Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Sodium zirconium cyclosilicate

Study Title: A study to learn how sodium zirconium cyclosilicate affects potassium levels in the blood

Thank you!

Thank you to the participants who took part in the clinical study for the study drug sodium zirconium cyclosilicate, also called ZS. You and all of the participants helped researchers learn more about ZS to help people who have high potassium levels in their blood.

AstraZeneca sponsored this study and thinks 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 you understand and feel proud of your 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 study started in March 2017 and ended in February 2018. The study included 267 participants in Japan, the Republic of Korea, Russia, and Taiwan.

The study had 2 parts, Part 1 and Part 2. The participants who were only in Part 1 were in the study for up to 10 days. The participants who were in both Part 1 and Part 2 were in the study for up to 45 days.

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 with high potassium levels in their blood. Before a drug can be approved for patients to take, researchers do clinical studies to find out how it works and how safe it is.

In this study, the researchers wanted to find out if ZS works in a number of participants around the world with high blood potassium levels. They also wanted to find out if the participants had any medical problems during the study.

Potassium is found in many foods. It helps the body control blood pressure, heart rhythm, and do other important tasks. When potassium levels in the blood become too high, the body may not be able to do these tasks well. This can lead to several medical problems. People can develop high potassium levels if their diet has too much potassium, or if their body cannot get rid of enough potassium through stool.

There are treatments for high potassium, but these treatments can cause constipation and other medical problems. So, researchers are looking for new ways to treat high potassium levels. ZS may be able to lower potassium levels by helping the body get rid of potassium through urine or stool.

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

- Did ZS help keep potassium levels normal?
- Did ZS affect the participants' overall health?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with high potassium levels. The participants in this study were 31 to 90 years old.

What kind of study was this?

Part 1 of the study was "open-label". This means the researchers and the participants knew that the participants took ZS during this part.

In Part 1, all of the participants took ZS by mouth.

Part 2 of the study was "double-blind". This means none of the participants, doctors, or other study staff knew which treatment each participant took during this part. Some studies are done this way because knowing what treatment the participants are taking can affect the results of the study. When the study ended, the research sponsor found out which treatment the participants took so they could create a report of the study results.

In Part 2, the participants took either ZS or a placebo by mouth. A placebo looks like a drug but does not have any medicine in it. Researchers use a placebo to make sure any of the effects they see in the participants who take a drug are actually caused by that drug.

A computer program was used to randomly choose the treatment each participant took in Part 2. 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.

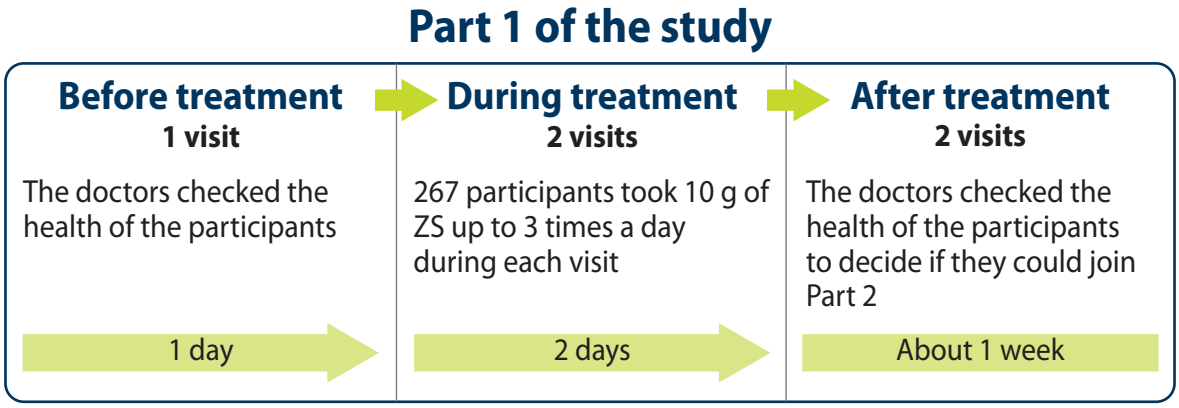
What happened during the study?

Before treatment and throughout the study, the doctors checked the participants' health to make sure they could continue in the study. The doctors did tests and exams, gave surveys to ask how the participants were feeling, and measured the participants' potassium levels.

During Part 1, the participants visited their study site up to 2 times. These visits happened once a day for 2 days in a row. During both visits, the participants took ZS by mouth as a powder with water. Doses were measured in grams, also called g. The participants took 10 g of ZS up to 3 times a day at both visits.

After taking ZS in Part 1, the participants visited their study site 1 more time so the doctors could check their health and potassium levels again. If a participant's potassium had reached normal levels by the time of this visit, the participant could continue into Part 2. If a participant's potassium had not reached normal levels, the participant did not continue into Part 2 and came back to the site about 1 week later for the end of study visit.

