AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca

Drug Studied: Dapagliflozin

Study Title: This study was done to learn how dapagliflozin worked and about its safety in participants with a type of heart failure called HFrEF

Protocol Number: D169EC00002

Thank you!

Thank you for taking part in the clinical study for the study treatment dapagliflozin.

You and all of the participants helped researchers learn more about dapagliflozin to help people who have a type of heart failure called HFrEF. HFrEF stands for 'heart failure with reduced ejection fraction'. HFrEF happens when the heart is too weak to pump blood around the body normally.

AstraZeneca 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 better way to treat people who have a type of heart failure called HFrEF. Researchers already did studies that showed dapagliflozin worked for people with HFrEF who were in those studies. In this study, the researchers wanted to find out more about how dapagliflozin works.

What treatments did the participants take?

The participants in this study took dapagliflozin or a placebo. A placebo looks like a treatment 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:

- **After 16 weeks, did the participants feel that dapagliflozin helped their overall heart failure symptoms?**

  Yes. Overall, the participants who took dapagliflozin felt that it helped their overall heart failure symptoms after 16 weeks.

- **After 16 weeks, did the participants feel that dapagliflozin helped their physical symptoms caused by heart failure?**

  No. Overall, the participants who took dapagliflozin did not feel that it helped their physical symptoms caused by heart failure after 16 weeks.

- **After 16 weeks, could the participants who took dapagliflozin walk farther in 6 minutes?**

  No. Overall, the participants who took dapagliflozin could not walk farther in 6 minutes after 16 weeks.

What medical problems did the participants have during this study?

There were 9.6% of participants who had medical problems that the study doctors thought might be related to the study treatment during the study. This was 30 out of 313 participants who took study treatment. The most common medical problem was low blood pressure.

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 a type of heart failure called HFrEF. The participants in this study were 30 to 93 years old when they joined. People with other types of heart failure did not participate in this study.

The study included 313 participants in 9 countries. These were Brazil, Canada, Denmark, Japan, Slovakia, South Africa, South Korea, Sweden and the United States.

Why was the research needed?

Researchers are looking for a different way to treat people who have heart failure with reduced ejection fraction, also called HFrEF. Researchers already did studies that showed dapagliflozin worked for the people with HFrEF who participated in those studies.

In this study, the researchers wanted to find out if dapagliflozin improved how a large number of participants with HFrEF felt and functioned in their everyday lives. They also wanted to find out if the participants had any medical problems during the study.

HFrEF happens when the heart is too weak to pump as much blood as it normally would each time it beats. This means that the heart cannot pump as much blood around the body as it normally would.

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 treatment, dapagliflozin, is used as a treatment for people with type 2 diabetes and also for people with HFrEF.

What was the purpose of this study?

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

- After 16 weeks, did the participants feel that dapagliflozin helped their overall heart failure symptoms?
- After 16 weeks, did the participants feel that dapagliflozin helped their physical symptoms caused by heart failure?
- After 16 weeks, could the participants who took dapagliflozin walk farther in 6 minutes?
- What medical problems did the participants have during the study?

The answers to these questions are important to know to understand how dapagliflozin can help improve the health of people with HFrEF.

What treatments did the participants take?

In this study, the participants took either dapagliflozin or 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.

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. 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 the participants took so they could create a report of the study results.

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 dapagliflozin or the placebo as a tablet by mouth once a day, for 16 weeks. The dose of dapagliflozin was 10 milligrams, also called mg.

The chart below shows the number of participants in the study and treatments they were given.

