Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drug Studied: RDEA3170 and febuxostat

Study Title: This study was done to learn how taking RDEA3170 and febuxostat together worked in patients with type 2 diabetes who have protein in their urine.

Thank you!

Thank you to the participants who took part in the clinical study for the study drugs RDEA3170 and febuxostat. You and all of the participants helped researchers learn more about using RDEA3170 and febuxostat together to help people with type 2 diabetes who have protein in their urine.

AstraZeneca sponsored this study and thinks 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 doctor or staff at your study site.

What is happening with the study now?

The participants were in the study for up to about 34 weeks. But, the entire study took 15 months to finish. The study started in May 2017 and ended in August 2018. The study included 60 participants in 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?

Researchers are looking for a better way to treat people whose type 2 diabetes is causing their kidneys to leak protein into their urine. 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 taking RDEA3170 and febuxostat together works in a small number of participants with type 2 diabetes who have mild to moderate amounts of protein in their urine. They also wanted to find out if the participants had any medical problems during the study.

Diabetes is the most common cause of chronic kidney disease. In people with diabetes, the kidneys may not work as well as they should and let protein leak into the urine. This may get worse over time and eventually the kidneys may stop working.

Uric acid is a waste product of the body and is found in urine and blood. Lowering the level of uric acid in the blood may prevent or slow kidney damage in people with type 2 diabetes.

RDEA3170 works by increasing the amount of uric acid that leaves the body in the urine. Febuxostat works by decreasing the amount of uric acid that the body makes. Both drugs work in different ways to lower the amount of uric acid in the body. Researchers want to find out if taking more than 1 treatment to lower the amount of uric acid has an effect on the kidneys in people with type 2 diabetes.

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

- Did RDEA3170 and febuxostat affect how much protein leaks into the urine?
- What medical problems did the participants have during the study?

To answer the questions in this study, researchers asked for the help of men and women who had type 2 diabetes, mild or moderate amounts of protein leaking into the urine, and high levels of uric acid in their blood. The participants in this study were 41 to 82 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.

The participants in this study either took RDEA3170 and febuxostat together, or they took placebos. Each placebo looked like one of the study drugs but did not have any medicine in it. Researchers use a placebo to help make sure any of the effects they see in participants who take a treatment are actually caused by the treatment.

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 treatment, the doctors checked the overall health of the participants to make sure that they could join the study. This included taking blood and urine samples, and using a magnetic resonance imaging scan, also called an MRI, to check the kidney and heart health of the participants. Doctors also checked the heart health of the participants using an electrocardiogram, also called an ECG.

If the doctors found that a participant was able to join the study, they asked them not to change any medication they were already taking to keep their kidneys healthy. This helped the doctors make sure any effects they saw during treatment were due to the treatment in this study.

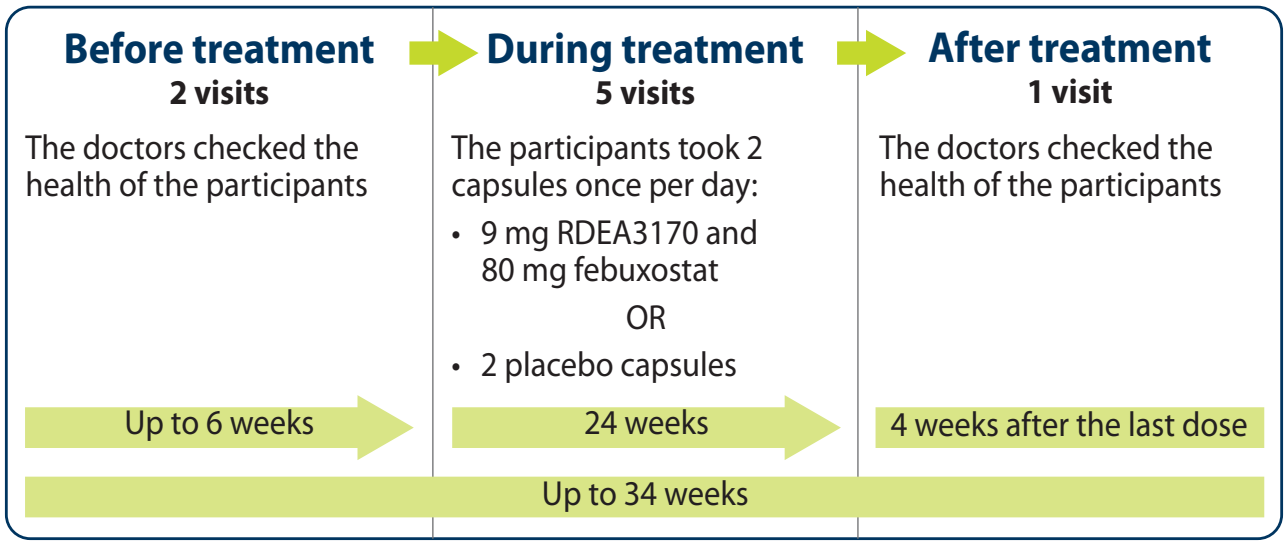
During treatment, the participants visited their study site 5 times. At the first visit, the participants were given either RDEA3170 and febuxostat capsules, or the placebo capsules.

The participants took 2 capsules every day. Each RDEA3170 capsule was 9 milligrams, also known as mg. Each febuxostat capsule was 80 mg.

At each visit, the doctors or study staff took blood and urine samples. Before the last visit, the doctors used another MRI to check the heart and kidney health of the participants.

After treatment, the participants visited their study site 1 time for a follow-up visit. At this visit, the doctors took blood and urine samples from the participants and asked how they were feeling.

