Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drugs Studied: Dapagliflozin and saxagliptin

Study Title: A study to learn more about how dapagliflozin and saxagliptin affect patients with type 2 diabetes and kidney damage

Thank you!

Thank you to the participants who took part in the clinical study for the study drugs dapagliflozin and saxagliptin. All of the participants helped researchers learn more about using these study drugs to help people who have type 2 diabetes and kidney damage.

AstraZeneca 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 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 doctor or staff at your study site.

What is happening with the study now?

The participants were in the study for up to about 8 months. But the entire study took about 2 years and 8 months to finish. The study started in September 2015 and ended in May 2018.

The study included 448 participants in Australia, Canada, Japan, Mexico, the Republic of Korea, South Africa, Spain, Taiwan, and 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 patients who have type 2 diabetes and kidney damage. Before a drug can be approved for patients to take, researchers do clinical studies to find out how it works and how safe it is. The study drugs, dapagliflozin and saxagliptin, are both available as treatments for people who have type 2 diabetes.

In people who have type 2 diabetes, the body does not use insulin as well as it should. Insulin is made by the pancreas and controls the levels of sugar in the blood. If a person's blood sugar levels become too high, he or she can have medical problems. One of the most common of these medical problems is damage to the kidneys.

The kidneys help the body control the levels of sugar in the blood. If sugar levels become too high, the kidneys lower the levels by getting rid of sugar through the urine. If the kidneys become damaged, they may not be able to do this as well as they should. This can cause a further increase in blood sugar levels.

Dapagliflozin may help lower the body's blood sugar levels by helping the kidneys remove sugar through the urine. Saxagliptin may help the body control blood sugar levels by increasing the amount of insulin the body makes.

In this study, the researchers wanted to learn more about using these drugs together to treat people who have type 2 diabetes. The researchers also wanted to find out if the participants had any medical problems during the study.

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

- Did the participants' kidney health change after taking the study drugs?
- Did the participants' blood sugar levels change after taking the study drugs together?
- What medical problems did the participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women who have type 2 diabetes and kidney damage. The participants in this study were 35 to 88 years old.

What kind of study was this?

The first 4 weeks of the study were "single-blind". This means the researchers knew what participants were taking but the participants did not.

Before taking any study treatment, all of the participants took a placebo for 4 weeks. 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 main part of this study was “double-blind”. 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.

During the main part of the study, the participants took 1 of 3 study treatments. All of the study treatments were taken as tablets by mouth. The doses of dapagliflozin and saxagliptin were measured in milligrams, also called mg. Below are the different treatment groups:

- 152 participants took 10 mg of dapagliflozin and 2.5 mg of saxagliptin
- 145 participants took 10 mg of dapagliflozin and a placebo
- 148 participants took 2 placebos, 1 that looked like dapagliflozin and 1 that looked like saxagliptin

A computer program was used to randomly choose the treatment that 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 the main part of the study, the participants visited their study site 3 times. At these visits, the doctors checked to make sure they could join the study. The doctors:

- did a physical examination
- took blood and urine samples
- checked the participants’ heart health using an electrocardiogram, also called an ECG
- checked the participants’ blood sugar levels and kidney health
- asked the participants about their medical history, how they were feeling, and what medicines they were taking

