Clinical Study Results

Research Sponsor: AstraZeneca KK

Drug Studied: Sodium zirconium cyclosilicate, also called ZS

Study Title: A study to learn how safe ZS is for Japanese participants with high levels of potassium in their 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. All of the participants helped researchers learn more about ZS to help people with high levels of potassium in their blood. This condition is also called hyperkalemia.

AstraZeneca KK 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 the participants understand and feel proud of their 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 participants were in the study for up to about 1 year, but the entire study took about 2 years to finish. The study started in September 2017 and ended in July 2019.

The study included 150 participants in Japan.

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 safe it is and how it works.

The researchers did earlier ZS studies in other groups of participants. When this study started, the researchers had gathered only a small amount of information on how ZS works in Japanese participants. In this study, the researchers wanted to find out if Japanese participants with high blood potassium had any medical problems while taking ZS.

People with high levels of potassium in their blood often don't have any symptoms that can be seen, but they may have problems with their heartbeat. This can be dangerous and in rare cases, it can lead to death.

ZS was designed to work by attaching to potassium in the gut and stopping it from getting into the blood.

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

- Did the participants' safety results change during the study?
- Did the participants feel their health was better after taking ZS?
- What medical problems did the participants have during the study that may have been caused by ZS?

To answer the questions in this study, the researchers asked for the help of men and women with high blood potassium. The participants in this study were 25 to 95 years old. People who had taken ZS within 30 days of the start of the study could not take part.

What kind of study was this?

This was an “open-label” study. This means the researchers and the participant knew what the participant was taking.

ZS was taken by mouth, as a powder mixed with water. The doses of ZS were measured in grams, also called g.

There were 2 parts to this study, and there were different treatments in each part.

Part 1

In this part of the study, all of the participants took 10 g of ZS. They took this dose 3 times a day for up to 3 days. The amount of time that each participant was in Part 1 was based on the participant’s blood potassium levels.

The chart below shows the treatments the participants took in Part 1:

Number of days in Part 1	Number of total doses	Total amount of ZS
1 day	3	30 g
2 days	6	60 g
3 days	9	90 g

If a participant’s blood potassium level was normal, they could join Part 2 of the study right away. At the end of Part 1 all participants had normal blood potassium levels and joined Part 2 of the study.

Part 2

In this part of the study, participants took ZS for up to a year. All of the participants took 5 g of ZS once a day when they started Part 2, but the doctor could increase or decrease their amount of ZS. This was based on how high their blood potassium was at their study site visits. During Part 2, the dose could be increased to 15 g each day, or decreased to either:

- 5 g every other day
- 2.5 g every day

What happened during the study?

Before the participants took the study treatment, they visited the study site 1 time so the doctors could get information about their medical history. Then, they visited the site again. At this visit, the doctors:

- checked the overall health of the participants to make sure that they could join the study
- took blood samples to check the participants' blood potassium levels
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also known as an ECG

These tests were done at the same visit that the participants started taking the study treatment.