The figure 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 the summary. If a full report of the study results is available, it can also be found on these websites.

Researchers usually need 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 RDEA3170 and febuxostat affect how much protein leaks into the urine?

Overall, the participants who took RDEA3170 and febuxostat together had less protein in their urine compared to the participants who took the placebos.

To answer this question, the researchers measured the participants' urine albumin-to-creatinine ratio, also called UACR. Albumin is a protein that controls the amount of water in cells and the blood. Albumin also helps to move nutrients, hormones and medicines through the bloodstream. When the kidneys are healthy, they do not allow albumin to leak from the blood to the urine.

Creatinine is a waste product made by muscles when they move. When the kidneys are healthy, they remove creatinine from the bloodstream into urine.

When the kidneys are not working properly, they do not remove creatinine from the blood as efficiently, and albumin leaks into urine. This means that the amount of albumin in urine goes up and the amount of creatinine goes down.

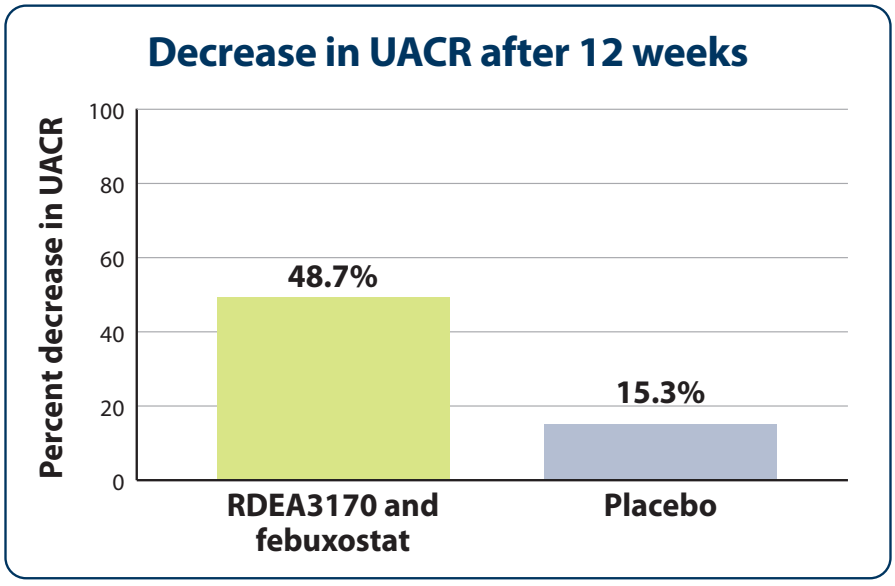
Low UACR means that there is less albumin than creatinine in urine, which means there is little or no kidney damage. High UACR means that the amount of albumin has increased relative to creatinine, which means there is more kidney damage. The researchers measured UACR before, during, and after participants took RDEA3170 and febuxostat or the placebos.

The researchers used the “least square mean” calculation to compare the difference in UACR after taking each treatment. This is a calculation that researchers use to account for any measurements taken before starting treatment. In this study, researchers used the least square mean to account for any differences between each participant’s UACR measurements before they started the treatment. This helps make sure that study results are as accurate as possible.

After 12 weeks of treatment, the UACR decrease compared to the start of the treatment was calculated.

- UACR was 48.7% lower in the participants who took RDEA3170 and febuxostat
- UACR was 15.3% lower in the participants who took the placebos

The figure below shows these results.



The researchers also calculated the overall difference in UACR decrease between the treatments using the least square mean calculation. They found that the UACR decrease was 39.4% lower in the participants who took RDEA3170 and febuxostat compared to the participants who took the placebos.

What medical problems did the participants have 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 treatment. 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.

Usually the results from several trials are used to determine if a drug causes a specific adverse reaction. At this stage, it is not known if these adverse reactions may be caused by 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.

How many participants had serious adverse reactions?

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

How many participants had adverse reactions?

Overall, there were 8.3% of participants who had adverse reactions to the treatment given during the study. This was 5 out of 60 participants.

What adverse reactions did the participants have?

The most common adverse reaction was diarrhea. The table below shows the most common adverse reactions that happened in this study. The study doctors thought that these adverse reactions were related to the study treatment, but did not know which treatment participants were taking.

Most common adverse reactions

	RDEA3170 and febuxostat (out of 32 participants)	Placebos (out of 28 participants)
Diarrhea	3.1% (1)	3.6% (1)
Nausea	3.1% (1)	0.0% (0)
Increased uric acid in the blood, joints, and tissues (gout)	3.1% (1)	0.0% (0)
Decreased kidney function	3.1% (1)	0.0% (0)
Blood clot in a vein that is deep below the skin of the legs	0.0% (0)	3.6% (1)

How has this study helped patients and researchers?

This study helped researchers learn how taking RDEA3170 and febuxostat together affect kidney function in people with type 2 diabetes who have protein in their urine. The researchers in this study found that the amount of protein in urine was lower in the participants who took RDEA3170 and febuxostat than in participants who took the placebos.

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 RDEA3170 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 "**NCT03118739**" into the search box and click "**Search**".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D5495C00007"** into the search box, and click **"Find a Study"**.

Full Trial Title: Effects of Intensive Uric Acid Lowering Therapy with RDEA3170 and Febuxostat in Patients with Albuminuria

National Clinical Trial number: NCT03118739

AstraZeneca Protocol Number: D5495C00007

AstraZeneca sponsored this study and has its headquarters in Wilmington, Delaware, USA.

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 participants.