Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Dapagliflozin

Study Title: A study to learn if taking dapagliflozin affected participants with heart failure

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 if dapagliflozin affects people with heart failure.

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 about 1 year and 6 months. But, the entire study took 2 years and 5 months to finish. The study started in February 2017 and ended in July 2019.

The study included 4,744 participants in Argentina, Brazil, Bulgaria, Canada, China, the Czech Republic, Denmark, Germany, Hungary, India, Japan, the Netherlands, Poland, Russia, Slovakia, Sweden, Taiwan, the United Kingdom, the United States, and Vietnam.

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 who have heart failure. 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 if dapagliflozin works in a large number of participants with heart failure. These participants had heart failure with reduced ejection fraction, also called HFrEF. The researchers also wanted to find out if the participants had any medical problems during the study.

Heart failure is a condition where the heart muscle becomes too weak to properly pump blood through the whole body. Heart failure is a long-lasting condition that can cause symptoms such as shortness of breath, tiredness, and swelling of certain tissues. In serious cases of heart failure, there is an increased risk of other heart problems, and of death.

The study drug, dapagliflozin, is used for people with type 2 diabetes. It helps the body remove sugar from the blood and leave the body in the urine. Researchers think dapagliflozin could help reduce the risk of heart failure.

In this study, the researchers wanted to find out more about if dapagliflozin affects participants who have heart failure.

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

- Did the participants who took dapagliflozin have fewer heart failure related hospital visits and fewer deaths from heart problems?
- Did the participants feel their heart failure symptoms were better after taking dapagliflozin?
- 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 heart failure who may or may not have type 2 diabetes. The participants were between the ages of 22 and 94.

What kind of study was this?

This was a “double-blind” study. This means none of the participants, doctors, or other AstraZeneca 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.

The participants in this study took either 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 took dapagliflozin or the placebo once a day, as tablets. The dose of dapagliflozin was 10 milligrams, also known as mg.

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

In this study, there were 2,373 participants in the dapagliflozin group and 2,371 participants in the placebo group.

During the study, the participants could continue taking any medication that they were already taking for their heart problems.

What happened during the study?

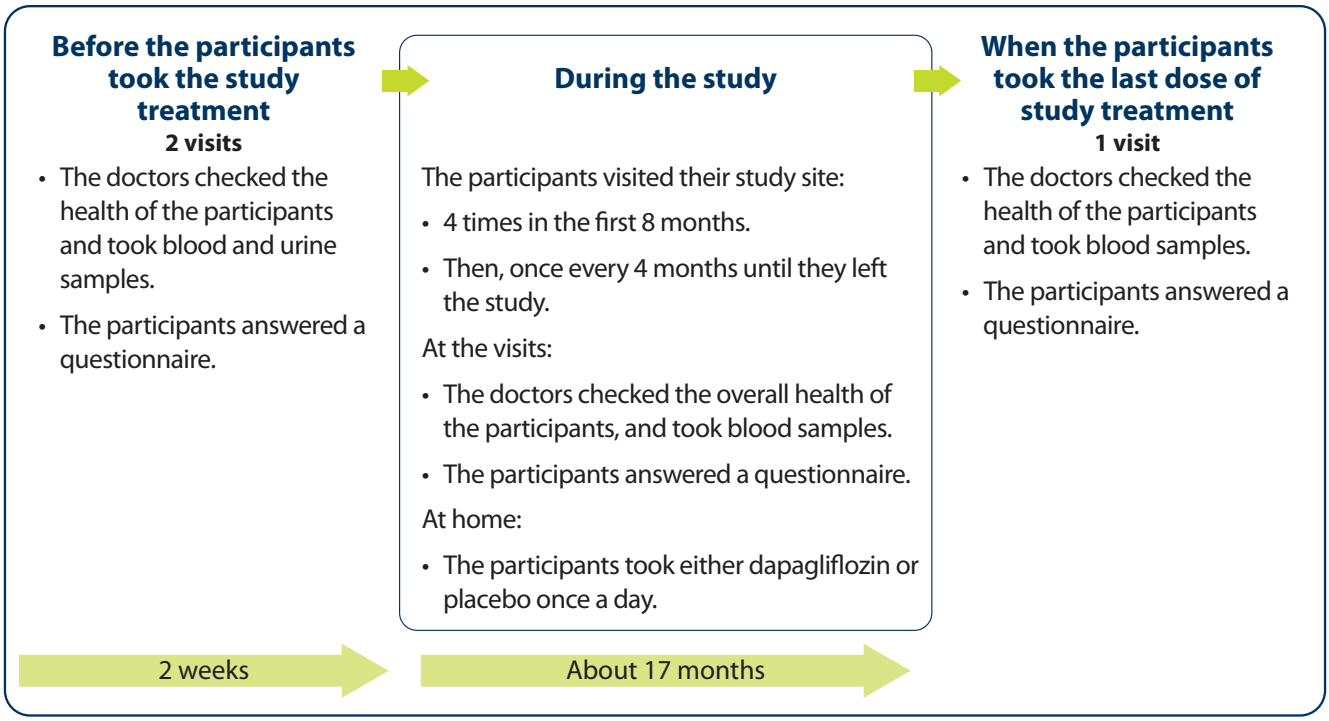
Before the participants took study treatment, they visited their study site 1 time. At this visit, the doctors checked their overall health to make sure they could join the study. The doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- took blood and urine samples
- tested the health of the participants' hearts using an electrocardiogram and an echocardiogram
- **During the study,** the doctors gave the participants their study treatment to take at home. The participants each took 1 tablet a day at home for about 17 months. They visited their study site 5 times in the first 8 months, and then once every 4 months until they left the study. At most visits, the participants answered a questionnaire about their symptoms. The doctors:
- did a physical exam
- took blood and urine samples
- asked the participants about any health problems or any medications they were taking

