the participants' heart health with an electrocardiogram (ECG), and checked vital signs. Then, the researchers compared the participants' results during the trial to their results from the start of the trial to see if there were any changes.

The researchers found that, on average, the participants who took AZD5462 had lower blood pressure and/or higher heart rate compared to the participants who took the placebo. Some participants who took AZD5462 and some participants who took the placebo also showed small changes in other tests and measurements. But, the researchers did not consider any of these results to be clinically meaningful.

The trial doctors also kept track of the "adverse events" that the participants had.

In this summary, there is information about 2 different types of medical problems that the participants had during this trial after taking the trial treatment. An **adverse event** is **any** medical problem that a participant has during a trial. Doctors keep track of all adverse events that happen in trials, whether or not these may be related to the trial treatment. An **adverse reaction** is different from an adverse event because it is reported by the doctor as **possibly related** to the trial treatment. An adverse event or adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care.

Adverse reactions are adverse events that the trial doctors think may be related to the trial treatments



Adverse events are all of the medical problems the participants had during this trial.

Adverse reactions are medical problems the participants had during this trial that the doctor reported as possibly related to the trial treatment.

The information below is a summary of the **adverse events** that happened in this trial.

Part A

	AZD5462 20 mg (out of 6 participants)	**AZD5462 80 mg** (out of 6 participants)	**AZD5462 400 mg** (out of 6 participants)	**AZD5462 400 mg** (Japanese Group) (out of 6 participants)	**AZD5462 750 mg** (out of 6 participants)	**AZD5462 750 mg** (Japanese Group) (out of 6 participants)	**AZD5462 1,000 mg** (out of 6 participants)	**Placebo** (out of 14 participants)
How many participants had any adverse events?	none	33.3% (2)	33.3% (2)	16.7% (1)	50.0% (3)	16.7% (1)	50.0% (3)	7.1% (1)
How many participants had serious adverse events?	none	none	none	none	none	none	none	none
How many participants stopped taking trial treatment due to adverse events?	none	none	none	none	none	none	none	none

Part B						
	AZD5462 40 mg (out of 6 participants)	**AZD5462 120 mg** (out of 6 participants)	**AZD5462 250 mg** (out of 7 participants)	**AZD5462 500 mg** (out of 6 participants)	**AZD5462 500 mg** (Japanese Group) (out of 7 participants)	**Placebo** (out of 10 participants)
How many participants had any adverse events?	50.0% (3)	16.7% (1)	42.9% (3)	66.7% (4)	42.9% (3)	20.0% (2)
How many participants had serious adverse events?	none	none	none	none	none	none
How many participants stopped taking trial treatment due to adverse events?	none	16.7% (1)	14.3% (1)	none	14.3% (1)	none

There were no serious adverse events that happened during this trial.

The most common adverse events in **Part A** were:

- Headache
- Itchy and swollen skin where a medical device was placed (also called medical device site dermatitis)
- Nausea

The most common adverse events in **Part B** were:

- Dizziness
- Headache
- Feeling sleepy (Somnolence)
- Nausea
- Vomiting
- Chills
- A greater than usual increase in heart rate after standing up

What medical problems did the doctors report as possibly related to the trial treatment?

This section is a summary of the medical problems that the participants had during this trial that the doctors reported as **possibly related** to the trial treatment. 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. The results from several trials are needed to decide if a treatment causes an adverse reaction.

In this trial, the doctors did not know what the participants were taking when the medical problems happened. So, some adverse reactions may be reported in participants who took the placebo, even though the placebo does not directly cause medical problems.

The websites listed at the end of this summary may have other information about adverse reactions or other medical problems that happened during this trial.

Did any adverse reactions happen during this trial?

There were 18.4% of participants who had adverse reactions in this trial. This was 18 out of 98 participants.

