Clinical Study Results

AstraZeneca

Research Sponsor: AstraZeneca

Drugs studied: Dapagliflozin and saxagliptin

Study Title: A study to learn how dapagliflozin and saxagliptin affect the HbA1c levels in people with type 2 diabetes who are already taking metformin

Thank you!

Thank you to the participants who took part in the clinical trial for the study drugs dapagliflozin and saxagliptin. You and all of the participants helped researchers learn more about how these drugs affect the hemoglobin A1c, also known as HbA1c, levels in the blood of people with type 2 diabetes who were already taking metformin.

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

What is happening with the study now?

The participants were in the study for up to about 27 weeks. But the entire study took about a year and a half to finish.

The study started in February 2016 and ended in July 2017. The study included 883 participants in Canada, the Czech Republic, Germany, Mexico, the Russian Federation, and the United States. The information for participants from 1 site was not included in the final results because the researchers were not able to accurately collect the data.

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 with type 2 diabetes. Before a drug can be approved for patients to take, researchers do clinical studies to find out how safe it is and how it works.

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

- How did dapagliflozin and saxagliptin affect the HbA1c levels of the participants?
- 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 that help find out if dapagliflozin and saxagliptin could improve the health of people with type 2 diabetes who are already taking metformin.

Insulin is a substance that is naturally made by the body. It helps the body use sugar, also known as glucose, for energy. In people with type 2 diabetes, the body does not make and use insulin normally. This makes the amount of sugar in the blood too high. High blood sugar levels can lead to several medical problems.

Dapagliflozin, saxagliptin, and metformin are drugs that are already approved to treat type 2 diabetes. But some doses of these drugs have not yet been approved to be taken together.

To answer the questions in this study, the researchers measured the levels of HbA1c in the blood. The HbA1c test measures how much blood sugar is bound to a protein called hemoglobin, which is found in the red blood cells. Since red blood cells live for about 3 months, the HbA1c test measures the average levels of sugar in the blood for the past 3 months.

The researchers asked for the help of men and women with type 2 diabetes who were already taking metformin for at least 8 weeks before joining the study. Everyone in the study was 21 to 88 years of age when they joined.

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 drug treatment each participant took during the study. Some studies are done this way because knowing what drug treatment the participants are taking can affect the results of the study. When the study ended, the research sponsor found out which drug treatment the participants took so they could create a report of the study results.

The participants in the study took 1 of 3 drug treatments:

- dapagliflozin, saxagliptin, and metformin
- dapagliflozin, a placebo, and metformin
- saxagliptin, a placebo, and metformin

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.

A computer program was used to randomly choose the drug treatment each participant took. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each drug treatment is as accurate as possible.

All of the drugs in this study were taken in tablet form by mouth.

What happened during the study?

Before the study started, the participants visited their study site twice over the course of 3 weeks. During these visits, the doctors:

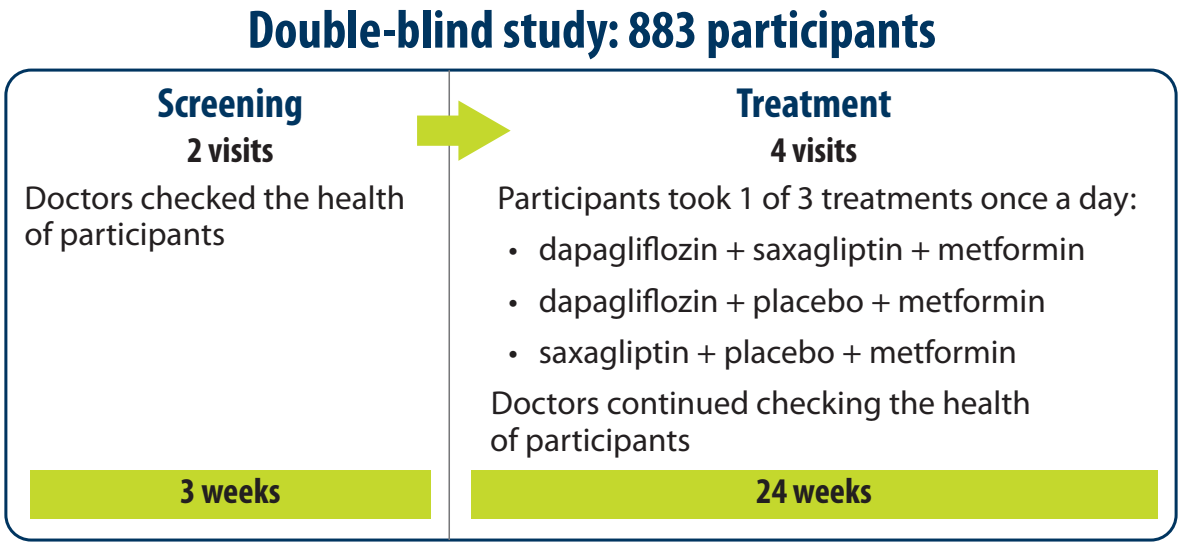
- did a physical examination
- took blood and urine samples
- checked the HbA1c levels of the participants
- asked about the medical history of the participants, how they were feeling, and what medicines they were taking

During the study, the participants visited their study site up to 4 more times over the course of 24 weeks.

During this period, the 883 participants were scheduled to take 1 of 3 drug treatments once a day.

Throughout the study, the doctors continued checking the health of the participants and asking how they were feeling. The doctors also took more blood and urine samples and checked the HbA1c levels of the participants.

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 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.

Some of the 883 participants left the study before it ended. So the researchers could not study the results and medical problems for all of the participants.

How did dapagliflozin and saxagliptin affect the HbA1c levels of the participants?

