Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Saxagliptin and dapagliflozin

Study Title: A study to find out how dapagliflozin, saxagliptin, and metformin work together to affect blood sugar levels in participants with type 2 diabetes compared to glimepiride and metformin

Thank you!

Thank you for taking part in the clinical study for the study drugs saxagliptin, dapagliflozin, glimepiride, and metformin. You and all of the participants helped researchers learn more about dapagliflozin, saxagliptin, and metformin compared to glimepiride and metformin to help people with type 2 diabetes. Type 2 diabetes is also called T2DM.

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 could each have been in the study for about 3 years, but the entire study took over 4 years to finish. The study started in August 2015 and finished in September 2019.

This study included a total of 444 participants in the Czech Republic, Germany, Hungary, Mexico, Poland, Romania, Russia, Sweden, the United Kingdom, 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 T2DM. 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.

In this study, the researchers wanted to find out how well dapagliflozin, saxagliptin, and metformin work together in a large number of participants with T2DM to lower blood sugar levels. They also wanted to find out if the participants had any medical problems during the study.

In people with T2DM, the body does not make enough insulin. Insulin controls the level of blood sugar, which is also called glucose. T2DM causes blood glucose levels to rise higher than normal. This can cause medical problems.

Blood glucose levels can be measured by looking at a protein in red blood cells called hemoglobin. In people with T2DM, the hemoglobin changes shape and is called HbA1c when red blood cells are carrying glucose. Lower levels of HbA1c mean improved blood glucose levels.

In this study, the researchers wanted to find out how 3 approved T2DM treatments, dapagliflozin, saxagliptin, and metformin, affected HbA1c levels in participants with T2DM when taken together. These participants had high levels of HbA1c. The researchers compared these treatments to another approved T2DM treatment called glimepiride, taken with metformin. All of the participants were already taking metformin before they started the study.

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

- Did the HbA1c levels in the participants' blood decrease after 1 year?
- 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 with T2DM. The participants in this study were aged 27 to 78 and did not have any other serious heart, kidney, or liver problems. The participants were already taking at least 1,500 milligrams of metformin for at least 8 weeks before the study, but their blood glucose levels were still not under control.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, doctors, or other study staff knew if the participants were taking saxagliptin and dapagliflozin or glimepiride. 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.

In this study, the participants either took dapagliflozin and saxagliptin or glimepiride once a day. The participants continued taking their regular doses of metformin. All of the treatments were taken as a tablet by mouth. Doses were measured in milligrams, also known as mg.

The participants also took a placebo. A placebo looks like a drug but does not have any medicine in it. The participants took a placebo so that they were taking the same number of tablets whether they took dapagliflozin and saxagliptin or glimepiride. This way, they would not know what treatment they were 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.

The chart below shows the treatments that the participants were planned to take in the study.

Saxagliptin and dapagliflozin and metformin (227 participants)	The participants took their treatment once a day by mouth: • 10 mg of dapagliflozin and 5 mg of saxagliptin • A placebo that looked like glimepiride • Their usual dose of metformin
Glimepiride and metformin (217 participants)	The participants took their treatment once a day by mouth: • Glimepiride at a starting dose of 1 mg. The dose of glimepiride could increase or decrease every 3 weeks for 12 weeks depending on each participants’ health, with a maximum dose of 6 mg. • A placebo that looked like dapaglifozin • A placebo that looked like saxagliptin • Their usual dose of metformin

What happened during the study?

Up to 4 weeks before the participants took treatment, the participants visited their study site 2 times. The study doctors checked the overall health of the participants to make sure that they could join the study. The study doctors:

- asked about the participants' health and did a physical exam
- asked about any medications the participants were taking
- gave the participants advice about diet and exercise
- took blood and urine samples from the participants
- tested the participants' HbA1c levels

The study doctors also did these tests and measurements throughout the study.

