Study Title for Study Participants: Testing osimertinib as a treatment for lung cancers with an EGFR exon 20 change

Official Study Title for Internet Search on https://ClinicalTrials.gov:

EA5162: Phase II Study of AZD9291 (Osimertinib) in Advanced NSCLC Patients with Exon 20 Insertion Mutations in EGFR

What is the usual approach to my lung cancer?

You are being asked to take part in this research study because you have advanced lung cancer with an EGFR exon 20 genetic change which has grown or has recurred. People who are not in a study are usually treated with chemotherapy, which can reduce symptoms and may stop the tumor from growing for several months or more.

What are my other choices if I do not take part in this study?

If you decide not to take part in this study, you have other choices for your care. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different research study, if one is available
- or you may choose not to be treated for cancer but you may want to receive comfort care to relieve symptoms.

Why is this study being done?

The purpose of this study is to test any good and bad effects of the study drug called osimertinib. Osimertinib could shrink your tumor but it could also cause side effects. Researchers hope to learn if the study drug will shrink the tumor by at least one-quarter compared to its present size. Osimertinib is FDA-approved (Food and Drug Administration approved) to treat other types of lung cancer. The study is testing the effects of a higher dose of osimertinib (160 mg) than the dose that is approved by the FDA (80 mg.) There will be about 20 people taking part in this study.

What are the Study Groups?

All study participants will get the same study drug, osimertinib. This is a pill which is taken by mouth once daily. Missed doses will not be taken later. You will be given a study drug diary to record when you take osimertinib at home.

Because the study drug has the potential to interact with other medications, you will be given a drug information handout and wallet card as a resource for yourself, caregivers and other health care providers.

How long will I be in this study?

You will receive osimertinib for as long as your cancer is shrinking or not growing and the study drug is not causing serious side effects that cannot be managed. After you finish osimertinib, your doctor will continue to watch you for side effects and follow your condition for up to 5 years by telephone or office visit.

What extra tests and procedures will I have if I take part in this study?

Most of the exams, tests, and procedures you will have are part of the usual care for your cancer. However, there are some extra tests that you will need to have if you take part in this research study.

Before you begin the study:

You will need to have the following extra tests to find out if you can be in the study:

- ECHO/MUGA scan to monitor the pumping of your heart
- A pregnancy test if you are a women having child-bearing potential

Samples of your diagnostic tumor tissue that are already in pathology will be sent for research testing. Tumor tissue samples are required because the research on the tumor tissue is an important part of the study.

Your privacy is very important and the researchers will make every effort to protect it. Your test results will be identified by a unique code and the list that links the code to your name will be kept separate from your samples and health information. The results will not be available to you or your study doctor. Neither you nor your health care plan/insurance carrier will be billed for the research tests.

Any tumor tissue leftover may be used for the research tests discussed in the Additional Studies Section at the end of the consent.

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, then you will need the following extra tests during your participation in the study. They are not part of the usual approach for your type of cancer.

During the study:

- EKG to monitor the electric activity of your heart every 3 weeks
- Study Drug Diary is filled out at home every day for the duration of the study
- Regular office visits to monitor for side effects and safety

What possible risks can I expect from taking part in this study?

If you choose to take part in this research study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual
- You may be asked sensitive or private questions which you normally do not discuss

The drugs used in this research study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

There is also a risk that you could have side effects from the study drug

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may interfere with your ability to have children.
- Some side effects may be serious and may even result in death.
- Do not start/take any new medication, over-the-counter drug, or herbal preparation without first checking with study staff to determine if it is safe. Sometimes other medications can significantly increase or decrease the amount of AZD9291 (osimertinib) your body absorbs and so all new medications must be approved by your study team.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.
- The study doctor may adjust the study drugs to try to reduce side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible Side Effects of AZD9291 (osimertinib) (Version 2.5, August 21, 2019)

COMMON, SOME MAY BE SERIOUS In 100 people receiving AZD9291 (osimertinib), more than 20 and up to 100 may have:
• Diarrhea • Infection, especially when white blood cell count is low • Dry skin • Rash