The chart below shows how Part 1 of the study was done.



Out of the 267 participants in Part 1, there were 248 participants who continued into Part 2. The other 19 participants left for 1 of the following reasons:

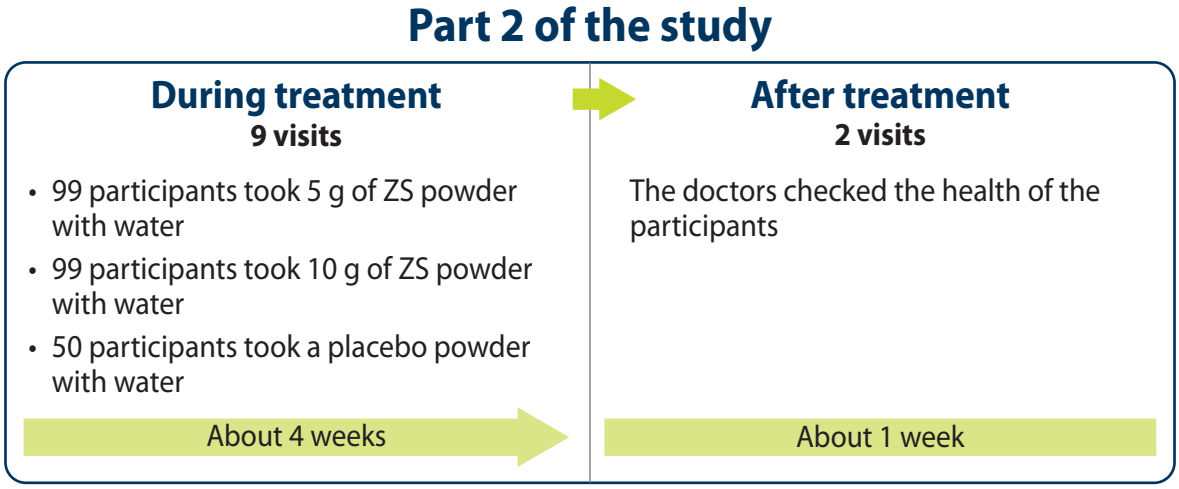
- not healthy enough to join Part 2
- did not follow study instructions
- personal reasons

During Part 2, the participants visited their study site up to 9 times over the course of about 4 weeks. During this time period, the participants took 1 of the below treatments once a day by mouth:

- 5 g of ZS powder with water
- 10 g of ZS powder with water
- a placebo powder with water

After taking ZS or the placebo in Part 2, the participants visited their study site 2 more times so the doctors could check their health and potassium levels.

The chart below shows how Part 2 of the study was done.



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. More information about the questions the researchers wanted to answer can be found on the websites listed at the end of this summary. A full report of the study results may also be available on these websites.

Researchers usually need 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.

Did ZS help keep potassium levels normal?

Yes. Overall in Part 2, the researchers found that more participants who took ZS had their potassium stay at normal levels compared to the participants who took the placebo.

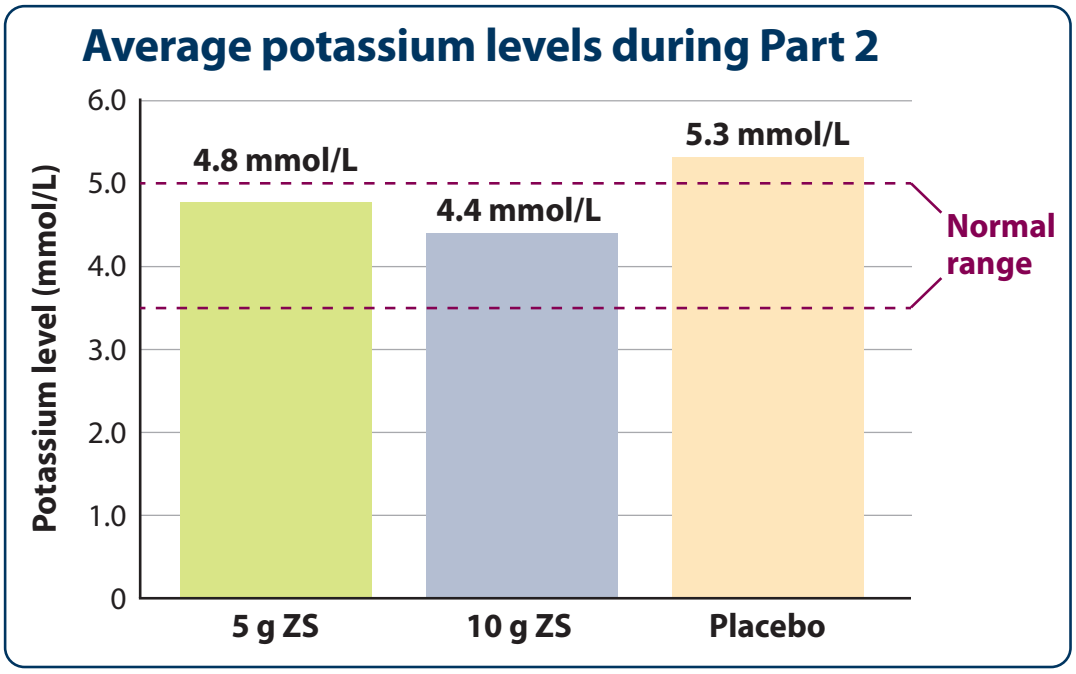
To answer this question, the researchers studied the potassium levels of the participants in Part 2. These participants had high potassium levels at the beginning of the study, but their potassium had reached normal levels before they entered Part 2.

