Clinical Study Results

Research Sponsor: AstraZeneca AB

Drug Studied: Dapagliflozin

Study Title: A study to find out if dapagliflozin affects blood sugar levels in participants with type 2 diabetes

Thank you!

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

You and all of the participants helped researchers learn more about dapagliflozin to help people with type 2 diabetes mellitus, 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 better way to treat people with T2DM. Before a drug can be approved for participants to take, researchers do clinical studies to find out how it works and how safe it is.

What treatments did the participants take?

This study was divided into 2 parts. All of the participants took dapagliflozin in 1 part of the study and a placebo in the other part. A placebo looks like a drug but does not have any medicine in it. The 2 parts of the study were 6 to 8 weeks apart.

What were the results of the study?

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

- Did dapagliflozin affect the amount of glucose that left the participants' blood?
- What medical problems did the participants have during the study?

Overall, the researchers found that dapagliflozin did not change the amount of glucose that left the participants' blood compared with the placebo.

During the study, none of the participants had any medical problems that the study doctors thought might be related to the study treatment.

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 can also be found on those websites.

Who took part in the study?

The researchers asked for the help of men and women with T2DM. When they joined the study, the participants could already be taking:

- a T2DM treatment called metformin
- a type of treatment called a DPP-IV inhibitor
- no T2DM treatment at all

The participants in this study were 56 to 71 years old when they joined and did not have any other serious medical conditions.

The study included 26 participants in the Netherlands.

Why was the research needed?

Researchers are looking for a better way to treat people with T2DM. Before a drug can be approved for people to take, researchers do clinical studies to find out how it works and how safe it is.

Researchers already did studies that showed that dapagliflozin worked for the people with T2DM who were in those studies.

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

The study drug, dapagliflozin, works by helping the kidneys remove glucose from the blood and clear it away through the urine. In this study, the researchers wanted to find out if dapagliflozin affected how much glucose left the participants' blood.

What was the purpose of this study?

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

- Did dapagliflozin affect the amount of glucose that left the participants' blood?
- 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 to find out if dapagliflozin helps improve the health of people with T2DM.

What treatments did the participants take?

This study was divided into 2 parts. It was planned that all of the participants would take dapagliflozin in one part of the study and a placebo in the other part of the study. 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.

Each part lasted for 5 weeks. After completing Part 1, the participants waited 6 to 8 weeks before taking the study treatment in Part 2.

A computer program was used to randomly choose the order of treatments 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.

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.

The participants took dapagliflozin and the placebo once a day as a tablet by mouth. The dose of dapagliflozin was 10 milligrams, also known as mg.

There was 1 participant who left the study after taking dapagliflozin in Part 1. So, this participant is not included in the group who took the placebo in Part 2.

The table below shows the treatments the participants took.

Part 1	Part 2
12 participants took dapagliflozin	11 participants took a placebo that looked like dapagliflozin
14 participants took a placebo that looked like dapagliflozin	14 participants took dapagliflozin
Once a day	Once a day

What happened during the study?

The participants were in the study for up to 22 weeks. But, the entire study took 20 months to finish. The study started in March 2018 and ended in November 2019. The chart below shows what happened during the study.

Before the participants took study treatment

1 visit

At this visit the study doctors:

- checked the health of the participants to make sure they could join the study
- took blood and urine samples
- did a physical exam and asked about the participants' medications and any medical problems
- checked the participants' heart health using an electrocardiogram, also called an ECG

Up to 3 weeks

While the participants took study treatment

3 visits in each part

At the visits, the study doctors:

- did a physical exam and asked about the participants' medications and any medical problems
- did a scan to find out the percentages of muscle, bone, and fat in the participants' body
- took blood and urine samples
- took a muscle biopsy
- gave the participants infusions of insulin and glucose to measure the amount of glucose that left the participants' blood
- did an MRI scan to measure fat levels after the participants exercised

The participants:

- took daily doses of dapafliglozin or the placebo
- did a cycling test so the study doctors could check how much oxygen they took in (only during Part 1)
- stayed in a small room for 1.5 days so that the study doctors could measure how much energy and what nutrients their body used

5 weeks in each part

In between Part 1 and Part 2, the study doctors called the participants to ask about their medications and any medical problems they were having.

After the participants took study treatment

1 visit

At this visit, the study doctors:

- asked about any medical problems the participants had

Up to 10 days

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. 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.

