AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Dapagliflozin

Study Title: A study to learn how dapagliflozin affects the kidneys in participants with chronic kidney disease

Protocol Number: D169AC00001

Thank you

Thank you to the participants who took part in the clinical study for the study drug dapagliflozin. All of the participants helped researchers learn more about dapagliflozin to help people who have chronic kidney disease, also called CKD.

AstraZeneca AB sponsored this study and thinks it is important to share the results of the study with the participants and the public. An independent non-profit organization called CISCRP helped prepare this summary of the study results. We hope it helps the participants to understand and feel proud of their 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 treat people who have chronic kidney disease, also called CKD. 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.

What treatments did the participants take?

The participants in this study took dapagliflozin or a placebo. 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.

The participants also continued taking any CKD treatments they were taking before the study started.

What were the results of this study?

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

- **Did dapagliflozin help prevent the participants' CKD from getting worse compared to the placebo?**

  Yes. Overall, the researchers found that dapagliflozin helped prevent the participants' CKD from getting worse compared to the placebo.

- **What serious medical problems happened during the study?**

  There were 2.3% of participants who took dapagliflozin who had serious medical problems during the study that the study doctors thought might be related to study treatment.

  There were 2.1% of participants who took the placebo who had serious medical problems during the study that the study doctors thought might be related to study treatment.

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 CKD. The participants were 18 to 93 years old when they joined.

The study included 4,304 participants in Argentina, Brazil, Canada, China, Denmark, Germany, Hungary, India, Japan, Mexico, Peru, the Philippines, Poland, the Republic of Korea, Russia, Spain, Sweden, Ukraine, the United Kingdom, the United States, and Vietnam.

Why was the research needed?

Researchers are looking for a better way to treat people who have chronic kidney disease, also called CKD. 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 healthy people, the kidneys help the body to control and remove fluid and unnecessary substances in the urine. In people who have CKD, the kidneys cannot do this as well as they should. This can lead to medical problems that can sometimes be serious. Kidney-related and heart-related medical problems are common with CKD, and kidney function can worsen. This can increase the risk of so-called end-stage kidney disease, also called ESKD. ESKD means that a person's kidneys can no longer remove sufficient amounts of extra substances from the body.

People with ESKD may need dialysis treatment, which is like an artificial kidney, or a kidney transplant to help manage their CKD.

The study drug, dapagliflozin, is currently used to treat people who have type 2 diabetes. Dapagliflozin works by helping the kidneys remove blood sugar through the urine. In this study, the researchers wanted to learn if dapagliflozin could help prevent people's CKD from getting worse regardless of whether they had type 2 diabetes or not.

What was the purpose of this study?

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

- Did dapagliflozin help prevent the participants' CKD from getting worse compared to the placebo?
- What medical problems happened during the study?

The answers to these questions are important to know before dapagliflozin can be approved to help improve the health of people who have CKD.

What treatments did the participants take?

The participants in this study took dapagliflozin or a placebo. 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 a drug are actually caused by the drug. The participants also continued taking any CKD treatments they were taking before the study started.

Both dapagliflozin and the placebo were taken as tablets by mouth. The treatment doses were measured in milligrams, also called mg.

This was 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.

Of the 4,304 participants who joined the study, 3 participants in each treatment group left the study before receiving study treatment. So, the chart below includes 4,298 participants.

The chart below shows the treatments that the participants took during the study.

	Dapagliflozin	Placebo
	2,149 participants	2,149 participants
	10 mg of dapagliflozin as a tablet by mouth	Placebo as a tablet by mouth
	Once a day for up to about 3 years	

What happened during this study?

The participants were in the study for up to about 3 years, but the entire study took about 3.5 years to finish. The study started in February 2017 and ended in June 2020.

The researchers had planned for the study to last almost 4 years. But, they ended the study early because they had already found that dapagliflozin helped prevent the participants' CKD from getting worse compared to the placebo.

The chart below shows what happened during the study.

Before the participants took study treatment

2 visits

The study doctors:

- checked the participants' health to make sure they could join the study
- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- checked the participants' heart health using an electrocardiogram, also called an ECG

The participants:

- answered questionnaires about their symptoms

About 2 weeks

While participants took study treatment

Up to 12 visits

The study doctors:

- did physical exams and checked the participants' kidney health and their overall health
- took blood and urine samples

The participants:

- took dapagliflozin or the placebo once a day and continued taking their CKD medicine

Up to about 3 years

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 that the 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 dapagliflozin help prevent the participants' CKD from getting worse compared to the placebo?

