AstraZeneca

Clinical Study Results

Research Sponsor: AstraZeneca AB

Treatment Studied: Radio-labelled osimertinib

Study Purpose: This study was done to learn how radio-labelled osimertinib acts in the brains of participants with non-small cell lung cancer that has spread to the brain

Protocol Number: D5160C00043

Thank you!

Thank you for taking part in the clinical study for the study drug osimertinib, also called AZD9291.

AstraZeneca AB 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 people with non-small cell lung cancer, also called NSCLC. All of the participants:

- had a change in a gene called "epidermal growth factor receptor" in their tumors
- had cancer cells that had spread from the lungs to the brain

A change in a gene is also known as a "mutation".

The study included 8 participants in the European Union.

Why was the research needed?

Researchers are looking for a better way to treat participants who have NSCLC that has spread to the brain. Before a drug can be approved for people to get, researchers do clinical studies to find out how safe it is and how it works.

In people with cancer, the body is not able to control the growth of some cells. The extra cells can form tumors. NSCLC is a type of lung cancer. Lung cancer cells can spread to other parts of the body, including the brain.

The study drug, osimertinib, was designed to stop different proteins in the body from allowing the tumors to grow. Osimertinib is already available as a treatment for people with certain types of NSCLC.

Sometimes, a drug that works in some parts of the body does not work in the brain. This can happen if a drug cannot get into the brain. A cell barrier, called the "blood-brain barrier", can stop some drugs from getting into the brain. Researchers need to know if osimertinib can pass through this barrier to know if it might be able to treat NSCLC that has spread to the brain.

In this study, the researchers wanted to learn if osimertinib spreads to different regions of the brain. They used a special form of osimertinib that was labelled with a small amount of a radioactive substance, known as "radio-labelled osimertinib".

This made it easier for the researchers to monitor how osimertinib acted in the participants' brains.

This was a "phase 1" study. In this study, the researchers wanted to learn how radio-labelled osimertinib acts in the brains of participants with NSCLC that has spread to the brain.

What was the purpose of this study?

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

- How much radio-labelled osimertinib got into the participants' brains when given at different times during the study?
- What medical problems did the participants have during the study?

The answers to these questions are important to know before other studies can be done to find out if osimertinib helps improve the health of people with NSCLC that has spread to the brain.

What treatments did the participants get?

In this study, the participants were planned to get both "normal" osimertinib and radio-labelled osimertinib.

This was an "open-label" study. This means the participants, researchers, study doctors, and other study staff knew what each participant was getting.

Normal osimertinib was taken as a tablet by mouth. Radio-labelled osimertinib was given through a needle into a vein, also known as an IV infusion. The participants got radio-labelled osimertinib at 3 different times:

- for dose 1, they got radio-labelled osimertinib by itself
- for dose 2, they took 1 normal osimertinib tablet just before they got radio-labelled osimertinib
- for dose 3, they took 1 normal osimertinib tablet once a day for at least 3 weeks, then they got the third dose of radio-labelled osimertinib

The doses of normal osimertinib were measured in milligrams, also known as "mg". The doses of radio-labelled osimertinib were measured in micrograms, also known as "µg".

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

	Dose 1	Dose 2	Dose 3
	8 participants		
	Less than 10 µg of radio-labelled osimertinib as an IV infusion		
	No normal osimertinib	80 mg of normal osimertinib as a tablet	80 mg of normal osimertinib as a tablet
	• Radio-labelled osimertinib 1 time	• Normal osimertinib 1 time • Radio-labelled osimertinib 1 time	• Normal osimertinib once a day for at least 3 weeks • Radio-labelled osimertinib 1 time

What happened during this study?

The participants could be in the study for up to 15 weeks. But, the entire study took a little more than 17 months to finish. The study started in October 2018 and ended in March 2020.

The study was stopped early because the study site closed during the COVID-19 pandemic. So, only 4 of the 8 participants got all of the study treatments. But, the researchers thought that the data collected was enough to complete the study.

