Clinical Trial RESULTS

AstraZeneca

Research Sponsor:	AstraZeneca AB
Drugs Studied:	Dapagliflozin and metformin
National Clinical Trial #:	NCT02637037
Eudra Clinical Trial #:	2015-000448-41
Protocol #:	D1691C00008
Study Date:	December 2015 to April 2016
Short Study Title:	A study to compare 2 different doses of dapagliflozin and metformin manufactured at 2 different facilities in healthy participants with and without food

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 the body affects dapagliflozin and metformin.

AstraZeneca AB, 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 that this summary 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.

What's happened since my study ended?

Your study started in December 2015 and ended in April 2016. It included 80 participants at 1 study site in the United States. 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?

Researchers in your study tested 2 drugs called dapagliflozin and metformin combined in 1 pill to see if they had a similar effect on participants, regardless of which of the 2 different manufacturing plants the pill came from. Dapagliflozin works through the kidneys to treat type 2 diabetes by allowing the body to get rid of extra sugar. Metformin treats the same disease by affecting the liver and causing blood sugar in the body to be lowered.

Researchers wanted to compare the same doses of the 2 different drugs from the 2 different facilities to see if they had a similar effect on the participants. To do this, researchers gave the participants the same doses of these drugs from the 2 different facilities and studied the drugs' effects.

Specific questions researchers wanted to answer were:

- Does a pill with 5 milligrams (mg) of dapagliflozin and 500 mg of metformin (5/500 mg) made in Mount Vernon, Indiana have a similar effect on healthy participants as a pill with the same drugs and dose made in Humacao, Puerto Rico?
- Does a pill with 10 mg dapagliflozin and 1000 mg of metformin (10/1000 mg) made in Mount Vernon have a similar effect on healthy participants as a pill with the same drugs and dose made in Humacao?
- What medical problems did participants have?

Your study had 80 healthy men and women in it, aged 18 to 55.

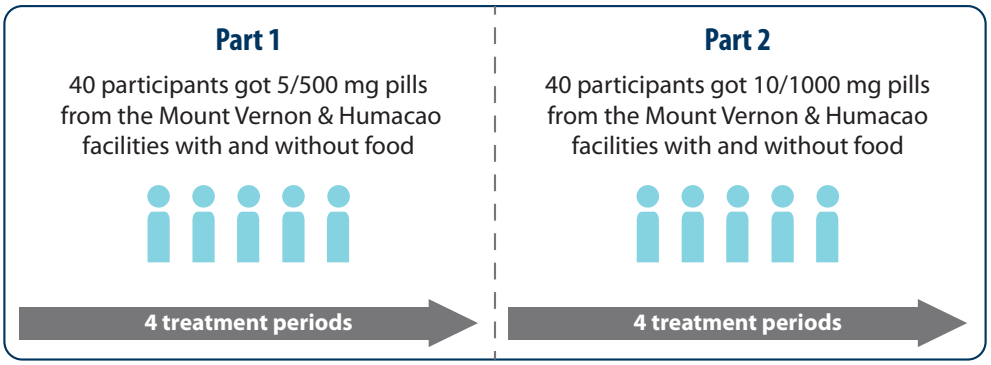
What kind of study was this?

This was an "open-label" study with 2 parts. "Open-label" means that both the researchers and the participants knew what drug each participant took.

This was also a "crossover" study. This means that all participants received each treatment in their treatment group in a random order. 40 participants took dapagliflozin and metformin 5/500 mg tablets from both the Mount Vernon and Humacao facilities, with and without food, and 40 participants took dapagliflozin and metformin 10/1000 mg tablets from both facilities, with and without food.

What happened during the study?

This study had 2 parts. The figure below shows how the study was done.



Before you started the study, researchers asked about your medical history. You had a physical examination and other tests to make sure you could participate. All 80 participants took all of the treatments in either Part 1 or Part 2.

During the study, researchers did tests to check participants' health, such as blood pressure tests and electrocardiograms, or ECGs. You and other participants had 12 total visits during the study. Your last visit was about 3 days after taking the last dose in either Part 1 or Part 2. At this visit, researchers repeated several of the tests to make sure you and other participants were still healthy.

Part 1
Participants were randomly assigned to take all 4 treatments below. Every participant took the drugs in a different order. Each treatment period lasted 3 days.