In general, after 24 weeks of treatment, the researchers found that the participants who took both dapagliflozin and saxagliptin together with metformin had the largest decrease in their HbA1c levels.

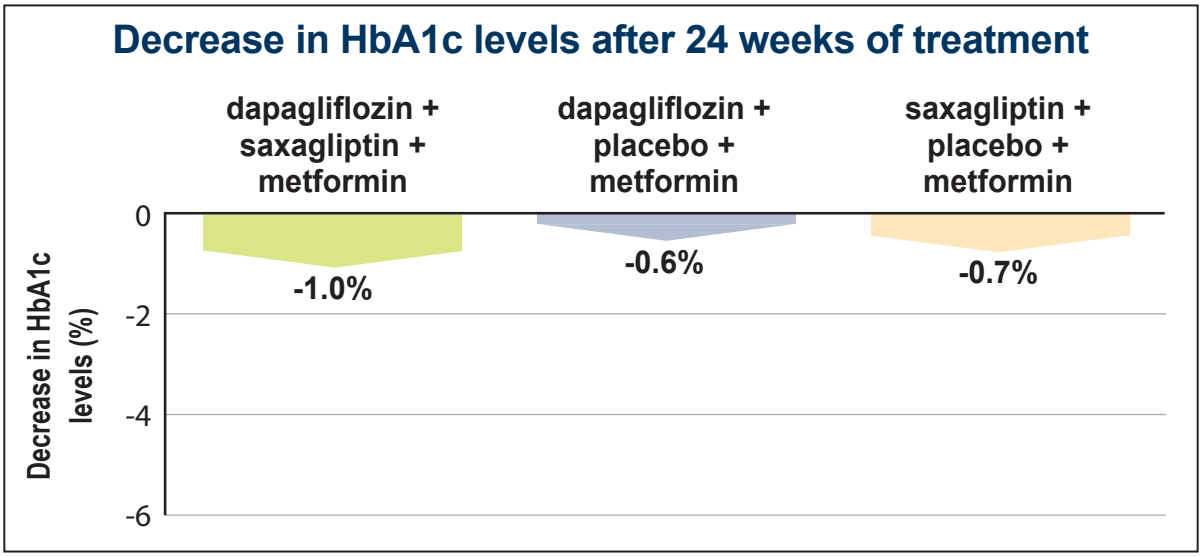
The participants who took dapagliflozin and the placebo with metformin had a similar decrease in their HbA1c levels compared to the participants who took saxagliptin and the placebo with metformin.

To answer this question, the researchers measured the HbA1c levels of the participants throughout the study.

After 24 weeks of treatment, the researchers found that on average:

- the participants who took all 3 drugs had a 1.0% decrease in their HbA1c levels
- the participants who took dapagliflozin and the placebo with metformin had a 0.6% decrease in their HbA1c levels
- the participants who took saxagliptin and the placebo with metformin had a 0.7% decrease in their HbA1c 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 more information about the adverse reactions or other medical problems that happened during this study.

How many participants had serious adverse reactions that doctors thought were related to study treatment?

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

There were 0.3% of participants who died during the study. This was 3 out of 881 participants.

- 1 participant died in a motorcycle accident
- 1 participant with a history of high blood pressure died from a heart attack
- 1 participant with a history of high cholesterol and high blood pressure died from heart failure that was caused by rapid heartbeat

The researchers did not think any of these deaths were related to the study drugs.

How many participants had adverse reactions that doctors thought were related to study treatment?

There were 9.6% of participants who had adverse reactions during the study. This was 85 out of 881 participants:

- There were 13.3% of participants who took all 3 drugs who had adverse reactions during the study. This was 39 out of 293 participants.
- There were 10.9% of participants who took dapagliflozin and the placebo with metformin who had adverse reactions during the study. This was 32 out of 293 participants.
- There were 4.7% of participants who took saxagliptin and the placebo with metformin who had adverse reactions during the study. This was 14 out of 295 participants.

None of the participants stopped treatment because of adverse reactions.

What adverse reactions did the participants have that doctors thought were related to study treatment?

The most common adverse reactions were lowering of kidney function and urinary tract infection.

The table below shows the most common adverse reactions that happened in at least 3 participants in any treatment group. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

	Dapagliflozin + Saxagliptin + Metformin (Out of 293 participants)	Dapagliflozin + Placebo + Metformin (Out of 293 participants)	Saxagliptin + Placebo + Metformin (Out of 295 participants)
Lowering of kidney function	1.7% (5)	0.7% (2)	0.3% (1)
Urinary tract infection	0.7% (2)	1.0% (3)	1.0% (3)
Frequent need to urinate	2.0% (6)	0.3% (1)	0.0% (0)
Nausea	1.4% (4)	0.7% (2)	0.3% (1)
Swelling at top of the penis	1.0% (3)	0.3% (1)	0.0% (0)

How has this study helped patients and researchers?

These results helped researchers learn more about how dapagliflozin and saxagliptin affect the HbA1c levels in people with type 2 diabetes who are already taking metformin when the 2 drugs are taken together, compared to when taken separately.

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 are not 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 **"NCT02681094"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2015-005406-11"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D1683C00005"** into the search box and click **"Find a Study"**.

Full trial title: A Multi-Center, Randomised, Double-Blind, Active-Controlled, Parallel Group, Phase III Trial to Evaluate the Safety and Efficacy of Saxagliptin 5 mg Co-administered with Dapagliflozin 5 mg compared to Saxagliptin 5 mg or Dapagliflozin 5 mg all given as Add-on therapy to Metformin in Patients with Type 2 Diabetes who have Inadequate Glycaemic Control on Metformin Alone

AstraZeneca Protocol number: D1683C00005

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 participants.

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.

CISCRP
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