

**Research Sponsor:** AstraZeneca

**Treatment Studied:** Dapagliflozin and metformin

**Study Purpose:** This study was done to learn if a combined dapagliflozin and metformin tablet works in a similar way to separate tablets in healthy Chinese adults

**Protocol Number:** D1691C00011

## Thank you

Thank you for taking part in the clinical study for the study drugs dapagliflozin and metformin.

AstraZeneca sponsored this study and believes it is important to share the results. An independent non-profit organization called CISCRP helped prepare this summary of the study results for you.

If you participated in the study and have questions about the results, please speak with the study doctor or staff at your study site.



## Who took part in this study?

The researchers asked for the help of healthy Chinese men and women. The participants in this study were between 19 and 50 years old when they joined.

The study included 80 participants at a single study site in China.



## Why was the research needed?

Researchers are looking for a better way to treat people with type 2 diabetes. Before drugs can be approved for people to take, researchers do clinical studies to find out how safe they are and how they work. In some studies, the research is done in healthy people before further studies are done in people who have the condition the drugs are intended to treat.

In people with type 2 diabetes, the body does not make enough insulin or does not use insulin as well as it should. Insulin controls the level of sugar in the blood, which is also called “glucose”. Type 2 diabetes causes blood glucose levels to rise higher than normal. This can cause medical problems.

Dapagliflozin and metformin are both taken as tablets. They are approved for treating type 2 diabetes in the United States, the European Union, and some parts of Asia including China.

Some people need only 1 type of treatment to help control their diabetes, while others need several treatments. Controlling blood sugar levels can often mean taking multiple treatments. If a tablet that combines dapagliflozin and metformin in a single tablet is shown to work the same or in a similar way to separate tablets, it may be a helpful treatment option for Chinese men and women with type 2 diabetes.



## What was the purpose of this study?

The purpose of this study was to see if a combined dapagliflozin and metformin tablet worked in the same way as separate tablets in healthy Chinese adults.

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

- ▶ Does a combined dapagliflozin and metformin tablet work in the same way as separate dapagliflozin and metformin tablets?
- ▶ What medical problems did the participants have during the study?

The answers to these questions are important to know to help understand if a combined dapagliflozin and metformin tablet can help people with type 2 diabetes control their blood glucose levels.



## What treatments did the participants take?

In this study, all the participants took dapagliflozin and metformin. The doses of study treatments were measured in milligrams, also known as “mg”.

This was an “open-label” study. This means the participants, researchers, study doctors, and other study staff knew what each participant was taking during each treatment part.

In this study, there were:

- ▶ 4 different combinations of study treatments: **A**, **B**, **C**, and **D**
- ▶ 2 treatment groups: **Group 1** and **Group 2**
- ▶ 2 treatment parts: **Part 1** and then **Part 2**

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

Group 1 40 participants		Group 2 40 participants	
Treatment <b>A</b>	Treatment <b>B</b>	Treatment <b>C</b>	Treatment <b>D</b>
Single 5 mg dapagliflozin tablet <b>and</b> Single 500 mg metformin tablet	Single tablet containing: <ul style="list-style-type: none"><li>• 5 mg dapagliflozin</li><li>• 500 mg metformin</li></ul>	Single 10 mg dapagliflozin tablet <b>and</b> 2 tablets of 500 mg metformin each	Single tablet containing: <ul style="list-style-type: none"><li>• 10 mg dapagliflozin</li><li>• 1,000 mg metformin</li></ul>