Some participants may have also been in other parts of the study. In one part, some participants got a wearable continuous glucose monitoring device, also called a CGM device. In another part, some participants had magnetic resonance imaging scans, also called MRI scans. These participants may have had more study site visits.

During the first year of the study, the participants visited their study site 9 times. The participants kept a study diary and completed several questionnaires. At each site visit, the study doctors checked the participants' health. At the first 4 visits, the participants taking glimepiride may have had their dose increased or decreased.

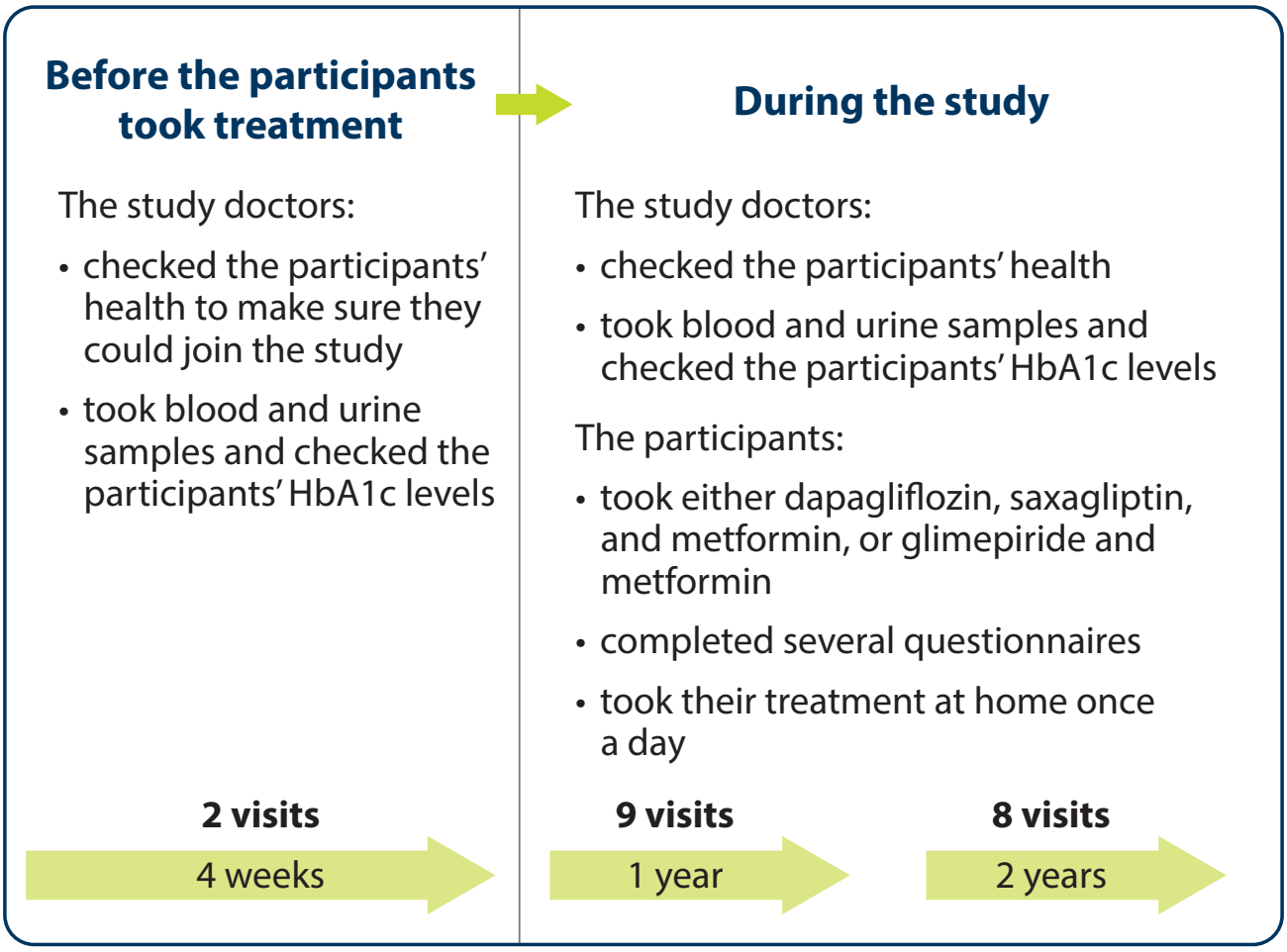
At some of these visits, the study doctors checked the participants' heart health using an electrocardiogram, also called an ECG.

