AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Saxagliptin

Study Title: This study was done to learn how saxagliptin worked and about its safety in participants with type 2 diabetes mellitus who also have heart failure

Protocol Number: D1680C00016

Thank you!

Thank you for taking part in the clinical study for the study drug saxagliptin.

You and all of the participants helped researchers learn more about saxagliptin to help people with type 2 diabetes mellitus and heart failure. Type 2 diabetes mellitus is also called T2DM.

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

Overview

Why was the research needed?

Researchers are looking for a different way to treat T2DM in people who also have heart failure. Researchers already did studies that showed saxagliptin worked for the people with T2DM who were in those studies. In this study, the researchers wanted to find out more about how saxagliptin works in people with T2DM and heart failure.

What treatments did the participants take?

The participants in this study took saxagliptin, or another T2DM treatment called sitagliptin, or a placebo. A placebo looks like a drug but does not have any medicine in it.

What were the results of the study?

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

> **Did saxagliptin have any effect on the participants' heart function?**

No. Overall, the researchers found that saxagliptin did not affect the participants' heart function.

> **What medical problems did the participants have during this study?**

Some of the participants had medical problems during the study that the study doctors thought might be related to the study drug. These happened in:

- 2.7% of the participants who took saxagliptin. This was 3 out of 112 participants.
- 3.5% of the participants who took sitagliptin. This was 4 out of 115 participants.
- None of the participants who took the placebo.

The most common medical problem was low blood sugar. This happened in 2 participants who took sitagliptin. All the other adverse reactions only happened in 1 person each.

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 with T2DM and heart failure. The participants in this study were 38 to 88 years old when they joined.

The study included 348 participants in 10 countries. These were Bulgaria, Canada, Chile, Hungary, Romania, Russia, South Korea, Thailand, Ukraine, and the United States.

Why was the research needed?

Researchers already did studies that showed saxagliptin worked for the people with T2DM who were in those studies. In this study, the researchers wanted to find out more about how saxagliptin works and if it has any effect on the heart.

In people with T2DM, the body does not use insulin as it should. Insulin controls the level of blood sugar, which is also called glucose. T2DM causes blood glucose levels to rise and be higher than normal. This can cause medical problems. In some cases, high blood glucose levels can cause changes in the heart muscle, leading to heart failure. Saxagliptin is used as a treatment for T2DM. It works by helping the body make and use insulin properly.

There are treatments for T2DM, but sometimes these treatments can make heart failure symptoms worse. In this study, the researchers wanted to find out whether saxagliptin affected how well the participants' hearts worked.

Sitagliptin is another T2DM treatment. It works in the same way as saxagliptin and has been shown to not make heart symptoms worse. In this study, the researchers also wanted to learn more about the safety of saxagliptin and sitagliptin compared with placebo.

What was the purpose of this study?

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

- Did saxagliptin have any effect on the participants' heart function?
- What medical problems did the participants have during this study?

The answers to these questions are important to know to find out if saxagliptin can be used to treat T2DM without having any negative effects on the heart.

What treatments did the participants take?

In this study, all of the participants took either:

- saxagliptin and a placebo, or
- sitagliptin and a placebo, or
- 2 placebos

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.

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.

The participants took their randomly chosen study treatment as tablets or capsules by mouth once a day for 24 weeks. The doses of saxagliptin and sitagliptin were measured in milligrams, also called mg. The dose that each participant received was based on their kidney function.