	Part A							
	AZD5462 20 mg (out of 6 participants)	**AZD5462 80 mg** (out of 6 participants)	**AZD5462 400 mg** (out of 6 participants)	**AZD5462 400 mg** (Japanese Group) (out of 6 participants)	**AZD5462 750 mg** (out of 6 participants)	**AZD5462 750 mg** (Japanese Group) (out of 6 participants)	**AZD5462 1,000 mg** (out of 6 participants)	**Placebo** (out of 14 participants)
How many participants had any adverse reactions?	none	16.7% (1)	33.3% (2)	16.7% (1)	16.7% (1)	16.7% (1)	33.3% (2)	7.1% (1)
How many participants had serious adverse reactions?	none	none	none	none	none	none	none	none
How many participants stopped taking trial treatment due to adverse reactions?	none	none	none	none	none	none	none	none

	Part B					
	AZD5462 40 mg (out of 6 participants)	**AZD5462 120 mg** (out of 6 participants)	**AZD5462 250 mg** (out of 7 participants)	**AZD5462 500 mg** (out of 6 participants)	**AZD5462 500 mg** (Japanese Group) (out of 7 participants)	**Placebo** (out of 10 participants)
How many participants had any adverse reactions?	16.7% (1)	16.7% (1)	14.3% (1)	66.7% (4)	14.3% (1)	10.0% (1)
How many participants had serious adverse reactions?	none	none	none	none	none	none
How many participants stopped taking trial treatment due to adverse reactions?	none	16.7% (1)	14.3% (1)	none	none	none

What serious adverse reactions happened during this trial?

There were no serious adverse reactions that happened during this trial.

What adverse reactions happened during this trial?

The most common adverse reaction in **Part A** was headache.

The most common adverse reactions in **Part B** were:

- Dizziness
- Feeling sleepy (Somnolence), and
- A greater than usual increase in heart rate after standing up

The adverse reactions below happened in 2 or more participants total. There were other adverse reactions, but each of those happened in only 1 participant.

Part A

Adverse reaction	AZD5462 20 mg (out of 6 participants)	AZD5462 80 mg (out of 6 participants)	AZD5462 400 mg (out of 6 participants)	AZD5462 400 mg (Japanese Group) (out of 6 participants)	AZD5462 750 mg (out of 6 participants)	AZD5462 750 mg (Japanese Group) (out of 6 participants)	AZD5462 1,000 mg (out of 6 participants)	Placebo (out of 14 participants)
Headache	none	none	16.7% (1)	none	none	none	33.3% (2)	none
Nausea	none	none	none	16.7% (1)	none	none	none	7.1% (1)

Part B

Adverse reaction	AZD5462 40 mg (out of 6 participants)	AZD5462 120 mg (out of 6 participants)	AZD5462 250 mg (out of 7 participants)	AZD5462 500 mg (out of 6 participants)	AZD5462 500 mg (Japanese Group) (out of 7 participants)	Placebo (out of 10 participants)
Dizziness	none	16.7% (1)	14.3% (1)	none	none	none
Feeling sleepy (Somnolence)	none	none	none	33.3% (2)	none	none
A greater than usual increase in heart rate after standing up	16.7% (1)	none	none	none	14.3% (1)	none

What did researchers learn from this trial?

This trial helped researchers learn more about how safe different dose levels of AZD5462 are in healthy people. These results will give researchers an idea of how safe AZD5462 would be in people with heart failure. The researchers concluded that there were no major safety or tolerability concerns with AZD5462 in this trial.

Researchers look at the results of many trials to decide which treatments work best and are safest. This summary shows only the main results from this one trial. Other trials may provide new information or different results.

At the time this summary was made and approved by the sponsor, further clinical trials with AZD5462 were planned.

Where can I learn more about this trial?

You can find more information about this trial on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **NCT04994106** into the "Other terms" search box and click "Search".
- www.AstraZenecaClinicalTrials.com Once you are on the main page of the website, scroll down to "Find a clinical trial". Then, type **D9090C00001** into the search box, and click "Search clinical trial".

Full Trial Title: A Phase I randomized, single-blind, placebo-controlled study to assess the safety, tolerability, and pharmacokinetics of AZD5462 following single and multiple ascending dose administration to healthy volunteers

National Clinical Trials Number: NCT04994106

AstraZeneca Protocol Number: D9090C00001

AstraZeneca AB sponsored this trial and has its headquarters at Södertälje, Sweden. The phone number for the AstraZeneca Information Center is 1-877-240-9479.

Thank you

Clinical trial 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 trials, nor is it involved in conducting clinical trials.

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

Version 1.0 2024_01_11