When the participants took the last dose of study treatment, they visited the study site 1 more time. At this visit, the participants answered a questionnaire about their symptoms. The doctors:

- did a physical exam
- took blood samples
- asked the participants about any health problems or any medications they were taking

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 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 who took dapagliflozin have fewer heart failure related hospital visits and fewer deaths from heart problems?

Yes. Overall, the participants who took dapagliflozin had fewer heart failure related hospital visits and fewer deaths from heart problems compared to the participants who took the placebo.

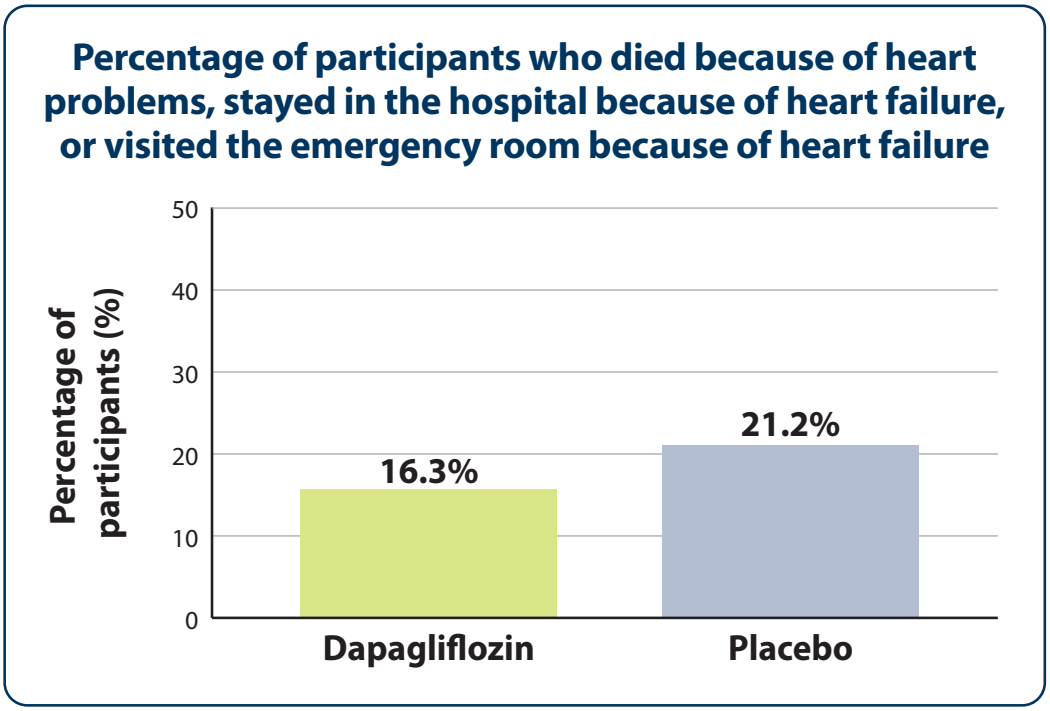
To answer this question, the researchers counted the total number of participants who:

- died because of heart problems
- stayed in the hospital because of heart failure
- visited the emergency room because of heart failure

The researchers compared these results for the participants who took dapagliflozin and the participants who took the placebo. They found that during the study, the percentage of participants who died because of heart problems, stayed in the hospital because of heart failure, or visited the emergency room because of heart failure was:

- 16.3% in the dapagliflozin group. This was 386 out of 2,373 participants.
- 21.2% in the placebo group. This was 502 out of 2,371 participants.

The figure below shows these results:



Did the participants feel their heart failure symptoms were better after taking dapagliflozin?

Yes. Overall, the researchers found that after 8 months of study treatment, more participants who took dapagliflozin felt that their heart failure symptoms were better compared to the participants who took the placebo.

To answer this question, the doctors gave the participants the Kansas City Cardiomyopathy Questionnaire, also called the KCCQ. This questionnaire asks about heart failure symptoms. The KCCQ is scored out of 100 and a higher score means better heart failure symptoms.