Some participants completed the study after the first year and did not continue in the study.

During the next 2 years of the study, the participants visited their study site 8 times. At each site visit, the study doctors checked the participants' health. At some of these visits, the study doctors did an ECG and asked the participants to complete several questionnaires.

After the participants finished taking treatment, they did not visit their study site again.

The chart below shows what happened during the study.



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.

There was 1 participant who left the study before taking any treatment and there were 79 participants who did not complete all of the tests and measurements. So, the results below are for 364 participants.

Did the HbA1c levels in the participants' blood decrease after 1 year?

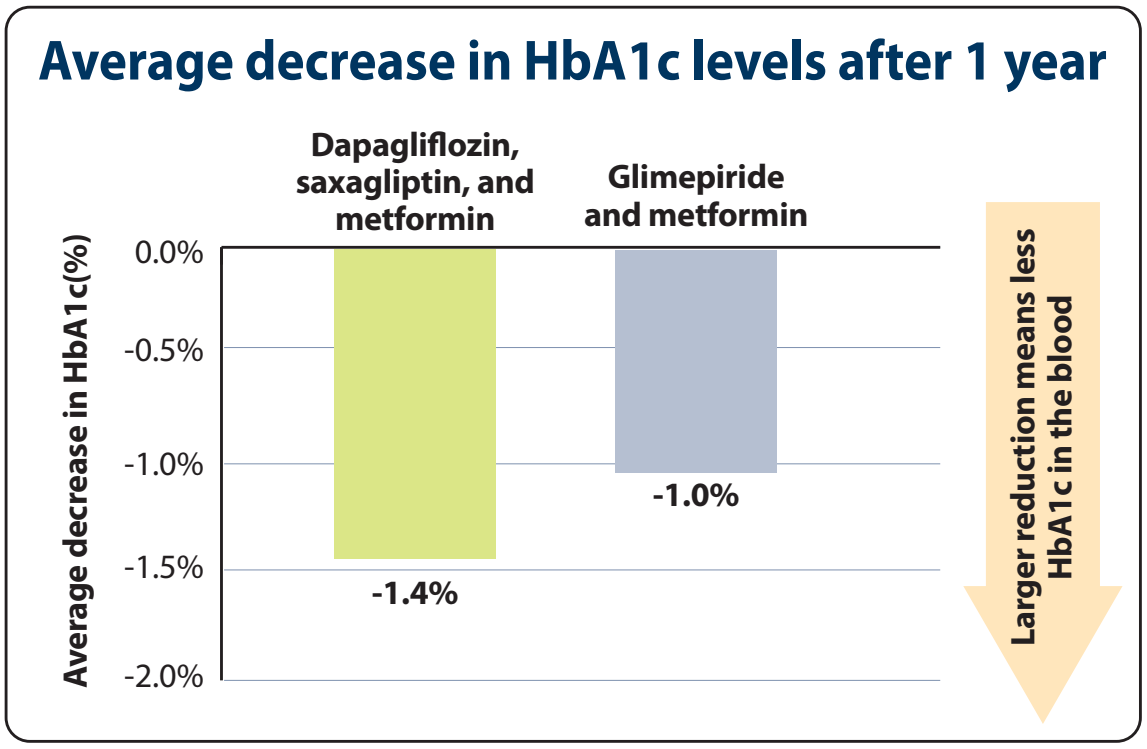
Yes. Overall, the researchers found that the HbA1c levels decreased over 1 year in the participants who took dapagliflozin, saxagliptin, and metformin and in those who took glimepiride and metformin. They found that there was a bigger overall decrease in the participants who took dapagliflozin, saxagliptin, and metformin.