Yes. Overall, the researchers found that dapagliflozin helped prevent the participants' CKD from getting worse compared to the placebo.

To answer this question, the study doctors recorded the number of participants who had at least 1 of the CKD-related problems below. They kept track of whether the participants:

- had a 50.0% worsening in their kidney function
- developed ESKD
- needed dialysis treatment
- needed a kidney transplant
- died from a medical problem related to the kidneys
- died from a medical problem related to the heart

They found that during the study the percentage of participants who had these CKD-related problems was:

- 9.2% in the dapagliflozin group. This was 197 out of 2152 participants.
- 14.5% in the placebo group. This was 312 out of 2152 participants.

What medical problems happened during the study?

In clinical studies, researchers keep track of the medical problems that participants have that study doctors think 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.

In this study, the researchers only wanted to learn if the participants taking dapagliflozin had specific adverse reactions and to learn about all serious adverse reactions. They did not require information on all adverse reactions to be collected.

This section is a summary of these specific adverse reactions and all serious adverse reactions that the study doctors thought might be related to dapagliflozin. In this summary, these are called "adverse reactions of interest" and "serious adverse reactions".

These adverse reactions of interest and serious adverse reactions may or may not be caused by dapagliflozin. When the participants had these adverse reactions of interest and serious adverse reactions, the study doctors did not know if they were taking dapagliflozin or the placebo.

There were 3 participants in each treatment group who left the study before receiving study treatment. So, the results below include information for 4,298 of the 4,304 participants.

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.

Did any adverse reactions happen during this study?

There were participants who had adverse reactions in this study.

How many participants had serious adverse reactions?

- 2.3% of participants who took dapagliflozin had serious adverse reactions. This was 50 out of 2,149 participants.
- 2.1% of participants who took the placebo had serious adverse reactions. This was 45 out of 2,149 participants.

How many participants stopped taking study treatment due to adverse reactions?

- 1.5% of participants stopped taking dapagliflozin due to adverse reactions. This was 33 out of 2,149 participants.
- 1.4% of participants stopped taking placebo due to adverse reactions. This was 30 out of 2,149 participants.

What serious adverse reactions happened during this study?

The most common serious adverse reaction during the study was sudden kidney damage.

The table below shows the serious adverse reactions that happened in at least 4 participants during this study. There were other serious adverse reactions that happened, but those happened in fewer participants.

Most common serious adverse reactions during this study

Serious adverse reaction	Dapagliflozin (out of 2,149 participants)	Placebo (out of 2,149 participants)
Sudden kidney damage	0.5% (11)	0.3% (7)
Urinary tract infection	0.2% (4)	0.2% (5)
Decreased blood sugar	0.1% (2)	0.2% (5)
Stroke	0.1% (2)	0.1% (2)

None of the participants who took the placebo died due to serious adverse reactions. There were 0.1% of participants who took dapagliflozin who died due to serious adverse reactions. This was 2 out of 2,149 participants. These adverse reactions were:

- heart attack
- stroke

What adverse reactions happened during this study?

Because the researchers did not collect information about all medical problems in the study, they could not calculate the most common adverse reactions overall.

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

Adverse reactions of interest during this study

Adverse reaction of interest	Dapagliflozin (out of 2,149 participants)	Placebo (out of 2,149 participants)
Symptoms of low levels of liquids in the body	2.5% (54)	1.4% (30)
Kidney problems	1.6% (35)	1.3% (27)
Any bone fractures	0.2% (4)	0.1% (3)
Amputation	0.1% (3)	0.1% (2)
Decreased blood sugar problems	0.1% (2)	0.3% (6)
High levels of ketones in the blood caused by low levels of insulin	0.0% (0)	0.1% (1)

How has this study helped patients and researchers?

This study helped researchers learn how dapagliflozin affects the kidneys in participants who have CKD.

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 dapagliflozin 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 **"NCT03036150"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu. Once you are on the website, click "Home and Search", then type **"2016-003896-24"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D169AC00001"** into the search box, and click **"Find a Study"**.

Full Study Title: A Study to Evaluate the Effect of Dapagliflozin on Renal Outcomes and Cardiovascular Mortality in Patients with Chronic Kidney Disease.

AstraZeneca AB Protocol Number: D169AC00001

National Clinical Trials number: NCT03036150

EudraCT Number: 2016-003896-24

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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