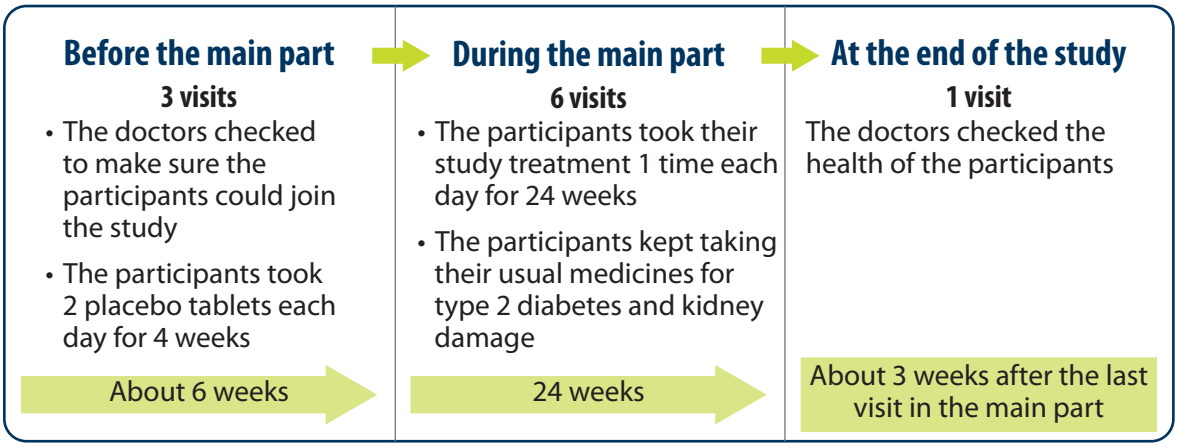
After the doctors made sure the participants could join the study, the participants took 2 placebo tablets each day for 4 weeks. They also kept taking their usual medicines for type 2 diabetes and kidney damage. At the end of this time, the participants returned to their study site. At this visit, the doctors checked the participants’ health again to make sure they could start the main part of the study.

During the main part of the study, the participants visited their study site 6 times over the course of 24 weeks. During this time, they took their study treatments 1 time each day. The participants also kept taking their usual medicines for type 2 diabetes and kidney damage.

Throughout the study, the doctors took blood and urine samples and checked the participants’ blood sugar levels, kidney health, and overall health.

At the end of the study, the participants visited their study site 1 more time. At this visit, the doctors asked the participants how they were feeling and checked their blood sugar levels, kidney health, and overall health.

The chart 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 this summary. If 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 the participants' kidney health change after taking the study drugs?

Yes. Overall, the researchers found that the participants who took dapagliflozin together with saxagliptin and the participants who took dapagliflozin and the placebo had healthier kidneys at the end of the study compared to before the study.

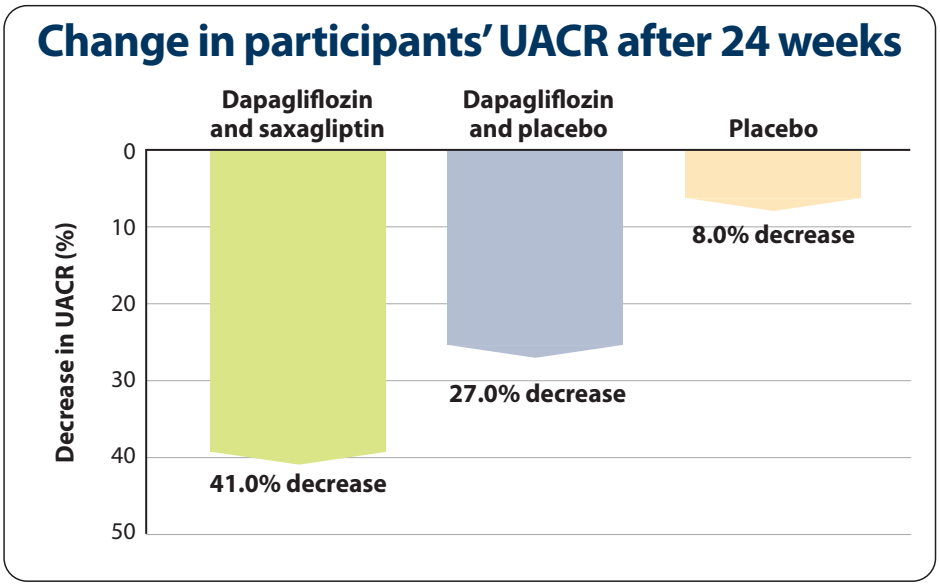
To answer this question, the researchers studied participants' kidney health throughout the study. They did this by measuring the amounts of a protein called albumin in participants' urine. Then, they compared these amounts to the amounts of a substance called creatinine in the urine.