To answer this question, the researchers measured the amount of HbA1c in the participants' blood before and after they took treatment in the study. HbA1c is measured as a percentage. They calculated the decrease in the participants' HbA1c levels for each treatment after 1 year.

The researchers found that the average decrease in HbA1c levels after 1 year in the participants' blood was:

- 1.4% in the participants who took dapagliflozin, saxagliptin, and metformin
- 1.0% in the participants who took glimepiride and metformin

This is shown in the graph below.



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?

There were 0.9% of participants who had serious adverse reactions during the 3 year study period. This was 4 out of 443 participants.

- 1.3% of participants who took dapagliflozin, saxagliptin, and metformin had serious adverse reactions during the study. This was 3 out of 227 participants.
- 0.5% of participants who took glimepiride and metformin had serious adverse reactions during the study. This was 1 out of 216 participants.

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

Serious adverse reaction	Dapagliflozin, saxagliptin, and metformin (out of 227 participants)	Glimepiride and metformin (out of 216 participants)
Overdose	0.4% (1)	0.5% (1)
Throat infection, also called laryngitis	0.4% (1)	0.0% (0)
Low blood sugar, also called hypoglycemia	0.4% (1)	0.0% (0)

How many participants had adverse reactions?

There were 13.8% of participants who had adverse reactions during the 3 year study period. This was 61 out of 443 participants.

- 18.1% of participants who took dapagliflozin, saxagliptin, and metformin had adverse reactions during the study. This was 41 out of 227 participants.
- 9.3% of participants who took glimepiride and metformin had adverse reactions during the study. This was 20 out of 216 participants.

There were 1.3% of participants who stopped taking dapagliflozin and saxagliptin because of adverse reactions they had during the 3 year study period. This was 3 out of 227 participants.

None of the participants stopped taking glimepiride because of adverse reactions they had during the study.

What adverse reactions did the participants have?

The most common adverse reaction was a urinary tract infection.

The table below shows the most common adverse reactions that happened in 3 or more participants in each treatment group during the 3 year study period. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions during the study

Adverse reaction	Dapagliflozin, saxagliptin, and metformin (out of 227 participants)	Glimepiride and metformin (out of 216 participants)
Urinary tract infection	4.8% (11)	2.8% (6)
Weight loss	1.8% (4)	0.0% (0)
Fungal genital infection	1.3% (3)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about how dapagliflozin, saxagliptin, and metformin worked in participants with T2DM compared with glimepiride and metformin.

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 are planned, but not with saxagliptin.

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 this website, type "**NCT02419612**" into the search box and click "**Search**"
- www.clinicaltrialsregister.eu Once you are on the website, click "Home and Search", then type "**2014-003721-18**" in the search box and click "Search".
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type "**D1689C00013**" into the search box, and click "**Find a Study**".

Full Trial Title: A 52-week International, Multicenter, Randomized, Double-Blind, Active-Controlled, Parallel Group, Phase 3b Trial with a Blinded 104-week Long-term Extension Period to Evaluate the Efficacy and Safety of Saxagliptin Co-administered with Dapagliflozin in Combination with Metformin Compared to Glimepiride in Combination with Metformin in Adult Patients with Type 2 Diabetes Who Have Inadequate Glycemic Control on Metformin Therapy Alone

National Clinical Trials number: NCT02419612

AstraZeneca Protocol Number: D1689C00013

AstraZeneca sponsored this study and has its headquarters in Cambridge, UK.

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.

CISCRP

TThe 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
One Liberty Square, Suite 1100 • Boston, MA 02109
1-877-MED-HERO • www.ciscrp.org