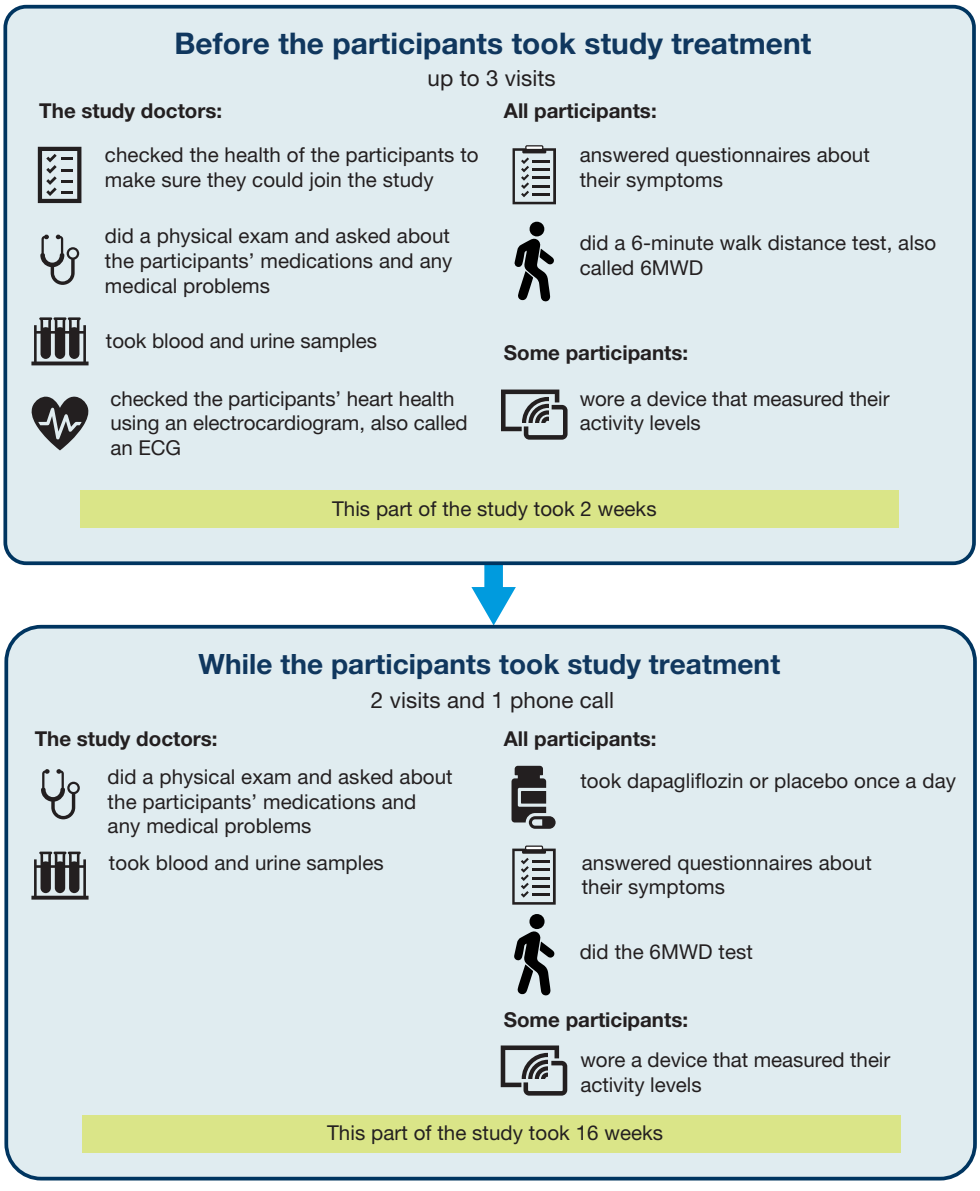
	Dapagliflozin	Placebo
	• 156 participants	• 157 participants
	• 10 mg of dapagliflozin	• Placebo
	• 1 tablet by mouth once a day for 16 weeks	• 1 tablet by mouth once a day for 16 weeks

What happened during this study?

Each of the participants was in the study for up to just over 20 weeks. But, the entire study took 11 months to finish.

The study started in April 2019 and ended in March 2020.

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.

The table below shows the different methods the researchers used to find out if dapagliflozin was helping the participants.

	KCCQ-TSS	KCCQ-PLS	6MWD
What does it stand for?	Kansas City Cardiomyopathy Questionnaire – Total Symptom Score	Kansas City Cardiomyopathy Questionnaire – Physical Limitation Score	6 Minute Walk Distance
What does it measure?	Overall heart failure symptoms	Physical symptoms caused by heart failure	How far a person can walk in 6 minutes
What does the test involve?	Answering 7 questions about overall heart failure symptoms	Answering 6 questions about physical symptoms	The participant walks for 6 minutes and the study doctor measures how far they walked
What do the scores mean?	The questionnaires are scored from 0 to 100. A higher score means fewer heart failure symptoms or less severe physical symptoms		The distance the participant walked is measured in meters, also called m. A longer distance means less impact of severe symptoms on the participant's ability to walk
When were these tests done during the study?	At study site visits		
Which participants' results were included?	The participants' results were only included if they: • had completed the tests at the start and end of the study, or • died during the study		
How did the researchers use these test results in the study?	For all 3 tests, the study doctors compared the participants' scores at the start of the study with their scores 16 weeks after starting study treatment. Then, they compared the results between the participants who took dapagliflozin and those who took a placebo. To do this, they used a type of average called a median. In a set of numbers, the median is the middle number between the lowest and highest numbers.		

