Clinical Trial RESULTS

AstraZeneca

Research Sponsor:	AstraZeneca AB
Drug Studied:	AZD9291 (osimertinib)
National Clinical Trial #:	NCT02491944
Eudra CT #:	2015-000448-41
Protocol #:	D5160C00020
Study Date:	July 2015 to August 2015
Short Study Title:	A study in healthy males to see how much of osimertinib is taken up by the body when taken by mouth compared with an injection into the vein

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 osimertinib, a newly approved drug being developed to treat lung cancer. You and all of the participants helped researchers learn how osimertinib is affected by 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 organisation called CISCRP prepared this summary of the study results for you with the help of a medical writing organisation. 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.

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What's happened since my study ended?

This study started in July 2015 and ended in August 2015. It included 10 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?

Research studies must be done to show that the drug is safe and effective, but also to understand how the drug is absorbed, broken down, and removed from the body. Some cancer medications can be safely studied using healthy volunteers so that the test results are more controlled compared to testing in patients. For example, the liver breaks down many drugs and patients may have diseases or cancer involving the liver so testing on patients would produce test results which may not affect other patients.

Researchers in this study tested a drug called osimertinib, which was developed to treat lung cancer. They wanted to find out how much of osimertinib reaches the blood in the body when taken as a tablet compared to when injected directly into the vein. When the drug is taken by mouth, there is a certain percentage of drug that is not absorbed but when the drug is injected directly into a vein, 100% of the drug goes in the blood stream.

Researchers wanted to know:

- How much of the study drug reaches the blood after participants take osimertinib in tablet form?
- How does the body break down osimertinib when it is swallowed in tablet form compared to when it is injected?
- How safe is osimertinib to take and what medical problems did participants have?

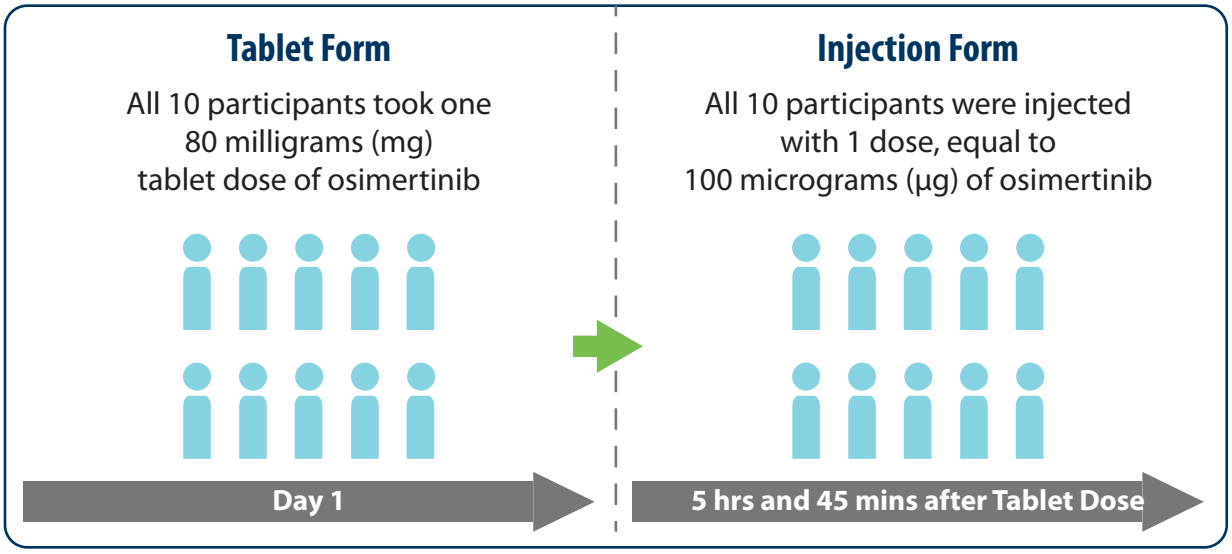
This study had 10 healthy men, ages 21 to 61.

What kind of study was this?

This study was an "open-label" study. "Open-label" means that both the researchers and the participants knew what the participants were taking. All participants got osimertinib, both in a tablet and in an injection. The injection was given in a vein slowly over 15 minutes.

The drug in the injection was radiolabelled. This means that a substance with radiation was used to help the researchers track where the drug is in the body and to tell the differences between the drug in the tablet form and the drug in the injection form.

The figure below shows how the study was done.



What happened during the study?

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

After being accepted into the study, all 10 participants stayed in the clinical unit for 7 days and 6 nights.

Each participant got one dose of the study drug in a tablet first and then one dose injected in a vein. The injection was given 5 hours and 45 minutes after the tablet. All participants got the same amount of drug, 80 mg in the tablet form and 100 µg in the injection form.

Study participants had 5 more visits during the study.

Starting with the clinical unit visit, the study doctors took about 30 blood samples over 22 days to learn how much of the drug remains in the blood at different times. They also did different tests at different visits to make sure participants were safe. These included testing urine, measuring blood pressure, pulse rate, and temperature; and checking the heart rhythm using an electrocardiogram (ECG).

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. Further clinical studies with osimertinib are ongoing.

How much of the study drug reaches the blood after participants take osimertinib in tablet form?

Researchers measured an amount and then calculated an average for osimertinib that reached the blood after participants took the tablet form followed by the injection form. After taking the 80 mg of tablet, participants had an average of 6791 nanomole hours (nM*h) of osimertinib in their blood. Nanomole hours are a unit of measurement that researchers use to see how much of the study drug is in participants' blood over time. After getting the 100 µg injection of osimertinib, participants had an average of 12.1 nM*h of osimertinib in their blood. Overall, researchers found that an average of 70% of the study drug reached participants' blood after taking the dose orally as a tablet compared to injecting the dose straight into the blood.

How does the body break down osimertinib when it is swallowed in tablet form compared to when it is injected?

Researchers took blood samples from participants after they took osimertinib in tablet form and then injection form.

They found the following:

- **Tablet form:** The highest amount of osimertinib in the blood (118.00 nM) was reached at 7 hours after taking the tablet. Half of the osimertinib left the blood within 60 hours.
- **Injection form:** The highest amount of osimertinib in the blood (0.58 nM) was reached at 15 minutes after taking the injection. Half of the osimertinib left the blood within 55 hours.

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, 2 of the 10 participants (20%) had a total of 3 medical problems. Researchers thought that one participant's medical problem (diarrhoea) was related to the study drug. No participants stopped taking the study drug because of medical problems.

What were the most common medical problems in the study?

The most common medical problems were:

- Cough
- Diarrhoea
- Pain in the muscles and/or joints

All 3 medical problems were considered mild, which means that the participants were aware of the medical problems but could easily tolerate them. One participant had a cough, which was resolved after 8 days, and diarrhoea, which was resolved after 1 day. One participant had pain in his or her muscles and/or joints, which was resolved after 2 days.

How many participants in this study 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 in this study.

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/NCT02491944.

Official study title: A Phase I, Open-label, Single-Dose, Single-Centre Study to Assess the Absolute Bioavailability of a Single Oral Dose of AZD9291 with Respect to an Intravenous Microdose of [^{14}C] AZD9291 in Healthy Male Subjects

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 Centre 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.

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The Centre for Information & Study on Clinical Research Participation (CISCRP) is a non-profit organisation 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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