If a person's urine contains a high amount of albumin, he or she may have damaged kidneys. The researchers in this study measured the amount of albumin by using a ratio between the amounts of albumin and creatinine in the urine. This ratio is called the urine albumin-to-creatinine ratio, which is also called the UACR. A decrease in UACR means better kidney health.

Before treatment, the participants in each treatment group had UACRs that were higher than normal. After 24 weeks of treatment, the researchers found that overall:

- The participants who took dapagliflozin and saxagliptin together had a 41.0% decrease in their UACR.
- The participants who took dapagliflozin and the placebo had a 27.0% decrease in their UACR.
- The participants who took the placebo treatment had an 8.0% decrease in their UACR.

The figure below shows these results.



Did the participants' blood sugar levels change after taking the study drugs together?

Yes. The researchers found that the participants who took dapagliflozin and saxagliptin together had a change in their blood sugar levels.

To answer this question, the researchers compared the blood sugar levels in the participants who took dapagliflozin and saxagliptin with the levels in the participants who took the placebo treatment.

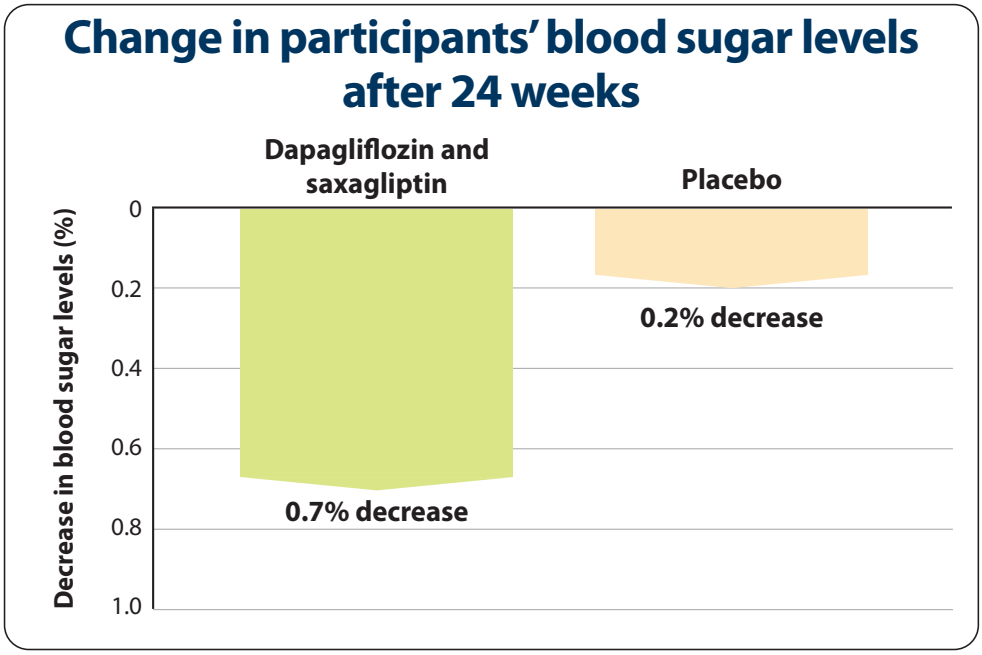
To do this, the doctors did hemoglobin A1c tests before the main part of the study and throughout the study. The hemoglobin A1c test is also called the HbA1c test. It measures how much blood sugar is attached to a protein called hemoglobin, which is found in red blood cells. Since red blood cells live for about 3 months, the HbA1c test measures the average levels of sugar in the blood over the past 3 months.

