Clinical Trial RESULTS

AstraZeneca

Research Sponsor: AstraZeneca AB
Drugs Studied: Dapagliflozin and metformin
National Clinical Trial #: NCT02722239
Eudra CT #: 2015-000448-41
Protocol #: D1691C00012
Study Date: March 2016 to April 2016
Short Study Title: A study to compare 2 similar doses of dapagliflozin and metformin in healthy volunteers when taken as a single tablet or in multiple tablets manufactured by different companies

Thank you!

As a clinical study participant, you belong to a large community of participants around the world. You help researchers answer important health questions and discover new medical treatments.

Thank you for taking part in the clinical study for the drugs dapagliflozin and metformin. These drugs are approved to treat type 2 diabetes. You and all of the participants helped researchers learn how dapagliflozin and metformin affect the body.

AstraZeneca MC Russia, the sponsor of this study, thanks you for your help and thinks it is important for you to know the results of your study. An independent non-profit organization called CISCRP prepared this summary of the study results for you with the help of a medical writing organization. We hope it helps you understand and feel proud of your important role in medical research. If you have questions about the results, please speak with the doctor or staff at your study site.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

What's happened since my study ended?

Your study started in March 2016 and ended in April 2016. It included 40 participants at 1 study site in Russia. When the study ended, the sponsor reviewed the data and created a report of the results. This is a summary of that report.

Why was the research needed?

Before a new drug, or combination of drugs, can be given to patients, the company developing the treatment must do research studies to show that it is safe and effective. The first step in studying a new combination of drugs is to test it in healthy people, or people without any serious health problems. The study drugs, dapagliflozin and metformin, have both been approved in Russia to treat diabetes separately, but not together.

Researchers in your study tested a pill made from both dapagliflozin and metformin. Researchers already know how each study drug is absorbed, broken down, and removed from the body alone. But, in this study researchers wanted to know how the body absorbs, breaks down, and removes the study drugs when they are taken together.

Researchers wanted to know:

- How did the combination tablet of dapagliflozin and metformin together act compared to dapagliflozin and metformin alone?
- What medical problems did participants have after they took the study drugs in the combination tablet or alone?

What kind of study was this?

This study was an "open label" study. This means that the participants and the study staff knew what study drug each participant took. Participants were "randomized" into 2 groups. This means that each participant had the same chance of being put into each group. Half of the participants were put into Group 1, and half of the participants were put into Group 2. Participants stayed in the same group for the whole study.

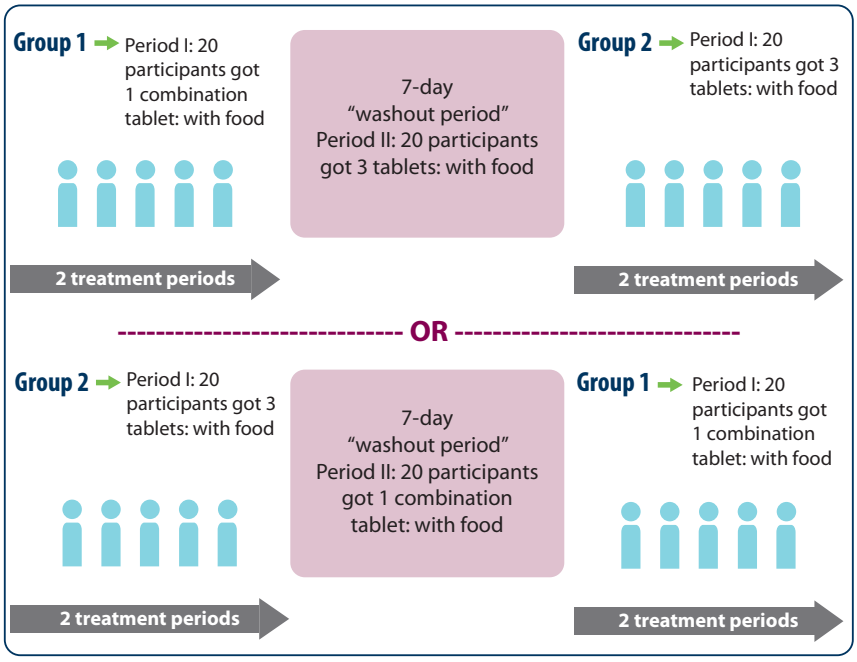
The study was a "crossover" study. In a "crossover" study, all participants get the same treatments and tests, but the treatments are given in a random order. This means that all participants received the same treatments but in a different sequence.