Treatment A: Dapagliflozin/metformin 5/500 mg pill from the Mount Vernon facility with food

Treatment B: Dapagliflozin/metformin 5/500 mg pill from the Humacao facility with food

Treatment C: Dapagliflozin/metformin 5/500 mg pill from the Mount Vernon facility without food

Treatment D: Dapagliflozin/metformin 5/500 mg pill from the Humacao facility without food

You and all the other participants stopped taking any study drugs for 7 to 14 days between treatments. This helped get rid of any effects from the previous treatment.

Part 2
Participants were randomly assigned to take all 4 treatments below. Every participant took the drugs in a different order. Each treatment period lasted 3 days.

Treatment E: Dapagliflozin/metformin 10/1000 mg pill from the Mount Vernon facility with food

Treatment F: Dapagliflozin/metformin 10/1000 mg pill from the Humacao facility with food

Treatment G: Dapagliflozin/metformin 10/1000 mg pill from the Mount Vernon facility without food

Treatment H: Dapagliflozin/metformin 10/1000 mg pill from the Humacao facility without food

You and all the other participants stopped taking any study drugs for 7 to 14 days between treatments, just like in Part 1. This helped get rid of any effects from the previous treatment.

What were the study results?

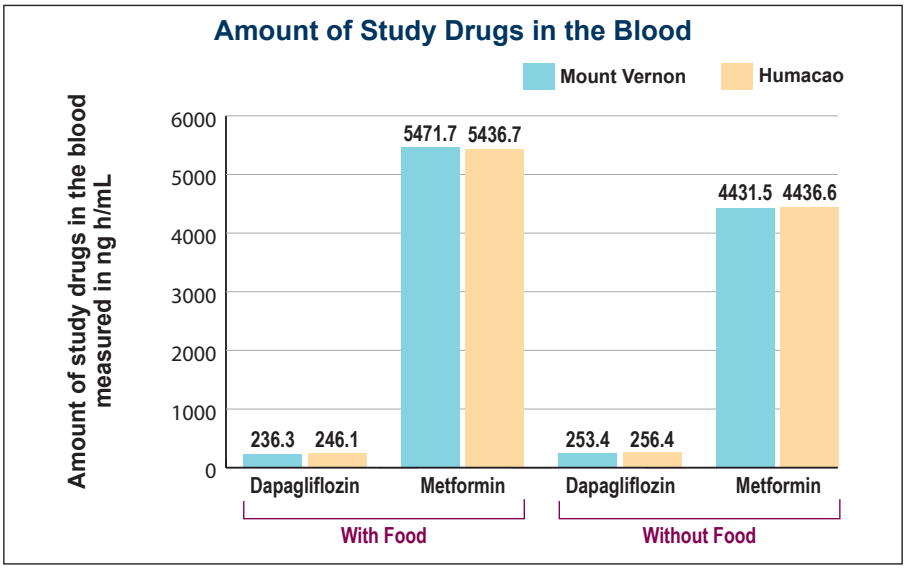
Below is a summary of the results of some of the questions the researchers asked. It is important to know that researchers look at the results of many studies to decide which drugs work best and are safest for patients, even approved drugs that are already on the market like dapagliflozin and metformin.

Does a pill with 5/500 mg of dapagliflozin and metformin made in Mount Vernon, Indiana have a similar effect on healthy participants as a pill with the same drugs and dose made in Humacao, Puerto Rico?

Yes. Researchers took blood samples to compare the effects of the 5/500 mg pill of dapagliflozin and metformin from the 2 facilities. They learned about:

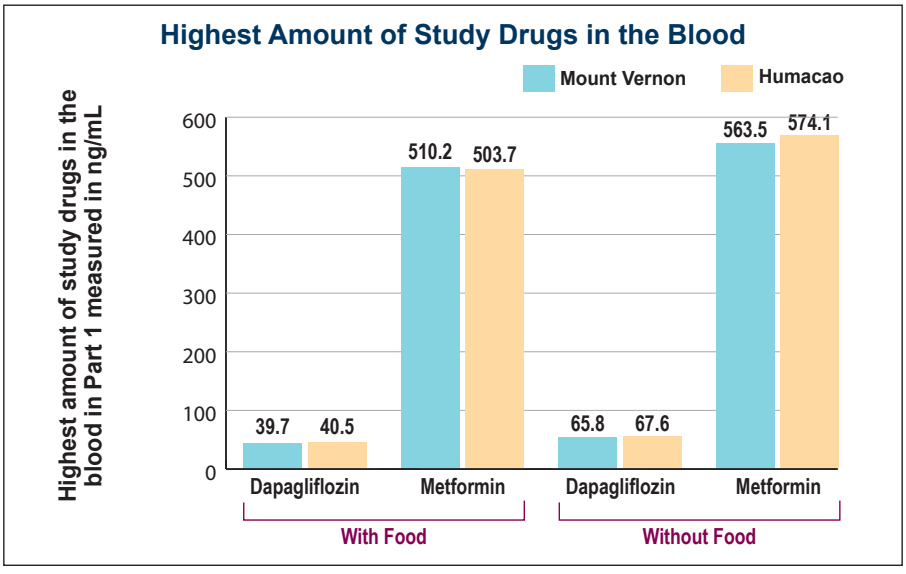
The amount of the study drugs in participants' blood
Researchers measured the amount of study drugs in participants' blood using nanogram hours per milliliter (ng h/mL). This is a scientifically accepted unit of measure. Researchers found that participants had similar amounts of the study drugs in their blood, whether the pills were made in Mount Vernon or Humacao. They also found similar amounts whether participants took the drugs with or without food.