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving AZD9291 (osimertinib), from 4 to 20 may have:
• Anemia which may require blood transfusion • Sores in the mouth which may cause difficulty swallowing • Nausea, vomiting • Change in the heart rhythm • Bruising, bleeding • Loss of appetite • Damage to the lungs which may cause shortness of breath • Change in or loss of some or all of the finger or toenails • Itching, acne • A hole or tear in the skin which may cause pain

RARE, AND SERIOUS In 100 people receiving AZD9291 (osimertinib), 3 or fewer may have:
• Heart failure which may cause shortness of breath, swelling of ankles, and tiredness • Dry eye • Visual disturbances • Swelling and redness of the eye • Change in heart function • Fluid around lungs

Let your study doctor know of any questions you have about possible side effects. You can ask the study doctor questions about side effects at any time.

Reproductive risks:

You should not get pregnant, breastfeed, or father a baby while in this study. The osimertinib used in this study could be very damaging to an unborn baby. Check with the study doctor about what types of birth control, or pregnancy prevention, to use while in this study and for 6 weeks after the last dose of protocol treatment for women of childbearing potential and 4 months after the last dose of protocol treatment for males who are sexually active with a women of childbearing potential.

What possible benefits can I expect from taking part in this study?

This research study has only a small chance of helping you because we do not know if the study drug/study approach is effective. This study may help researchers learn things that may help other people in the future.

Can I stop taking part in this study?

Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:

- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study rules
- If the study is stopped by the sponsor, IRB or FDA.

What are my rights in this study?

Taking part in this research study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.
For questions about your rights while in this study, you may contact the Operations Office of the National Cancer Institute (NCI) Central Institutional Review Board (CIRB) at 888-657-3711.

What are the costs of taking part in this study?

The osimertinib will be supplied at no charge while you take part in this study. The cost of getting the osimertinib ready and giving it to you is also provided at no charge. It is possible that the osimertinib may not continue to be supplied while you are on the study. Although not likely, if this occurs, your study doctor will talk to you about your options.

You and/or your health plan/insurance company will need to pay for all of the other costs of treating your cancer while in this study, including the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests are supplied at no charge.

Before you decide to be in the study, you should check with your health plan or insurance company to find out exactly what they will pay for.

You will not be paid for taking part in this study

What happens if I am injured or hurt because I took part in this study?

If you are injured or hurt as a result of taking part in this research study and need medical treatment, please tell your study doctor. Contact information for your study doctor is listed on the consent cover page. The study sponsors will not offer to pay for medical treatment for injury. Your insurance company may not be willing to pay for research study-related injury. If you have no insurance, you would be responsible for any costs.

If you feel this injury was a result of medical error, you keep all your legal rights to receive payment for this even though you are in a research study.

No funds have been set aside to compensate you in the event of injury.

Who will see my medical information?

Your privacy is very important to us and the researchers will make every effort to protect it. Your information may be given out if required by law. For example, certain states require doctors to report to health boards if they find a disease like tuberculosis. However, the researchers will do their best to make sure that any information that is released will not identify you. Some of your health information, and/or information about your specimen, from this study will be kept in a central database for research. Your name or contact information will not be put in the database.

The ECOG-ACRIN Cancer Research Group is conducting this study. ECOG-ACRIN is a cancer research group that conducts studies for the National Cancer Institute. Your doctor is a member of ECOG-ACRIN or another group that is participating in this study. To help protect your privacy, ECOG-ACRIN has obtained a Confidentiality Certificate from the Department of Health and Human Services (DHHS). With this Certificate, ECOG-ACRIN cannot be forced (for example, by court subpoena) to disclose information that may identify you in any federal, state or local civil, criminal, administrative, legislative or other proceeding. Disclosure will be necessary, however, upon request of DHHS for audit or program evaluation purposes.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- Montana Cancer Consortium
- The study sponsor and the drug company supporting the study

- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- The Food and Drug Administration and the National Cancer Institute in the U.S.

Additional Studies Section:

This section is about optional studies you can choose to take part in.

