AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Sodium zirconium cyclosilicate

Study Title: This study was done to learn how sodium zirconium cyclosilicate worked in participants with heart failure

Protocol Number: D9484C00001

Thank you

Thank you for taking part in the clinical study for the study drug sodium zirconium cyclosilicate, also called SZC.

You and all of the participants helped researchers learn more about SZC to help people with heart failure.

AstraZeneca AB sponsored this study and believes it is important to share the results of the study with you and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you. 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 study doctor or staff at your study site.

Overview of this study

Why was the research needed?

Researchers are looking for a better way to make sure people with heart failure who have, or are likely to have, high blood potassium levels can take target doses of some medications called RAAS inhibitors. The "target dose" is the dose of an RAAS inhibitor that many doctors think will have the most benefit in treating that person's heart failure. Before a drug can be approved for people to take, researchers do clinical studies to find out how safe it is and how it works.

What treatments did the participants take?

The participants in this study took SZC or a placebo. A placebo looks like a drug but does not have any medicine in it.

The researchers could not continue the study as planned during the COVID-19 pandemic, so the study closed early and did not include as many participants as they had expected.

What were the results of this study?

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

- **Did SZC affect how many participants could take RAAS inhibitors without having blood potassium levels that were too high?**

  No. The researchers found that the differences between the participants who took SZC and those who took the placebo were small.

- **What medical problems did the participants have during this study?**

  There were 6.1% of participants who had medical problems that the study doctors thought might be related to the study drug or to the placebo during the study. The most common medical problems were heart failure and constipation.

More details about the results of this study are included later in this summary.

Where can I learn more about this study?

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

Who took part in this study?

The researchers asked for the help of men and women who had heart failure with reduced ejection fraction, also called HFrEF. The participants in this study had or were at risk of having high potassium levels in their blood. The participants were 51 to 92 years old when they joined. All the participants were taking less than the target dose of some heart failure medications called RAAS inhibitors, also called renin–angiotensin–aldosterone system inhibitors.

The study included 182 participants in Brazil, Bulgaria, Canada, Hungary, Poland, Romania, Russia, Slovakia, and the United States.

Why was the research needed?

Researchers are looking for a better way to make sure people with heart failure who have, or are likely to have, high blood potassium levels can take target doses of RAAS inhibitors. The "target dose" is the dose of an RAAS inhibitor that many doctors think will have the most benefit in treating that person's heart failure. Before a drug can be approved for people 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 SZC makes it easier for a small number of participants with heart failure to be treated with target doses of RAAS inhibitors. They also wanted to find out if the participants had any medical problems during the study.

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. RAAS inhibitors are a common treatment for heart failure, but they can increase the amount of potassium in the blood. This can cause other heart problems.

Because of the possible increase in blood potassium levels, some people with heart failure do not take RAAS inhibitors. Or, they take lower doses than the target doses that are recommended to treat their heart failure.

SZC is currently available as a treatment for high blood potassium levels. SZC works by trapping potassium in the gut and stopping it from getting into the blood. In this study, the researchers wanted to find out if SZC could help the participants take their target doses of RAAS inhibitors without raising blood potassium levels.

What was the purpose of this study?

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

- Did SZC affect how many participants could take RAAS inhibitors without having blood potassium levels that were too high?
- 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 SZC helps improve the health of people with heart failure.

What treatments did the participants take?

In this study, all of the participants took either SZC or a placebo by mouth. 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.

This was planned as a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew what treatment 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 SZC or the placebo as a powder mixed with water. The doses of SZC were measured in grams, also called g. The doses of SZC and the placebo that each participant took at any given time during the study depended on their blood potassium levels, kidney health, blood pressure, and on what the doctors thought was safest for the participants.

At the beginning of the study, all of the participants were taking 1 of these 3 types of RAAS inhibitors:

- angiotensin-converting enzyme inhibitors, called ACEis
- angiotensin receptor blockers, called ARBs
- angiotensin receptor/neprilysin inhibitors, called ARNIs

Some participants were also taking lower than target doses of another type of RAAS inhibitor, called an aldosterone receptor antagonist, or also known as an MRA.

After the first week of taking study treatment, each participant's dose of the study drug and their doses of combined RAAS inhibitors were increased or decreased as recommended by the doctors.

The chart below shows the treatments the participants took in this study.