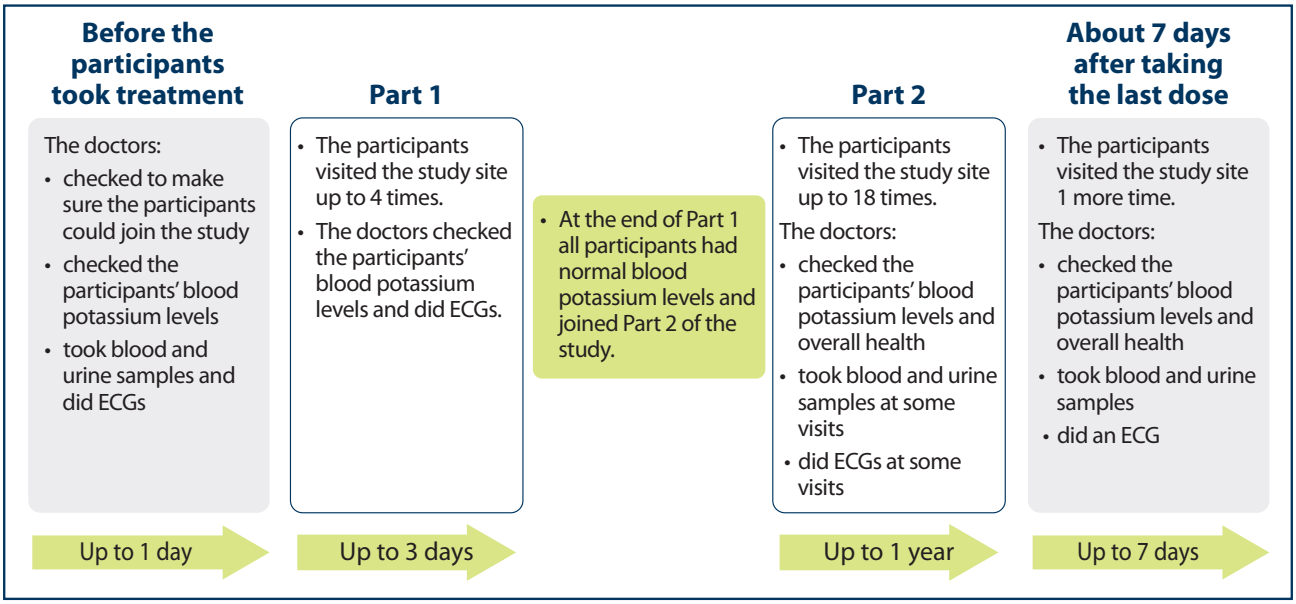
During Part 1, the participants visited the study site up to 4 days in a row. At each visit, the participants took ZS 1 time. The participants could take the 2 other doses at home later that day. The doctors checked the participants' blood potassium levels, heart health, and overall health at every visit.

Any participants who had normal blood potassium levels could start Part 2 of the study right away, even if they had not had the full 3 days of treatment.

During Part 2, the participants visited the study site 18 times. At these visits, the doctors checked the participants' blood potassium levels, their overall health, their heart health, and took blood and urine samples.

About 7 days after taking the last dose of ZS, the participants visited the study site 1 more time. At this visit, the doctors checked their blood potassium levels, their overall health, and their heart health, and took blood and urine samples.

The chart below shows what happened during the study.



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. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. If a full report of the study results is available, it can also be found on these websites.

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.

Did the participants' safety results change during the study?

No. Overall, the participants' safety results did not change during the study.

To answer this question, the doctors did tests and measurements before and after the participants took ZS. The doctors did physical exams and tested the participants' blood and urine samples to check their overall health. They also did ECGs to check the participants' heart health. Overall, the researchers found that there were some small changes in the results of these tests and measurements. But, the researchers did not consider these to be significant.

The doctors also kept track of the "adverse events" that the participants had. An adverse event is any medical problem that happens during the study. Adverse events are considered "serious" when they are life-threatening, cause lasting problems, or require hospital care. Adverse events may or may not be caused by the study drugs. This section talks about adverse events that happened during the study. Some of these adverse events are also included in the "What medical problems did participants have during the study?" section.

In Part 1 of the study:

How many participants had adverse events?

- 3.3% of participants had adverse events. This was 5 out of 150 participants.
- 0.7% of participants had serious adverse events. This was 1 out of 150 participants. This serious adverse event was diabetes.
- There were no deaths due to adverse events, and none of the participants stopped taking ZS because of adverse events.

What serious adverse events did the participants have?

The only serious adverse event in Part 1 of the study was diabetes.

What adverse events did the participants have?

The table below shows the adverse events that happened in Part 1 of the study.

Adverse reactions during Part 1 of the study

	ZS 3 times a day (out of 150 participants)
A cold and sore throat	0.7% (1)
Diabetes	0.7% (1)
Irregular heartbeat	0.7% (1)
Fatty liver	0.7% (1)
Generally feeling unwell	0.7% (1)

In Part 2 of the study:

How many participants had adverse events?

- 87.3% of participants had adverse events. This was 131 out of 150 participants.
- 18.0% of participants had serious adverse events. This was 27 out of 150 participants.
- 1.3% of participants died due to adverse events. This was 2 out of 150 participants.
- 8.0% of participants stopped taking ZS because of adverse events. This was 12 out of 150 participants.

What serious adverse events did the participants have?

The most common serious adverse event was heart failure. Heart failure is a condition in which the heart is not able to pump enough blood around the body. The table below shows the serious adverse events that happened in 2 or more participants. There were other serious adverse events, but these happened in fewer participants.