This part of the consent form is about optional studies that you can choose to take part in. You will not get health benefits from any of these studies. The researchers leading this optional study hope the results will help other people with cancer in the future.

The results will be added to your medical records and you or your study doctor will know the results.

You will not be billed for these optional studies. You can still take part in the main study even if you say 'no' to any or all of these studies. If you sign up for but cannot complete any of the studies for any reason, you can still take part in the main study.

Optional Sample Collections for Laboratory Studies

Researchers are trying to learn more about cancer, diabetes, and other health problems. Much of this research is done using samples from your tissue, blood, urine, or other fluids. Through these studies, researchers hope to find new ways to prevent, detect, treat, or cure health problems.

Some of these studies may be about genes. Genes carry information about features that are found in you and in people who are related to you. Researchers are interested in the way that genes affect how your body responds to treatment.

If you choose to take part, we are requesting that you allow the submission of tumor tissue from your diagnostic biopsy, as well as tumor tissue from the biopsy performed as part of your routine care if your cancer starts to grow despite treatment for research.

Additionally, we are requesting that you allow the collection and submission of blood for research to determine how well your cancer is responding to treatment.

What Is Involved?

If you agree to take part, here is what will happen next:

1. Tumor tissue leftover after the research tests (described above) as well as tumor tissue from the routine care biopsy performed if your cancer begins to grow will be sent for research. Only tumor tissue from procedures performed as part of your standard of care will be sent.

2. About eight (8) teaspoons of blood will be collected from a vein in your arm before the start of therapy, at cycle 1, day 8 (after one (1) week of treatment), at the start of cycle 3, day 1 (time your first scan will be done), every six (6) weeks to coincide with each restaging scan, and if your cancer starts to grow. The blood will usually be collected at the same time as the blood collected for your clinical tests to monitor your health. In most cases an additional needle stick will not be required to collect the blood.
3. Your specimens and some related health information will be sent to researchers for use in the studies described above and remaining specimens stored in the Biobank, along with specimens and information from people who take part in this or other research studies. The specimens will be kept until they are used up. Information from your medical record will be updated from time to time.
4. Only qualified researchers can submit a request to use the materials stored in the Biobanks. A committee of experts at ECOG-ACRIN, and/or the National Cancer Institute, will review each request to use the specimens for research. All research projects using these specimens will also be reviewed by an ethics or institutional review board to ensure that the request is necessary and proper. Researchers will not be given your name or any other information that could directly identify you.
5. Neither you nor your study doctor will be notified when research will be conducted or given reports or other information about any research that is done using your specimens.
6. Results from the research may be placed in centralized storage systems called databases. It is possible that some of your genetic information and your health information may be placed in these databases. It is also possible that some of these databases may be public.

What are the possible risks?

1. The most common risks related to drawing blood from your arm are brief pain and possibly a bruise.
2. There is a risk that someone could get access to the personal information in your medical records or other information researchers have stored about you.
3. There is a risk that someone could trace the information in a central database back to you. Even without your name or other identifiers, your genetic information is unique to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.
4. In some cases, this information could be used to make it harder for you to get or keep a job or insurance. There are laws against the misuse of genetic information, but they may not give full protection. There can also be a risk in knowing genetic information. New health information about inherited traits that might affect you or your blood relatives could be found during a study. The researchers believe the chance these things will happen is very small, but cannot promise that they will not occur.

How will information about me be kept private?

Your privacy is very important to the researchers and they will make every effort to protect it. Here are just a few of the steps they will take:

1. When your specimens are sent to the researchers, no information identifying you (such as your name) will be sent. Specimens will be identified by a unique code only.
2. The list that links the unique code to your name will be kept separate from your specimens and health information. Any Biobank and ECOG-ACRIN staff with access to the list must sign an agreement to keep your identity confidential.
3. Researchers to whom ECOG-ACRIN sends your specimens and information will not know who you are. They must also sign an agreement that they will not try to find out who you are.
4. Information that identifies you will not be given to anyone, unless required by law.
5. If research results are published, your name and other personal information will not be used.

What are the Possible Benefits?

You will not benefit from taking part.

