Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drug Studied: Sodium zirconium cyclosilicate

Study Title: A study to learn how sodium zirconium cyclosilicate affects blood potassium levels in patients who have kidney failure and are getting hemodialysis

Thank you!

Thank you to the participants who took part in the clinical study for the drug sodium zirconium cyclosilicate, also called SZC. All of the participants helped researchers learn more about SZC to help people who have kidney failure and high levels of potassium 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 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 study started in December 2017 and ended in November 2018. The participants were in the study for up to about 3 months. But, the entire study took about 1 year to finish.

The study included 196 participants. The participants were in Japan, Russia, the United Kingdom, and the United States.

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?

In this study, the researchers wanted to find out if sodium zirconium cyclosilicate, also called SZC, works in many participants who have kidney failure and high levels of potassium in their blood. They also wanted to find out if the participants had any medical problems during the study.

Potassium is found in many foods, such as bananas and potatoes. It helps the body perform several important functions, including maintaining a normal blood pressure and heart rhythm. When levels of potassium in the blood become too high, the body may not be able to perform these functions well. This can lead to medical problems.

A common cause of high potassium levels is kidney failure. Healthy kidneys remove toxins and potassium from the body through urine, which keeps potassium at normal levels in the blood. In people who have kidney failure, the kidneys may not be able to remove these substances. This can lead to high blood potassium levels. Researchers think that SZC may be able to help lower blood potassium levels by helping the body get rid of potassium through stool.

In earlier studies, researchers found that SZC lowered potassium levels in a large number of participants who had kidney failure and high blood potassium levels. In this study, the researchers wanted to find out how SZC works in participants with high blood potassium levels and kidney failure who need hemodialysis treatment. In this treatment, a patient is attached to a machine that acts like healthy kidneys to remove substances from his or her body.

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

- Did the participants' blood potassium levels become normal after taking SZC?
- What new medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of people with high potassium levels and kidney failure who had been getting hemodialysis for at least 3 months before joining the study. The men and women in this study were 20 to 86 years old.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, doctors, or other study staff knew what treatment each participant took. 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 participants took so they could create a report of the study results.

In this study, some of the participants took SZC by mouth as a powder mixed with water. The other participants took a placebo by mouth as a powder mixed with water. 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 SZC doses were measured in grams, also called g.

During the study, the participants were also allowed to take a treatment chosen by the doctors for their kidney failure. This treatment was called a “rescue treatment”. Doctors use rescue treatments in studies if they think it can help participants manage their disease without affecting the study results.

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.

What happened during the study?

Before the study started, the participants visited their study site 3 times. At these visits, the doctors checked to make sure the participants could join the study. The doctors:

- did a physical examination
- took blood samples
- checked the participants’ heart health using an electrocardiogram, also called an ECG
- checked the participants’ blood potassium levels
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

During the study, the participants visited their study site 19 times over the course of about 8 weeks. Each week, the participants:

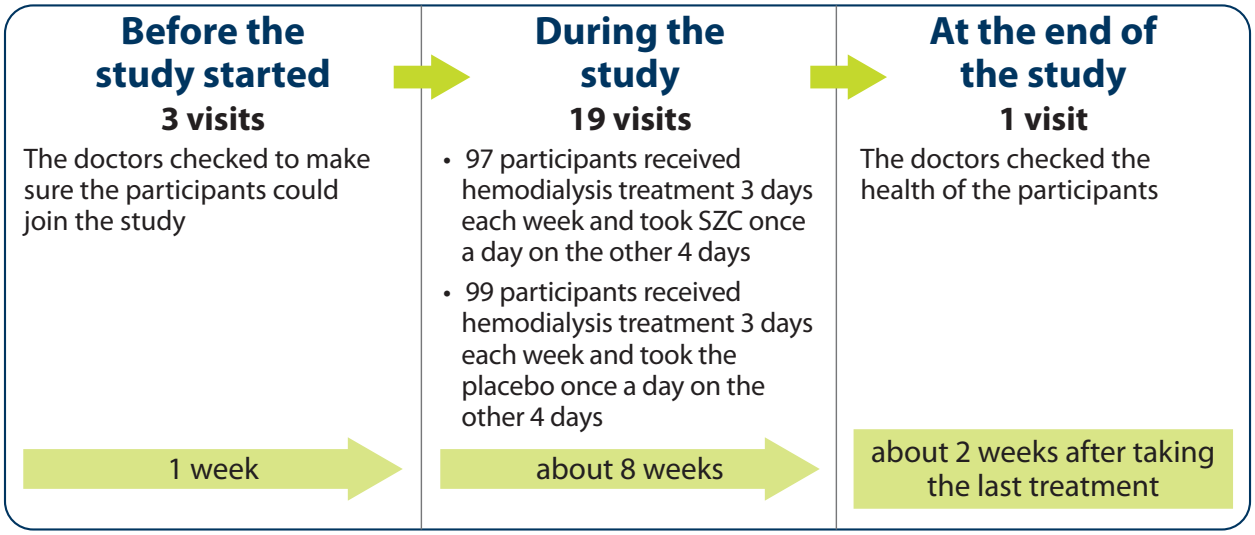
- received hemodialysis treatment for 3 days
- took SZC or the placebo once a day on the other 4 days
- took rescue treatment if needed

The participants who took SZC started by taking a dose of 5 g. The doctors studied the participants' blood potassium levels every week during the first 4 weeks. If a participant's potassium levels did not improve, the doctors could increase the SZC dose up to a total of 15 g over the course of these 4 weeks. The dose that each participant was taking at the end of these first 4 weeks was the same dose that he or she took for the next 4 weeks.

Throughout the study, the doctors took blood samples and checked the participants' blood potassium levels.

At the end of the study, the participants visited their study site 1 time. At this visit, the doctors checked the participants' blood potassium levels and asked them how they were feeling.

The chart below shows how 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. A full list of the questions the 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' blood potassium levels become normal after taking SZC?

Yes. Overall, the researchers found that more participants who took SZC had their blood potassium reach normal levels compared to the participants who took the placebo.

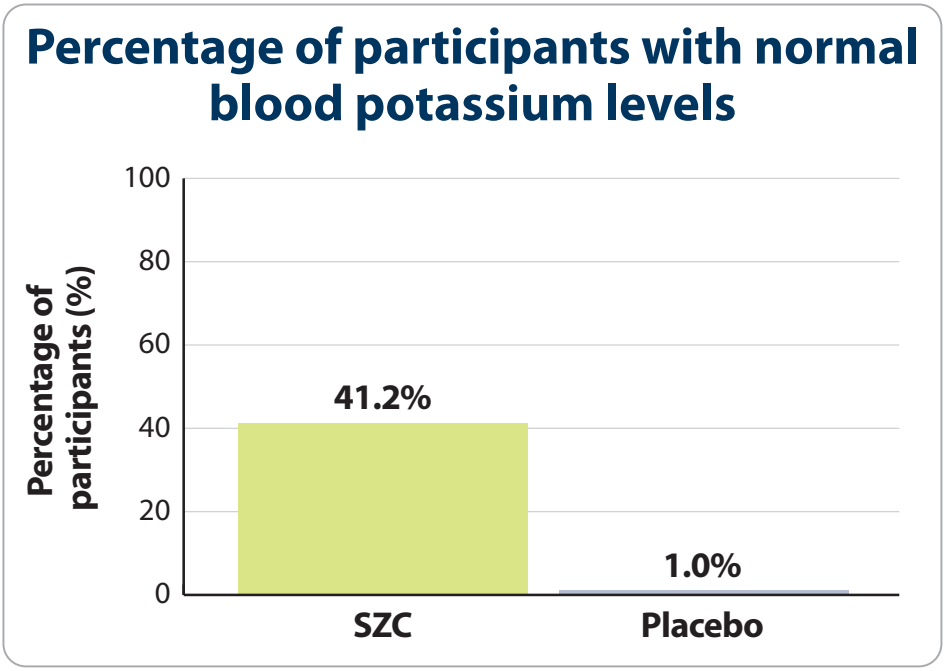
To answer this question, the researchers measured the participants' blood potassium levels throughout the study. Blood potassium levels are measured in millimoles per liter, also called mmol/L. In this study, the researchers considered normal blood potassium levels to be between 4.0 mmol/L and 5.0 mmol/L. This is a widely accepted range in the global scientific community.