After 16 weeks, did the participants feel that dapagliflozin helped their overall heart failure symptoms?

Yes. Overall, the participants who took dapagliflozin felt that it helped their overall heart failure symptoms after 16 weeks.

The numbers of participants whose results were included in this part of the study were:

- 153 participants who took dapagliflozin
- 147 participants who took placebo

Overall, the researchers found that the median changes in total symptom scores 16 weeks after starting the study treatment were:

- 2.1 points for the participants who took dapagliflozin
- 0.0 points for the participants who took the placebo

The researchers then did extra statistical tests on these results that showed dapagliflozin did not help the participants' overall heart failure symptoms.

After 16 weeks, did the participants feel that dapagliflozin helped their physical symptoms caused by heart failure?

No. Overall, the participants who took dapagliflozin did not feel that it helped their physical symptoms caused by heart failure after 16 weeks.

The numbers of participants whose results were included in this part of the study were:

- 150 participants who took dapagliflozin
- 146 participants who took a placebo

Overall, the researchers found that the median changes in physical symptom scores 16 weeks after starting the study treatment were:

- 4.2 points for the participants who took dapagliflozin
- 0.0 points for the participants who took a placebo

The researchers then did extra statistical tests on these results that showed that dapagliflozin did not help the participants' physical symptoms caused by heart failure.

After 16 weeks, could the participants who took dapagliflozin walk farther in 6 minutes?

No. Overall, the participants who took dapagliflozin could not walk farther after taking study treatment.

The numbers of participants whose results were included in this part of the study were:

- 150 participants who took dapagliflozin
- 148 participants who took a placebo

Overall, the researchers found that the participants could walk a median of:

- 20.0 m farther than at the start of the study, for the participants who took dapagliflozin
- 13.5 m farther than at the start of the study, for the participants who took the placebo

The researchers then did extra statistical tests on these results that showed that dapagliflozin did not help the participants walk farther.

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 treatment. 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 treatment. 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 the study treatment.

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 shows what percentage of participants had adverse reactions during the study. The numbers in parentheses are the number of participants who had an adverse reaction.

	Dapagliflozin (out of 156 participants)	**Placebo (out of 157 participants)**
What percentage of participants had adverse reactions?	11.5% (18)	7.6% (12)
What percentage of participants had serious adverse reactions?	1.3% (2)	1.3% (2)
What percentage of participants stopped taking study treatment due to adverse reactions?	2.6% (4)	4.5% (7)

What serious adverse reactions happened during this study?

The table below shows the serious adverse reactions that happened during the study. The numbers in parentheses are the number of participants who had an adverse reaction.

Serious adverse reactions

Serious adverse reaction	Dapagliflozin (out of 156 participants)	Placebo (out of 157 participants)
Narrowing of the arteries in the arms and legs	0.6% (1)	0.0% (0)
High blood sugar	0.6% (1)	0.0% (0)
Liver not working properly	0.0% (0)	0.6% (1)
Sudden kidney damage	0.0% (0)	0.6% (1)

None of the participants died due to serious adverse reactions.

What adverse reactions happened during this study?

The most common adverse reaction was low blood pressure.

The table below shows the adverse reactions that happened in 2 or more participants during the study. There were other adverse reactions, but these happened in only 1 participant each. Some participants may have had more than 1 adverse reaction. The numbers in parentheses are the number of participants who had an adverse reaction.

Most common adverse reactions

Adverse reaction	Dapagliflozin (out of 156 participants)	Placebo (out of 157 participants)
Low blood pressure	1.9% (3)	1.3% (2)
Cough	1.3% (2)	0.0% (0)
Painful urination	1.3% (2)	0.0% (0)
Kidney function getting worse	0.6% (1)	0.6% (1)

How has this study helped patients and researchers?

This study helped researchers learn more about if dapagliflozin affected how participants with HFrEF felt and functioned in their everyday lives.

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 dapagliflozin are ongoing.

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 **"NCT03877237"** into the search box and click **"Search"**.
- http://www.clinicaltrialsregister.eu Once you are on the website, click **"Home and Search",** then type **"2018-003442-16"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D169EC00002"** into the search box, and click **"Find a Study"**.

Full Study Title: An International, Multicentre, Parallel-group, Randomised, Double-blind, Placebo-controlled, Phase III Study Evaluating the effect of Dapagliflozin on Exercise Capacity in Heart Failure Patients with Reduced Ejection Fraction (HFrEF)

AstraZeneca Protocol number: D169EC00002

National Clinical Trials number: NCT03877237

EudraCT number: 2018-003442-16

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

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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