There was 1 participant who did not take any treatment. So, the chart only includes the 181 participants who took at least 1 dose of treatment.

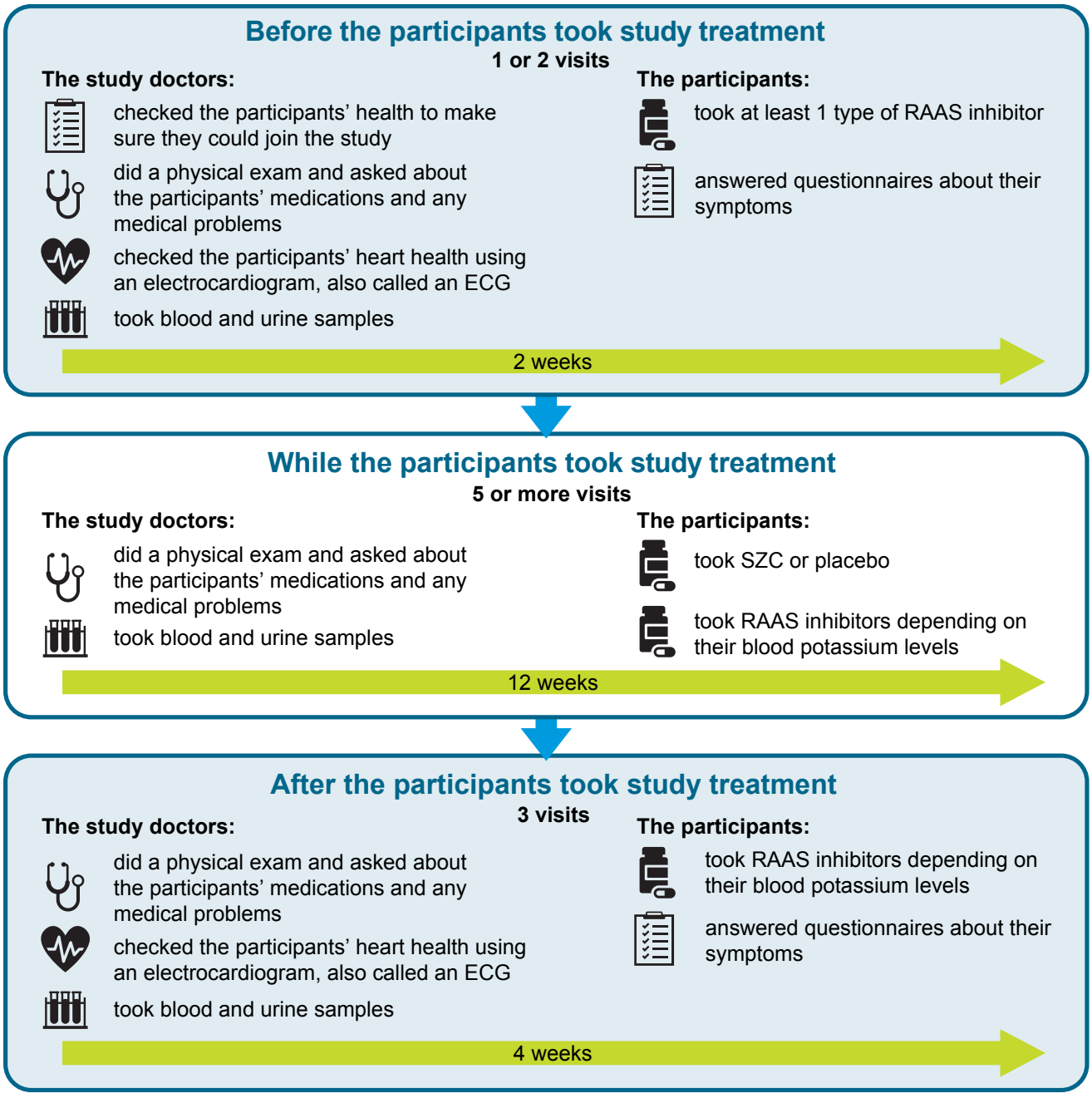
	SZC 91 participants	**Placebo** 90 participants
1 week	First 2 days: 5 g SZC once a day or 10 g SZC 3 times a day Next 5 days: 5 g SZC once a day	First 2 days: Placebo once a day or 3 times a day Next 5 days: Placebo once a day
	RAAS inhibitors	RAAS inhibitors
11 weeks	5 g SZC every other day, increasing to 15 g SZC every day	Placebo every other day
	RAAS inhibitors	RAAS inhibitors

What happened during this study?