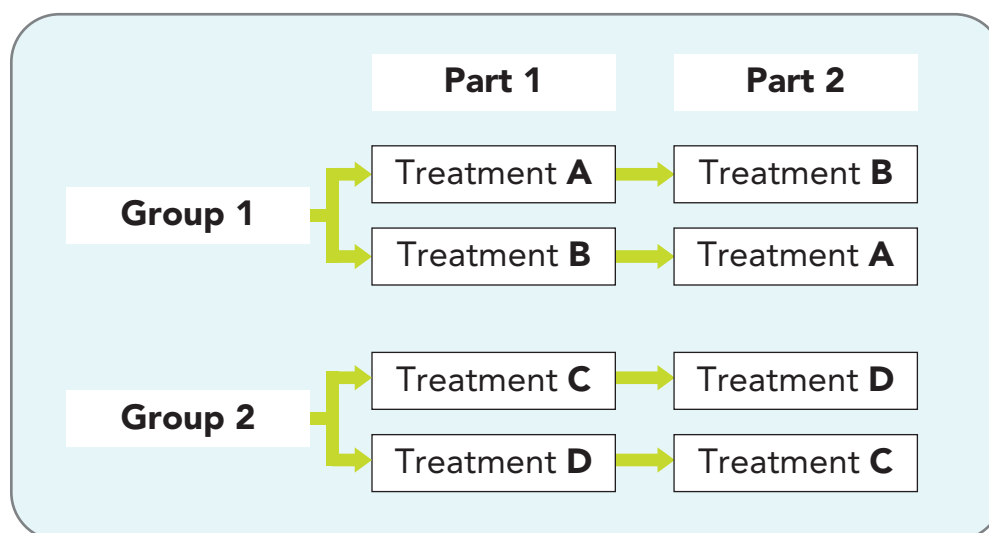
A computer program was used to randomly choose the treatments each participant took during each treatment part. This helps make sure the groups are chosen fairly. Researchers do this so that comparing the results of each treatment is as accurate as possible.

There were 2 main Parts to the study. There was a gap of more than 4 days between Part 1 and Part 2. This was for the study treatments to fully leave the participants’ bodies, also called “washing out”.

In **Group 1**, 20 participants were chosen to receive Treatment A first while the other 20 participants received Treatment B first in Part 1. After the washout gap, the treatments were swapped, so the Groups then took Treatment B or Treatment A in Part 2.

In **Group 2**, 20 participants were chosen to receive Treatment C first while the other 20 participants received Treatment D first in Part 1. After the washout gap, the treatments were swapped, so the Groups then took Treatment D or Treatment C in Part 2.

The chart below shows how the treatments were taken during the study.



## What happened during this study?

The study started in April 2021 and ended in June 2021.

**Before the participants took their study treatment,** they visited the study site to make sure they could join the study. The study doctor:

- ▶ did physical exams and asked about the participants' medications and any medical problems they were having
- ▶ took blood and urine samples
- ▶ checked the participants' heart health using an electrocardiogram, also called an ECG

This part of the study lasted up to 21 days to allow the doctors to receive and check any test results.

The participants stayed at the study site for the whole study. There were 2 main Parts to the study. There was a gap of more than 4 days between Part 1 and Part 2. This was for the study treatments to wash out of the participants' bodies.

**On Day 1 of each Part,** the study doctor:

- ▶ gave the participants their study treatment
- ▶ did physical exams and asked about any medical problems the participants were having
- ▶ took blood samples
- ▶ checked the participants' heart health using an ECG

**On Days 2 and 3 of each Part,** the study doctor:

- ▶ did physical exams and asked about any medical problems the participants were having
- ▶ took blood samples

**On Day 4 of each Part,** the study doctor:

- ▶ did physical exams and asked about any medical problems the participants were having
- ▶ took blood samples
- ▶ checked the participants' heart health using an ECG

**At the end of Part 2,** after the study doctor decided that the participant was doing well, the participant left the study site.



## 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.

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 websites listed at the end of this summary may have more information about the study results.

There was 1 participant in Group 2 who did not take any study treatment. So, the results shown in this summary are for 79 participants.

Does a combined dapagliflozin and metformin tablet work in the same way as separate dapagliflozin and metformin tablets?

The study results showed that a combined dapagliflozin and metformin tablet works in the same way as separate dapagliflozin and metformin tablets.

