AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drugs Studied: Verinurad, allopurinol, cyclosporine, and rifampicin

Study Purpose: This study was done to learn if taking cyclosporine or rifampicin together with verinurad affected how much verinurad remained in the participants' blood during the study

Protocol Number: D5495C00013

Thank you!

Thank you for taking part in the clinical study for the study drugs verinurad, allopurinol, cyclosporine, and rifampicin.

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 20 to 55 years old when they joined.

The study included 14 participants in Germany.

Why was the research needed?

Researchers are looking for a better way to treat chronic kidney disease, also known as "CKD". 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.

Verinurad is being developed as a possible treatment for CKD. Verinurad decreases the blood levels of a chemical in the body known as uric acid. It does this by stopping the activity of a protein in the kidneys called URAT-1. This helps the kidneys to remove the uric acid from the blood into the urine, instead of reabsorbing it back up into the blood. Researchers think that high levels of uric acid in the blood may cause more kidney damage. They believe that limiting the amount of uric acid that is taken back up into the body may help people with CKD.

People with CKD often take several other drugs. These drugs might affect how the body breaks down verinurad, which could lead to levels of verinurad in the blood that are too high or too low. Researchers need to know if taking cyclosporine or rifampicin affects how the body breaks down verinurad to learn if taking other medications may also affect how verinurad acts in the body.

In this study, the researchers wanted to learn if taking either cyclosporine or rifampicin affected how much verinurad remained in the participants' blood during the study.

What was the purpose of this study?

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

- Did taking cyclosporine or rifampicin together with verinurad affect how much verinurad remained in the participants' blood during the study?
- 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 verinurad helps improve the health of people who have CKD.

What treatments did the participants take?

In this study, all of the participants took:

- Treatment 1: verinurad with allopurinol
- Treatment 2: verinurad with allopurinol and cyclosporine
- Treatment 3: verinurad with allopurinol and rifampicin

All of the participants took all 3 treatments in the order shown above. They took verinurad and cyclosporine as capsules by mouth, and the other drugs as tablets by mouth.

The participants in this study took verinurad together with allopurinol, which decreases the amount of uric acid made by the body. Allopurinol is an approved drug that has been used in other clinical studies with verinurad.

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

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

	Treatment 1	Treatment 2	Treatment 3
	14 participants		
	• Verinurad as a capsule by mouth • Allopurinol as a tablet by mouth	• Verinurad as a capsule by mouth • Allopurinol as a tablet by mouth • Cyclosporine as a capsule by mouth	• Verinurad as a capsule by mouth • Allopurinol as a tablet by mouth • Rifampicin as a tablet by mouth
	• Once	• Once, 5 days after Treatment 1	• Once, at least 2 weeks after Treatment 2

What happened during this study?

Each participant was in the study for up to 11 weeks. But, the entire study took about 3 months to finish. The study started in September 2020 and ended in November 2020.

Before the participants took study treatment, they visited their study site 1 time. 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.

The study doctors 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
- did COVID-19 tests

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

While the participants took study treatment, they visited their study site 2 times. This part of the study lasted about 5 weeks.

At the first visit, the participants stayed overnight for 11 days. During this visit, they took Treatment 1, waited 5 days, and then took Treatment 2. At the second visit, the participants stayed overnight for 6 days and took Treatment 3.

Between the first and the second visits, the participants stayed at home for at least 10 days and did not take any study drugs.

After the participants had taken all study treatments, they visited their study site 1 time. This part of the study lasted for up to 2 weeks. At these visits, 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.

Did taking cyclosporine or rifampicin together with verinurad affect how much verinurad remained in the participants' blood during the study?

Yes. Overall, the researchers found that taking either cyclosporine or rifampicin together with verinurad increased the amount of verinurad in the participants' blood.

To answer this question, the researchers took blood samples throughout the study. In these samples, they measured:

- the average of the highest amount of verinurad in the participants' blood
- the average of the total amount of verinurad in the participants' blood over time

Then, the researchers compared the results for each treatment group:

- verinurad with allopurinol
- verinurad with allopurinol and cyclosporine
- verinurad with allopurinol and rifampicin

Overall, the researchers found that the average amounts of verinurad in the participants' blood were higher when they took verinurad and allopurinol with either cyclosporine or rifampicin compared to when they took verinurad and allopurinol alone. So, the researchers concluded that taking either cyclosporine or rifampicin increased the amount of verinurad in the 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 drugs. 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 drugs. 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 drugs.

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 left the study early and did not take Treatment 3. So, the results below for Treatment 3 include only 13 of the 14 participants.

Did any adverse reactions happen during this study?

	Treatment 1 (out of 14 participants)	Treatment 2 (out of 14 participants)	Treatment 3 (out of 13 participants)
How many participants had adverse reactions?	14.3% (2)	64.3% (9)	15.4% (2)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	0.0% (0)	7.1% (1)	0.0% (0)

What serious adverse reactions happened during this study?

There were no serious adverse reactions that happened during this study.

What adverse reactions happened during this study?

The most common adverse reaction was feeling hot.

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

Adverse reactions

Adverse reaction	Treatment 1 (out of 14 participants)	Treatment 2 (out of 14 participants)	Treatment 3 (out of 13 participants)
Feeling hot	0.0% (0)	57.1% (8)	0.0% (0)
Unusual urine color	0.0% (0)	0.0% (0)	15.4% (2)
Feeling tired	0.0% (0)	14.3% (2)	0.0% (0)
Head discomfort	0.0% (0)	14.3% (2)	0.0% (0)
Rash	7.1% (1)	7.1% (1)	0.0% (0)
Stomach pain	0.0% (0)	7.1% (1)	0.0% (0)
Diarrhea	0.0% (0)	7.1% (1)	0.0% (0)
Dry mouth	7.1% (1)	0.0% (0)	0.0% (0)
Headache	0.0% (0)	7.1% (1)	0.0% (0)
Nausea	0.0% (0)	7.1% (1)	0.0% (0)
Pain in arms and legs	0.0% (0)	7.1% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn if taking cyclosporine or rifampicin affected how much verinurad remained in the participants' blood during the study.

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 verinurad, allopurinol, cyclosporine, and rifampicin are ongoing at this time.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"NCT04532918"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2020-000937-42"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D5495C00013"** into the search box, and click **"Find a Study"**.

Full Study Title: An Open-label, 3-Treatment, 3-Period, Fixed Sequence Study in Healthy Subjects to Assess the Pharmacokinetics of Verinurad and Allopurinol when Administered Alone, and in Combination with Single Doses of Cyclosporine or Rifampicin

AstraZeneca AB Protocol Number: D5495C00013

National Clinical Trials Number: NCT04532918

EudraCT Number: 2020-000937-42

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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