The researchers found that after 24 weeks of treatment, both treatment groups had a decrease in their blood sugar levels. The participants who took dapagliflozin and saxagliptin together had a larger decrease in their blood sugar levels compared to the participants who took the placebo treatment.

The researchers found that:

- The participants who took dapagliflozin and saxagliptin together had a 0.7% decrease in their blood sugar levels.
- The participants who took the placebo had a 0.2% decrease in their blood sugar levels.

The figure below shows these results.



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 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.

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?

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

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

Serious adverse reactions during the study			
	Dapagliflozin and saxagliptin (out of 152 participants)	**Dapagliflozin and placebo (out of 145 participants)**	**Placebo (out of 148 participants)**
Irregular heartbeat	0.7% (1)	0.0% (0)	0.0% (0)
Genital infection	0.0% (0)	0.7% (1)	0.0% (0)
Heart not pumping blood as well as it should	0.0% (0)	0.7% (1)	0.0% (0)
Brain damage from reduced blood flow in the body	0.0% (0)	0.0% (0)	0.7% (1)
Urinary tract infection	0.0% (0)	0.0% (0)	0.7% (1)

How many participants had adverse reactions?

The table below shows how many participants had adverse reactions during the study.

Adverse reactions during the study			
	Dapagliflozin and saxagliptin (out of 152 participants)	**Dapagliflozin and placebo (out of 145 participants)**	**Placebo (out of 148 participants)**
How many participants had adverse reactions during the study?	11.8% (18)	14.5% (21)	6.1% (9)
How many participants had serious adverse reactions during the study?	0.7% (1)	1.4% (2)	1.4% (2)
How many participants stopped treatment because of adverse reactions?	3.3% (5)	1.4% (2)	2.7% (4)

What adverse reactions did the participants have?

The most common adverse reaction during the study was a frequent need to urinate.

The table below shows the adverse reactions that happened in at least 2 participants in any treatment group during the study. There were other adverse reactions that happened during the study, but those happened in fewer participants.

Most common adverse reactions during the study

	Dapagliflozin and saxagliptin (out of 152 participants)	Dapagliflozin and placebo (out of 145 participants)	Placebo (out of 148 participants)
Frequent need to urinate	2.0% (3)	2.1% (3)	0.0% (0)
Passing large amounts of urine	1.3% (2)	1.4% (2)	0.0% (0)
Feeling thirsty, despite drinking fluids	1.3% (2)	0.7% (1)	0.0% (0)
Frequent need to urinate at night	1.3% (2)	0.7% (1)	0.0% (0)
High amount of uric acid in the blood, which can lead to medical problems	0.0% (0)	1.4% (2)	0.7% (1)
Urinary tract infection	0.0% (0)	0.7% (1)	1.4% (2)
Kidneys not working as well as they should	1.3% (2)	0.0% (0)	0.0% (0)
Kidney damage	0.0% (0)	1.4% (2)	0.0% (0)
Swelling at tip of the penis	0.0% (0)	1.4% (2)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about using dapagliflozin and saxagliptin to treat people who have type 2 diabetes and kidney damage.

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 dapagliflozin and saxagliptin taken together in patients who have kidney damage are not planned. A large clinical study with dapagliflozin in patients who have kidney damage is ongoing.

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 "**NCT02547935**" into the search box, and click "**Search**".
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-002676-24"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D1690C00023"** into the search box, and click **"Find a Study"**.

Full Trial Title: An Exploratory Phase II/III, Randomised, Double-Blind, Placebo Controlled, Parallel Design Study to Evaluate the Efficacy, Safety and Pharmacodynamics of Dapagliflozin and Dapagliflozin in Combination with Saxagliptin in CKD Patients with Type 2 Diabetes Mellitus and Albuminuria Treated with ACEi or ARB

AstraZeneca Protocol Number: D1690C00023

AstraZeneca sponsored this study and has its headquarters at
1800 Concord Pike in Wilmington, Delaware.

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.