The researchers compared the results of the questionnaire from the beginning of the study with the results after the participants had taken study treatment for 8 months. They counted how many participants scored at least 5 points higher after 8 months, and how many scored at least 5 points lower or died. They compared the results between the dapagliflozin and placebo groups.

There were 596 participants who did not answer the questionnaire at the beginning of the study and after 8 months. So, the results below include information for 4,148 participants.

The researchers found that the percentage of participants whose total score got higher by at least 5 points was:

- 57.4% in the dapagliflozin group. This was 1,198 out of 2,086 participants.
- 50.0% in the placebo group. This was 1,030 out of 2,062 participants.

The percentage of participants whose total score got lower by at least 5 points, or who died, was:

- 25.1% in the dapagliflozin group. This was 524 out of 2,086 participants.
- 33.1% in the placebo group. This was 682 out of 2,062 participants.

What medical problems did participants have 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. 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”.

The 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 doctors did not know whether they were taking dapagliflozin or the placebo.

The websites listed at the end of this summary may have information about other medical problems that happened during this study.

The results below are for 4,736 participants who took at least 1 dose of study treatment.

How many participants had serious adverse reactions?

Overall, 2.0% of participants had a serious adverse reaction. This was 94 out of 4,736 participants.

- 1.9% of participants in the dapagliflozin group had a serious adverse reaction. This was 45 out of 2,368 participants.
- 2.1% of participants in the placebo group had a serious adverse reaction. This was 49 out of 2,368 participants.

The table below shows the serious adverse reactions that happened in more than 1 participant during the study. There were other serious adverse reactions, but these happened in fewer participants.

Most common serious adverse reactions

Serious adverse reaction	Dapagliflozin (out of 2,368 participants)	Placebo (out of 2,368 participants)
Chronic or continuous heart failure	0.34% (8)	0.34% (8)
Urinary tract infection	0.30% (7)	0.17% (4)
Kidney injury	0.08% (2)	0.21% (5)
Heart failure caused by a build-up of fluid around the heart	0.08% (2)	0.17% (4)
Death of brain tissue from lack of blood flow	0.08% (2)	0.04% (1)
Sudden death	0.08% (2)	0.0% (0)
Low blood pressure	0.04% (1)	0.13% (3)
Fainting	0.04% (1)	0.13% (3)
Acute or urgent heart failure	0.04% (1)	0.08% (2)
Heart attack	0.04% (1)	0.04% (1)
Low blood volume	0.04% (1)	0.04% (1)
Kidney infection	0.04% (1)	0.04% (1)
Kidney failure	0.04% (1)	0.04% (1)
Abnormal heart rhythm	0.04% (1)	0.04% (1)

The researchers collected information on all serious adverse reactions that led to the death of any participants. There were 0.2% of participants who died from a serious adverse reaction during the study. This was 11 out of 4,736 participants.

- 0.3% of participants in the dapagliflozin group died from a serious adverse reaction. This was 6 out of 2,368 participants.
- 0.2% of participants in the placebo group died from a serious adverse reaction. This was 5 out of 2,368 participants.

How many participants had adverse reactions?

Because the researchers did not collect information about all medical problems in the study, they could not calculate how many participants had adverse reactions overall.

The researchers collected information on **all** adverse reactions that led to any participants stopping their study treatment. There were 1.7% of participants who stopped taking their study treatment because of an adverse reaction. This was 79 out of 4,736 participants.

- 1.7% of participants in the dapagliflozin group stopped taking their study treatment because of an adverse reaction. This was 40 out of 2,368 participants.
- 1.6% of participants in the placebo group stopped taking their study treatment because of an adverse reaction. This was 39 out of 2,368 participants.

What adverse reactions did the participants have?

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 reaction of interest	Dapagliflozin (out of 2,368 participants)	Placebo (out of 2,368 participants)
Loss of fluid in the body	2.87% (68)	2.24% (53)
Kidney problems	1.39% (33)	1.18% (28)
Bone fracture	0.13% (3)	0.04% (1)
Amputation	0.04% (1)	0.04% (1)
High amounts of acid in the blood caused by diabetes	0.04% (1)	0.00% (0)
Extremely low blood sugar	0.00% (0)	0.04% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about if taking dapagliflozin affected participants with heart failure.

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 study drug are 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 **"NCT03036124"** into the search box, and click **"Search"**.
- www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search"**, then type **"2016-003897-41"** in the search box, and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D1699C00001"** into the search box, and click **"Find a Study"**.

Full Trial Title: Study to Evaluate the Effect of Dapagliflozin on the Incidence of Worsening Heart Failure or Cardiovascular Death in Patients with Chronic Heart Failure with Reduced Ejection Fraction.

National Clinical Trials number: NCT03036124

EudraCT Number: 2016-003897-41

AstraZeneca Protocol Number: D1699C00001

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

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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