Clinical Trial RESULTS

AstraZeneca

Research Sponsor: AstraZeneca AB
Drug Studied: AZD9977
National Clinical Trial #: NCT02532998
EudraCT #: 2015-002224-11
Protocol #: D6400C00004
Study Date: September 2015 to November 2015
Short Study Title: A study in healthy males to investigate a new drug for the potential treatment of chronic kidney disease

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 study drug AZD9977. AZD9977 is a new drug being developed to treat kidney disease, including kidney disease from diabetes. You and all of the participants helped researchers learn how AZD9977 affects the body.

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 and a medical writing organization called Synchrogenix prepared 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 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?

This study started in September 2015 and ended in November 2015. It included 23 participants at 1 study site in the United Kingdom. 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 medicine can be approved, research studies must be done to show that it is safe and effective. The first step in studying a new medicine is to test it in healthy volunteers, before testing it in people with the disease the medicine will treat.

Researchers in this study tested a drug called AZD9977 as a possible treatment for chronic kidney disease. Chronic kidney disease can cause an imbalance in the amount of sodium and potassium in urine, which can make people very sick. Researchers wanted to know how AZD9977 affected the amount of sodium and potassium in urine.

To study how AZD9977 works, researchers compared it to another drug called eplerenone. Eplerenone is used to treat heart failure. Researchers wanted to know if AZD9977 affects the kidneys in the same way as eplerenone. They also compared AZD9977 and eplerenone to a placebo. A placebo looks like a real drug but doesn't have any medicine in it.

Researchers wanted to know:

- How did AZD9977 alone affect the amount of sodium and potassium in the urine compared to AZD9977 and eplerenone together?
- How did AZD9977 alone affect the passing of sodium and potassium in the urine and the amount of urine produced compared to AZD9977 and eplerenone together or to a placebo?
- How did AZD9977 and eplerenone act in the body?
- What medical problems did participants have?

This study had 23 healthy men between the ages of 22 and 50 years.

WHAT KIND OF STUDY WAS THIS?

This was a "single-blind" study. "Single-blind" means that researchers knew what participants were taking but the participants did not know. All participants took AZD9977, eplerenone, a placebo, and a drug called fludrocortisone. Fludrocortisone affects how sodium and potassium are passed out of the body through urine. Researchers used this drug to make sure all participants passed the same amount of sodium and potassium in their urine before they took AZD9977, eplerenone, and/or a placebo.

WHAT HAPPENED DURING THE STUDY?

Before starting this study, study doctors asked about each participant's medical history, did a physical exam and other tests, and took blood and urine samples to make sure each participant could participate.

During the study, the study doctors and staff did an exam and other tests, and took blood and urine samples.

There were 4 different treatments in the study:

- Fludrocortisone and a placebo
- Fludrocortisone and AZD9977
- Fludrocortisone, eplerenone, and a placebo
- Fludrocortisone, eplerenone, and AZD9977

In each treatment, participants got 5 doses of fludrocortisone and a single dose each of placebo, AZD9977, or eplerenone.

During each treatment, the participants took 200 milligrams (mg) of AZD9977, 100 mg of eplerenone, and up to 1.0 mg of fludrocortisone.

All of the participants got all 4 treatments. The order of the treatments was assigned by chance, like the tossing of a coin. Each treatment lasted 3 or 4 days. Each participant stopped taking a treatment for at least 7 days before starting the next treatment.

After the last treatment, participants had a final visit 5 to 7 days later so researchers could check their health. Each participant was in the study for about 2 months.

WHAT WERE THE STUDY RESULTS?

Below is a summary of the results of some of the questions 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. Further clinical studies with AZD9977 are not currently planned.

How did AZD9977 alone affect the amount of sodium and potassium in the urine compared to AZD9977 and eplerenone together?