What happened during the study?

You and other participants were in the study for up to 25 days. Before the study started, there was a "washout period" of 14 days. During the "washout period", participants were not allowed to take certain medications. This means that when participants started the study, their bodies had processed all of the medications in their blood, and the medications were "washed out" of their bodies

This study had 2 sequences of treatment. All participants took both types of medications, but in a different order. Participants completed another 7 day "washout period" between the 2 treatments.

The first treatment was 1 combination tablet of 10 mg of dapagliflozin and 1000 mg of metformin, which participants took 30 minutes after eating breakfast 1 time. The second treatment was one 10 mg tablet of dapagliflozin and two 500 mg tablets of metformin, which participants took 30 minutes after eating breakfast 1 time. Participants in Group 1 took the combination tablet first, then the 3 tablets. Participants in Group 2 took the 3 tablets first, then the combination tablet. Throughout the study, doctors checked participants' blood pressure, heart rate, body temperature, and took blood samples before and after taking their tablets.



Throughout the study, researchers did tests to check participants' blood pressure and overall health. Researchers also checked participants' heart rate using electrocardiograms, or ECGs. At the final visit, researchers repeated some of the same tests they did during the study to make sure you and the other participants were still healthy.

What were the study results?

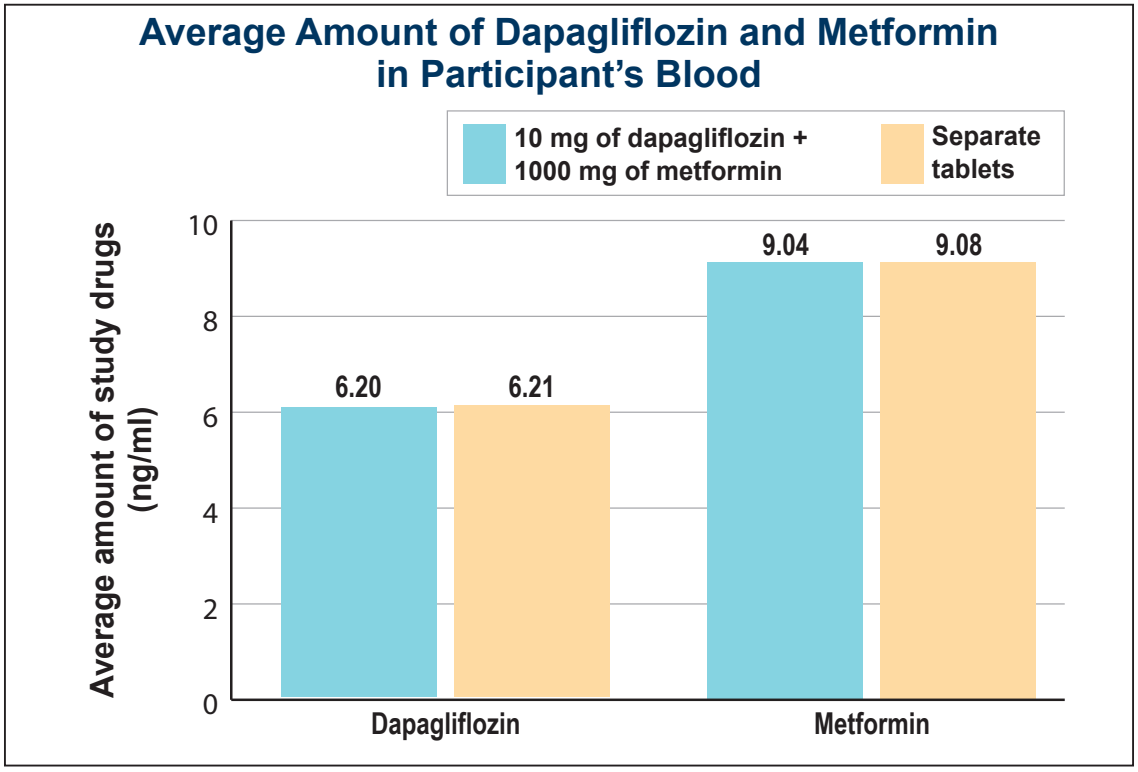
Below is a summary of the results of some of the questions the researchers asked during this study. It is important to know that researchers look at the results of many studies to decide which medicines work best and are safest for patients.