The participants were in the study for up to 4.3 months. But, the entire study took nearly 2 years to finish.

The study started in June 2018 and was stopped earlier than planned in May 2020 because of the COVID-19 pandemic.

The chart below shows what happened during the study.



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. A full list of the questions researchers wanted to answer can be found on the websites listed at the end of this summary. When 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 SZC affect how many participants could take RAAS inhibitors without having blood potassium levels that were too high?

No. The researchers found that the differences between the participants who got SZC and those who got the placebo were small.

To answer this question, the researchers measured the levels of potassium in the participants' blood and did other health measurements, such as blood pressure. Then, they determined whether all of these measurements were in a range that allowed the participants to get their target dose of RAAS inhibitors.

The researchers calculated how many participants fell into the following 4 categories after 12 weeks of treatment with SZC or placebo:

- could not take an ACEi, ARB, or ARNI, or could only take less than the target dose of these drugs, and did not take an MRA
- could take a target dose of an ACEi, ARB, or ARNI, and did not take an MRA
- could take an MRA, but at less than the target dose
- could take an MRA at the target dose

Overall, the differences between the participants who took SZC and those who took the placebo in all 4 categories were small and not significant. So, this study did not show that SZC affected how many participants could take RAAS inhibitors.

The participants who could take an MRA at the target dose were the group who received the greatest protection against heart failure. The researchers found that more participants who took SZC could take an MRA at the target dose compared with those who took the placebo. But, this difference was not significant.

What medical problems happened 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, SZC, or to the placebo. 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. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for the study drug.

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.

There was 1 participant who did not take any treatment. So, the information below is for the 181 participants who took at least 1 dose of treatment.

Did any adverse reactions happen during this study?

	SZC (out of 91 participants)	Placebo (out of 90 participants)
How many participants had adverse reactions?	5.5% (5)	6.7% (6)
How many participants had serious adverse reactions?	1.1% (1)	0.0% (0)
How many participants stopped taking study treatments due to adverse reactions?	2.2% (2)	0.0% (0)

What serious adverse reactions happened during this study?

There was 1 serious adverse reaction that happened during this study. This serious adverse reaction was swelling all over the body caused by trapped liquids.

This serious adverse reaction happened in 1.1% of participants who took SZC. This was 1 out of 91 participants. None of the participants who took the placebo had a serious adverse reaction.

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

What adverse reactions happened during this study?

The most common adverse reactions were heart failure and constipation.

The chart below shows the adverse reactions that happened during this study.

Adverse reactions		
Adverse reaction	**SZC** (out of 91 participants)	**Placebo** (out of 90 participants)
Heart failure	2.2% (2)	2.2% (2)
Constipation	2.2% (2)	0.0% (0)
Nausea	1.1% (1)	0.0% (0)
Irregular heartbeat	1.1% (1)	0.0% (0)
Long-standing kidney disease, also called chronic kidney disease	1.1% (1)	0.0% (0)
Swelling all over the body caused by trapped liquids in the whole body	1.1% (1)	0.0% (0)
Diarrhea	0.0% (0)	1.1% (1)
Feeling weak	0.0% (0)	1.1% (1)
Indigestion	0.0% (0)	1.1% (1)
Not feeling well	0.0% (0)	1.1% (1)
Swelling caused by trapped liquids	0.0% (0)	1.1% (1)
Swelling in the face	0.0% (0)	1.1% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about how SZC works in participants with heart failure.

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 1 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 more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on the website, type **"NCT03532009"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click "Home and Search", then type **"2018-000175-33"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D9484C00001"** into the search box, and click **"Find a Study"**.

Full Study Title: A Phase II, Randomised, Double-Blind, Placebo-Controlled, Parallel-Group, Multicentre, Three Month Duration Potassium Reduction Initiative to Optimise RAAS Inhibition Therapy with Sodium Zirconium CyclosilicatE in Heart Failure (PRIORITIZE HF)

AstraZeneca AB Protocol Number: D9484C00001

National Clinical Trials number: NCT03532009

EudraCT Number: 2018-000175-33

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

Participants in clinical studies 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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