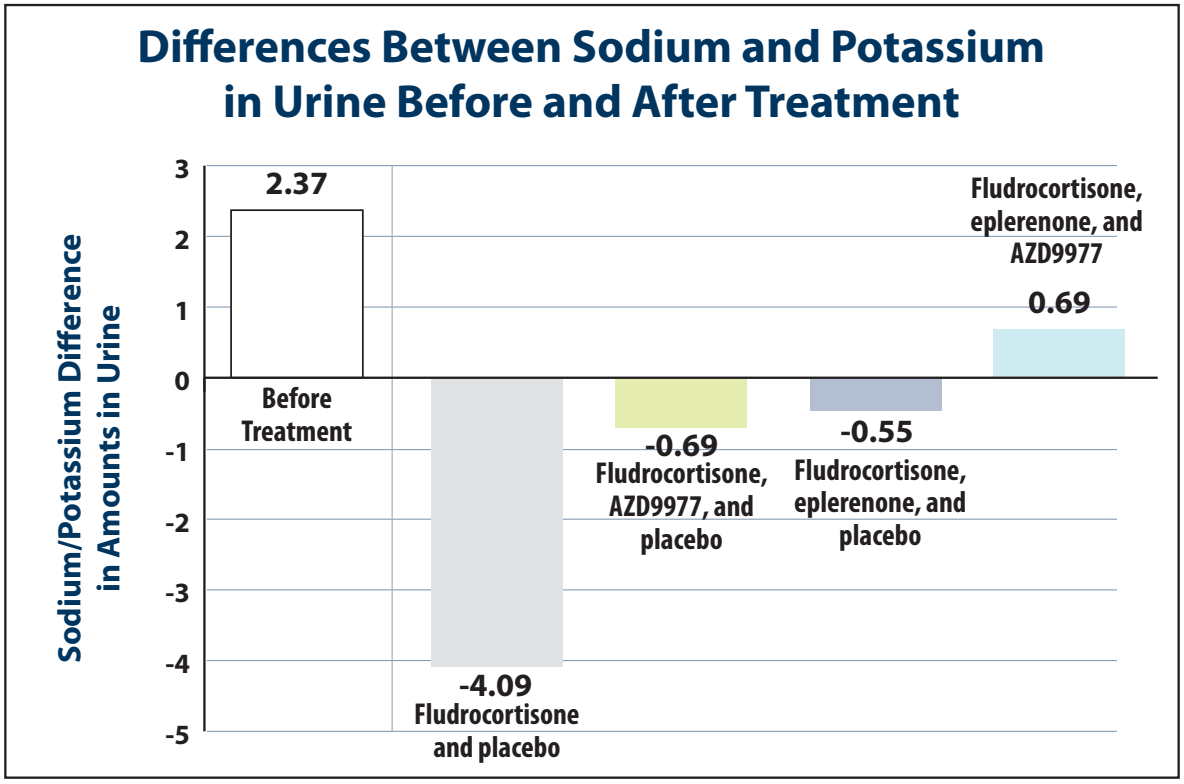
To see how eplerenone and AZD9977 affected sodium and potassium in the urine, researchers measured the amount of sodium and potassium in the participant's urine before and after treatment.

In order to find the difference between sodium and potassium, researchers used a mathematical formula called a logarithm to measure the difference between sodium and potassium in the urine. A difference larger than zero means there was more sodium than potassium in the urine. A difference smaller than zero means there was more potassium than sodium in the urine.

After treatment:

- **Participants who took fludrocortisone and placebo** had a difference between sodium and potassium of -4.09. The researchers thought this would happen because fludrocortisone decreases the amount of sodium in urine and also increases the amount of potassium in urine.
- **Participants who took fludrocortisone, AZD9977, and placebo** had a difference between sodium and potassium of -0.69. This made it seem like AZD9977 had an effect on how fludrocortisone worked in the body.
- **Participants who took fludrocortisone, eplerenone, and placebo** had a difference between sodium and potassium of -0.55. This made it seem like eplerenone had an effect on how fludrocortisone worked in the body.
- **Participants who took fludrocortisone, eplerenone, and AZD9977** had a difference between sodium and potassium of 0.69. This made it seem like eplerenone and AZD9977 worked together in how they affected the difference between sodium and potassium in the urine.

The graph below shows the differences between sodium and potassium before and after treatment.



How did AZD9977 alone affect the passing of sodium and potassium in urine and the amount of urine produced compared to AZD9977 and eplerenone or to a placebo?