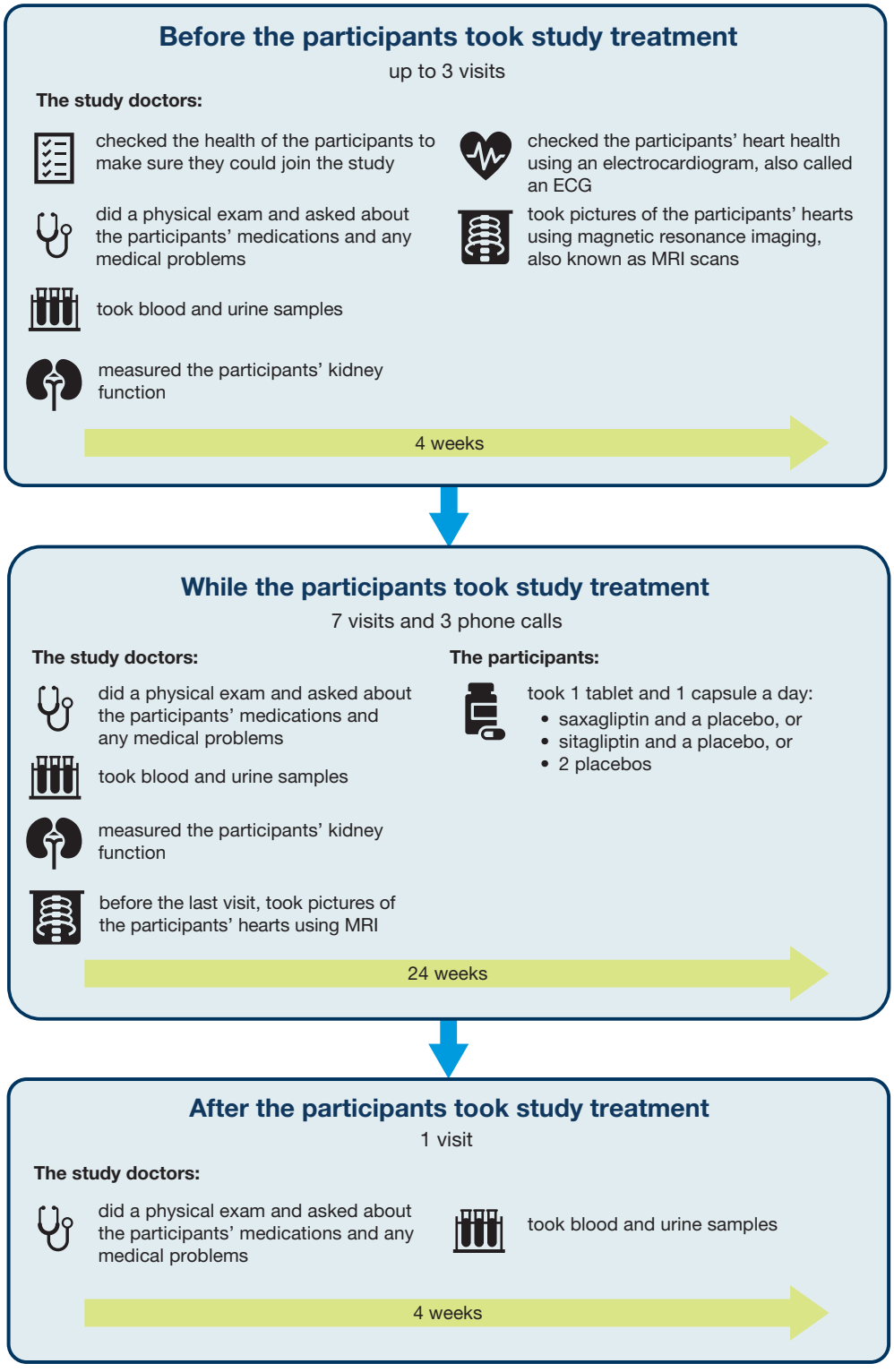
The chart below shows the treatments the researchers planned to study.

	Saxagliptin	Sitagliptin	Placebo
	112 participants	115 participants	121 participants
	5 mg or 2.5 mg of saxagliptin	100 mg or 50 mg of sitagliptin	2 placebos
	A placebo	A placebo	
	1 tablet and 1 capsule once a day for 24 weeks		

What happened during this study?

The study started in January 2017 and ended in August 2019. Individual participants were in the study for up to 32 weeks.

The chart below shows what happened during the study.



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 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 saxagliptin have any effect on the participants' heart function?

No. Overall, the researchers found that saxagliptin did not affect the participants' heart function.