The researchers, using the specimens from you and others, might make discoveries that could help people in the future.

Are there any costs or payments?

There are no costs to you or your insurance. You will not be paid for taking part. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

What if I change my mind?

If you decide you no longer want your specimens to be used, you can call the study doctor, who will let the researchers know. Contact information for your study doctor is listed on the consent cover page. Then, any specimens that remain in the bank will no longer be used and related health information will no longer be collected. Specimens or related information that have already been given to or used by researchers will not be returned.

What if I have more questions?

If you have questions about the use of your specimens for research, contact the study doctor. Contact information for your study doctor is listed on the consent cover page.

Please circle your answer to show whether or not you would like to take part in each option:

SAMPLES FOR THE LABORATORY STUDIES:

May we have samples of your tumor tissue and blood for laboratory research studies?

- **I agree to have my samples collected and I agree that my samples and related information may be used for the laboratory studies described above.**

YES **NO**

SAMPLES FOR FUTURE RESEARCH STUDIES:

May we keep any tumor tissue and blood leftover after the laboratory research studies for future research?

- **My samples and related information may be kept in a Biobank for use in future health research.**

YES **NO**

This is the end of the section about optional studies.

TREATMENT BEYOND PROGRESSION CONSENT:

You may be able to continue to receive osimertinib even after X-Rays suggest your cancer has begun to grow again if you and your doctor believe you may still benefit from osimertinib and if you meet certain requirements for the research study.

Continuing osimertinib after X-Rays show that the cancer is growing is experimental and not considered a standard of care for your cancer. You should discuss with your doctor if there may be other treatment options available to you at that time. You may choose to pursue other treatment options, or to consider joining a different research study. Discuss with your study doctor which treatment plan is best for you.

- **I agree to treatment beyond progression with osimertinib.**

YES **NO**

Where can I get more information?

You may visit the NCI Web site at http://cancer.gov/ for more information about studies or general information about cancer. You may also call the NCI Cancer Information Service to get the same information at: 1-800-4-CANCER (1-800-422-6237).

A description of this clinical trial will be available on https://ClinicalTrials.gov, as required

by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Who can answer my questions about this study?

You can talk to the study doctor about any questions or concerns you have about this study or to report side effects or injuries. Contact information for your study doctor is listed on the consent cover page.

Signature:

This study has been explained to me, and I have been told what my enrollment in the study involves. I have read all pages of this consent and have had my questions answered to my satisfaction at this time. I consent to participate in this study and any additional studies where I circled 'yes'. I understand that by signing this form I have not given up any of my legal rights. I will be given a copy of this consent form. I may also request a copy of the protocol (full study plan).

Participant Signature: _____

Date: _____

Signature of Person Obtaining Consent: _____

Date: _____

Time of consent: _____ (AM) (PM)
(Required for initial consent only)

Study Calendar

Visit	**Patient Activities**
Visit 1: Screening (within four to five weeks of start of treatment)	• History and physical examination • Routine blood tests • EKG • Pregnancy test (if you are a woman who could become pregnant) • ECHO/MUGA scan to monitor the pumping of your heart • Imaging (CT scans; MRI or other scans for known brain tumors) to look at your cancer • Blood collection (only if you agree to the Additional Studies)
Visit 2: Start of treatment	• History and physical examination • Routine blood tests • Start taking osimertinib • Study drug diary is filled out at home every day for the duration of the study
Visit 3: 1 week after start of treatment	• Side effects assessment • Routine blood tests • EKG • Continue taking osimertinib • Blood collection (only if you agree to the Additional Studies)
Visits 3 and beyond: Ongoing treatment evaluations about every 21 days	• History and physical examination • Side effects assessment • Routine blood tests • EKG • Collection of study drug diary • Continue taking osimertinib • Imaging (CT scans; MRI or other scans for known brain tumors) to assess how your cancer is responding to treatment every 6 weeks. • Blood collection every 6 weeks (only if you agree to the Additional Studies)
End of treatment	• Side effects assessment • Routine blood tests • EKG • Collection of study drug diary
Follow up: Every three months for five years	• Conversation with your doctor about your health.