The chart below shows how much of each study drug was in participants' blood in Part 1.



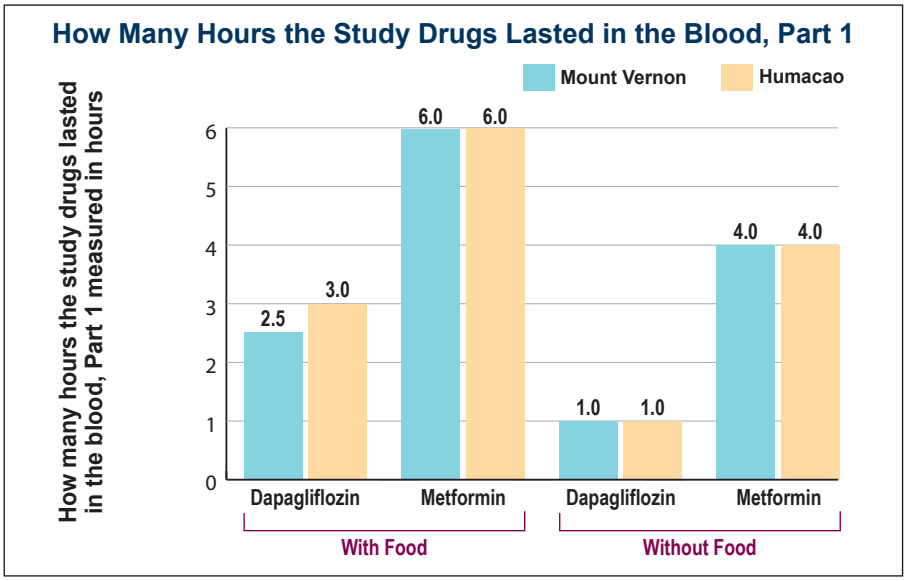
Highest amount of the study drugs in participants' blood over time
Researchers measured the highest amount of the study drugs in participants' blood at any time. They found the highest amounts from the Mount Vernon facility and the Humacao facility were similar, with and without food.

The chart below shows the highest amount of each study drug in participants' blood in Part 1.



How long the study drugs lasted in participants' blood
Researchers checked how many hours the study drugs lasted in participants' blood. They found that drugs from the Mount Vernon and Humacao facilities lasted in the blood a similar amount of time, with and without food.

The chart below shows how long each study drug stayed in participants' blood in Part 1.