There was 1 participant who left the study before completing Part 2. The study doctors were also not able to use the results from 3 other participants. So, the results below include 22 out of 26 participants.

Did dapagliflozin affect the amount of glucose that left the participants' blood?

No. Overall, the researchers found that compared with the placebo, dapagliflozin did not affect the amount of glucose that left the participants' blood.

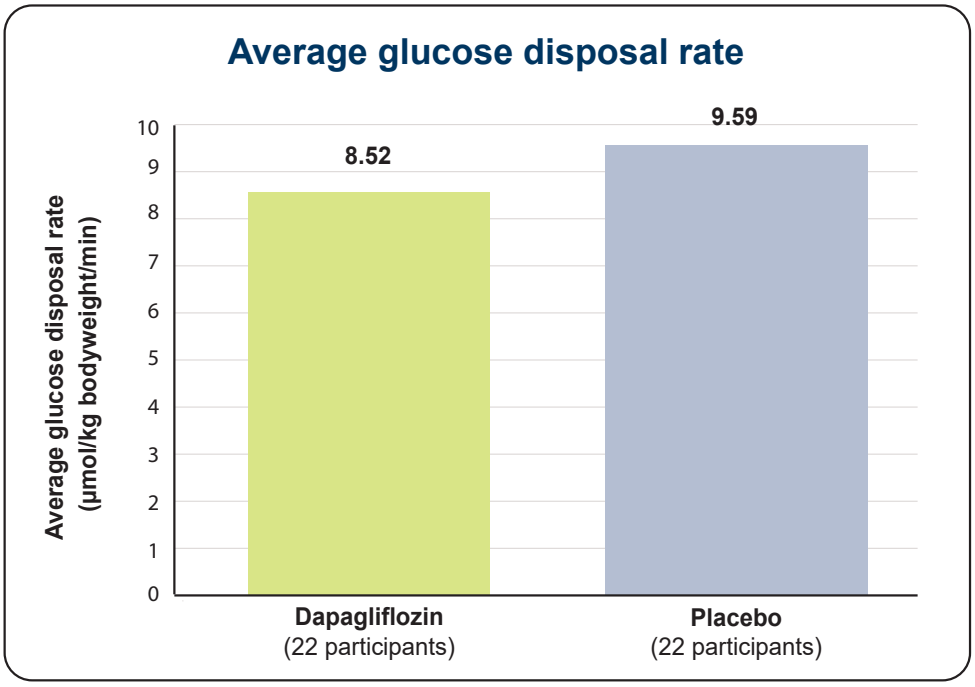
To answer this question, the study doctors measured the rate at which glucose left the participants' blood after they took study treatment for 5 weeks. This is called the "glucose disposal rate". The glucose disposal rate is measured in micromoles per kilogram body weight per minute, also known µmol/kg body weight/min.

The study doctors measured the glucose disposal rate after Part 1 and after Part 2 for each participant. Then, they calculated the average for all of the participants. The study doctors compared the results when the participants took dapagliflozin to the results when they took the placebo.

The researchers found that the average glucose disposal rate was similar between the study treatments:

- 8.52 µmol/kg body weight/min when the participants took dapagliflozin
- 9.59 µmol/kg body weight/min when the participants took the placebo

The chart below shows these results.



What medical problems happened 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 drug. 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 drug. A lot of research is needed to know whether a drug 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 drug.

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?

None of the participants had adverse reactions during this study.

How has this study helped patients and researchers?

This study helped researchers learn more about how dapagliflozin works in people with T2DM. 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 the 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 more information about the study results is available, it can also be found here.

- www.clinicaltrials.gov. Once you are on this website, type **"NCT03338855"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2016-003991-27"** in the search box and click **"Search"**.
- www.AstraZenecaClinicalTrials.com. Once you are on the website, type **"D1690C00047"** into the search box, and click **"Find a Study"**.

Full Study Title: DAPAMAAST: A Double-blind, Randomized, Phase IV, Mechanistic, Placebo-controlled, Cross-over, Single-center Study to Evaluate the Effects of 5 Weeks Dapagliflozin Treatment on Insulin Sensitivity in Skeletal Muscle in Type 2 Diabetes Mellitus Patients

AstraZeneca Protocol Number: D1690C00047

National Clinical Trials number: NCT03338855

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

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.

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