AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: AZD9977

Study Purpose: This study was done to learn how AZD9977 worked compared to spironolactone in participants with heart failure who have mild or moderate kidney disease

Protocol Number: D6401C00004

Thank you!

Thank you for taking part in the clinical study for the study drug AZD9977.

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 this study?

The researchers asked for the help of men and women with heart failure and mild or moderate kidney damage. The participants in this study were 51 to 89 years old when they joined.

The study included 68 participants in Bulgaria, the Czech Republic, Poland, and the United Kingdom.

Why was the research needed?

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

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 make the heart change shape. It can also cause fluid to build up in the arms and legs. There are treatments for heart failure, but some of these treatments can increase the amount of potassium in the blood. High potassium levels may also develop in people with kidney disease.

People with high levels of potassium in their blood often do not have any symptoms that can be detected. But, they may have problems with their heartbeat. This can be dangerous and in rare cases, can lead to death.

In this study, the researchers wanted to find out if AZD9977 increased the participants' blood potassium levels less than a drug for heart failure called spironolactone.

What was the purpose of this study?

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

- How did AZD9977 affect the participants' blood potassium levels?
- 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 to find out if AZD9977 helps improve the health of people with heart failure and kidney damage.

What treatments did the participants take?

In this study, all of the participants took either AZD9977 or spironolactone as capsules by mouth.

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was taking.

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.

The participants took their randomly chosen study treatment once a day for 4 weeks. The doses of AZD9977 and spironolactone were measured in milligrams, also called mg.

- For the first 2 weeks of the study, the participants took 100 mg AZD9977 or 25 mg of spironolactone.
- For the last 2 weeks of the study, the participants took 200 mg of AZD9977 or 50 mg of spironolactone.

The study doctors monitored each participant's blood potassium during the study. If it got too high, the participant stopped taking the study treatment and left the study.

The chart below shows the treatments the researchers planned to study.

	AZD9977	Spironolactone
	• 33 participants	• 35 participants
	• 100 mg of AZD9977 • Then, 200 mg of AZD9977	• 25 mg of spironolactone • Then, 50 mg of spironolactone
	• The first dosage once a day in the morning for 2 weeks • Then, the next dosage once a day in the morning for 2 weeks for a total of 4 weeks	

What happened during this study?

The study started in November 2018 and ended in March 2020.

Before the participants took study treatment, they visited their study site 1 time. This part of the study lasted for 2 weeks. 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 samples to check the participants' blood potassium levels
- took blood and urine samples for testing
- checked the participants' heart health using an electrocardiogram, also known as an ECG

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

While the participants were taking study treatment, most of the participants visited their study site 5 times. Because of country requirements, the participants in the United Kingdom visited their study site more often. They visited up to a total of 8 times and had extra tests to measure their blood potassium levels. This part of the study lasted 4 weeks.

After the participants took study treatment, they visited their study site 1 time. This part of the study lasted 1 week. At these visits, the study doctors checked the health of the participants.

What were the results of this 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.

How did AZD9977 affect the participants' blood potassium levels?

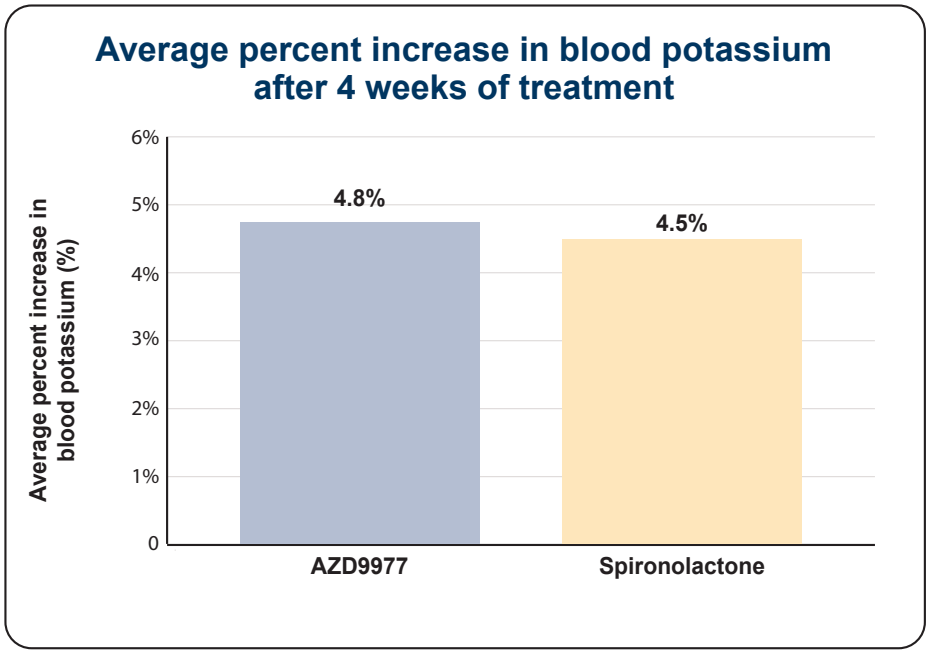
Overall, the researchers found that AZD9977 increased the amount of potassium in the participants' blood by about the same amount as spironolactone did.

To answer this question, the study doctors measured the amount of potassium in the participants' blood. The researchers compared the participants' blood potassium at the start of the study with their blood potassium after taking the study treatment for 4 weeks. They calculated the difference as a percentage. Then, they compared these results between the participants who took AZD9977 and those who took spironolactone.

Overall, the researchers found that after 4 weeks of treatment, the average percentage increase in blood potassium was:

- 4.8% for the participants who took AZD9977
- 4.5% for the participants who took spironolactone

The graph below shows these results.



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 the study treatments. 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 treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for AZD9977.

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.

Did any adverse reactions happen during this study?

The table below shows how many participants had adverse reactions during the study.

	AZD9977 (out of 33 participants)	Spironolactone (out of 35 participants)
How many participants had adverse reactions?	9.1% (3)	5.7% (2)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	3.0% (1)	5.7% (2)

None of the participants had to stop taking AZD9977 because their blood potassium got too high.

What serious adverse reactions happened during this study?

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

None of the participants in this study died due to serious adverse reactions.

What adverse reactions happened during this study?

The table below shows the adverse reactions that happened during the study. Some of the participants had more than 1 adverse reaction.

Adverse reactions

Adverse reaction	AZD9977 (out of 33 participants)	Spironolactone (out of 35 participants)
Diarrhea	3.0% (1)	0.0% (0)
Headache	3.0% (1)	0.0% (0)
High blood pressure	3.0% (1)	0.0% (0)
Nausea	3.0% (1)	0.0% (0)
Itchy skin	3.0% (1)	0.0% (0)
Kidney failure	0.0% (0)	2.9% (1)
Kidneys not working properly	0.0% (0)	2.9% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how AZD9977 worked in participants with heart failure and mild or moderate kidney disease.

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 AZD9977 are planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. When a full report of the study results is available, it also can be found here.

- www.clinicaltrials.gov Once you are on the website, type **"NCT03682497"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search",** then type **"2018-000707-16"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D6401C00004"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase I, Open Label, Randomised, Parallel Group, Multicentre Study to Compare the Effect of AZD9977 and Spironolactone on Serum Potassium [sK^+] during 28 Days in Patients with HFmrEF or HFpEF and eGFR in the Range of ≥ 40 and ≤ 70 mL/min/1.73 m^2

AstraZeneca AB Protocol Number: D6401C00004

National Clinical Trials Number: NCT03682497

EudraCT Number: 2018-000707-16

AstraZeneca sponsored this study and has its headquarters at Cambridge, UK.

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

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