AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Sodium zirconium cyclosilicate

Study Purpose: This study was done to learn how sodium zirconium cyclosilicate works in healthy participants

Protocol Number: D9480C00012

Thank you

Thank you to the participants who took part in the clinical study for the study drug sodium zirconium cyclosilicate, also called "SZC".

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 healthy men and women. The participants in this study were 18 to 50 years old when they joined.

The participants could join the study if they:

- had never had a medical condition that could make it unsafe to take part in this study.
- had never had a medical condition that could change how the study treatments worked in the body.

The study included 62 participants in Germany.

Why was the research needed?

Researchers are looking for a better way to treat people with high levels of potassium in their blood. This condition is also called "hyperkalemia".

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

High blood potassium can be caused by certain medicines. These include tacrolimus and cyclosporin, which are designed to decrease the activity of the immune system. Decreasing the activity of the immune system is important in treating some diseases, or to avoid complications after an organ transplant.

Researchers think that the study drug, SZC, could help prevent high blood potassium in people taking tacrolimus and cyclosporin.

But, SZC can make the stomach less acidic. This can make it harder for some other medicines to get into the blood, and can be a problem for people who take multiple medicines.

In this study, the researchers wanted to find out if taking SZC affected how much tacrolimus or cyclosporin got into the participants' blood.

What was the purpose of this study?

In this study, the researchers wanted to learn how SZC works in healthy participants.

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

- Did the amount of tacrolimus or cyclosporin that got into the participants' blood differ when taken with SZC?
- What medical problems did the participants have during the study?

What treatments did the participants take?

In this study, there were 2 groups:

- In the **tacrolimus** group, all of the participants took 1 dose of tacrolimus **on its own** and 1 dose of tacrolimus **with SZC**.
- In the **cyclosporin** group, all of the participants took 1 dose of cyclosporin **on its own** and 1 dose of cyclosporin **with SZC**.

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

The first treatment the participants took was called **"treatment 1"** and the second treatment they took was called **"treatment 2"**. After the participants took treatment 1, they did not take any study treatment for at least 2 weeks. This was done so that treatment 1 could leave the participants' bodies before they took treatment 2.

A computer program was used to randomly choose which group each participant was in, and which study treatment they took as treatment 1 and treatment 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.

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

	Tacrolimus group	Cyclosporin group
	31 participants	31 participants
	• Tacrolimus as a **capsule** by mouth • SZC as a **liquid** by mouth	• Cyclosporin as a **capsule** by mouth • SZC as a **liquid** by mouth
	• **Treatment 1** once. This was either tacrolimus on its own or tacrolimus with SZC. • **Treatment 2** once, 2 weeks later. This was whichever treatment the participant had not yet taken.	• **Treatment 1** once. This was either cyclosporin on its own or cyclosporin with SZC. • **Treatment 2** once, 2 weeks later. This was whichever treatment the participant had not yet taken.

What happened during this study?

The study started in March 2021 and ended in September 2021.

The participants were in the study for up to about 2 months. But, the entire study took about 6 months to finish.

Before the participants took study treatment, they visited their study site once. This part of the study lasted for up to 4 weeks. At this visit, the study doctors made sure the participants could join the study. They also:

- did physical exams and asked about the participants' medications and any medical problems they were having
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an "ECG"
- checked if the participants had COVID-19

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

While the participants took study treatment, they visited their study site twice. For each visit, the participants stayed at the study site for 5 days and took their study treatment on the second day.

The participants stayed at home for 10 days between each visit to the study site. During that time, the participants did not take any study treatment. This was done so that treatment 1 could leave the participants' bodies before they took treatment 2.

After the participants took study treatment, they visited their study site once. This happened up to 10 days after the participants took their last dose of study treatment. At this visit, 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 more information about the study results.

There were 3 participants who did not take both of their study treatments. So, the results below are for:

- 31 participants who took tacrolimus
- 30 participants who took tacrolimus with SZC
- 31 participants who took cyclosporin
- 29 participants who took cyclosporin with SZC

Did the amount of tacrolimus or cyclosporin that got into the participants' blood differ when taken with SZC?

To answer this question, the study doctors took blood samples from the participants throughout the study. In these samples, the study doctors measured:

- the average **total** amount of tacrolimus or cyclosporin in the participants' blood over time
- the average **highest** amount of tacrolimus or cyclosporin in the participants' blood

Then, the researchers compared the results after the participants took tacrolimus or cyclosporin on their own with the results after they took them with SZC.

In the tacrolimus group:

Yes. Overall, the researchers found that taking SZC **did** affect how much tacrolimus got into participants' blood:

- The **average total amount of tacrolimus** in the participants' blood over time was **lower** when the participants took tacrolimus with SZC compared to when they took tacrolimus by itself.
- The **average highest amount of tacrolimus** in the participants' blood was **lower** when the participants took tacrolimus with SZC compared to when they took tacrolimus by itself.

In the cyclosporin group:

No. Overall, the researchers found that there were some small changes in how much cyclosporin got into the participants' blood when they took SZC. But, the differences were too small for the researchers to know if taking cyclosporin on its own, or with SZC, affected how much cyclosporin got into participants' blood.

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 drug causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for SZC.

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.

Since there were 3 participants who did not take both of their study treatments, the information below does not include these results.

Did any adverse reactions happen during this study?

	Tacrolimus (out of 31 participants)	**Tacrolimus + SZC** (out of 30 participants)	**Cyclosporin** (out of 31 participants)	**Cyclosporin + SZC** (out of 29 participants)
How many participants had adverse reactions?	6.5% (2)	23.3% (7)	6.5% (2)	6.9% (2)
How many participants had serious adverse reactions?	none	none	none	none
How many participants stopped taking study treatment due to adverse reactions?	none	none	none	none

What serious adverse reactions happened during this study?

No serious adverse reactions happened during this study.

What adverse reactions happened during this study?

The most common adverse reaction was **headache**.

The table below shows the adverse reactions that happened during the study.

Adverse reactions

Adverse reaction	Tacrolimus (out of 31 participants)	Tacrolimus + SZC (out of 30 participants)	Cyclosporin (out of 31 participants)	Cyclosporin + SZC (out of 29 participants)
Headache	6.5% (2)	10.0% (3)	3.2% (1)	6.9% (2)
Nausea	3.2% (1)	3.3% (1)	none	none
Fatigue	none	none	none	3.4% (1)
Diarrhea	none	3.3% (1)	none	none
Muscle pain	none	3.3% (1)	none	none
Pain in upper part of the stomach	none	3.3% (1)	none	none
Feeling hot	3.2% (1)	none	none	none
Stomach pain	none	none	3.2% (1)	none
Vomiting	3.2% (1)	none	none	none

How has this study helped patients and researchers?

This study helped researchers learn more about whether taking SZC affected how much tacrolimus or cyclosporin got into the blood of healthy participants.

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 ongoing.

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 **"NCT04788641"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2020-000515-68"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D9480C00012"** into the search box and click **"Find a Study"**.

Full Study Title: A Two-Cohort, Randomised Sequence, Cross-over, Open-label Study to Assess the Effect of a Single Dose of Sodium Zirconium Cyclosilicate (SZC) on the Pharmacokinetics of Tacrolimus and Cyclosporin in Healthy Subjects

AstraZeneca AB Protocol Number: D9480C00012

National Clinical Trials Number: NCT04788641

EudraCT Number: 2020-000515-68

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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