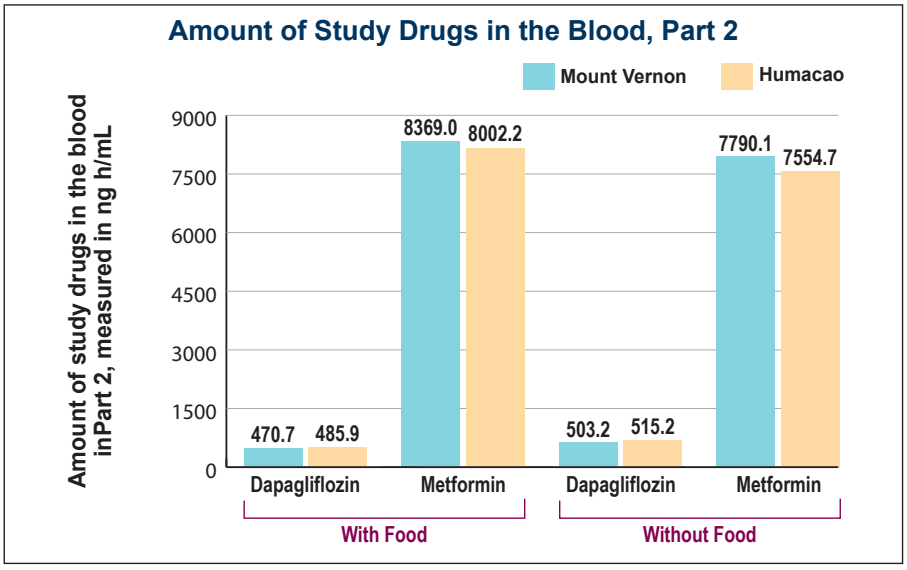


Does a pill with 10/1000 mg of dapagliflozin and metformin made in Mount Vernon, Indiana, have a similar effect on healthy participants as a pill with the same drugs and dose made in Humacao, Puerto Rico?

Yes. Researchers collected blood samples to compare the effects of the 10/1000 mg pill of dapagliflozin and metformin from the 2 facilities. Researchers found the following results for some of the tests they did.

The amount of the study drugs in participants' blood

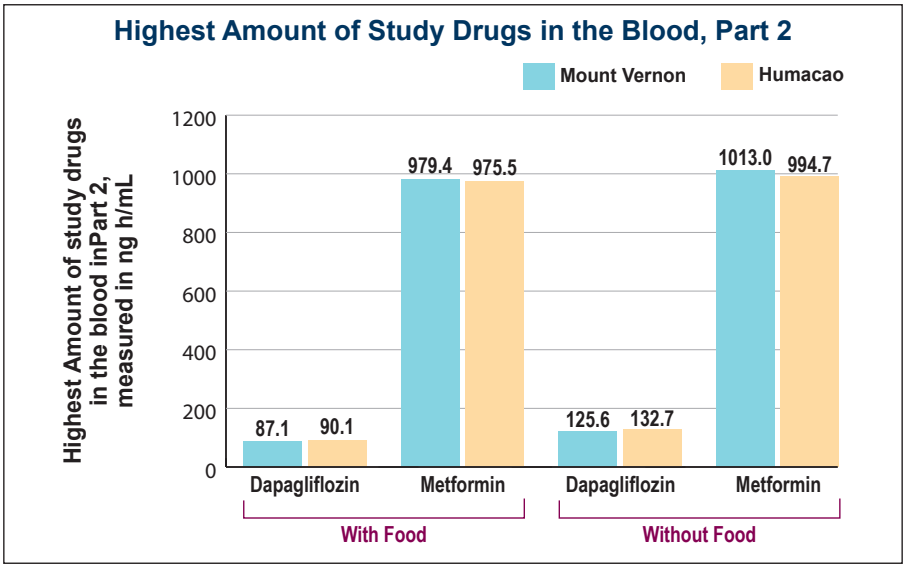
In Part 2, researchers used ng h/mL to measure the amount of study drugs in participants' blood. They found that participants had similar amounts of the study drugs in their blood, whether the pills were from Mount Vernon or Humacao. They also found similar amounts whether participants took the drugs with or without food. The chart below shows how much of each study drug was in participants' blood in Part 2.



Highest amount of the study drugs in participants' blood over time

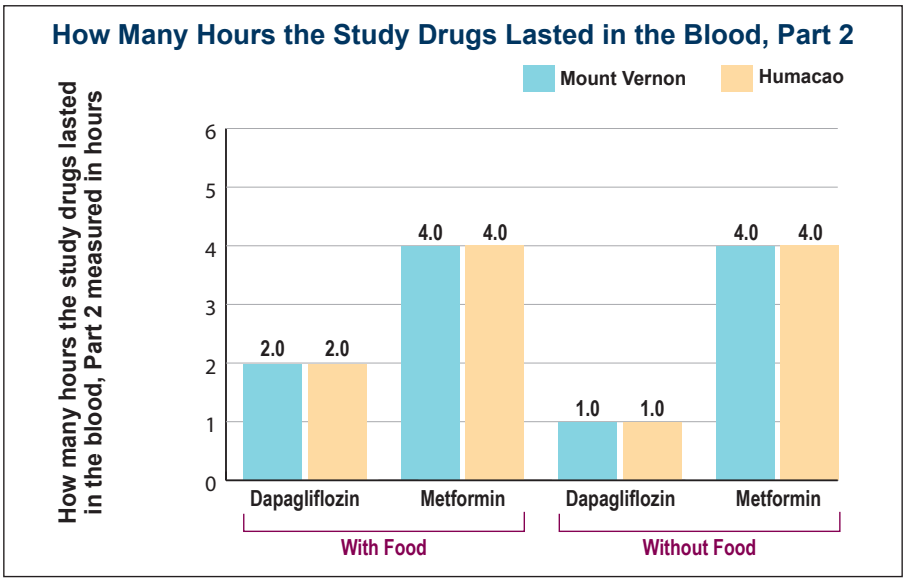
Researchers measured the highest amount of the study drugs in participants' blood at any time. They found the highest amounts from the Mount Vernon facility and the Humacao facility were similar, with and without food.