Before the participants got study treatment, they visited their study site 1 time. If all measurements could not be taken during this visit, the participants visited their study site 1 more time. This part of the study lasted for up to 4 weeks. At these visits, the study doctors made sure the participants could join the study. They also:

- did a physical exam and asked about the participants' medications and any medical problems they were having
- checked the participants' blood flow

- did an eye exam
- took samples of blood, urine, and the fluid that surrounds the brain and the spinal cord
- took pictures of the participants' tumors using CT and MRI scans
- checked the participants' heart health using an echocardiogram and an electrocardiogram, also called an ECG
- checked how well the participants were able to do their usual daily activities
- asked the participants about their symptoms

The study doctors also did some of these tests and measurements throughout the study.

While the participants were getting study treatment, they visited their study site 5 times. This part of the study lasted for up to 5 weeks. At these visits, the study doctors:

- gave the participants radio-labelled osimertinib as an IV infusion
- gave the participants normal osimertinib as a tablet
- did a PET scan

The participants received their IV infusion at 3 visits and a single normal osimertinib tablet at 2 visits. The participants also took normal osimertinib once a day at home between their second and fourth visits to the study site.

After the participants got study treatment, they visited their study site 1 time. At this visit, the study doctors checked the health of the participants. This part of the study lasted for up to 6 weeks.

All of the participants also had the option to continue taking normal osimertinib tablets once a day after the main part of the study ended for as long as the study doctors thought the treatment was helping, or until the participants decided to stop taking the treatment. If they chose to continue taking normal osimertinib tablets, the participants visited the study site 6 weeks after taking their last normal osimertinib tablet. At this visit, the study doctors checked the health of the participants.

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 a full report of the study results.

The results below are for the 4 out of 8 participants who completed the study.

How much radio-labelled osimertinib got into the participants' brains when given at different times during the study?

To answer this question, the researchers took brain images and blood samples after the participants got an IV infusion of radio-labelled osimertinib. The participants got radio-labelled osimertinib at 3 different times:

- before the participants took any normal osimertinib tablet
- right after the participants took 1 normal osimertinib tablet
- after the participants had taken 1 normal osimertinib tablet once a day for at least 3 weeks

Overall, the researchers found that a similar amount of radio-labelled osimertinib got into the participants' brains at all 3 time points. They also found that it spread similarly throughout the different regions of the brain.

What medical problems happened during this study?

The medical problems that the participants had during this study are not in this summary. Because there was a very small number of participants, leaving this information out helps protect their identities.

The medical problems participants have during clinical studies that the study doctors think might be related to the study drug are called "adverse reactions". An adverse reaction is considered "serious" when it is life-threatening, causes lasting problems, or requires hospital care. There were no serious adverse reactions in this study.

The adverse reactions that happen in a study may or may not be caused by the study drug. A lot of research is needed to know whether a drug causes an adverse reaction. 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.

How has this study helped patients and researchers?

This study helped researchers learn more about osimertinib by using radio-labelled osimertinib to monitor how it acts in the brains of participants with cancer cells from NSCLC that has spread to the brain.

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 radio-labelled osimertinib are not planned.

Where can I learn more about this study?

You can find more information about this study on the websites listed below.

- www.clinicaltrials.gov Once you are on the website, type **"NCT03463525"** into the search box and click **"Search"**.
- www.clinicaltrialsregister.eu. Once you are on the website, click **"Home and Search"**, then type **"2018-000262-10"** in the search box and click "Search"
- www.AstraZenecaClinicalTrials.com Once you are on the website, type **"D5160C00043"** into the search box, and click **"Find a Study"**.

Full Study Title: An Open-label Positron Emission Tomography (PET) Study to Determine Brain Exposure of Osimertinib after Intravenous Microdose Administration of [11C] Osimertinib and Therapeutic Oral Doses of Osimertinib to Patients with EGFR Mutated Non-Small Cell Lung Cancer and Brain Metastases

AstraZeneca Protocol Number: D5160C00043

National Clinical Trials Number: NCT03463525

EudraCT Number: 2018-000262-10

AstraZeneca AB sponsored this study and has its headquarters at Södertälje, Sweden.

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

Thank you!

Clinical study participants and their families 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.

CISCRP

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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