Clinical Study Results

Research sponsor: AstraZeneca K.K.

Drug studied: Dapagliflozin

Study title: A study to learn if dapagliflozin combined with insulin is safe to take and how these combined drugs affect the body

Thank you!

Thank you for taking part in the clinical trial for the study drug dapagliflozin. You and all of the participants helped researchers learn more about dapagliflozin to help people with type 1 diabetes.

AstraZeneca K.K. 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?

You were in the study for about 15 months. But the entire study took about 21 months to finish.

The study started in October 2015 and ended in June 2017. The study included 151 participants at 29 study sites in Japan.

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 type 1 diabetes. Before a drug can be approved for patients to take with other drugs, researchers do clinical studies to find out how it works and how safe it is.

In this study, researchers wanted to find out how dapagliflozin affects the body when it is taken with insulin in a large number of participants with type 1 diabetes. They also wanted to find out if the participants had any medical problems during the study.

Dapagliflozin is already approved to treat type 2 diabetes. But, dapagliflozin has not yet been approved to treat type 1 diabetes.

Type 1 diabetes is a disease that causes the body to not make enough insulin. Insulin helps control the amount of glucose, also known as sugar, in the blood. If the body doesn't make enough insulin, the amount of sugar in the blood can be too high.

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

- How did dapagliflozin combined with insulin affect the body?
- What medical problems did participants have during the study?

To answer the questions in this study, the researchers asked for the help of men and women with type 1 diabetes who had been taking insulin for at least 12 months before joining the study. The participants in this study were 21 to 73 years old.

What kind of study was this?

This was an "open-label" study. This means the researchers and the participants knew what the participants were taking.

In this study, all of the participants took dapagliflozin and insulin. The amount of insulin each participant took was decided by the study doctors, but the dose of dapagliflozin was chosen randomly.

A computer program was used to randomly choose the dose of dapagliflozin 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.

What happened during the study?

The participants were in this study for about 15 months. They visited the study site 15 or 16 times.

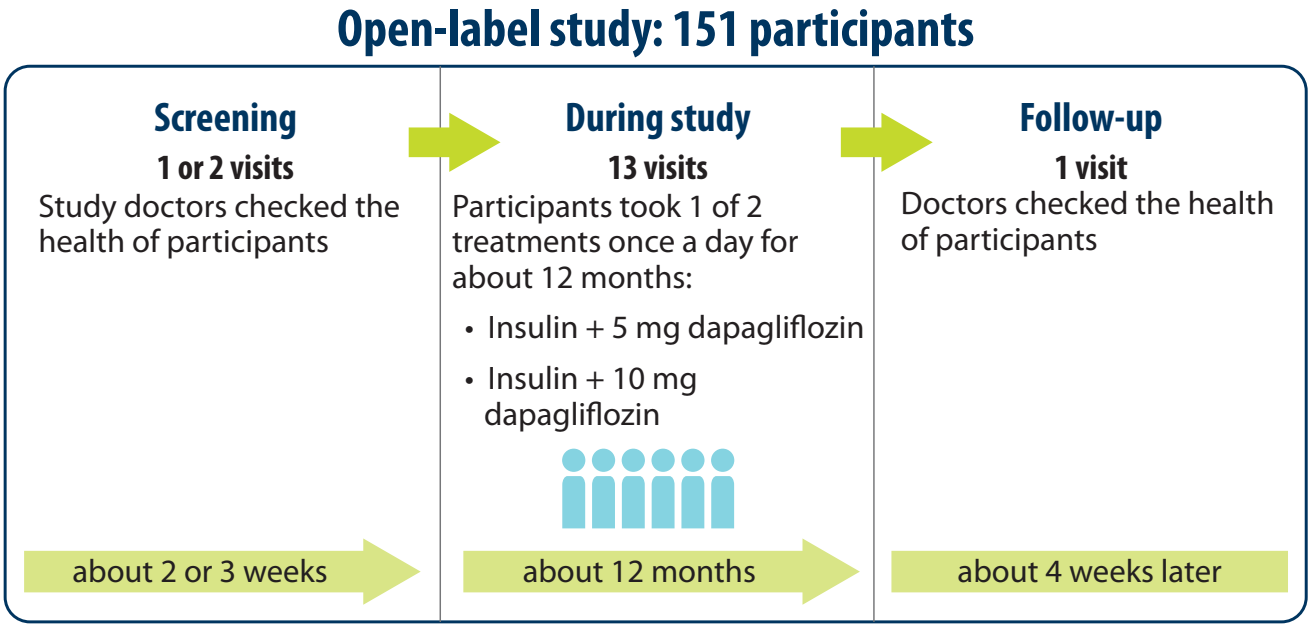
To see if the participants could join the study, study doctors did a physical examination to check their overall health. Study doctors also checked the heart health of the participants using an electrocardiogram, also known as an ECG. They also asked about the medical history of the participants, how they were feeling, and what medicines they were taking.