Serious adverse events in 2 or more participants during Part 2 of the study

	ZS once a day or every other day (out of 150 participants)
Heart failure caused by a build-up of fluid around the heart	2.7% (4)
Lung infection	2.0% (3)
Vision problems (cataract)	1.3% (2)

2 participants died during the study. The researchers did not think that these deaths were related to ZS. 1 participant died from cancer and the other died from heart failure.

What adverse events did the participants have?

The most common adverse event was a cold and cough. The table below shows the adverse events that happened in 5 or more participants. There were other adverse events, but these happened in fewer participants.

Adverse events in 5 or more participants during Part 2 of the study

	ZS once a day or every other day (out of 150 participants)
A cold and cough	24.0% (36)
High blood pressure	15.3% (23)
Swelling in arms and legs	15.3% (23)
Constipation	13.3% (20)
Vision problems (cataract)	4.7% (7)
General swelling	4.7% (7)
Joint pain	4.0% (6)
Back pain	4.0% (6)
Bruising	4.0% (6)
Cough	4.0% (6)
Low blood sugar	4.0% (6)
Lung infection	4.0% (6)
Type 2 diabetes	4.0% (6)
Heart failure caused by a build-up of fluid around the heart	3.3% (5)
Too much uric acid in the blood	3.3% (5)

Did the participants feel their health was better after taking ZS?

No. Overall, the participants felt that their health was the same after taking ZS.

To answer this question, the doctors used a survey called the 36-item Short Form Survey, also called SF-36. The participants answered this survey before and after taking ZS. The doctors asked the participants if they felt their health was the same as, better, or worse than 1 year earlier.

Before taking ZS:

- 18.0% of participants said that their health was better than 1 year ago. This was 27 out of 150 participants.
- 60.7% of participants said that their health was the same as 1 year ago. This was 91 out of 150 participants.
- 21.3% of participants said that their health was worse than 1 year ago. This was 32 out of 150 participants.

There were 22 participants who did not complete Part 2. So, only 128 participants are included in the results below.

After taking ZS:

- 26.6% of participants said that their health was better than 1 year ago. This was 34 out of 128 participants.
- 62.5% of participants said that their health was the same as 1 year ago. This was 80 out of 128 participants.
- 10.9% of participants said that their health was worse than 1 year ago. This was 14 out of 128 participants.

What medical problems did 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.

These adverse reactions may or may not be caused by the study drug. A lot of research is needed to know whether a drug causes an adverse reaction.

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?

There were 0.7% of participants who had serious adverse reactions during the study. This was 1 out of 150 participants. This serious adverse reaction was an irregular heartbeat that stopped the heart from pumping blood properly.

None of the participants died due to a serious adverse reaction during this study.

How many participants had adverse reactions?

There were 20.0% of participants who had adverse reactions during the study. This was 30 out of 150 participants.

All of these adverse reactions happened during Part 2 of the study.

There were 8.0% of participants who stopped taking ZS because of adverse reactions they had during the study. This was 12 out of 150 participants.

What adverse reactions did the participants have?

The most common adverse reaction was constipation. This happened in 6.7% of participants during the study. This was 10 out of 150 participants.

The table below shows the most common adverse reactions that happened in more than 1 participant during the study. There were other adverse reactions, but each of these only happened in 1 participant. All of the adverse reactions happened in Part 2.

Most common adverse reactions in Part 2 during the study

	ZS once a day (out of 150 participants)
Constipation	6.7% (10)
Swelling in the arms and legs	4.0% (6)
High blood pressure	2.7% (4)
Retaining fluid in the body	1.3% (2)
Heart failure caused by a build-up of fluid around the heart	1.3% (2)
General swelling	1.3% (2)

How has this study helped patients and researchers?

This study helped researchers learn about the safety of ZS in a large number of Japanese patients with high blood potassium.

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 **"NCT03172702"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D9482C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase 3 Multicenter Open-label Maintenance Study to Investigate the Long-term Safety of ZS (Sodium Zirconium Cyclosilicate) in Japanese Subjects with Hyperkalemia

National Clinical Trials number: NCT03172702

AstraZeneca Protocol Number: D9482C00001

AstraZeneca KK, sponsored this study and has its headquarters in Osaka, Japan.

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.