The potassium levels were measured in millimoles per liter, also called mmol/L. This measurement is commonly used by researchers to study blood and other fluids in the body. Researchers generally consider normal potassium levels to be between 3.5 mmol/L and 5.0 mmol/L.

At the end of Part 2, the researchers found:

- The participants who took 5 g of ZS had an average potassium level of 4.8 mmol/L
- The participants who took 10 g of ZS had an average potassium level of 4.4 mmol/L
- The participants who took the placebo had an average potassium level of 5.3 mmol/L

The figure below shows these results.



Did ZS affect the participants' overall health?

No. The researchers found that throughout the study, the participants had very little change in their overall health.

To answer this question, the researchers gave the participants surveys throughout the study that asked them how they were feeling. In general, participants' survey scores did not change throughout the study.

What medical problems did the participants have during the 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 drug.

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.

Usually the results from several studies are needed to decide if a treatment causes an adverse reaction. At the time of this study, it was not known if these adverse reactions were or were not caused by the study treatment.

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?

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

None of the participants died because of adverse reactions during the study.

How many participants had adverse reactions?

There were 0.4% of participants who had adverse reactions during Part 1 of the study. This was 1 out of 267 participants.

There were 5.2% of participants who had adverse reactions during Part 2 of the study. This was 13 out of 248 participants.

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

Adverse reactions during the study

	Part 1 (out of 267 participants)	Part 2 (out of 248 participants)		
	10 g ZS (out of 267 participants)	5 g ZS (out of 99 participants)	10 g ZS (out of 99 participants)	Placebo (out of 50 participants)
How many participants had adverse reactions during the study?	0.4% (1)	4.0% (4)	8.1% (8)	2.0% (1)
How many participants had serious adverse reactions during the study?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
How many participants stopped treatment because of adverse reactions?	0.4% (1)	3.0% (3)	3.0% (3)	2.0% (1)

What adverse reactions did the participants have?

The most common adverse reaction during the study was constipation. The table below shows the adverse reactions that happened during the study.

Adverse reactions

	Part 1 (out of 267 participants)	Part 2 (out of 248 participants)		
	10 g ZS (out of 267 participants)	5 g ZS (out of 99 participants)	10 g ZS (out of 99 participants)	Placebo (out of 50 participants)
Constipation	0.0% (0)	1.0% (1)	3.0% (3)	0.0% (0)
Swelling in the lower limbs	0.4% (1)	1.0% (1)	0.0% (0)	0.0% (0)
Swelling in the body	0.0% (0)	0.0% (0)	2.0% (2)	0.0% (0)
Increase in potassium levels in the blood	0.0% (0)	1.0% (1)	0.0% (0)	0.0% (0)
Irregular heartbeat	0.0% (0)	1.0% (1)	0.0% (0)	0.0% (0)
Decrease in potassium levels in the blood	0.0% (0)	0.0% (0)	1.0% (1)	0.0% (0)
Diarrhea	0.0% (0)	0.0% (0)	1.0% (1)	0.0% (0)
Swelling in the body caused by kidney disease	0.0% (0)	0.0% (0)	1.0% (1)	0.0% (0)
Blockage in the airway to the lungs	0.0% (0)	0.0% (0)	0.0% (0)	2.0% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about using ZS to treat people with high blood potassium levels.

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 ZS 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 "**NCT02875834**" into the search box, and click "**Search**".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D9480C00002"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase 3 Multicentre, Prospective, Randomised, Double-Blind, Placebo-Controlled Study to Investigate the Safety and Efficacy of Sodium Zirconium Cyclosilicate (ZS) in Patients with Hyperkalaemia—HARMONIZE Global

AstraZeneca Protocol Number: D9480C00002

AstraZeneca sponsored this study and has its headquarters at 1800 Concord Pike in Wilmington, Delaware.

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.