How did the combination tablet of dapagliflozin and metformin together act compared to dapagliflozin and metformin alone?

Researchers from an analytical laboratory took blood samples to compare the effects of the 10 mg of dapagliflozin + 1000 mg of metformin together to the 10 mg tablet of dapagliflozin and the two 500 mg tablets of metformin.

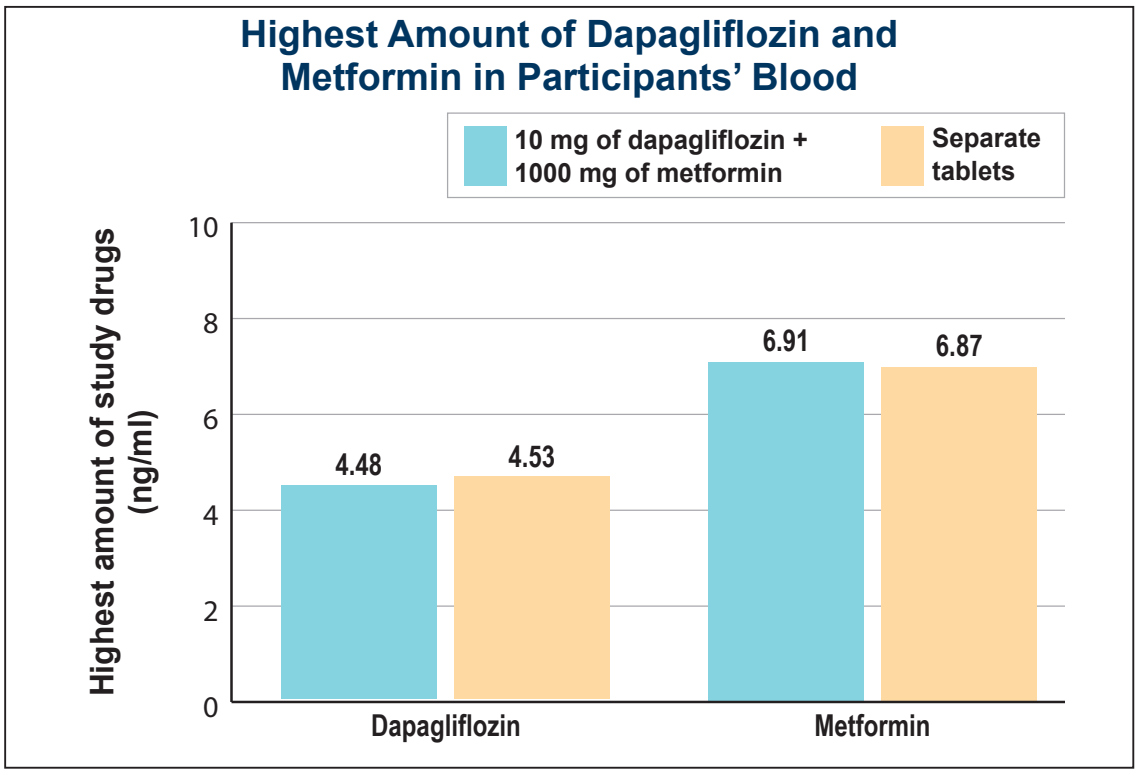
Researchers measured the average amount of study drugs in participants' blood using nanograms per milliliter (ng/ml). This is a scientifically accepted unit of measure. Researchers found that participants had similar average amounts of dapagliflozin in their blood when they took the 10 mg of dapagliflozin + 1000 mg of metformin together compared to the 10 mg tablet of dapagliflozin alone. They found similar results when they also looked at the average amount of metformin they took in the 10 mg of dapagliflozin + 1000 mg of metformin together compared to the two 500 mg tablets of metformin alone.