During the study, the participants took the study drug once a day for 12 months with insulin injections. Participants took either:

- 5 milligrams, also known as mg, in pill form
- 10 mg in pill form

About 4 weeks after the treatment period, the participants had a follow-up visit. During this visit, the study doctors checked the health of participants again.

The figure below shows how the study was done.



What were the study results?

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 website listed at the end of this summary. If a full report of the study results is available, it can also be found on this website.

How did dapagliflozin combined with insulin affect the body?

The researchers wanted to learn how dapagliflozin affected the body when it was taken with an insulin injection. So, they took blood samples to study changes in the blood sugar levels of the participants and checked the weight of the participants throughout the study.

After the 12-month treatment period, the researchers found that:

- The participants in both treatment groups had their blood sugar levels reach normal and healthy levels
- The participants in both treatment groups had their weight decrease
- The participants in both treatment groups needed less insulin over the course of the treatment period
- The participants in both treatment groups who had high blood pressure had their blood pressure decrease over the course of the treatment period

What medical problems did the participants have?

This section is a summary of the medical problems the participants had during this 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. The website listed at the end of this summary may have more information about the adverse reactions or other medical problems that happened in this study.

How many participants had serious adverse reactions?

There were 3.3% of participants in this study who had serious adverse reactions. This was 5 out of 151 participants.

The table below shows the serious adverse reactions the participants had during this study. None of the participants died during this study.

Serious adverse reactions

	5 mg of dapagliflozin + insulin (Out of 76 participants)	10 mg of dapagliflozin + insulin (Out of 75 participants)	Total (Out of 151 participants)
Too much acid in the blood from diabetes	2.6% (2)	1.3% (1)	2.0% (3)
Pregnancy miscarriage	1.3% (1)	0.0% (0)	0.7% (1)
Coma from low blood sugar levels	0.0% (0)	1.3% (1)	0.7% (1)

How many participants had adverse reactions?

There were 29.8% of participants who had adverse reactions during this study. This was 45 out of 151 participants.

There were 5.3% of participants who stopped taking dapagliflozin because of adverse reactions they had during this study. This was 8 out of 151 participants.

What adverse reactions did the participants have?

The most common adverse reaction the participants had during this study was frequent need to urinate.

The table below shows the most common adverse reactions the participants had during this study. These adverse reactions happened in 4.0% or more of all of the participants. There were other adverse reactions, but these happened in fewer participants.

Most common adverse reactions

	5 mg of dapagliflozin + insulin (Out of 76 participants)	10 mg of dapagliflozin + insulin (Out of 75 participants)	Total (Out of 151 participants)
Frequent need to urinate	9.2% (7)	6.7% (5)	7.9% (12)
Too many ketones in the body (substance created by the body that affects energy levels)	3.9% (3)	6.7% (5)	5.3% (8)
Thirst	5.3% (4)	4.0% (3)	4.6% (7)

How has this study helped participants and researchers?

The results presented here are for a single study. These results helped researchers learn if dapagliflozin combined with insulin is safe to take and how these combined drugs affect the body.

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. Always talk to a doctor before making any treatment changes.

Where can I learn more about this study?

You can find more information about this study on the website 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 **"NCT02582814"** into the search box called **"Other Terms"**. Then, click **"Search"**.

The full title of your study is: A clinical pharmacology and long-term study to evaluate the safety, efficacy, pharmacokinetics, and pharmacodynamics of dapagliflozin therapy in combination with insulin in Japanese subjects with type 1 diabetes who have inadequate glycemic control

The protocol number of your study is: D1695C00001 (Part B)

AstraZeneca K.K., a member of the AstraZeneca Group, sponsored this study and has headquarters at 1800 Concord Pike, Wilmington, DE 19850.

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 participants.