To answer this question, the study doctors took pictures of the participants' hearts using magnetic resonance imaging, also called MRI. In these pictures, the study doctors looked at the shape and size of the part of the heart called the left ventricle. They then used this information to calculate the "left ventricular end diastolic volume index", also called the LVEDV index.

The higher a person's LVEDV index score, the worse their heart function is. The LVEDV index measures how many milliliters of blood the left ventricle can hold compared to the surface area of the body in square meters, also called mL/m^2. In this study, the researchers considered a participant's heart function to be "worse" if their average LVEDV index scores at the end of the study were 10.5 mL/m^2 more than the placebo scores.

The researchers compared the participants' LVEDV index scores at the start of the study with their scores after taking saxagliptin or a placebo for 24 weeks. They calculated the average change in LVEDV index scores in each group. Then, they compared the results.

There was 1 participant in the placebo group who did not take any study treatment. So, the results in this summary are for the 112 participants who took saxagliptin and the 120 participants who took the placebo.

The researchers found that the LVEDV index scores changed only by a small amount in the participants who took saxagliptin and in those who took the placebo.

Overall, the researchers found that the average increase in the participants' LVEDV index scores after 24 weeks was:

- 0.9 mL/m^2 in the participants who took saxagliptin
- 3.5 mL/m^2 in the participants who took the placebo

The saxagliptin score was 2.6 mL/m^2 less than the placebo score. This means that saxagliptin did not affect the participants' heart function.

What medical problems happened during this 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 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.

These adverse reactions may or may not be caused by the study treatments. A lot of research is needed to know whether a treatment causes an adverse reaction. These adverse reactions have been, and will continue to be, reviewed together with all of the available data for saxagliptin.

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?

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

	Saxagliptin (out of 112 participants)	Sitagliptin (out of 115 participants)	Placebo (out of 120 participants)
How many participants had adverse reactions?	2.7% (3)	3.5% (4)	0.0% (0)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	2.7% (3)	2.6% (3)	0.0% (0)

What serious adverse reactions happened during this study?

None of the participants had a serious adverse reaction or died because of a serious adverse reaction during the study.

What adverse reactions happened during this study?

The most common adverse reaction was low blood sugar.

The table below shows the adverse reactions that happened in the participants during the study. Same participants may have had more than 1 adverse reaction.

Adverse reactions

Adverse reaction	Saxagliptin (out of 112 participants)	Sitagliptin (out of 115 participants)	Placebo (out of 120 participants)
Low blood sugar	0.0% (0)	1.7% (2)	0.0% (0)
Bloating	0.9% (1)	0.0% (0)	0.0% (0)
Vomiting	0.9% (1)	0.0% (0)	0.0% (0)
Skin irritation caused by an allergy	0.9% (1)	0.0% (0)	0.0% (0)
Rash	0.9% (1)	0.0% (0)	0.0% (0)
Nausea	0.0% (0)	0.9% (1)	0.0% (0)
Heart failure	0.0% (0)	0.9% (1)	0.0% (0)

How has this study helped patients and researchers?

This study helped researchers learn more about if saxagliptin affects heart function in participants with T2DM and heart failure. It also helped researchers learn about the safety of saxagliptin.

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 saxagliptin are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below. When a full report of the study results is available, it also can be found here.

- www.clinicaltrials.gov Once you are on the website, type **"NCT02917031"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search",** then type **"2015-004825-14"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D1680C00016"** into the search box, and click **"Find a Study"**.

Full Study Title: MEchAniStic evalUation of glucose-loweRing strategiEs in patients with Heart Failure (MEASURE-HF). A 24-Week, Multicenter, Randomised, Double-blind, Parallel Group, Placebo-controlled Study to Investigate the Effects of Saxagliptin and Sitagliptin in Patients with Type 2 Diabetes Mellitus and Heart Failure

AstraZeneca AB Protocol Number: D1680C00016

National Clinical Trials number: NCT02917031

EudraCT number: 2015-004825-14

AstraZeneca AB sponsored this study and has its headquarters at Södertälje, Sweden.

The phone number for the AstraZeneca Information Center is +1-877-240-9479.

Thank you!

Clinical study participants and their families 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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