To answer this question, the researchers looked at the blood samples taken throughout the study. They wanted to see how the drugs in each treatment group were absorbed into the body and moved through the blood. This is called “pharmacokinetics”, also known as PK.

If the pharmacokinetics are similar, it means that the different tablets release the drugs into the blood at a similar amount and at a similar rate.

The results showed that:

- ▶ The pharmacokinetics for **Treatment A** were similar to **Treatment B**.
- ▶ The pharmacokinetics for **Treatment C** were similar to **Treatment D**.

The chart below also shows these results:

Group 1		Group 2	
Treatment <b>A</b>	Treatment <b>B</b>	Treatment <b>C</b>	Treatment <b>D</b>
Single 5 mg dapagliflozin tablet <b>and</b> Single 500 mg metformin tablet	Single tablet containing: <ul style="list-style-type: none"><li>• 5 mg dapagliflozin</li><li>• 500 mg metformin</li></ul>	Single 10 mg dapagliflozin tablet <b>and</b> 2 tablets of 500 mg metformin each	Single tablet containing: <ul style="list-style-type: none"><li>• 10 mg dapagliflozin</li><li>• 1,000 mg metformin</li></ul>
The results showed that: The pharmacokinetics for Treatment A <b>were similar to</b> Treatment B		The results showed that: The pharmacokinetics for Treatment C <b>were similar to</b> Treatment D	



## 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 dapagliflozin and metformin.

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?

	Group 1		Group 2	
	Treatment A (out of 40 participants)	Treatment B (out of 39 participants)	Treatment C (out of 39 participants)	Treatment D (out of 39 participants)
How many participants had adverse reactions?	30.0% (12)	20.5% (8)	23.1% (9)	25.6% (10)
How many participants had serious adverse reactions?	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
How many participants stopped taking study treatment due to adverse reactions?	2.5% (1)	0.0% (0)	0.0% (0)	0.0% (0)

### What serious adverse reactions happened during this study?

There were no serious adverse reactions during the study.

There were 2.5% of participants who stopped taking study treatment due to an adverse reaction of liver damage. This was 1 out of 40 participants in Group 1. This participant took Treatment A but did not go on to take Treatment B.

## What adverse reactions happened during this study?

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 fewer participants.

Most common adverse reactions				
	Group 1		Group 2	
Adverse reaction	Treatment A (out of 40 participants)	Treatment B (out of 39 participants)	Treatment C (out of 39 participants)	Treatment D (out of 39 participants)
White blood cells found in the urine	12.5% (5)	5.1% (2)	5.1% (2)	5.1% (2)
Increased level of an enzyme called bilirubin found in the blood	0.0% (0)	0.0% (0)	5.1% (2)	2.6% (1)
Protein found in the urine	2.5% (1)	2.6% (1)	5.1% (2)	0.0% (0)
Slow heartbeat	7.5% (3)	10.3% (4)	2.6% (1)	5.1% (2)



## What did researchers learn from this study?

This study helped researchers learn more about whether a combined dapagliflozin and metformin tablet works in a similar way to separate dapagliflozin and metformin tablets in healthy Chinese adults.

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 a combined dapagliflozin and metformin tablet are not 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](http://www.clinicaltrials.gov). Once you are on the website, type **"NCT04856007"** into the search box and click **"Search"**.
- ▶ [www.AstraZenecaClinicalTrials.com](http://www.AstraZenecaClinicalTrials.com). Once you are on the website, type **"D1691C00011"** into the search box and click **"Find a Study"**.

**Full Study Title:** A Single-center, Parallel-cohort, Randomized, Open-label, Two-period, Cross-over, Bioequivalence Study of the Fixed Dose Combination of Dapagliflozin/Metformin XR Relative to Coadministration of the Individual Components in Two Cohorts of Healthy Chinese Subjects in the Fed State

**AstraZeneca Protocol Number:** D1691C00011

**National Clinical Trials Number:** NCT04856007

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

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

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## 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.

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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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