The chart below shows the highest amount in participants' blood in Part 2.



How long the study drugs lasted in participants' blood

Researchers checked how many hours the study drugs lasted in participants' blood. They found that drugs from the Mount Vernon and Humacao facilities lasted a similar amount of time, with and without food. The chart below shows how long each study drug stayed in participants' blood in Part 2.



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 Part 1 of your study, 14 of the 40 participants (35.0%) had medical problems. The table below shows how many participants in each treatment group had medical problems in Part 1.

How Many Participants had Medical Problems in Part 1?

	Treatment A (Out of 40 participants)	Treatment B (Out of 38 participants)	Treatment C (Out of 37 participants)	Treatment D (Out of 36 participants)
How many participants had medical problems?	5 participants (12.5%)	7 participants (18.4%)	4 participants (10.8%)	5 participants (13.9%)

In Part 2 of your study, 13 of the 40 participants (32.5%) had medical problems. The table below shows how many participants in each treatment group had medical problems in Part 2.

How Many Participants had Medical Problems in Part 2?

	Treatment A (Out of 39 participants)	Treatment B (Out of 40 participants)	Treatment C (Out of 39 participants)	Treatment D (Out of 39 participants)
How many participants had medical problems?	4 participants (10.3%)	5 participants (12.5%)	7 participants (17.9%)	4 participants (10.3%)

In Part 1, 1 participant out of 40 (2.5%) stopped taking the study drugs because of medical problems. No participants stopped taking the study drugs because of medical problems in Part 2.

How many participants had serious medical problems?

A medical problem is considered serious when it is life-threatening, causes you lasting problems, or if you need hospital care. No participants had 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 that happened to more than 1 participant in Part 1.

What were the most common medical problems in Part 1 of the Study?

Medical Problem	Treatment A (Out of 40 participants)	Treatment B (Out of 38 participants)	Treatment C (Out of 37 participants)	Treatment D (Out of 36 participants)
Headache	1 participant (2.5%)	3 participants (7.9%)	0 participants (0.0%)	1 participant (2.8%)
Diarrhea	0 participants (0.0%)	2 participants (5.3%)	1 participant (2.7%)	1 participant (2.8%)

The table below shows the most common medical problems that happened to more than 1 participant in Part 2.

What were the most common medical problems in Part 2 of the Study?

Medical Problem	Treatment A (Out of 39 participants)	Treatment B (Out of 40 participants)	Treatment C (Out of 39 participants)	Treatment D (Out of 39 participants)
Diarrhea	0 participants (0.0%)	2 participants (5.0%)	3 participants (7.7%)	2 participants (5.1%)
Headache	2 participants (5.1%)	0 participants (0.0%)	0 participants (0.0%)	1 participant (2.6%)
Abdominal pain	0 participants (0.0%)	0 participants (0.0%)	1 participant (2.6%)	1 participant (2.6%)
Tiredness	0 participants (0.0%)	2 participants (5.0%)	1 participant (2.6%)	0 participants (0.0%)

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. As of the spring of 2017, you will be able to find more information about your study online at www.clinicaltrials.gov/ct2/show/results/NCT02637037.

Official study title: A two part bioequivalence study to compare two fixed dose combination (FDC) tablets of dapagliflozin/metformin XR 5/500 mg (Part 1) and 10/1000 mg (Part 2) manufactured at two different plants (Humacao, Puerto Rico and Mount Vernon, United States [US]) in healthy subjects under fasting and fed conditions

AstraZeneca AB, the sponsor of this study, is a member of the AstraZeneca Group of companies and has its headquarters at 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850 USA.

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

The results presented here are for a single study. Other studies may provide new information or different results. You should not make changes to your therapy based on the results of a single study without first consulting your healthcare professional.

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 this 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.

CISCRP
56 Commercial Wharf East
Boston, MA 02110

1-877-MED-HERO

www.ciscrp.org