The researchers considered a participant's blood potassium to have reached normal levels if his or her levels were between 4.0 mmol/L and 5.0 mmol/L at 3 of the 4 hemodialysis visits during the final 4 weeks of treatment. The researchers focused on the results during this time because the participants who took SZC did not have a change in their SZC dose during these 4 weeks. The researchers also focused on the participants who did not need rescue treatment during this time.

The researchers found that during the final 4 weeks of treatment:

- 41.2% of the participants who took SZC and did not need rescue treatment had their blood potassium reach normal levels. This was 40 out of 97 participants.
- 1.0% of the participants who took the placebo and did not need rescue treatment had their blood potassium reach normal levels. This was 1 out of 99 participants.

The figure below shows these results.



What new medical problems did the participants have during the study?

This section is a summary of the new medical problems the participants had during the study that the study doctors thought might be related to the study treatment.

New medical problems that study doctors think might be related to study treatment 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 treatment. A lot of research is needed to know whether a treatment causes an adverse reaction.

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

The researchers could only study the below results for 195 of the 196 participants. This was because 1 participant in the SZC group did not receive study treatment.

How many participants had serious adverse reactions?

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

None of the participants died from serious adverse reactions during the study.

How many participants had adverse reactions overall?

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

Adverse reactions during the study

	SZC (out of 96 participants)	Placebo (out of 99 participants)
How many participants had adverse reactions during the study?	7.3% (7)	7.1% (7)
How many participants had serious adverse reactions during the study?	0.0% (0)	0.0% (0)
How many participants stopped treatment because of adverse reactions?	0.0% (0)	2.0% (2)

What adverse reactions did the participants have?

The most common adverse reaction during the study was diarrhea.

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

Adverse reactions during the study

	SZC (out of 96 participants)	Placebo (out of 99 participants)
Diarrhea	1.0% (1)	3.0% (3)
Constipation	2.1% (2)	1.0% (1)
Chest pain not related to the heart	1.0% (1)	0.0% (0)
Headache	1.0% (1)	0.0% (0)
High blood pressure	1.0% (1)	0.0% (0)
Increased heart rate	1.0% (1)	0.0% (0)
Nausea	1.0% (1)	0.0% (0)
Numbness in the mouth	1.0% (1)	0.0% (0)
Irregular heartbeat	0.0% (0)	1.0% (1)
Muscle spasms	0.0% (0)	1.0% (1)
Rash	0.0% (0)	1.0% (1)
Stomach discomfort	0.0% (0)	1.0% (1)
Swelling in the legs	0.0% (0)	1.0% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how SZC affects blood potassium levels in patients who had kidney failure who were receiving hemodialysis.

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 SZC 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 **"NCT03303521"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2017-003029-14"** into the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D9480C00006"** into the search box, and click **"Find a Study"**.

Full Trial Title: A Phase 3b, Multicentre, Prospective, Randomised, Double-Blind, Placebo-Controlled Study to Reduce Incidence of Pre-Dialysis Hyperkalaemia with Sodium Zirconium Cyclosilicate (DIALIZE)

AstraZeneca Protocol Number: D9480C00006

AstraZeneca AB, sponsored this study and has its headquarters in 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.

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