The chart below shows how much of each study drug was in participants' blood.



Researchers from an analytical laboratory also measured the highest amount of the study drugs in participants' blood at any time. They found that the highest amounts of both dapagliflozin and metformin in the blood were similar when participants took the combined tablet of 10 mg of dapagliflozin + 1000 mg of metformin compared to when participants took the dapagliflozin tablet and the metformin tablet individually.

The chart below shows the highest amount of both study drugs in participants' blood.



How quickly the study drugs reached participants' blood

Researchers from an analytical laboratory were also interested in seeing how quickly both study drugs reached the blood circulation in participants' bodies, known as the rate of absorption. Researchers found that the rate of absorption was similar when participants took the single tablet of 10 mg of dapagliflozin + 1000 mg of metformin together compared to when participants took the separate dapagliflozin tablet and the metformin tablets.

What medical problems did participants have?

A lot of research is needed to know whether a drug causes a medical problem. So when new drugs are being studied, researchers keep track of all medical problems that participants have during the study. These medical problems are also called "adverse events". They may or may not be caused by the study drug.

How many participants had medical problems in this study?

For the participants in Group 1, 12 of the 20 participants (60.0%) had medical problems. Among the participants in Group 2, 16 of the 20 participants (80.0%) developed had medical problems. The table below shows how many participants in each treatment group developed medical problems.

How Many Participants Developed Medical Problems in Both Groups?

	Group 1 (20 participants)	Group 2 (20 participants)
How many participants developed medical problems?	12 participants (60.0%)	16 participant (80.0%)

How many participants developed serious medical problems?

A medical problem is considered serious when it is life-threatening or causes lasting problems or you need hospital care. No participants developed serious medical problems in this study, and no participants died.

What were the most common medical problems in the study?

The table below shows the most common medical problems in both groups. Researchers determined that 93.8% of the medical problems were due to how dapagliflozin works in the body. All medical problems in both groups were not very severe and had fully gone away by the end of the study.

Most Common Medical Problems	Group 1 (20 participants)	Group 2 (20 participants)
pH in urine decreased	8 participants (40.0%)	12 participants (60.0%)
Glucose in urine	6 participants (30.0%)	9 participants (45.0%)
Decrease in concentration of urine	6 participants (30.0%)	4 participants (20.0%)
Blood in urine	1 participant (5.0%)	0 participants (0.0%)
Increase in percentage of red blood cells	0 participants (0.0%)	2 participants (10.0%)
Increase in red blood cells	0 participants	1 participant (5.0%)

Where can I learn more about the study?

If you have questions about the results, please speak with the doctor or staff at your study site. You can find more information about your study online at www.clinicaltrials.gov/show/results/ NCT02722239.

Official study title: An open-label, randomized, crossover study of comparative pharmacokinetics and bioequivalence of Dapagliflozin + Metformin modified release film-coated tablets, 10 mg + 1000 mg (AstraZeneca AB, Sweden) versus the combined use of Forxiga™ (Dapagliflozin), film-coated tablets, 10 mg (Bristol Myers Squibb Company, USA) and two Glucophage® Long (Metformin), ER tablets, 500 mg (Merck Santé S.A.S., France), co-administered to healthy volunteers under standard fed conditions.

The phone number for the AstraZeneca Information Centre is 1-877-240-9479.

The results presented here are for a single study. Other studies may provide new information or different results.

Thank you

It is said that the greatest gift is one which is given anonymously, giving when you do not know whether you will get direct personal benefit.

This is the gift that you have given by taking part in a clinical trial. It is a brave and selfless act, one that advances medical knowledge and benefits public health.

Thank you for the gift of your participation in clinical research.

CISCRP
THE CENTER FOR INFORMATION & STUDY ON CLINICAL RESEARCH PARTICIPATION

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 trials, nor is it involved in conducting clinical trials.

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