AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Verinurad and allopurinol

Study Title: A study to learn if the amount of verinurad in the blood affected how the heart beats in healthy participants

Protocol Number: D5495C00012

Thank you!

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

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 the study?

The researchers asked for the help of healthy men and women. The participants in this study were 20 to 50 years old when they joined.

The study included 24 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.

The study drug, verinurad, is being developed as a treatment for CKD. It decreases blood levels of uric acid by helping the kidneys to excrete the uric acid from the blood into the urine, instead of reabsorbing it. Uric acid is a chemical made by the body. Researchers think that levels of uric acid that are too high in the blood may increase the risk of CKD. They think that limiting the amount of uric acid that is taken back up in the kidneys may help people with CKD.

When someone has too much uric acid in their blood and takes verinurad alone, there is a risk that the extra uric acid can form crystals in the kidneys. These crystals can damage the kidney. So, verinurad is taken together with a type of drug that decreases the amount of uric acid that the body makes. This means that when the drugs are taken together, there is less uric acid in the kidneys and a lower risk that crystals are formed in the kidneys. A drug that decreases the amount of uric acid made by the body is called allopurinol. It is an approved drug that has been used in other clinical studies with verinurad.

Before larger studies with verinurad can be done in participants with CKD, the researchers needed to learn how verinurad affects how the heart beats. In this study, the researchers wanted to learn if the amount of verinurad in the participants' blood affected how the heart beats. The participants in this study also took allopurinol.

What was the purpose of this study?

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

- Did the amount of verinurad that got into the blood affect how the heart beats?
- What medical problems did the participants have during this study?

The answers to these questions are important to know before other larger studies can be done to find out if verinurad helps improve the health of people with CKD.

What treatments did the participants take?

In this study, all of the participants took each of the following treatments by mouth:

- verinurad as a capsule and allopurinol as a tablet
- a placebo that looks like verinurad and a placebo that looks like allopurinol

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 treatment are actually caused by the treatment.

This was a "double-blind" study. This means none of the participants, researchers, study doctors, or other study staff knew the order that each participant took their treatments.

There were 6 groups of participants, and each group took the treatments in a different order. The doses of verinurad and allopurinol were measured in milligrams, also known as mg.

A computer program was used to randomly choose the order that each participant would take their treatments. 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 that were planned during the study.

	24 participants 6 groups of 4 participants		
	• 24 mg of verinurad • 300 mg of allopurinol	• 40 mg of verinurad • 300 mg of allopurinol	• A placebo that looked like verinurad • A placebo that looked like allopurinol
	• Each treatment once, with a 1 week gap before taking the next treatment • A different treatment each week for a total of 3 weeks		

What happened during the study?

The study started in March 2020 and ended in September 2020. The participants were in the study for about 10 weeks. After the study started, it was paused due to the COVID-19 pandemic. So, there was a delay of about 4 months between the study starting and the participants taking any study treatment.

Before the participants took study treatment, they visited their study site 1 time. This part of the study lasted for 4 weeks. At this visit, the study doctors checked the participants' health to make sure they could join the study. The study doctors:

- did a physical exam 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

The study doctors also did these tests and measurements during the study visits.

While the participants took study treatment, they visited their study site 3 times. This part of the study lasted nearly 3 weeks.

- At each of the 3 visits, the participants stayed overnight at the study site for 4 days.
- On the first day of each visit, the participants had a throat swab done to test for COVID-19 infection.
- The participants took study treatment on the second day of each study site stay.
- The study doctors used an ECG to check the participants' heart rate regularly for 2 days after the participants took study treatment.
- There was a gap of at least 7 days between each study treatment. This was done so that each treatment could leave the participants' bodies before they took the next treatment.

After the participants took study treatment, they visited their study site 1 time. This part of the study lasted up to 10 days. At this visit, the study doctors checked the health of the participants.

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.

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 a full report of the study results.

Did the amount of verinurad that got into the blood affect how the heart beats?

To answer this question, the study doctors measured the amount of verinurad in the participants' blood after they took each treatment. The study doctors also measured how the heart beats using standard ECG. The researchers wanted to learn if the participants had any abnormal heart activity after taking verinurad. If they did have abnormal heart activity, the researchers wanted to learn if it was related to the amount of verinurad in the blood. The researchers used a mathematical model to find out if the amount of verinurad in the blood affected how the heart beats.

Overall, the researchers found that the amount of verinurad in the blood had no effect on how the heart beats.

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. 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.

Not all of the participants took all of the treatments during the study. The results below show the medical problems for the number of participants who took each of the treatments.

Did any adverse reactions happen during this study?

- There were 4.5% of participants who took 24 mg of verinurad and 300 mg of allopurinol who had adverse events. This was 1 out of 22 participants.
- There were 16.7% of participants who took 40 mg of verinurad and 300 mg of allopurinol who had adverse events. This was 4 out of 24 participants.
- There were 8.7% of participants who took the placebo who had adverse events. This was 2 out of 23 participants.

None of the participants stopped taking study treatment due to adverse reactions.

What serious adverse reactions happened during this study?

None of the participants had serious adverse reactions in this study.

None of the participants died 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 in during this study.

Adverse reactions

Adverse reaction	**24 mg of verinurad and 300 mg of allopurinol** (out of 22 participants)	**40 mg of verinurad and 300 mg of allopurinol** (out of 24 participants)	**Placebo** (out of 23 participants)
Headache	4.5% (1)	12.5% (3)	0.0% (0)
Feeling sick	0.0% (0)	0.0% (0)	4.3% (1)
Feeling sleepy	0.0% (0)	4.2% (1)	0.0% (0)
Unusual smelling urine	0.0% (0)	0.0% (0)	4.3% (1)
Pain when urinating	0.0% (0)	4.2% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn if the amount of verinurad in the blood affected how the heart beats in healthy participants when they took it with allopurinol.

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 verinurad 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 **"NCT04256629"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2019-003657-28"** in the search box and click "Search".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5495C00012"** into the search box, and click **"Find a Study"**.

Full Study Title: A Single-Centre, Randomised, Double-Blind, Placebo-Controlled, 3-Period, Cross-Over Phase I Study to Investigate the Effect on the QTcF Interval of a Single Dose of 2 Different Doses of Verinurad, Each in Combination with Allopurinol 300 mg, Compared with Placebo In Healthy Volunteers.

AstraZeneca Protocol Number: D5495C00012

National Clinical Trials number: NCT04256629

EudraCT number: 2019-003657-28

AstraZeneca AB sponsored this study and has its headquarters at 151 85 Södertälje, Sweden.

The phone number for the AstraZeneca Information Center is +1-877-240-9479 and the email is information.center@astrazeneca.com.

Thank you!

Clinical study participants and their families 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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