Sodium:

The amount of sodium passed out of the body in urine was:

- Sometimes higher for AZD9977 and eplerenone compared to eplerenone and a placebo.
- Sometimes higher for AZD9977 alone compared to a placebo.

Potassium:

The amount of potassium passed out of the body in urine was:

- Similar for AZD9977 alone compared to eplerenone and a placebo.
- Lower for AZD9977 alone compared to a placebo.
- Lower for AZD9977 and eplerenone compared to eplerenone and a placebo.

Amount of Urine:

At certain times during the study, the amount of urine passed out of the body in urine was more for:

- AZD9977 and eplerenone compared to eplerenone and a placebo.
- AZD9977 alone compared to a placebo.

How did AZD9977 and eplerenone act in the body?

The amounts of fludrocortisone, AZD9977, and eplerenone in the body were measured. The drugs did not seem to have an effect on each other or affect their ability to work in the body.

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. 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?

Overall, 10 participants (43.5%) had at least 1 medical problem. No participants stopped participating in the study because of medical problems. The table below shows how many participants had medical problems during the study by treatment.

Medical Problems in this Study for all 23 Participants

	Placebo	AZD9977	Placebo + Eplerenone	AZD9977 + Eplerenone
How many participants had medical problems?	2 participants (8.7%)	3 participants (13.0%)	2 participants (8.7%)	4 participants (17.4%)

How many participants had serious medical problems?

A medical problem is considered serious when it is life-threatening, causes lasting problems or a participant needs hospital care. No participants had serious medical problems.

What were the most common medical problems?

The most common medical problems were common cold and headache. The table below shows all the medical problems in this study.

Medical Problems in this Study

	Placebo (Out of 23 Participants)	AZD9977 (Out of 23 Participants)	Placebo + Eplerenone (Out of 23 Participants)	AZD9977 + Eplerenone (Out of 23 Participants)
Common cold	1 participant (4.4%)	1 participant (4.4%)	1 participant (4.4%)	0 participants (0%)
Headache	1 participant (4.4%)	0 participants (0%)	0 participants (0%)	2 participants (8.7%)
Bloating	0 participants (0%)	1 participant (4.4%)	0 participants (0%)	0 participants (0%)
Dizziness	0 participants (0%)	1 participant (4.4%)	0 participants (0%)	0 participants (0%)
Fever	0 participants (0%)	0 participants (0%)	0 participants (0%)	1 participant (4.4%)
Gas	0 participants (0%)	1 participant (4.4%)	0 participants (0%)	0 participants (0%)
Red eye	0 participants (0%)	1 participant (4.4%)	0 participants (0%)	0 participants (0%)
Runny nose	0 participants (0%)	0 participants (0%)	0 participants (0%)	1 participant (4.4%)
Skin irritation	0 participants (0%)	0 participants (0%)	0 participants (0%)	1 participant (4.4%)
Sneezing	1 participant (4.4%)	0 participants (0%)	0 participants (0%)	0 participants (0%)
Splinter	0 participants (0%)	0 participants (0%)	0 participants (0%)	1 participant (4.4%)
Stomach pain	0 participants (0%)	0 participants (0%)	1 participant (4.4%)	0 participants (0%)

WHERE CAN I LEARN MORE ABOUT THE STUDY?

You can find more information about your study online at

www.clinicaltrials.gov/show/results/NCT02532998. If you have questions about the results, please speak with the doctor or staff at your study site.

Official study title: A Phase I, Randomized, Single-Blind, Crossover Study to Assess the Pharmacodynamics of AZD9977 Following Single-Dose Administration to Healthy Male Subjects

AstraZeneca AB, the sponsor of this study, has its headquarters in Södertälje, Sweden.

The phone number for general information 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 trial 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 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

synchrogenix
Powered by ClinGenuity™

Synchrogenix is a worldwide medical and regulatory writing organization and is not involved in recruiting participants or in conducting clinical trials.

Synchrogenix Headquarters
2 Righter Parkway, Suite 205
Wilmington, DE 19803

1-302-892-4800

www.synchrogenix.com